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HAYAT SAĞLIK VE SOSYAL HİZMETLER VAKFI

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HAYAT SAĞLIK VE SOSYAL HİZMETLER VAKFI

Seyir Defteri: Bilimsel Yolculuğun Etik Pusulası

Bir denizcinin okyanusta yol alırken yıldızları kaybettiği, rüzgârın yön değiştirdiği o an gelir. O an, denizcinin elinde sadece pusulası kalır; yolunu bulabileceği tek şey, o küçük manyetik ibrenin gösterdiği istikamettir. Bilim de işte böylesine engin ve bilinmezlerle dolu bir denizdir. Yolculuğumuz, bilgiyi arayış ve gerçeklere ulaşma çabasıyla sürerken, bilim insanlarının pusulası ise etik değerlerdir. Etik, bilimi güvenilir ve sağlam kılan temel direklerden biridir.

Bilimde etik, sadece doğru olanı yapma zorunluluğu değildir; aynı zamanda insanlığa karşı sorumluluğumuzdur. Bilimsel araştırmalar, geleceği şekillendirme potansiyeline sahipken, bu gücün doğru kullanılması da etik prensiplere bağlıdır. Kötüye kullanıldığında, bilginin sınırlarını zorlamak değil, insanlığa zarar vermek de mümkündür. İşte bu yüzden bilimin yolculuğu; dürüstlük, şeffaflık ve bilim insanlarının sorumluluklarıyla şekillenir.

Editörden

Anadolu Kliniği Tıp Bilimleri Dergisi olarak, bilimin bu geniş okyanusunda ilerlerken etik değerleri pusulamız olarak görüyoruz. Yayın sürecimizdeki her aşamada, bilimin tarafsızlığını ve güvenilirliğini koruma ilkemizi her zaman ön planda tutuyoruz. Bilimsel bilginin değeri, yalnızca ortaya çıkan sonuçlarda değil, o sonuca nasıl ulaşıldığında gizlidir. Bu nedenle, makalelerin değerlendirilmesinden hakemlik sürecine kadar her adımda şeffaflık ve dürüstlük ilkesini benimsemekteyiz.

Dergimizin yazarlar, hakem ve editörleri bu sorumluluk bilinciyle bilimsel ilerlemeye katkıda bulunmayı hedeflemektedir. Hakemlerimizin ve yazarlarımızın ortak çabasıyla, sağlık bilimleri alanında insanlığa fayda sağlayacak yeni bilgileri ortaya çıkarmaya devam ediyoruz.

Anadolu Kliniği Tıp Bilimleri Dergisi olarak, tüm bilim insanlarını etik pusulanın izinden gitmeye ve bu zorlu fakat bir o kadar da aydınlatıcı yolculukta bizlerle birlikte olmaya davet ediyoruz. Bilimsel araştırmaların etik ilkeler çerçevesinde değerlendirildiği, şeffaf ve adil bir süreci desteklemeye devam edeceğiz.

Anadolu Kliniği Tıp Bilimleri Dergisi, siz değerli okuyucularımıza 16 araştırma makalesi ve 1 derlemeden oluşan yeni sayımızı sunmanın mutluluğunu yaşıyor.

Kıymetli yazarlarımız ve değerli okuyucularımız başta olmak üzere, yoğun çalışma temposuna rağmen özveriyle emek veren hakemlerimize, editörlerimize ve teknik ekibimize paha biçilmez destekleri için gönülden teşekkür ederiz. Katkılarınızın ve desteğinizin artarak devam etmesini temenni ediyor, gelecek zamanın tüm insanlığa sağlık, mutluluk ve huzur getirmesini diliyoruz.

Saygılarımızla,

Doç. Dr. Sedat Akbaş

TIP DALLARINDAKİ GELİŞMELERİN TARİHİ

EDİTÖRLER

HAKAN ERTİN, AHMET SALDUZ
ZEYNEB İREM YÜKSEL SALDUZ

Tıp, saf bilimden ziyade, bilim ile sanatın birleşmesiyle oluşan bir disiplindir. Pozitif bilimlerin çoğu alanını tanımlamayı amaçlarken, tıp bilimsel metod ve prensipleri insanlığın yararına kullanılan bir maharete dönüştürür. Bir başka deyişle, tıp başlı başına bir şifa verme sanatıdır.

Hekimlik mesleğini bütün bu öğeleri ile hakkını vererek yapabilme, yaşadığımız anı idrak edebilme, geçmişte yapılan hataları tekrarlamama ve bir ölçüde ileriyi öngörebilme söz konusu olduğunda tıp tarihine vakıf olmanın önemi inkar edilemez. Mesleğinin teknik yönleri kadar tarihini de öğrenmek için çaba gösterenler başarıya ulaşma yolunda bir adım önde olacaklardır. Herakleitos'un yüzyıllar öncesinden ifade ettiği *'Değişmeyen tek şey değişimin kendisidir'* sözü uyarınca bilginin de dönüşüp değiştiği, zaman içinde evrildiği aşikardır. Bir bilimi oluşturan teoriler, keşifler, yenilikler insanlığın binlerce yılda oluşturduğu bilgi birikiminin ürünüdür. Günümüz tıbbı da geçmişten bu yana basamak basamak çıkılan bir merdiven gibi, gerçeğe ulaşan yoldaki tüm bilgi ve tecrübelerin sentezidir. Yarının bilimine ise bugünden aktardığımız bilgi ve tecrübelerimiz temel olacaktır.

Alanında ehil, değerli bilim insanı hocalarımızın katkılarıyla ortaya çıkan ve tıp dallarının tarihini hekim gözüyle anlatmayı hedefleyen bu kitabın tıbba, hekimliğe ve sağlığa ilgi duyan tüm okurlar için bir kaynak eser olmasını umuyoruz.

BETİM KİTAPLIĞI

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Türk nüfusunda intrahepatik ve ekstrahepatik safra kanalı varyasyonlarının manyetik rezonans kolanjiyopankreatografi değerlendirilmesi

Magnetic resonance cholangiopancreatography evaluation of intrahepatic and extrahepatic bile duct variations in Turkish population

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Öz

Amaç: Safra kanalları bilinen anatomik dağılımları dışında birçok varyasyona sahip, komşu yapılarla sıkı bağlantıları olan oluşumlardır. İntrahepatik veya ekstrahepatik safra yollarında görülebilen anatomik varyasyonlar, laparoskopik cerrahi ve karaciğer nakli gibi operasyonlarda çeşitli sorunlara neden olabilir. Bu anatomik varyasyonları bilmek, operasyon yaralanma riskini azaltmak için faydalı olacaktır. Bu çalışmada toplumumuzda safra ağacı anatomisinin sık ve nadir görülen paternlerinin yaygınlığını manyetik rezonans kolanjiyopankreatografide (MRKP) ortaya çıkarmak amaçlanmıştır.

Yöntemler: Bu çalışmada, 1 Ocak 2012 ile 1 Ocak 2016 yılları arasında çekilen 663 hastanın MRKP görüntüleri retrospektif olarak değerlendirildi. MRKP taramaları, faz dizili koil kullanılarak 1.5 Tesla manyetik rezonans ünitesinde gerçekleştirildi. Single-shot fast spin echo yöntemi ile bT2 ağırlıklı görüntüler değerlendirildi.

Bulgular: Değerlendirilen hastaların 224'ünde (%33,8) anatomik varyasyon saptandı. Varyasyonlar dört ana perspektifte değerlendirildi. Bunlar sırasıyla intrahepatik safra kanalı varyasyonları, ekstrahepatik safra kanalı duplikasyonları, sistik kanal varyasyonları ve diğer varyasyonlar olarak gruplandırıldı. İntrahepatik safra kanalı seviyesindeki en yaygın varyasyon trifurkasyon (%9,4) olarak saptandı. Literatürde nadiren bildirilen bir varyasyon olan ekstrahepatik safra kanalı duplikasyonu olgularımızın 3'ünde (%0,5) mevcuttu. Sistik kanal düzeyindeki en yaygın varyasyon uzun sistik kanal (distal bağlantı) idi ve en sık görülen diğer varyasyonlar pankreas divizum ve ortak hepatik kanala vasküler bası idi.

Sonuç: MRKP ile safra kanalları iyonizan radyasyona maruz kalmadan, kontrast madde kullanmadan ve herhangi bir komplikasyon olmaksızın çok kısa sürede noninvaziv olarak görüntülenebilmektedir. Pankreatobiliyer invaziv girişim veya operasyon planlanan hastalarda MRKP ile safra kanalı varyasyonlarının saptanması ve belirtilmesi olası iatrojenik travmaların önüne geçecektir.

Anahtar Sözcükler: Anatomik varyasyon; safra kanalları, manyetik rezonans kolanjiyopankreatografi; manyetik rezonans görüntüleme.

Abstract

Aim: Bile ducts are formations that have many variations other than their known anatomical distribution and have tight connections with the adjacent structures. Anatomical variations that can be seen in intra or extrahepatic bile ducts might cause various problems in operations like laparoscopic surgery and liver transplantation. Knowing these anatomical variations will be useful for lowering the operational injury risk. This study aimed to reveal the prevalence of common and rare patterns of biliary tree anatomy in our society using magnetic resonance cholangiopancreatography (MRCP).

Methods: In this study, MRCP images of 663 patients taken between January 1, 2012 and January 1, 2016 were evaluated retrospectively. MRCP scans were performed on a 1.5 Tesla magnetic resonance unit by using phased-array coil. Heavily T2 weighted images were obtained with single-shot fast spin echo technique.

Results: Anatomical variations were detected in 224 (33.8%) of the patients evaluated. Variations were evaluated in four main perspectives. Those were grouped respectively as intrahepatic bile duct variations, extrahepatic bile duct duplications, cystic duct variations and other variations. The most common variation in the intrahepatic bile duct level was detected as trifurcation (9.4%). Extrahepatic bile duct duplication which is a rarely reported variation in the literature was present in 3 of our cases (0.5%). The most common variation in the cystic duct level was long cystic duct (distal connection) and the most seen other variations were pancreas divisum and vascular compression to the common hepatic duct.

Conclusion: Bile ducts can be visualized noninvasively in a very short period without any exposure to ionizing radiation, use of contrast material and without any complication with MRCP scan. In the patients who are planned to have pancreatobiliary invasive procedure or operation, detecting and stating the bile duct variations with MRCP scan will prevent the possible iatrogenic traumas.

Keywords: Anatomical variation; bile ducts; magnetic resonance cholangiopancreatography; magnetic resonance imaging.

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GİRİŞ

Safra kesesi ve safranın iletimini sağlayan kanallardan oluşan yapı, hepatik duktal sistemini oluşturur ve aynı zamanda safra salgısının depolandığı bir sistemdir. Safra sıvısının depolanmasının yanında, konsantre hale gelmesini de sağlayan safra kesesi ve iletimi sağlayan safra yolları çok sayıda varyasyonu olan ve komşuluğundaki yapılar ile yakın ilişkili oluşumlardır. Bu yapıların anatomisi ve varyasyonlarının bilinmesi cerrahi açısından önem arz etmektedir. Safra kanalları, intra ve ekstrahepatik olmak üzere ikiye ayrılmaktadır. Couinaud'un tanımlamış olduğu şekilde karaciğer, sekiz ayrı segmentten oluşmaktadır ve bunların her birinin ayrı portal venöz akımı, hepatik venöz ve biliyer duktal drenajı bulunmaktadır (1). İntrahepatik safra yollarının dağılımı, karaciğerin segmental anatomisi ile uyumlu bir şekilde gerçekleşir. Hepatik dallar (sağ ve sol), segmental hepatik safra kanallarının birleşmesi ile oluşmaktadır. Sağ ve sol lobun drenajını sağlayan ana hepatik kanallar, birleşerek ortak hepatik kanalı oluşturur. Daha distalde, sistik kanalın da ortak hepatik kanala katılmasıyla koledok meydana gelir. Pankreas kanalıyla birleşen koledok, duodenumun ikinci kısmında oddi sfinkterine açılmaktadır (2,3).

Biliyer sistem, gelişimsel açıdan intrahepatik veya ekstrahepatik düzeylerde varyasyonlar gösterebilir (4-7). Bu kompleks biliyer anatomik varyasyonları bilmenin önemi, daha çok laparoskopik kolesistektomi, karaciğer nakli canlı donör, hepatik tümör rezeksiyonu ve teröpatik biliyer drenaj gibi hepatobiliyer girişimlerde ortaya çıkmaktadır (6). Bu kanalların yanlışlıkla bağlanması veya rezeksiyonu, komplikasyon riskini artırabilir. Ayrıca, bu varyasyonların safra kanallarında taş oluşumu, pankreatit, kolanjit ve biliyer maligniteleri gelişimine zemin hazırlaması, morbiditeyi artıran diğer nedenler arasında yer almaktadır (6,8). Manyetik rezonans kolanjiopankreatografi (MRKP), pankreatik ve biliyer sistem anatomi ve patolojilerini non-invaziv bir şekilde değerlendirmek için kullanılan bir manyetik rezonans görüntüleme (MRG) tekniğidir. Bu yöntem, intra ve ekstrahepatik safra kanallarının anatomisini kontrast madde kullanılmaksızın, hızlı ve güvenilir bir biçimde, komplikasyon riski olmaksızın inceleme olanağı sağlar. Bu süreçte ağır T2 sekansları kullanılmaktadır.

Çalışmamızın amacı, literatürdeki son verileri de gözden geçirerek toplumumuzda safra yolları anatomisinin yaygın ve nadir varyasyonlarının görülme sıklığını MRKP ile araştırmaktır.

GEREÇ VE YÖNTEMLER

Çalışma Popülasyonu ve Etiği

Çalışmamızda 1 Ocak 2012 ile 1 Ocak 2016 yılları arasında çekilmiş olan toplam 771 MRKP tetkiki incelendi. MRKP incelemesi yetersiz kalitede olan 108 hasta çalışma dışı bırakıldı. Bu sebeple çalışmamıza 663 hasta kabul edildi. Değerlendirme yapılırken MRKP tetkikinin normal olması ya da patolojik olması göz önünde bulundurulmadı. Bu retrospektif çalışma Hatay Mustafa Kemal Üniversitesi Sağlık Uygulama ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurul tarafından onaylanmıştır (tarih: 06.05.2015, karar no: 20).

MRG Tekniği

Standart vücut sargısının kullanıldığı MRKP incelemeleri 1.5 Tesla magnet gücüne sahip MR cihazında (Achieva, Philips Medical System, Netherland) gerçekleştirildi. Bu teknikte, 4-5 saatlik açlık sonrasında gerçekleştirilen incelemelerde, 2 boyutlu 'single-shot fast spin echo' tekniği kullanılarak ağır T2 görüntüler elde edildi. Bu incelemede, koronal pilot üzerinde koledoğun yeri belirlenerek, porta hepatisin birkaç santimetre yukarısından ampulla Vater'e kadar olan bölge, aksiyel planda, kesit aralığı bırakılmaksızın ve kesit kalınlığı 5 mm olarak seçilerek tarandı. Aksiyel plandaki kaynak görüntülerde koledok merkezi kabul edilerek, her biri bu merkezden geçen, koronal veya koronal oblik düzlemde 40-70 mm kalınlığında bir hacmi içerecek şekilde kesitler alındı. Her bir kalın kesit alınırken hastaların nefes tutma süresi 7 saniye olarak belirlendi.

MRKP incelememizde parametrelerimiz şunlardan oluşmaktaydı: TR:1204 msn, TE:650 msn, bant genişliği: 0.784/277.0 kHz, FOV: 260 mm, görüntüleme matriksi: 256x205 ve NEX: 2 olarak uygulandı. Bunlara ek olarak koronal planda BTFE sekansı TR: 500; efektif TE: 2.1; FA: 90, NEX: 1, matriks: 312x249; FOV: 350x350 mm; bant genişliği 0.339/641 Hz/piksel olarak uygulandı. İnceleme esnasında oral ya da intravenöz kontrast madde kullanılmadı.

Tablo 1. Safra yolu varyasyonlarımız

Varyasyon adı	n	%
İntrahepatik safra yolları varyasyonu		
Trifurkasyon	60	9,0
Sol hepatik kanala açılan sağ posterior segment dal	41	6,1
Aberan sağ posterior kanal (sistik kanal proksimalinde ana hepatik kanala açılma)	17	2,5
Kuadrifurkasyon	11	1,6
Aberan sağ posterior kanal (sağ posterior inferior dal ana hepatik kanala, posterior süperior dal sol hepatik kanala açılmakta)	3	0,4
Aberan sağ posterior kanal (sağ posterior süperior dal ana hepatik kanala, posterior inferior dal sol hepatik kanala açılmakta)	1	0,1
Sağ anterior segment dal sistik kanal ile birleşip ana hepatik kanala açılmakta	1	0,1
Aksesuar sağ hepatik kanal	1	0,1
Varyasyon adı		
Ekstrahepatik safra yolları varyasyonu		
Duplikasyon varyantı (sistik kanal sağ hepatik kanal ile birleşerek ampulla proksimalinde sol hepatik kanal ile birleşmekte	3	0,4
Sistik kanal varyasyonları		
Uzun sistik kanal (distal birleşim)	57	9,2
Medialden birleşme	24	3,6
Ana hepatik kanal ve sistik kanalın ayrı seyredip distalde ampullaya birlikte açılması	4	0,6
Kısa sistik kanal	2	0,3
Diğer varyasyonlar		
Ortak hepatik kanala vasküler bası	17	2,5
Pankreas divizium	16	2,4
Yukarı yerleşimli safra kesesi	3	0,4

n: Olgu sayısı, %: Yüzde değeri

Tablo 2. Sağ hepatik safra yolunun Huang sınıflamasına göre tiplendirmesi ve bu sınıflamaya göre bizim oranlarımız

Tip	Sağ posterior hepatik kanala açılma	n	%
A1	Sağ posterior hepatik kanal sol anterior kanala açılmakta	439	66,2
A2	Trifurkasyon	60	9,4
A3	Sağ posterior hepatik kanal sol hepatik kanala açılmakta	41	6,6
A4	Sağ posterior hepatik kanal ana hepatik kanala açılmakta	21	3,4
A5	Sağ posterior hepatik kanal sistik kanala açılmakta	1	0,2

n: Olgu sayısı, %: Yüzde değeri

Görüntü değerlendirme

Osirix yazılımlı tıbbi iletişim ve dijital görüntülemede ayrı iki radyoloji doktoru tarafından MR sekansları değerlendirildi (Pixmeo Labs, Geneva, Switzerland).

Safra Yolları Varyasyonları

Literatürde safra yolları varyasyonları ile pek çok sınıflama mevcuttur (2,3,6,9-11). Biz de bu çalışmamızda safra yolları varyasyonlarını dört ana başlıkta ele aldık. Bunlar sırasıyla intrahepatik safra yolları varyasyonları, ekstrahepatik safra yolları duplikasyonları, sistik kanal varyasyonları ve diğer olarak belirlendi. Literatürde farklı anatomik sınıflandırmalar ve anatomik varyasyonlar mevcut olmakla birlikte özelikle intrahepatik varyasyonlarımızı Huang ve ark.'ın yaptığı tiplendirmeye göre sınıflandırdık (12).

İstatistiksel analiz

Çalışmadaki tüm istatistiksel analizler Statistical Package for the Social Sciences package program version 25.0 (SPSS Inc., Chicago, IL, USA) kullanılarak yapıldı. Deskriptif veriler sayısal verilerde ortalama ve standart sapma, nominal ya da sıralı değişkenlere ait dağılımlar sayı ve yüzde şeklinde verildi. Kategorik değişkenler açısından gruplar arasındaki karşılaştırmalar Ki Kare testi ile yapıldı. Sürekli değişkenlerin normal dağılıma uygun olup olmadığı Kolmogorov-Smirnov Testi ile analiz edildi. Sürekli değişkenler açısından

Tablo 4. Varyasyonlar arasında ortalama yaşa göre karşılaştırma

	Yaş	
	Ortalama	**SS**
Normal	56,8	18,3
İntrahepatik safra yolları varyasyonu	56,2	20,0
Sistik kanal varyasyonları	59,5	19,0
Ekstrahepatik safra yolları varyasyonu + Diğer varyasyonlar	61,0	15,2
Çoklu varyasyonlar	58,1	17,1
Genel	57,2	18,4

p=0,665, Kruskal Wallis testi kullanılmıştır, SS: Standart sapma.

çoklu gruplar arasındaki ortalama değerlerin karşılaştırmaları Kruskal Wallis testi ile analiz edildi. Sonuçlar %95 güven aralığında değerlendirildi ve p<0,05 değerleri anlamlı kabul edildi.

BULGULAR

Çalışmamıza dahil edilen 663 hastanın yaş ortalaması 57 idi (6-100 yaş). Bunların 333'ü erkek, 330'u kadındı. Çalışma kapsamına alınan 663 olgudan 261'inde (%39,4) çeşitli düzeylerde varyasyon tespit edildi.

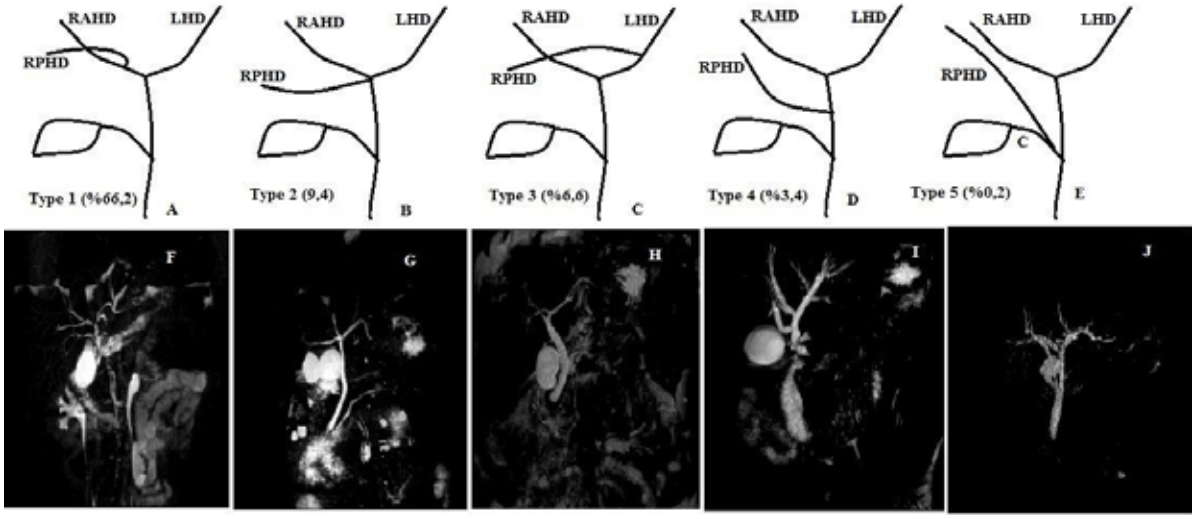
Çalışmamızda normal anatomi dediğimiz intrahepatik safra yolu varyasyonu 439 olguda (%66,2) tespit edildi. Varyasyon tespit edilen 261 olgunun, 135'inde intrahepatik safra yolları varyasyonları, 3'ünde ekstrahepatik safra yolları duplikasyonları, 87'sinde sistik kanal varyasyonları ve 36'sında pankreas divisium, ortak hepatik kanala vasküler bası, yukarı yerleşimli safra kesesi gibi diğer varyasyonlar tespit edildi (Tablo 1). Bazı vakalar birden fazla varyasyon içermekteydi. İntrahepatik safra yolları ile ilgili literatürde farklı anatomik sınıflandırmalar ve anatomik varyasyonlar mevcut olmakla birlikte genelde yapılan çalışmalar Huang ve ark.'ın sağ hepatik safra yolları üzerindeki yaptığı tiplendirmeye göre sınıflandırılmaktadır (13) (Tablo 2). İntrahepatik olarak en çok üzerinde çalıştığımız sağ hepatik safra yolları düzeyindeki en sık varyasyonlarımız sırasıyla; tip A1 %66,2 (439 vaka), tip A2 %9,4 (60 vaka), tip A3 %6,6 (41 vaka), tip A4 %3,4 (21 vaka), tip A5 %0,2 (1 vaka) idi (Resim 1).

Çalışmamız neticesinde daha önce sınıflandırılmamış ve nadir görülen kompleks biliyer anatomik varyasyonlar tespit ettik. Bu sınıflandırmaya dahil edilmeyen ve literatürde nadir rastladığımız intrahepatik düzeyde görülen varyasyonlarımızdan aberran sağ posterior segment dalının kendi içinde farklı varyasyonları 4 vakada, kuadrifurkasyon varyasyonu 11 vakada gözlendi (Resim 2-3-4). Sadece bir vakada aksesuar sağ hepatik kanal tespit edildi (Resim 5). Ekstrahepatik sağ ve sol ana hepatik kanalın duplikasyonu üç vaka olup literatürde ve son çalışmalarda pek karşılaşmadığımız vakalardandı (Resim 6). Bir vakada sistik kanalın sağ anterior kanala drene olması ve bir vakada da sistik kanalın sağ hepatik kanala drenajı olan aynı zamanda da duplikasyon olarak adlandırdığımız vakalar gözlendi (Resim 7-8). Diğer varyasyonlardan ise en sık görülenler pankreas divizium 16 vakada ve ana hepatik kanala vasküler bası 17 vakada tespit edildi (Resim 9-10). Safra kesesi uzun aksı ve fundusunun yukarı yerleşimli olması üç vakamızda gözlendi (Resim 11).

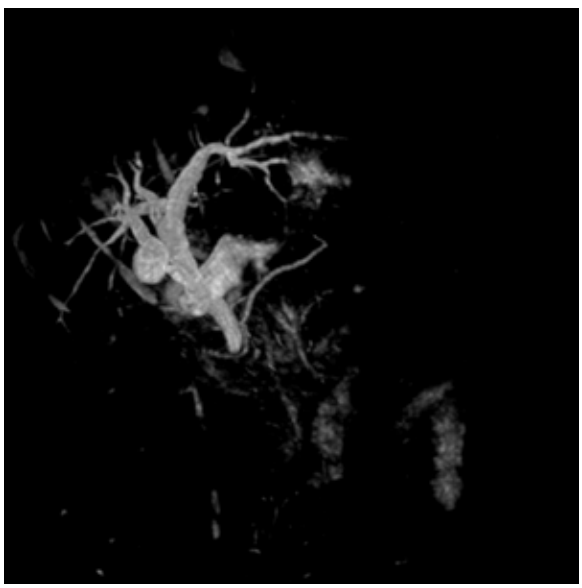
Varyasyon bulgularına göre yapılan gruplar arasında cinsiyet dağılımı (p=0,998) (Tablo 3) ve ortalama yaş (p=0,665) (Tablo 4) açılarından anlamlı farklılık saptanmadı.

TARTIŞMA VE SONUÇ

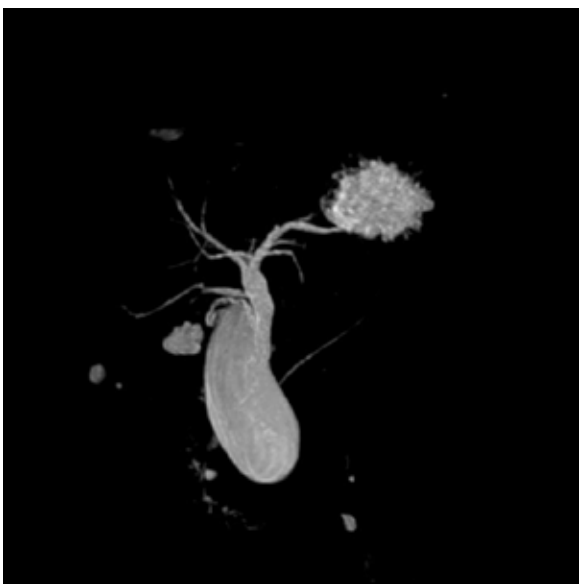
Safra yolları anatomik varyasyonlarının ve patolojilerinin değerlendirilmesinde noninvaziv olarak ultrasonografi (US), bilgisayarlı tomografi (BT), MRKP, kolesintigrafi gibi inceleme yöntemleri kullanılmaktadır. Safra yollarında genişleme olduğunda US ve BT artı değer sağlayabilmekte olup varyasyonları göstermede yeri sınırlıdır. Direkt kontrast madde enjeksiyonu ile safra yollarının görüntülenmesi endoskopik retrograd kolanjiopankreatografi (ERKP), perkütan transhepatik kolanjiyografi (PTK), T-tüp ya da intraoperatif kolanjiyografi gibi tekniklerle yapılmaktadır (8). ERKP, yüksek çözünürlüklü görüntüleri sayesinde safra yolları anatomisini ve varyasyonlarını yüksek sensitivite



Resim 1. Huang ve ark. tiplendirmesine göre sağ hepatik safra yolu dağılım paterni. Üst sıra imajlar(A-E) tip 1'den tip 5'e kadar şematik çizim ve alt sıra imajlar (F-J) MRKP'ye karşılık gelen figürleri. RPHD: Sağ posterior hepatik kanal, RAHD: Sağ anterior hepatik kanal, LHD: Sol hepatik kanal, CD: Sistik kanal.



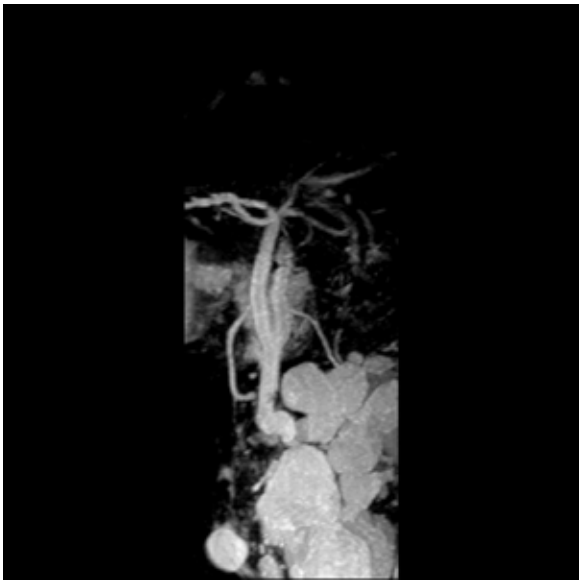
Resim 2. Sağ posterior süperior dal ana hepatik kanala, posterior inferior dal sol hepatik kanala açılmakta



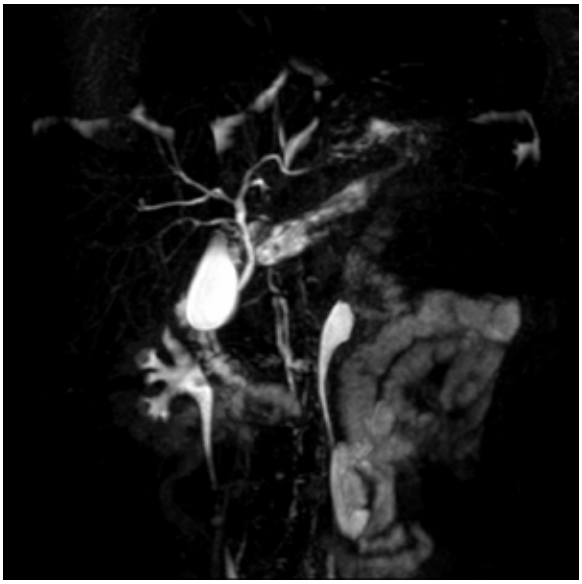
Resim 3. Sağ posterior inferior dal ana hepatik kanala, posterior süperior dal sol hepatik kanala açılmakta

ve spesifite ile doğru bir şekilde gösterebilmektedir. Ancak, operatöre bağımlı ve invaziv bir teknik olması, ayrıca pankreatit, kolanjit, sepsis, safra kanalı veya duodenum perforasyonu gibi önemli komplikasyonları içermesi nedeniyle, kolesistektomi öncesinde rutin kullanımı önerilmemektedir (6,7,9,10).

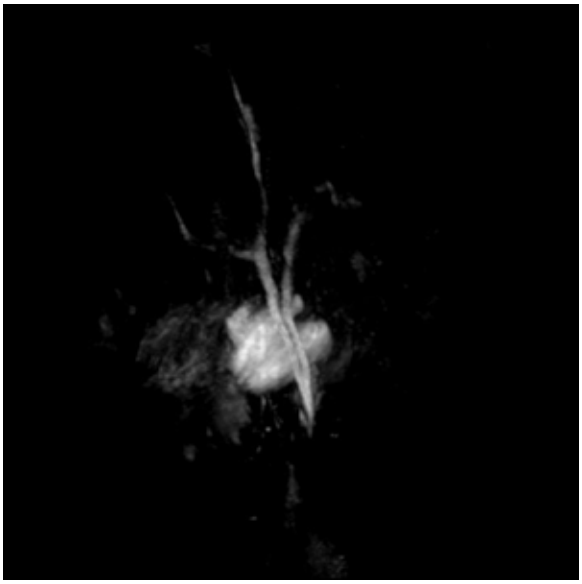
MRKP ise, safra ve pankreatik kanalın morfolojik özelliklerini doğru olarak saptayan noninvaziv görüntüleme tekniğidir (11). Pankreatobiliyer hastalıklarda, ERKP kadar yüksek doğruluk oranlarına sahip olan bir diğer yöntem MRKP'dir. ERKP'ye göre avantajları arasında iyonizan radyasyon içermemesi, daha ekonomik olması, komplikasyon oluşturmaması, kontrast madde ve premedikasyon gerektirmemesi, pankreatit ve kolanjitin akut atakları sırasında kullanılabilmesi, darlığın hem proksimalindeki hem de distalindeki saf-



Resim 4. Kuadrifurkasyon



Resim 5. Sağ aksesuar hepatik kanal ortak hepatik kanala açılmakta



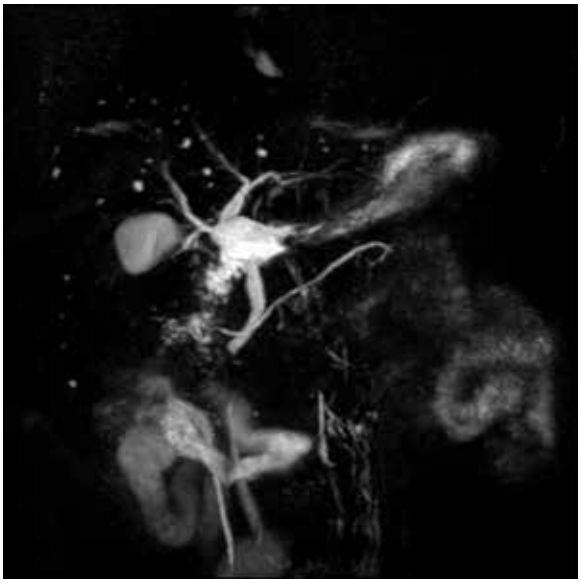
Resim 6. Duplikasyon

Resim 7. Sağ anterior hepatik kanal sistik kanala açılmakta

ra kanallarını gösterebilmesi bulunmaktadır. Ancak, MRKP'nin çözünürlük gücünün düşük olması, küçük duktal patolojileri gösterememesi ve işlem sırasında terapötik girişimlerin yapılamaması, kullanımını sınırlayan özellikleridir.

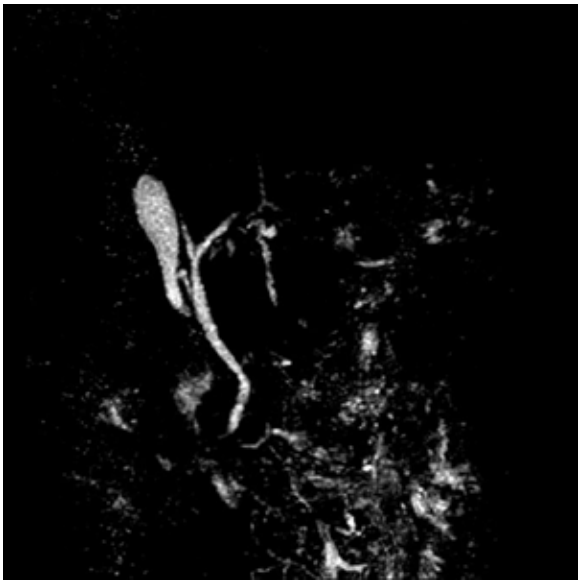
Safra yollarında bilinen normal anatomik dağılım dışında birtakım varyasyonlar görülmektedir. Biliyer sistem varyasyonları genellikle klinik açıdan önemsiz olabilir; ancak, tanısal incelemelerde karışıklığa neden olabilir, endoskopik veya perkütan girişimleri karmaşıklaştırabilir ve açık veya laparoskopik kolesistektomi operasyonlarında zorluklara ve iyatrojenik travmalara neden olabilir (2,5-7,13). Her ne kadar laparoskopik ameliyatlar daha az invaziv olmasına rağmen sınırlı görme alanı ve yanlış algılama nedeniyle safra kaçağı ve kontralateral safra kanalı yaralanması (yaklaşık %0,5) gibi biliyer komplikasyonlara sebep olabilmektedir (14). Örnek olarak aberran sağ posterior segment

Resim 8. Sağ hepatik kanala açılan sistik kanal ve duplikasyon



Resim 9. Pankreas divisium

Resim 10. Ortak hepatik kanala vasküler kompresyon



Resim 11. Yukarıya doğru lokalize safra kesesi

dalının ana hepatik kanala veya sistik kanala drene olması ve sistik kanalın sağ posterior kanala drene olması gibi varyasyonların olması operasyon esnasında bu kanalların bağlanmasına veya yaralanmasına neden olabilmektedir. Bu çalışmamızda bir vakada aberran sağ posterior segment dalının laparoskopik kolesistektomi esnasında ligasyonu ve buna bağlı olarak dilatasyonu gibi komplikasyonları dikkati çekmektedir (Resim 12).

Günümüzde karaciğer rezeksiyonu ve transplantasyonları gibi operasyonların da çok sık yapılıyor hale gelmesi, safra kanallarının anatomisinin ve varyasyonlarının doğru bir şekilde gösterilmesini gerektirmektedir (2,7,15).

Literatürde safra yolları varyasyonları ile ilgili değişik oranlar bildirilmiştir (2,3,8,14-15). Yapılan bu çalışmaların sonucunda safra yollarıyla ilgili %24-37 oranında varyasyon görmek mümkündür (6,7,16).

Resim 12. Laparoskopik kolesistektomi sırasında ligasyona bağlı aberran sağ arka segment dalının dilatasyonu

Bizim çalışmamız sonucunda da varyasyon oranımız %33,8 olup literatür ile uyumlu idi.

Literatürde şimdiye kadar genelde sadece sağ hepatik veya sol hepatik olmak üzere intrahepatik safra yolları ile ilgili veya sadece ekstrahepatik düzeyde ana hepatik, sistik kanal ve pankretobiliyer düzeyde olan anatomik varyasyonlar ile ilgili çalışmalar yapılmıştır. Bizim çalışmamızda ise yukarıda saydığımız grupların çoğunluğu dâhil edilmiş olup sol hepatik safra yolları ile ilgili dikkati çekici belirgin bir anatomik farklılık tespit edilmemiştir. Nayman ve ark. Türk toplumunda yaptıkları çift merkezli 2143 olgulu geniş bir çalışmaya göre buldukları varyasyonları Yoshida ve ark.'ın yaptıkları tiplendirmeye göre sınıflandırmışlardır (14-15). Bu tiplendirmede ilk dört varyasyon bizim kullandığımız Huang sınıflandırmasıyla aynı olup sırasıyla buldukları oranlar Tip 1 (Tip A1) %62, Tip 2 (Tip A2) %9, Tip 3 (Tip A3) %11, Tip 4 (Tip A4) %7 idi. Bu ve diğer çalışmalarda olduğu gibi en sık gözlenen ve normal anatomi dediğimiz Tip A1 bizim çalışmamızda da en sık tespit ettiğimiz varyasyondu. Nayman ve ark.'da olduğu gibi daha önceki çalışmalara baktığımızda da genelde tip A3 varyasyonun tip A2'den daha yaygın olduğu, ancak bizim çalışmamızda ise tip A2'nin daha yüksek oranda olduğu dikkatimizi çekmektedir.

Sınıflandırmaya girmeyen ekstrahepatik sağ ve sol ana hepatik kanalın duplikasyonu şeklinde tespit ettiğimiz varyasyonlarımız ise üç vaka olup literatürde ve son çalışmalarda pek karşılaşmadığımız vakalardandı. Sistik kanal üzerinde yapılan çalışmalarda şimdiye kadar belirgin bir sınıflandırma mevcut olmayıp yapılan çalışmalarda farklı isimlendirmeler kullanılmaktadır. Swain ve ark.'ın yaptığı çalışmaya göre de en sık görülen varyasyonlar posterior spiral insersiyon (%42,8) ve right lateral insersiyon (%39,3) idi (17). Hussein ve ark. yaptıkları çalışmada 238 vakanın %75'inde right lateral insersiyon buldular (18). Sawaragi ve ark. yalnızca sistik kanal üzerinde yaptıkları 198 vakalık çalışmalarında 102 vakada (%51,5) sistik kanalın normal lateral insersiyonu tespit ettiler (19). En nadir buldukları vakalar; 1 vakada sistik kanalın sağ hepatik duktusa drene olması ve 1 vakada sağ posterior hepatik duktusun sistik kanala drene olmasıydı. Bizim çalışmamızda en sık gördüğümüz –ve normal anatomik yerleşim olarak değerlendirdiğimiz- sistik kanalın lateralden ortak hepatik kanala açılmasıydı. Ayrıca çalışmamızda benzer şekilde tespit ettiğimiz en nadir olanları; 1 vakada sistik kanalın sağ anterior kanala drene olması ve diğer vaka da sistik kanalın sağ hepatik kanala drenajı olan ve aynı zamanda duplikasyon gördüğümüz vakadır. Ancak sistik kanal anatomisinin farklılığı nedeniyle çoğu çalışmada sınıflandırılmamış kompleks anatomiye sahip varyasyonlar görülebilmektedir. Sistik kanal varyasyon oranlarının göreceli yüksek olması kendi içindeki sınıflandırmadan ve intrahepatik veya diğer varyasyonlarla birlikte görülebilmesinden kaynaklanmaktadır.

Diğer varyasyonlardan ise en sık görülenler pankreas diviziumun bazen sebebi bulunamayan pankreatit etyolojisinde yer alması ve ortak hepatik kanala vasküler basının ise yanlışlıkla taşa bağlı sinyal olarak algılanması nedeniyle bu varyasyonların tanı ve tedavide etkisi olabileceği göz önünde bulundurulmalıdır. Safra kesesi uzun aksı ve fundusunun yukarı yerleşimli olması üç vakamızda dikkatimizi çekmektedir. Yine operasyon öncesi safra kesesi lokalizasyonunu bilmek, ameliyat süresini ve dolayısıyla hastanın alacağı anestezik madde dozunu azaltacaktır. Hasta sayımızın az olması, bazı hastaların tetkik sırasındaki uyum problemi ve buna bağlı görüntü kalitesinin yetersiz olması sonucu değerlendirilememesi çalışmamızın limitasyonu olarak gösterilebilir. Bu konuda daha geniş serilerle ve tetkik öncesi hasta uyumunu artıracak unsurları göz ününde bulundurarak çalışmalar yapılabilir.

İntrahepatik ve ekstrahepatik safra yollarında genellikle klinik açıdan önemsiz birçok anatomik varyasyon gözlemlenebilir. Bu varyasyonların tespiti her geçen gün daha da önemli hale gelmektedir. Safra yollarındaki varyasyonları değerlendirmede noninvaziv altın standart yöntem MRKP görüntülemedir. Hepatobiliyer sisteme yönelik girişimsel işlemlerin arttığı günümüzde özellikle işlem öncesi safra yolları varyasyonlarını MRKP tetkiki ile hızlı, güvenilir ve noninvaziv bir biçimde değerlendirmek önem arz etmektedir. Aksi takdirde bu varyasyonların iyatrojenik travmalara sebep olup özellikle postoperatif dönemde mortalite ve morbidite oranlarını artıracağı bir gerçektir.

Çıkar çatışması ve finansman bildirimi

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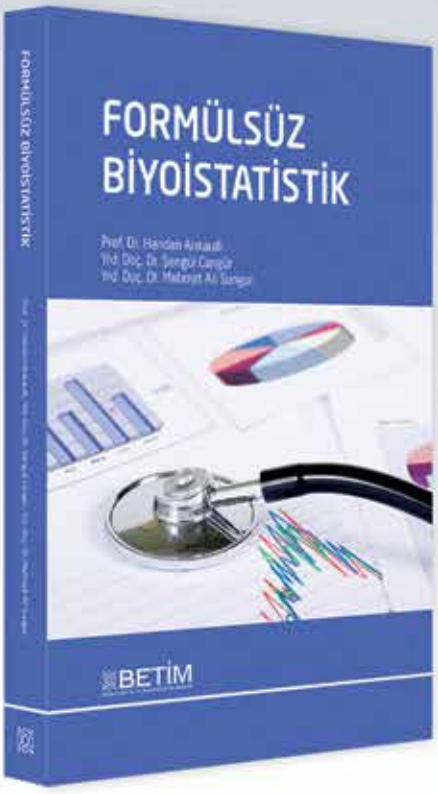

Formülsüz Biyoistatistik

Handan Ankaralı - Şengül Cangür - Mehmet Ali Sungur

Biyoistatistik yöntem ve prensiplerden yararlanırken önemli olan, doğru veriyi seçmek, doğru yerde kullanmak, doğru yöntemlerle değerlendirmek ve elde edilen sonuçları doğru bir şekilde sunmaktır. Bu bilgiler ışığında ve günümüz teknolojisi sayesinde elle çözüme neredeyse hiç ihtiyaç duyulmadığı gerçeğinden hareketle, bu kitapta yalın bir anlatım tekniği seçilmiş ve formül vermemek tercih edilmiştir. Bu anlatım tekniğiyle, biyoistatistik bilimi ve araçlarını, korkulacak bir bilim dalı olmaktan çıkararak sevilen ve ilgi duyulan bir bilim haline getirmek, ayrıca araştırmacıların temel düzeyde istatistik değerlendirmelerini yapabilecek donanıma sahip olmalarını sağlamak, en azından nerede yardım almaları gerektiği konusunda bilinç düzeylerini artırmak amaçlanmıştır.

BETİM KİTAPLIĞI

Attitude of nurses and nursing students towards preventing pressure injury: A relational cross-sectional study

Hemşirelerin ve hemşirelik öğrencilerinin basınç yaralanmalarını önlemeye yönelik tutumları: İlişkisel kesitsel bir çalışma

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Abstract

Aim: This study aims to measure the attitude of senior nursing students and practicing nurses toward preventing pressure injury and to provide recommendations for improving the necessary education based on their feedback.

Methods: A descriptive-cross-sectional relationship-seeking design was used. 229 nurses and 93 senior nursing students were included in the study. The study data were collected using the "descriptive characteristics questionnaire form" and "attitude towards pressure injury prevention scale".

Results: The attitude scores of nurses for the prevention of pressure injury were 26.98 ± 3.33 and 25.52 ± 3.64 of the nursing students. The scores of the sub-dimensions of the attitude towards pressure injury prevention scale of nurses and nursing students were examined and showed that the nurses obtained the highest score from the "priority" dimension, and the lowest score from the "effectiveness of prevention" dimension.

Conclusions: It is necessary to raise awareness first to develop a positive attitude towards pressure injury prevention. The curriculum for nurses and nursing students should be reviewed and the identified knowledge gaps should be filled with effective teaching methods. More topics should be covered in hospitals, classrooms, and labs through simulation or clinical practice.

Keywords: Attitude; education; nurses; nursing students; pressure injury

Öz

Amaç: Bu çalışma hemşirelik son sınıf öğrencilerinin ve hemşirelerin basınç yaralanmasını önlemeye yönelik tutumlarını ölçmek ve geri bildirimlerine dayanarak gerekli eğitimin geliştirilmesi için önerilerde bulunmak amacıyla yapılmıştır.

Yöntemler: Tanımlayıcı-kesitsel bir ilişki arama deseni kullanılmıştır. Çalışmaya 229 hemşire ve 93 hemşirelik son sınıf öğrencisi dâhil edilmiştir. Araştırmanın verileri "tanımlayıcı özellikler anket formu" ve "basınç yaralanmasından korunmaya yönelik tutum ölçeği" kullanılarak toplanmıştır.

Bulgular: Hemşirelerin basınç yaralanmasını önlemeye yönelik tutum puanları 26.98 ± 3.33 ve hemşirelik öğrencilerinin puanları 25.52 ± 3.64 bulunmuştur. Hemşirelerin ve hemşirelik öğrencilerinin basınç yaralanmasını önlemeye yönelik tutum ölçeği alt boyut puanları incelendiğinde hemşirelerin en yüksek puanı "öncelik" boyutundan, en düşük puanı ise "önlemenin etkinliği" boyutundan aldıklarını göstermiştir.

Sonuç: Basınç yaralanmasını önlemeye yönelik olumlu bir tutum geliştirmek için öncelikle farkındalık oluşturmak gerekir. Hemşireler ve hemşirelik öğrencileri için müfredat gözden geçirilmeli ve belirlenen bilgi boşlukları etkili öğretim yöntemleri ile doldurulmalıdır. Simülasyon veya klinik uygulama yoluyla hastanelerde, sınıflarda ve laboratuvarlarda daha fazla konu ele alınmalıdır.

Anahtar Sözcükler: Bası yarası; eğitim; hemşireler; hemşirelik öğrencileri; tutumlar

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INTRODUCTION

A pressure injury is often a preventable problem in health care services and is crucial for patients, nurses, and institutions to monitor. It causes prolonging of the healing process, and complications such as infection. It also increases the workload of nurses and the treatment costs. Pressure injuries, which increase the risk of morbidity and mortality, are accepted as an indicator that determines the standards of care in nursing (1-5).

A research study determined that the prevalence of pressure injuries varies between 9-18% in European countries (6). The meta-analysis study conducted by Chaboyer et al. found the prevalence of a pressure sore to be 16.9-23.8%, and Kayser et al. found the prevalence to be 9.2% in their study (7). In studies conducted in Turkey, the prevalence of Pressure injury was reported to be between 8.1% and 10.3% (8-10). Demarre et al. stated that the cost of preventing a pressure injury varies between 2.65 and 87.57 Euros, and the cost of treating a pressure injury varies between 1.71 and 470.49 Euros (11). A study conducted in Canada estimated that the monthly cost for each spinal cord injury patient receiving pressure injury treatment in Ontario was Canadian dollars 4,750 (12).

A pressure injury, a common problem in patients worldwide, should be prevented before it occurs as its care/treatment is difficult and costly. Although the fight against pressure injury requires multidisciplinary teamwork, nursing care plays a key role in the prevention and treatment of pressure injuries. It is possible to prevent pressure injury by nurses evaluating patients at risk of developing a pressure injury, and by planning and implementing preventive interventions. Therefore, the occurrence of pressure injury has been presented as an important indicator of inadequate quality of care since the 1980s (13).

Nurses must have sufficient knowledge, skills, and critical thinking and problem-solving skills to provide quality and effective pressure injury care. However, studies emphasize that nurses lack knowledge on this issue (5,14). In addition, the attitudes of nurses towards pressure injury are as important as their knowledge level and clinical skills. A study revealed that although the average knowledge score of nurses about pressure injury was 71.5%, their attitude scores were not at a satisfactory level (15). Nurses have a very important role in evaluating patients for pressure injuries, determining the factors that may cause them, taking precautions to reduce risks, and treating them. However, one of the reasons for the development of pressure injuries is seen as the lack of knowledge of nurses. Therefore, this study aims to contribute to the literature and to guide the education curricula and in-service training programs using the obtained results. For these reasons, it is crucial to determine the attitude of working nurses and nursing students who will step into the nursing profession towards pressure injury. In this study, it was aimed to investigate the attitude of nurses and nursing students toward preventing pressure injury. Research questions followed:

1. What is the level of nurses' attitude towards preventing pressure injury?
2. What is the level of nursing students' attitude towards preventing pressure injury?
3. Are there differences between the attitudes of nurses and nursing students toward preventing pressure injury?
4. Do nurses' socio-demographic characteristics affect their attitudes towards preventing pressure injury?
5. Do nursing students' socio-demographic characteristics affect their attitudes towards preventing pressure injury?

MATERIAL AND METHODS

Design, participants, and setting

The study's descriptive, cross-sectional, and relationship-seeking design was intended to determine the attitude of nurses and nursing students toward preventing pressure injuries. The sample of the research consisted of 482 nurses in the training and research hospital and 105 final-year nursing students in the nursing department of the Faculty of Health Sciences. The sample of the study was determined according to the frequency formula in cases where the sample is known (nurses=229 and students=93). 229 nurses and 93 students who voluntarily participated were included in the research.

Table 1. Distribution of nurses' introductory characteristics (n=229)

Variable		n	%
Age	18-25	77	33.6
	26-30	61	26.6
	31-40	61	26.6
	41 +	30	13.1
Gender	Female	196	85.6
	Male	33	14.4
Working year	0-5	78	34.1
	6-10	52	22.7
	11-15	55	24.0
	16-20	17	7.4
	21 +	27	11.8
Number of pressure wound care	Never	33	14.4
	Less than 10	78	34.1
	11-20	46	20.1
	21 +	72	31.4
Out-of-school education regarding pressure sores	Yes	59	25.8
	No	170	74.2
Competence in caring for pressure injuries	Sufficient	104	45.4
	Partly sufficient	101	44.1
	Insufficient	24	10.5
The most commonly used method in pressure wound care	Position Change	144	62.9
	Air Bad	70	30.6
	Massage	15	6.6
Who should do pressure wound care?	Nursing	206	90.0
	Doctor	11	4.8
	Staff member	12	5.2

n: number, %: percentage

Table 2. Distribution of nursing students' introductory characteristics (n=93)

Variable		n	%
Gender	Female	73	78.5
	Male	20	21.5
Pressure wound care status	Yes	84	90.3
	No	9	9.7
Out-of-school education regarding pressure sores	Yes	14	15.1
	No	79	84.9
Competence in caring for pressure injuries	Sufficient	22	23.7
	Partly sufficient	57	61.3
	Insufficient	14	15.1
The most commonly used method in pressure wound care	Position change	68	73.1
	Air bad	22	23.7
	Massage	3	3.2
Who should do pressure wound care?	Nursing	89	95.7
	Doctor	4	4.3

n: number, %: percentage

Table 3. Distribution of *ATPIPS* sub-dimension scores according to the promotional characteristics of nurses (n=229)

Variables	Competency	Priority	Impact	Responsibility	Effectiveness of prevention	Total
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Age						
18-25a	6.77 ± 1.34	8.14 ± 0.82	5.31 ± 1.45	4.04 ± 0.85	3.44 ± 0.91	27.70 ± 2.79
26-30[b]	6.89 ± 1.87	8.26 ± 0.95	4.67 ± 1.46	3.82 ± 1.27	3.10 ± 1.08	26.74 ± 3.88
31-40[c]	6.41 ± 1.36	8.48 ± 0.89	4.43 ± 1.65	3.70 ± 1.09	3.15 ± 1.18	26.16 ± 3.18
41 +[d]	6.53 ± 1.96	8.23 ± 0.77	5.20 ± 1.71	4.00 ± 1.29	3.33 ± 1.21	27.30 ± 3.44
F: ANOVA,	1.09/356	1.70/0.167	4.56/0.**004/0.06**	1.24/0.297	1.47/0.224	2.68/0.**048/0.04**
			a>b, a>c			a>c
Variable of working						
0-5[a]	6.55 ± 1.22	8.26 ± 0.83	5.14 ± 1.44	3.77 ± 0.77	3.40 ± 0.92	27.12 ± 2.89
6-10[b]	7.42 ± 1.68	8.15 ± 0.92	5.00 ± 1.51	4.25 ± 1.24	3.31 ± 1.02	28.13 ± 3.38
11-15[c]	6.42 ± 1.69	8.36 ± 0.95	4.62 ± 1.62	3.78 ± 1.24	3.00 ± 1.05	26.18 ± 3.38
16-20[d]	6.41 ± 1.12	8.59 ± 0.71	4.24 ± 1.72	3.41 ± 0.80	3.29 ± 1.72	25.94 ± 3.19
21 +[e]	6.26 ± 1.99	8.19 ± 0.83	4.93 ± 1.84	4.04 ± 1.32	3.26 ± 1.13	26.67 ± 3.91
F / p / η2	4.15/0.**003/0.07**	1.02/0.398	1.72/0.147	2.78/0.**028/0.05**	1.15/.0.332	2.96/0.**021/0.05**
	b>a, b>c, b>d, b>e			b>d		b>c
The number of patients with pressure ulcers the nurses took care						
None[a]	7.12 ± 1.92	8.39 ± 0.79	4.70 ± 1.76	3.88 ± 0.99	3.52 ± 1.40	27.61 ± 3.61
10 ve altı	7.08 ± 1.46	8.22 ± 0.78	4.99 ± 1.38	3.97 ± 1.14	3.41 ± 0.96	27.67 ± 2.86
11-50[c]	6.57 ± 1.33	8.24 ± 1.08	5.17 ± 1.78	3.91 ± 1.11	3.17 ± 1.08	27.07 ± 3.47
51 +[d]	6.10 ± 1.56	8.31 ± 0.87	4.69 ± 1.55	3.78 ± 1.10	3.03 ± 0.99	25.90 ± 3.37
F: ANOVA η2: Eta squared	6.16/0.**000/0.08**	0.37/0.776	1.13/0.338	0.41/0.748	2.39/0.070	4.18/0.**007/0.05**
	a>d, b>d					b>d
Nurses' education on pressure ulcers						
Yes	6.47 ± 2.04	8.25 ± 1.09	4.58 ± 1.65	3.71 ± 1.23	2.98 ± 1.09	26.00 ± 3.89
No	6.74 ± 1.40	8.28 ± 0.79	5.00 ± 1.54	3.95 ± 1.05	3.35 ± 1.06	27.32 ± 3.06
t: t-test	-1.11/0.268	-0.21/0.832	-1.79/0.076	-1.42/0.157	-2.30/0.**023/0.34**	-2.66/0.**008/0.37**
Finding the applications related to pressure wounds sufficient						
Sufficient[a]	6.25 ± 1.43	8.23 ± 0.93	4.93 ± 1.52	3.80 ± 1.12	3.26 ± 1.03	26.47 ± 3.37
Partially sufficient[b]	6.90 ± 1.60	8.31 ± 0.83	4.79 ± 1.67	3.91 ± 1.11	3.15 ± 1.06	27.06 ± 3.19
Insufficient[c]	7.54 ± 1.72	8.33 ± 0.82	5.13 ± 1.45	4.17 ± 0.96	3.71 ± 1.23	28.88 ± 3.15
F / p / η2	8.87/0.**000/0.07**	0.25/0.777	0.50/0.610	1.14/0.320	2.67/0.072	5.32/0.**006/0.05**
	b>a, c>a, c>b					c>b, c>a

n: number, %: percentage, SD: Standard deviation

Instruments

The data of the study were collected using the "descriptive characteristics questionnaire form" and the "attitude towards pressure injury prevention scale".

Descriptive characteristics questionnaire form: The questionnaire prepared by the researchers contained eight questions that included information about the introductory characteristics of the nurses (age, gender, work experience, knowledge of pressure injury care, having had any field training about pressure injury, whether they found any sufficient pressure injury applications, their most frequently used method in caring for pressure injury, and their thoughts on who should perform pressure injury care). Six questions included information about the introductory characteristics of the students (gender, knowledge of car-

Table 4. Distribution of *ATPIPS* the sub-dimension scores according to the promotional characteristics of the nursing students (n=93)

Özellik	Competency	Priority	Impact	Responsibility	Effectiveness of prevention	Total
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Gender						
Female	6.73 ± 1.76	8.74 ± 0.78	3.75 ± 1.50	3.32 ± 1.10	2.68 ± 0.97	25.22 ± 3.53
Male	6.30 ± 1.59	8.45 ± 0.83	4.95 ± 1.88	3.60 ± 1.14	3.35 ± 1.66	26.65 ± 3.94
t / p / Cohen's d	0.98/0.330	1.45/0.150	-2.99/0.**004/0.71**	-1.02 / 0.313	-2.29/0.**024/0.49**	-1.57/0.121
Nurses' education on pressure ulcers						
Yes	5.64 ± 1.91	8.43 ± 1.02	4.43 ± 2.07	3.36 ± 1.39	3.29 ± 1.68	25.14 ± 5.04
No	6.81 ± 1.64	8.72 ± 0.75	3.94 ± 1.57	3.38 ± 1.07	2.75 ± 1.06	25.59 ± 3.38
t / p / Cohen's d	-2.39/0.**019/0.66**	-1.27/0.206	1.03/0.307	-0.07/0.945	1.59/0.115	0.43/0.671
Finding the applications related to pressure wounds sufficient						
Sufficient [a]	5.41 ± 1.87	8.77 ± 0.75	3.59 ± 1.65	3.23 ± 1.19	2.64 ± 1.00	23.64 ± 4.46
Partially sufficient [b]	6.74 ± 1.25	8.77 ± 0.73	4.09 ± 1.63	3.30 ± 1.05	2.70 ± 0.91	25.60 ± 2.95
Insufficient [c]	8.14 ± 1.92	8.14 ± 0.95	4.36 ± 1.74	3.93 ± 1.14	3.64 ± 1.95	28.21 ± 3.29
F / p / η2	14.16/0.**000/0.24**	3.95/0.**023/0.08**	1.08/0.343	2.11/0.127	4.26/0.**017/0.09**	7.77/0.**001/0.15**
	b>a, c>a, c>b	a>c, b>c			c>a, c>b	c>a, c>b

n: Sayı, %: Yüzde, SD: Standard deviation

Table 5. Distribution of nurses and nursing students' *ATPIPS* sub-dimension scores

	Nurses (n:229)		**Nursing students (n:93)**		**t**	***p***
	Mean	**SD**	**Mean**	**SD**		
Competency	6.67	1.59	6.63	1.72	0.190	0.849
Priority	8.28	0.87	8.68	0.80	-3.843	**0.000**
Impact	4.89	1.58	4.01	1.65	4.473	**0.000**
Responsibility	3.89	1.10	3.38	1.11	3.763	**0.000**
Effectiveness of prevention	3.26	1.10	2.83	1.18	3.161	**0.002**
Total	26.98	3.33	25.53	3.65	3.457	**0.001**

n: Sayı, %: Yüzde, SD: Standard deviation

ing for pressure injury, having had any out-of-school training about pressure injury, whether they found any sufficient pressure injury applications, their most frequently used method in caring for pressure injury, and their thoughts on who should care for pressure injury).

Attitude Towards Pressure Injury Prevention Scale (ATPIPS): The Cronbach Alpha value of the ATPIPS scale developed by Beeckman et al. used to determine the attitude of nurses towards pressure injury prevention was 0.79 (16). The Cronbach Alpha value of its Turkish version which was adapted by Üstün, was found to be 0.71 in this study (17). The ATPIPS contains 13 items in five sub-dimensions. The sub-dimensions of the scale are as follows: attitude towards individual competence in pressure injury prevention (3 items), attitude towards the priority of pressure injury prevention (3 items), attitude towards the impact of pressure injury (3 items), attitude towards personal responsibility in preventing pressure injury (2 items), and attitude towards the effectiveness of pressure injury prevention (2 items). While the minimum score that can be obtained from the scale is 13, the maximum score is 52. It is expected that the attitude will be more positive as the total average score of the ATPIPS increases.

Data collection

Data were collected by face-to-face interview technique between 01.12.2021 and 01.02.2022. Before the data were collected, the nurses and nursing students were informed about the study by the researchers. The

purpose of the research was explained and it was emphasized that the research would be kept confidential and voluntarily. After the content of the consent form was read, the forms were distributed to those who agreed to participate in the study. Participants voluntarily consented and were told that they could withdraw from the study at any time without prejudice. After the tools were completed, they were collected by the researchers. Data collection took approximately 15-20 minutes.

Statistical analyses

The data obtained in the research were analyzed using the Statistical Package for the Social Sciences package program version 23.0 (SPSS Inc., Chicago, IL, USA). The number, percentage, mean and standard deviation were used as descriptive statistical methods in the evaluation of the data. The Kolmogorov-Smirnov test was applied to determine whether the data was normally distributed. The t-test was used to compare the quantitative continuous data between two independent groups, and the one-way Analysis of Variance (ANOVA) test was used to compare the quantitative continuous data among more than two independent groups. Cronbach's α coefficients were calculated for validity and reliability. Eta squared and Cohen's d coefficients were used to calculate the effect size. The findings were evaluated at the 95% confidence interval at a 5% significance level.

RESULTS

The sociodemographic and nurses' introductory characteristics are given in Table 1. 33.6% of the nurses that participated in the study were between the ages of 18-25 years, 85.6% were female, 34.1% had 0-5 years work experience, 34.1% cared for pressure injury less than 10 times, 74.2% did not receive any training on pressure injury outside of school, 45.4% found pressure injury applications sufficient, 62.9% used the repositioning method the most for pressure injury care, and 90.0% stated that nurses should care for pressure injury (Table 1).

The distribution of the introductory characteristics of nursing students is given in Table 2. 78.5% of the students that participated in the study were female, 90.3% cared for pressure injury, 84.9% did not receive training on pressure injury outside of school, 61.3% found pressure injury applications partially sufficient, 73.1% used the repositioning method the most often for pressure injury care, and 95.7% stated that nurses should care for pressure injury (Table 2).

Table 3 shows the distribution of nurses' *ATPIPS* sub-dimension scores. The nurses' sub-dimension scores were as follows: competence (6.67±1.59), priority (8.28±0.87), impact (4.89±1.58), responsibility (3.89±1.10), the effectiveness of prevention (3.26±1.10), and *ATPIPS* total score (26.98±3.33). The scales that were used in this study were found to be highly reliable according to the research results. There was no significant difference between the nurses' age variable and the mean scores of *ATPIPS* competency, priority, responsibility, and effectiveness of prevention ($p>0.05$). A statistically significant difference was found between the age variable and the impact sub-dimension mean scores at a moderate level ($p<0.05$; eta-square: 0.06), and the scale total mean score at a low level ($p<0.05$; eta-square:0.04). The impact scores of the nurses in the age range of 18-25 years were higher than those in the age ranges of 26-30 and 31-40 years, and the total scale scores were higher than those in the 31-40 age range. No significant difference was found between the variable of working years and the nurses' mean scores of *ATPIPS* priority, impact, and effectiveness of prevention sub-dimensions ($p>0.05$). A statistically significant difference was found between the variable of working years and the competence sub-dimension mean score at a moderate level ($p<0.05$; eta-square:0.07), the responsibility sub-dimension mean score ($p<0.05$; eta-square:0.05) at a low level, and the total scale mean score at a low level ($p<0.05$; eta-square: 0.05). The competence scores of the nurses for 6-10 years were found to be higher than the others, their responsibility scores were higher than those working for 16-20 years, and their total scale scores were higher than those working for 11-15 years (Table 3).

No significant difference was found between the number of patients with pressure injury in the nurses' care and their mean scores of *ATPIPS* priority, impact, responsibility, and effectiveness of prevention sub-dimensions ($p>0.05$). A statistically significant differ-

ence was found between the number of patients with pressure injury in the nurses' care and the mean scores of the competence sub-dimension at a moderate level (p<0.05; eta-square: 0.08), and the scale mean score at a low level (p<0.05; eta-square: 0.05). The competence scores of the nurses who cared for 51 or more patients with pressure injury were found to be lower than the scores of those who did not care for patients such as these and the scores of those who cared for less than 10 patients, and their total scale scores were lower than the scores of those who cared for less than 10 patients. There was no significant difference between the nurses' education on pressure injury and their mean scores of *ATPIPS* competence, priority, impact, and responsibility sub-dimensions (p>0.05). A statistically significant difference was found between the nurses' education on pressure injury and the effectiveness of prevention sub-dimension mean score (p<0.05; Cohen's d: 0.03) at a moderate level, and the total scale mean score at a moderate level (p<0.05; Cohen's d: 0.04). The scores of those who did not receive education were found to be higher than the rest. There was no significant difference between the variable of finding pressure-injury-related practices sufficient and the nurses' mean scores of *ATPIPS* priority, impact, responsibility, and effectiveness of prevention sub-dimensions (p>0.05). A statistically significant difference was found between the variable of finding pressure-injury-related practices sufficient and the mean scores of the competence sub-dimension at a moderate level (p<0.05; eta-square:0.07), and the total scale mean score at a low level (p<0.05; eta-square:0.05). The competence scores of the nurses who found the practices related to pressure injury sufficient were lower than the rest, and the scores of those who found them to be partially sufficient were lower than the scores of those who found them to be insufficient. The total scale scores of the nurses who found the practices related to pressure injury inadequate were found to be higher than the scores of the rest. (Table 3)

Table 4 shows the distribution of nursing students' *ATPIPS* sub-dimension scores. There was no significant difference between the student's gender and their *ATPIPS* competence, priority, responsibility, and total scale mean scores (p>0.05). A statistically significant difference was found between gender and the impact sub-dimension mean scores at a high level (p<0.05; Cohen's d: 0.71) and the effectiveness of prevention mean scores at a moderate level (p<0.05; Cohen's d: 0.04). The scores of the male students were higher than the scores of the female students. There was no significant difference between the students' education on pressure injury and their *ATPIPS* priority, impact, responsibility, effectiveness of prevention, and total scale mean scores (p>0.05). A statistically significant difference was found between the students' education on pressure injury and their competence sub-dimension mean scores at a moderate level (p<0.05; Cohen's d: 0.66). The scores of those students who did not receive education were found to be higher than those who had. There was no significant difference between the variable of finding the practices related to pressure injury sufficient and the students' *ATPIPS* impact and responsibility mean scores (p >0.05). A statistically significant difference was found between the variable of finding the practices related to pressure injury sufficient and the competence sub-dimension mean scores at a low level (p<0.05; eta-square:0.24), the priority sub-dimension mean scores at a moderate level (p<0.05; eta-squared:0.08), the effectiveness of prevention at a moderate level (p<0.05; eta-square:0.09), and the total scale mean scores at a high level (p<0.05; eta-square:0.15). The competence scores of the students who found the applications related to pressure injury sufficient were lower than the rest, and the scores of those who found them to be partially sufficient were lower than the scores of those who found them to be insufficient. The priority scores of those who found the applications to be inadequate were lower than the scores of the rest, and their effectiveness of prevention and total scale mean scores were found to be higher than the scores of the rest (Table 4).

In Table 5, the *ATPIPS* sub-dimension scores of nurses and nursing students are given. A t-test was conducted to determine whether the *ATPIPS* sub-dimension mean scores of the nurses and nursing students who participated in the study showed a significant difference. The difference between priority, impact, responsibility, effectiveness of prevention, and total mean scores were statistically significant (p<0.05). The nurses' impact, responsibility, effectiveness of prevention, and total scores were higher than the students' scores, and their priority scores were lower. The differ-

ence between the nurses' and the students' competence mean scores were not found to be statistically significant (p>0.05) (Table 5).

DISCUSSION AND CONCLUSION

Nurses need to update their knowledge of pressure injuries to help prevent pressure injuries and to improve the quality of patient care. Nursing education aims to provide knowledge and skills related to pressure injury, and nurses play a key role in pressure injury prevention. The attitudes of nursing students and nurses towards pressure injury prevention were determined in this study.

Attitude of nurses and nursing students toward preventing pressure injury

This study showed that nursing students and nurses had low scores on attitude towards pressure injury prevention. The studies by Khojastehfar et al. (2020) with 328 nurses and by Balan et al. (2021) with 164 nurses determined that the attitude of nurses towards pressure injury prevention was not at the desired level. The studies conducted by Özyürek and Kuzucuk (2023) assessed nurses' knowledge and attitudes regarding the prevention of pressure injuries. The observations indicated that nurses exhibited notably low levels of positive attitudes toward the effectiveness of preventing pressure injuries (18-19). Contrary to this study, the studies by Sucu and Kılıç (2022) conducted with 259 nursing students, by Ghazanfari et al. (2022) with 183 intensive care nurses, by Kısacık and Sönmez with 753 nursing students, by Ekim and Sabuncu with 131 nurses and by Usher et al. (2018) with 2949 nursing students determined that they exhibited positive attitude towards pressure injury prevention (20-24). There are different results in the literature regarding attitudes toward pressure injury prevention. This result could be due to the low prevalence of patients with pressure injuries in the hospital where the study was conducted.

It is key to have positive role models to develop students' attitudes towards pressure injury prevention. This study showed that although the nurses' attitudes towards pressure injury prevention are more positive than the attitudes of nursing students, they are not at the desired level. Students interact with nurses during their clinical experience. The higher the nurses' attitude scores, the higher the students' awareness. Similar to this study, Cukljek et al. (2022) conducted a study with nursing students and nurses, and nurses' attitude scores toward pressure injury prevention were found to be higher than those of nursing students (25). The fact that nurses have more clinical experience, care for patients with pressure injuries, and attend training and courses that are useful in updating their knowledge about pressure injuries leads them to obtain higher scores than the students (25). This result supports the results in the literature.

The scores of the sub-dimensions of the *ATPIPS* of the nurses and nursing students were examined, which showed that the nurses obtained the highest score for the "Priority of Pressure Injury Prevention" dimension, and the lowest score from the "Effectiveness of Pressure Injury Prevention" dimension. Similar to this study, the studies by Aydoğan et al. (2019) with 340 intensive care nurses, and by Şen (2019) with 110 intensive care nurses showed that nurses scored lower in the "effectiveness of prevention" sub-dimension (26-27). The studies conducted by Aslan and Van Giersbergen (2016) with 660 nurses working in surgical clinics and intensive care units, by Usher et al. (2018), and by Aydoğan et al. (2019) found that the highest score was obtained from the "priority of prevention" sub-dimension (24,26,28). Nurses and nursing students think that it is important to prevent pressure injuries, but they also think that pressure injuries cannot be prevented in high-risk patients. This study result may be due to the inability to prevent pressure injury because of the lack of information, time, number of nurses, and materials.

The difference between the attitude of nurses and nursing students toward preventing pressure injury

The scores of the nurses in the sub-dimensions of attitude towards the impact of pressure injury, attitude towards personal responsibility in preventing pressure injury, and attitude towards the effectiveness of pressure injury prevention were found to be significantly higher than those of nursing students, and their scores of priority of pressure injury prevention were found to be significantly lower. This study result suggests that while nursing students work in the clinic with a focus on care, their priorities may change because nurses have responsibilities in the clinic other than care.

The attitude of health professionals contributes greatly to pressure injury prevention. Attitude are developed and acquired during nursing education. All the lessons during training contribute to the development of a positive attitude toward pressure injury prevention. Although knowledge raises awareness, attitude, and experience are important elements in preventing pressure injury (29). The high level of knowledge of nurses and nursing students, their positive attitude towards pressure injury, and the elimination of the obstacles they encounter in prevention will greatly contribute to the prevention of pressure injury and will decrease its incidence (30). This study revealed that some revisions are needed to improve the attitude of nurses and nursing students toward pressure injury prevention and care.

However, a relationship was found between age, work experience, the number of patients with pressure injuries cared for, and *ATPIPS* total scores. Contrary to this study, it found that nurses' age, education level, and year of clinical work experience did not have a significant effect on nurses' attitudes (31,32,33).

A pressure injury is an important clinical problem that affects the quality of life, health care costs, and treatment results in patients, therefore it is important for nurses to develop a positive attitude towards pressure injury prevention. The results of this study revealed that the attitude of nurses and nursing students towards pressure injury prevention was negative, and nurses showed a more positive attitude than students, although not at the desired level. It is necessary to raise awareness first to develop a positive attitude towards pressure injury prevention. The curriculum for nurses and nursing students should be reviewed and the identified knowledge gaps should be filled with effective teaching methods. It is recommended to include more topics in hospitals, classrooms, and laboratories through simulation or clinical practice.

Clinical Relevance

This study emphasizes the importance of nurses and nursing senior students' attitudes toward preventing pressure injury. Although the fight against pressure injury requires multidisciplinary teamwork, nursing care plays a key role in the prevention and treatment of pressure injuries. It is possible to prevent pressure injury by evaluating patients at risk of pressure injury by nurses and planning and implementing prevention interventions. Nurses must have sufficient knowledge, skills, critical thinking, and problem-solving skills to provide quality and effective pressure injury care. Senior nursing students who will graduate are also required to be competent in the basic areas of nursing care and to give priority to all the care necessary for the comfort and recovery of their patients. The results of this study revealed that the attitudes of nurses and nursing students towards preventing pressure injury are negative and that nurses exhibit more positive attitudes than students, although not at the desired level. To develop a positive attitude towards the prevention of pressure injuries, it is necessary to raise awareness first. Curriculum for nurses and nursing students should be revised and identified knowledge gaps should be filled with effective teaching methods. More issues need to be addressed in hospitals, classrooms, and laboratories through simulation or clinical practice.

Study Limitation

The limitation of this study is that the knowledge and practices of nurses and nursing students regarding pressure injuries were not evaluated.

Ethical approval

Written permission was obtained from the ethics committee of Kastamonu University Clinical Research (date: 12.16.2021, decision no: 2020-KAEK-143-137) where the research was conducted, and from the Faculty of Health Sciences and the Provincial Health Directorate for the implementation of the research. Permission was obtained from the researcher who carried out the validity and reliability study of the scale via e-mail. In addition, it was clearly stated to the participants that their data would be confidential, that they could withdraw from the study at any time, and that it was voluntary. Consent was obtained from the nurses and students who agreed to participate. All expenses of the research were covered by the researchers. The research was conducted according to the principles stated in the Declaration of Helsinki.

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Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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Gelmiş Geçmiş En Büyük Katil:
1918 "İSPANYOL" GRİBİ

İKİNCİ BASKI

Dr. M. Kemal Temel

Grip, her yıl olağan bölgesel grip salgınları sırasında dünya genelinde yaklaşık 500.000 ölüme yol açmasına karşın, yaşlılar ve kronik hastalar gibi gruplar dışında genellikle hafif seyreden bir hastalık olduğundan, bugüne dek pek önemsenmemiştir. Daha seyrek görülen küresel grip salgınları, yani grip pandemileri sırasında ise, çok daha büyük kayıplar kaydedilmektedir. Kayıtlı tarihte onlarca grip pandemisi gerçekleşmiş olduğu bilinmektedir ve bunların en şiddetlisi olan 1918 "İspanyol" gribi pandemisi, bir yıldan kısa süre içinde 40 ila 100 (ortalama 50) milyon insanı ölüme götürmüştür. Üstelik en ağır seyrettiği grup, sıra dışı bir biçimde sağlıklı genç yetişkinler olmuştur. Çok sarsıcı sosyal, demografik ve ekonomik sonuçları nedeniyle 1918 "İspanyol" gribi pandemisi, sağlık otoritelerince solunum yoluyla yayılan salgınlar için olabilecek "en kötü senaryo" kabul edilegelmiştir. Sürmekte olan COVID-19 pandemisi sırasında bu kıyas ve ikaz, T.C. Sağlık Bakanlığı tarafından da yapılmıştır.

Yabancı dillerdeki eserlere karşın, bu yıkıcı pandemiyi ele alan Türkçe çalışmalar oldukça az sayıdadır. İlkin 2015 yılında yayımlanmış olan *Gelmiş Geçmiş En Büyük Katil: 1918 "İspanyol" Gribi,* kapsamlı bir araştırmanın ardından bu konudaki başlıca bilgi ve belgeleri Türkçe literatüre kazandırmayı amaçlayan bir ilk eserdir. Kitapta pandeminin köken, neden ve sonuçlarına; morbidite, mortalite ve üç dalgalı seyrine; Birinci Dünya Savaşı ile ilişkisine; genel küresel yayılımına ve bölgesel farklılıklarına; klinik semptom ve karakteristiklerine; dünyada ve Osmanlı İmparatorluğu'nda pandemiye karşı alınan önlemlere; yabancı kaynaklardan hastalığın teşhis ve tedavisi ile ilgili bildirim, anekdot ve gözlemlere; Osmanlı basınından hastalığın semptomları, seyri, payitaht İstanbul'a gelişi, hasta istatistikleri ile ilgili haberlere ve de yerli doktorların açıklama, karşılaştırma ve otopsi bulgularına yer verilmiştir. Ayrıca, gribin de yeni koronavirüs hastalığının da solunumsal salgın hastalıklar olması paydasında, genişletilmiş ikinci baskı güncel COVID-19 pandemisi ile mukayeseler de içermektedir.

BETİM KİTAPLIĞI

Lokal sistoskopi öncesi görsel bilgilendirmenin, anksiyete ve ağrı üzerine etkisi

The effect of visual information before local cystocopy on anxiety and pain

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Öz

Amaç: Çalışmamızda işlem öncesi video tabanlı eğitimin, mesane kanseri takibi amacıyla lokal sistoskopi yapılacak hastalarımızda anksiyete ve ağrı üzerindeki etkisini değerlendirmeyi amaçladık.

Yöntemler: Görsel bilgilendirme yapılan 28 hasta (grup 1) ve görsel bilgilendirme yapılmayan 32 hasta (grup 2) olmak üzere toplam 60 hasta çalışmaya dâhil edildi. Grup 1'e preoperatif video temelli bilgi verildi. Grup 2'ye ise sadece sözel bilgilendirme yapıldı. Avrupa Üroloji Derneği (EAU) hasta bilgilendirme videosu kullanıldı. Amsterdam Ameliyat Öncesi Anksiyete ve Bilgi Ölçeği (APAIS) ve Durumluk-Süreklilik Kaygı Envanteri (STAI) ameliyat öncesi tüm hastalar tarafından doldurduldu. Postoperatif ağrı vizüel analog skala (VAS) kullanılarak ölçüldü. Her hasta VAS'ı ve isteklilik anketini operasyon sonrası 2. saatte doldurdu.

Bulgular: APAIS ve VAS ve STAI durumluk skoru, görsel bilgilendirme yapılan grupta istatistiksel olarak anlamlı olarak düşük hesaplandı (sırasıyla; p=0,021, p=0,016, p<0,001). İsteklilik skoru görsel bilgilendirme yapılan grupta anlamlı olarak daha yüksekti (p=0,002). Bireyin içinde bulunduğu durum ve koşullardan bağımsız olarak kendini nasıl hissettiğini belirleyen STAI süreklilik skorunda ise gruplar arasında istatistiksel olarak anlamlı fark saptanmadı (p=0,380).

Sonuç: İşlem öncesinde görselliğe dayalı ve çok daha anlaşılır olan video bilgilendirme uygulamaları, geleneksel yöntemler olan sözlü ve yazılı bilgilendirmeye kıyasla çok daha anlaşılır ve açıklayıcı olur. Operasyon öncesi video bilgilendirme hastanın operasyon öncesi kaygısını önemli ölçüde azaltır. Bunun yanı sıra postoperatif ağrı ve operasyon için isteklilik durumları üzerinde de olumlu etkileri olacaktır.

Anahtar Sözcükler: Ağrı; anksiyete; sistoskopi

Abstract

Aim: In our study, we aimed to evaluate the effect of pre-procedural video-based education on anxiety and pain in patients who will undergo local cystoscopy for bladder cancer follow-up.

Methods: A total of 60 patients were included in the study, with 28 patients receiving visual information (group 1) and 32 patients not receiving visual information (group 2). Group 1 received preoperative video-based information, while Group 2 received only verbal information. The European Association of Urology (EAU) patient information video was used. The Amsterdam Preoperative Anxiety and Information Scale (APAIS) and the State-Trait Anxiety Inventory (STAI) were administered to all patients preoperatively. Postoperative pain was measured using the visual analog scale (VAS). Each patient completed the VAS and willingness questionnaire at 2 hours after the surgery.

Results: APAIS and VAS scores, as well as STAI state scores, were significantly lower in the group that received visual information (p=0.021, p=0.016, p<0.001, respectively). The willingness score was significantly higher in the group that received visual information (p=0.002). The STAI trait score, which determines how an individual feels regardless of their current circumstances, did not show a statistically significant difference between the groups (p=0.380).

Conclusion: Preoperative video-based education applications, which are visually more comprehensible, are more informative compared to traditional methods of verbal and written information. Preoperative video education significantly reduces the patient's preoperative anxiety. In addition, it will have positive effects on postoperative pain and willingness for the operation.

Keywords: Anxiety; cystoscopy; pain

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GİRİŞ

Sistoskopi; alt üriner sistemi anatomik açıdan tanısal olarak değerlendirme olanağı sağlayan, oldukça yaygın olarak kullanılan invaziv bir işlemdir. Temel olarak alt üriner sistem semptomları olan hastaların değerlendirilmesinde, ürolojik malignitelerin tanı ve takibinde kullanılır. Özellikle mesane kanserinin tanı ve takibinde altın standart yöntem olarak kabul edilir (1,2).

Lokal sistoskopi; kolay, güvenli ve etkili bir biçimde kullanılan yaygın bir yöntemdir. İnvaziv bir işlem olması nedeniyle hastada ağrı ve anksiyeteye yol açabilmektedir. Bu sebeple başarılı bir sistoskopi prosedüründe temel hedefler; hastayı rahatsız etmeden ve sedatif anestezi ihtiyacı gerektirmeden, eksiksiz bir inceleme yapabilmeyi kapsar. Literatürde sistoskopiye bağlı ağrı durumunu değerlendiren birçok çalışma bulunmaktadır. Prosedürle ilgili teknik işlemlerin ve çevresel belirleyicilerin, işleme bağlı ağrı ve anksiyete üzerinde etkili olduğu gösterilmiştir (3,4).

Hastalar cerrahi prosedürler öncesinde oldukça değişken bir skalada kaygı yaşamaktadır. Bunun temel sebepleri olarak ağrı duyusu, bilinmeyenin korkusu, iyileşememe ve organ yaralanması korkusu sayılabilir. Preoperatif aşamada tüm hastalar çeşitli yöntemler kullanılarak işlem hakkında bilgilendirilir. Günlük cerrahi pratiğimizde yaygın olarak kullanılan sözlü ve yazılı bilgilendirme çoğu kez hasta tarafından yeterli düzeyde anlaşılır olmayabilir. Bu durum ise hasta üzerinde stres ve kaygı için bir risk faktörüdür. Bilgilendirmede kullanılacak görsel öğeler, daha kolay anlaşılabileceği için preoperatif kaygıyı azaltabilir (5,6). Literatürde perkütan nefrolitotomi, transrektal prostat biyopsisi ve inguinal herni onarımı gibi farklı işlem türleri öncesi preoperatif video tabanlı bilgilendirme ile anksiyetenin azaldığına dair çok sayıda çalışma bulunmaktadır (7-9).

Biz de bu çalışmamızda, mesane kanseri takibi amacıyla kontrol sistoskopi planlanan hastalarda, işlem öncesi video tabanlı bilgilendirmenin anksiyete ve ağrı üzerindeki etkisini değerlendirmeyi amaçladık.

GEREÇ VE YÖNTEMLER

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Çalışmamıza, daha önce mesane tümörü nedeniyle spinal anestezi altında transüretral mesane tümörü rezeksiyonu (TUR-MT) yapılan ve kılavuzlarda belirtilen sürelerde kontrol sistoskopi planlanan hastalar dâhil edildi. İlk TUR-MT işlemi genel anestezi altında yapılan hastalar, spinal anestezi ile karşılaştırıldığında, operasyon sırasında görsel ve işitsel duyuları tamamen kapalı olmasından dolayı çalışmaya dâhil edilmedi. Daha önceki kontrol sistoskopilerinde lokal anestezi ile işlem yapılan hastalar, işlemle ilgili tecrübesi olduğu ve çalışmanın standardizasyonunu etkileyebileceği için çalışmaya dâhil edilmedi. Okuma-yazma bilmeyen, sorulara cevap verme beklentisi düşük olan hastalar, çalışmada kullanılan anketleri ve skorlamaları uygun şekilde cevaplayamayacağı için çalışmaya dâhil edilmedi. Yaygın anksiyete bozukluğu veya depresyon tanısı olan hastalarda, çalışmada kullanılan ölçek skorları yüksek beklenmektedir. Bu nedenle ölçek skorlarını etkileyecek psikiyatrik bozukluğu olan hastalar çalışma dışı bırakıldı. Bilinen üretra darlığı olan ve operasyon öncesi görüntüleme yöntemlerinde tümör saptanan hastalarda, lokal anestezi uygun bir seçenek olmamaktadır ve bu hastalarda spinal veya genel anestezi uygulaması gerekmektedir. Ayrıca bir önceki TUR-MT veya sistoskopi ile yeni planlanan sistoskopi arasında makroskopik hematüri tarifleyen veya nüks oranlarını daha fazla beklediğimiz yüksek riskli mesane kanseri hastalarında yine aynı şekilde sistoskopide tümör saptanma ihtimali daha fazladır ve lokal anestezi uygun bir seçenek olarak görülmemektedir. Genel veya spinal anestezi uygulamasının daha uygun bir seçenek olarak görüldüğü bu hastalar çalışmaya dâhil edilmedi. Çalışmamıza, mesane kanseri takibi nedeniyle lokal sistoskopi planlanan 74 hasta dâhil edildi. Hastalar www.randomizer.org internet sitesi kullanılarak iki gruba randomize edildi. 6 hasta lokal sistoskopiyi tolere edemedi, 8 hastada ise anestezi eşliğinde rezeke edilmesi gereken nüks tümöral oluşum izlendi. 14 hasta çalışma dışı bırakıldı ve sonuç olarak görsel bilgilendirme yapılan 28 hasta (Grup 1) ve görsel bil-

gilendirme yapılmayan 32 hasta (Grup 2) olmak üzere toplam 60 hasta ile çalışmaya devam edildi.

Hastaların demografik ve klinik verileri (yaş, cinsiyet, komorbidite, tümör evresi, sistoskopi bulguları vb.) kaydedildi. Grup 1'e preoperatif video temelli bilgi verildi. Grup 2'ye ise sadece sözel bilgilendirme yapıldı. Avrupa Üroloji Derneği (EAU) hasta bilgilendirme videosu tarafımızca dilimize çevrilerek tekrar dublaj yapılmıştır (10). Animasyonlu video EAU'nun izniyle kullanılmıştır. Sistoskopinin tüm aşamaları hakkında detaylı bilgi içeren video, tüm grup 1 hastalarına aynı klinisyen tarafından sunuldu. Hastalara video ile ilgili soru sormaları teşvik edildi. Grup 1 ve Grup 2'ye tüm preoperatif sözel operasyon bilgileri aynı klinisyen tarafından verildi.

Amsterdam Ameliyat Öncesi Anksiyete ve Bilgi Ölçeği (APAIS) ve Durumluk-Süreklilik Kaygı Envanteri (STAI) ameliyat öncesi tüm hastalara uygulandı (11,12). APAIS, Moerman ve arkadaşları tarafından operasyon öncesi kaygıyı değerlendirmek amacıyla geliştirilmiştir. Testte 6 soru bulunmaktadır ve yüksek puanlar, yüksek kaygı ve daha fazla bilgi alma isteğini göstermektedir. STAI, durumluk ve süreklilik kaygı düzeylerini ölçen yirmişer sorudan oluşan Likert tipi bir ölçektir. Her iki bölüm için de düşük puanlar hastanın daha az kaygısı olduğunu göstermektedir.

Tüm ameliyatlar 19 Fr rijid sistoskop ile lokal anestezi altında yapıldı. Lokal anestezi için operasyondan 10 dakika önce 20 cc bupivakain ve lidokain içerikli kaydırıcı jel olan 11 ml Lubragel® intraüretral olarak uygulandı. Tüm hastalara sistoskopi işlemi aynı cerrahi aletle (19-Fr; Karl Storz, Rigid Cystoscope, Tuttlingen, Almanya) ve aynı cerrah tarafından gerçekleştirildi. Postoperatif ağrı vizüel analog skala (VAS) kullanılarak ölçüldü. Hastalar ağrı şiddetini tanımlamak için 0 ile 10 arası bir puan seçtiler. 0; hiç ağrının olmaması, 10 ise en şiddetli ağrıyı ifade etmektedir. Gelecek zamanlarda gerekebilecek tekrar sistoskopiye girme isteği, 0 ila 4 arası sayısal bir ölçek kullanılarak belirlendi. Her hasta VAS'ı ve isteklilik anketini operasyon sonrası 2. saatte doldurdu.

İstatistiksel analiz

Çalışma verilerinin istatisiksel analizi Statistical Package for the Social Sciences package program version 20.0 (SPSS Inc., Chicago, IL, USA) programı ile yapıldı. Değişkenlerin normal dağılıma uygunluğu Kolmogorov-Smirnov (K-S) testi kullanılarak incelendi. İkili grupların karşılaştırılmasında; normal dağılım gösteren parametreler için Student's T testi, anormal dağılım gösteren parametreler için Mann-Whitney U testi uygulandı. Çok gözlü çapraz tabloların değerlendirilmesi Ki-kare testi ya da Fisher Exact testi ile yapıldı. Yaş ve diğer parametrelerin ilişkisi yerine göre Spearman korelasyon testi ve Pearson korelasyon testi kullanılarak incelendi. $p<0,05$ olduğunda sonuçlar istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Çalışmaya katılan 60 hastanın ortalama yaşı 53,32±13,30 (min=28, max=77) idi. Gruplar arasında istatistiksel anlamlı yaş farkı saptanmadı (p=0,210). Çalışmaya katılan 39 (%65) hasta erkek, 21 (%35) hasta kadındı. Gruplar arasında cinsiyet açısından anlamlı fark yoktu (p=0,233). Cinsiyet ile APAIS, VAS, isteklilik, STAI durumluk ve süreklik puanları arasında istatistiksel olarak anlamlı fark saptanamadı (sırasıyla; p=0,145, p=0,741, p= 0,885, p=0,734, p=0,870). APAIS, VAS ve STAI durumluk skoru, görsel bilgilendirme yapılan grupta istatistiksel olarak anlamlı olarak düşük saptandı (sırasıyla; p=0,021, p=0,016, p<0,001). İsteklilik skoru görsel bilgilendirme yapılan grupta anlamlı olarak daha yüksekti (p=0,002). Bireyin içinde bulunduğu durum ve koşullardan bağımsız olarak kendini nasıl hissettiğini belirleyen STAI süreklilik skorunda ise gruplar arasında istatistiksel olarak anlamlı fark saptanmadı (p=0,380) (Tablo 1).

Yaş, APAIS, VAS, isteklilik, STAI durumluk ve süreklilik parametreleri arasında yapılan korelasyon analizinde; yaş ile diğer parametreler arasında korelasyon saptanmazken, isteklilik skoru ile APAIS ve VAS skoru arasında orta düzeyde negatif bir korelasyon izlendi ve istatistiksel olarak anlamlıydı (sırasıyla; r=-0,547 p<0,001, r=-0,590 p<0,001) (Tablo 2).

TARTIŞMA VE SONUÇ

Sistoskopi, özellikle mesane kanserinin takibinde kullanılan altın standart tanı yöntemidir. Lokal sistoskopi ise günübirlik şartlarda ve anestezi gerektirmeden yapılan bir işlem olmasına rağmen anksiyete ve kaygıya neden olabilmektedir (2).

Tablo 1. Gruplar arası demografik veriler ve ölçeklerin karşılaştırılması

	Grup 1 (Görsel bilgilendirme yapılan) n=28	Grup 2 (Görsel bilgilendirme yapılmayan) n=32	p
Yaş	50,93±11,33	55,41±14,67	0,210
Cinsiyet			
Erkek	16 (%57,1)	23 (%71,9)	0,233
Kadın	12 (%42.9)	9 (%28,1)	
APAIS	6,21±2,64	8,50±4,45	*0,021*
VAS	2,75±1,55	4,31±2,55	*0,016*
İsteklilik	1,96±1,37	0,91±0,96	*0,002*
STAI durumluk	38,07±5,31	43,88±5,04	*<0,001*
STAI süreklik	45,68±5,55	46,97±5,56	0,380

The data obtained in the research were analyzed using the Statistical Package for the Social Sciences package program version 23.0 (SPSS Inc., Chicago, IL, USA).

Tablo 2. Yaş ve diğer parametrelerin korelasyon analizi

		Yaş	APAIS	VAS	İsteklilik	STAI durumluk	STAI süreklilik
Yaş	r						
	p						
APAIS	r	0,122					
	p	0,351					
VAS	r	0,094	0,439				
	p	0,475	*<0,001*				
İsteklilik	r	-0,219	-0,547	-0,590			
	p	0,093	*<0,001*	*<0,001*			
STAI durumluk	r	0,029	0,101	0,215	-0,232		
	p	0,825	0,444	0,098	0,075		
STAI süreklilik	r	0,004	0,114	0,129	-0,063	0,136	
	p	0,977	0,385	0,327	0,631	0,300	

The data obtained in the research were analyzed using the Statistical Package for the Social Sciences package program version 23.0 (SPSS Inc., Chicago, IL, USA).

Yapılan bir meta-analiz sonucunda preoperatif anksiyete yaygınlığı %48 olarak bildirilmiştir. Bu anksiyete sonucunda nöroendokrin yolaklar devreye girerek; anestezi gereksinimini, analjezik ihtiyacını ve postoperatif ağrı şiddetini artırabilir. Başka bir çalışma ise işlem öncesinde yetersiz bilgilendirmenin anksiyeteyi artırıcı sonuçları olabileceğini ortaya koymuştur (13-15).

Koroner anjiyografi işlemi öncesi video bilgilendirmenin avantajlarını değerlendiren bir çalışmada, video bilgilendirmeden sonra hastalarda anksiyete, stres ve depresyon oranlarında anlamlı derecede azalma gözlemlenmiştir (16). Başka bir çalışmada ise, abdominal cerrahiler öncesinde video bilgilendirme uygulamalarının hasta kaygı düzeyini azalttığı ve hasta memnuniyetini artırdığı gösterilmiştir (17). Yakın dönemde Karalar ve arkadaşlarının, böbrek taşı tedavisi için uygulanan fleksible üreteroskopi operasyonlarında hastalar iki gruba ayrılarak bir kısmına operasyonun aşamalarını anlatan video görseli izletilmiştir. Video bilgilendirme yapılan hastalarda kaygı düzeyinin diğer gruba göre anlamlı olarak azaldığı tespit edilmiştir (18). Biz de çalışmamızda benzer şekilde, video bilgilendirmenin kaygıyı anlamlı derecede azalttığını tespit ettik.

Hastaların operasyon öncesinde yeterli düzeyde bilgilendirilmesi çok önemlidir. Bu amaçla sözlü ve yazılı materyaller kullanılmakta olsa da bilgilendirmenin standardizasyonu ve hasta uyumu her zaman istenilen seviyede olmayabilir. Hasta-hekim iletişimi, hekimin iş-

lemi anlaşılır bir biçimde açıklaması ve hastanın okuryazarlık durumu, hastanın yeterli düzeyde bilgilendirilmesi için önemli belirleyicilerdir. Video bilgilendirme ise oldukça kolay anlaşılırdır (19). Çalışmamızda lokal sistoskopi öncesi video eğitim alan hastalar, daha düşük kaygı düzeyine sahipti. APAIS ve STAI durumluk skoru, görsel bilgilendirme yapılan grupta istatistiksel olarak anlamlı olarak düşük bulundu. STAI süreklilik skorunda ise anlamlı farklılık saptanmadı.

Ameliyat süreci; hastanın ameliyathaneye girişi ile başlayıp, ameliyathaneden çıkarılması ile biten bütüncül bir işlem olarak değerlendirilmelidir. Bu süreç içerisinde hastaya uygulanan anestezi şeklinin de hastanın anksiyete ve ağrı düzeyine etki etmesi beklenmelidir. APAIS skorlaması içerisinde anestezi ile ilgili sorular da yer almaktadır. Çalışmamızda tüm hastalara lokal anestezi uygulanarak, anestezi şeklinden oluşabilecek yanlılık en aza indirilmiştir. Ayrıca hastanın operasyon öncesi ve sonrasında yataklı serviste değerlendirildiği süreçte yaşadığı anksiyete, ameliyat sürecini de etkileyebilmektedir. Hastanın hekimini tanıması ve operasyonu gerçekleştirecek hekimden doğrudan bilgi alması en uygun yöntem gibi görünmektedir. Hekim ile hasta arasındaki iyi bir iletişim, hastaların motivasyonlarını artırabilir ve bu da sağlık sonuçlarını olumlu etkileyebilir. Hekimlerin iş yükü nedeniyle yeterli zaman ayıramaması ve hastaların endişeleri bu iletişimi olumsuz olarak etkileyebilmektedir (20). Bizim çalışmamızda da tüm hastalara operasyonu gerçekleştirecek olan aynı hekim tarafından yeterli zaman ayrılarak bilgilendirme yapılmıştır.

Tarhan ve ark.'ın transrektal prostat biyopsisi öncesi video tabanlı bilgilendirme yaptığı bir çalışmada, video bilgilendirme yapılan grupta STAI-durumluk puanlarında anlamlı olarak azalma meydana geldiği bildirilmiştir (7). Yang ve ark'ın flexible üreteroskopik litotripsi yapılan hastaların anksiyeteyi değerlendirdiği bir çalışmada, operasyon sırasında hekim hasta iletişiminin gerçek zamanlı video ile birleştirilmesinin kaygıyı anlamlı derecede azalttığı gösterilmiştir (21). Yapılan başka bir çalışmada ise sistoskopi sırasında hastalara gerçek zamanlı olarak operasyon videosu izletilmiş ve video izleyen erkek hastalarda ağrı algısında anlamlı bir azalma saptanmamıştır (22).

Kadınlarda kolposkopi öncesi video eğitimin sonuçlarını değerlendiren randomize kontrollü bir çalışmada, video bilgilendirmenin postoperatif ağrı durumu üzerinde anlamlı bir değişiklik yaratmadığı belirtilmiştir (23). Bizim çalışmamızda, VAS skorunun görsel bilgilendirme yapılan grupta anlamlı derecede düşük olduğu ve video bilgilendirmenin postoperatif ağrı üzerinde olumlu etkileri olduğu sonucuna ulaştık. Ayrıca hastaların gerekirse tekrar aynı tedaviyi görmek isteyip istemediklerini de araştırdık; video ile bilgilendirilen hastalar daha istekliydi.

Sanal gerçeklik; teknolojinin gelişmesi ile birlikte, hastanın kaygısını ve ağrısını azaltmak için sağlık alanında kullanılan yeni bir yöntemdir. Bu yöntemde ara yüzler kullanılarak, sanal video ile kişi arasında etkileşim oluşturulmaktadır. Hasta kendini sanal gerçeklik ortamın içerisinde hissetmekte ve dikkatini gördüğü çevreye aktarmaktadır. Algısı bu ortama yönelen kişinin ağrısının azaltılması hedeflenmektedir (24,25). Cerrahi girişimler sırasında sanal gerçeklik ve görsel dikkat dağıtma yöntemi kullanılan çalışmalarda; hastaların ağrı ve kaygı düzeylerinde azalma olduğu izlenmiştir (26-28).

Tekrar aynı tedaviyi görme isteğini değerlendiren isteklilik skoru ile ağrı ve anksiyeteyi değerlendiren VAS ve APAIS skorları arasında negatif ve anlamlı bir korelasyon saptadık. Preoperatif kaygı düzeyi düşük olan ve daha az ağrı hisseden hastaların, tekrar aynı işlemi yaptırmaya istekliliklerinin yüksek olması tespit ettiğimiz ve beklediğimiz bir durumdur.

Çalışmamızın kısıtlılıkları; düşük hasta sayısı, hastanın günlük yaşantısındaki olayların da operasyon anksiyetesi ve istekliliğini etkileyebilmesi ve hastaların ağrıya verdiği tepkinin kişiye özgü olmasından dolayı tam olarak objektif bir değerlendirme yapılamamasıdır. Çalışmamızın güçlü yanları ise; homojen bir hasta grubunda çalışılmış olması, hastalara sözel ve görsel bilgilendirmenin aynı hekim tarafından yapılmış olması, tüm hastalara aynı lokal anestezinin uygulanması ve elde edilen tüm verilerin korelasyonunun incelenmesidir.

Lokal sistoskopi günübirlik şartlarda ve anestezi gerektirmeden yapılan bir işlem olsa da hasta için tüm cerrahi girişimler gibi kaygı ve stresi beraberinde getirmektedir. İşlem öncesinde görselliğe dayalı ve çok daha anlaşılır olan video bilgilendirme uygulamaları, geleneksel yöntemler olan sözlü ve yazılı bilgilendirmeye kıyasla çok daha anlaşılır ve açıklayıcı olabilir.

Sonuç olarak operasyon öncesi video bilgilendirme hastanın operasyon öncesi kaygısını önemli ölçüde azaltmaktadır. Bunun yanı sıra postoperatif ağrı ve operasyon için isteklilik durumları üzerinde de olumlu etkileri olmaktadır. Uygulamasının hem kolay hem de oldukça etkili olan video bilgilendirme yöntemleri operasyon öncesinde yaygın olarak kullanılabilir ve hasta uyumunu artırabilir.

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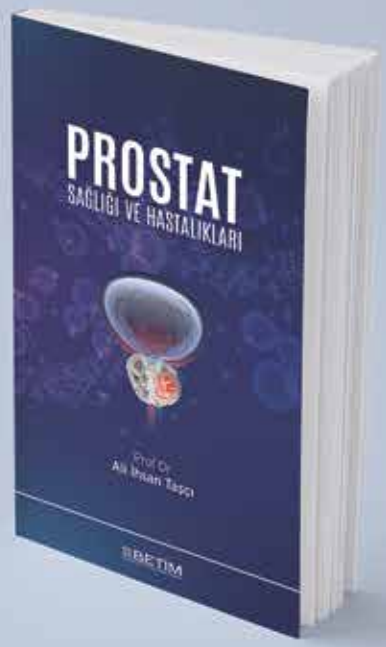

PROSTAT
SAĞLIĞI VE HASTALIKLARI

Prof Dr
Ali İhsan Taşçı

Bazen gençlerde, daha sıklıkla da yaşlanma ile birlikte, erkeklerin birçoğunda prostat ve idrar yolları ile ilgili hastalıklar görülebilmektedir. Prostat konusunda doğru bilgiye ulaşmak isteyenler için hazırlanmış bu kitapta; prostatın yapısı, fonksiyonları, hastalıkları, hastalıklardan korunma, alternatif ve tamamlayıcı tıp uygulamaları sade bir dille anlatılmaya çalışılmıştır.

BETİM KİTAPLIĞI

Automatic stroke classification: Domain knowledge injection augmented transfer learning approach

Otomatik inme sınıflaması: İmkansız piksellerin eliminasyonuyla etkinleştirilmiş transfer öğrenme yaklaşımı

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Abstract

Aim: To build an artificial intelligence model to classify stroke into ischemic or hemorrhagic classes using the labeled stroke computer tomography (CT) slices that were shared in the 2021 Teknofest artificial intelligence in health competition.

Methods: We developed a set of methods that can inject domain knowledge into the models to provide a more refined search space for the model for better performance. We used pre-trained MobileNet and EfficientNet architectures and fine-tuned them for our 2-class output model. We discarded impossible pixel values and pixel spatial locations to provide a space that was conditioned into only possible spatial locations and signal values using our knowledge of brain anatomy, stroke pathology, and imaging.

Results: With the dataset which we just used [0-1] normalization and adjusted the input dimension into 224*224, accuracy values of 0.74 with adapted MobileNetV2 and 0.72 with adapted EfficentNetB0 were obtained in the group without further pre-processing. In the data transformation group where bone structures were removed and pixel values were restricted by eliminating impossible values, an accuracy level of 0.91 with MobileNetV2 and 0.88 with EfficientNetB0 at test time were achieved.

Conclusion: In conclusion, CT-based slice prediction of mechanism of stroke as ischemic or hemorrhagic was achieved with high accuracy by integrating human knowledge into the pre-trained off-the-shelf models which was promising to shorten the time of the triage of stroke patients which can potentially improve stroke patient outcomes.

Keywords: Artificial intelligence; stroke; machine learning; deep learning

Öz

Amaç: Derin öğrenme yöntemleri ve özellikle evrişimsel sinir ağları (CNN) tıbbi görüntü sınıflamasında otomatizasyon açısından geliştirilen uygulamalarda altın standart niteliğindedir. İnme görüntülemesinde zaman oldukça kritik olup hızlı müdahale ile morbidite ve mortalite azaltılabilmektedir. Bu çalışmada amacımız hızlı inme triajı ve uygun tedavi seçimi sağlayacak iskemik inme ile hemorajik inmeyi birbirinden ayırt edebilen otomatize yöntem geliştirmektir.

Yöntemler: Teknofest sağlıkta yapay zekâ yarışması tarafından sağlanan kimliksizleştirilmiş ve anonimleştirilmiş 2000 adet iskemik inme, 2000 adet hemorajik inme içeren bilgisayarlı tomografi (BT) kesitleri kullanılarak, MobileNet ve EfficientNet CNN mimarileri transfer öğrenme metodolojisi ile, özel bir imkansız piksel değeri ve uzamsal lokalizasyonları dışlama stratejisi kullanılarak arama uzayı daraltılmış ve otomatik inme sınıflaması sağlanmıştır.

Bulgular: [0-1] normalizasyon ve 224*224' e girişin ayarlanması dışında ön işleme yapılmayan grupta adapte MobileNetV2 ile 0.74 ve adapte EfficentNetB0 ile 0.72 doğruluk değerleri elde edildi. Öte yandan kemik yapıların çıkarıldığı ve piksel değerlerin imkânsız değerler elimine edilerek kısıtlandığı veri dönüşümü uygulanan grupta MobileNetV2 ile 0.91 ve EfficientNetB0 ile 0.88 doğruluk düzeyine ulaşıldı.

Sonuç: Derin öğrenme yöntemleri kullanılarak inme teşhisi, radyoloji uzmanı olmayan inme görüntülemeye aşina olmayan ancak inme triaj ve sağaltımında aktif rol oynayan sağlık personelleri için özellikle yararlı olabilir. Bu şekilde tedaviden fayda görecek hastanın seçimi ve tedavi kararının verilme hızı artırılabilir. Sonuç olarak iskemik-hemorajik inme sınıflandırmada yüksek doğruluk oranlarına ulaşan çalışmamız, otomatik inme tespitine katkı sağlayabilir ve hekimlerin hızlı ve uygun tedavi kararları vermelerine yardımcı olabilir.

Anahtar Sözcükler: Derin öğrenme; inme; makine öğrenimi; yapay zekâ

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INTRODUCTION

Deep learning methods form the basis of artificial intelligence methods in image classification and segmentation problems. AlexNet, VGG16/19, GoogleNet (Inception), and ResNet artificial neural networks achieved higher success than humans on the ImageNet dataset in the International Large Scale Computer Vision (ILSCV) competition (1-5). Medical imaging has also benefitted from these developments and has become an important application area. In this respect, stroke is a very attractive application area, both because it has high mortality and morbidity rates and because it can benefit greatly from automated applications that may help initiate appropriate treatment promptly. Indeed, a significant number of startups developing artificial intelligence applications in radiology have developed stroke-related applications and are trying to improve them further (6). When it comes to stroke treatment, every minute that passes can cause another piece of brain tissue to be irreversibly damaged. Therefore, the first step in deciding on treatment is to understand whether it is an ischemic or hemorrhagic stroke and start thrombolytic therapy early in ischemic lesions. For this purpose, in patients presenting with suspicion of stroke, non-contrast computer tomography (CT) imaging is performed quickly to try to rule out bleeding. (Figure 1)

One of the most important catalysts in the development of artificial intelligence projects in radiology worldwide is the anonymization of large numbers of medical images and making them available for public use through platforms such as Kaggle. The main driving force behind the products that can be developed regarding stroke is the labeled brain hemorrhage data set publicly presented in the 2018 Kaggle competition (7). Radiological Society of North America (RSNA) stroke dataset, CQ500, and University College of London Hospitals (UCLH) stroke datasets are important public datasets in this field (7,8,9).

In order to eliminate this labeled radiological data scarcity in our country, Teknofest, has created a platform where the best strategies for solutions are sought as a project pool with the artificial intelligence competition in health, the first of which was held in 2021. Based on the success of this platform, it was decided to repeat it every year, and in 2022, data was provided for models to classify the causes of acute abdomen, and in 2023, data was provided for cancer and breast density classification in mammograms. Our aim in this study was to develop an artificial intelligence model to classify stroke using the labeled hemorrhagic and ischemic stroke CT slices shared in the 2021 Teknofest artificial intelligence in health competition (10).

MATERIAL AND METHODS

Patients and dataset

The dataset shared by Teknofest contained 2000 ischemia and 2000 hemorrhage slices from different patients and at different anatomic levels (11). After the data embargo period which ended in 2022, the dataset could be freely used by the participitants for academic research. Therefore ethical board approval was not required for this study. The slices included both posterior fossa and supratentorial levels and were randomly distributed both anatomically and etiologically, including intraventricular, subdural, epidural, subarachnoid, intraparenchymal hemorrhage, and embolic, large vessel and border zone infarcts. Since deep learning systems require many data points, it was necessary to develop strategies to overcome data limitations. One of these strategies is to apply a transfer learning strategy. In transfer learning, networks trained using many natural images can be applied to a medical imaging problem. The data set frequently used for this purpose is ImageNet (5). Indeed, ImageNet has played an important catalyst role for developments in this field, both by providing a comparison environment in computer vision applications and by providing labeled data to those who want to develop models containing over 10 million labeled natural images. Thus, teaching the special features of the target domain to the models that have already learned image primitives such as edges, corners, and circles from natural images becomes much easier than teaching all the information from scratch.

Preprocessing

Images were resized into 224x224 for MobileNet and EfficientNet pre-trained networks (12,13). While normal gray matter shows values of 37-41 Hounsfield units (HU) and white matter shows values of 29-33 HU, bleeding can show densities of 30-90 HU, and

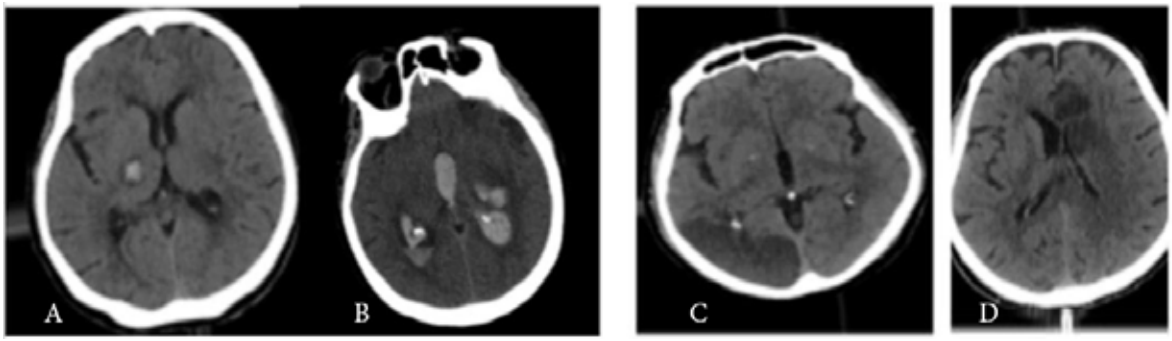

Figure 1: Hemorrhagic and ischemic stroke CT images. The sections are randomly distributed in the posterior fossa and supratentorial intra- and extra-axial hemorrhage and ischemia spectrum and localizations. A) Thalamic parenchymal hemorrhage B) Intraventricular hemorrhage C) Posterior circulation ischemic stroke D) Anterior circulation ischemic stroke

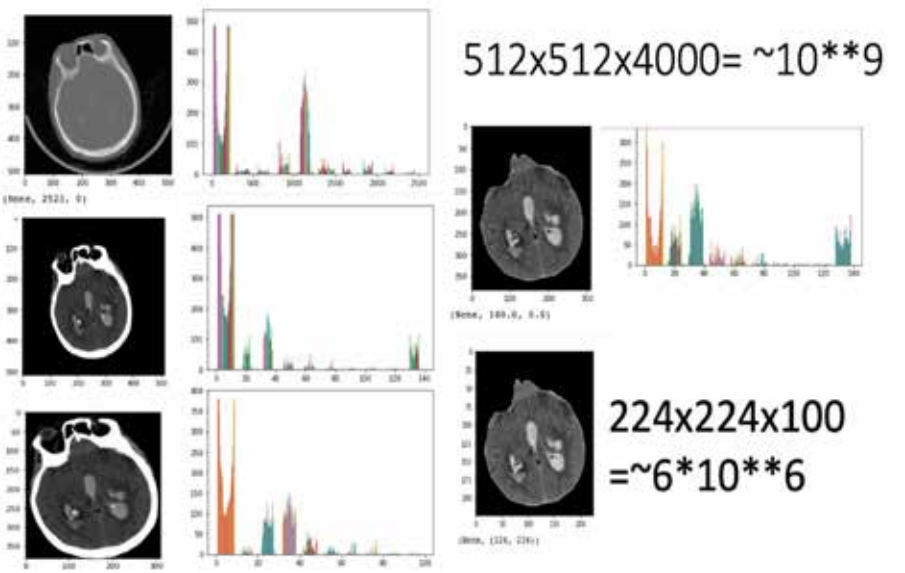

Figure 2: Various structures on CT can mimic bleeding or ischemia with their density features. While those that mimic ischemia with low density are cisterns containing cerebrospinal fluid, ventricles, developmental cysts and sequelae spaces, those that mimic bleeding with high density are bones and calcifications.

ischemia can show densities ranging from 0 HU to 30 HU. Along with bleeding, various conditions such as basal ganglia, epiphysis, falx, and vascular calcifications can be observed as hyperdense on the tomography. (Figure 2)

On the other hand, cerebrospinal fluid, lesions that reflect previous sequela lesions, areas of encephalomalacia, and cystic brain lesions are in the low-density band close to water density. Therefore, while it may not be easy to solve the problem with simple thresholding, eliminating impossible density values and spatial positions from the image can significantly narrow the search space of the model and enable it to reach the global minimum point more easily and quickly. For this reason, the images were subjected to a 5-step preprocessing process. These operations were carried out in the order as follows. The black space around the skull was removed and the remaining image was resized to 224x224. Then, RescaleIntercept and RescaleSlope values were found from the image metadata, and numerical values were converted to HU values according to the equation "Real HU = Pixel value * Slope + Intercept". Thus, HU values that are important for classification are kept limited.

Then, the skull was removed from the image using the Otsu threshold method and morphological op-

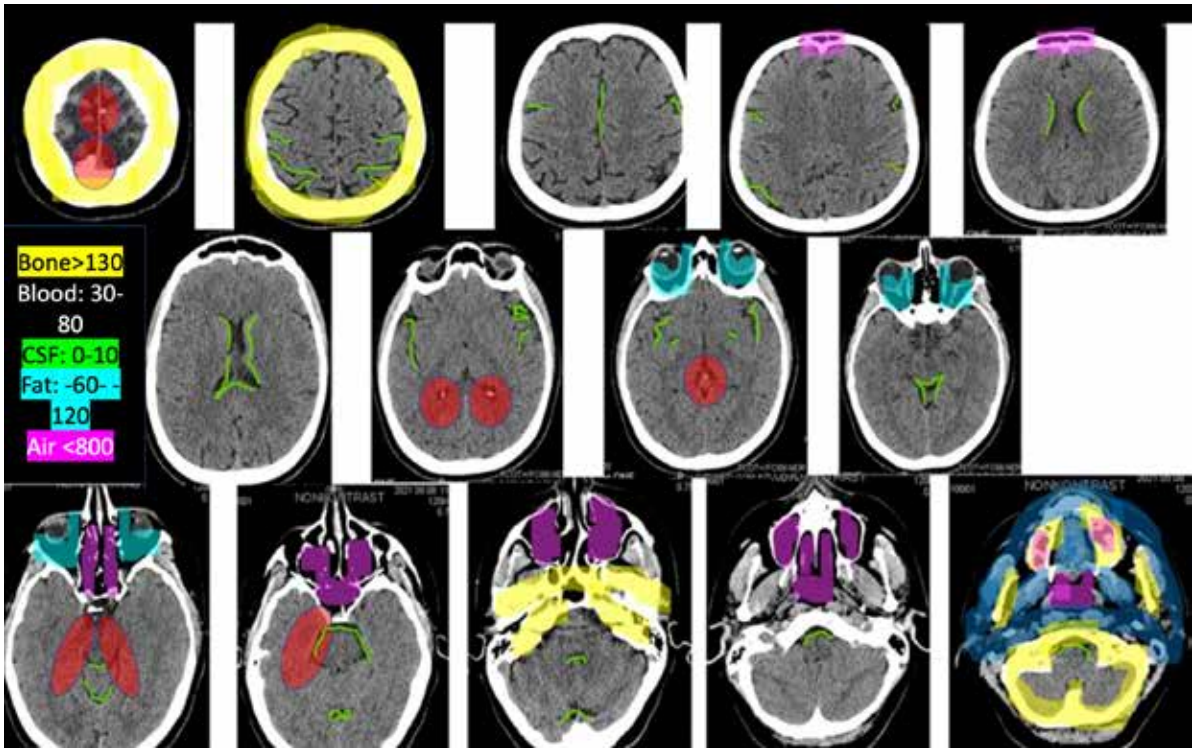

Figure 3: Intracranial field images remaining with diluted information after preprocessing. Histograms can reveal how the search space is diluted by table cleaning, windowing to the appropriate range, discarding the surrounding spaces, discarding the bone, and density normalization, respectively.

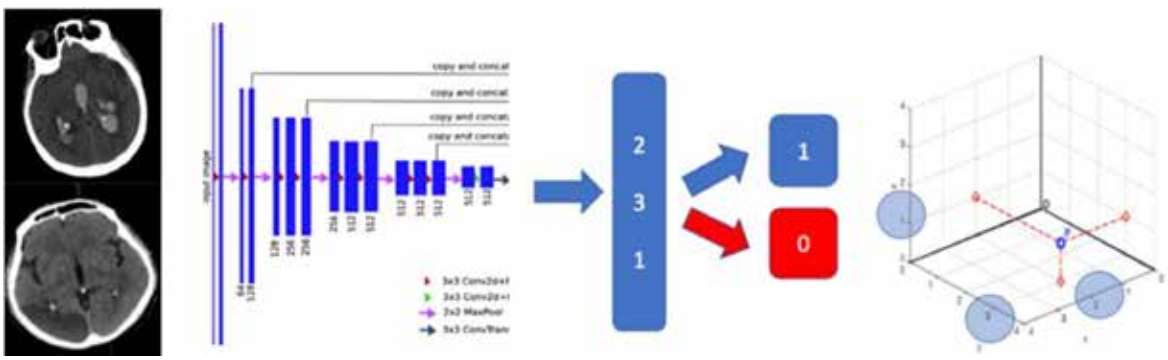

Figure 4: The artificial neural network projects the image to become a point in the feature space. It then searches for the interface separating these points.

erations. Density values were limited to the range of 0-150 with the np.clip function in the numpy library of the standard Python programming language. Finally, normalization was applied, and the pixel values were reduced to the range 0-1. (Figure 3)

In this way, all information in the image that could be noise for the classifier was removed and only the necessary signal was left. This led to a kind of refinement such that, unnecessary pixel localizations and values, which constitute more than 90% of the image, were eliminated and the model was enabled to converge more easily.

In classification with artificial neural networks, the image and the features obtained from the image are compressed, unnecessary ones are eliminated, and each example is reflected in the feature space. Thus,

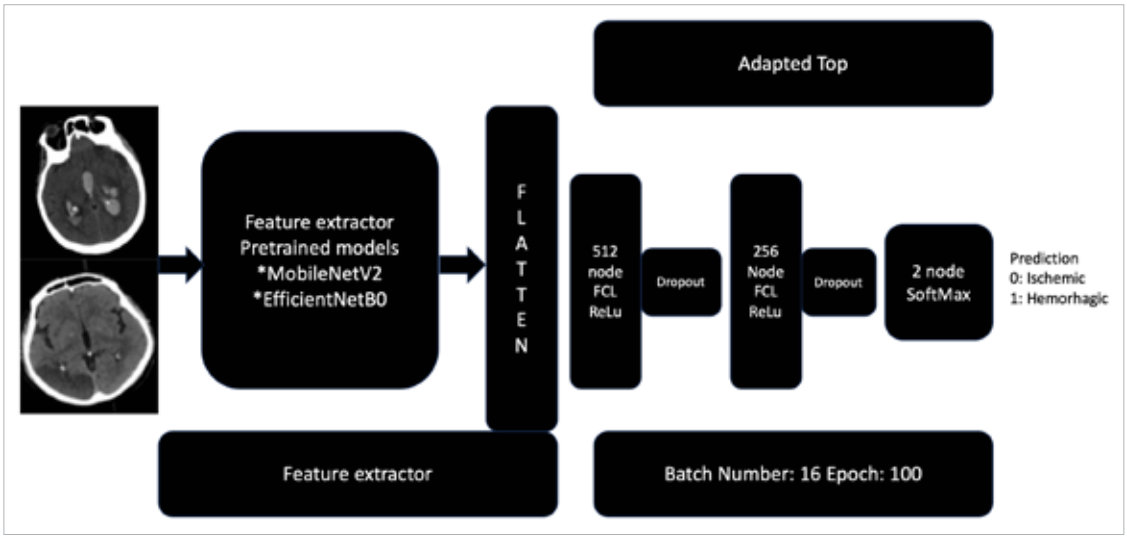

Figure 5: MobilenetV2 and EfficientNetB0, initialized with pre-trained weights and adapted to our problem, were used as classifiers.

each image becomes a point in a feature space whose number of coordinates is equal to the number of features. The purpose of the classifier is to determine the boundary hyperplane that correctly separates the points in different classes (Figure 4).

In cases where access to the required number of data is limited, such as medical image classification, additional strategies are required to reach the necessary number of samples. Data augmentation can be used for this purpose. In the dictionary used for augmentation purposes in our experiments, parameters such as {rotation:10 degrees, random_magnification= 0.1, random_horizontal_shift = 0.2, random_vertical_ shift = 0.1, horizontal_mirror_view = Yes} were used. Thus, it has become possible to obtain a much larger number of images by producing various versions of an image that are slightly rotated, shifted, or enlarged. 150 slices from the hemorrhagic and 150 slices from the ischemic classes were reserved for validation and the remaining 3700 slices were used for training. Additionally, 150 ischemia and 150 hemorrhage sections provided in the final stage of the competition were used as an independent test set.

Model building

The spread of cloud-based services, the development of automatic machine learning methods, the design of easier-to-use libraries, and easier access to data have paved the way for artificial intelligence studies and brought spring again after a long artificial intelligence winter period. On the other hand, Sigmoid and Tanh activation functions, previously used in intermediate layers, were causing gradient vanishing in deep networks. However, this problem has been largely solved with rectified linear units (ReLU) and similar activation functions. The use of residual units implemented with the ResNet architecture has also enabled the gradient not to vanish and to be propagated back more easily. In ResNet, residual blocks are connected with skip connections. This allows the compressed information to be copied and move more smoothly between layers (4). The cost of this is that the number of parameters increases greatly. Solving this problem is an active area for artificial intelligence studies. For this purpose, Mobilenet V2 architecture has been developed in recent years. This architecture, built on inverted bottleneck units, makes it possible to achieve similar performance without increasing the number of parameters too much. It is possible to think of inverted bottleneck units as ResNet blocks in reverse order. In this architecture, channels are first expanded, then compressed, and their number is reduced to establish skip connections between them. Thus, higher efficiency can be achieved with fewer parameters (12). The next development in this regard was the addition of scaling on all three channels to the inverted bottlenecks. Thus, the EfficientNet family was born (13). MobilenetV2 and EfficientNet are modern convolutional artificial neural

Table 1: Performance metrics of the models

Models		Validation Accuracy	Testing Accuracy	Testing ROC_AUC
Without Domain Knowledge	MobileNetV2	0.78	0.74	0.86
	EfficientNetB0	0.77	0.72	0.85
With Domain Knowledge	MobileNetV2	0.93	0.91	0.94
	EfficientNetB0	0.90	0.88	0.92

networks that can perform effective image classification with a smaller number of parameters.

In our study, we took the pre-trained versions of the MobileNetV2 and EfficientNetB0 models and applied additional training in the form of fine-tuning with the data set we had. For this purpose, we separated the feature extractor part of these models from the classifier part, vectorized the resulting feature maps, and added a 2-layer fully connected layer (FCN) containing 512 and 256 nodes. Finally, we connected the final 2-class classifier with the Softmax layer. To prevent overfitting, we added the DropOut operator, which selects nodes with a 30% probability between layers. (Figure 5)

We applied 100 epochs of training by giving 16 image batch sizes that were on the fly synthesized from the data set using the data augmentation techniques.

Statistical analyses

Python scripting language with a scikit-learn package was used for statistical analysis. Tensorflow and Keras libraries with Python were used for model building and analysis.

RESULTS

In the data set that we used in our study, a total of 4300 CT slices, 2150 of which were ischemic (50%: 2150/4300) and 2150 hemorrhagic (50%: 21500/4300) were used. The distribution of both classes was equal. On the other hand, since the patients were deidentified and anonymized, which is a mandatory step to make the data set available to the public, it was not possible to make comparisons about their age and gender distributions. However, considering that this image set was prepared to automatically detect the distinction between ischemic/hemorrhagic stroke and that it was presented as an award-winning competition and hoped to attract the attention of many researchers and find a solution to the problem, we can think that it was prepared balanced between the two groups. With the dataset which we just used [0-1] normalization and adjusted the input dimension into 224*224, accuracy values of 0.74 with adapted MobileNetV2 and 0.72 with adapted EfficentNetB0 in test time and 0.78 and 0.77 in the training set respectively were obtained in the group without preprocessing. On the other hand, in the data transformation group where bone structures were removed and pixel values were restricted by eliminating impossible values, an accuracy level of 0.91 with MobileNetV2 and 0.88 with EfficientNetB0 in test time and 0.93 and 0.90 in the validation set respectively were achieved (Table 1). This approach is an example of injecting domain knowledge into the model by narrowing the search space of the model, and its application to the problem of ischemic/hemorrhagic automatic stroke classification in the literature is the first to our knowledge. It has been a concrete example of the usefulness of domain knowledge in developing more effective models. Because the model can work more effectively by directing its search to the target without wasting time with impossible pixel locations and values.

DISCUSSION AND CONCLUSION

In this study, a model that can automatically classify stroke from anonymous axial CT images containing 2150 ischemic and 2150 hemorrhagic stroke diagnoses was developed. An accuracy value of 0.91 was achieved with MobileNetV2, which was prepared by eliminating impossible pixels and localizations.

Transfer learning approach was used in training the dataset prepared for stroke detection. MobileNetV2 and EfficientNet-B0 CNN architectures, pre-trained with the ImageNet dataset, were used for transfer learning (12,13).

Nazari-Farsani et al. achieved 73% accuracy in stroke detection with a data set consisting of Diffusion weighted imaging (DWI) and ADC images of 192 samples, including 106 strokes and 86 healthy cases (14).

In a study evaluating the success of the CNN model in detecting stroke using a dataset containing non-contrast CT images of ischemic stroke, hemorrhagic stroke, and normal images, an accuracy of 90% was obtained (15). However, only 45 CT images were available in this study. Additionally, for the test set, each class consisted of only 5 images. For these reasons, it can be said that the research findings are far from being generalizable.

Pereira et al. achieved the most successful results in stroke detection with CNN and non-contrast CT. These researchers evaluated the accuracy of the CNN model they developed on a cross-sectional basis using a data set of 300 slices (100 ischemic stroke, 100 hemorrhagic stroke, 100 normal) and obtained approximately 99% accuracy (16). In this study, which used the methodology closest to ours, a cross-section-based classification approach was used, and the small number of cross-sections used makes it difficult to generalize the results. Indeed, while 4300 slices were used for 2 classes in our study, 300 slices were used for 3 classes in this study. Considering that as the number of classes increases, the number of samples to be used must also increase, it is more reasonable to think that the 99% value reflects overfitting. To reduce overfitting, the authors did not mention an additional strategy. In our study, the measures taken to prevent overfitting were the greater number of samples, the application of data augmentation methods, and the use of a more homogeneous data set by purifying the signal from noise and feeding it to the model. Indeed, in the models we developed without taking precautions to adapt the signal into the desired range, the accuracy we achieved remained at 0.74, similar to Nazarani et al., even though the number of data we used was much higher. With the added methodology of narrowing the search space of the model using domain knowledge, the accuracy reached 0.91.

China et al. reached over 90% accuracy for ischemic stroke detection on non-contrast CT and Marbun et al. reached 90% classification accuracy for multi-class stroke prediction. (17,18)

In a study using GoogleNet to detect hemorrhagic stroke in the basal ganglia, 80% specificity, area under the curve (AUC=1) and 100% sensitivity were obtained (19). Arabbhsian et al. achieved 80% specificity, 73% sensitivity and AUC = 0.846 in their model for the triage of head CT scans for the detection of intracranial hemorrhage. With this model, the pathology detection time was reduced from 512 to 19 minutes (20).

In the study using the largest cohort for stroke detection, Oman and colleagues addressed the problem of middle cerebral artery (MCA) stroke detection using computed tomographic angiography (CTA) source images. Takahashi and colleagues used support vector machines (SVM) to identify the dot sign on noncontrast CT as a candidate for thromboembolism. They reached 93% and 82% accuracy, respectively (21,22). These studies also addressed the automatic classification of the stroke problem, and although the data sets and methodology they used were quite different from our study, they were able to obtain similar or less accurate values.

The limitations of our study were that due to its preprocessed data set and retrospective nature, the effect of patient demographics on the results cannot be evaluated optimally. However, it is a desirable feature for automatic classifiers to be able to make correct decisions regardless of demographics and acquisition conditions. Another important limitation was that slice-wise classification was employed due to the characteristics of the data set we have, and therefore there were limitations in generalizing the results obtained to the patient level.

Today, thrombolysis in the early stages and in appropriate patients is the gold standard in stroke treatment, and pre-hospital thrombolysis is on the agenda, which increases the importance of automatic stroke diagnosis (23). Stroke diagnosis using deep learning methods may be particularly useful for healthcare personnel who are not radiologists and are not familiar with stroke imaging but play an active role in stroke diagnosis and treatment. In this way, the selection of the patient who will benefit from the treatment and the speed of treatment decision making can be increased. In conclusion, this study, which achieved high accuracy rates in ischemic-hemorrhagic stroke classification, may contribute to automatic stroke detection and

help physicians make rapid and appropriate treatment decisions.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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Does occupational self-competence perception relate to functional outcomes after total knee arthroplasty?

Total diz artroplastisi sonrası aktivite öz yeterlik algısının fonksiyonel sonuçlarla ilişkisi var mı?

Abstract

Aim: The study investigates the effect of occupational self-perception level on the functional status in the early period after total knee arthroplasty (TKA).

Methods: Occupational Self Assessment (OSA), Canadian Occupational Performance Measure (COPM), Knee Injury and Osteoarthritis Outcome Score (KOOS), and Timed Up and Go Test (TUG) tests were administered before and at the 3rd and 6th week after surgery. Changes in COPM, KOOS, and TUG tests were analyzed using Friedman test. The relationship of OSA was examined using the Pearson correlation test.

Results: Self-perception score was statistically in relation to TUG (r =- 0.600; p = 0.001). It was not significantly related with other assessment scores (p>0.05).

Conclusion: Occupational self-competence perception of individuals affect their actual performance levels therefore; high occupational self-perception level may affect the recovery positively.

Keywords: Activities of daily living; recovery of function; total knee replacement

Öz

Amaç: Bu çalışma total diz artroplastisi (TDA) sonrası erken dönemde aktivite öz yeterlilik algısı düzeyinin fonksiyonel duruma etkisini araştırmaktadır.

Yöntemler: Aktivite Öz Değerlendirme ölçeği (AÖDÖ), Kanada Aktivite Performans Ölçeği (KAPÖ), Diz Yaralanması ve Osteoartrit Sonuç Skoru (KOOS), Zamanlı Kalk ve Yürü Testi (TUG) testleri ameliyat öncesi ve ameliyat sonrası 3. ve 6. haftalarda uygulandı. KAPÖ, KOOS, TUG testlerindeki değişimler Friedman testi kullanılarak analiz edildi. OSA ilişkisi Pearson korelasyon testi kullanılarak incelendi.

Bulgular: OSA puanı TUG ile istatistiksel olarak ilişkiliydi (r =- 0.600; p = 0.001). Diğer değerlendirme puanları ile anlamlı bir ilişki yoktu (p>0.05).

Sonuç: Bireylerin aktiviteler hakkında öz yeterlilik algıları, onların fonksiyonel performans düzeylerini etkilemektedir dolayısıyla; yüksek öz yeterlilik algısı iyileşmeyi olumlu yönde etkileyebilir.

Anahtar Sözcükler: Fonksiyonun geri kazanılması; günlük yaşam aktiviteleri; total diz replasmanı

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INTRODUCTION

Total knee arthroplasty (TKA) is a widely employed surgical procedure aimed at alleviating pain resulting from severe joint damage, particularly in cases of osteoarthritis, and enhancing both functionality and overall quality of life (1, 2). The demand for this surgery has been observed to be on the rise (3). Patients typically experience a reduction in pain-related symptoms within the initial four weeks, allowing for an accelerated return to daily activities six weeks post-surgery, contributing to functional recovery (4, 5). Studies indicate sustained, positive changes in terms of pain relief, functional recovery, and increased independence in daily life activities in the long-term following the surgery (6, 7).

The primary outcome following any treatment is functionality. Numerous factors that affect long-term functional post-surgery outcomes are discussed in the literature. These include significant systemic issues and obesity, cardiovascular diseases, and physical/surgical/biomechanical factors such as motor loss due to peroneal nerve damage, compromised knee joint biomechanics, and the occurrence of infection, all of which have been demonstrated to adversely impact the functional recovery process in TKA (8-11). Additionally, a few studies have noted that participants' beliefs about recovery may also influence functional outcomes (12, 13).

According to Geiger, individuals with high self-perception tend to recover more swiftly after surgery and resume routine activities more effortlessly. Conversely, there is a call for research to investigate the impact of participants' personal factors, such as self-efficacy, self-perception, and their health perspective, on the recovery process (13, 14). The influence of participants' self-perception regarding occupations, motivations for engaging in activities, and the values they ascribe to these activities on functional outcomes following TKA remains unclear. It is believed that individuals' personal beliefs and expectations about themselves before surgery may affect early recovery and functional status.

This study aimed to assess functional recovery and occupational participation levels during the early recovery period and establish a connection between occupational self-perception and early functional outcomes after TKA.

MATERIAL AND METHODS

Study protocol

Hacettepe University Non-Interventional Clinical Research Ethics Committee approved this study (date: 04.09.2018, decision no: GO 18/671-02). The purpose and procedures of the study were explained to the participants and written informed consent forms were obtained for participation in the study.

Participants

Research data were collected in the orthopedics service of Düzce Atatürk State Hospital. Research invitations were distributed to individuals who were scheduled for surgery and came to visit the orthopedic clinic. The research procedure was explained in detail to individuals interested in participating in the study and their contact information was obtained.

Power analysis was performed to determine the number of participants. Individuals who met the inclusion criteria were included in the study. Inclusion criteria were to undergo total knee arthroplasty surgery, to be over 45 years old, and to be literate. Exclusion criteria were not having any communication problems (n = 2), not having obesity (n = 4), not developing post-surgical infection (n = 2), and not having a history of falling after surgery (n = 1). The study was completed with the participation of forty-three individuals.

Study design

Individuals who volunteered to participate in the study were interviewed and evaluated in the orthopedic service on the day before surgery. Evaluations took approximately one hour, and written consent was obtained from the participants. Individuals were called and invited to the hospital for evaluations in the third and sixth weeks after surgery, and the evaluations were repeated.

Outcome measures

Participants' demographic details were collected. This included inquiries about age, gender, height, weight, presence of chronic diseases, educational and occupational status, surgical history, experience of falls, and the duration of employment. Additionally, the Body Mass Index of participants was computed to identify the presence of obesity. Occupational Self-Assessment

(OSA), a Likert-type scale, was used to evaluate individuals' occupational self-competence perceptions. This scale consists of 21 items and is scored between 0-100 points (15, 16). Patient-reported Canadian Occupational Performance Measure (COPM), Knee Injury and Osteoarthritis Outcome Score (KOOS) and performance-reported Timed Up and Go Test (TUG) were used to evaluate functional expectations and changes. COPM determines occupational preferences and priorities; It evaluates perceived occupational performance and satisfaction while performing occupation. It is used as both goal setting and outcome measure in clinical education (17). Within the scope of this evaluation, a semi-structured interview identifies and lists the problems the participants encounter in the field of occupational performance (18). The Knee Injury and Osteoarthritis Outcome Score (KOOS) comprises five distinct subscales: pain, daily living, sports and recreational activities, symptoms, and quality of life related to the knee. Each subscale is evaluated independently, and the score for each ranges from 0 to 100. A score of 100 implies the absence of symptoms, while 0 points indicate the presence of severe symptoms (19, 20). In the TUG test, individuals are asked to stand up, walk 3 m with the assistive device, turn around, and return to the chair as quickly as possible. The time required to perform the action is timed using a stopwatch. Patients complete two trials and the average time it takes to complete the test in the hospital room is recorded in seconds (21).

Statistical analysis

The study's recorded data underwent statistical analysis using the Statistical Package for the Social Sciences package program version 24.0 (SPSS Inc., Chicago, IL, USA). Sociodemographic details of the participants were documented. The normal distribution of variables was assessed through visual methods (such as histograms and probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test). Mean and standard deviation values were used for numerical variables in participants' demographic information, while ratio values and frequency tables were employed for categorical variables. To assess the participants' level of improvement, scores for symptoms, pain, function, daily life, sports and leisure activities, and knee-related quality of life in the KOOS test were examined. This included analyzing changes in COPM performance and satisfaction scores over time, as well as changes in TUG scores over time, using the Friedman test. Subsequently, Pearson correlation tests were utilized to evaluate the associations between OSA, COPM, KOOS, and TUG scores.

RESULTS

Forty-three participants with an average age of 62.4±4.33 years were included in the study. Demographic data of the participants are summarized in Table 1.

In the COPM evaluation, problems were noted in functional mobility (12.5%), productivity activities (see Fig 1), and spiritual activities (32.5%) among daily living activities. More than 80% of the participants stated that they work for more than 12 hours a day in jobs that require physical strength. The average daily time that participants spent in income generating activities were 8.64 ± 3.81 hours. The basic productivity activities of participants were shown in Figure 1.

There was a significant difference between the functional skills of the participants in the six-week postoperative period ($p<0.05$). The increase in performance and satisfaction levels of the activities in COPM was statistically significant ($p <0.05$). An increase was found in both the activity performance and satisfaction levels of the participants. However, the change in performance and satisfaction levels between assessments was not clinically significant (less than 2 points change). According to the KOOS test, a reduction in symptoms, pain, ADL, sports, and recreational activities was detected in the six-week period ($p <0.05$); there was no significant change in knee-related quality of life ($p> 0.05$). The change found in the TUG test was statistically significant ($p <0.05$). The functional recovery findings of the participants are summarized in Table 2.

The OSA- Competence score was significantly correlated with TUG results ($r =-0.600$; $p = 0.001$). On the other hand, it was not in relation with other assessment scores significantly ($p>0.05$). The COPM satisfaction variable was found to be significant in terms of occupational self-perception level ($p<0.05$). Individuals with high perception levels also had high levels of satisfaction Table 3.

Table 1. Demographic characteristics of the participants.

	Descriptive	n (%)
Gender	*Female*	37 (86%)
	Male	6 (14%)
Total knee prosthesis	*Right*	20 (46.5%)
	Left	14 (32.5%)
	Bilateral	9 (%21)
Education level	*lliterate*	18 (41.8%)
	Primary school	23 (53.4%)
	Collage	2 (4.6%)
Different surgical history	*Yes*	36(83.7%)
	No	7(16.3%)

n: number, %: percentage

Table 2. The functional recovery findings of the participants.

Outcome	Time	Mean±SD	p		p'
COPM Performance	1	2.75±0.13	0.0001	1-2	0.013*
	2	3.37±0.13		1-3	0.001**
	3	4.02±0.15		2-3	0.013*
KOOS Symptoms	1	38.97±18.36	0.001	1-2	0.22
	2	47.31±15.60		1-3	0.10
	3	53.84±14.36		2-3	0.001**
KOOS Pain	1	22.97±20.50	0.0001	1-2	0.03*
	2	33.54±18.48		1-3	0.0001**
	3	42.81±15.90		2-3	0.0001**
KOOS ADL	1	30.61±19.73	0.0001	1-2	0.02*
	2	38.06±18.49		1-3	0.002**
	3	44.86±16.72		2-3	0.001**
KOOS Sport and Rec	1	4.50±10.60	0.0001	1-2	0.86
	2	8.50±10.20		1-3	0.48
	3	11.61±10.73		2-3	0.04
TUG Test	1	43.91±18.62	0.002	1-2	0.001
	2	37.35±9.80		1-3	0.001
	3	30.11±7.69		2-3	0.001

1: Preoperative evaluation. 2: Postoperative 3rd week. 3: Postoperative week 6; * p <0.05 ** p <0.001; p': corrected p value for Bonferonni correction

ADL: Activities of daily living; COPM:Canadian Occupational Performance Measure; KOOS: Knee Injury and Osteoarthritis Outcome Score; TUG: Timed Up and Go Test; OOL; Quality of Life; Rec: Recovery; SD: Standard deviation, n: Number, %: Percentage

DISCUSSION AND CONCLUSION

This study revealed that occupational self-perception is related to functional performance in the early period after TKA. However, individual's statements about functional recovery (patient-reported evaluations) were not related to the level of self-perception. In addition, while knee-related results progressed positively in the early postoperative period, the changes in the level of quality of life were not significant. This study also stated an activity profile of the patients as a secondary result, which may give valuable information for planning measures. Most patients treated for knee osteoarthritis with total knee replacement have shown high rates of perfection and good early functional results(22). When evaluating functional results

Table 3. The Relationships between occupational self perception and functional outcomes

Pearson correlation test	***OSA occupational competence***		***OSA occupational value***	
	r	**p**	**r**	**p**
COPM performance	0.233	0.062	0.049	0.766
COPM satisfaction	0.782	0.001	0.653	0.002
TUG test	-0.600	0.001	-0.770	0.001
KOOS symptoms	-0.036	0.826	-0.095	0.526
KOOS pain	-0.179	0.695	-0.041	0.801
KOOS ADL	-0.021	0.896	-0.017	0.915
KOOS sport and recreation	-0.160	0.924	-0.228	0.158

ADL: Activities of Daily Living, COPM: Canadian Occupational Performance Measure, KOOS: Knee Injury and Osteoarthritis Outcome Score, OSA: Occupational Self Assessment, TUG: Timed Up and Go Test; QOL; Quality of Life, p<0.05; r: Correlation coefficent

in individuals with TKA, objective outcome measurements and patient-reported outcome measurements (PROMs) are encountered (23, 24). Physical assessments such as TUG generally provide good results. The Timed Up and Go test is a recommended assessment of functionality, balance, and walking ability for people with knee osteoarthritis and is one of the most commonly used performance-based outcome measures for TKA (21, 25), performance-based measures such as TUG provide a more objective response than patient-reported outcome measures in the acute phase after TKA (23). Therefore, it is thought that measures such as TUG may help to identify patients early who may need additional rehabilitation to reduce the potential for poor outcomes after surgery. In this study, positive changes were also found in both perceived and performance-based functional results of individuals in the early period after TKA. However, surprisingly it was determined that there was no improvement in the quality of life levels of the participants in the early period. Quality of life is not only bound with physical measures, it is a biophysicososocail measure that reflects motive, social status, psychology, etc (26).

Although many studies have stated that the quality of life of individuals increased after TKA (27-29). Canovas and Dagneaux that there was no change in the quality of life of approximately 30 percent of patients (30). As our study revealed similar results with Canovas and Dagneaux we offer individual factors, and unrealistic occupational goals desired to be achieved in the early period may have caused the individuals' quality of life to not increase at the expected level. Studies may focus on the factors related to quality of life.

Factors such as personal and cultural influences that affect results after TKA are still not sufficiently clear (31). In joint replacement, depressed mood was consistently associated with less improvement in osteoarthritis symptoms following surgery, while greater self-efficacy was variably associated with better (32). Self-perception holds many cultural, personal factors. However, the effects of personal characteristics such as pre-surgical self-perception and self-efficacy are not yet clear in the literature(33, 34). A significant result of this study is that occupational self-competence perception of individuals affects actual performance levels, but not perceived performance levels. This study revealed a relationship between occupational self-perception level and objective evaluation of walking performances. In other words, the changes in the functional performance of the individuals during the surgical process are affected by the individuals' activity identities and the sense of self-efficacy about the activities. High occupational self-perception levels affected the recovery positively.

Rossi stated that individuals' functional improvement expectations, i.e. perceived activity performance and actual performance levels, differ after TKA (24). Therefore, while examining the recovery, expectations of the individuals and their functionality should be examined separately. Studies have shown that surgical expectations are multidimensional and affected by patient characteristics and clinical features. Also, preoperative patient expectations may affect functional outcomes. Therefore, a more comprehensive understanding of pa-

tients' surgical outcome expectations is required (35). In this study, it can be stated that the functional expectations of the patients before the surgery were not fully met after the surgery. It can be said that this situation stems from the unrealistic expectations of the patients or their low self-efficacy perceptions.

This study showed that KOOS and COPM performance scores were not correlated with the OSA score but in the meantime, the COPM satisfaction variable was found to be significant in terms of occupational self-perception. And the change in participants' performance levels in COPM was not clinically significant. Individuals with high perception levels also had high levels of satisfaction. Participants' low perception levels about surgical processes and activities led individuals to set unrealistic recovery goals and eventually reached a level of professional engagement below expectations. Living in rural areas, a low education level and sociocultural level may cause individuals to have a lower perception of occupations. This may also affect the expected relation of OSA with COPM results. The universe in which a person lives, person's social and cultural environment, life roles, opportunities and resources has in accessing occupations can change his view of the occupation (36). Patient expectations are sometimes unrealistic. Individuals may have expectations such as having a new knee joint with surgery and thinking of returning to their old functions. These expectations vary mostly in relation to the cultural dimension of the activity.

In a study conducted with individuals with TKA in Scotland, when the activities individuals want to do after surgery were questioned; expectations rose, such as playing golf or gardening (37). In this study, individuals had expectations of gaining independence in religious activities such as praying. This results shows us that people have a pain-free life expectancy for different activities, and analysis of the activities performed and expected can also be a factor in deciding which surgeries will be performed. Cultural influence should not be forgotten either.

This study examined the recovery process in the early period after TKA from the occupational perspective and the perception of people. In this study, occupational self- perception levels of the participants in the early period after TKA surgery were shown to affect their walking performance. However, occupational self-perception level had no effect on patient-reported functional improvement outcomes. Also, it was seen that the individuals could not reach the level of functional independence and quality of life they wanted to achieve in the early period. Therefore; determining realistic occupational goals and holding occupational therapy interviews with individuals before the TKA surgery can positively contribute to the recovery process of the individuals.

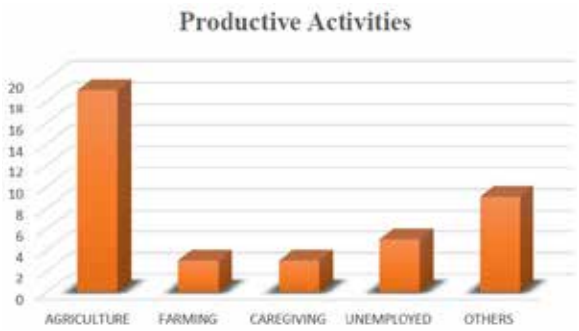

Figure 1. Productivity activities of participants

The study had some limitations. Individuals had difficulty in understanding OSA. Another limitation of our study was the coexistence of individuals who underwent unilateral and bilateral arthroplasty, which heterogenized the group structure.

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Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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Evaluation of falling risk and quality of life in the elderly

Yaşlılarda düşme riski ve yaşam kalitesinin değerlendirilmesi

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Abstract

Aim: The aim of this study is to determine the risk of falling, which is one of the conditions that threaten the health of the elderly, and to evaluate its relationship with quality of life.

Methods: A cross-sectional study was conducted in a province located in the west of Türkiye between September and November 2022. The questionnaire was conducted face-to-face in family health centers after obtaining informed consent from the participants. In this study, a questionnaire including sociodemographic characteristics, features related to falls, the fall risk for the older in the community (FROP-Com) screening scale, and the EQ-5D quality of life scale was used.

Results: The study was completed with 413 participants. The prevalence of falls within the last year in the study group was 21.1%. According to FROP-Com screen; 8.0% of the participants had a low fall risk and 92.0% had a high fall risk. The median EQ-5D index score was 0.7 (minimum=-0.2; maximum=1.0). FROP-Com fall risk was accepted as the dependent variable, the risk of falling; It was found that it increased 2.5 times in those who did not exercise, 5.1 times in those who did have balance problems, and 3.6 times in those who used assistive devices compared to those who did not.

Conclusion: In the Central District of Kütahya, one out of every five people over the age of 65 had a history of falling within the last year. In the study, it is remarkable that there is a relationship between exercise status and the risk of falling. Falls can be prevented or reduced by increasing exercise status.

Keywords: Accidental falls; aged; quality of life

Öz

Amaç: Bu çalışmanın amacı, yaşlıların sağlığını tehdit eden durumlardan biri olan düşme riskini belirlemek ve yaşam kalitesi ile ilişkisini değerlendirmektir.

Yöntemler: Çalışma, Türkiye'nin batısında yer alan bir ilde Eylül-Kasım 2022 tarihleri arasında yürütülen kesitsel bir çalışmadır. Anket, katılımcıların bilgilendirilmiş onamları alındıktan sonra aile sağlığı merkezlerinde yüz yüze uygulandı. Anket formu; sosyodemografik özellikler, düşmeye ilişkin özellikler, toplumdaki yaşlılarda düşme riski (FROP-Com) tarama ölçeği ve EQ-5D yaşam kalitesi ölçeğini içermekte idi.

Bulgular: Araştırma 413 katılımcıyla tamamlandı. Çalışma grubunda son bir yılda düşme görülme sıklığı %21,1 idi. FROP-Com taramasına göre; katılımcıların %8,0'ı yüksek düşme riskine, %92,0'ı düşük düşme riskine sahipti. EQ-5D indeks puan ortancası 0,7 (minimum=-0.2; maksimum=1.0) idi. FROP-Com düşme riski bağımlı değişken olarak kabul edildiğinde, düşme riski; egzersiz yapmayanlarda 2,5 kat, denge sorunu olanlarda 5,1 kat, yardımcı cihaz kullananlarda ise kullanmayanlara göre 3,6 kat arttığı belirlendi.

Sonuç: Kütahya'nın Merkez ilçesinde 65 yaş üstü her beş kişiden birinde son bir yıl içinde düşme öyküsü vardı. Çalışmada, egzersiz durumu ile düşme arasındaki ilişki dikkat çekmektedir. Egzersiz durumunun artırılması ile düşmeler önlenebilecek ya da azaltılabilecektir.

Anahtar Sözcükler: Düşme; yaşam kalitesi; yaşlılık

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INTRODUCTION

Falls are the second leading cause of unintentional injury death worldwide, and they are a major public health concern (1). Adults over the age of 60 have the highest number of fatal falls. Approximately one-third of the elderly worldwide fall, and an estimated 684,000 people die from falls each year, with over 80% of these deaths occurring in low- and middle-income countries (2,3). Declines in fertility and mortality in recent years have increased life expectancy at birth, and the world's elderly population is growing. In 2019, the elderly population will comprise about 1 billion people and is projected to increase to 1.4 billion in 2030 and 2.1 billion in 2050 (4). In Türkiye, it is seen that the population aged 65 and over, which is considered the elderly population, increased from 8.3% (6.5 million people) in 2016 to 9.7% (8.2 million people) in 2021 (5).

The incidence of falls is an important health problem among the elderly due to its physical, psychological, and social consequences, as well as being a preventable problem. Therefore, it is very important to identify the risk factors associated with falls in the elderly and to develop different algorithms to prevent falls, improve quality of life and reduce healthcare costs (6).

Although the causes and risk factors for falls in the elderly differ according to studies, many risk factors for falls have been defined. Environmental factors (loose carpets, slippery bathtubs, poor lighting, unsafe stairs, unsuitable shoes), medications (antidepressants, sedatives, and hypnotics), medical conditions and changes associated with aging (poor vision, cognitive impairment), nutrition (calcium, which can be classified into five categories as vitamin D deficiency), and exercise deficiency are all factors that contribute to falls (7). As the number of these risk factors increases, so does the risk of falling (6). As well as physical injury, the psychological consequences, such as the fear associated with falling, can be equally harmful to the individual in the long term. It can lead to the need for care, loss of self-confidence, limitation of daily activities, isolation from society, and loss of independence, all of which have a significant impact on a person's quality of life (8).

According to the World Health Organization (WHO), the main goal of health care, in addition to increasing life expectancy, is to "add life to years", recognizing the importance of high quality of life for people (8). The fact that the elderly spend their years with the least health problems, with preventive measures, with activities that increase their physical and cognitive capacity, and with a positive outlook on life is defined as healthy aging. "Healthy elderly" are defined as those who, on average, have little or no functional decline for their age group (9). There are variations and different classifications in the scales used in the assessment of quality of life. The most commonly used scales to evaluate general health status are the Short Form SF-36, EQ-5D, and World Health Organization Quality of Life-Brief Form (WHOQOL-BREF) scales (10).

Old age is a period in which the physical abilities of the individual decrease, the individual's dependence on others increases, and the quality of life is negatively affected. As age progresses, cognitive deterioration increases, and in parallel with this destruction, the daily activities and quality of life of the elderly are negatively affected. The risk and fear of falling are important health problems that cause loss of independence in daily living activities for the elderly and negatively affect their quality of life (11).

The aim of this study is to determine the risk of falling, which is one of the conditions that threaten the health of the elderly, and to evaluate its relationship with quality of life.

MATERIAL AND METHODS

A cross-sectional study was conducted in a province located in the west of Türkiye between September and November 2022. The study population consisted of 38817 people over 65 years of age in the central district of Kütahya. The sample size was calculated as 381 individuals with a confidence level of 95%, a prevalence of 50% (for unknown cases), and a margin of error of 5%. The study was conducted in six randomly selected family health centers (22 of the 84 Family Medicine Units in the central district are located in selected Family Health Centers) in the central district of Kütahya among people over 65 years of age who were registered with the relevant family medicine units (10542

Table 1. Relationship between falling status in the last year and sociodemographic characteristics

	Total (n)	Fall status		Statistical analysis*	Fall risk (FROP-Com)		Statistical analysis*
		None (n(%))	Yes (n(%))	X^2; p	Low risk (n(%))	High risk (n(%))	X^2; p
Gender							
Man	200	162 (81,0)	38 (19,0)	0,995; 0,319	184 (92,0)	16 (8)	0,000; 1,000
Woman	213	164 (77,0)	49 (23,0)		196 (92,1)	17 (7,9)	
Age							
65-74	299	244 (81,6)	55 (18,4)	5,642; 0,060	283 (94,6)	16 (5,3)	17,020; ***<0,001***
75-84	98	72 (73,5)	26 (26,5)		86 (87,8)	12 (12,2)	
85 and over	16	10 (62,5)	6 (37,5)		11 (68,8)	5 (31,2)	
Marital status							
Not married	104	81 (77,9)	23 (22,1)	0,092; 0,761	92 (88,5)	12 (11,5)	1,779; 0,182
Married	309	245 (79,3)	64 (20,7)		288 (93,2)	21 (6,8)	
Education status							
Primary school and less	224	175 (78,1)	49 (21,9)	0,193; 0,660	206 (92,0)	18 (8)	0,000; 1,000
Middle school and above	189	151 (79,9)	38 (20,1)		174 (92,1)	15 (7,9)	
Income status							
Income more than expenses	70	55 (78,6)	15 (21,4)	0,394; 0,821	64 (91,4)	6 (8,6)	0,080; 0,961
Income equal to expenses	272	213 (78,3)	59 (21,7)		251 (92,3)	21 (7,7)	
Income less than expenses	71	58 (81,7)	13 (18,3)		65 (91,5)	6 (8,5)	
Personal daily care							
Can't	21	9 (42,9)	12 (57,1)	17,319; ***<0,001***	13 (61,9)	8 (38,1)	27,275; ***<0,001***
Can	392	317 (80,9)	75 (19,1)		367 (93,6)	25 (6,4)	
Exercise status							
Do not	159	116 (73,0)	43 (27,0)	5,558; ***0,018***	134 (84,3)	25 (15,7)	19,353; ***<0,001***
Do	254	210 (82,7)	44 (17,3)		246 (96,9)	8 (3,1)	
Sleep status							
Irregular	137	96 (70,1)	41 (29,9)	9,682; ***0,002***	118 (86,1)	19 (13,9)	8,476; ***0,004***
Regular	276	230 (83,3)	46 (16,7)		262 (94,9)	14 (5,1)	
Walking problem							
Yes	177	122 (68,9)	55 (31,1)	18,658; ***<0,001***	148 (83,6)	29 (16,4)	27,721; ***<0,001***
No	236	204 (86,4)	32 (13,6)		232 (98,3)	4 (1,7)	
Balance problem							
Yes	123	79 (64,2)	44 (35,8)	22,786; ***<0,001***	97 (78,9)	26 (21,1)	38,681; ***<0,001***
No	290	247 (85,2)	43 (14,8)		283 (97,6)	7 (2,4)	
Use of assistive devices							
None	251	218 (86,9)	33 (13,1)	24,127; ***<0,001***	245 (97,6)	6 (2,4)	25,387; ***<0,001***
Yes	162	108 (66,7)	54 (33,3)		135 (83,3)	27 (16,7)	
Fall risk (FROP-Com)							
Low risk	380	324 (85,3)	56 (14,7)	114,548; ***<0,001***			
High risk	33	2 (6,1)	31 (93,9)				

FROP-Com: Fall Risk for Older People in the Community, n: Number, %: Percentage, *X2: Chi-square test

individuals). Individuals aged 65 and older who applied to the relevant Family Health Center and agreed to participate in the study were included. Participants who did not agree to participate and those who provided incomplete or incorrect information during the survey interview were excluded from the study. The data of the study were obtained by face-to-face interview method by the researchers after obtaining the informed consent of the participants with a questionnaire form including sociodemographic characteristics, fall risk factors, fall status in the last year, personal characteristics, Fall Risk Screening Scale for the Elderly in the Community and EQ-5D General Quality of Life Scale prepared by the researchers based on the literature.

The study was approved by the Ethics Committee of Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (date: 17.08.2022, decision no: 2022/08-18).

In the post-hoc power analysis, since the fall prevalence was found to be 21.1% in a study with 413 participants, the power of the study was determined to be 99.9%.

Table 2. Relationship between EQ-5D index score and sociodemographic characteristics

		EQ5D Index score Median (min-max)	Statistical analysis*	
			MWU/KWT	p
Gender				
	Man	0,7641 (-0,0748 - 1)	-5,138	***<0,001***
	Woman	0,6607 (-0,1584 - 1)		
Age				
	65-74[a]	0,7444 (-0,1584 - 1)	26,734	***<0,001****
	75-84[b]	0,6589 (-0,0748 - 1)		
	85 and over[c]	0,4728 (0,0194 - 1)		
Marital status				
	Not married	0,61275 (-0,1584 - 1)	-5,789	***<0,001***
	Married	0,7444 (-0,0748 - 1)		
Education status				
	Primary school and less	0,6699 (-0,1584 - 1)	-3,655	***<0,001***
	Middle school and above	0,7641 (-0,0748 - 1)		
Income status				
	Income more than expenses	0,6897 (-0,0748 - 1)	4,365	0,113
	Income equal to expenses	0,7234 (-0,0013 - 1)		
	Income less than expenses	0,6607 (-0,1584 - 1)		
Personal daily care				
	Can't	0,4728 (-0,1584 - 1)	-4,509	***<0,001***
	Can	0,6897 (-0,0013 - 1)		
Exercise status				
	Do not	0,6392 (-0,1584 - 1)	-5,760	***<0,001***
	Do	0,7444 (0,1031 - 1)		
Sleep status				
	Irregular	0,607 (-0,1584 - 1)	-5,665	***<0,001***
	Regular	0,7444 (-0,0013 - 1)		
Walking problem				
	Yes	0,5863 (-0,1584 - 1)	-8,396	***<0,001***
	No	0,7641 (-0,0013 - 1)		
Balance problem				
	Yes	0,5863 (-0,1584 - 1)	-6,402	***<0,001***
	No	0,7444 (-0,0013 - 1)		
Use of assistive devices				
	None	0,7641 (-0,1584 - 1)	-6,903	***<0,001***
	Yes	0,5863 (-0,0748 - 1)		
Falling status in the last one year				
	None	0,7444 (-0,0748 - 1)	-4,548	***<0,001***
	Yes	0,6299 (-0,1584 - 1)		
Falling risk				
	Low risk	0,7333 (-0,0748 - 1)	-5,562	***<0,001***
	High risk	0,5762 (-0,1584- ,7733)		

*MWU: Mann-Whitnet U test, KWT: Kruskal Wallis test; ** Significance arises between groups a-b and a-c, min: Minimum, max: Maximum, a: 65-74 age group, b: 75-84 age group, c: 85 and over age group

Falls Risk for Older People in the Community (FROP-Com) Screen Scale

The score was obtained from the FROP-Com screen scale, which consists of 3 questions (fall history, activities of daily living, balance) and was developed by Russell et al., (12). The answer to each question is scored between 0 and 3, the minimum score from the scale is 0 and the maximum score is 9. On the scale, 0–3 points are considered low risk, and 4–9 points are considered high risk. The necessary permission to use the scale in Türkiye was obtained from the researcher who developed the scale. There is no Turkish validity and reliability study for the FROP-Com screening tool. Permission to use the scale was obtained from the author who developed it. The comprehensibility, validity and reliability of the scale questions were tested in a group of ten people (Cronbach's alpha = 0.790). In the data of our study, the reliability of the FROP-Com screen was 0.740.

Table 3. Multiple logistic regression analysis of some personal characteristics with fall risk

Risk Group		Odds Ratio	95% C.I. for OR		p
			Lower	Upper	
Age	65-74	1			
	75-84	1,079	0,430	2,708	0,871
	85 and over	1,824	0,428	7,770	0,416
Personal daily care	Can't	1			
	Can	3,000	0,921	9,773	0,068
Exercise status	Do	1			
	Do not	2,532	1,010	6,346	***0,047***
Sleep status	Regular	1			
	Irregular	1,233	0,524	2,904	0,631
Walking problem	No	1			
	Yes	2,881	0,884	9,390	0,079
Balance problem	No	1			
	Yes	5,119	1,990	13,165	***0,001***
Use of assistive devices	None	1			
	Yes	3,596	1,290	10,020	***0,014***

C.I. for OR: Confidence Interval for Odds ratio, p: p value

Table 4. Correlation relationship between EQ-5D index and FROP-Com Score and some variables

		EQ5D Index	FROP-Com Score
Age	r	-0,273	0,269
	p	***<0,001***	***<0,001***
Education status	r	,221	-0,108
	p	***<0,001***	***0,028***
Income status	r	-0,075	0,019
	p	0,127	0,693
Falling status in the last one year	r	-0,442	0,840
	p	***<0,001***	***<0,001***
Current health score	r	0,417	-0,299
	p	***<0,001***	***<0,001***
EQ5D Index score	r	1,000	-0,464
	p	-	***<0,001***
FROP-Com score	r	-0,464	1,000
	p	***<0,001***	-

FROP-Com: Fall Risk for Older People in the Community

EQ-5D General Quality of Life Scale

The scale, which consists of five dimensions: movement, self-care, usual activities, pain or discomfort, and anxiety or depression, was developed by the European Quality of Lİfe (Euro-Qol) in 1987 (13). Responses to each dimension have three options as 'no problem', 'some problem' and 'important problem' and the scale describes 243 (3^5) possible different outcomes. The 5 dimensions of the scale are used to calculate an index score ranging from -0.59 to 1. A score of 0 indicates death, a score of 1 indicates perfect health, and negative scores indicate conditions such as unconsciousness and being bedridden. The Turkish validity and reliability of the scale was conducted by Kahyaoğlu Süt (14).

Statistical analyses

The data of the study were evaluated with the Jamovi statistical package program version 2.2.5. Descriptive data were presented as number, percentage, median, minimum, and maximum values. Pearson chi-square test (Yates correction and Fisher's chi-square test when necessary) was used to compare categorical variables. Mann-Whitney U Test and Kruskal-Wallis test were used to compare groups with continuous variables that did not fit the normal distribution. In univariate analyses examining the relationship between the risk of falls and independent variables, a multiple logistic regression model was created with independent variables with $p<0.1$ values. The correlation between variables was examined using Spearman correlation test. For statistical significance level of $p<0.05$ was accepted.

RESULTS

The study was completed with 413 participants, 200 (48.4%) men and 213 (51.6%) women. The mean age of the participants was 71.5±6.1 (min=65, max=93), and 72.4% (n=299) were in the 65–74 age range, 23.7% (n=98) were 75–84, and 3.9% (n=16) were 85 and over. 74.8% (n=309) of the participants were married; 54.2% (n=224) had a primary school education or less; and 65.9% (n=272) had income equal to their expenses (Table 1).

The prevalence of falls within the last year in the study group was 21.1% (n = 87). Among the participants, those who could not do their personal daily care (p<0.001), those who did not exercise (p=0.018), those with irregular sleep status (p=0.002), those with walking and balance problems (p<0.001), and those who used assistive devices (p<0.001), those with a high risk of falling FROP-Com (p<0.001) The rate of falling in the last year was higher. There was no relationship between the falling status in the last year and the variables of gender, age group, marital status, education level, and income status (p>0.05).

FROP-Com is higher in those with a high age group (p<0.001), those who cannot do their personal daily care (p<0.001), those who do not exercise (p<0.001), those with irregular sleep status (p=0.004), those who have walking and balance problems (p<0.001), those who used assistive devices (p<0.001), and those who had a fall in the last year (p<0.001) (Table 1).

When the quality of life of the participants was evaluated, the median EQ-5D index score was 0.7 (min=-0.2; max=1.0). The EQ-5D quality of life index score was found to be significantly lower in those who have female gender (p<0.001), those who are in the high age group (p<0.001), those who are not married (p<0.001), those who have a primary school and below education level (p<0.001), those who cannot do personal daily care (p<0.001), those who do not exercise (p<0.001), those who have irregular sleep status (p<0.001), those who have walking and balance problems (p<0.001), those who use assistive devices (p<0.001), those who had a fall in the last year (p<0.001) and in those with a high FROP-Com risk of falling (p<0.001) (Table 2).

FROP-Com fall risk was accepted as the dependent variable, the risk of falling; It was found that it increased 2.5 times (p=0.047) in those who did not exercise, 5.1 times (p=0.001) in those who did not have balance problems, and 3.6 times (p=0.014) in those who used assistive devices compared to those who did not (Table 3). The correlation between the participants' EQ-5D index values and FROP-Com scores with some variables is presented in Table 4.

DISCUSSION AND CONCLUSION

It is known that falls, which are an important health problem for the elderly in society, have a negative impact on quality of life. Determining the risk of falling and the prevalence of falls is considered to be crucial for the proper implementation of protective measures (15,16). In this study, which examined falls, which are both an important health problem and reduced quality of life due to various consequences, approximately two in ten participants had a history of falling within the last year, while 8% of participants were found to be at high risk of falling. Furthermore, those who had a history of falling in the previous year had a lower quality of life than those who had not, and those with a high risk of falling had a lower quality of life than those with a low risk of falling.

The prevalence of falls within the last year was found to be 21.1%. A review of the literature shows that the prevalence of falls in the elderly ranges from 18% to 60.3% (9,17–19). This wide range may be due to the place, time, and socio-cultural structure of the society. In addition, because our study asked retrospectively about falls within the previous year, the prevalence may have been lower due to reasons such as recall and not taking falls seriously.

In our study, although the risk of falling and having fallen in the last year increased with age, only the relationship between the risk of falling and age was found to be statistically significant. Some studies show that being older increases the risk of falling (3,17,20). No relationship was found between gender, marital status, education, income status, and the risk of falling or falling status. Similar to our study, no relationship was found between gender and marital status and the risk of falling in one study (6). In the study of Wu and Ouyang, the risk of falling has been reported to be higher in women, married people, and those with physical

dysfunction (18). In another study conducted in China, it was shown that the risk of falling is higher in women and those living alone (19). It can be thought that these differences in the relationship between fall risk and sociodemographic variables may be due to the structure of the society or the characteristics of the place and time of the study.

The risk of falling was found to be 2.5 times higher in those who did not exercise, 5.1 times higher in those with balance problems, and 3.6 times higher in those who used assistive devices. There are studies reporting that the risk of falling is high in people with low physical activity and walking problems (17,19,21). An Indian study of individuals aged 60 to 95 years, found that those with balance problems were 3.1 times more likely to fall than those who used assistive devices (22). It has been reported that deterioration of balance, which is one of the most important reactive elements in preventing falls, can lead to increased injury, disability and falls, and reduced quality of life (23). Considering that individuals with an increased risk of falling and with walking and balance problems use assistive devices, it is not unexpected that more falls will be observed in the population using assistive devices, although their purpose is to prevent falls.

Some studies that have looked at aging and quality of life have found that the elderly have a moderate quality of life (24,25). In our study, the elderly people included in the study were found to have a low quality of life. The findings in these studies are similar to the findings in our study in terms of the relationship between falls and quality of life (24). This is an expected situation because of the old age period; it is a period in which factors such as physical and social regression and chronic diseases are experienced more common (26,27). It should also be noted that the results may vary depending on the diversity of quality of life scales and differences in scoring. According to our study, the quality of life of the elderly is lower in older age, in women, in the elderly with low education, in the unmarried, and in those who do not exercise. Studies examining quality of life in the elderly support the findings of our study (28). In addition to sociodemographic characteristics, other factors also affect quality of life. Although the relationship between health status and quality of life is important at all ages, it is said to be more pronounced with age (26,28). In our study, in addition to the sociodemographic characteristics that affect the quality of life of the elderly, it was determined that some health conditions and functional levels also reduced the quality of life. Among them are irregular sleep, walking problems, balance problems, and the use of assistive devices. According to these findings, as the health and functionality of the elderly decrease, their quality of life also decreases.

Other factors affecting the quality of life are the risk of falling and the fact that the elderly has fallen in the last year. Studies investigating the relationship between falling and quality of life in the elderly have found significant relationships between the falling status of individuals and their quality of life (15,16). The findings of our study are similar to the findings of these studies in the literature. In particular, the quality of life was found to be significantly lower in the elderly with a high risk of falling than in the elderly with a low risk. According to our study, the high risk of falling affects the quality of life of the elderly more than experiencing a fall. The fact that the risk of falling is high may decrease the quality of life since the elderly experience constant anxiety, which decreases their functionality and limits their social participation and activities of daily living. From this point of view, reducing the fall risk of the elderly can increase both the number of falls and the quality of life by reducing the perception of a lower risk of falling. Therefore, this finding suggests that it is particularly important to determine the risk of falling and the factors that increase the risk of falling.

Among the limitations of the study are the ignoring of the effect on the prevalence of falls, since those who lost their lives due to falls could not be determined and the fact that the elderly, who could not apply to a health institution, could not be reached because the study was carried out in family health centers.

In conclusion, the prevalence of falls within the last year was found to be 21.1%. The risk of falling was discovered to be 5.1 times higher in those with balance issues, and 3.6 times higher in those who used assistive devices. Quality of life was affected by many sociodemographic and personal characteristics. The quality of life decreased as the age increased, the educational status decreased, and the risk of falling increased in those with a history of falling.

Considering that the world population has an increasing proportion of elderly people, it is extremely important to prevent falls, which are an important cause of morbidity and mortality in this population. It is important for local governments to create protective environments to prevent falls in the elderly. Although some findings in this study indicate that exercise status may be related to the risk of falling, further research is needed to determine the causality of this relationship. Nevertheless, we believe that increasing exercise status can prevent or reduce falls. Falls can be prevented or reduced by increasing exercise status. Researchers recommend that policymakers focus on the importance of exercise in the elderly. It should be taken into account that every attempt to reduce the risk of falling will not only reduce the health problems caused by falls in the elderly but also increase the quality of their lives.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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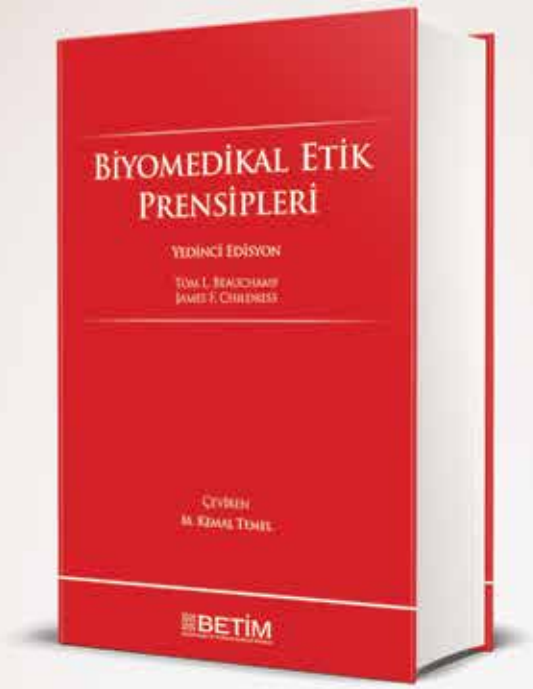

Biyomedikal Etik Prensipleri

Yedinci Edisyon

Tom L. Beauchamp - James F. Childress

Çeviren
M. Kemal Temel

Amerikan filozoflar Tom L. Beauchamp ve James F. Childress tarafından yazılmış olan ve birçok ülkede benimsenen ana akım tıp etiği paradigmasının temelini oluşturan Biyomedikal Etik Prensipleri, Türkiye'de de klinik uygulama ve araştırmalarda, tıp eğitimi, etiği ve hukukunda esas alınan başlıca ilkelerin kaynağıdır. Bu kitap, İngilizce temel eserin yedinci edisyonu ve ilk Türkçe baskısıdır. İstanbul Tıp Fakültesi Tıp Tarihi ve Etik Anabilim Dalı mensubu Uzm. M. Kemal Temel tarafından tercüme edilmiş ve üç yıllık kusursuz bir çalışma sonucunda basılmıştır. Başta tıp ve insani bilimler olmak üzere, Türkiye'de bilimsel gelişim ve üretime adanmış bir kurum olan, Hayat Sağlık ve Sosyal Hizmetler Vakfı bünyesindeki Beşikçizade Tıp ve İnsani Bilimler Merkezi—BETİM, bu tercümeyi Türk akademisyen ve okurların istifadelerine iftiharla sunar.

Betim Kitaplığı

The effect of somatosensory perception and proprioception on upper extremity functional skills in children with hemiparetic and diparetic cerebral palsy

Hemiparetik ve diparetik serebral palsili çocuklarda somatosensoriyel algı ve propriyosepsiyonun üst ekstremite fonksiyonel becerilerine etkisi

Abstract

Aim: The aim of the current research is to determine the impacts of somatosensory perception and proprioception on upper extremity functional skills in children with hemiparetic and diparetic cerebral palsy (CP).

Methods: Children with hemiparetic (n=15) and diparetic (n=15) CP at Gross Motor Function Classification System (GMFCS) I-III and Manual Ability Classification System (MACS) I-III levels and healthy children (n=15) with a mean age of 10.71± 4.09 were enrolled in the research. Somatosensory perception was evaluated with the Ayres' Southern California Sensory Integration and Praxis Test (SIPT) sub-parameters, kinesthesia (KIN), touch stimulus localization (TSL), double-touch stimulus localization (DTL), finger recognition (FR), and right-left discrimination (RLD) tests. Proprioception measurements were performed with a goniometer on the shoulder, elbow, and hand-wrist. Upper extremity functional skills were evaluated by the Jebsen-Taylor Hand Function Test (JTHFT).

Results: Somatosensory perception and proprioception of the control group were determined to be significantly better than those of both groups with CP ($p<0.05$). The somatosensory perception, proprioception, and JTHFT test results of children with CP were significantly better in the hemiparetics in comparison with the diparetics ($p<0.05$).

Conclusion: The study showed that children with CP had lower somatosensory perception levels in their upper extremities and had proprioceptive losses in their upper extremities in comparison with their healthy peers. It was shown that diparetic children had lower scores than hemiparetic children in somatosensory perception and proprioception tests compared to their healthy peers.

It was determined that children with CP had lower hand skills compared to their healthy peers and hemiparetic children were better than diparetic group in hand skills. It was revealed that children with CP had lower manual dexterity than their healthy peers, and hemiparetic children had better skills than the diparetic group.

Keywords: Cerebral palsy; hand; perception; proprioception

Öz

Amaç: Bu çalışmanın amacı hemiparetik ve diparetik Serebral Palsi (SP)'li çocuklarda somatoduyusal algı ve propriosepsiyonun üst ekstremite fonksiyonel becerilerine etkilerini belirlemektir.

Yöntemler: Çalışmaya yaş ortalamaları 10,71± 4,09 olan, Kaba Motor Fonksiyon Sınıflama Sistemi (GMFCS) 1-2 ve 3 ile El Beceri Sınıflama Sistemi (MACS) 1-2-3 düzeyindeki 15 hemiparetik SP'li çocuk, 15 diparetik SP'li çocuk ve 15 sağlıklı çocuk (24 erkek/21 kız) dahil edildi. Somatoduyusal algı Ayres Güney Kaliforniya Duyu Bütünleme ve Praxis Testi (SIPT)'nin alt parametreleri olan kinestezi, dokunma uyarısının lokalizasyonu, çift dokunma uyarısı lokalizasyonu, parmak tanıma ve sağ-sol ayırımı testleriyle değerlendirildi. Propriosepsiyon değerlendirmesi için omuz, dirsek, el-el bileğine gonyometrik ölçümü yapıldı. Üst ekstremite fonksiyonel becelerileri Jebsen Taylor El Fonksiyon Testi (JTEFT) değerlendirildi.

Bulgular: SP'li çocuklar ile kontrol grubu arasında somatoduyusal algı ile propriosepsiyonun farklı olduğu ve bu parametrelerin de el becerileriyle anlamlı olarak ilişkili olduğu bulundu ($p<0.05$). Kontrol grubunun somatoduyusal algı ve propriosepsiyonlarının SP'li gruplara göre anlamlı düzeyde daha iyi olduğu bulundu ($p<0.05$). SP'li çocukların somatoduyusal algı, propriosepsiyon ve JTEFT testlerinde; hemiparetik grubun diparetik gruba göre anlamlı düzeyde daha iyi olduğu bulundu ($p<0.05$).

Sonuç: SP'li çocukların sağlıklı yaşıtlarına göre üst ekstremitelerinde daha düşük somatosensoriyel algı düzeylerine sahip olduğu ve üst ekstremitelerinde propriyoseptif kayıpların olduğu belirlendi. Sağlıklı akranlarına göre somatosensoriyel algı ve propriyosepsiyon testlerinde diparetik çocukların hemiparetiklerden daha düşük skorlarının olduğu gösterildi. SP'li çocukların sağlıklı akranlarına göre daha düşük el becerilerine sahip oldukları, hemiparetik çocukların ise diparetik gruba göre daha iyi düzeyde olduğu belirlendi.

Anahtar Sözcükler: Algı; üst ekstremite; propriyosepsiyon; serebral palsi

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INTRODUCTION

Cerebral palsy (CP) represents a non-progressive neurodevelopmental disorder characterized by posture and movement disorders due to perinatal brain injury (1). Hence, sensory-motor impairment, which takes place under the influence of systems including proprioception, tactile, and vestibular systems, is the primary problem in CP (2, 3).

The somatosensory system is active from the early stages of life and plays an important role in sensory-motor development. The tactile sense develops the earliest among all senses (4). The somatosensory system is very important in gross and fine motor development. Infants use tactile cues to reach an object throughout their lives, even at the early stages of life. Correct tactile and proprioceptive sensory input is crucial for motor development during childhood and is especially significant for fine motor development during the preschool period (5).

Research has indicated that children with CP have impaired tactile discrimination skills (5). This impairment is closely related to motor losses. It has been observed that motor skills are also impacted in individuals with impaired somatosensory perception processing and cause significant functional impairments (6). Studies have indicated that children with CP also experience loss of stereognosis, two-point discrimination, and tactile senses (6). As a result of sensory losses, motor learning required for fine hand skills is also delayed and may result in clumsiness, decreased sensitivity, or inability to use extremities in individuals (6). It is known that poor tactile perception will cause functional impairment in children with hemiparetic CP (7). While no difference has been observed in the senses of pain, light touch, and vibration between the affected side and the less affected side in these children, a difference has been detected in tactile, proprioception, and two-point discrimination senses (8). Children with diparetic CP are stated to have poor tactile discrimination skills (9).

Proprioception is the somatosensory system that uses afferent stimuli from muscles, joints, and skin (10). Proprioception is a sense that ensures the sense of joint position, kinesthesia, the perception of the resistance and pressure created by the movement in the joint, and the perception of the body position in space (10). It provides postural control by working with the somatosensory, visual, and vestibular systems. Owing to the somatosensory receptors in the body, appropriate adaptive sensory and motor responses are created by the integration of the senses from the body (11). Loss of proprioception in CP arises from the lesion in the Central Nerve System (CNS) and proprioceptive inputs to the sensory afferent muscle spindle, Golgi tendon organ, joint, and cortex is affected. The most common sensory deficits in CP are stereognosis and proprioception, which are affected bilaterally (3). The superficial sense is usually normal in these children, but the senses of proprioception, stereognosis, and kinesthesia are adversely impacted. Due to these problems, it becomes more challenging for children with functional disabilities in the upper extremity to fulfill their roles in society (12). Difficulties in writing have been observed in children due to loss of proprioception, which has also been associated with poor coordination skills. This leads to difficulties and delays in motor learning while children acquire new skills (12). Sensory inputs take a significant place in developing motor function and acquiring functional independence in children with CP. Deficiencies in sensory input may delay learning new motor movements, which may cause disuse of the extremities and sensitivity (12).

Deficiencies in upper extremity functions due to their involvement are among the most significant factors influencing activities of daily living (ADL) in children with CP (13). Limitations leading to the restriction of normal joint movements due to hypertonia in the upper extremity, loss of grip strength due to isolated finger movements that cannot be performed with a normal pattern, cortical thumb deformity, inadequacies in manipulation skills, and loss of speed and coordinated movement skills are observed in children with CP (13). The aim of the current study is to research the impacts of somatosensory perception and proprioception on upper extremity functional skills in children with hemiparetic and diparetic CP.

MATERIAL AND METHODS

Participants

Children with hemiparetic and diparetic CP who were diagnosed by a specialist physician and presented to the research and treatment unit of SANKO University Physiotherapy and Rehabilitation Depart-

ment and their families were included in the study. When the sample size was calculated with α=0.05 and power=0.80 in the power analysis, it was decided to include 20±5 children in each group consisting of children diagnosed with hemiparetic and diparetic CP and healthy children. The study was completed with 45 children since there were children who could not participate in the evaluations due to the pandemic and various reasons (Figure 1). Children with hemiparetic and diparetic CP aged between 6-18 who were able to receive verbal commands, did not have any intellectual disability, had Gross Motor Function Classification System (GMFCS) Level≤III, had upper extremity muscle spasticity≤2 in accordance with the Modified Ashworth Scale (MAS), had the Manual Ability Classification System (MACS)≤III, had not undergone surgery or received Botulinum Toxin (Botox) treatment in the last 6 months, and whose family consent was obtained were enrolled in the research. All of the children's parents signed the informed volunteer consent form for this study. Children with joint contractures in the shoulder, elbow, and hand-wrist and any hearing or vision problems were excluded from the study. pproval for the research was received from the SANKO University Non-Interventional Clinical Research Ethics Committee (date: 07.07.2020, decision no: 2020/07), and the study was performed in accordance with the Declaration of Helsinki. The clinical trial number is NCT05213715.

Outcome measures

The children's sociodemographic characteristics were recorded. The somatosensory perception test (touch stimulus localization test (TSL), double-touch stimulus localization test (DTSL), finger recognition test (FR), right-left discrimination test (RLD), Jebsen-Taylor Hand Function Test (JTHFT), Modified Ashworth Scale (MASH), Gross Motor Function Classification System (GMFCS), Manual Ability Classification System (MACS), and goniometer and kinesthesia tests (KIN) in proprioception evaluation were used in all children. A table, chair, and stretcher suitable for the child who was performed were used in all evaluations.

Somatosensory perception assessment: The subtests of Ayres' Southern California Sensory Integration and Praxis Test (SIPT) (touch stimulus localization test, double-touch stimulus localization test, finger recognition test, and right-left discrimination test) were used (14). Before the assessment, the children were explained how the tests would be conducted. Before the test, the children's eyes were closed, or an eye patch was used. All assessments were carried out bilaterally in the following order:

Touch stimulus localization test (TSL): During the test, the child's hand, wrist, and forearm, respectively, were touched once with a pencil first, and he/she was requested to show the touched area with his/her finger. The distance between the place touched with the pencil and the place pointed by the child was measured with a ruler and recorded in centimeters (cm). If the distance between the touched location and the distance touched by the child was far from the touched location, it indicated poor tactile perception (14).

Double-touch stimulus localization test (DTSL): Two different points, left hand-right cheek, right hand-left hand, left cheek-right cheek, left hand-left cheek, right hand-left cheek, and right hand-right cheek, were touched simultaneously with two separate pencils. The child was requested to show both points touched. The total score was written by giving 2 points if the child knew both points, 1 point if he/she knew one point, and 0 points if he/she did not know any of the points. In the scoring in which the best value was measured out of 12, the lower this value was, it was interpreted as the worse tactile perception to the same extent. (14).

Finger recognition test (FR): The child was requested to put his/her hands on the table, and 16 different points (right-left) were touched with a pencil. The child was requested to show the touched points with his/her finger. It was scored as 1 point in case of a correct answer and 0 points in case of an incorrect answer. The total score was acquired by summing the scores of both hands. A higher score indicates good tactile perception (14).

Right-left discrimination test (RLD): The child was asked to repeat 10 commands, respectively: 'Show me with your right hand, touch your left ear, hold this pen with your right hand, touch my right hand, etc' If the correct answer was given in the first three seconds, 2 points were scored; if the correct answer was given in ten seconds 1 point scored; if no answer was given

Table 1. Comparison of demographic information between groups

	Hemiparetic (n:15)	Diparetic (n:15)	Control (n:15)	*Test statistics*	*p*
	mean±SD	mean±SD	mean±SD		
Age (y)	8.67 ± 3.64	11.87 ± 3.7	11.6 ± 4.37	KW-H=6.718	***0.035**ac*
Height	1.29 ± 0.12	1.42 ± 0.16	1.5 ± 0.21	KW-H=9.619	***0.008**ac*
Weight (kg)	28 ± 11.57	40.53 ± 17.33	46.07 ± 16.89	KW-H=9.958	***0.007**ac*
BMI	16.11 ± 3.4	19.29 ± 4.91	19.64 ± 3.53	F=3.528	***0.038**ac*
Sex (m/f)	5/10	8/7	11/4	KW-H=4.714	***0.003**a*
Percent (%)	33.3/66.7	53.3/46.7	73.3/26.7		

*p<0,05; SD: Standart Deviation, n: Number, m: Male, f: Female, F: One way Anova, KW-H: Kruskal-Wallis test, a: Hemiparetic-control, b: Diparetic-control, c: Hemiparetic-diparetic, kg: kilograms, y: year, BMI: Body Mass Index

Table 2. Comparison of categorical variables between groups

	Hemiparetic (n:15)	Diparetic (n:15)	Control (n:15)	X^2	*p*
	n (%)	n (%)	n (%)		
Dominance					
Right	12 (80)	11 (73.3)	11 (73.3)	0.246	0.884
Left	3 (20)	4 (26.7)	4 (26.7)		
Gross Motor Function Classification System (GMFCS)					
1	15 (100)	9 (60)	15 (100)	15.150	***0.001***
2	0 (0)	6 (40)	0 (0)		
Manuel Ability Classification System (MACS)					
1	12 (80)	2 (13.3)	15 (100)	33.178	***0.001***
2	3 (20)	10 (66.7)	0 (0)		
3	0 (0)	3 (20)	0 (0)		

p<0,01; n: number, %: Percent, X^2:** Chi-square test

Table 3. Comparison of somatosensory perception tests of groups

Somatosensory Perception	Hemiparetic (n=15)	Diparetic (n=15)	Control (n=15)	*Test statistics*	*p*
	mean±SD	mean±SD	mean±SD		
KIN (right)	35.24 ± 7.35	31.86 ± 4.51	39.93 ± 4.95	KW-H=10.301	***0.006**b*
KIN (left)	34.55 ± 5.83	30.47 ± 5.92	39.35 ± 3.55	KW-H=15.812	***0.001**ab*
Right-hand touch stimulus localization test (TSL)	6.33 ± 2.4	7.65 ± 2.38	5.01 ± 2.56	F=4.383	***0.019**b*
Left-hand touch stimulus localization test (TSL)	8.36 ± 3.28	10.14 ± 4.1	6.75 ± 2.8	F=3.646	***0.035**b*
Double-touch stimulus localization test (DTSL)	13.53 ± 0.92	12.73 ± 1.53	13.8 ± 0.41	KW-H=6.804	***0.033**b*
Finger recognition (FR)	14.67 ± 1.59	14.33 ± 1.84	15.67 ± 0.62	KW-H=6.962	***0.031**ab*
Right-left discrimination (RLD)	16.53 ± 2.47	16 ± 3.09	18.47 ± 1.81	KW-H=7.417	***0.025**ab*

*p<0,05; SD: Standart deviation, F: One way Anova, KW-H: Kruskal-Wallis test, a: Hemiparetic-control, b: Diparetic-control, c: Hemiparetic-diparetic, KIN: Kinesthesia

Table 4. Comparison of proprioception of the groups

	Hemiparetic (n:15)	Diparetic (n:15)	Control (n:15)	*p*
Shoulder flexion (right)	9 ±5.87	13.06 ± 6.54	6.60± 5.87	***0.026**b*
Shoulder flexion (left)	11± 4.35	15.06± 7.43	7.46± 5.79	***0.009**b*
Shoulder abduction (right)	9.66 ± 5.43	19.93± 8.47	9.93 ± 5.45	***0.002**bc*
Shoulder abduction (left)	12.26 ± 5.72	22.86± 8.02	12± 5.87	***0.000**bc*
Elbow flexion (right)	3.96 ± 3.50	8.30± 5.22	4.76± 4.38	***0.018**c*
Elbow flexion (left)	5.10 ± 3.35	6.63± 4.42	5.63± 5.39	0.623
Elbow extension (right)	4.50 ± 3.72	7.96± 5.46	3.43± 3.43	***0.018**b*
Elbow extension (left)	6.10 ± 4.17	10.70± 7.58	4.43 ± 3.61	***0.023**b*
Supination (right)	4.40 ± 2.13	10.06± 5.56	4.60± 4.38	***0.008**bc*
Supination (left)	6.40± 2.94	11.53± 6.10	3.86± 2.61	***0.001**b*
Pronation (right)	4.60 ± 2.87	9.26± 4.94	4 ± 3.44	***0.003**bc*
Pronation (left)	6.86 ± 4.42	10.26± 4.75	3.66 ± 2.38	***0.001**b*
Wrist flexion (right)	5.80± 3.27	12.60± 6.73	2.73 ± 3.05	***0.000**bc*
Wrist flexion (left)	6.80± 3.07	14 ± 3.44	5.46 ± 3.06	***0.000**bc*
Wrist extension (right)	4± 2.36	7.13± 3.60	2.60 ± 2.66	***0.001**b*
Wrist extension (left)	4.06 ± 2.08	8.13± 3.99	4.13 ± 3.15	***0.006**bc*

*p<0,05, n: Number, Kruskal-Wallis test, a: Hemiparetic-control, b: Diparetic-control, c: Hemiparetic-diparetic

Table 5. Comparison of jebsen taylor hand function test (JTHFT) values between groups

JTHFT	Hemiparetic (n:15)	Diparetic (n:15)	Control (n:15)	*Test statistics*	*p*
	mean±SD	mean±SD	mean±SD		
Card flip (right)	7.35 ± 1.96	11.21 ± 7.86	4.32 ± 1.18	KW-H=25.084	***0.001**ab*
Card flip (left)	8.91 ± 2.88	12.31 ± 8.69	4.28 ± 0.71	KW-H=28.582	***0.001**ab*
Putting objects in the can (right)	10.57 ± 1.99	14.69 ± 5.41	7.19 ± 1.3	F=18.206	***0.009**abc*
Putting objects in the can (left)	13.21 ± 3.87	16.16 ± 7.42	7.01 ± 1.47	KW-H=27.842	***0.001**ab*
Stacking checkers (right)	6.83 ± 3.3	11.26 ± 8.29	2.66 ± 0.99	KW-H=27.204	***0.001**ab*
Stacking checkers (left)	8.71 ± 5.78	12.19 ± 7.95	2.95 ± 0.88	KW-H=27.331	***0.001**ab*
Move empty cans (right)	7.05 ± 2.49	9.27 ± 4.15	3.43 ± 0.73	KW-H=27.204	***0.001**ab*
Move empty cans (left)	8.29 ± 3.08	10.81 ± 4.69	3.75 ± 1.15	KW-H=27.331	***0.001**ab*
Move full cans (right)	8.72 ± 2.89	10.94 ± 4.94	4.18 ± 1.17	F=15.682	***0.001**ab*
Moving full cans (left)	9.27 ± 4.15	12.32 ± 4.92	4.19 ± 1.18	F=17.742	***0.001**abc*
Picking beans with a spoon (right)	23.34 ± 6.56	34.08 ± 15.67	14.99 ± 11.69	KW-H=18.218	***0.005**ab*
Picking beans with a spoon (left)	31.09 ± 8.07	39.06 ± 18.39	15.31 ± 8.03	KW-H=19.117	***0.001**ab*

*0,05; SD: Standart deviation, n: Number, %: Percent, F: One-way Anova, KW-H: Kruskal-Wallis test, a: Hemiparetic-control, b: Diparetic-control, c: Hemiparetic-diparetic, JTHFT: Jebsen Taylor Hand Function Test

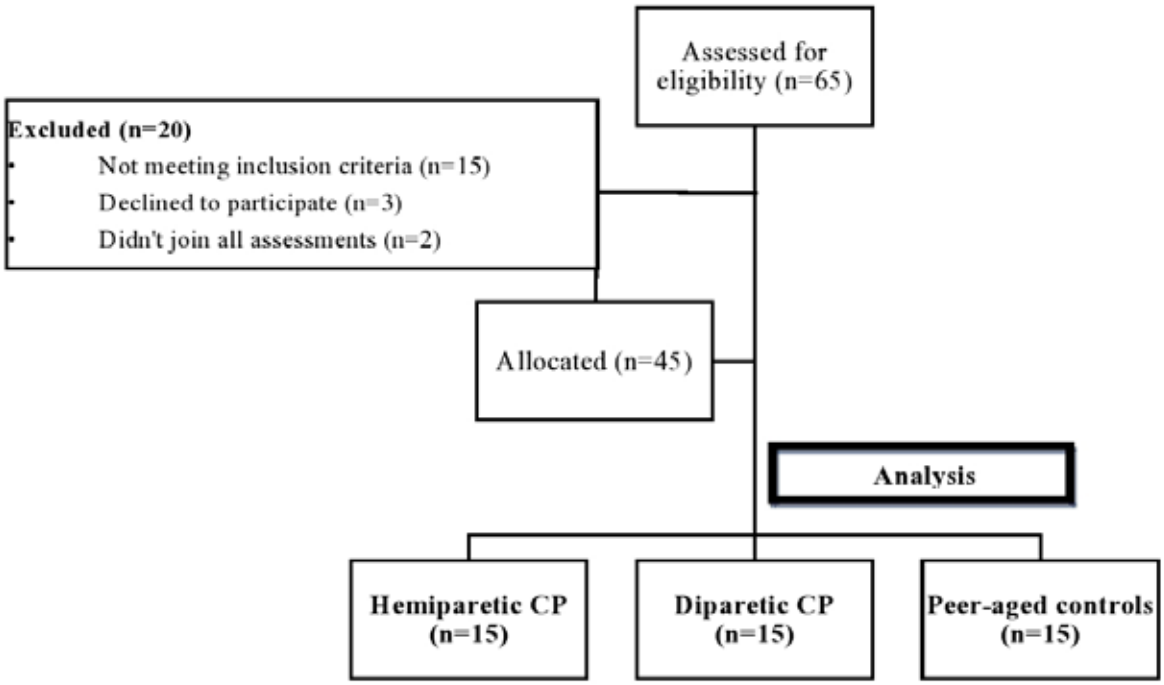

Figure 1. Flow chart showing the experimental design of the study (n: Number)

0 points scored. The total score was recorded by summing all of the questions scored (14).

Jebsen-Taylor Hand Function Test (JTHFT): The JTHFT, which is utilized in the 6-18 age range, comprises 6 subtests that represent hand function in daily life. The application time is 15-45 minutes (min). A scaled board is utilized to ensure a standard arrangement of objects in the test. The time during which all activities are performed is recorded with a stopwatch (15). Activities in the test's sub-parameter are turning over 5 cards, putting 6 objects in a can, stacking 4 checkers, picking up an empty can, picking up a full can, collecting 5 kidney beans with a dessert spoon, and writing. All parameters except writing were measured in this study. Before the assessment, the child was told how to perform the steps in the test. The child started the test with the start command. When he/she finished the activity, the stopwatch was stopped, and the activity completion time was recorded in seconds.

Modified Ashworth Scale (MAS): It is the most frequently used clinical scale for assessing spasticity. It is used to assess muscle tone during passive movement of the muscle in the affected extremity. Muscle tone is scored from 0 to 4 (16). This scale, whose applicability in Turkish has been tested in children with CP, has been determined to be the most effective and reliable method for evaluating spasticity. All of the upper extremity muscles' tone was measured in the supine position.

Gross Motor Function Classification System (GMFCS): It represents a standard classification system for categorizing the gross motor skills of children with CP between levels I and V (17).

Manual Ability Classification System (MACS): It represents a classification system formed in order to classify the hand skills of children with CP aged between 4-18, e.g., grasping and releasing objects in daily life, and how they utilize their hands while holding objects. The MACS is defined at five levels (I-V). Level I shows that the child can grasp and use objects easily and successfully, while Level V demonstrates that the child cannot use objects independently and there is a severe decrease in function performance (18).

Proprioception: The goniometric measurement was used for upper extremity shoulder flexion-abduction, elbow flexion-extension, forearm supination-pronation, and hand-wrist flexion. The child was requested to close his/her eyes or turn the head

opposite to the assessed side and perform the movements slowly during the test. First, the physiotherapist showed the movement passively in the full range with the eyes open so that the child could fully perceive the movement. Then, after stopping for 3 seconds at the last point reached, the child returned to the starting position. The child was requested to repeat the same movement. The point at which the child came was measured angularly. Afterward, he/she was asked to do the movement in half range. The physiotherapist showed the same movement of the child in half range. After stopping for 3 seconds at the point reached, the child returned to the starting position. The child was requested to perform the same movement. The angular value of the last point reached was measured. Finally, the difference between the value for the full range and the value for the half range was recorded. Angular values determined for the measurement were evaluated with Kendall McCreary degrees (19).

Kinesthesia test (KIN): This test is one of Ayres' somatosensory perception tests evaluating motion perception. 10 lines are intersecting each other on a 28X43 cm test form, for the right and left hand, in separate directions and of different lengths. The child's eyes were closed, and starting from the right hand, he/she was asked to move his/her index finger of the right hand from the starting point to the end point of every line. Afterward, the child's index finger was placed again at the starting point, and he/she was asked to repeat the movement. The difference in distance between the point where the child ended the movement and the endpoint of the real line was measured using a ruler and recorded. The total value for the right and left acquired was subtracted from 50 and recorded (20).

Statistical analysis

Statistical Package for the Social Sciences package program version 24.0 (SPSS Inc., Chicago, IL, USA was used in statistical analysis. As descriptive statistics, mean±standard deviation values were given for numerical variables, while number and percentage values were given for categorical variables. The conformity of the data to the normal distribution was tested by the Shaphiro-Wilk test, and the Kruskal-Wallis and Dunn's multiple comparison tests were carried out in comparing the non-normally distributed variables in three independent groups, and the one-way ANOVA and LSD multiple comparison tests were employed for the normally distributed variables in three independent groups. The chi-square test was conducted to test the correlation between categorical variables. The correlation between two continuous variables was assessed by Pearson's correlation coefficients. P-value <0.05 was accepted as statistically significant in all measurements.

RESULTS

The mean age of all children in the study (n=45) (hemiparetic (n=15), diparetic (n=15), and healthy control (n=15)) was 10.71±4.09. Of the children, 24 (53.3%) were male, and 21 (46.7%) were female. Upon comparing the demographic data of the children in the research, a significant difference was detected between the three groups concerning age, height, weight, and body mass index (BMI) ($p<0.05$). In the pairwise comparison of the groups, age, height, weight, and BMI values were revealed to be significantly higher in favor of the control group between the hemiparetic and control groups (p=0.032, p=0.002, p=0.002, p=0.020**,** respectively). Age, height, weight, and BMI values were determined to be significantly higher in favor of the diparetic group between the hemiparetic and diparetic groups (p=0.02, p=0.046, p=0.035, p=0.036**,** respectively). The diparetic and control groups were similar in terms of age, height, weight, and BMI ($p<0.05$) (Table 1).

The three groups were similar in terms of dominant extremity. However, a significant difference was identified between the groups with regard to GMFCS and MACS levels (p=0.001). The GMFCS and MACS levels of the diparetic group were revealed to be significantly lower than those of the hemiparetic and control groups (GMFCS p=0.001, p=0.001, respectively) (MACS p=0.001, p=0.001, respectively) (Table 2).

Upon comparing the somatosensory perception tests of the hemiparetic, diparetic, and control groups, a significant difference was determined between the groups in all sub-parameters ($p<0.05$). When the groups were compared in pairs, a significant difference was detected between the hemiparetic and control groups in favor of the control group in terms of

left-hand KIN, FR, and RLD values (p=0.023, p=0.049, p=0.028, respectively). Upon comparing the diparetic and control groups, a significant difference was observed in favor of the control group in all sub-parameters of the somatosensory perception test (p<0.05). However, no significant difference was revealed in any of the sub-parameters when the hemiparetic and diparetic groups were compared (p>0.05) (Table 3).

Upon comparing the proprioception of all groups, a significant difference was determined between the groups in all parameters except left elbow flexion (p<0.05). In the pairwise comparison of the groups, no significant difference was revealed in any parameter between the hemiparetic and control groups (p>0.05). When the diparetic and control groups were compared, a significant difference was identified in favor of the control group in all parameters except right-left elbow flexion (p<0.05). In the comparison of the hemiparetic and diparetic groups, a significant difference was observed in favor of the hemiparetic group in right-left shoulder abduction, right elbow flexion, right forearm supination, right forearm pronation, right-left wrist flexion, and left wrist extension (p=0.005, p=0.002, p=0.026, p=0.049, p=0.025, p=0.039, p=0.000, p=0.027, respectively) (Table 4).

When the JTHFT completion times were compared, a significant difference was determined between the three groups (p<0.01). The JTHFT test completion time of the control group for all sub-parameters was significantly lower compared to those of the hemiparetic and diparetic groups (p<0.01). In the pairwise comparison of the hemiparetic and diparetic groups, a difference was determined in favor of the hemiparetic group only in the parameters of putting 6 objects in the can with the right hand and displacing 5 full cans with the left hand, among the JTHFT sub-parameters (p=0.002, p=0.032) (Table 5).

DISCUSSION AND CONCLUSION

This study examined the impacts of somatosensory perception and proprioception on upper extremity functional skills in children with hemiparetic and diparetic CP and compared them to their healthy peers. It was determined that children with CP had lower somatosensory perception levels in their upper extremities and experienced proprioception losses in all joints of the upper extremities compared to their healthy peers. In terms of hand skills, it was revealed that children with CP were adversely affected in comparison with their healthy peers, and the hand skills of hemiparetic children were at a better level in some sub-parameters of the JTHFT in comparison with the diparetic group. Concerning somatosensory perception parameters, hemiparetic children were more impacted than their healthy peers in terms of only KIN, FR, and RLD. However, diparetic children were found to be more affected in all somatosensory perception levels than their healthy peers, whereas no difference was detected between the upper extremity somatosensory perception levels of hemiparetic and diparetic children. In terms of upper extremity proprioception, it was seen that children with CP were adversely affected in comparison with healthy children, but proprioception effects in all upper extremity joints of diparetic children were higher than those of hemiparetic children.

As a result of damage to the central nervous system, about 90% of children with CP have tactile and proprioceptive dysfunctions (21, 22). Upon reviewing studies on somatosensory perception, they are observed to focus on children with autism spectrum disorder, and studies on children with CP have not examined the impacts in terms of different clinical types (23, 24). Among the studies in the literature, the research by Megan et al. indicated that most children with hemiparetic CP had poor tactile perception, and as a result, functional disorders were observed (7). A study carried out by Sagner et al. on children with CP revealed that children with CP had poor tactile perception in comparison with the healthy group (9). Cooper et al. found that sensory loss in hemiparetic children was higher than in healthy children, which affected both body halves in hemiparetic children (22). Our study determined that the tactile perception levels of healthy children were better than children with CP in terms of upper extremity somatosensory perception sub-parameters. The results of healthy children in the KIN (left) FR, and RLD tests were better in comparison with hemiparetic children. The difference in kinesthesia on the left was associated with the lower number of children's left-dominant extremity preference.

These results suggested that hemiparetic children who could not recognize fingers and discriminate between right and left might have difficulties perceiving tactile stimuli. All somatosensory perceptions of children with diparetic CP were worse than those of the hemiparetic and control groups. As a result, it was concluded that children with CP perceived tactile stimuli less, and the tactile systems of children with diparetic CP were more impacted. Unlike the literature, this situation demonstrated the importance of conducting upper extremity somatosensory perception tests in clinics for children with diparetic CP in terms of forming evaluation and treatment programs.

Kinesthesia disorder was more common in children with CP (25). Another study using the Ayres kinesthesia test researched the impacts of dance therapy on praxis in children with dyslexia. Dance was found to be significant in the perception of kinesthesia (26). In the present research, it was found that children with CP had worse kinesthetic sense than healthy children. The kinesthetic sense was most affected in the diparetic group. The above-mentioned findings are in line with the literature in that they demonstrate certain levels of kinesthetic losses in different clinical types in children with CP. Evaluation of the upper extremity kinesthetic sense in children with CP of different clinical types will contribute to inadequate studies in the literature.

Studies have shown that children with CP experience losses in proprioception, stereognosis, tactile sense, and two-point discrimination compared to healthy individuals (7, 25). In a study evaluating the proprioception of the upper extremity in children with hemiparetic CP and healthy children, Lewis et al. concluded that children with hemiparetic CP had worse proprioceptive sense than healthy children (27). Duque et al. assessed and compared the senses of pressure, proprioception, and stereognosis in the upper extremity between congenital hemiparetic children and their peers. In conclusion, they reported that pressure, proprioceptive, and stereognosis senses were affected in hemiparetic children (28). Other studies examined elbow proprioception in the goal-directed target-matching task of children with hemiparetic CP and concluded that they made more matching errors in the arm on the affected side (29). In their study carried out with children with CP and healthy children, Hoon et al. found that children with CP experienced losses in their tactile sense and proprioception (30). Our study in which we evaluated proprioception in the upper extremities revealed that healthy children had better proprioception than children with CP, similar to the literature. It was observed that upper extremity proprioception was affected more in children with diparetic CP compared to hemiparetic children. Our study determined that children with hemiparetic CP had better levels of proprioceptive senses in many joints of the upper extremity than healthy children. This is thought to originate from the fact that the dominant hand of hemiparetic children is mostly on the right side and their MACS and GMFCS levels are high. Our study results also differ from the literature in that hemiparetic children, in case of high functional levels and hand skills, can reach proprioception levels similar to their healthy peers when using their dominant hand.

Upper extremity problems in children with CP are among the most important things that adversely affect daily life (13). In children with CP who have deficiencies in hand skills, difficulties are observed in activities requiring the use of both hands when the clinical picture is accompanied by functional and sensory losses in the upper extremity and various postural disorders (31). Accordingly, we think it is important to investigate upper extremity functional skills, somatosensory perception tests, and upper extremity proprioception in children with CP. Identifying deficiencies that affect upper extremity dysfunction with these evaluations may contribute to the rehabilitation programs of pediatric physiotherapists clinically.

Hand functions consisting of gross and fine motor skills are important for a person's independence in ADL. Furthermore, cognitive, motor, and sensory losses adversely affect independence in daily life. Upper extremity involvement is observed in all clinical types, regardless of the clinical type, severity, or distribution of CP. In addition to combined reactions in hemiparetic CP, conditions such as loss of upper extremity function, decreased movement quality, and a slowdown in movement, can be observed, especially with hand-wrist problems (32). In diparetic CP, deficiencies in fine motor skills and decreased en-

durance are observed in the upper extremities. This adversely affects functionality by revealing abnormal movement patterns in the child. Although children with diparetic and hemiparetic CP have similar upper extremity tone levels, children with hemiparetic CP have slightly more severe deformities and relatively worse motor control than the diparetic group (33). In the literature, it was seen that the proximal regions were usually included in studies evaluating upper extremity skills, and the clinical types of children with CP were mostly spastic hemiparetic children in these studies (29). Studies investigating the functional skills of children with diparetic CP are rare (34). Our study found that the functional skills of children with CP were worse compared to their healthy peers. However, it was observed that children with hemiparetic and diparetic CP did not differ in terms of functional hand skills. The reason for this is thought to be due to the high number of children in the hemiparetic group with better functional levels according to MACS and GMFCS. This demonstrated that children with CP experienced losses of hand skills, independent of clinical type, tone, and deformities. These results indicate that diparetic children should also be evaluated in terms of hand skills.

The study by Elbasan et al. compared children with diparetic CP and their healthy peers and evaluated the independence levels and functional hand skills of these children in daily life. It was observed that children with CP were adversely affected in comparison with the control group in all evaluation parameters (34). Another study evaluated the hand skills of children with hemiparetic CP and healthy peers by the JTHFT. As a result, it was found that the functions and physical properties of hemiparetic CP on the affected side were worse compared to the dominant side of the healthy group in the same age group. In another study assessing hand function in the literature, the JTHFT was used in children with hemiparetic and quadriparetic CP, similar to our study. This study revealed that the hand function of those with hemiparetic CP was better than those with quadriparetic CP, except for the writing parameter, and they completed the tests faster (35). In our study, it was concluded that the hand skills of children with CP were adversely affected compared to their healthy peers, but the hand skills of the diparetic and hemiparetic groups did not differ. In this respect, our results demonstrated the importance of evaluating hand skills not only in the spastic hemiparetic and quadriparetic groups but also in individuals with spastic diparetic CP. It was seen that children with diparetic CP were slower than hemiparetic children in the JTHFT sub-parameter of throwing small objects with the right hand and displacing 5 full cans (left). As a result, it was determined that children with hemiparetic and diparetic CP completed the JTHFT more slowly and in a longer time in comparison with healthy children. Hence, it was concluded that the hand skills of both CP groups were adversely affected compared to their healthy peers (34). In this respect, the results of our study also support the literature, showing that hand skills should be considered important in diparetic children with bilateral spastic involvement as well as in spastic hemiparetic children.

This study suggested that the group with more proprioception involvement had a longer JTHFT time and proprioceptive losses in children with diparetic CP caused a longer JTHFT time. It was found that the JTHFT completion times were shorter since the control group had better proprioception than children with CP. Better proprioception in the hemiparetic group compared to the diparetic group resulted in shorter JTHFT times of the hemiparetic group than the diparetic group. Based on the obtained results, it can be interpreted that proprioception affects hand skills, and the weak proprioception on the affected side in children with CP causes them to not use their hands actively, leading to the decreased quality of movement and a prolongation of its duration. All sensory systems, such as proprioception and somatosensory perception, interact with each other in children with CP. Hence, we think that sensory systems, also including hand functionality in the upper extremity, are impacted, which is an element that should be considered in the evaluation. According to these results, we think that somatosensory perception and proprioception affect functional skills in the upper extremities, and the current study will contribute to the literature in this respect.

This study's limitation is that proprioception measurements were performed using only a goniometer. It has been suggested that the use of advanced pro-

prioceptive measurements such as isokinetic devices in children with CP may yield more objective results. Furthermore, in terms of somatosensory perception tests, detailed evaluations such as the SIPT are recommended to be carried out in children with CP of different clinical types with a higher population in further research. Another limitation of our study is that since the children participating in the study were generally young, the SIPT assessments were done with their eyes closed, and their focusing time was short. Therefore, it is suggested that the test interval time can be extended in future research. In addition, there was a significant difference between the MACS levels of children with CP in this study. However, we believe that the inclusion of homogeneous groups of children with CP with similar MACS levels in further studies may yield more reliable results.

The current study demonstrated that children with CP had lower somatosensory perception levels in their upper extremities than their healthy peers and proprioception losses were observed in all joints of the upper extremity. It was observed that the somatosensory perceptions of hemiparetic children were lower compared to their healthy peers. However, it was revealed that diparetic children were impacted more than their healthy peers in all somatosensory perception levels, whereas there was no difference between the upper extremity somatosensory perception levels of hemiparetic and diparetic children. It was found that children with CP had proprioceptive losses in the upper extremity compared to healthy children, but proprioceptive losses in all upper extremity joints of diparetic children were higher than those of hemiparetic children. The hand skills of children with CP were lower than those of their healthy peers, and hemiparetic children were at a better level in some parameters compared to the diparetic group. It was revealed that the proprioception and somatosensory perception disorders of children with CP adversely affected their hand activities in daily life, and it was also important to evaluate their somatosensory perception levels to increase the level of independence in upper extremity hand functions. Also, this study revealed that more research about somatosensorial and proprioseptive therapy models like sensory integration therapies in children with cerebral palsy should be investigated.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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Miyop hastalarda sikloplejinin korneal keratometrik ölçümlere etkisi

Effect of cycloplegia on corneal keratometric measurements in myopic patients

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Öz

Amaç: Bu çalışmanın amacı oftalmolojik muayenede sikloplejik-midriyatik olarak kullanılan %1 siklopentolat hidroklorür damlanın korneal keratometrik değerlere etkisini araştırmak, siklopleji-midriazis sonrası ölçülen keratometrik değerlerin refraktif cerrahi ve biyometrik hesaplamalarda kullanılıp kullanılamayacağını ortaya koymaktır.

Yöntemler: Kesitsel prospektif planlanan çalışmaya, Ocak 2022-Nisan 2023 tarihleri arasında rutin göz muayenesi için polikliniğe başvuran sağlıklı erişkin 110 hastanın sağ gözü dâhil edildi. Standart otorefraktokeratometreyle (Topcon KR 8100) ölçülen korneal keratometrik veriler (K1, K1mm, K1 aks, K2, K2mm, K2 aks, K ortalama, korneal astigmatik değer) %1 siklopentolat hidroklorür 3 defa damlatıldıktan 45 dakika sonra elde edilen siklopleji sonrasındaki keratometrik ölçümlerle karşılaştırıldı.

Bulgular: Olguların medyan yaşı 25 (minimum 18-maksimum 40 yıl) idi. Cinsiyet dağılımı eşitti. Olguların siklopleji öncesi ölçülen K1, K1mm, K1 aks, K2, K2mm, K2 aks, K ortalama, korneal astigmatik değerlerinde siklopleji-midriyazis sonrasında istatiksel olarak anlamlı fark saptanmadı (p>0,05).

Sonuç: Sağlıklı erişkin bireylerde korneal keratometrik değerler %1 siklopentolat ile oluşturulan siklopleji-midriyazisten etkilenmemektedir.

Anahtar Sözcükler: Astigmatizm, kornea, midriyaz, siklopentolat, siklopleji

Abstract

Aim: The purpose of this study was to investigate the effect of 1% cyclopentolate hydrochloride drops used as cycloplegic-mydriatic in ophthalmologic examination on corneal keratometric values and to determine whether keratometric values measured after cycloplegia-mydriasis can be used in refractive surgery and biometric calculations.

Methods: The cross-sectional prospective study included the right eye of 110 healthy adult patients who presented to the outpatient clinic for routine ophthalmologic examination between January 2022 and April 2023. Corneal keratometric data (K1, K1mm, K1 axis, K2, K2mm, K2 axis, K mean, corneal astigmatic value) measured with a standard autorefractokeratometer (Topcon KR 8100) were compared with keratometric measurements after cycloplegia obtained 45 minutes after 3 instillations of 1% cyclopentolate hydrochloride.

Results: The median age of the patients was 25 years (minimum 18-maximum 40 years). Gender distribution was equal. There were no statistically significant differences in corneal keratometric values (K1, K1mm, K1 axis, K2, K2mm, K2 axis, K mean, corneal astigmatic value) before and after induction of cycloplegia (p>0.05).

Conclusion: Corneal keratometric values are not affected by cycloplegia-mydriasis induced by 1% cyclopentolate in healthy adult subjects.

Keywords: Astigmatism, cyclopentolate, cycloplegia, cornea, mydriasis

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GİRİŞ

Sikloplejik ajanlar günümüz oftalmoloji pratiğinde; akomodasyonun engellenmek istendiği refraksiyon muayenelerinde, intraoküler inflamasyonlarda (üveit, endoftalmi) iris sifinkterinin gevşetilerek (midriyazis) posterior sineşilerin önlenmesinde, kornea ülserlerinde siliyer spazma bağlı ağrının giderilmesinde ve kuvvetli pupil dilatasyonunun istendiği intraoküler cerrahiler öncesinde sıklıkla kullanılırlar. Muskarinik asetil kolin reseptörlerine bağlanarak parasempatolitik etkiyle sifinkter pupilla kasını ve siliyer adaleyi felç ederek etki gösterirler. Refraksiyon muayenesi esnasında kullanıldığında latent kırma kusurlarının manifest hale geçmesini sağlarlar. Bu sebepten ötürü refraktif kusurların saptanmasında akomodasyon spazmının engellenmesi için sikloplejik ajanların kullanılması kritik öneme sahiptir (1-3). Günümüzde sikloplejik-midriyatik etki elde etmek için topikal olarak kullanılan antimuskarinik (antikolinerjik) beş adet ajan bulunmaktadır. Bunlar; homatropin hidrobromid, skopolamin hidrobromid, atropin sülfat, siklopentolat hidroklorid ve tropikamiddir. Atropin, sikloplejik ajan olarak her ne kadar altın standart olarak kabul edilse de etkisinin yavaş başlaması, uzun sürmesi, sistemik ve lokal yan etkilerinin daha sık olması nedeniyle yerini tropikamid ve siklopentolata bırakmıştır (4). Siklopentolat ise tropikamide göre daha kuvvetli ve uzun süreli sikloplejı ve midriazis sağlar (5).

Sentetik antikolinerjik bir ajan olan siklopentolat hidroklorür 1950'li yılların başında kullanıma sunulmuştur (6,7). Lokal ve sistemik yan etkilerinin atropine göre daha az olması, etkisinin hızlı başlaması sebebiyle oküler parasempatolitik etki arzu edilen durumlarda atropine alternatif olmuş ve günümüzde göz polikliniklerinde kullanılan temel sikloplejik ajan haline gelmiştir (8). Dünyada %0,5-1-2'lik dozları mevcutken ülkemizde yalnızca %1'lik ticari preparatı (Sikloplejin®, Abdi İbrahim İlaç San, İstanbul) bulunur. Sikloplejik etkisi damlatıldıktan 25-75 dk sonra başlar ve etkisi 6-24 saat içinde son bulur (9). Sikloplejik refraksiyon muayenesinde standart protokol olarak bir ya da iki damla %0,5 veya %1'lik solüsyonu damlatıldıktan 30 ile 60 dk sonra ölçüm yapılması önerilmektedir (10). Siklopentolatın oküler yan etkileri iritasyon, sulanma, alerjik blefarokonjonktivit, konjonktival hiperemi, artmış göz içi basıncı iken, sistemik yan etkileri ise uyuşukluk, ataksi, oryantasyon bozukluğu, tutarsız konuşma, huzursuzluk ve görsel halüsinasyonlardır. Prematüre bebeklerde karında distansiyon ve nekrotizan enterokolit de bildirilmiştir (11-13).

Keratometri kornea kurvatürünün ölçülmesidir. Kornea sağlığının göstergelerinden biri olarak kabul edilir. En doğru ve kesin keratometrik ölçümler keratokonus gibi ektazik hastalıkların saptanmasında, refraktif cerrahi uygulamalarında, kontakt lens pratiğinde ve katarakt cerrahisi öncesinde göz içi merceğinin gücünün hesaplanmasında vazgeçilmez değere sahiptir. Astigmatizmanın korneal ya da lentiküler kaynaklı olup olmadığının ortaya konulmasında, korneanın en dik ve en düz aksının belirlenmesinde korneal keratometrik ölçümler mutlaka yapılmalıdır. Meridyenler arası anormal keratometrik farklılık korneal astigmatizmaya yol açarak ciddi ametropi yaratıp erken yaşlardan itibaren ambliyopinin bir sebebi olabilir (14-17). Keratometri ölçümünde altın standart yöntem manuel yöntem olan Javal keratometresi olarak kabul edilmekle birlikte günümüzde daha çok dijital cihazlar; otorefraktokeratometre, korneal topografi/tomografi cihazları ve biyometri cihazları kullanılmaktadır. Bu çeşitli cihazların Javal keratometrisiyle benzer sonuçlar verdiği gösterilmiştir (18).

Bu çalışmanın amacı %1 siklopentolat kullanılarak yapılan sikloplejı sonrası elde edilen keratometrik değerlerin sikloplejı öncesi yapılan ölçümlerle karşılaştırmak ve böylece sikloplejı sonrasında ölçülen korneal keratometrik verilerin refraktif cerrahi ve biyometrik hesaplamalarda kullanılıp kullanılamayacağını ortaya koymaktır.

GEREÇ VE YÖNTEMLER

Ocak 2022-Nisan 2023 tarihleri arasında rutin göz muayenesi veya gözlük talebiyle polikliniğimize başvuran, sikloplejik muayenesi yapılmış, 18-40 yaş arası 110 hastanın (55 erkek, 55 kadın) sağ gözünün tıbbi kayıtları çalışmaya dâhil edildi. Çalışma için Helsinki Deklarasyonu çerçevesinde Ondokuz Mayıs Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan izin alındı (tarih 11.05.2023, karar no:2023/159). Daha önce herhangi bir göz cerrahisi (katarakt, refraktif, pterjium, glokom, vitrektomi vb) geçirenler, herhangi bir

Tablo 1. Olguların siklopleji öncesi ve sonrası keratometrik verileri ve p değerleri

Keratometrik değer	Siklopleji öncesi	Siklopleji sonrası	p
	Medyan (min-maks)	Medyan (min-maks)	
K1(D)	43,12 (40,25-46,50)	43,25 (40,25-46)	0,679*
K1(mm)	7,83 (7,26-8,38)	7,82 (7,32-8,38)	0,984*
K1 (aks)	160 (5-180)	160 (5-180)	0,359*
K2 (D)	44,24 (41,25-47)	44,25 (41,25-46,75)	0,733*
K2 (mm)	7,64 (7,18-8,17)	7,62 (7,22-8,17)	0,247*
K2 (aks)	85 (5-180)	85 (5-180)	0,888*
K (ort)-D	43,75 (41,13-46,75)	43,87 (40,75-46,38)	0,925*
Astig K-D	0,75 (0-4,75)	0,75 (0-4,75)	0,751*

D: Diyoptri, mm: Milimetre, min: Minimum, maks: Maksimum, K1: Düz keratometri, K2: Dik keratometri, Astig K: Korneal astigmatizma, *Wilcoxon testi, ort: ortalama

edinsel ya da kalıtsal korneal patolojiye sahip olanlar, siklopentolat alerjisi öyküsü olanlar, aktif keratit ya da konjonktivit olanlar, korneal skar, nistagmus ya da albinizmi olanlar, hipermetrop olanlar, ölçümleri etkileyebilecek her türlü korneal, lentiküler, vitreus ya da retinal patolojisi olanların tıbbi kayıtları çalışmadan dışlandı. Snellen eşeliyle ölçülen görme keskinliği 1,0 tam olan, miyop ve/veya astigmat kırma kusuruna sahip gözler çalışmaya dâhil edildi.

Tüm hastalara öncelikle refraksiyon muayenesi daha sonrasında ön segment ve fundus muayenesini içeren tam bir oftalmolojik muayene yapıldı. Sikloplejik muayene için olgulara 5 dk ara ile 3 kez %1 siklopentolat (Sikloplejin®, Abdi İbrahim İlaç Sanayi ve Ticaret AŞ, Türkiye) damlatıldı. 45 dk sonra keratometrik ölçümler aynı hekim tarafından tekrarlandı. Topcon KR 8100 (Tokyo, Japonya) otorefraktometre ile ölçülen keratometrik değerler (en düz-K1 ve en dik-K2 korneal kırıcılık diyoptrisi, korneal eğrilik yarıçapları, korneal eğrilik aksları, ortalama keratometri, korneal astigmatizm) siklopleji öncesi ve sonrası birbirleriyle karşılaştırıldı. Ortalama keratometrik değer (K ort) ve korneal astigmatizma (Astig K) hesaplamasında aşağıdaki formüller kullanıldı.

Ortalama Keratometrik Değer = (K1+K2)/2

Korneal Astigmatizma=K2-K1

Siklopleji sonrası ölçülen keratometrik değerlerden siklopleji öncesi değerlerin çıkartılmasıyla elde edilen delta (Δ) değerlerinin sferik ekuvalanla korelasyonu da değerlendirildi.

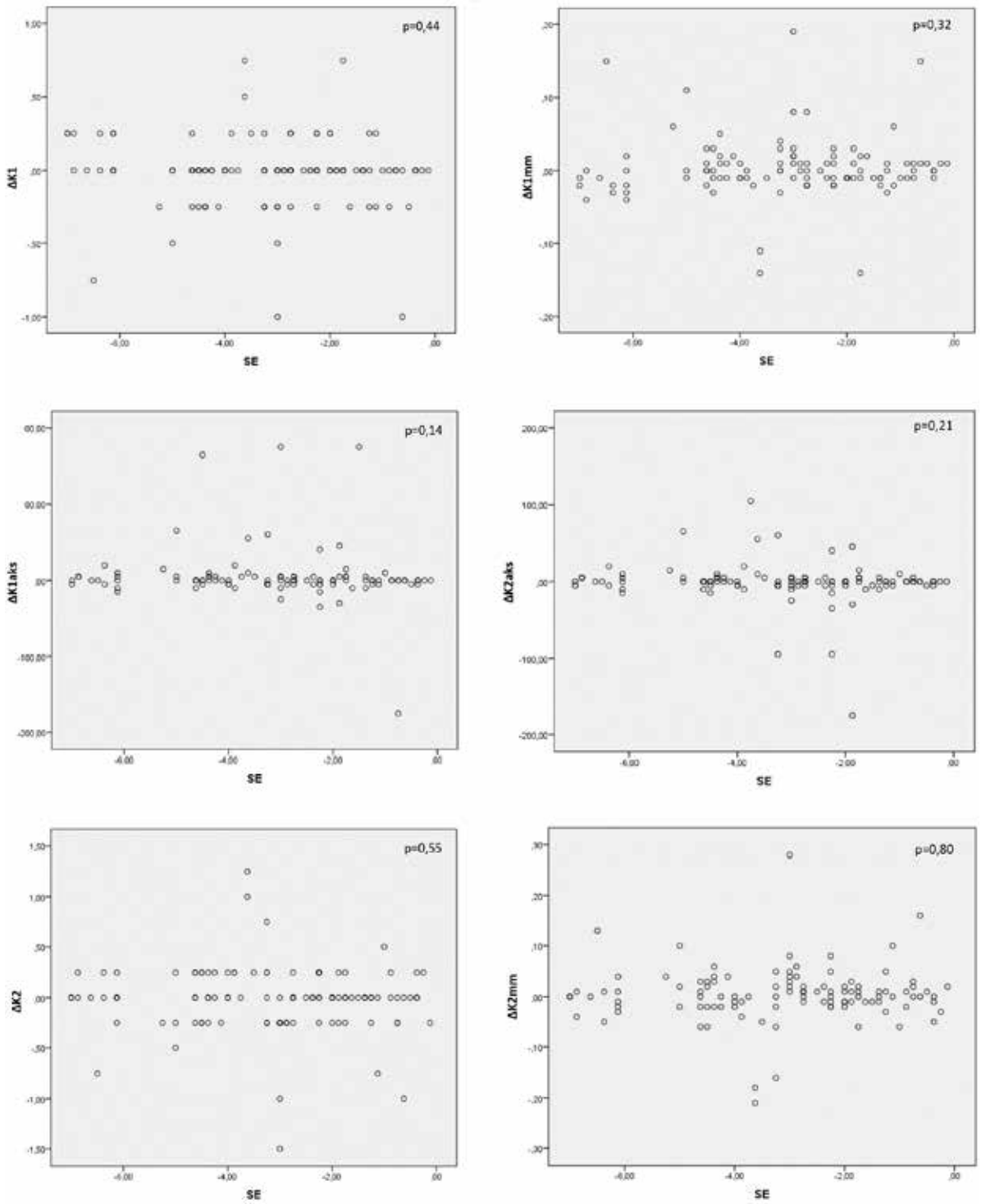
İstatistiksel analiz

Verilerin istatistiksel değerlendirmesinde SPSS (Statistical Package for the Social Sciences software for Windows, version 22.0, IBM, Chicago, IL, USA) bilgisayar paket programı kullanılmıştır. Öncelikle verilerin normal dağılım gösterip göstermediği Kolmogorov-Smirnov testi ile analiz edildi. Normal dağılım gösteren sürekli değişkenler ortalama ± standard sapma, göstermeyenler medyan (minimum-maksimum) olarak, kategorik veriler sayı ve yüzde olarak ifade edildi. Siklopleji öncesi ve sonrası ölçülen verilerin eşit dağılmadığının görülmesi üzerine data Wilcoxon testi ile analiz edildi. Değişkenler arasında korelasyon olup olmadığına Spearman korelasyon analizi ile bakıldı. Tüm analizlerde $p<0,05$ değeri istatistiksel olarak anlamlı kabul edildi.

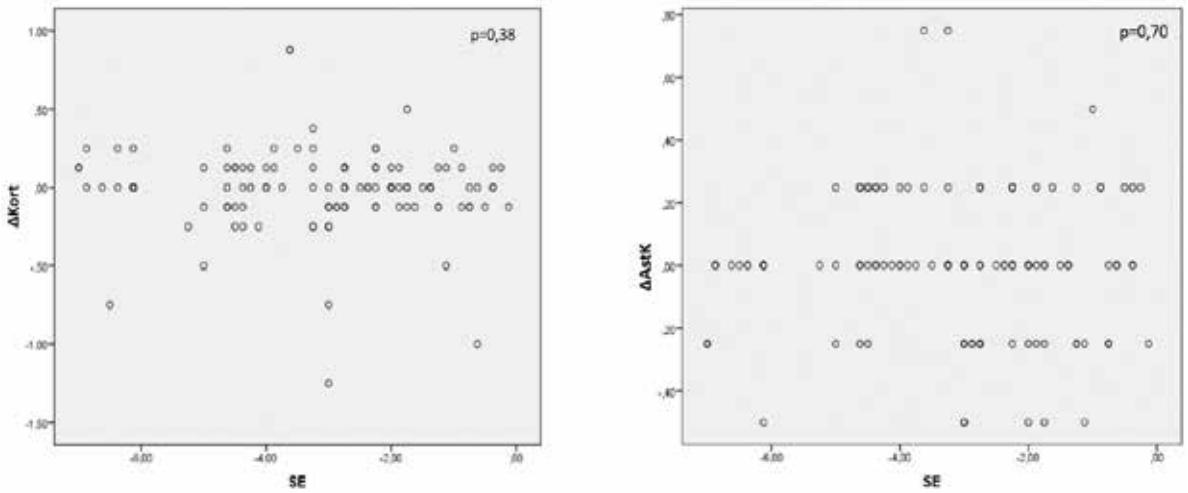
BULGULAR

Çalışmaya dâhil edilen 110 olgunun medyan yaşı 25 yıl idi. Cinsiyet dağılımı eşitti. Olguların kırma kusurlarının sferik ekuvalanı medyan -2,93 diyoptri (D) (min -7,00 maks -0,12 D) idi. Siklopleji öncesi medyan K1 değerleri 43,12 (D), 7,83 mm, aks 160 derece; medyan K2 değerleri ise 44,24 D, 7,64 mm, aks 90 derece, medyan ortalama keratometrik değer K(ort) 43,75 D, medyan korneal astigmatizma (Astig K) 0,75 D olarak saptandı.

Siklopleji sonrası medyan K1 değerleri 43,25 D, 7,82 mm, aks 160 derece; medyan K2 değerleri 44,25 D, 7,62 mm, aks 85 derece, medyan ortalama kerato-



Resim 1. Siklopleji öncesi ve sonrası ölçülen keratometrik verilerin farkının sferik ekuvalanla korelasyonu



Resim 2. Siklopleji öncesi ve sonrası ölçülen keratometrik verilerin farkının sferik ekuvalanla korelasyonu

metrik değer K (ort) 43,87 D, medyan korneal astigmatizma (Astig K) 0,75 D olarak ölçüldü. Siklopleji öncesi ve sonrası tüm keratometrik değerler Tablo 1'de özetlendi.

Siklopleji öncesi ve sonrası ölçülen keratometrik değerlerde; K1(D), K1 (mm), K1 (aks), K2 (D), K2 (mm), K2 (aks), K (ort), Astig K istatistiksel olarak anlamlı fark saptanmadı. Tüm p değerleri Tablo 1'de özetlendi.

Siklopleji sonrası elde edilen keratometrik değerlerden, siklopleji öncesi değerlerin çıkartılmasıyla elde edilen delta (Δ) değerlerle (ΔK1, ΔK1mm, ΔK1aks, ΔK2, ΔK2mm, ΔK2aks, ΔKort, Δ Astig K) sferik ekuvalan arasında herhangi bir korelasyon olmadığı saptandı. Tüm p değerleri Resim 1 ve 2'deki grafiklerde gösterildi.

TARTIŞMA VE SONUÇ

Gözün toplam kırıcılık gücünün üçte ikisi kornea tarafından sağlanmaktadır. Korneanın kırıcılık gücünün ve kurvatürünün ölçülmesine ise keratometri denilmektedir. Korneal keratometrik verilerin en doğru şekilde ölçülmesi, korneal astigmatizmanın değerlendirilmesinde, korneal ektazik hastalıkların tanısında, refraktif cerrahi planlamasında, kontakt lens uygulamalarında ve katarakt cerrahisi öncesi göz içi merceğin gücünün hesaplanmasında vazgeçilmez öneme sahiptir.

Bu çalışmada, sağlıklı erişkin olgu popülasyonunda 110 olgunun 110 sağ gözünde standart otorefraktokeratometreyle ölçülen korneal keratometrik değerlerin, %1 siklopentolat hidroklorür damlayla oluşturulan siklopleji-midriyazis sonrasında istatistiksel olarak anlamlı değişim göstermediği saptandı.

Saitoh ve ark. 28 hastanın 28 gözünde (yaş ortalaması 31,1±5,6 yıl) Orbscan topografi cihazıyla, midriyazis ve miyozisin korneanın ön ve arka yüzüne etkilerini araştırmışlardır (19). Tropikamid-fenilefrin kombinasyonuyla elde ettikleri siklopleji-midriyazis sonrasında, korneanın ön ve arka yüzünün düzleştiğini, pilokarpin kullanarak oluşturdukları miyozis sonrasında ise kornea ön ve arka yüzünün dikleştiğini saptamışlardır. Ortalama aksiyel keratometrik gücün ise midriyazisten etkilenmediğini bildirmişlerdir (19). Mevcut çalışmada korneal eğrilik yarıçapının midriyazisten etkilenmemesi Saitoh ve ark.'ın çalışmasıyla karşıtlık oluştururken ortalama aksiyel keratometrik gücün değişmemesi ise benzerlik göstermektedir. Bu karşıtlık, Saitoh ve ark.'ın standart otorefraktometre yerine topografi cihazı tercih etmiş olmalarından, farklı midriyatikler kullanmalarından ve çalışmalarındaki olgu sayısının düşük olmasından kaynaklanmış olabilir. Cheng ve ark. ise çalışmalarında yaş ortalaması 9,1±2,8 yıl olan 114 pediatrik hastanın 114 sağ gözünde, parsiyel optik koherent interferometre (IOL Master, Carl Zeiss, Jena Almanya) cihazıyla tropikamid ile elde edilen siklopleji nin refraktif ölçümlere ve biyometrik değerlere olan etkisini araştırmışlardır (20). Tropikamid kullanımıyla sağlanan siklopleji-midriyazis sonrasında ortalama, minimum ve maksimum

keratometrik değerlerde anlamlı düşüş saptamışlar, korneanın siklopleji sonrası siliyer kasların gevşemesiyle daha düz bir hal aldığını belirtmişlerdir. Maksimum keratometrik değerden minimum keratometrik değeri çıkartarak hesapladıkları korneal astigmatizma değerinin ise sikloplejiden etkilenmediğinin altını çizmişlerdir. Maksimum ve minimum keratometrik değerlerde düşüş bulmaları mevcut çalışmanın sonuçlarıyla karşıtlık oluşturmaktadır. Bu farklılık Cheng ve ark.,'ın olgu popülasyonunun pediatrik yaş grubundan seçilmesinden, siklopentolat yerine tropikamid tercih edilmesinden ve bu yaş grubunda sklera ve korneanın daha elastik bir yapısının olmasından kaynaklandığını düşündürmektedir. Bir diğer sebep ise mevcut çalışmada kullanılan standart otorefraktometre yerine IOL Master biyometri cihazı kullanmalarından olabilir. Pediatrik olgu popülasyonundaki bir diğer çalışmada (8,5±2,1 yıl) Ho ve ark. %0,125 atropin ile oluşturulan sikloplejinin oküler parametrelere olan etkisini irdelemiş standart otorefraktokeratometre kullanarak (Topcon KR-8800, Tokyo, Japonya) ölçülen ortalama keratometrik değerlerin sikloplejiden etkilenmediğini rapor etmişlerdir. Pediatrik popülasyonda atropin ile standart otorefraktokeratometre kullanılarak yapılan bu çalışma, erişkinlerde %1 siklopentolat ve standart otorefraktokeratometreyle yapılan mevcut çalışmayla benzer sonuçlar bildirirken, Cheng ve ark.'ın yine benzer yaş grubunda tropikamid ve IOL Master kullanarak yaptıkları çalışmanın sonuçlarıyla ters düşmektedir. Benzer pediatrik yaş grubunda (9,20±1,65 yıl), Hashemi ve ark. %1 siklopentolat ve Allegro Biograph (WaveLight AG, Erlangen, Almanya) biyometri cihazıyla yaptıkları çalışmada ise ortalama korneal keratometrik değerin sikloplejiden etkilenmediğini belirtmişlerdir (22). Erişkinlerde optik düşük koherent reflektometre biyometri cihazıyla (Lenstar LS 900, Haag-Streit AG, Koeniz, İsviçre) farklı iki sikloplejik-midriyatik ajanın (%1 siklopentolat - %0,5 tropikamid) ön segment parametrelerine ve göz içi mercek hesaplamalarına olan etkilerini araştırdıkları çalışmalarında Taşçı ve ark. her iki midriyatik-sikloplejik ajanın maksimum ve minimum keratometrik değerleri etkilemediği sonucuna ulaşmışlardır (23). Erişkinlerde ikili Scheimpflug kamera sistemi içeren Galilei cihazıyla (Ziemer, Zurih, İsviçre) %1 siklopentolat kullanarak yaptıkları çalışmada Bagheri ve ark. da Taşcı ve ark.'ın paralelinde, korneal astigmatizmanın sikloplejiden etkilenmediğini rapor etmişlerdir (24). Megwas ve ark. erişkin popülasyonda, Javal keratometrisiyle elde ettikleri korneal ortalama eğrilik yarıçapının %1 siklopentolat kullanımı sonrası 30-60 ve 90. dakikada etkilemediğini göstermişlerdir (25).

Literatürdeki çalışmaların birbirleriyle farklı ya da benzer sonuçlar bildirmesi, kullanılan sikloplejik ajanların ve keratometri cihazlarının farklı olmasından, çalışma popülasyonlarının yaş aralıklarının değişmesinden kaynaklanmış olabilir.

Sonuç olarak bu çalışmada göz hastalıkları polikliniklerinde en yaygın kullanılan midriyatik-sikloplejiklerden biri olan %1 siklopentolat hidroklorürün, yine refraktif muayenede ve keratometrik ölçümlerde en sık kullandığımız cihazlardan biri olan standart otorefraktokeratometrenin korneal keratometrik verilerini sağlıklı erişkinlerde etkilemediği saptandı. Mevcut çalışmanın farklı yaş grupları ve daha geniş serilerle teyit edilmesi literatüre daha fazla katkı sağlayacaktır.

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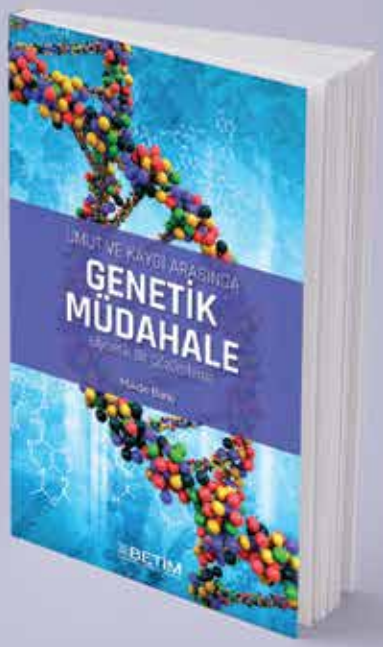

UMUT VE KAYGI ARASINDA

GENETİK MÜDAHALE

Biyoetik Bir Çözümleme

Maide Barış

Dünyadaki biyoetik literatürü genetik müdahale konusundaki tartışmalar bağlamında her geçen gün daha da zenginleşirken, Türkçe olarak yapılmış çalışmaların sayısı oldukça kısıtlıdır. Bu çalışma soy hattına yönelik genetik müdahalenin kategorik bir şekilde ahlaken yanlış olarak değerlendirilip değerlendirilemeyeceğine ilişkin kapsamlı bir tartışma yürütmektedir. CRISPR/Cas9 teknolojisinin geliştirilmesi ile birlikte pratik olarak mümkün hale gelen soy hattına yönelik genetik müdahaleler, laboratuvar dışına çıkmak (ve kliniğe doğru ilerlemek) için son hazırlıklarını tamamlamaktadır. Elinizdeki bu kitapta, tüm insanlığı ve gelecek nesilleri etkileme potansiyeli bulunan ve hem umut hem de kaygı kaynağı addedilen soy hattına yönelik genetik müdahale teknolojisi, dünya ile eş zamanlı olarak detaylı bir şekilde ele alınarak biyoetik bir analiz gerçekleştirilmiştir.

BETİM KİTAPLIĞI

The effect of acute and chronic harmaline administration on penicillin-induced epileptiform activity in rats

Sıçanlarda akut ve kronik uygulanan harmalinin penisilin ile oluşturulmuş epileptiform aktivite üzerine etkisi

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Abstract

Aim: Harmaline (HR) is a monoamine oxidase inhibitor (MAOi) and antioxidant alkaloid obtained from Banisteriopsis caapi and Peganum harmala, where experimental studies have been conducted to support modern medicine. The electrophysiological impact of short-term and long-term HR treatment on the penicillin G-induced epileptic model in rats was examined in this study.

Methods: Eighty-four adult male Wistar rats were randomly assigned to two groups: one received a single dose/day of HR, and the other received repeated doses/days of HR. Each group was further divided into six subgroups based on the dose of HR (10, 50, and 100 mg/kg). Epileptiform activity (EA) was triggered in the experimental groups with intracortical penicillin administration. Electrophysiological data were collected and analyzed using electrocorticography (ECoG). The serum levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GR) were measured using the Enzyme-Linked Immuno Sorbent Assay (ELISA) method to assess the free radical scavenger effects of HR. The latency, frequency, and amplitude of EA waves and serum antioxidant marker levels were analyzed statistically.

Results: There was no observed EA in the sham group. Nevertheless, the results showed that both acute and chronic HR treatment increased the seizure threshold dose-dependently ($p<0.05$). It was observed that the acute HR group reduced the frequency and amplitude of spike-wave discharges up to the 10th period, compared to the control and other groups, and did not affect these parameters in the remaining periods. No significant difference was observed in the chronic groups in terms of spike wave frequency and spike-wave amplitude, except for some time periods. In addition, while there was a significant increase in antioxidant enzyme levels of the chronic HR group compared to the control and other groups ($P<0.05$), there was no significant difference in the acute groups.

Conclusion: It was observed that HR did not affect spike wave frequencies and amplitudes in all acute groups, except for the 10th period and in chronic HR groups. HR prolonged the latency to first EA onset in acute and chronic groups and may have an antioxidant effect with long-term use.

Keywords: Antioxidants; electrocorticography; epilepsy; harmaline; monoamine oxidase

Öz

Amaç: Harmalin (HR), modern tıbbı desteklemek amacıyla deneysel çalışmaların yapıldığı Banisteriopsis caapi ve Peganum harmala bitkilerinden elde edilen, monoamin oksidaz inhibitörü (MAOi) ve antioksidan bir alkaloiddir. Bu çalışmada kısa süreli ve uzun süreli HR tedavisinin sıçanlarda penisilin G ile indüklenen epileptik model üzerindeki elektrofizyolojik etkisi incelenmiştir.

Yöntemler: Seksen dört yetişkin erkek Wistar sıçan rastgele iki gruba ayrıldı. Akut gruba tek doz/gün HR, kronik gruba tekrarlayan doz/gün HR verildi. Her grup ayrıca HR (10, 50 ve100 mg/kg) dozuna göre altı alt gruba ayrıldı. İntrakortikal penisilin uygulamasıyla deney gruplarında epileptiform aktivite (EA) tetiklendi. Elektrofizyolojik veriler, elektrokortikografi (ECoG) kullanılarak izlendi ve analiz edildi. HR'nin serbest radikal temizleyici etkilerini değerlendirmek için süperoksit dismutaz (SOD), katalaz (CAT), glutatyon peroksidaz (GPx) ve glutatyon redüktazın (GR) serum seviyeleri Enzim Bağlı İmmüno-Sorbent testi (ELISA) yöntemi kullanılarak ölçüldü. EA dalgalarının latensi, frekansı ve amplitüdü ile serum antioksidan belirteç düzeyleri istatistiksel olarak analiz edildi.

Bulgular: Sham grubunda EA görülmedi. Ancak sonuçlar hem akut hem de kronik HR tedavisinin nöbet eşiğini doza bağlı olarak arttırdığını gösterdi ($p<0.05$). Akut HR grubu kontrol ve diğer gruplarla karşılaştırıldığında diken dalga deşarjlarının sıklığı ve genliğinde 10. periyoda kadar düşürürken, kalan periyotlarda bu parametreleri etkilemediği gözlendi. Kronik gruplarda diken dalga frekansı ve diken dalga genliği açısından bazı zaman dilimleri dışında anlamlı fark görülmedi. Ayrıca kronik HR grubunun antioksidan enzim düzeylerinde kontrol ve diğer gruplara göre anlamlı bir artış görülürken ($P<0.05$) akut gruplarda anlamlı fark oluşmadı.

Sonuç: Harmalinin Kronik HR gruplarında ve akut HR gruplarının 10. periyotundan sonra diken dalga frekanslarını ve genliklerini etkilemediği görüldü. HR akut ve kronik gruplarda ilk EA başlama latensini uzattı ve uzun süreli kullanımda antioksidan etkiye sahip olabilir.

Anahtar Sözcükler: Antioksidanlar; elektrokortikografi; epilepsi; harmalin; monoamin oksidaz

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INTRODUCTION

Epilepsy, distinguished by recurring and sudden seizures, ranks as the fourth most prevalent neurological disorder, following stroke, migraine, and Alzheimer's disease. Despite encompassing diverse structural alterations such as genetic factors, traumatic brain injury, central nervous system infections, or brain tumors, approximately 65% of patients exhibit no discernible cause (1). Currently, around 65 million people worldwide receive treatment for epilepsy (2). Despite the treatment with classical, second, or third-generation antiepileptic drugs targeting the underlying pathophysiological processes of epileptogenesis, approximately 30% of epilepsy patients still exhibit resistance to these drugs (3). Additionally, the existing antiepileptic medications used in treatment often come with significant side effects, necessitating the use of two or more antiepileptic drugs for some patients. Epileptic seizures develop due to an increase in excitatory neurotransmitters such as glutamate or a decrease in inhibitory neurotransmitters like gamma-aminobutyric acid (GABA). Hence, antiepileptic drugs either augment GABA activity in the brain or manifest their impact through the inhibition of glutamate receptors (4). Therefore, these substances acting on neurons may generally cause a delay in epileptiform activity. For this purpose, the harmaline we used in the study may affect the pathways involved in the formation of epilepsy (Hypothesis 1, H_1).

- **H_1: Harmaline prolongs the latency of epileptiform activity.**

Abnormal discharges and spike waves appear in the electroencephalography (EEG) during epileptogenesis. Several epilepsy models using experimental animals, such as cats and rats, have been developed to understand the pathways in epilepsy. In these studies, epilepsy models were created by administering penicillin G intraperitoneally, and electroencephalographic recordings were obtained. Spike wave discharges were recorded, and various drug efficacies were evaluated. Furthermore, local application of penicillin to the cortex surface or interior also reported the induction of epileptiform activity. Recent research has turned to medicinal plants intending to suppress epileptic seizures (Hypothesis 2, H_2).

- **H_2: Harmaline reduces the EA frequency and amplitude of spike waves.**

The antioxidant properties of various experimental models have demonstrated a reducing effect on the severity and frequency of seizures. Many plants are known to have anticonvulsant effects, and various electrophysiological studies are being conducted with these anticonvulsant and antioxidant plants. One such medicinal plant is Peganum harmala (5). These alkaloids were first isolated from Peganum harmala and Banisteriopsis caapi in 1847 (6). The seeds of the plant have been employed in the treatment of various ailments such as fever, diarrhea, subcutaneous tumors, joint diseases, cough, diabetes, hypertension, and asthma (7-8). However, the traditional use of Peganum harmala has increased in the past two decades. Studies on the use of Peganum harmala seeds date back to 1980, while research on harmaline began in 2000. These studies predominantly focus on revealing the analgesic, antitumor, anti-inflammatory, bronchodilator, anticonvulsant, and antiepileptic properties of harmaline. There are also studies investigating the anticonvulsant properties of Peganum harmala and the effect of harmaline on seizure thresholds (9).

The dry seeds of the plant contain approximately 5.6% harmaline, 4.3% harmin, 0.6% harmalol, and 0.1% tetrahydroharmine, which are known as human monoamine oxidase (MAO) inhibitors (10). Moreover, the beta-carboline harmaline, with a molecular formula of C13H14N2O, has been reported to exhibit antidepressant, anxiolytic, anticonvulsant, sedative, hallucinogenic stimulant, excitatory stimulant, and antitumor effects. Studies by Rahimian (2023) reported that intraperitoneal harmaline administration reduced seizure threshold in mice. Hence, the study demonstrates that Peganum harmala, through its prevention of complex neuronal damage resulting from neurodegeneration caused by oxidative stress, is effective against various neurodegenerative diseases, including epilepsy (11). An imbalance between oxidative and antioxidant systems can lead to the detrimental effects of free radicals. Flavonoids such as harmaline have been shown to mitigate the potential harmful effects of free radicals in diseases related to neuronal degeneration, including epilepsy. Experimental evidence clearly indicates that flavonoids, structurally

similar to benzodiazepines, modulate the GABAA-Cl channel complex, exhibiting antiepileptic activity (12, 13). Therefore, due to their phenolic structures, flavonoids may play a modulating role in the treatment of neurodegenerative diseases by disrupting cellular oxidative processes in the central nervous system (14, 15). Oxidative stress originates from an overabundance of reactive oxygen species, encompassing hydroxyl radicals (HO), superoxide anion radicals (O2), hydrogen peroxide (H2O2), peroxyl radicals (HOO), and elevated levels of nitric oxide. The brain is particularly susceptible to harm owing to its heightened oxygen demand and extensive mitochondrial activity. Additionally, seizures increase the production of reactive oxygen molecules, leading to oxidative damage to biomolecules (16).

Therefore, the following hypotheses were investigated and their compatibility with the literature was examined (Hypothesis 3, H_3).

- **H_3: Due to its antioxidant properties, harmaline is neuroprotective, has monoamine oxidase inhibitor (MAOi) properties, and protects against epileptiform activity.**

Peganum harmala, containing beta-carboline group alkaloids such as harmaline, norharman, harman, harmol, and harmin, has been the subject of recent research into its antidepressant, antitumor, antidiabetic, analgesic, anti-addictive, antihypertensive, anticoagulant, antimicrobial, antioxidant, anti-inflammatory, and anticonvulsant effects (17). In this research, we examined the antioxidant impact of intraperitoneal harmaline applications in a dose-dependent manner, alongside their effects on EA, in order to explore the hypotheses formulated. The primary objective of this study is to investigate the effects of harmaline on EA and its potential neuroprotective role attributed to its antioxidant properties, in alignment with the formulated hypotheses. Through experimental models involving intraperitoneal administration of harmaline at varying doses, the study aims to elucidate whether harmaline prolongs the latency of epileptiform activity, reduces the frequency and amplitude of spike waves associated with EA, and exhibits neuroprotective effects against epileptiform activity by acting as a monoamine oxidase inhibitor (MAOi).

MATERIALS AND METHODS

Animals

Wistar male rats, aged 2-3 months and weighing 270±30 grams, were accommodated in optimal conditions, maintaining a room temperature of 23 °C, 60±5% humidity, and a 12:12 light-dark cycle (N=84). The experimental animals employed in this research were sourced from the Duzce University Experimental Animals Research and Application Center (Düzce, Türkiye). They were provided ad libitum access to both feed and water. The study received ethical approval from the Duzce University Animal Research Local Ethics Committee (date: 16.04.2018, decision no: 2018/1/1).

Inclusion Criteria

- Male Wistar Breed Rats: Only male Wistar breed rats were included in the study to maintain uniformity and minimize potential confounding factors related to gender differences.
- Controlled Feeding: Rats received controlled feeding from birth until they reached the age of 2-3 months to ensure consistent nutritional intake and minimize variability in physiological parameters.
- Regular Weight Monitoring: Animal weight was measured every other day to track growth patterns and ensure that rats were within the specified weight range for inclusion in the study.
- Content Analysis of Feeds: The feeds consumed by the animals underwent content analysis to ensure that they met the daily nutritional requirements without exceeding the recommended amounts.
- Controlled Water Consumption: Water consumption of the animals was controlled to maintain hydration levels and minimize potential confounding factors related to dehydration.
- Monitoring of Physiological Parameters: Urination rates, body temperatures, and body mass indexes were recorded regularly to monitor the overall health and well-being of the animals throughout the study period.
- Anesthesia Suitability Assessment: Prior to the experiment, suitability for anesthesia was assessed by measuring blood glucose levels to ensure that animals could safely undergo experimental procedures without complications.

Table. 1: Experimental groups, substances doses and administration route

Group	Substance	Dose	Route	Acute group (n)	Chronic group (n)
Sham (SG)	Saline	1 ml/kg/day	I.P.	7	7
Only Harmalin (OHG)	Harmaline	100 mg/kg/day	I.P.	7	7
Control (Penicillin G, CG)	Saline	1 ml/kg/day	I.P.	7	7
10 mg/kg Harmaline (HR10)	Harmaline	10 mg/kg/day	I.P.	7	7
50 mg/kg Harmaline (HR50)	Harmaline	50 mg/kg/day	I.P.	7	7
100 mg/kg Harmaline (HR100)	Harmaline	100 mg/kg/day	I.P.	7	7

SG: Sham group, CG: Control group, HR10: 10 mg/kg Harmaline, HR50: 50 mg/kg Harmaline, HR100: 100 mg/kg Harmaline, I.P.: Intraperitoneal, n: Number of animals, min: Minute

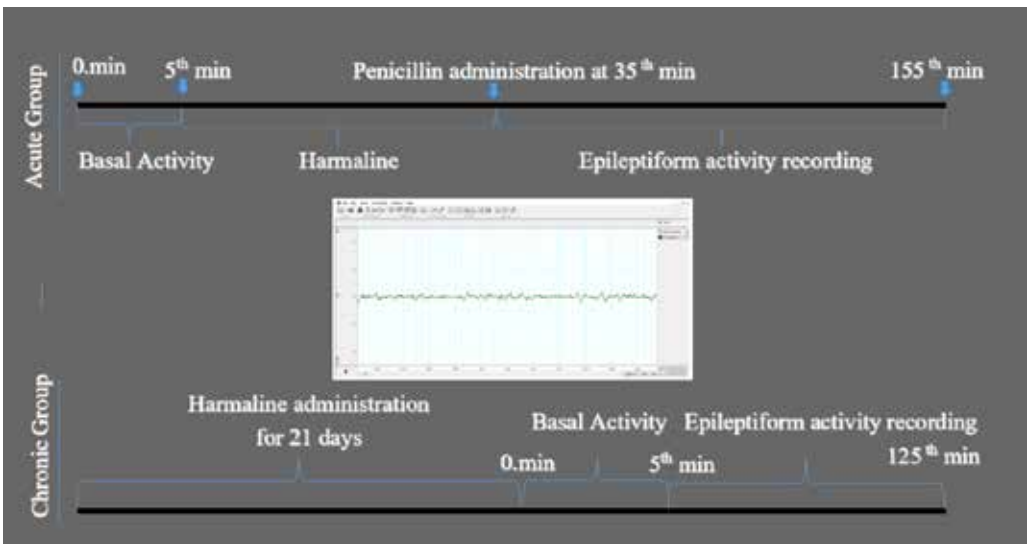

Figure 1. Duration of administration of substances in acute and chronic harmaline groups (min:Minute)

- Supervised Monitoring: Daily monitoring and examination of animals under the supervision of a veterinarian ensured their health and welfare throughout the study.
- Minimum Weight Requirement: Animals with a live weight of 270±30 grams or less on the day of the study were excluded from the study to ensure consistency and reliability of experimental results.

Exclusion Criteria

- Less than 2% of animals cared for at the experimental animal center were excluded from the study if they did not meet the specified inclusion criteria. The study incorporated an adequate sample size, determined through power analysis, to guarantee statistical power and the reliability of the experimental outcomes.

Substances and doses

Harmaline (Chemical abstract service number: 304-21-2) was administered intraperitoneally (I.P.) to the rats at doses of 10, 50, and 100 mg/kg in our study (Sigma-Aldrich, Missouri, USA). It was dissolved in dimethyl sulfoxide (DMSO) mixture and diluted with saline (Merk, Darmstadt, Germany). The induction of epilepsy was achieved by intracortical (I.C.) administration of Penicillin G potassium salt (İ.E. Ulagay İlaç, Istanbul, Türkiye) at a volume of 2 µl, containing 500 IU. Anesthesia was induced using urethane (Sigma-Aldrich, Missouri, USA) at a dosage of 1.25 g/kg administered intraperitoneally (I.P.).

Surgical procedure

The animals were anesthetized with urethane and positioned in a stereotaxic frame (Harvard Instruments,

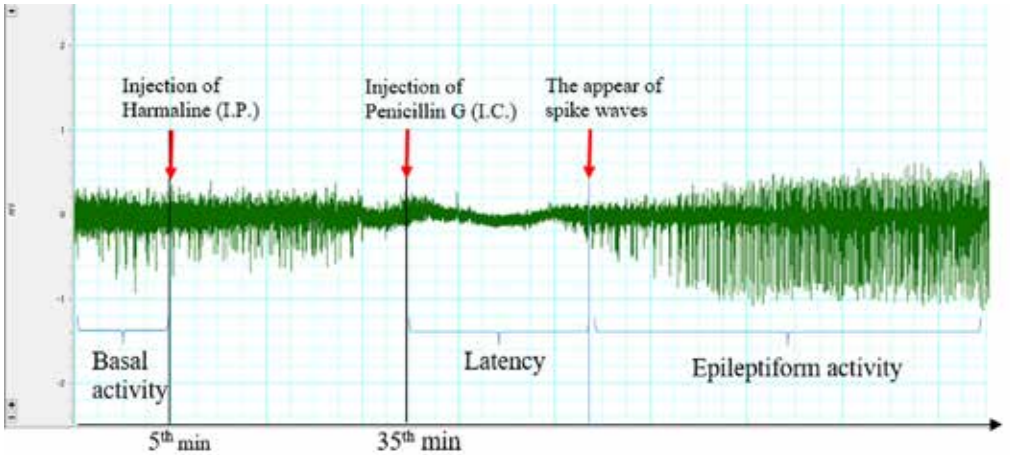

Figure 2. Epileptiform activity recording obtained by intracortical penicillin injection (I.P.:Intraperitoneal, I.C.:Intracortical, min: Minute)

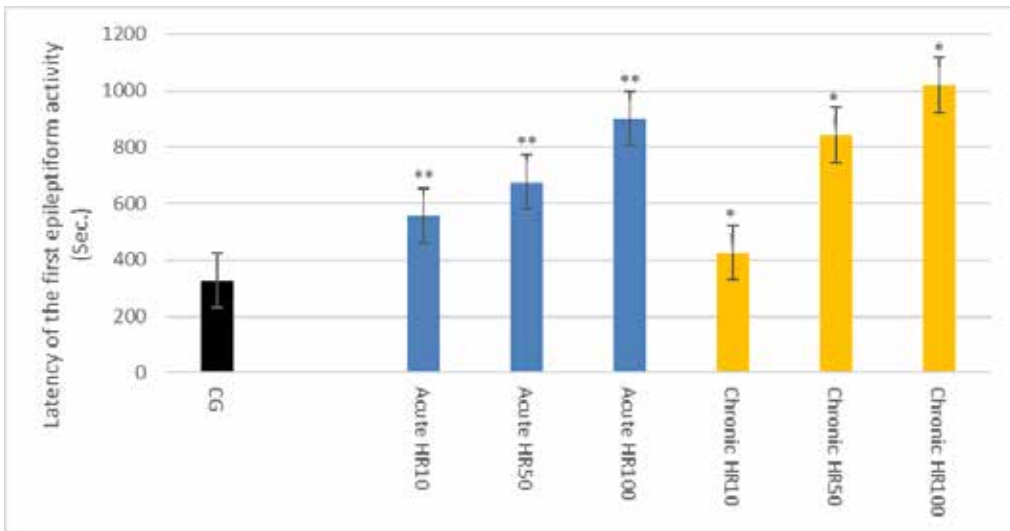

Figure 3. (CG; Control Group, Acute HR10; Acute 10mg/kg harmaline, Acute HR50; Acute 50mg/kg harmaline, Acute HR100; Acute 100mg/kg harmaline, Chronic HR10; Chronic 10mg/kg harmaline, Chronic HR50; Chronic 50mg/kg harmaline, Chronic HR100; Chronic 100mg/kg harmaline, sec: Second (*; p=0.003, **; p=0.009).

MA, USA) under the supervision of a veterinarian, ensuring vital signs were evaluated and electrophysiological observations were conducted in accordance with literature studies (16). After shaving the head region, the scalp was incised midline from front to back with a scalpel. Subsequently, the bony portion over the left cerebral cortex was delicately thinned using a microdrill (FST Rechargeable Microdrill, KF Technology, Rome, Italy) and carefully removed.

Experimental groups

Before commencing the experiment, rats were categorically divided into two primary groups: chronic administration (n=42) and acute administration (n=42) (Table 1). In the SG group, only surgical procedures were performed. OHG group, which only received 100 mg/kg of harmaline. CG group, which only received Penicillin G (500IU/2 µl, i.c.). HR10, HR50, and HR100 groups, which received HR+Penicillin G. Except for penicillin, all of the substances used in

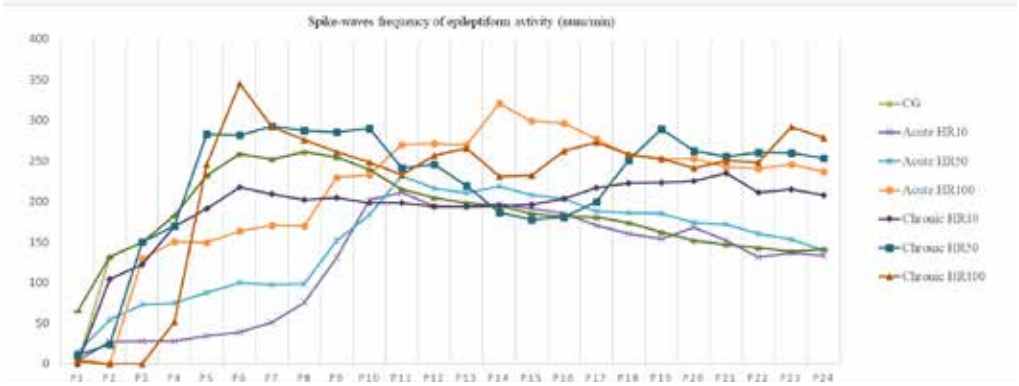

Figure 4. CG; Control Group, Acute HR10; Acute 10mg/kg harmaline, Acute HR50; Acute 50mg/kg harmaline, Acute HR100; Acute 100mg/kg harmaline, Chronic HR10; Chronic 10mg/kg harmaline, Chronic HR50; Chronic 50mg/kg harmaline, Chronic HR100; Chronic 100mg/kg harmaline; P. 5 minute period

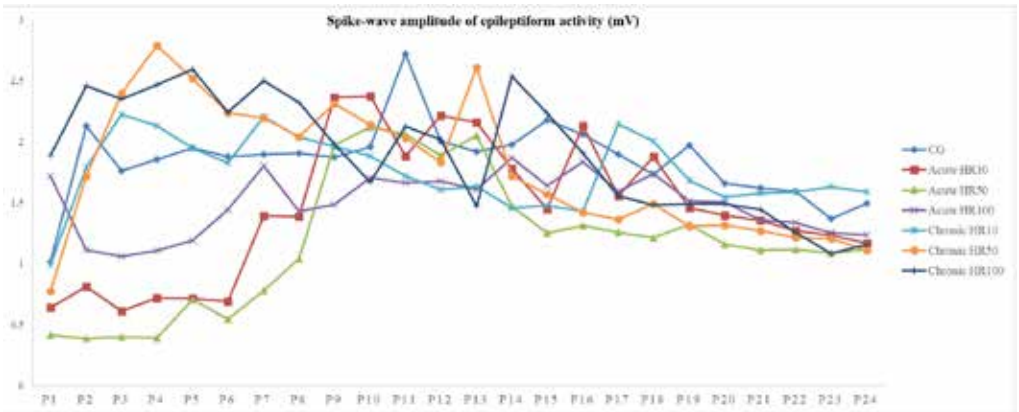

Figure 5. CG; Control Group, Acute HR10; Acute 10mg/kg harmaline, Acute HR50; Acute 50mg/kg harmaline, Acute HR100; Acute 100mg/kg harmaline, Chronic HR10; Chronic 10mg/kg harmaline, Chronic HR50; Chronic 50mg/kg harmaline, Chronic HR100; Chronic 100mg/kg harmaline; P. 5 minute period

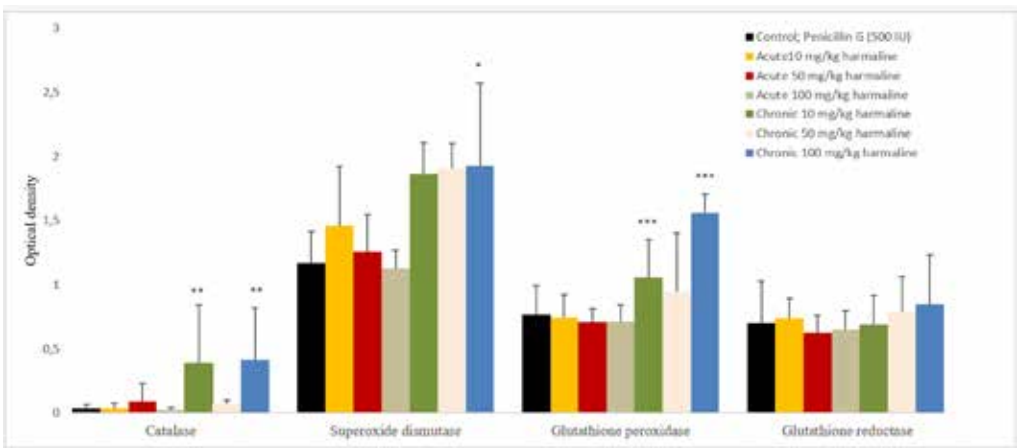

Figure 6. Effect on antioxidant optic density levels after harmaline administration in acute and chronic harmaline groups (* ; p=0.001, **; p=0.003, ***; p=0.002)).

the study were administered intraperitoneally for 21 days in the chronic group. The harmaline-only group (OHG) was given only harmaline. The substances were administered to the animals in the acute group during the experiment (Figure 1).

Creation of penicillin-induced epileptiform activity

Intracortical penicillin administration triggered the initiation of epileptiform activity. The induction of epileptiform activity through penicillin administration involved the intracortical injection of 500 IU/2 µl of penicillin. The administration of penicillin to the somatomotor cortex was conducted using a microinjector (Hamilton, Reno, USA). The injection coordinates were set at 2 mm lateral, 1 mm anterior and 1.2 mm deep to the Bregma line (18).

Electrophysiological records

Rats in the chronic group were prepared for surgery at the end of the 21st day, and rats in the acute group were prepared for surgery on the same day that harmaline was administered. First, animals were administered 1.25 g/kg urethane i.p. Anesthesia was applied. The left portion of the skull bone was then removed and two silver/silver chloride electrodes were placed in the somatomotor cortex area. After the electrodes were placed, electrocorticographic (ECoG, PowerLab/8SP, ADInstruments, NSW, Australia) recordings were obtained during the experiment. Rats were appropriately anesthetized, and after the removal of the skull region (blue area) as illustrated in Figure 1, the injection was performed at the point indicated by the black dot located 2 mm lateral to and 1 mm anterior to the bregma. Five-minute basal activity records were taken before epileptiform activity was initiated with penicillin. Intracortical administration of penicillin (500 IU / 2 ul) resulted in epileptiform activity (EA). Data analysis was conducted utilizing the PowerLab Chart v.8.0 software package (ADInstruments Pty Ltd., CO, US). Each animal underwent ECoG recordings lasting 125 minutes. Bipolar spike and spike-wave complexes, indicative of EA, were scrutinized. Additionally, within 120-minute intervals of ECoG recordings for each animal, the mean, median, minimum, and maximum values of spike-wave frequency and amplitudes per 5 minutes were quantified and utilized as data.

Determination of antioxidant activity

Subsequent to the ECoG procedure, rat blood samples were collected into tubes with yellow caps and subjected to centrifugation at 4,000 rpm for 15 minutes. (Heraeus labofuge 400, Thermo Scientific, Waltham, Massachusetts, USA). The serum obtained after centrifugation was stored at -20 °C until the day of testing. The enzyme-linked immunosorbent assay (ELISA) kits for superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GSR) levels in the serum were used (Shanghai Sunred Biological Technology Co., Ltd, Shanghai, China). Optical density values were obtained by performing the ELISA test according to the procedure in the kit manual.

Statistical analysis

The sample size was calculated by considering the correlation coefficient of 0.40, which is stated in the literature as the limit for a moderate relationship in the variables whose clinical relationships were examined. The G*Power (G*Power ver. 3.0.10, Franz Faul, Universität Kiel, Germany) package program was used to determine the required sample size for the study. As a result of the analysis (with 0,85 power, α=0.05 type I error, β=0.10 type II error, critical F value= 2,267), a correlation coefficient of at least 0.40 was found to be significant (19). The total required minimum sample size in each large group was determined to be 42 animals.

The initiation time of the initial epileptiform activity, spike-wave frequency, and spike-wave amplitude were automatically computed from the records acquired for each animal using computer software (Lab Chart 8, ADInstruments Pty Ltd, Castle Hill, NSW, Australia). Epileptiform activity records were segmented into five-minute intervals for analysis. Group differences in the onset time of the first epileptiform activity, spike-wave frequency, and amplitude measurements within each period were evaluated through the one-way ANOVA test, and homogenous subgroups were identified using the multiple comparison method. To compare groups regarding ELISA SOD, CAT, GR, and GPx values, the ANOVA test was employed, and homogenous sub-

groups were identified for distinct groups using the multiple comparison method. Statistical Package for the Social Sciences package program version 23.0 (SPSS Inc., Chicago, IL, USA) was used for the analyses. One-way ANOVA was employed as a statistical analysis to assess differences in antioxidant activity within groups periodically. Differences with a P value below 0.05 were considered statistically significant.

Potential primary outcomes from the study

Delay in the Time of Onset of Epileptiform Activity: Both acute and chronic administration of harmaline can cause a dose-dependent delay in the time of onset of penicillin-induced EA. This delay may reveal the potential antiepileptic effect of harmaline.

Decrease in Spike-Wave Frequency: Acute harmaline administration can lead to a statistically significant decrease in spike-wave frequency at certain intervals; such a finding may indicate a potential modulation of epileptiform activity. However, in chronic harmaline groups, this effect may not occur due to some metabolic dysregulation.

Increase in Antioxidant Enzyme Levels: Chronic administration of harmaline can significantly increase the levels of antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx). This demonstrates the potential neuroprotective effect of harmaline thanks to its antioxidant properties.

Secondary outcomes from the study

Effect on Spike Wave Amplitude: While harmaline showed some statistically significant effects on spike-wave amplitude during acute administration, these effects were not consistent across all time periods. Overall, harmaline did not significantly alter spike wave amplitude during epileptiform activity.

Antiepileptic and Neuroprotective Effects: The study confirms previous findings suggesting that harmaline has antiepileptic properties, as evidenced by its ability to delay the onset time of EA and modulate spike-wave frequency. In addition, the increase in antioxidant enzyme levels in chronic harmaline groups supports the hypothesis that harmaline may have a neuroprotective effect thanks to its antioxidant properties.

The findings imply that harmaline warrants exploration as a promising candidate for epilepsy therapy, potentially owing to its ability to modulate monoamine transmission and exert antioxidant properties. However, further investigation is imperative to unravel the precise molecular mechanisms driving its antiepileptic and neuroprotective actions, as well as to assess its viability as a novel therapeutic intervention for epilepsy.

RESULTS

Electrocorticographic results

The substance harmaline was exclusively examined in the harmaline groups (OHG) to assess its potential impact on the basal brain activities of rats. The investigation revealed that doses of 10, 50, and 100 mg/kg of harmaline administered in both acute and chronic groups did not elicit any discernible effect on basal activity. Additionally, it is noteworthy to mention that no epileptic activity was observed in the Sham groups throughout the entirety of the experiment.

Analysis of penicillin-induced epileptiform activity

The induction of epileptic activity was achieved through intracortical administration of 500 IU/2 µl of penicillin at a depth of 1.2 mm, utilizing a Hamilton microinjector. Epileptic discharges, characterized by spike-wave formations, emerged 3-8 minutes post-penicillin injection, as depicted in Figure 2. According to the electrocorticographic (ECoG) recordings obtained within the initial five minutes following penicillin injection in the control groups, an average amplitude of 1.01 mV was observed. The amplitude generated waves of approximately 2 mV until the 30th minute. Subsequently, an increase was noted at the 50th minute, reaching its maximum value between the 50th and 55th minutes, followed by a declining trend throughout the recording period.

In the first five minutes after penicillin injection, 132 spike-wave complexes were identified in the ECoG records of the control groups. The intervals with the highest number of spike-wave complexes were observed between the 21st and 25th minutes, totaling 258 spike-wave complexes. Although the values remained relatively consistent thereafter, a decrease in

the number of spike-wave complexes was observed after the 50th minute. By the 120th minute, the number of spike-wave complexes had decreased to 130.

Onset Latency of Initial Epileptiform Activity

The appearance of spike waves indicative of epileptiform activity commenced between the 5th and 10th minutes following penicillin administration. Upon comparison of the short and long-term harmaline groups with the control group (penicillin), it was observed that the acute harmaline application groups exhibited a dose-dependent increase in seizure onset time ($p = 0.003$). Similarly, in the chronic groups, harmaline prolonged the onset time of epileptiform activity in a dose-dependent manner, mirroring the trend observed in the acute groups ($p = 0.009$) (see Figure 3). These findings confirm that harmaline prolongs the latency of epileptiform activity in both acute and chronic groups, thereby supporting our H1 hypothesis.

Time-dependent effect of harmaline on the Spike-Wave Frequency of Epileptiform Activity

The acute administration of harmaline at doses of 10 mg/kg, 50 mg/kg, and 100 mg/kg resulted in notable differences in epileptiform activity spike wave counts compared to the control group. Specifically, at the 10 mg/kg dose, significant differences were observed up to the 40th minute, while at the 50 mg/kg dose, this effect extended to the 45th minute, and at the 100 mg/kg dose, it persisted until the 35th minute ($p=0.01$). However, beyond these time points, although the spike-wave counts remained lower than the control group from the 40th to the 120th minute, statistical significance was not reached except for specific intervals.

In the chronic harmaline groups, a similar pattern was observed. For instance, the chronic administration of 10 mg/kg harmaline resulted in a non-statistically significant decrease in spike wave counts up to the 30th minute compared to the control group. Subsequent intervals showed statistically significant differences, particularly between the 36th and 45th minutes and from the 96th to 120th minutes.

Likewise, the chronic administration of 50 mg/kg harmaline demonstrated significant differences in spike-wave counts during specific intervals, notably in the initial 5-minute period and from the 80th to 120th minutes. Moreover, the chronic administration of 100 mg/kg harmaline led to a statistically significant decrease in spike wave counts up to the 15th minute and subsequent intervals from the 21st to the 30th minute. However, no statistical differences were found during certain intervals despite higher spike wave counts compared to the control group. Overall, it was observed that harmaline did not significantly affect spike wave frequencies throughout the recording period. Thus, despite partial decreases in spike-wave frequencies, our H2 hypothesis was rejected.

Harmaline Effect on Spike-Wave Amplitude

In our investigation, animals receiving an acute dose of 10 mg/kg harmaline exhibited statistically significant differences in spike-wave amplitudes compared to the control group in every 5-minute interval up to the 40th minute ($p=0.01$). While between the 41st and 65th minutes, with the exception of the interval between 51-55 minutes where significance was maintained compared to the control group, spike wave amplitudes were higher without statistical significance. Subsequently, from the 66th to the 110th minute (excluding intervals between 76-80 and 86-90 minutes where amplitudes were higher but not statistically significant), each 5-minute period showed significantly lower spike wave amplitudes compared to the control group ($p=0.02$). However, no statistical significance was observed between the 111th and 120th minutes, despite lower amplitudes compared to the control group.

In the acute harmaline group receiving a dosage of 50 mg/kg, statistically significant differences in spike-wave amplitudes compared to the control group were observed at every 5-minute interval up to the 40th minute ($p=0.01$). Despite higher amplitude values compared to the control group between the 41st and 50th minutes, statistical significance was not reached. Similarly, during each 5-minute period between the 51st and 70th minutes, although spike wave values were lower than the control group, no statistical difference was observed. However, from the 71st to the 120th minutes (excluding the 61-65 minute interval), significant differences in spike-wave amplitudes compared to the control group were noted ($p=0.015$).

In the acute harmaline group administered a dosage of 100 mg/kg, statistically significant differences in spike wave amplitudes compared to the control group were observed in every 5-minute interval up to the 30th minute (excluding the 0-5 minute interval) (p=0.01). Although amplitude values were lower than the control group between the 31st and 35th minutes and between the 36th and 40th minutes, no statistical difference was observed. From the 41st to the 60th minutes, significant differences in spike-wave amplitudes compared to the control group were noted in each 5-minute interval. However, between the 61st and 120th minutes (excluding intervals between 71-75 and 76-80 minutes), although spike wave amplitudes were lower than the control group, no statistical significance was observed.

In the chronic harmaline group receiving a dosage of 10 mg/kg, although spike wave amplitude was lower than the control group up to the 10th minute, statistical significance was not reached. Subsequent intervals between the 11th and 20th minutes showed higher amplitude values than the control group and were statistically significant. Intervals between 21-25, 36-40, 41-45, 81-85, 86-90, and 51-55, 56-60, 66-70, 71-75, 76-80 minutes exhibited lower spike wave amplitudes compared to the control group and were statistically significant. However, between the 91st and 120th minutes (excluding intervals between 111-115 minutes), no statistical significance was observed despite lower spike wave amplitudes compared to the control group.

In the chronic harmaline group administered a dosage of 50 mg/kg, spike wave amplitude was significantly lower than the control group up to the 10th minute. Between the 11th and 30th minutes, amplitude values were higher than the control group and statistically significant. Although spike wave amplitudes were higher than the control group up to the 50th minute, no statistical significance was observed. However, from the 51st to the 120th minutes (excluding the 61-65 minute interval), spike-wave amplitudes were lower than the control group and statistically significant.

In the chronic harmaline group administered a dosage of 100 mg/kg, spike-wave amplitude was higher than the control group and statistically significant up to the 25th minute. Although amplitude values were higher than the control group between the 26th and 45th minutes, no statistical significance was observed. Intervals between 46-55, 61-65, and 81-120 minutes exhibited lower spike wave amplitudes compared to the control group and were statistically significant (p=0.01). Despite the statistically significant decreases in certain intervals during EA recordings induced by harmaline, no significant impact on spike-wave amplitudes was observed. Thus, our H2 hypothesis was rejected.

Antioxidant effect of harmaline

Upon analyzing the CAT optical density levels obtained from the ELISA test, the chronic HR10 and HR100 groups exhibited statistically significant differences compared to both the control and other groups ($p = 0.003$). Similarly, SOD levels in animals from the chronic HR100 group showed statistical significance compared to both the control and other groups (p=0.01). Furthermore, GPx levels in the chronic HR10 and HR100 groups were statistically significant compared to the control and other groups (p=0.02). Conversely, when comparing the GR levels among the groups, no statistically significant difference was observed (p=0.06) (Figure 6). These results suggest that long-term administration of harmaline may possess neuroprotective properties, thus confirming our H3 hypothesis.

DISCUSSION AND CONCLUSION

The beta-carboline alkaloids present in nature have been reported in various plants, including Banisteriopsis caapi and Peganum harmala (20). These compounds are known to bind to benzodiazepine, serotonin, opioid, and imidazoline receptors in the human body and brain. Additionally, they interact with enzymes such as cytochrome P450 and MAO (21). Due to these properties, they exhibit a wide range of psychopharmacological effects (22). The present study investigated the effects of harmaline administration on electrocorticographic (ECoG) activity and penicillin-induced epileptiform activity in rats, as well as its potential antioxidant properties. Our findings contribute to understanding harmaline's impact on epileptiform activity and its neuroprotective potential. Harmaline derived from Peganum harmala seeds demonstrated

negligible impact on seizures in a mouse model of maximal electroshock. These findings confirm the prolongation of EA latency with H_1. However, the co-administration of 3 mg/kg diazepam alongside doses of 50 mg/kg and 100 mg/kg harmaline revealed an antiepileptic effect in both groups. In the presented study, the impact of chronic and acute doses of harmaline, administered intraperitoneally (I.P.), on the onset time, frequency, and amplitude of penicillin G-induced epileptiform activity was investigated in male Wistar rats. Additionally, the potential protective effect of harmaline on the biochemical mechanisms of epilepsy was examined based on its antioxidant properties (11). Harmaline, administered in doses of 10, 50, and 100 mg/kg in both acute and chronic settings, did not demonstrate any discernible effect on basal brain activities. This suggests that harmaline does not significantly alter normal brain function under the conditions tested. Additionally, no epileptic activity was observed in the Sham groups throughout the experiment, indicating the specificity of harmaline's effects on epileptiform activity induced by penicillin. This finding showed that harmaline used for long or short periods does not cause epileptic seizures. Nevertheless, both the acute and chronic harmaline groups exhibited a delayed onset time of epileptiform activity in comparison to the control group, and this delay was dose-dependent. Assessment of spike-wave frequency and amplitude in the acute harmaline group revealed a statistically significant reduction compared to the control group. Conversely, in the chronic groups, no notable differences were observed in spike-wave frequency and amplitude of epileptiform activity compared to the control group. Previous studies have elucidated the neuroprotective effects of harmala alkaloids, specifically their modulation of calcium channels (23). However, these findings do not mean that harmaline has a reducing effect on spike-wave amplitudes and frequencies (H_2). Penicillin-induced epileptiform activity, characterized by spike-wave formations, emerged within 3-8 minutes post-administration, as expected. Our analysis of ECoG recordings revealed a time-dependent increase in spike-wave amplitude following penicillin injection, peaking between the 50th and 55th minutes before declining. Spike-wave complexes were most prevalent between the 21st and 25th minutes, reflecting the dynamic nature of epileptiform activity induced by penicillin.

Regarding the onset latency of initial epileptiform activity, harmaline administration prolonged the seizure onset time in a dose-dependent manner, both acutely and chronically. This supports the hypothesis that harmaline extends the latency of epileptiform activity, suggesting a potential antiepileptic effect.

The time-dependent effect of harmaline on spike-wave frequency demonstrated significant differences compared to the control group, particularly at lower doses and earlier time points. However, beyond certain intervals, harmaline did not significantly affect spike-wave frequencies, indicating a limited impact on the overall frequency of epileptiform activity over time. In terms of spike-wave amplitude, harmaline administration led to significant differences compared to the control group, especially in the acute phase and at lower doses. However, while statistically significant differences were observed during specific intervals, harmaline did not exert a consistent effect on spike-wave amplitudes throughout the recording period. Harmaline, in particular, blocks voltage-gated calcium channels, reducing calcium entry into cells. The neuroprotective effect of harmaline was more pronounced in the chronic groups in our study. Another study in rat dorsal root ganglia showed that harmaline dose-dependently inhibited voltage-gated calcium, sodium, and potassium channels, mainly acting on L and N types of calcium channels. The interaction of harmala alkaloids with the imidazoline contained in Peganum harmala was also shown to have antiepileptic effects (24).

Monoamine oxidase catalyzes the oxidative deamination of amines and neurotransmitters, playing a role in mood disorders, depression, and oxidative stress. The investigation into harmaline's antioxidant properties revealed significant differences in catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) levels in the chronic harmaline groups compared to controls. This suggests that long-term administration of harmaline may confer neuroprotective benefits, possibly through its antioxidant effects. Studies on Peganum harmala have shown that these plants suppress the MAO enzyme, improving mood and mental perception. Considering epilepsy treatment mechanisms, studies have suggested that thera-

peutic options targeting the NMDA receptor complex, which our study used harmaline for, are more effective. Harmaline, used in our study, is believed to block the NMDA receptor by binding to the glycine site, thereby reducing intracellular calcium entry and exhibiting antiepileptic effects. Chemicals acting as glycine antagonists have been shown to block NMDA and exert antiepileptic effects in previous studies (25).

When considering epilepsy treatment mechanisms, alongside new genetic models, gaining more knowledge about different aspects of monoaminergic neurotransmission using human genetic biomarkers can elucidate the complex roles of monoamines in the pathophysiology of epilepsy (26). It is thought that the adrenergic neuron-modulating property of harmaline reduces the development of epileptiform activity (27-28). The effects of harmaline, which has an MAOi property, on brain monoamine transmission have been investigated. The role of monoamines in epilepsy mechanisms was first demonstrated in a study using the adrenergic neuron blocker, reserpine. After reserpine administration, it was observed that the onset time of convulsions was prolonged. Another study in MAO-deficient mice showed slower development of seizures compared to the control group, attributed to elevated levels of serotonin and norepinephrine neurotransmitters (29). In the study conducted by Abdulrahman and Alsahrani (2016), harmaline was shown to be anticonvulsant (18, 30).

Furthermore, in addition to the obtained electrocorticogram (ECoG) recordings, the effects of harmaline on blood levels of free radicals were investigated. Free radical levels were examined in all the same groups in this study. Superoxide dismutase, catalase, glutathione reductase, and glutathione peroxidase levels were assessed to determine free radical levels. Only in the group receiving chronic harmaline application, CAT, SOD, GPx, and GR were significantly increased. The results of the study indicate that harmaline has antiepileptic and free radical-scavenging effects (31, 32). To support this effect, further studies can explore glutamate and GABA levels and receptor distribution in the same groups (33,34,35).

In the chronic harmaline application groups, the levels of antioxidant enzymes were found to be statistically significant compared to the control group. Long-term use of harmaline reduces the levels of free radicals (H_3). Recent studies have implicated increased levels of free radicals in the pathophysiology of epilepsy (36,37,38). Oxidative stress is involved in the pathogenesis of many neurodegenerative diseases, including Alzheimer's, Parkinson's, and epilepsy (39,40,41,42,43).

In the presented study, harmaline was found to have an experimental anti-epileptic effect when applied in rats with induced epilepsy models, suggesting its antioxidant properties. Therefore, it is considered to be antiepileptic. Additionally, further studies may reveal that drugs developed from harmaline could play a significant role in the treatment of epilepsy through monoamine transmission and glutamate blockade. One of the primary limitations of this study is the absence of molecular analysis to determine the negative or positive feedback mechanisms of the molecules involved in the Monoamine Oxidase Inhibitor (MAOi) pathways within the brain tissues of rats with epileptiform activity (EA). This limitation hinders a comprehensive understanding of the intricate biochemical interactions underlying harmaline's effects on epileptiform activity and its antioxidant properties. The translational relevance of the findings may be limited due to the use of animal models, specifically rats, in this study. While animal models provide valuable insights into the biological mechanisms underlying disease processes, the extrapolation of these findings to human epilepsy treatment requires careful consideration of species-specific differences and potential variations in drug responses. However, this is the first study to electrophysiologically examine the effects of acute and chronic HR in a penicillin-induced epileptiform activity model. We can say that 10, 50, and 100 mg/kg doses of harmaline in acute groups have an effect in short periods. We can also see its antioxidant properties in long-term use. Future studies can investigate the molecular connection pathways of MAOi mechanism and antioxidant effect.

In conclusion, our study provides insights into the effects of harmaline on epileptiform activity and its potential antioxidant properties. Harmaline prolonged the latency of epileptiform activity, particularly in the acute and chronic phases, supporting its potential antiepileptic properties. While harmaline exerted significant effects on spike-wave frequency and ampli-

tude during specific intervals, its overall impact was limited, suggesting a nuanced relationship between harmaline and epileptiform activity. Additionally, the observed alterations in antioxidant enzyme levels indicate a potential neuroprotective role for harmaline, which warrants further investigation. Overall, our findings contribute to understanding harmaline's pharmacological effects and its therapeutic potential in epilepsy and neuroprotection.

Conflict-of-Interest and Financial Disclosure

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Delayed versus simultaneous implant placement with ramus block grafts: A retrospective cohort study

Ramus blok grefti ile geç ve eş zamanlı implant yerleştirme prosedürlerinin karşılaştırılması: Retrospektif kohort çalışması

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Abstract

Aim: This study compared the graft stability and implant success of delayed implantation versus simultaneous implantation with autogenous grafts.

Methods: The study sample comprised a population of patients who underwent autogenous block bone grafting using the ramus of the mandible. Patients with data from 1 year of follow-up were divided into two groups according to implantation approach: delayed implantation and simultaneous implantation. Outcome variables were 3D volume changes (the bone graft volumes at post-implantation and 1-year follow-up, resorption volume, and resorption rate of the bone graft), 2D linear changes (the bone graft width at post-implantation and 1-year follow-up, 2D resorption amount, and resorption rate of the bone graft), marginal bone loss, and implant success.

Results: The final sample comprised 21 subjects, and 33 implants were investigated. In total, 51.5% (n=17) were placed with a simultaneous approach and 48.5% (n=16) with a delayed approach. The simultaneous approach resulted in a higher rate of graft resorption in both the 3D and 2D measurements compared to the delayed implantation (p=0.001 and p=0.014, respectively). There was no difference between the two groups in terms of graft volume, graft width, marginal bone loss, or implant success at the 1-year follow-up (p=0.958, p=0.039, p=0.168, and p=1.000, respectively).

Conclusion: Although simultaneous implantation resulted in a higher resorption rate than delayed implantation, the graft volume and width, marginal bone loss, and implant success were similar at the 1-year follow-up.

Keywords: Alveolar bone grafting; alveolar ridge augmentation; dental implantation; three-dimensional image

Öz

Amaç: Bu çalışmada, otojen greftlerle eş zamanlı ve geç yerleştirilen implantlarda greft stabilitesi ve implant başarısı karşılaştırılmıştır.

Yöntemler: Çalışma örneklemi, mandibula ramusu kullanılarak otojen blok kemik grefti uygulanan hasta popülasyonundan oluşmuştur. Bir yıllık takip verilerine sahip hastalar implantasyon yaklaşımına göre iki gruba ayrılmıştır: geç implantasyon ve eş zamanlı implantasyon. Sonuç değişkenleri 3B hacim değişiklikleri (implantasyon sonrası ve 1 yıllık takipteki kemik grefti hacimleri, rezorpsiyon hacmi ve kemik greftinin rezorpsiyon oranı), 2B lineer değişiklikler (implantasyon sonrası ve 1 yıllık takipteki kemik grefti genişliği, 2B rezorpsiyon miktarı ve kemik greftinin rezorpsiyon oranı), marjinal kemik kaybı ve implant başarısı idi.

Bulgular: Nihai örneklem 21 denekten oluşmuş ve 33 implant incelenmiştir. Toplamda, %51,5'i (n=17) eşzamanlı ve %48,5'i (n=16) geç implantasyon yaklaşımla yerleştirilmiştir. Eş zamanlı yaklaşım, geç implantasyona kıyasla hem 3B hem de 2B ölçümlerde daha yüksek greft rezorpsiyonu oranıyla sonuçlanmıştır (sırasıyla p=0,001 ve p=0,014). İki grup arasında 1 yıllık takipte greft hacmi, greft genişliği, marjinal kemik kaybı veya implant başarısı açısından fark yoktu (sırasıyla p=0.958, p=0.039, p=0.168 ve p=1.000).

Sonuç: Eş zamanlı implantasyon, geç implantasyona göre daha yüksek rezorpsiyon oranıyla sonuçlansa da, 1 yıllık takipte greft hacmi ve genişliği, marjinal kemik kaybı ve implant başarısı benzerdi.

Anahtar Sözcükler: Alveolar kemik grefti; alveoler bombe ögmentasyonu; diş implantasyonu; üç boyutlu görüntü

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INTRODUCTION

In augmented alveolar bone, the timing of implantation affects the total treatment time, mechanical loading time of the bone graft, morbidity, and treatment costs (1,2,3). A delayed implantation approach is often preferred (4). If the type of defect allows implant placement with sufficient primary stability in the ideal prosthetic position, a simultaneous implantation approach may be preferred (2). The timing of implantation in augmented alveolar bone remains a controversial issue of debate in the literature. When augmentation is performed with autogenous block grafts, some researchers support the preference for simultaneous implantation because the resorption of bone grafts is not a linear process, and this process is predictable (5). However, researchers advocating delayed implantation have argued that osseointegration and implant success could be compromised when an augmentation-related complication occurs with simultaneous implantation (6,7). In addition, some researchers have suggested that the delayed implantation approach allows higher bone-implant contact and greater implant stability compared to the simultaneous implantation approach (8).

Autogenous block grafts show 0–25% resorption in the early period (9). This resorption rate may affect treatment results, especially following simultaneous implantation. Many studies have shown the effects of the timing of implantation on implant success and marginal bone loss as measured by 2D radiography (6,10,11). Although 2D radiographs are useful for planning and implant follow-up in implantology, they cannot provide sufficient information about volumetric changes in the bone graft in horizontally augmented alveolar bone. Thus, 3D radiographic examinations are needed. However, a limited number of studies have evaluated the effects of the timing of implantation on the dimensional changes in augmented bone in 3D radiographs (7). Selecting the region of interest (ROI) is a critical aspect of volumetric analysis. In many studies examining volumetric changes in autogenous grafts, ROIs include all or part of the jaws, including implants placed, and their borders are determined manually (12,13,14,15). Manual determination of the borders of ROIs is not reliable enough for reproducible measurement areas in cone-beam computed tomography (CBCT) images scanned at different time points. Furthermore, because ROIs can contain multiple objects and layers of anatomical structures, acquiring graft volume measurements is challenging (16).

The present study hypothesized that the timing of implantation may affect the dimensional changes in the bone graft and that these changes may affect the success of the implant, which is estimated according to the Implant Quality of Health Scale. (17). Thus, this study aimed to address the following question: Does the simultaneous implantation technique, compared to the delayed implantation approach, influence implant success and the stability of bone grafts in alveolar crests that have undergone lateral augmentation using autogenous grafts? To answer this question, we compared simultaneous and delayed implants after 1 year of prosthetic loading in patients who underwent horizontal reconstruction of the mandible posterior with mandibular ramus grafts. In addition to measuring implant success, marginal bone loss, and bone graft width, we also evaluated 3D bone stability using a measurement method that allowed only the volume of augmented bone to be evaluated.

MATERIAL AND METHODS

Study design

The investigators designed and implemented a retrospective cohort study to compare the graft stability and implant success of delayed implantation versus simultaneous implantation with autogenous grafts. The present study was performed according to the guidelines of the 2013 revision of the Helsinki Declaration and complied with the STROBE guidelines (18). Ethical approval was obtained from the Marmara University Institute of Health Sciences Ethics Committee (date: 15.11.2021, decision no: 127). Every patient signed a written informed consent form.

Study sample

The study sample was derived from the population of patients who underwent autogenous block bone grafting using the ramus of the mandible at the Department of Oral and Maxillofacial Surgery, Marmara University between May 2018 and April 2021. All patients who

met the inclusion criteria were included in the study. The patients' augmentation operations and implant-related data were obtained from the patients' electronic health records. The inclusion criteria were as follows: (1) >18 years of age (2) not smoking; (3) severe horizontal atrophy of the alveolar ridge in the mandibula posterior (Class IV, i.e., knife-edge ridge with adequate height but inadequate width of 4 mm or less) (19); (4) reconstruction with autogenous block bone graft using the ramus of the mandible; (5) simultaneous implantation with autogenous grafts or delayed implantation after augmentation operation; (6) single tooth or partial tooth deficiency (4 teeth) restored with screw-retained fixed implant-supported prosthesis; (7) presence of keratinized gingiva at least 2 mm around the implant; and (8) follow-up for at least 1 year after prosthetic loading. The exclusion criteria were as follows: (1) systemic or local contraindications to implant surgery; (2) vertical alveolar ridge augmentation; (3) poor oral hygiene; (4) implants narrower than 3.5 mm in diameter and shorter than 8 mm in length; and (5) refusal to participate in the study.

Treatment procedures

The performed approach (simultaneous or delayed implantation) was chosen based on the intraoperative CBCT evaluation of each case. The width and shape of the bone ridge were assessed. Simultaneous implantation was preferred if the implants could be expected to achieve primary implant stability of at least 20 Ncm in the appropriate prosthetic position (Figure 1). All surgical procedures were performed by two surgeons (GG and SAE) under local anesthesia.

Delayed implantation approach

The recipient and donor sites were exposed through midcrestal and vertical incisions. Crestal, lateral, and apical osteotomies to harvest the bone block graft were performed using piezoelectric surgical instruments (Piezosurgery White, Mectron S.P.A., Italy). Surgical chisels were used to mobilize the graft. The graft was recontoured to the recipient site using a diamond burr. Using screws, the block graft was fixed to the residual crest so that there was no movement of the block graft seen following fixation. (Ramed Medikal, Turkey). Particulate autogenous grafts were collected from the external oblique ridge using a bone scraper (Safe Scraper Twist, Osteogenics Biomedical, Canada). The spaces between the recipient site and the block graft are filled with particulate autogenous bone grafts. A periosteal-releasing incision was made to allow passive primary closure of the flap. The flap was sutured using simple and mattress-absorbable sutures (Dogsan Medical Supplies Industry, Turkey). Four months later, the implantation operation was performed. The recipient site was exposed to a midcrestal incision. Fixation screws were removed. Implant osteotomies were performed, and implants were placed at the bone level The cover screws for the implants were placed, and the flap was closed primarily (Figure 2).

Simultaneous implantation approach

Autogenous block and particulate graft harvesting were performed in a manner similar to the delayed implantation approach. Before the block grafts were fixed to the recipient site, osteotomies of the implants were performed, and the implants were placed at the level of the lingual bone. Block grafts were fixed to the recipient site using 1.6 mm fixation screws. The spaces between the implants and the block graft are filled with particulate autogenous bone grafts. The flap was closed primarily using resorbable sutures without tension (Figure 3).

Except for autogenous graft material, no graft material, membrane, or platelet-rich concentrates were used in either group. The implant stability quotient (ISQ) values during the implantation were measured using an Osstell device (Osstell ISQ, Integration Diagnostics Ltd., Sweden). After surgeries, antibiotics (amoxicillin + clavulanic acid 1 g, two times a day for 7 days), pain medication (naproxen sodium 550 mg + codeine phosphate 30 mg, every 8 hours as needed), and rinsing irrigation (0.12% chlorhexidine gluconate + 0.15% benzydamine hydrochloride, three times daily for 7 days) were administered. The sutures were removed 14 days after the operation. No patients used fixed or removable temporary prostheses during the recovery period. After a healing time of 4 months (simultaneous implantation) or 2 months (delayed implantation), the healing abutments were inserted. Approximately 3 weeks after the placement of the healing abutment, prosthetic procedures were started when soft tissue

Table 1. Health scale for dental implants (17)

Implant Quality Scale Group	Clinical Conditions
I. Success (optimum health)	a) No pain or tenderness upon function b) 0 mobility c) 2 mm radiographic bone loss from initial surgery d) No exudates history
II. Satisfactory survival	a) No pain on function b) 0 mobility c) 2–4 mm radiographic bone loss d) No exudates history
III. Compromised survival	a) May have sensitivity on function b) No mobility c) Radiographic bone loss 4 mm (less than 1/2 of implant body) d) Probing depth 7 mm e) May have exudates history
IV. Failure (clinical or absolute failure)	Any of following: a) Pain on function b) Mobility c) Radiographic bone loss 1/2 length of implant d) Uncontrolled exudate e) No longer in mouth

>18 years of age

Table 2. Demographic data of patients

		Patient (n:21)
Age (years)		42.84±12.04
Gender	Female	18 (85.7)
	Male	3 (14.3)
Systemic disease	None	18 (85.7)
	Allergic asthma	1 (4.76)
	Gastritis	1 (4.76)
	Hypertension	1 (4.76)

n: Number, %: Percentage, SD: Standard deviation

Table 3. Description of implant-related variables between simultaneous and delayed implantation groups.

		Simultaneous implantation	Delayed implantation	p
Sample size		17(51.5)	16(48.5)	
Implant manufacturer	Straumann Bone Level	3 (17.6)	4 (25.0)	
	Megagen ST	9 (52.9)	6 (37.5)	[a]0.730
	Megagen Anyone	5 (29.4)	6 (37.5)	
Follow-up after prosthetic loading (months)		14.12±1.17	15.63±2.45	[b]0.157
Implant diameter (mm)		4.22±0.30	3.90±0.42	[b]0.058

* a : Fisher Freeman Halton Test, b. : Mann Whitney U Test; n (%), Mean±SD, mm: millimeter, n: Number, %: Percentage, SD: Standard deviation

Table 4. The descriptive statistics of outcome variables between simultaneous and delayed implantation groups.

Outcome Variables		Simultaneous implantation (n=17)	Delayed implantation (n=16)	*p*
3D Volume Changes	3D resorption rate (%)	57.18±22.75	31.98±17.55	[a]***0.001***
	Volume1(mm^3)	209.54±94.83	122.02±32.46	[a]***0.003***
	Volume2(mm^3)	80.22±42.29	85.18±38.77	[a]0.958
	3Dresorp (mm^3)	128.26±78.75	35.88±17.91	[a]***0.001***
2D Linear Changes	2D resorption rate (%)	54.81±30.88	38.44±18.86	[a]***0.014***
	Width1(mm)	3.13±1.08	2.28±0.87	[a]***0.014***
	Width2(mm)	1.55±1.47	1.60±0.87	[a]0.309
	2Dresorp (mm)	1.64±1.08	0.75±0.52	[a]***0.017***
Marginal Bone Loss (mm)		1.15±0.47	0.88±0.60	[a]0.168
Implant success	Success (optimum health)	16 (94.1)	15 (93.7)	[b]1.000
	Satisfactory survival	1 (5.9)	1 (6.3)	

* a:Mann Whitney U Test, b:Fisher's Exact Test; Mean±SD, mm3: Cubic millimeter, n: Number, %: Percentage, SD: Standard deviation

healing was complete. Single or 2-tooth deficiencies were restored with implant-supported, screw-retained single crowns. 3-tooth deficiencies were restored with two implant-supported, 3-unit screw-retained dental prostheses. The cantilever design was not used in any patients. At the control appointments 1 year after prosthetic loading, the implants were evaluated clinically and radiologically. CBCT scans were carried out preoperatively (T0), post-implantation (T1), and a year following prosthetic loading (T2). Intraoral radiographs were taken post-implantation (T1) and a year following prosthetic loading (T2).

Study variables

The predictor variable was the timing of implantation (simultaneous or delayed approaches). The primary outcome variable was the 3D resorption rate of the bone graft after 1 year of prosthetic loading. Secondary outcome variables were 3D volume changes, 2D linear changes, marginal bone loss, and the success of the implant. The 3D volume changes were volume1 (the bone graft volume at post-implantation), volume2 (the bone graft volume at 1-year follow-up), and 3Dresorp (resorption volume of the bone graft). The 2D linear changes were width1 (the bone graft width at post-implantation), width2 (the bone graft width at 1-year follow-up), 2Dresorp (2D resorption amount of the bone graft), and 2D resorption rate. The variables were assessed separately for each implant if a patient had more than one implant.

Outcome measures

All data were collected by a single investigator (SAE). Intraexaminer calibration was determined by reassessing 3D measurements, 2D measurements, and marginal bone loss for 10 randomly selected implants, including duplicate measurements performed on different days, before evaluating the entire implant sample. The intraclass correlation coefficients for intraexaminer reliability were 0.947, 0.864, and 0.912 for the 3D measurements, 2D measurements, and marginal bone loss, respectively.

3D CBCT measurements

The same machine (Planmeca Promax 3D Mid, Helsinki, Finland) and the same protocol (90 kVp, 10 mA, 10.08 s, 0.20 mm voxel, 160x160 mm field of view [FOV]) were used for all CBCT scans. Images were exported with the Planmeca Romexis Viewer 4.6.2.R software (Planmeca, Helsinki, Finland). The procedures recommended in previous studies were followed when determining both 2D and 3D measurement protocols (16).

The CBCT data scanned at T0, T1, and T2 were used for 3D measurements. CBCT images were exported in DICOM format and uploaded to Slicer 5.2.2 software (Slicer Community) (20). Regarding the anatomical points, all CBCT scans were superimposed based on the T1 CBCT scans for each patient. The same threshold value was used for mandible segmentation in CBCT scans taken at different times for each patient. After that, background noise or artifacts were

eliminated slice by slice following the cortical border of the mandibular alveolar bone, and segmentation was completed manually in the axial, coronal, and sagittal planes. Implant segmentation was performed at the appropriate threshold value in the T1 CBCT images. To standardize the measurement area, 10 × 10 × 10 mm cubes were segmented. While the cubes were superimposed, the cervical border of the cubes was placed at the most coronal point of the implant and the lingual border at the most lingual point of the implant. The cubes were aligned so that the implants were centered in the axial plane and that their axis was parallel to the implant's long axis. All data were exported in STL format and uploaded to the Meshmixer program (AutoDesk, CA, USA). In this software, the measurement area was constructed by separating the implant segment from the cube segment to examine only the volume change in the bone graft. To identify ROIs, the areas that the mandible segments covered within the measurement area were digitally identi-

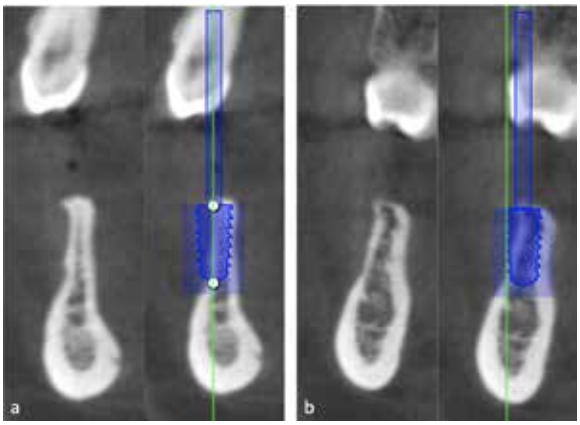

Figure 1. Choosing the implantation approach based on the CBCT examination **a)** Delayed implantation due to inadequate primary stability **b)** Simultaneous implantation due to adequate primary stability

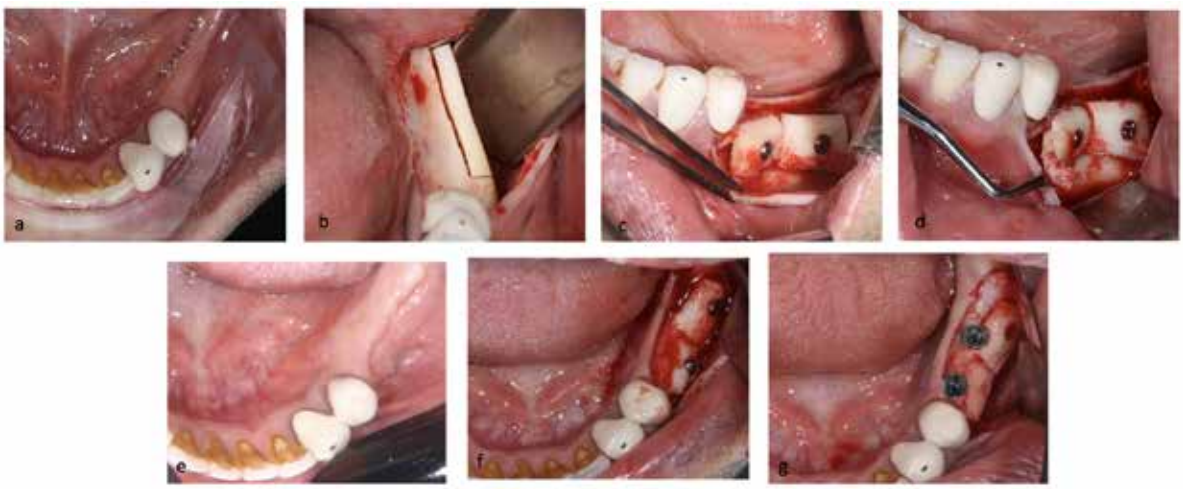

Figure 2. Delayed implantation approach **a-d)** Lateral alveolar ridge augmentation with ramus block graft **e-g)** Delayed implant placement 4 months after the augmentation procedure

Figure 3. Simultaneous implantation approach with augmentation procedure
a) Horizontally inadequate alveolar crest **b)** Implant placement and defect in buccal aspect **c)** Block graft fixation and filling of gaps with particulate grafts

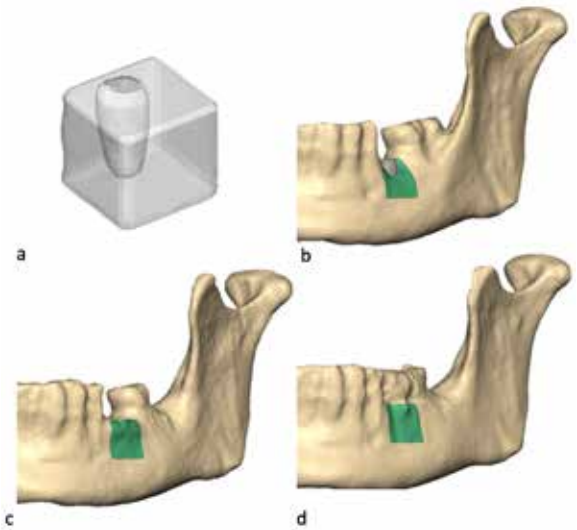

Figure 4. Identification of ROIs **a)** Separation of the implant segment from the cube segment to create a measurement area **b)**The green area represents ROI-0 **c)**The green area represents ROI-1 **d)** The green area represents ROI-2

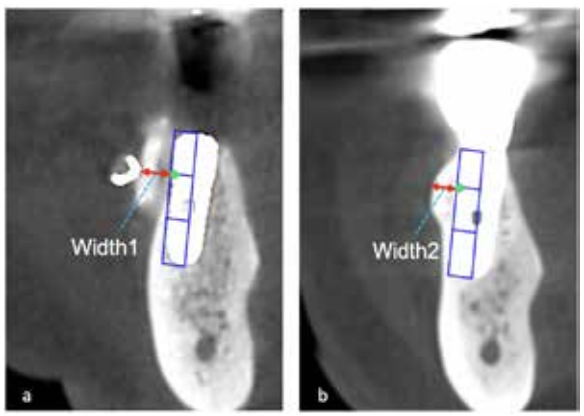

Figure 6. Determination of the 2D linear measuring points **a)** The bone graft width at post-implantation (Width1) **b)** The bone graft width at 1-year follow-up (Width2)

fied. Since the measurement area was superimposed at the same location in all mandible segments, it allowed measurement in a reproducible and standardized area specific to each implant. A total of 3 ROIs were created for each implant: preoperative ROI (ROI-0), post-implantation ROI (ROI-1), and 1-year follow-up ROI (ROI-2) (Figure 4). Volume1 was calculated by subtracting ROI-0 from ROI-1. Volume2 was calculated by subtracting ROI-0 from ROI-2. 3Dresorp was calculated by subtracting ROI-1 from ROI-2 (Figure 5). The 3D resorption rate was calculated using the following formula:

Figure 5. 3D volume measurements **a)** The purple area represents Volume1 **b)** The blue area represents Volume2 **c)** The red area represents 3Dresorp

$$\text{3D resorption rate} = 100 \times \frac{\text{Volume1} - \text{Volume2}}{\text{Volume1}}$$

2D CBCT measurements

The 2D measurements were made in Planmeca Romexis Viewer 4.6.2.R software using CBCT data scanned at T1 and T2. The procedures recommended by previous studies were followed to ensure that each spline on the axial view was the same for each patient through a series of scans taken at each measurement point (21). Measurements were taken on a cross-sectional image passing through the center of each implant. To establish the measurement point, a box parallel to the implant's long axis was made. The box's cervical border was lined up with the implant's most coronal point, the apical border was lined up with its most apical point, the lingual border was lined up with the implant's midline, and the buccal border was lined up with the implant's buccal line. This box was divided vertically into three equal parts. The width of the bone graft was determined by measuring the distance from the most buccal and coronal points of the middle part of the buccal bone in the direction perpendicular to the long axis of the implant (Figure 6).

The difference in the width of the bone graft between the T1 and T2 CBCT images was evaluated as the amount of 2Dresorp. The 2D resorption rate was calculated using the following formula:

$$\text{2D resorption rate} = 100 \times \frac{\text{Width1} - \text{Width2}}{\text{Width1}}$$

Marginal bone loss

Intraoral radiographs were obtained at T1 (baseline) and at T2 using the same device (Belmont Phot-X II

Model 303-CM, New Jersey, USA) with the aid of Kerr Super-Bite (KerrHawe SA, Switzerland) to achieve parallelism. Images were scanned using the VistaScan Mini Plus (DÜRR Dental SE, Almanya) device and exported with DBSWIN software (DÜRR Dental SE, Almanya) before being saved in JPEG format. Measurements were made using Digimizer Image Analysis Software Version 6.0 (MedCalc Software Ltd., Belgium). To minimize the distortion factor, the images were calibrated based on the implant length. The distance between the implant shoulder and the lowest point of the crestal bone in intimate contact with the implant was measured. For each implant, marginal bone loss was a single score recorded as the greatest value from either the mesial or distal measurements.

Implant success

The success of the implants was evaluated at T2 using the ICOI Implant Health Scale(17) (Table 1). Pain or tenderness during function was questioned on clinical examination. Through visual inspection, probing, and applying pressure, suppuration and implant mobility were evaluated. Probing depth measurements were made at six points of the implants (mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual), and a probing depth value was obtained for each implant by considering the largest value.

Statistical analysis

The Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) program was used for the statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, and maximum) were used to evaluate the study data. The conformity of the quantitative data to the normal distribution was determined using the Shapiro–Wilk test and graphical examinations. The Mann–Whitney U test was used for comparisons between two groups of quantitative variables that did not show a normal distribution. Fisher's exact test and the Fisher–Freeman–Halton test were used to compare the qualitative data. Statistical significance was accepted as $p < 0.05$. Statistical significance was accepted as $p < 0.05$. Post hoc analysis was performed based on the 3D resorption rate, which is the primary outcome, to investigate the power of the study.

RESULTS

During the study period, 56 subjects were screened for eligibility. The final sample comprised 21 subjects with a mean age of 42.8 ± 12 years, and 18 (89.5%) were female. In total, 33 implants were investigated, 51.5% (n = 17) of which were placed using a simultaneous approach and 48.5% (n = 16) using a delayed approach. In the delayed implantation approach group, the interval between augmentation and implantation operations ranged between 4 and 7 months, with a mean of 4.87 ± 0.83 months.

Three implant brands with platform-switching designs were used. (Straumann Bone Level, Institut Straumann AG, Basel, Switzerland; Megagen Anyone, MegaGen, Daegu, Korea; Megagen ST, MegaGen, Daegu, Korea) Demographic data and implant-related variables are compiled in tables (Table 2 and Table 3).

In both groups, the ISQ values of all implants were above 60 at implantation. No postoperative graft infection, graft loss complications, or prosthesis-related complications occurred in any of the patients. The descriptive statistics for 3D volume change, 2D linear change, marginal bone loss, and implant success between the simultaneous and delayed implantation groups are summarized in a table (Table 4).

The 3D volume measurements showed that the 3D resorption rate, volume1, and 3Dresorp values were higher in the simultaneous implantation group than in the delayed group. This difference was statistically significant ($p = 0.001$, $p = 0.003$, and $p = 0.001$, respectively). According to the results of the post hoc analysis based on the 3D resorption rate, the power of the study was 99.4%.

The 2D linear measurements showed that the 2D resorption rate, width1, and 2Dresorp values were higher in the simultaneous implantation group than in the delayed group. This difference was statistically significant ($p = 0.014$, $p = 0.014$, and $p = 0.017$, respectively)

There were no significant differences between the two groups with respect to volume2, width2, marginal bone loss, and implant success at the 1-year follow-up ($p = 0.958$, $p = 0.309$, $p = 0.168$, and $p = 1.000$, respectively).

DISCUSSION and CONCLUSION

This retrospective study aimed to demonstrate the effects of the timing of implantation on the dimensional changes in the bone graft and implant success in ridges augmented with autogenous grafts. The results showed that the simultaneous implantation approach demonstrated a higher rate of graft resorption compared to delayed implantation. This finding supports the hypothesis that the timing of implantation affects the dimensional changes in the bone graft.

Graft resorption is a natural consequence of graft healing. Studies have shown that 18–60% of the autogenous block graft volume is resorbed (22,23,24,25,26,27). In our study, autogenous graft stability in alveolar crests implanted using simultaneous implantation approaches was evaluated utilizing 3D measurement methods and compared with delayed implantation. In studies examining the volume changes in autogenous grafts in alveolar crests implanted with delayed implantation, both the graft volume gained and the resorbed graft volume values were higher than in the present study (12,13,14,15). The ROIs in these studies included the whole jaw or the whole region where grafting was performed. In patients undergoing augmentation, CBCTs obtained after implantation contain both the bone graft and the implant, which are absent in preoperative CBCT images. In the event of bone graft resorption over time, the implant continues to exist outside the pre-augmentation crest margins. In this case, if the implant is not removed in the measurement area, the implant volume is identified by the software as bone graft volume. In addition, if there is no mechanical stimulation on the bone graft for 6 months after augmentation, the bone graft begins to resorb, and its volume decreases (28,29). In the ROIs including the entire augmented area or the jaw, resorptions observed at unloaded graft sites may be misleading. Given these facts, this study focused on changes in peri-implant bone graft volume, and implant volume was not included in the digitally determined ROI borders. This method of determining ROI borders resulted in lower volume values compared to the literature. However, this allowed measurements to be made in a standardized and reproducible manner at different time points at each implant site.

The results of our study indicated that the width1 and volume1 in both the 2D and 3D CBCT evaluations were significantly higher in the simultaneous implantation group than in the delayed group. This result is consistent with a meta-analysis reporting higher width gains as a result of the simultaneous approach compared to the delayed approach (30). The thickness of the external oblique ridge restricts the graft's size in the ramus block graft procedure (31). In the simultaneous approach, due to the placement of the implant between the residual crest and the graft, the blocks are fixed away from the residual crest, and more bone thickness can be obtained. Additionally, in the present study, post-implantation evaluations were performed immediately with the augmentation in the simultaneous approach and 4 months after the augmentation in the delayed approach. During implantation, autogenous block grafts resorb at a rate ranging from 0% to 25% (9). Performing measurements 4 months after the grafting procedure may have been a factor in the delayed implantation group's lower volume1, width1, 3Dresorp, and 2Dresorp values compared to those of the simultaneous implantation group.

The present study's findings revealed that there was no difference between the two groups in terms of graft volume, graft width, marginal bone loss, and implant success at the 1-year follow-up. This result rejects the hypothesis that the timing of implantation influences implant success and showed that the two groups had similar results, at least at the 1-year follow-up. There is no consensus in the literature on the results of simultaneous and delayed implantation approaches. Tosun et al. evaluated autogenous bone graft resorption using 2D linear measurements in CBCT. The higher graft resorption rate as a result of the simultaneous implantation approach compared to the delayed implantation approach reported in this study is consistent with our study (7). Some researchers who compared simultaneous and delayed implantation approaches in alveolar crests augmented with autogenous grafts observed that marginal bone loss was higher following the simultaneous implantation approach (6,7,11) Aloy-Prósper et al. indicated that marginal bone loss was higher in the simultaneous group, but when bone grafting was successful, marginal bone loss was not significantly different between the groups. (6) In the present study, no

graft-related complications occurred. On the contrary, several researchers have indicated that marginal bone loss was not different between the two groups (10). Similarly, studies have reported that implant success and survival are higher following the delayed implantation approach, while others have reported that they are similar regardless of the approach (6,11,32).

Limitations of the present study include its short follow-up period, retrospective design, and small sample size. Additionally, dividing groups based on preoperative CBCT evaluations may cause bias. However, the present study has the strength is that comparable results are obtained by creating a standardized measurement area for each implant at different times.

The results of the study showed that although the simultaneous implantation approach was associated with a higher rate of graft resorption than the delayed implantation approach in crests augmented with autogenous grafts, the implants in the two groups showed similar results at the 1-year follow-up. The literature indicates that alveolar crests augmented with autogenous grafts acquire a stable bone level around the implant after 3 years, regardless of the timing of implantation (1,3,33) Therefore, the 1-year follow-up may not be the endpoint when it comes to measuring graft volume changes and implant success. Prospective comparative studies with longer follow-ups and larger sample sizes are needed to show the effects of the timing of implantation on implant success and graft stability in crests augmented with autogenous grafts.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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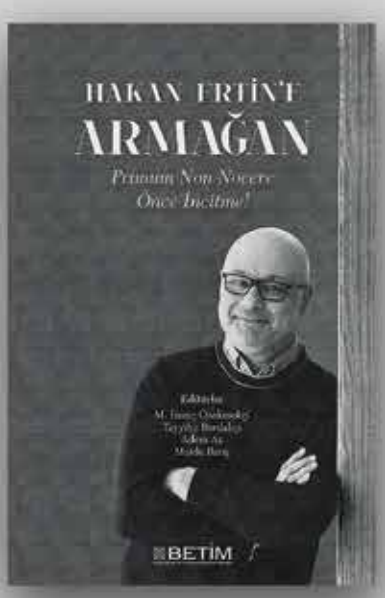

HAKAN ERTİN'E
ARMAĞAN

Primum Non Nocere
Önce İncitme!

Editörler
M. İnanç Özekmekçi, Tayyibe Bardakçı
Adem Az, Maide Barış

Hakan Ertin, akademide eşine az rastlanır incelikte ve bilgelikte, merhametli, anlayışlı, öğrencisine her zaman vakti olan, yeri geldiğinde yakın bir arkadaş, yeri geldiğinde bir baba, ama her zaman en sevilen hocalardan biri oldu. Türkiye'nin ilk ve halihazırda tek tıpta insan bilimleri merkezi olan Beşikçizade Tıp ve İnsani Bilimler Merkezi - BETİM'i kurdu. BETİM'de çok sayıda etkinlik, dersler, çalıştaylar düzenlenmesinde, "tıpta insan bilimleri" ve "biyoetik" alanlarının ülkemizde duyulmasında çok önemli bir rol üstlendi. Öğrencilerine sürekli tıbbın öznesinin olduğu kadar nesnesinin de 'insan' olduğunu vurguladı. Tıbbın ilk kuralı "*primum non nocere*", yani "önce zarar verme" Hakan Hocamızın hem öğrencilerine öğrettiği hem de kendi hayatında titizlikle uyguladığı bir ilkeydi. Ve bu ilkenin maddi boyutu kadar manevi boyutunun da önem taşıdığının bilincindeydi. Hakan Hoca, modern hayatın empoze ettiği kalp kırıp kırmadığını önemsemeyen benmerkezci ve pragmatik tutuma inat, hayatı boyunca, incinse de incitmemek için gayret etti. Biz de bu yüzden ona armağan ettiğimiz bu kitapta, hocamızın bu düsturunu bir rehber kabul ederek "önce incitme!" dedik.

BETİM KİTAPLIĞI

Fasiyal sinirin intraparotidal dallanma paternleri ve cerrahi önemi

Intraparotidal branching patterns of the facial nerve and it's surgical significance

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Öz

Amaç: Bu çalışmanın amacı fasiyal sinirin intraparotidal dallanma paternlerini, anastomozlarını ve anatomik varyasyonlarını araştırmak ve dallanma paternlerinin cerrahi önemini vurgulamaktır.

Yöntemler: Bu çalışmaya 2018-2023 yılları arasında parotis kitlesi nedeniyle total veya yüzeyel parotidektomi uygulanan ve ameliyat sonunda intraparotidal fasiyal sinirin ana trunkustan itibaren seyrini gösteren fotoğrafları mevcut olan hastalar dâhil edildi. Hastaların fasiyal sinir dallanma ve anastomoz sınıflaması Katz ve Catalano'nun sınıflamasına göre yapıldı ve buna göre analiz edildi.

Bulgular: Çalışmaya dâhil edilme kriterlerini sağlayan 48 hasta dâhil edildi. Hastaların 18 tanesi kadın, 30 tanesi erkek idi. Hastaların yaş ortalaması 57,37 idi. Fasiyal sinir dallanma paternleri analiz edildiğinde en sık olan dallanma paterninin tip 1 olduğu görülmüştür (%41,6). İkinci sıklıkta ise tip 2 (%27,08) dallanma paterni görülmüştür. Tip 3 dallanma hastaların % 20,83'ünde, tip 4 ise hastaların %6,25'inde görülmüştür. En az görülen tipin ise tip 5 dallanma paterni olduğu bulunmuştur (%4,16).

Sonuç: Bu çalışma ülkemizdeki erişkinlerde yapılan, kadavra çalışması olmayan ve fasiyal sinirin intraparotidal dallanma paternini araştıran ilk çalışmadır. Çalışma sonucunda en sık görülen dallanma paterninin tip 1 dallanma paterni olduğu görülmüştür. Parotis bezi cerrahisi ile uğraşan hekimlerin fasiyal sinir intraparotidal dallanma paternlerine hâkim olmasının, başarılı ve komplikasyonsuz bir cerrahi gerçekleştirilebilmesi için önemli olabileceği düşünülmüştür.

Anahtar Sözcükler: Fasiyal sinir; parotis bölgesi

Abstract

Aim: The aim of this study is to investigate the intraparotidal branching patterns, anastomoses, and anatomical variations of the facial nerve and to emphasize the surgical importance of branching patterns.

Methods: This study included patients who underwent total or superficial parotidectomy for parotid mass between 2018 and 2023 and had available photographs taken at the end of the surgery showing the intraparotid facial nerve course from the main trunk. Classification of facial nerve branching and anastomosis was performed according to the classification of Katz and Catalano and analyzed accordingly.

Results: Forty-eight patients who met the inclusion criteria were included in the study. 18 of the patients were women and 30 were men. The average age of the patients was 57.37. When facial nerve branching patterns were analyzed, the most common branching pattern was type 1 (41.6%). The second most common branching pattern was type 2 (27.08%). Type 3 branching pattern was seen in 20.83% of the patients and type 4 was seen in 6.25% of the patients. The least common type was type 5 (4.16%).

Conclusion: This is the first study in our country to investigate the intraparotidal branching pattern of the facial nerve in adults. As a result of the study, it was observed that the most common branching pattern was type 1. It is thought that surgeons dealing with the parotid gland may benefit from being familiar with intraparotid facial nerve branching patterns in order to perform a successful and uncomplicated surgery.

Keywords: Facial nerve; parotid region

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GİRİŞ

Parotis bezi tümörleri tüm baş boyun bölgesi tümörlerinin yaklaşık %2'sini, tüm tükürük bezi tümörlerinin ise yaklaşık %70-80'ini oluşturmaktadır (1). Parotis tümörlerinde cerrahi tedavi fasiyal sinir ve dallarının tanınarak korunduğu, tümörün çevresindeki tükürük bezi dokusuyla birlikte tamamen çıkarılmasını içeren yüzeyel ya da total parotidektomidir.

Parotidektomi, tedavi edici bir cerrahi işlem olmasının yanında fasiyal sinirin yüz kasları, mimikler ve yüz görünümündeki önemi nedeniyle aynı zamanda kozmetik yönü de çok önemli olan bir cerrahidir. Bu cerrahinin başarılı sonuçlanmasındaki majör kriterlerden biri cerrahinin fasiyal sinirde iatrojenik hasar oluşmadan tamamlanabilmesidir.

Fasiyal sinir, parotid bölgede genellikle çeşitli dallanma ve anastomoz paternleri içerecek şekilde önce temporofasiyal ve servikofasiyal olmak üzere iki ana dala ayrılmakta ardından da temporal, zigomatik, bukkal, marjinal mandibüler ve servikal dallarını vermektedir (1,2). Farklı varyasyonlardaki dallanma paternleri, özellikle derin lob tümörlerinde parotidektomi sırasında sinir diseksiyonunu zorlaştıran nedenlerden biridir (1). Bu nedenle fasiyal siniri ilgilendiren cerrahi operasyonlarda fasiyal sinirde iatrojenik hasar oluşmaması için cerrahın fasiyal sinir anatomisine ve dallanma paternlerindeki tüm olasılıklara hâkim olması hayati önem taşımaktadır.

Fasiyal sinirin intraparotidal dallanmaları ile ilgili çalışmalar incelendiğinde ülkeler arasında hatta aynı ülkenin farklı alt bölgeleri arasında farklı dallanma paternlerinin olduğu bildirilmiştir. Ülkemizde yapılan çalışmalar değerlendirildiğinde ise çok kısıtlı sayıda çalışmanın mevcut olduğu ve bu çalışmaların tamamının kadavra üzerinde ve fetüs ya da çocuklarda yapıldığı görülmüştür (3-6).

Bu nedenle bu çalışmanın amacı ülkemizdeki erişkin popülasyonunda fasiyal sinirin intraparotid dallanma paternlerini, anastomozlarını ve anatomik varyasyonlarını araştırmak ve dallanma paterlerinin cerrahi önemini vurgulamaktır.

GEREÇ VE YÖNTEMLER

Bu çalışma retrospektif olarak, Balıkesir Üniversitesi Rektörlüğü Sağlık Bilimleri Girişimsel Olmayan Araştırmalar Etik Kurulu onayı alındıktan sonra (tarih: 02.04.2024, karar no:2024/55) Helsinki Deklarasyonu'na uygun olarak üçüncü basamak sağlık kuruluşunda gerçekleştirilmiştir.

Hastaların demografik ve klinik bilgileri hastaların medikal kayıtlarından, klinik takip kartlarından ve ana bilim dalı fotoğraf arşivinden elde edilmiştir. Bilgileri kullanılan tüm hastalara çalışma ile ilgili bilgi verilmiş ve hastaların medikal bilgilerini kullanabilmek için onam alınmıştır.

Bu çalışmaya 2018- 2023 yılları arasında parotiste kitle nedeniyle total veya yüzeyel parotidektomi uygulanmış olan hastalar dâhil edildi. Tüm hastaların cerrahi kararları ultrasonografi eşliğinde ince iğne aspirasyon biyopsisi sonucu, bilgisayarlı tomografi (BT) veya Manyetik rezonans (MR) görüntülemesi değerlendirildikten sonra verilmiştir. Parotidektomi operasyonları genel anestezi altında, Modifiye Blair insizyonu (Preauriküler alandan başlayıp, auriküla lobülünden arkaya mastoid apekse doğru dönüp oradan da sternokleidomastoid kası ön kısmına doğru devam edecek şekilde insizyon) ile yapılmıştır. İnsizyonu takiben cilt flebi elevasyonu süperfisiyal muskulo-aponörotik sistem altından olacak şekilde yapılmıştır. Takiben digastrik kasın posterior karnı, styloid proses, tragal pointer ve mastoid apeks referans noktaları alınarak fasiyal sinir ana trunkusu bulunmuştur. Fasiyal sinir ana trunkusu bulunduktan sonra pes anserinusa kadar ilerlenip önce temporofasiyal sonra servikofasiyal kısmı proksimalden distale doğru diseke edilerek fasiyal sinirin tüm dalları ve anastomozları takip edilerek tümör patolojisi ve yerleşim yerine göre yüzeyel ya da total parotidektomi operasyonu uygulanmıştır. 2020 yılından sonraki tüm vakalarda fasiyal sinir monitörizasyonu kullanılmıştır. Cerrahi bitiminde tüm hastaların fasiyal sinirlerini ana trunkustan itibaren gösterecek şekilde fotoğrafları ve videoları çekilerek hastaların ameliyat notları ile birlikte ana bilim dalı arşivine eklenmiştir.

Rekürren parotis cerrahisi yapılmak, preoperatif fasiyal parezi ya da paralizili olmak, cilde infiltre tümörü olmak ve herhangi bir dalın intraoperatif olarak rezeke edilmesini gerektiren malign parotis tümörü bulunmak, takip kartlarındaki verileri ya da intraoperatif çekilmiş olan fotoğrafları eksik olmak, Türkiye Cumhuriyeti vatandaşı olmamak ve yabancı uyruklu olmak çalışmadan dışlama kriteri olarak belirlendi.

Tablo 1. Parotidektomi yapılan hastaların ameliyat sonrası histopatoloji sonuçları

Ameliyat sonrası histopatalojik tanı	Sayı
Pleomorfik adenom	17
Warthin tümörü	18
Squamöz hücreli karsinom	4
Karsinoma ex pleomorfik adenom	2
Lipom	1
Bazal hücreli karsinom	1
Malign melanoma	1
Sekretuar hücreli karsinom	1
Asinik hücreli karsinom	1
Onkositoma	1
Kronik lenfositer lösemi	1

Hastaların fasiyal sinir dallanma ve anastomoz sınıflaması Katz ve Catalano'nun çalışmalarında kullandıkları fasiyal sinir dallanma sınıflamasına göre yapıldı (7) (Şekil 1). Hastaların fasiyal sinir dallanmaları bu sınıflamaya göre yapıldıktan sonra çalışmaya dâhil edilen hastaların fasiyal sinirin dallanma paternleri bulundu ve çalışma sonucu olarak sunuldu.

Bu sınıflamaya göre fasiyal sinir 5 grupta sınıflandırılmıştır.

Tip I: Fasyial sinirin üst (temporozigomatik) ve alt (servikomandibüler) ana dalları birbiri ile anastomoz yapmazlar.

I A: Ana trunkustan iki ana dal ayrılır. Zigomatik ayrımdan çıkan ve yine zigomatik dal ile anastomoz yapan bir dal mevcuttur.

I B: Ana trunkustan iki ana dal ayrılır. Bukkal dal temporozigomatik ayrımdan doğar. Mandibüler dal kendisi ile anastomoz yapan ikinci bir dala sahiptir.

Tip II: Fasiyal sinir ana trunkustan üst ve alt dallara ayrıldıktan sonra zigomatik dal ile bukkal dal arasında anastomoz mevcuttur.

Tip III: Bukkal dalın diğer dallar ile majör anstomozu mevcuttur.

Tip III A: Bukkal dal ile zigomatik dal arasında anastomoz vardır.

***Tip III B*:** Bukkal dal ile zigomatik dal arasında anastomoz vardır ancak mandibüler dal ana trunkus yerine bukkal daldan ayrılır.

Tip III C: Bukkal dal ile mandibüler dal arasında majör anastomozlar vardır.

Tip IV: Dallar arasında multiple anastomozlar vardır.

Tip IVA: Bukkal dal servikomandilüler daldan çıkar. Zigomatik, bukkal ve mandibüler dallar arasında anastomozlar vardır.

Tip IV B: Bukkal dal hem alt hem de üst ana daldan çıkabilir. Tüm dallar arasında multiple anstomozlar görülür.

Type V: Majör ve minör olmak üzere iki ana trunkus vardır.

İstatistiksel analiz

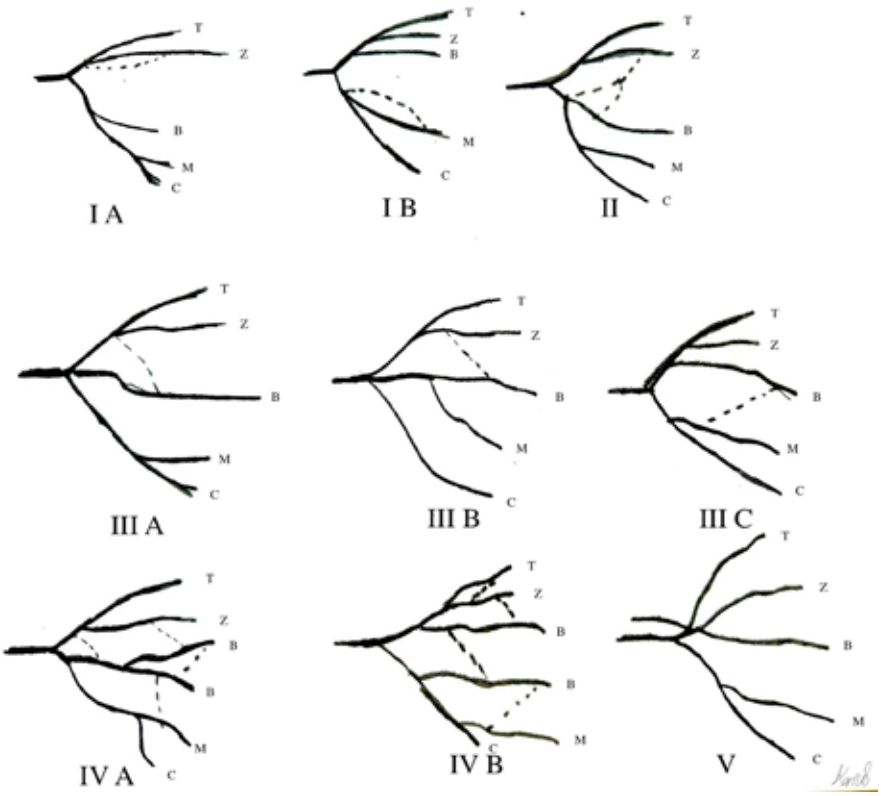
Araştırma verileri Statistical Package For Social Sciences for Windows version 22.0 (SPSS Inc. Chicago, IL,USA) aracılığıyla bilgisayar ortamına yüklenmiş ve değerlendirilmiştir. Çalışmadaki bulgular sayı ve yüzde olarak sunulmuştur. Çalışmada gruplar arası karşılaştırma içeren istatistiksel analiz yöntemi olmadığı için power analiz yapılmamıştır.

BULGULAR

Bu çalışmaya medikal verileri ve fotoğrafları tam olan 48 hasta dâhil edildi. Hastaların 18 tanesi kadın (%37,5), 30 tanesi erkek (%62,5) idi. Hastaların yaş ortalaması 57,37 idi.

Kırk bir hastaya yüzeyel partoidektomi, 7 hastaya total parotidektomi uygulandı. Parotidektomilerin 19 tanesi sol, 29 tanesi ise sağ parotidektomi idi. Hastaların ameliyat sonrası patoloji sonuçlarının değerlendirilmesi tablo halinde verilmiştir (Tablo 1).

Hastaların fasiyal sinir dallanma ve anastomoz paternleri değerlendirildiğinde; en sık tip 1 dallanma paterni görülmüştür (20 hastada (%41,6)). Takiben tip 2 dallanma paterni 13 hastada (%27,08) görülmüştür. Tip 3 dallanma 10 hastada (%20,83), tip 4 dallanma ise 3 hastada (%6,25) görülmüştür. En az görülen tip ise tip 5 dallanma olarak bulunmuştur (2 hastada (%4,16)). İntraoperatif çekilen fotoğraflarda fasiyal sinirin dallanma paternlerinin örnekleri resimler halinde sunulmuştur (Resim1-5).



Şekil 1. Katz ve Catalano'nun yaptıkları fasiyal sinir dallanma ve anastomoz sınıflaması (T: Temporal dal, Z: Zigomatik dal, B: Bukkal dal, M: Marjinal mandibüler dal, C: Servikal dal)

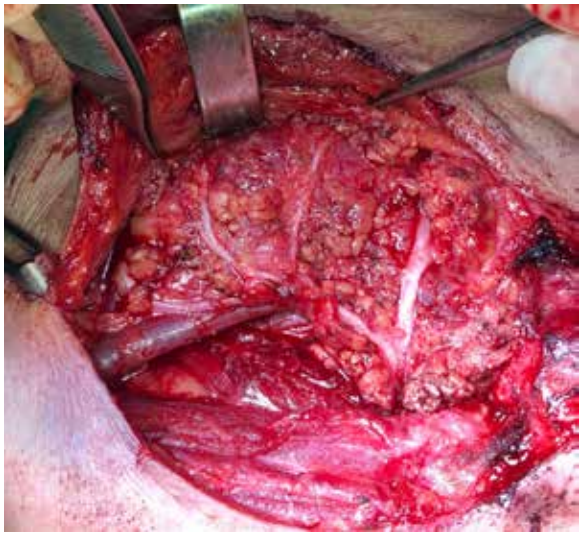
TARTIŞMA VE SONUÇ

Tükürük bezi tümörleri, baş boyun bölgesi tümörlerinin yaklaşık olarak %5-10'unu oluşturur. Tükürük bezi tümörleri en sık (%85) parotis bezinden köken alır. Parotis tömörlerinin ideal tedavisi iatrojenik fasiyal paraliziye neden olmadan, tümörün etraf tükürük bezi dokusuyla birlikte çıkarılmasını içeren yüzeyel ya da total parotidektomidir.

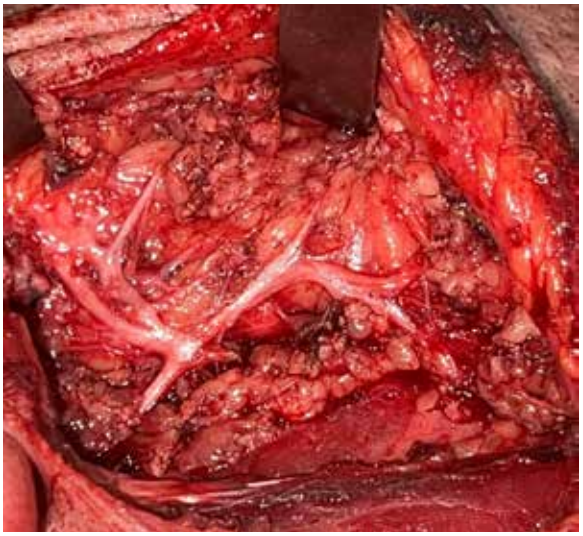
Parotidektomi gibi fasiyal siniri ilgilendiren cerrahilerde fasiyal sinirin tam olarak identifiye edilmesi ve tüm dallarıyla birlikte korunması başarılı ve komplikasyonsuz cerrahi için önemli kriterlerin başında gelmektedir (1,3). Bening parotis tümörlerinde parotidektomi sonrası geçici fasiyal paralizi meydana gelme olasılığı %20-55 iken kalıcı paralizi meydana gelme olasılığı %1-2'dir (1,8). Sinirin anatomik varyasyonunun mevcut olduğu durumlarda, malign tümörlerde, derin lob tümörlerinde ve revizyon parotis cerrahilerinde fasiyal sinirin hasar görme olasılığı daha da artmaktadır (1). Parotis bezi içerisindeki fasiyal sinirin dallanma paterni ve anastomozları oldukça çeşitli ve karmaşıktır (2). Fasiyal sinirin intraparotidal anatomisi ve anastomozları hakkında detaylı bilgi sahibi olmak, sinirin identifiye edilebilmesi ve paralizi olmadan cerrahinin tamamlanabilmesi için çok önemlidir (9).

Fasiyal sinirin parotis bezi içerisindeki dallanma paternleri ile ilgili olarak çeşitli araştırmacılar tarafından çalışmalar yapılmıştır. Yapılan çalışmalar değerlendirildiğinde farklı ülkelerde, farklı etnik kökenlerde hatta aynı ülke içerisindeki farklı coğrafik alt bölgelerde farklı dallanma paternlerinin mevcut olduğu literatürde bildirilmiştir (1,7,10-15). Yapılan literatür taramasında ülkemizde yapılan çalışmalar değerlendirildiğinde; çok kısıtlı sayıda çalışmanın mevcut olduğu ve bunların tamamının kadavra (etnik kökeni belirtilmeyen) çalışması olduğu görülmüştür (3-6). Bu nedenle bu çalışma ülkemizdeki erişkinlerde yapılan, kadavra çalışması olmayan ve fasiyal sinirin intraparotidal dallanma paternini ortaya koyan ilk çalışmadır.

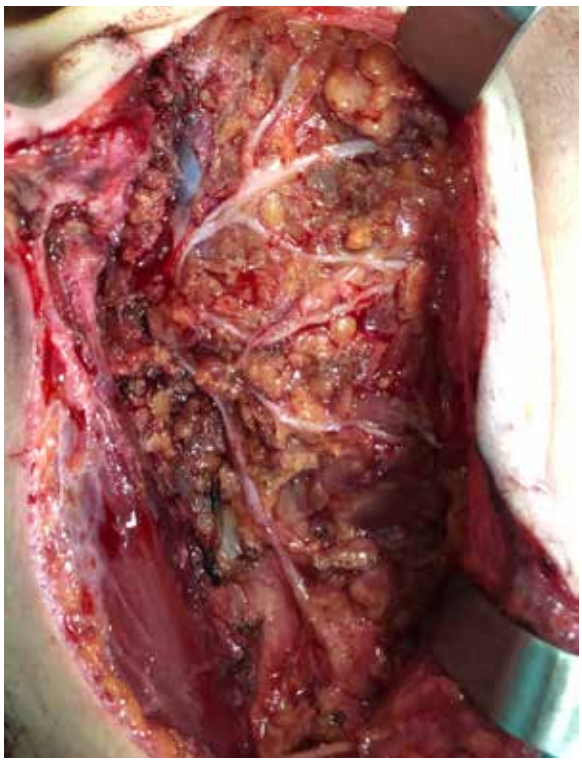
Çalışmada fasiyal sinir dallanma paternleri Katz ve Catalano'nun çalışmalarında kullandıkları fasiyal sinir



Resim 1. Tip 1 dallanma paterni (parotidektomi operasyonunda çekilmiş olan, fasiyal sinir ve dallanmasını gösteren fotoğraf)



Resim 2. Tip 2 dallanma paterni (parotidektomi operasyonunda çekilmiş olan fasiyal sinir ve dallanmasını gösteren fotoğraf)

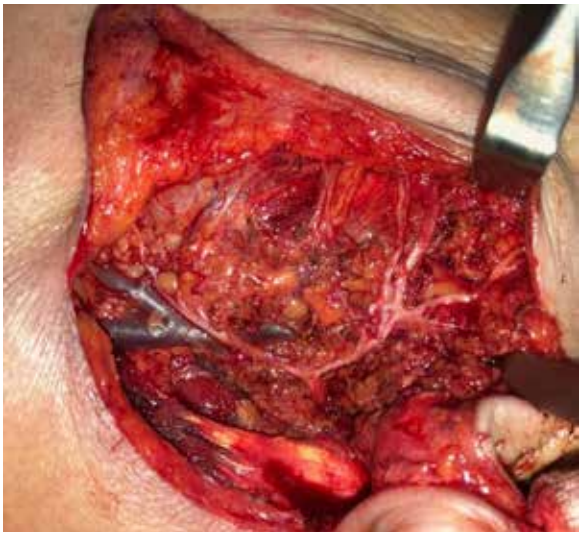


Resim 3. Tip 3 dallanma paterni (parotidektomi operasyonunda çekilmiş olan fasiyal sinir ve dallanmasını gösteren fotoğraf)

dallanma sınıflamasına göre sınıflandırılmış ve en sık görülen tip olarak tip 1 dallanma paterni bulunmuştur (7). Tip 1 dallanma paterninde fasiyal sinir ana trunkusu önce temporozigomatik ve servikofasiyal olarak iki ana dala ayrılır daha sonra da bu dallardan temporal dal, zigomatik dal, bukkal dal, marjinal mandibüler dal, servikal dal çıkar. Tip 1 dallanma paterninin en büyük özelliği alt ve üst ana dallar ve diğer beş dalın birbiri ile hiç anastomoz yapmamasıdır. Yani herhangi bir dalda meydana gelecek olan iatrojenik hasarın parezi ya da paralizi ile sonuçlanma olasılığı yüksektir. O nedenle dallanma paternlerine ve özelliklerine hâkim olunması ve özellikle tip 1 dallanma paterni olan hastalarda parezi ya da paralizi riskinin yüksek olması nedeniyle intraoperatif olarak ekstra dikkat sarf edilmesi önem arz etmektedir.

Çalışmada hastaların yaklaşık %20'sinde tip 3 dallanma paterni bulunmuştur. Bu dallanma paterninin özelliği bukkal dalın diğer dallar ile majör anastomozlar içeriyor olmasıdır. Klinik olarak önemi ise böyle bir dallanma paternine sahip bir hastada bukkal dalda, anastomoz hattının proksimalinde meydana gelecek olan iatrojenik sinir hasarının parezi ya da paralizi ile sonuçlanmayabilecek olmasıdır. Bu açıdan bu dallanma paterni avantajlı paternlerden biridir.

Çalışmada hastaların %6'sında tip 4 dallanma paterni görülmüştür. Bu dallanma paterni klinik olarak en avantajlı patern olarak sayılabilmektedir. Çünkü dallar arasında multiple anastomozlar vardır. Cerrahi sırasında, anastomoz sayısı fazla olduğu için diseksiyonu ve sinirin takibi daha zor olsa da iatrojenik sinir hasarlarının multiple anastomozlar nedeniyle postoperatif olarak parezi ya da paralizi ile sonuçlanmama



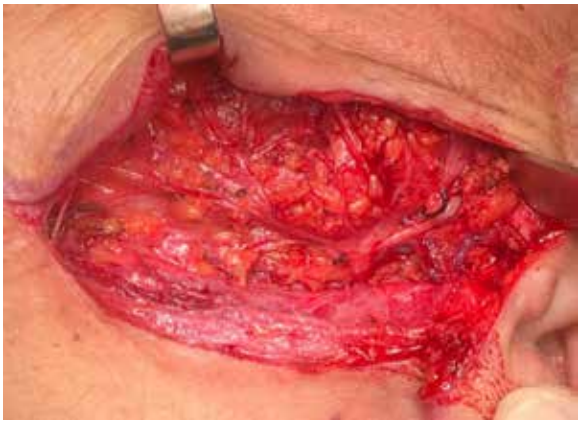
Resim 4. Tip 4 dallanma paterni (parotidektomi operasyonunda çekilmiş olan fasiyal sinir ve dallanmasını gösteren fotoğraf)

olasılığı yüksektir.

Bu çalışmada ve literatürdeki diğer çalışmalarda en az görülen ancak önemli bir dallanma paterni de tip 5'tir. Bu tipte majör ve minör olmak üzere iki ana trunkus mevcuttur. Bunun klinik önemi ise cerrahın ana trunkusu bulduğunda, her zaman ikinci bir ana trunkusun daha olabileceğini aklında bulundurmasının gerekliliğidir. Bu nedenle Pes anserinusu görene kadar ya da sinir monitöründe ana trunkustan yapılan uyarı sonucunda tüm yüzün hareketini tanıyana kadar herhangi bir eksizyon işleminden uzak durulmalıdır.

Bu konu ile ilgili yapılan diğer çalışmalar incelendiğinde; ülkemizde Alkan ve ark. ile Kopuz ve ark. tarafından yapılan çalışmalarda en sık tip 4 dallanma panterinin olduğu, Öksüz ve ark. tarafından yapılan çalışmada ise en sık tip 1 dallanma paterni olduğu görülmüştür (3-5). Bu çalışmaların tümünde fasiyal sinir incelemeleri kadavralar üzerinde yapılmıştır ve kadavraların kökenleri ile ilgili bir bilgi verilmemiştir. Bu nedenle bu çalışmaların ülkemizdeki fasiyal sinirin dallanma panterlerini yansıtıp yansıtmadığı tartışmalıdır.

Gataa ve Faris'in çalışmalarında, Devis ve ark.'ın çalışmasında ve Katz ve Katalano'nun çalışmalarında en sık tip 3 dallanma paterninin olduğu bulunmuştur (1,7,11). Thuku ve ark.'ın çalışmasında ise en sık tip 1 bulunmuştur (10). Çocukların dâhil olduğu çalışmalar incelendiğinde ise Ekinci'nin çalışması 27 çocuk



Resim 5. Tip 1 dallanma paterni (parotidektomi operasyonunda çekilmiş olan fasiyal sinir ve dallanmasını gösteren fotoğraf)

kadavrada yapılmış ve en sık tip 1 dallanma paterni bulunmuştur (16). Kopuz ve ark.'ın çalışmalarında ise tüm yaş grupları dâhil edildiğinde en sık tip 4 dallanma paterni bulmuş olmalarına rağmen sadece çalışmalarındaki çocuk hastalar ayrı değerlendirdiğinde en sık tip 1 dallanma paterni bulunmuştur (4). Kopuz ve ark. yaşın dallanma paterni üzerine etkili olup olmadığını araştırmak amacıyla regresyon analizi yapmışlar ve regresyon analizi sonucunda yaş arttıkça anastomozların da artabileceği soncuna ulaşmışlardır (4).

Hem ülkemizdeki hem de diğer ülkelerdeki çalışma sonuçları değerlendirildiğinde fasiyal sinirin dallanma paternlerinde ülkeden ülkeye hatta aynı ülkenin farklı bölümlerinde hatta farklı yaş gruplarında bile farklılık olabileceği görülmüştür. Bu nedenle bu çalışmanın sonuçlarının ülkemizde erişkinlerde yapılan ilk çalışma olması nedeniyle fasiyal sinir intraparotidal dallanma paterninin belirlenebilmesi açısından önemli olabileceği düşünülmüştür. Ancak çalışmanın çeşitli kısıtlılıkları mevcuttur. Bunlardan biri çalışmanın retrospektif olarak yapılmış olmasıdır, diğer bir kısıtlılık ise çalışmaya dâhil edilen hastaların sadece güney Marmara ve Kuzey Ege bölgesi popülasyonunu içermesidir. Bu nedenle bundan sonraki çalışmaların ülkemizde çok merkezli, tüm bölgeleri kapsayacak ve her yaş grubunu içerecek şekilde yapılmasının fasiyal sinirin ülkemizdeki intraparotidal dallanma paterninin tespitine ve fasiyal sinir cerrahisiyle uğraşan hekimlere faydalı olabileceği düşünülmüştür.

Sonuç olarak çalışmada parotidektomi yapılan erişkin hastalarda fasiyal sinirin intraparotid dallanma

paternleri araştırılmış ve en sık tip 1 dallanma paterninin, en az ise tip 5 dallanma paterninin mevcut olduğu bulunmuştur. Fasiyal sinirin intraparotidal anatomisine detaylı bir şekilde hâkim olunması parotidektomi yapan cerrahlar açısından önem arz etmektedir. Bu nedenle parotis bezi cerrahisi ile uğraşan hekimlerin çalıştıkları ülke ve bölge insanının fasiyal sinir intraparotidal dallanma paternlerine hâkim olmasının, sinirin tam olarak identifiye edilebilmesi ve sinirin tüm dallarının korunarak başarılı ve komplikasyonsuz bir cerrahi gerçekleştirilebilmesi için önemli olabileceği düşünülmüştür.

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TIBBİ VE SOSYAL YÖNLERİYLE

SÜNNET CERRAHİSİ

EDİTÖRLER
M. FATİH ŞİMŞEKOĞLU
BÜLENT ÖZALTAY

İnsanlık tarihi boyunca en çok uygulanan cerrahi işlemlerden olan sünnet (hitan) ile ilgili tıbbi ve sosyal alanda bugüne kadar çokça tartışmalar yürütülmüştür. Bu tartışmaların genellikle bilimsel veriler zemininde ele alınmaması ve farklı önyargıların tesiri altında kalması nedeniyle sünnet cerrahisi ile ilgili net kanaatlere ulaşmak mümkün olmamıştır.

Elinizdeki kitap sünnetin tıbbi, cerrahi ve sosyal yönlerine dair en güncel tartışmaları disiplinler arası işbirliği çerçevesinde sunmayı amaçlamaktadır. Bu çalışmanın sağlık çalışanları, akademisyenler ve sünnete dair rehberlik arayışında olan aileler için kaynak kitap olmasını umuyoruz.

BETİM KİTAPLIĞI

Comparison of the effects of remifentanil and fentanyl on awakening and hemodynamic parameters in probe curettage cases

Probe küretaj olgularında remifentanil ve fentanilin uyanma ve hemodinamik parametreler üzerine etkilerinin karşılaştırılması

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Abstract

Aim: We aimed to investigate the effects of two different opioids, fentanyl, and remifentanil, on waking parameters, hemodynamic effects, duration of stay in the post-anesthesia care unit (PACU), pain and nausea and vomiting in patients undergoing probe curettage surgery.

Methods: Sixty-six patients scheduled for probe curettage surgery were randomly divided into Fentanyl (Group F, n = 33) and Remifentanil (Group R, n = 33) groups. For induction of anesthesia, 2.5 mg/kg propofol was administered as a bolus in both groups, 2.5 mcg/kg fentanyl in Group F and 2-4 mcg/kg i.v. remifentanil in Group R. No muscle relaxant agent was used. The laryngeal mask size was selected according to the patient's body weight. For induction of anesthesia, 2.5 mg/kg propofol was administered as a bolus in both groups, 2.5 mcg/kg fentanyl in Group F, and 2-4 mcg/kg i.v. remifentanil in Group R. No muscle relaxant was used. The laryngeal mask size was selected according to the patient's body weight and the cuff pressure was adjusted to 60 cm H2O using a manometer.

Results: The demographic data of both groups were similar in our study. Extubation time was shorter in Group R. The difference between the groups was significant (p<0.001). The awakening time was also significantly shorter in Group R (p<0.001). Among the hemodynamic data, MAP values were lower in Group R at T1, T3, and T5 time intervals. HR values were significantly lower in Group R. There was a statistically significant difference between the groups in both time intervals (p: 0.014, p: 0.037)

Conclusions: In our study, remifentanil provided better hemodynamic stability, shorter extubation and awakening times, and lower incidence of nausea and vomiting than fentanyl in probe curettage cases. Therefore, we suggest that the use of remifentanil with supraglottic airway devices is a good alternative in anesthesia management.

Keywords: Awakening from anesthesia; curettage; day surgery; fentanyl; laryngeal mask airway; remifentanyl

ÖZ

Amaç: Supraglottik hava yolu cihazı ile havayolu güvenliğin sağladığımız çalışmamızda fentanil ve remifentanil gibi iki farklı opiodin probe küretaj ogularında uyanma parametreleri, hemodinamik etkiler, anestezi sonrası bakım ünitesi (PACU)' da kalış süresi, ağrı ve bulantı kusma üzerine etkilerini incelemeyi amaçladık.

Yöntemler: Probe küretaj cerrahisi planlanan 66 hasta Fentanil (Grup F, n = 33) ve Remifentanil (Grup R, n = 33) guruplarına randomize olarak dağıtıldı. Anestezi indüksiyonunda her iki grupta 2.5 mg/kg propofol i.v, Grup F' de 2.5 mcg/kg fentanil i.v, Grup R' de ise 2-4 mcg/kg i.v remifentanil bolus olarak uygulandı ve kas gevşetici bir ajan kullanılmadı. Hastanın vücut ağırlığına göre laringeal maske boyutu seçildi ve kaf basıncı bir manometre kullanılarak 60 cm H2O'ya ayarlandı. Anestezi indüksiyonunda her iki grupta 2.5 mg/kg propofol, Grup F' de 2.5 mcg/kg fentanil, Grup R' de ise 2-4 mcg/kg i.v remifentanil bolus olarak uygulandı ve kas gevşetici bir ajan kullanılmadı. Hastanın vücut ağırlığına göre laringeal maske boyutu seçildi ve kaf basıncı bir manometre kullanılarak 60 cm H2 O'ya ayarlandı.

Bulgular: Çalışmamızda her iki grubun demografik verileri benzerdi. Ekstübasyon ve uyanma süresi Grup R'de daha kısaydı. Gruplararası fark anlamlı idi (p<0,001). Hemodinamik verilerden ortalama arter basıncı (MAP) değerleri; T1, T3, T5 zaman aralığında Grup R' de daha düşüktü. Kalp atış hızı (HR) değerleri Grup R'de anlamlı olarak daha düşüktü. Her iki zaman aralığında gruplar arasında istatiksel olarak anlamlı fark vardı (p: 0,014, p: 0,037)

Sonuçlar: Çalışmamızda edilen probe küretaj olgularında remifentanilin fentanile göre daha iyi bir hemodinamik stabilite sağladığı, ekstübasyon ve uyanma sürelerini daha kısa olduğu, bulantı kusma insidansının daha az olduğu görüldü. Bu nedenle supraglottik hava yolu cihazlarıyla birlikte remifentanil kullanımının anestezi yönetiminde iyi bir alternatif olduğunu düşünmekteyiz.

Anahtar Sözcükler: Anesteziden uyanma; fentanil; günlük cerrahi; küretaj; laringeal maske havayolu; remifentanil

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INTRODUCTION

Day surgery is defined as the discharge of a patient who has undergone an interventional procedure on the same day or within 24 hours (1). Reducing the time spent in the hospital decreases wound infection, minimizes the loss of labor force and minimizes hospital costs (2). Recently, day surgery interventions have become increasingly common.

Patient groups undergoing day-case anesthesia have many comorbidities. This situation makes anesthesia management special. Postoperative pain, nausea-vomiting, and depth of sedation are important factors affecting the duration of hospitalization in surgical applications (3).

Therefore, the anesthesia method to be used in day surgery applications should provide a stable hemodynamic state, adequate depth of anesthesia, and rapid recovery (4). One of the goals of day surgery is the rapid return of patients to their daily activities (5).

Probe curettage is a surgical procedure that constitutes the most minimally invasive gynecologic intervention used in diagnosis and treatment for a long time. Probe curettage is also one of the daily surgical procedures (6).

The use of supraglottic airway devices in short-term minimal surgical procedures that do not carry the risk of regurgitation is seen as a good alternative to endotracheal intubation in probe curettage cases because it does not require the use of muscle relaxants and is less irritating to the airway. (7) .

Many anesthesia methods and anesthetic drugs have been used in anesthesia applications used in day surgery operations. There are not many studies in the literature comparing remifentanil and fentanyl in cases of probe curettage using laryngeal mask airway (LMA).

In our study in which we ensured airway safety with LMA, we aimed to investigate the effects of two different opioids such as fentanyl and remifentanil on waking parameters, hemodynamic effects, duration of stay in the post-anesthesia care unit (PACU), pain and nausea and vomiting in probe curettage cases.

MATERIAL AND METHODS

Protocol

This study was conducted in the Department of Anesthesiology and Reanimation, Inonu University, Faculty of Medicine, Turgut Özal Medical Center, with the approval of the Malatya Clinical Research Ethics Committee (date: 21.12.2022, decision no: 2022/105). The study was conducted according to CONSORT guidance (8).

Study Participants

Our study was conducted as a randomized, double-blind clinical trial. Subjects who voluntarily agreed to participate in the study were informed about the potential risks and predictable outcomes of the study. Written informed consent was then obtained. For randomization, patients were assigned to the study groups completely by chance. MedCalc, version-16 statistical software for Windows (medcalc.com.tr.) was used for this purpose. Sixty-six patients scheduled for probe curettage surgery were randomly assigned to Fentanyl (Group F, n = 33) and Remifentanil (Group R, n = 33) groups.

Patient Recruitment

ASA I-II patients aged 18-65 years who underwent probe curettage were included in our study. Patients with severe respiratory, hepatic, or renal dysfunction, neurological and psychiatric patients, history of allergy to anesthesia drugs, obese patients with body mass index (BMI) over 30, difficult airway findings (modified Mallampati class 4 or thyromental distance <65 mm), high risk of regurgitation or aspiration were excluded.

Preoperative Procedures

General anesthesia was standardized for all patients. Patients were given midazolam 0.05 - 0.1 mg/kg i.v. for premedication 20 minutes before the surgical procedure. The patients were taken to the operation room and pre-oxygenated with 100% O_2 for 5 min. Routine noninvasive blood pressure (NIBP), pulse oximetry (SpO_2), electrocardiogram (ECG), heart rate (HR), and end-tidal carbon dioxide ($EtCO_2$) monitoring were performed.

General Anesthesia

For induction of anesthesia, 2.5 mg/kg i.v propofol was administered as a bolus in both groups, 3-5 μg/kg fentanyl in Group F and 2-4 μg/kg i.v. remifentanil in Group R. No muscle relaxant agent was used. The laryngeal mask size was selected according to the pa-

Table 1. Characteristics of the groups

	Group F (Mean ± StD)	Group R (Mean ± StD)	p
Age, (year)	44,48 ± 13,38	41,81 ± 14,32	0,393
Weight, (kg)	67,06 ± 11,76	70,30 ± 10,61	0,136
ASA, n(%)			0,804
I	18 (54,5)	20 (60,6)	
II	15 (45,5)	13 (39,4)	
Mallampati, n(%)			0,621
1	19 (57,6)	17 (51,5)	
2	14 (42,4)	16 (48,5)	
Bradicardia, n(%)	1 (3,03)	2 (6,06)	0,403
Surgical duration, (min)	15,81 ± 2,78	17,21 ± 2,73	0,073
Anaesthesia duration, (min)	23,63 ± 4,52	21,96 ± 2,73	0,076
PACU duration, (min)	19,06 ± 3,82	13,03 ± 2,87	**<0,001***
Extubation duration, (min)	7,09 ± 1,37	4,81 ± 1,073	**<0,001***
Wake-up duration, (min)	6,72 ± 1,20	3,42 ± 0,83	**<0,001***

ASA: American Society of Anesthesiologists, PACU: Postanesthetic care unit, StD: Standart deviation, min: Minute, n: Number, %: Percentage

Table 2. Sedation values of the groups

	Group F n(%)	Group R n(%)	p
Sedation S5			<0,001*
1	5 (15,2)	0 (0)	
2	13 (39,4)	1 (3,0)	
3	11 (33,3)	14 (42,4)	
4	4 (12,1)	18 (54,5)	
5	0 (0)	0 (0)	
Sedation S15			<0,001*
1	0 (0)	0 (0)	
2	4 (12,1)	0 (0)	
3	9 (27,3)	2 (6,1)	
4	16 (48,5)	13 (39,4)	
5	4 (12,1)	18 (54,5)	

Sedation S5: PACU 5th minute, sedation; S15: PACU 15th minute, 1: Deep sleep; 2: Sleeping, slow response to verbal stimulation; 3: Prone to sleep; 4: Awake calm quiet; 5: Awake active .* Significant difference, min: Minute, n: Number, %: Percentage

tient's body weight and the cuff pressure was adjusted to 60 cm H_2O using a manometer.

After placement of the laryngeal mask, the position of the airway devices in both groups will be confirmed by the absence of leak sound, and chest expansion during ventilation, auscultation, and capnography.

Anesthesia maintenance was provided with 75 mcg/kg/min propofol and 50% O2/air mixture in each group, 1.5 mcg/kg/h fentanyl in Group F and 0.1-0.3 mcg/kg/min remifentanil in Group R. In both groups, the anesthesia device was set in volume-controlled mode with a tidal volume of 6-8 mL/kg and a respiratory rate of 35-45 mm Hg $EtCO_2$.

Hemodynamic parameters were recorded at the following time intervals: T0 before induction, T1 after LMA placement, T2 surgery at 5 min, T3 surgery at 10 min, T4 surgery at 15 min, T5 surgery at 25 min, and T6 surgery at 35 min. Demographic data, duration of anesthesia and surgery, recovery time, postanesthetic intensive care unit stay, pain, nausea and vomiting data were evaluated.

Postoperative Management

Patients who opened their eyes with warnings, whose spontaneous breathing was regular, respiratory rate was 14-20/min, and oxygen saturation was greater

Table 3. Pain values of the groups

	Group F n(%)	Group R n(%)	p
NRS			0,019*
0-1	12 (36,4)	7 (21,2)	
2-4	15 (45,5)	10 (30,3)	
5-7	6 (18,2)	14 (42,4)	
8-10	0 (0)	2 (6,1)	

NRS: Numerical rating scale, no pain (0-1 points), mild pain (2–4 points), moderate pain (5–6 points) and severe pain (7–10 points). * Significant difference, n: Number, %: Percentage

Table 4. PONV values of the groups

	Group F n(%)	Group R n(%)	p
PONV-5			0,110
0	12 (36,4)	20 (60,6)	
1	13 (39,4)	9 (27,3)	
2	5 (15,2)	2 (6,1)	
3	3 (9,1)	2 (6,1)	
PONV-15			**0,007***
0	16 (48,5)	28 (84,8)	
1	8 (24,2)	1 (3,0)	
2	4 (12,1)	4 (12,1)	
3	5 (15,2)	0 (0)	

PONV: Postoperative nausea and vomiting; PONV-5: Postoperative 5th minute; PONV-15: Postoperative 15'th minutes, n: Number, %: Percentage, * Significant difference

than 95% were extubated and taken to the recovery room. In the recovery unit, hemodynamically and respiratory stable patients with a Modified Aldrete score ≥ 9 were transferred to the relevant ward (9).

Outcome Measures

Anesthesia duration; the time from induction of anesthesia until extubation. Surgical time; the time from the first surgical incision until the end of the surgical procedure. Extubation time; the time from the completion of surgery and discontinuation of anesthetic drugs until extubation. Recovery time was defined as a meaningful response to simple verbal commands (open your eyes, etc.) given after extubation. Bradycardia (<50/min) was evaluated. PACU length of stay was defined as the time from admission of the patient to the recovery room to transfer to the relevant service.

Pain was assessed by a blinded anesthesiologist as postoperative pain on a numerical rating scale (NRS) (0-10 scale (0-1: mild, 2-4: moderate, 5-7: moderate, 8-10: severe). 15 mg/kg i.v. paracetamol was given as a rescue analgesic in cases with NRS ≥5.

Nausea and vomiting were assessed with a 4-point scale (0=no nausea, 1=moderate nausea, 2=severe nausea, 3= retching, vomiting or both). In cases of 'severe nausea', ondansetron 50 mcg/kg i.v. was administered as antiemetic. In our study, all outcome measures were assessed by a blinded observer.

Sample Size

While the type I error (alpha) is 0.05, the power of the test (1-beta) is 0.9, the effect size is 0.82 and the alternative hypothesis (H1) is two-way, the minimum sample size required to find a significant difference using this test should be 33 in each group and 66 in total (10). Power analysis was calculated with WSSPAS software (11).

Statistical analysis

PONV: Postoperative nausea and vomiting; PONV-5: Postoperative 5th minute; PONV-15: Postoperative

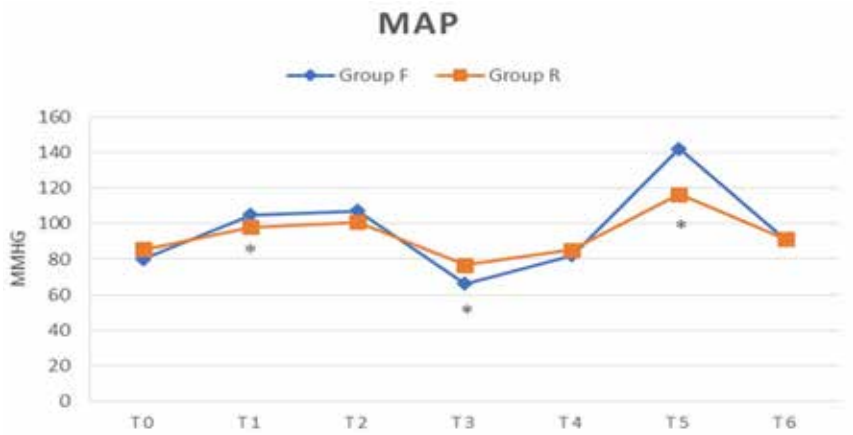

Figure 1. MAP values of the groups
MAP: Mean Arterial Pressure; T0: pre-induction; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference.

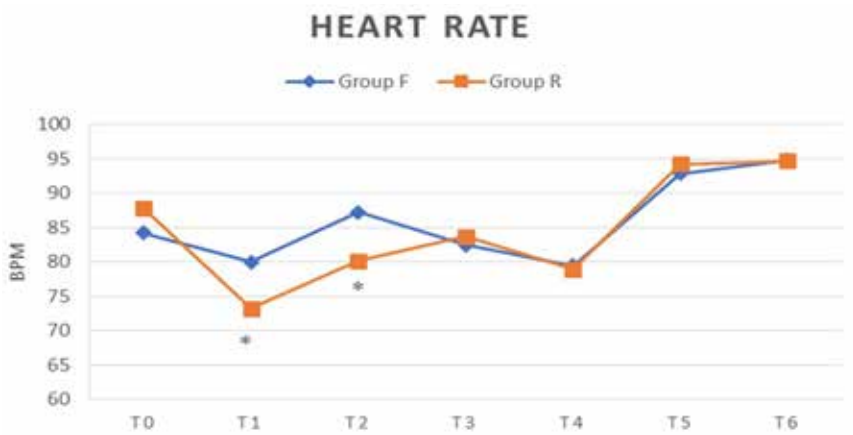

Figure 2. HR values of the groups
HR values of the groups. T0: pre-induction; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference, HR: Hearts rate, BPM: Beats per minute.

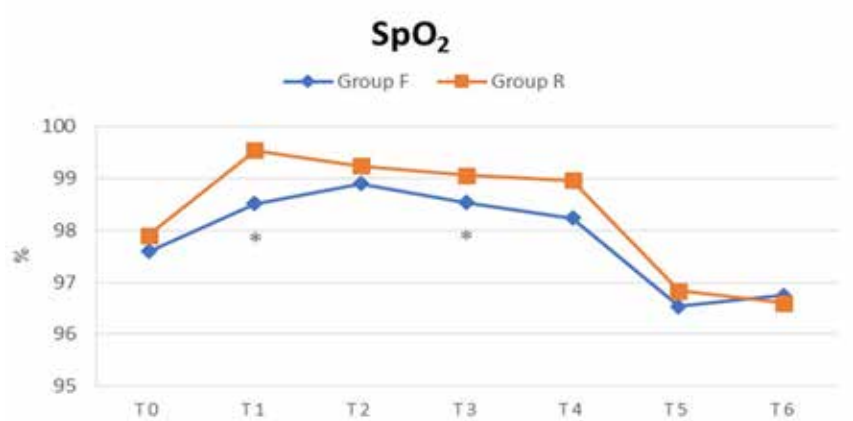

Figure 3. SpO_2 values of the groups
SpO_2: peripheral oxygen saturation; T0: pre-induction; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference.

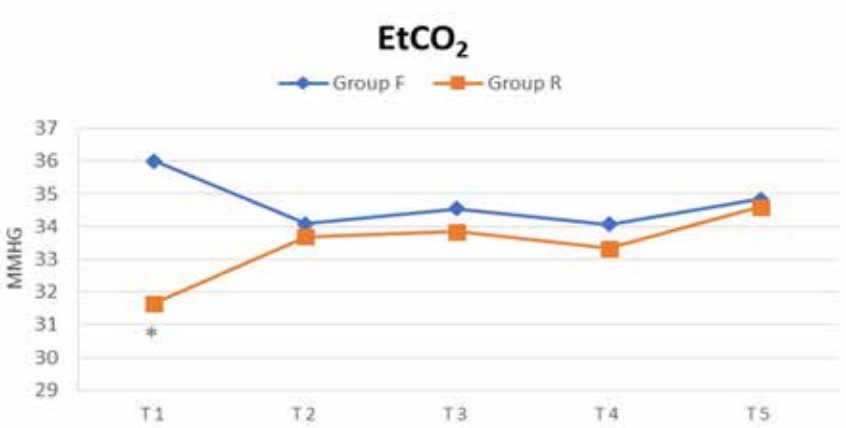

Figure 4. $EtCO_2$ values of the groups
$EtCO_2$: end-tidal carbon dioxide; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference.

15'th minutes, n: Number, %: Percentage, * Significant difference Shapiro-Wilk test, histogram distribution, and skewness-kurtosis parameters were used for normality analysis. Descriptive statistics are shown as mean ± standard deviation for variables with normal distribution, median (min-max) for variables with non-normal distribution, and the number of cases and (%) for nominal variables. The Chi-square and Fisher Exact tests were used to analyze the relationship between categorical variables. In evaluating the relationship between continuous variables, the Mann-Whitney U test was used if the variables were non-parametric, and Student's t-test was used if they were parametric. A p-value less than 0.05 was considered statistically significant.

RESULTS

The mean age of the patients in our study was 44.48 ± 13.38 years in Group F and 41.81 ± 14.32 years in group R. There was no significant difference between the groups (p>0,05). Weight, ASA and mallampati scores were similar between the groups and there was no statistically significant difference (p>0,05) . Bradycardia was observed in 1 patient in group F and 2 patients in Group R. The difference between the groups was not statistically significant. The duration of PACU stay was shorter in group R. The difference between the groups was statistically significant (p<0.001). Extubation time was shorter in Group R. The difference between the groups was significant (p<0.001). The awakening time was also significantly shorter in Group R (p<0.001). Demographic characteristics in our study are presented in Table 1.

Among the hemodynamic data, MAP values were lower in Group R at T1, T3 and T5 time intervals. There was a statistically significant difference between the groups (p: 0.024, p: 0.008, p: 0.006). There was no statistically significant difference between the groups at other time intervals (p>0,05) (Figure 1).

When HR values were analyzed, HR values were significantly lower in Group R at T1 and T2 time intervals. There was a statistically significant difference between the groups at both time intervals (p: 0.014, p: 0.037) (Figure 2).

When sedation values were measured at the 5th and 15th minute in PACU, sedation scores were higher in Group R at both time intervals. The difference between the groups was statistically more significant (p<0.001, p<0.001) (Table 2).

Postoperative pain scores were lower in Group F than in Group R when evaluated by NRS at 15 min in PACU. This difference was statistically significant (p: 0.019) (Table 3).

There was a statistically significant difference in SpO_2 values at T1 and T2 time intervals. There was no significant difference at other time intervals. EtCO2 values were significantly different between the groups

at T1. There was no significant statistical difference between the groups at other time intervals (Figure 3).

When postoperative nausea and vomiting scores were compared, there was no statistically significant difference in both groups at 5 minutes (p: 0.110). In the comparison of the other time interval of 15 minutes, the PONV values were lower in Group R. There was a statistically significant difference between the groups (p: 0.007).

DISCUSSION AND CONCLUSION

In this study, in which we applied TIVA, in daily probe curettage interventions using LMA We compared the effects of two different opioids (fentanyl and remifentanil) on hemodynamic data, awakening parameters, nausea, vomiting and pain. Extubation time and awakening time were significantly shorter in group R. Among hemodynamic parameters, MAP and HR values were more stable and lower at certain time intervals.

In PACU; pain intensity in NRS assessment was less in Group F. In PACU, nausea and vomiting were less in Group R in PONV-15th minute evaluation. The difference between the groups was statistically significant.

It is known that most of the surgical interventions are actually suitable cases for day surgery. Probe curettage cases are also considered in this group (12). In this study, we aimed to investigate important variables such as anesthesia awakening parameters of two different opioids and postoperative PACU stay time in probe curettage cases in which LMA was used for airway management.

Early discharge has many advantages in patients undergoing day surgery, and reduces the risk of infection, increases bed availability in hospitals and decreases the cost of treatment per patient (13).

Supraglottic airway devices are increasingly used as an alternative to endotracheal intubation in airway management in short-term day surgery applications requiring general anesthesia because they do not require the use of muscle relaxant agents, can be easily applied without the need for laryngoscopy which causes sympathetic discharge, cause less traumatic damage, provide better stability in hemodynamic data, less airway complications and provide better comfort in the postoperative period (14,15).

During endotracheal intubation, activation develops in the sympathoadrenal system due to supraglottic stimulation, and this leads to catecholamine discharge. This leads to unwanted increases in intracranial and intraocular pressure, especially arterial hypertension and tachycardia (16).

Tachycardia developing during the placement of supraglottic airway devices is one of the important hemodynamic parameters. This situation is especially important in terms of complications that may occur in patients with cardiac pathologies.

In a study by Zhang L. et al. comparing propofol-fentanyl and propofol-remifentanil combination for anesthesia in gastrointestinal endoscopy cases, HR values were lower in the remifentanil group (17). In another study comparing the effects of remifentanil and fentanyl on hemodynamic data, HR values were statistically significantly lower in the remifentanil group at all time intervals evaluated (18). In our study, in accordance with the literature, statistically significantly less tachycardia was observed in patients in whom remifentanil was used in the early period compared to patients in whom fentanyl was used.

Avoiding hypertensive episodes in airway management is critical in terms of morbidity. Suppression of hemodynamic response during intubation is one of the important parameters of a successful induction of anesthesia. In a study investigating cardiovascular response to intubation, MAP values were statistically significantly lower in the remifentanil group than in the fentanyl group at all time intervals determined, especially after induction (18). In our study, MAP values were similarly more stable in group R. MAP values were lower in group R at T1, T3 and T5 time intervals. There was no statistically significant difference between the groups at other time intervals.

Remifentanil has vagotonic and sympatholytic effects like other narcotics. radicardia is the most common side effect. Remifentanil is hydrolyzed by blood and tissue esterases independent of the liver and kidney. Therefore, it does not accumulate in tissues and its effect disappears rapidly (19).

Oğurlu M. et al. reported bradycardia in 4 (11.1%) patients in the remifentanil group and in 3 (8.3%) patients in the fentanyl group in probe curettage cases

(20). In our study, bradycardia was observed in 1 (3.03%) patient in group F and in 2 (6.06%) patients in group R. There was no statistically significant difference between the two groups.

Faster recovery time from anesthesia, earlier response to verbal commands and less time in the PACU are the desired outcomes in daily procedures such as probe curettage.

In a study comparing the effects of remifentanil and fentanyl in dilated curettage cases, the time to wake up, orientation and response to verbal commands after extubation was significantly shorter in the remifentanil group than in the fentanyl group (20).

In another study, in invasive hemato-oncologic procedures in which the efficacy of fentanyl and remifentanil were evaluated, it was shown that the time to open the eye with verbal stimuli and recovery time was statistically significantly shorter in the propofol-remifentanil group (21). In our study, extubation time, awakening time and PACU stay time were significantly shorter in the remifentanil group, consistent with the literature.

Postoperative nausea and vomiting are one of the most important complications in day surgery under general anesthesia, especially in gynecologic operations. In our study, the incidence of nausea and vomiting at 5-15 minutes in PACU was evaluated. While there was no significant difference in the incidence of nausea and vomiting in both groups at 5 minutes in PACU, nausea and vomiting was statistically significantly higher in the fentanyl group at 15 minutes. The effect of fentanyl lasts for 0.5 to 2 hours, depending on the dose. Remifentanil half-life is 3-6 minutes and terminal elimination half-life is 10-20 minutes (22). In this study, there was no statistical difference between the two agents in the evaluation of nausea and vomiting in the postoperative 6-24th hours. We think that late evaluation was effective in the formation of this picture (23).

Pain is one of the parameters affecting the length of hospital stay and patient comfort in patients undergoing day surgery. Analgesic properties of the agents used should be well evaluated (24). In a study comparing the effects of fentanyl and remifentanil in probe curettage cases, there was no significant difference in NRS values in the early postoperative period (5th min). However, NRS values were significantly higher in the remifentanil group at the 10th minute (25). In our study, pain intensity was found to be statistically higher in Group R at the NRS 15th-minute assessment. We think that the longer half-life of fentanyl was effective in the lower pain intensity in Group F in late pain scores.

In our study, remifentanil provided better hemodynamic stability, shorter extubation and awakening times, and lower incidence of nausea and vomiting than fentanyl in probe curettage cases accepted as day surgery. Therefore, we think that the use of remifentanil with supraglottic airway devices is a good alternative in anesthesia management.

Conflict-of-Interest and Financial Disclosure

The author declares that he has no conflict of interest to disclose. The author also declares that he did not receive any financial support for the study.

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SAĞLIKTA ADALET

Türkiye'de Sağlıkta Dönüşüm Programı'nın Etik Analizi

Dr Ahmet Özdinç

Sağlığın sadece bir tıp problemi olarak görülmediği günümüzde, tıp etiği konusu büyük bir önem kazanmıştır. Sosyal güvenlik kapsamında ve devletin kontrolünde yürütülen sağlık hizmetleri, adalet ve etiğin konusu haline gelmiştir. Devlete karşı yükümlülüklerini yerine getiren bireylerin sosyal güvencenin bir parçası olan sağlık taleplerine hukukî bir zemin oluşturulmaktadır. Bu organizasyonda devlet, sağlık hizmetlerini imkânları en iyi şekilde değerlendirip vatandaşlarına dağıtmakla sorumludur. Yine bu zeminde hastalarla hekimlerin hak ve sorumlulukları da devletin güvencesi ve denetimi altındadır. Planlamadan uygulamaya kadar yürütülen bütün faaliyetler, oldukça kapsamlı bir etik tartışmasını da beraberinde getirmiştir.

BETİM KİTAPLIĞI

The effect of postnatal weight gain and other risk factors on severe retinopathy of prematurity

Postnatal kilo alımı ve diğer risk faktörlerin şiddetli prematüre retinopatisi üzerindeki etkisi

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Abstract

Aim: To assess the effect of postnatal weight gain characteristics and multiple risk factors on treatment-required retinopathy of prematurity.

Methods: The medical records of preterm infants who were followed up for retinopathy of prematurity in a tertiary referral center were retrospectively reviewed. Infants were grouped as Treatment(-) (retinal maturation without treatment) and Treatment(+) (treatment required). Retinopathy of prematurity findings, weight gain and weight gain rates at the 4th and 6th weeks, and clinical features were noted. The best cut-off points for the weight gain and weight gain rate were assessed with the area under the receiver operating characteristic curve. Risk factors were determined by the logistic regression model.

Results: Twenty-eight of 201 preterm infants (13.5%) were in the treatment (+) group. Birth weight, gestational age, weight gain, and weight gain rate at the 4th and 6th weeks were lower, the duration of oxygen therapy and hospitalization was longer, and a history of bronchopulmonary dysplasia, necrotizing enterocolitis, prolonged mechanical ventilation, and erythrocyte transfusion was more common in the treatment (+) group ($p<0.05$). The best cut-off points (and area under the receiver operating characteristic curve) were calculated as 297.5 g (0.779) and 504.5 g (0.771) for weight gain and 21.02% (0.697) and 54.80% (0.670) for weight gain rates at the 4th and 6th weeks, respectively. History of bronchopulmonary dysplasia and prolonged mechanical ventilation were independently associated with severe retinopathy of prematurity.

Conclusion: Preterm infants with a history of low weight gain profile at the 4th week, bronchopulmonary dysplasia, and prolonged mechanical ventilation should be carefully monitored for the development of the treatment-required retinopathy of prematurity.

Keywords: Birth weight; bronchopulmonary dysplasia; mechanical ventilation; retinopathy of prematurity; weight gain

Öz

Amaç: Postnatal kilo alımı özelliklerinin ve çoklu risk faktörlerinin tedavi gerektiren prematüre retinopatisi üzerindeki etkisinin değerlendirilmesi.

Yöntemler: Üçüncü basamak bir sevk merkezinde prematüre retinopatisi nedeniyle takip edilen preterm infantların tıbbi kayıtları retrospektif olarak incelendi. İnfantlar Tedavi (-) (tedavisiz retinal matürasyon) ve tedavi (+) (tedavi gerekli) olarak gruplandırıldı. Prematüre retinopatisi bulguları, 4. ve 6. haftalardaki kilo alımı, kilo alımı oranları ve klinik özellikler not edildi. Kilo alımı ve kilo alımı oranı için en iyi kesim noktaları alıcı işletim karakteristik eğrisi altı alan ile değerlendirildi. Risk faktörleri lojistik regresyon modeli ile belirlendi.

Bulgular: İki yüz bir preterm infanttan 28'i (%13,5) tedavi (+) grubundaydı. Tedavi (+) grubunda doğum ağırlığı, gebelik yaşı, kilo alımı ile 4. ve 6. haftalardaki kilo alımı oranı daha düşük, oksijen tedavisi ve hastanede yatış süresi daha uzun ve bronkopulmoner displazi, nekrotizan enterokolit, uzamış mekanik ventilasyon ve eritrosit transfüzyonu öyküsü daha yaygındı ($p<0,05$). En iyi kesim noktaları (ve alıcı işletim karakteristik eğrisi altı alan) 4. ve 6. haftalardaki kilo alımı için sırasıyla 297,5 g (0,779) ve 504,5 g (0,771) ve kilo alımı oranları için %21,02 (0,697) ve %54,80 (0,670) olarak hesaplandı. Bronkopulmoner displazi öyküsü ve uzamış mekanik ventilasyon bağımsız olarak tedavi gerektiren prematüre retinopatisi ile ilişkiliydi.

Sonuç: Dördüncü haftada düşük kilo alımı profili, bronkopulmoner displazi ve uzamış mekanik ventilasyon öyküsü olan preterm infantlar tedavi gerektiren prematüre retinopatisi gelişimi açısından dikkatle izlenmelidir.

Anahtar Sözcükler: Ağırlık artışı; bronkopulmoner displazi; doğum ağırlığı; mekanik ventilasyon; prematüre retinopatisi

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INTRODUCTION

Retinopathy of prematurity (ROP) is an abnormal proliferative retinal vasculopathy that results from the relative ischemia of non-vascularized immature retinal areas in premature infants and may cause blindness in the advanced stages (1, 2). Therefore, it is necessary to determine the risk factors of patients carefully, perform their follow-up regularly, apply the appropriate treatment in a timely manner when necessary, and ensure continuous communication between the experienced and specialized ophthalmologist, neonatologist, and the infant's family in terms of ROP.

As a result of the studies conducted, it has been shown that premature birth is not a risk factor by itself, and ROP is a multifactorial disease. Low birth age and weight, application of high-concentration oxygen therapy in the neonatal intensive care unit (NICU), neonatal sepsis, erythrocyte transfusion (ET), history of bronchopulmonary dysplasia (BPD), perinatal asphyxia, intraventricular hemorrhage (IVH), apneic attacks, acidosis, and many other factors have been examined in terms of their role in the etiology of the disease (3-6). Some recent studies have shown that the weight gain of premature infants is effective on the incidence and stage of ROP (6-12). It has been shown that physiological weight gain during the postnatal period is related to serum Insulin-Like Growth Factor-1 (IGF-1) level, and it has been thought that low serum IGF-1 level in premature infants with very low birth weight is a risk factor for the development of ROP (1, 8, 13, 14). Although there have been studies associating weight gain with ROP, there are limited studies in which weight gain has been ratioed to birth weight, and this ratio has been associated with treatment-required ROP (15-18).

This study aims to retrospectively investigate the effects of weight gain characteristics during the neonatal intensive care unit (NICU) period and other risk factors on the development of the treatment-required ROP in premature infants enrolled in a screening and follow-up program for ROP in a tertiary referral center.

MATERIAL AND METHODS

The medical records of 207 infants who were hospitalized in the NICU of a tertiary referral center between September 2010 and September 2014 due to preterm birth and who were screened and followed up for ROP by an experienced ophthalmologist at the same center were retrospectively analyzed. All infants born in the 35th gestational week and/or with a birth weight under 1500 g and infants born after the 35th gestational week, for whom consultation had been requested by neonatologists because of the risk, were included in the study. The study was performed with the approval of the Bakirköy Dr. Sadi Konuk Educational and Research Hospital Clinical Research Ethics Committee (date: 12.12.2014, decision no: 2014-17-16), and the research protocol was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from the parents of the infants included in the study.

All previous ROP screening examinations had been scheduled according to the International ROP Classification, and all examination findings had been recorded according to the American Pediatric Ophthalmology and Strabismus Society criteria (19, 20). Infants were divided into two groups based on previous ROP examination findings: Cases who achieved retinal maturation without treatment were grouped as Treatment(-), whereas cases who required treatment due to the presence of Type 1 ROP or threshold ROP were grouped as Treatment(+).

Gestational age (in weeks), birth weight, duration of the NICU hospitalization, weekly weight gain, and the type and duration of oxygen therapy administered were obtained from medical records. Cases with a duration of mechanical ventilation >21 days were categorized as prolonged mechanical ventilation. Weight gain rates at the 4th and 6th weeks were calculated with the following formula:

*(actual weight at 4th or 6th week – birth weight) * 100 / birth weight*

Medical records of the cases were reviewed, and the history of necrotizing enterocolitis, sepsis, BPD, IVH, and ET were noted. The presence of intrauterine comorbidities such as oligo/polyhydramnios, multiple pregnancy, and maternal conditions were also collected from medical records. Cases with a history of pathologies that prevented weight gain, such as congenital gastrointestinal system anomalies, cases with pathologic weight gain profile, such as hydrocephalus

and massive edema, and cases with no weight gain data during the first postnatal period of 6 weeks, were excluded.

Statistical analyses

Statistical analysis was performed using the Statistical Package for the Social Sciences package program version 22.0 for Windows (SPSS Inc. Chicago, IL, USA). Continuous variables are presented as median and (interquartile range), and categorical variables are presented as numbers and (percentages). Pearson's chi-square test was used to compare categorical data, and continuous variables were compared with the Mann-Whitney U test. Receiver operator characteristic (ROC) curves were constructed for weight gain and weight gain rates in the 4th and 6th week, and the best cut-off values were determined based on specificity and sensitivity. The area under the ROC curve (AUC) was calculated. Binary logistic regression analysis was used to analyze the risk factors. $p<0.05$ was considered statistically significant.

RESULTS

Two hundred and one preterm infants were included in this study. The mean gestational age was 30.00 ± 2.59 weeks, and the mean birth weight was 1419.10 ± 415.61 g. During the follow-up period, 108 (53.7%) infants did not develop ROP, while ROP at any stage was observed in 93 (46.3%) infants. There were 173 infants (86.1%) in the Treatment(-) group and retinal maturation was completed without treatment in this group. The Treatment(+) group included 28 infants (13.9%) who received laser photocoagulation and/or intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment due to the presence of Type 1 ROP. None of the cases in the follow-up had ROP progression to stage 4 or above. Treatment(+) group had lower birth weight and gestational age compared to Treatment(-) group (p:0.002 and p:0.003, respectively) (Table 1).

The weight gain and weight gain rate in the 4th week were 370.00 (257.50) g and 27.80 (17.36) % in the Treatment (-) group and 222.50 (213.75) g and 19.54 (22.98) % in the Treatment (+) group ($p<0.001$ and p:0.001, respectively). The weight gain and weight gain rate at the 6th week were 760.00 (362.50) g and 55.56 (24.60) % in the Treatment (-) group and 495.00 (379.25) g and 44.25 (24.24) % in the Treatment (+) group ($p<0.001$ and p:0.004, respectively) (Table 1). According to ROC curve analysis, the best cut-off point of the weight gain in the 4th week was 297.5 g (67.6% sensitivity, 77.8% specificity, and the AUC was 0.776), and the best cut-off point of the weight gain in the 6th week was 504.5 g (86.7% sensitivity, 55.6% specificity, and the AUC was 0.771). When the weight gain rates were analyzed, the best cut-off point of the 4th week was 21.02% (70.5% sensitivity, 59.3% specificity, and the AUC was 0.694), while it was 54.80% (53.2% sensitivity, 74.1% specificity, and the AUC was 0.667) in the 6th week (Table 1) (Figure 1).

In terms of other risk factors, the presence of small for gestational age (SGA), IVH, sepsis, and maternal factors did not differ between the groups ($p>0.05$). In the Treatment(+) group, a history of BPD, necrotizing enterocolitis, and ET were more common, and the duration of NICU hospitalization was longer ($p<0.05$) (Table 2). The duration of all types of oxygen therapy was found to be longer in the Treatment(+) group ($p<0.05$), and the frequency of prolonged mechanical ventilation was higher in the Treatment(+) group ($p<0.001$) (Table 3). According to logistic regression analysis, BPD and prolonged mechanical ventilation statistically increased the risk of treatment-required ROP p:0.027 and p:0.047, respectively) (Table 4).

DISCUSSION AND CONCLUSION

Since ROP is one of the most preventable causes of blindness, guidelines have been established for the development of appropriate follow-up and screening programs. Many studies have been conducted to determine the risk factors that may be associated with ROP (5, 6, 21). Studies reporting the prevalence of ROP vary between 10% and 65% according to countries, socioeconomic and demographic characteristics, and inclusion criteria. In this study, the incidence of ROP development at any stage was 45.4%, and the incidence of ROP requiring treatment was 13.5%. In a multicenter study from Türkiye, the incidence was reported to be 30%, and in a recent multicenter study in the USA, this rate was reported to be 65.8% (22, 23).

Table 1. Comparison of the gestational age, birth weight, and weight gain characteristics between the groups.

	Treatment (-) n: 173 *median (IQR)*	**Treatment (+) n: 28** *median (IQR)*	***p****
Gestational age, week	30.00 (3.50)	28.50 (4.00)	**0.002**
Birth weight, g	1480.00 (605.00)	1155.00 (425.00)	**0.003**
4th-week weight gain, g	370.00 (257.50)	222.50 (213.75)	**<0.001**
4th-week weight gain rate, %	27.80 (17.36)	29.54 (22.98)	**0.001**
6th-week weight gain, g	760.00 (362.50)	495.00 (379.25)	**<0.001**
6th-week weight gain rate, %	55.56 (24.60)	44.25 (24.24)	**0.004**

n: Number of cases, IQR: Interquartile range, g: Gram, %: Percentage. *: Mann-Whitney U test. Bold p-values indicate statistical significance (p<0.05)

Table 2. Comparing the frequencies of risk factors between the groups.

	Treatment (-) n: 173	**Treatment (+) n: 28**	***p***
Maternal risk factor, n (%)	75 (43.4%)	12 (42.9%)	0.961*
Multiple gestations, n (%)	29 (16.8%)	3 (10.7%)	0.581**
Gender (female/male)	83/90	12/16	0.615*
Small for gestational age, n (%)	23 (13.3%)	4 (14.3%)	1.000**
Bronchopulmonary dysplasia, n (%)	63 (36.4%)	21 (75.0%)	**<0.001***
Necrotizing enterocolitis, n (%)	25 (14.5%)	11 (39.3%)	**0.001***
Erythrocyte transfusion, n (%)	67 (38.7%)	22 (78.6%)	**0.004***
Sepsis, n (%)	84 (48.6%)	19 (67.9%)	0.091*
Intraventricular hemorrhage, n (%)	36 (20.8%)	8 (28.6%)	0.500*
Prolonged mechanical ventilation, n (%)	15 (8.7%)	12 (42.9%)	**<0.001***

n: Number of cases, %: Percentage. *: Chi-squared test, **: Fisher's exact test. Bold p-values indicate statistical significance (p<0.05)

Table 3. Duration of oxygen therapies according to types and the duration of hospitalization in the groups

	Treatment (-) n: 173 *median (IQR)*	**Treatment (+) n: 28** *median (IQR)*	***p****
Duration of NICU hospitalization, days	38.00 (35.50)	74.00 (57.50)	**<0.001**
Invasive mechanical ventilation, days	1.00 (5.00)	10.50 (54.75)	**<0.001**
Nasal CPAP, days	3.00 (6.00	10.00 (15.00)	**<0.001**
Oxygen hood, days	4.00 (7.00)	9.50 (15.75)	**0.024**
Incubator oxygen, days	1.00 (4.00)	5.00 (9.75)	**0.002**

n: Number of cases, IQR: Interquartile range, NICU: Neonatal intensive care unit, CPAP: Continuous positive airway pressure, IQR: Interquartile range. *: Mann-Whitney U test. Bold p-values indicate statistical significance (p<0.05)

Table 4. Determination of the risk factors for treatment-required retinopathy of prematurity by logistic regression analysis.

	p	**Odds Ratio**	**95% CI**
Bronchopulmonary dysplasia	**0.027**	**3.096**	**1.139 – 8.413**
Necrotizing enterocolitis	0.143	2.314	0.735 – 7.104
Erythrocyte transfusion	0.122	2.204	0.810 – 5.998
Prolonged mechanical ventilation	**0.047**	**2.874**	**1.069 – 8.258**

CI: Confidence interval. Bold p-values indicate statistical significance (p<0.05).

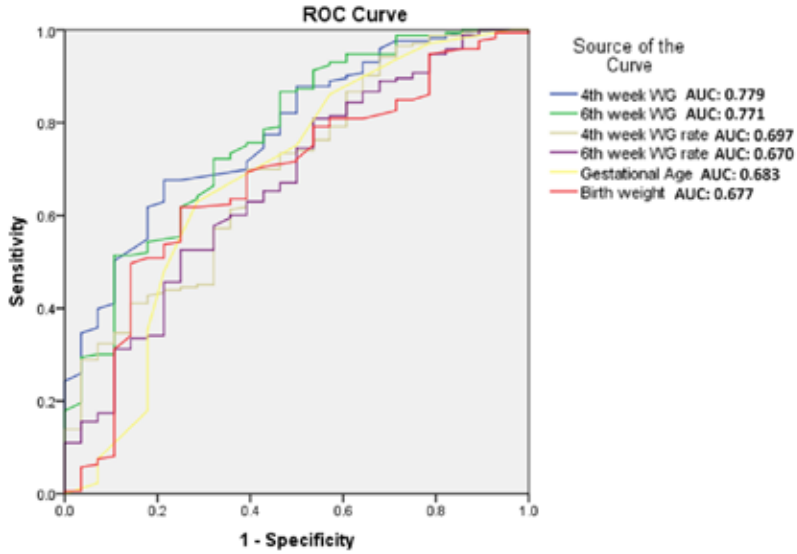

Figure 1. A graph demonstrating the area under the curve with the receiver operator characteristics (ROC) curves analysis of weight gain characteristics at 4th and 6th weeks, gestational age, and birth weight. WG: Weight gain, AUC: Area under the ROC curve

In this study, it is thought that a difference in incidence may have been detected because patients whose weight gain records could be obtained until the 6th week were included.

Many studies have been conducted to determine the risk factors of ROP, which is a multifactorial disease. Especially in the last two decades, studies have shown that birth weight and gestational age, as well as postnatal weight gain and serum IGF-1 levels, are effective on ROP development (8, 10, 13, 24-27). In addition, many prediction algorithms have been developed that include postnatal weight gain and/or IGF-1 level (6, 8, 27, 28). The IGF-1 production of preterm infants born before the 33rd gestational week is very slow until the 44th gestational week, and postnatal serum levels are regulated by total protein and caloric intake (10, 25). The WINROP (weight, IGF, neonatal ROP) algorithm described in 2006 aims to reduce the number of patients' examinations using weekly weight gain, IGF-1, IGFBP-3, birth weight, gestational age, and to detect the ROP development earlier (8). In another study conducted with the WINROP algorithm, it was observed that the algorithm gave the alarm in 319 of 407 patients, and it covered 45 of 47 (95.7%) patients who developed Type 1 ROP in the follow-up, and also by using the WINROP algorithm, it was thought that the number of painful and stressful examinations for preterm infants could be reduced by approximately 53% (29). In this study, the predictive efficacy of weight gain and weight gain rates at the 4th and 6th weeks were evaluated in terms of treatment-required ROP. However, recently published validation studies in various populations have reported controversial results regarding the ROP prediction of these algorithms (12, 17, 30-33). In the current study, weight gain and weight gain rates at both weeks 4 and 6 had statistically significant predictive efficacy. However, the accuracy of the weight gain and weight gain rate for the 4th week was higher than that for the 6th week. Furthermore, no superiority of weight gain rates compared to cumulative weight gain rates in terms of predicting ROP development was demonstrated. Filho et al. determined the best cut-off point for the weight gain proportion at the 6th week for the development of severe ROP in very low birth weight preterm infants as 51.2% and calculated the AUC for this proportion as 0.63 (34). This finding is consistent with the results found in the current study, and unlike the previous study, the rate of weight gain in the 4th week was also evaluated.

Low birth weight and low gestational age have been described as the primary risk factors for the development of ROP. In this study, lower birth weight and lower gestational age were observed in the Treat-

ment (+) group in accordance with previous studies. In addition to these risk factors, many studies have been conducted to define various risk factors for ROP, which is a multifactorial disease (6). However, controversial results have been reported in terms of other maternal and postnatal conditions. Considering clinical features of the preterm infants, although the history of ET, BPD, NEC, and prolonged mechanical ventilation were more frequent in the Treatment(+) group, only BPD and prolonged mechanical ventilation were associated with increased treatment requirement, as revealed by a logistic regression model with binary data showing statistical differences between the two groups. According to the results of a previous meta-analysis evaluating maternal blood pressure status, no evidence was found linking ROP to preeclampsia or eclampsia (35). Controversial results have also been reported in various studies examining the relationship between maternal glycemic status and ROP (36, 37). In the current study, the presence of both gestational diabetes and pre-eclampsia or eclampsia was defined as a "maternal risk factor", and no association of maternal blood pressure and/or glycemic status with severe ROP could be demonstrated. Prolonged oxygen therapy and the presence of BPD have been shown to be risk factors for ROP in previous studies (6). Consistent with previous findings, both BPD and mechanical ventilation for more than 21 days were found to be risk factors for ROP requiring treatment in the current study.

This study has some limitations. Since it was a single center, the number of cases, especially in the severe ROP group, was relatively small. However, it is thought that by including cases from a single center in the study, a standard intensive care process was obtained, and the effect of confounding factors originating from the NICU was minimized. In addition, a large series could not be reached due to the exclusion of cases without weight gain data until the 6th week and the exclusion of cases consulted for ROP follow-up from different NICU centers. Therefore, some of the cases with treatment-requiring ROP were excluded from the study. Although many of the cases included in the study had a history of oxygen therapy such as mechanical ventilation, nasal CPAP, etc., detailed information about the applied therapy (such as peak inspiratory pressure, respiratory rate, fraction of inspired oxygen level, target oxygen saturation) were not presented and analyzed in this study. The lack of information about the oxygen therapy administered can be considered a limitation of this study. However, as mentioned before, since the data were obtained from a single NICU, it can be considered that the oxygen therapy applied has certain standards. Another limitation of this study is that the data on weight gain were limited to postnatal 4th and 6th weeks. It was assumed that the death or NICU discharge of some cases would limit the sample size, especially the number of cases in the Treatment(+) group. Therefore, only the weight gain profiles of the first 6 weeks postpartum were evaluated in this study. Furthermore, the absence of an evaluation of blood levels of IGF-1, which is associated with postnatal weight gain, and the lack of specification of the components of oral or parenteral nutritional support can be considered additional limitations of this study.

In conclusion, the present study, which evaluated the weight gain and weight gain rates at the postnatal 4th and 6th weeks, demonstrated that the weight gain profile at the 4th week had a higher diagnostic efficiency in predicting treatment-requiring ROP compared to the 6th-week data. Moreover, the superiority of weight gain ratios over cumulative weight gain was not shown. In the evaluation of risk factors, it was revealed that prolonged mechanical ventilation and the history of BPD caused an independent increased risk for ROP requiring treatment. Future studies evaluating multiple risk factors and long-term weight gain profiles are needed.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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17. ve 18. asır sicil ve vakıf kayıtlarına göre İstanbul'da sağlıkta yardımlaşma: Tarihi ipuçları ve modern yansımaları

A study of health charity in Istanbul during the 17th and 18th centuries based on registry and foundation records: Historical clues and modern reflections

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Öz

Amaç: Bu çalışma, Osmanlı dönemine ait sicil ve vakıf kayıtları üzerinden İstanbul'da sağlıkta yardımlaşmanın nasıl gerçekleştirildiğini incelemeyi amaçlamaktadır. Vakıfların koruyucu hekimlik, tedavi ve ilaç yardımı gibi konularda topluma sunduğu hizmetler ve İslam medeniyetinde dinî ana metinlerin yardımlaşma kültürü üzerindeki etkisi ve bu kültürün Osmanlı toplumundaki yansımaları ele alınmaktadır.

Yöntemler: Çalışmada, Osmanlı dönemine ait Şer'iyye sicilleri ve vakıf kayıtları incelenmiştir. Şer'iyye sicillerinde, darp ve yaralama gibi adli vakaların sulh ile neticelendiği davalarda ilaç ve tedavi masraflarının nasıl kayıt altına alındığı araştırılmıştır. Ayrıca, hastalar odası adı verilen mekânlar, cerrah müdahaleleri ve frengi gibi dönemin tedavisi zor hastalıklarına dair kayıtlar da incelenmiştir. Vakıf kayıtlarında ise darüşşifaların vakfiyeleri ve gayrimüslimlerin sağlık hizmetlerine yönelik vakıflar detaylandırılmıştır.

Bulgular: İncelemeler sonucunda, vakıflarda koruyucu hekimlik ve tedaviye yönelik hizmetler bulunduğu görülmüştür. Şer'iyye sicillerinde, adli vakalarda ilaç ve tedavi masraflarının detaylı olarak kayıt altına alındığı, vakıf kayıtlarında ise sağlık hizmetlerine yönelik vakıfların hayırseverlik duygusu ile oluşturulduğu tespit edilmiştir. Ayrıca, koruyucu hekimlik ve tedavi hizmetlerinin toplumda önemli bir yer tuttuğu belirlenmiştir.

Sonuç: Bu çalışma, Osmanlı döneminde sağlıkta yardımlaşmanın arka planında yatan hayırseverlik duygusunun, vakıf kayıtları ve kadı sicillerinde açıkça görüldüğünü ortaya koymaktadır. Sicil ve vakıf kayıtlarının yeni belge ve bilgilerle incelenmeye devam edilmesi, sağlıkta yardımlaşma konusunda daha farklı bakış açıları ve detaylı bilgiler sunacaktır. Bu çalışma, Osmanlı dönemindeki sağlık yardımlaşma sisteminin ve toplumsal dayanışmanın tarihi kökenlerine ışık tutmaktadır.

Anahtar Sözcükler: Koruyucu hekimlik; Osmanlı imparatorluğu; sağlıkta yardımlaşma; Şer'iyye sicilleri; vakfiye

Abstract

Aim: The objective of this study is to examine how health charity was realised in Istanbul during the Ottoman period through the analysis of historical records. The services provided by the foundations to the society in areas such as preventive medicine, treatment and medication assistance, the impact of the main religious texts in Islamic civilisation on the culture of charity and the reflections of this culture in Ottoman society are discussed.

Methods: This study analyses the Shar'iyye registers and foundation records of the Ottoman period. The Shar'iyye registers are examined to ascertain how the costs of medicine and treatment were recorded in cases where judicial cases such as assault and wounding were concluded with a settlement. In addition, the records of the so-called patients' rooms, surgeon interventions and the records of difficult-to-treat diseases of the period such as syphilis are also analysed. Foundation records detail the foundations of darüşşifas and foundations for non-Muslim health services.

Results: The results of the analyses revealed that the foundations included services for preventive medicine and treatment. In the Shar'iyye registers, medicine and treatment costs in judicial cases were recorded in detail, and in the foundation records, it was determined that foundations for health services were created with a sense of philanthropy. Furthermore, it was established that preventive medicine and treatment services held a significant position within society.

Conclusion: This study demonstrates that the sense of philanthropy that underpinned cooperation in health during the Ottoman period is clearly evident in the foundation records and kadi registers. Continued analysis of the registers and foundation records with the incorporation of new documents and information will provide further insight.

Keywords: Charities; foundation; Ottoman empire; preventive medicine; Shar'iyye registers

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GİRİŞ

Sağlıkta yardımlaşma, bireylerin ve toplumların sağlık hizmetlerine erişimlerini kolaylaştırmak amacıyla maddi ve manevi destek sağlamayı ifade eder. Bu yardımlaşma, hem bireysel bağışlar hem de kurumsal vakıflar aracılığıyla gerçekleştirilir. İslam medeniyetinde ve Osmanlı İmparatorluğu'nda sağlıkta yardımlaşma, vakıf sistemi üzerinden yürütülmüş ve bu vakıflar, toplumun sağlık ihtiyaçlarını karşılamak için çeşitli hizmetler sunmuştur (1).

Sağlıkta Yardımlaşma Örnekleri

1. **Koruyucu Hekimlik**: Vakıflar, hastalıklardan korunma ve sağlıklı yaşamın teşviki için çeşitli hizmetler sunmuştur. Bu hizmetler arasında aşı kampanyaları, hijyen eğitimi ve sağlıklı yaşam koşullarının sağlanması bulunmaktadır. Örneğin, II. Bayezid Darüşşifası'nda, halkı bulaşıcı hastalıklardan korumak için düzenli olarak aşı kampanyaları düzenlenmiştir. Ayrıca, bu dönemde temizlik ve hijyen konularında da halka eğitim verilmiştir (2).
2. **Tedavi Hizmetleri**: Vakıflar, hastaların tedavi edilmesi için hastaneler, darüşşifalar ve klinikler kurmuştur. Bu sağlık kurumlarında hem genel sağlık hizmetleri hem de uzmanlık gerektiren cerrahi müdahaleler yapılmıştır. Örneğin, Süleymaniye Darüşşifası'nda çeşitli cerrahi operasyonlar gerçekleştirilmiş ve hastalara tıbbi bakım sağlanmıştır. Ayrıca, Haseki Sultan Darüşşifası, özellikle kadın hastalıkları ve doğum konusunda uzmanlaşmış bir merkez olarak hizmet vermiştir (3).
3. **İlaç ve Tıbbi Malzeme Yardımı**: Vakıflar, ihtiyaç sahiplerine ilaç ve tıbbi malzeme temin etmiştir. Bu yardım, özellikle yoksul ve muhtaç kişilerin tedavi masraflarının karşılanmasında büyük rol oynamıştır. Örneğin, Atik Valide Sultan Vakfı, yoksul hastalara ücretsiz ilaç dağıtımı yapmış ve bu ilaçların temini için düzenli olarak gelir sağlamıştır. Ayrıca, hastanelerde kullanılan tıbbi malzemelerin temini de bu vakıflar tarafından gerçekleştirilmiştir (4).

Sağlık vakıfları, sadece bireylerin sağlık ihtiyaçlarını karşılamakla kalmamış, aynı zamanda toplumun genel sağlık düzeyini yükseltmiştir. Bu vakıflar, sağlık hizmetlerinin sürekliliğini ve kalitesini artırarak toplum sağlığını korumada önemli bir rol oynamıştır. Ayrıca, sağlık vakıfları, tıp eğitimi ve araştırmalarına da katkıda bulunmuş, böylece sağlık alanında bilimsel ilerlemelerin önünü açmıştır (5).

Osmanlı döneminde vakıf sistemi, sağlık hizmetlerinin yaygınlaşması ve herkesin bu hizmetlerden faydalanabilmesi için etkin bir şekilde kullanılmıştır. Yıldırım Bayezid, Fatih, II. Bayezid, Haseki (Hürrem Sultan), Süleymaniye, Atik Valide Sultan, Yeni Valide (Gülnûş Emetullah) gibi pek çok darüşşifanın vakfiyelerinde sağlık hizmetlerine yönelik yardımlar detaylandırılmıştır (3). Bu vakıflar, toplumun sağlık ihtiyaçlarını karşılamak için çeşitli hizmetler sunmuş ve bu hizmetlerin sürekliliğini sağlamak için gerekli kaynakları temin etmiştir (6).

Osmanlı döneminde sadece vakıflar değil, bireylerin kişisel yardımları da sağlık sistemine önemli katkılarda bulunmuştur. Örneğin, dönemin zengin ve nüfuzlu kişileri, mahallelerinde hasta ve yoksul insanlara maddi destek sağlamış, ilaç ve tedavi masraflarını karşılamışlardır. Bu bireysel yardımlar, toplumun sağlık ihtiyaçlarının karşılanmasında önemli bir rol oynamıştır (7). Günümüz Türkiyesi'nde de benzer kişisel yardımlaşma örneklerine rastlanmaktadır. Özellikle köylerde ve küçük yerleşim yerlerinde, komşular arası yardımlaşma kültürü hala devam etmektedir. Zengin bireylerin sağlık alanında yaptıkları bağışlar ve hayır işleri, modern sağlık sisteminin önemli bir parçası haline gelmiştir (8).

Osmanlı İmparatorluğu'nda hayatın her alanına dair çeşitli vakıflar kurulmuştur. Bu vakıfların nasıl hizmet edeceği, mütevellisinin kimler olacağı ve gelirlerinin hangi hayrî hizmetlerde kullanılacağı vakfiyelerde belirtilmiştir. Sağlık, insanoğlu için vazgeçilmez hususların başında gelir. Sağlıkta yardımlaşma, özellikle zaruret içinde bulunan ihtiyaç sahiplerinin hayatını kolaylaştırmaktadır. Bu çalışmada, vakfiyelerde koruyucu hekimlik, tedavi ve ilaç yardımı gibi hususların nasıl yer aldığı üzerinde durulacaktır. İslam'ın temel kaidelerini belirleyen metin Kur'an-ı Kerim'dir. Kur'an'da "İyilik ve takvâ hususunda yardımlaşın, günah ve haksızlık yolunda yardımlaşmayın" (Maide Suresi, 2. Ayet) emri bulunmaktadır. Müslümanlar, bu ayet doğrultusunda yardımlaşma adına pek çok hayrî hizmet gerçekleştirmektedirler (9).

Bu çalışmanın amacı, Osmanlı döneminde İstanbul'da sağlık alanında yardımlaşmanın nasıl gerçekleştirildiğini ve bu yardımlaşmanın toplumsal etkilerini incelemektir. Şer'iyye sicilleri ve vakfiye kayıtları gibi tarihî belgeler üzerinden yürütülen bu araştırma, sağlık hizmetlerinin yaygınlaştırılması ve ihtiyaç sahiplerine ulaşılması konusundaki uygulamaları ortaya koymayı hedeflemektedir. Ayrıca, bu çalışmanın bir diğer amacı, Osmanlı dönemi sağlık sisteminin ve yardımlaşma kültürünün modern sağlık hizmetlerine olan etkilerini anlamak ve bu konuda yeni bakış açıları sunmaktır. Böylelikle, sağlık yardımlaşmasının tarihî gelişimini, işleyişini ve topluma sağladığı faydaları daha iyi kavramak mümkün olacaktır.

GEREÇ VE YÖNTEM

Veri toplama aracı

Bu çalışmada veri toplama aracı olarak, Osmanlı dönemi şer'iyye sicilleri ve vakfiye kayıtları kullanılmıştır. Şer'iyye sicilleri, Osmanlı dönemi kadı mahkemelerinin kayıtlarını içerir ve bu kayıtlar, darp ve yaralama başta olmak üzere adli vakaların yanı sıra sağlık hizmetlerine dair bilgileri de barındırır. Vakfiye kayıtları ise vakıfların kuruluş amaçlarını, faaliyet alanlarını ve finansal yapılarını detaylandıran belgelerden oluşmaktadır. Bu çalışma için etik kurul onayı gerekmemektedir. Çalışma tarihi metinler üzerinden yapılmıştır.

Veri analizi

Toplanan veriler, nitel araştırma yöntemleri kullanılarak analiz edilmiştir. Sicil ve vakfiye kayıtları, içerik analizi yöntemiyle incelenmiş, sağlıkta yardımlaşma ile ilgili bilgiler kategorilere ayrılmıştır. Elde edilen veriler, sağlık hizmetlerinin kapsamı, sağlık çalışanlarının rolleri, hastalara sunulan yardımlar ve bu yardımların toplum üzerindeki etkileri bağlamında değerlendirilmiştir.

Çalışma kısıtlılığı

Bu çalışmanın bazı kısıtlılıkları bulunmaktadır. İlk olarak, kullanılan sicil ve vakfiye kayıtları sadece belirli dönemlere ve bölgelere ait olup, genelleme yapılırken dikkatli olunmalıdır. Ayrıca, kayıtların dili ve terimleri zaman zaman anlaşılması güç olabilir ve bu durum, verilerin yorumlanmasında zorluklara yol açabilir. Son olarak, mevcut belgelerin tamamı günümüze ulaşmamış olabilir, bu da eksik veya yanlı bilgiye neden olabilir.

BULGULAR

Sicillerde yer alan hususlar

Şer'iyye sicilleri, Osmanlı dönemi kadılarının çeşitli görevleri nedeniyle pek çok konunun bulunduğu kayıtlardır. Darp ve yaralama davalarında ilaç ve tedavi masrafları mahkemece kayıt altına alınmıştır. Örneğin, 1748 tarihli Üsküdar sicilinde, hamurkârlık yapan bir kişinin yaralanması sonucu bir kuruşluk merhem ücreti ödenmiştir. Ayrıca, cerrah müdahalesi gereken durumlarda cerrah ücreti de zikredilmiştir (10).

Hastalar odası: Kayıtlarda hastalar odası adı verilen mekânlar da bulunmaktadır. Örneğin, meşhur Köprülü ailesinden olup aşçıbaşı kaymakamlığı görevinde bulunan Mehmed Ağa'nın terekesinden 1676 tarihli bir alacak davasında, hastalar odasının tamir ve yenilemesi için borç alındığı kaydedilmiştir. Bu odalar, özellikle saray aşçılarına mahsus mekânlardır (11).

Rıza kayıtları: Şer'iyye sicillerinde sağlık çalışanlarına yardımcı olma ve rıza kayıtları da önemli bir yer tutmaktadır. Fıtık ameliyatları için yapılan rıza kayıtları yaygın bir uygulamadır. Ünlü cerrah aileleri arasında, 17. yüzyılda Üsküdar'da yaşamış Cerrah Üstad Deniz ve ailesi örnek gösterilebilir (12). Yine bunun yanında H. 1073 - 1074 / M. 1663 tarihli Galata sicilinde İstati v. Yani adlı Rum'un meşhur cerrah olarak tebarüz ettiğini görmekteyiz (13).

Frengi hastalığı: Frengi hastalığı gibi dönemin tedavisi zor hastalıkları da sicil kayıtlarında yer almaktadır. Örneğin, 1614 senesinde Galata kazasına bağlı Kasımpaşa kasabasında yaşayan yetim Mustafa'nın frengi hastalığı nedeniyle yapılan harcamalar, kadı tarafından onaylanmıştır (14).

Akıl hastaları: Akıl hastası olarak tarif edilen mecnun kişilere yönelik yardımlar da dikkat çekicidir. Bu kişiler için mahalle sakinleri ve kadılar tarafından çeşitli önlemler alınmış, gereken durumlarda bimarhanelere gönderilmişlerdir (15).

Resim 1. Topçubaşı Osman Ağa b. Cafer'in vakfiyesi Tophane no.38 vr.110b-111a

Vakıf kayıtlarında yer alan hususlar

Vakıf kayıtlarında sağlık konusunda yardımlaşma örnekleri sıkça görülmektedir. II. Osman dönemi vezirlerinden Dilaver Paşa'nın vakfiyesinde, Haleb darüşşifaları ve fukaralarına yardım edilmiştir. Ayrıca, Tophane sicilinde yer alan bir kayda göre, bir hayırseverin vakfettiği mülklerden elde edilen gelirler hasta ve alil olanların tedavisine tahsis edilmiştir (16).

Darüşşifalar: Osmanlı döneminde kurulan darüşşifaların vakfiyeleri, tıp tarihi araştırmacılarının ilgisini çeken önemli belgeler arasında yer almaktadır. Yıldırım Bayezid, Fatih, II. Bayezid, Haseki (Hürrem Sultan), Süleymaniye, Atik Valide Sultan, Yeni Valide (Gülnûş Emetullah) gibi pek çok darüşşifanın vakfiyelerinde sağlık hizmetlerine yönelik yardımlar detaylandırılmıştır (3).

Gayrimüslim vakıflar: Gayrimüslimlerin de sağlık hizmetlerine yönelik vakıfları bulunmaktadır. Örneğin, 1670 tarihli Üsküdar sicilinde, Yorgi v. Kostantin'in İstavros köyünde Hıristiyan fukarası ve hastaları için bir bağ vakfettiği kaydedilmiştir (17).

TARTIŞMA VE SONUÇ

Bu çalışmada elde edilen bulgular, Osmanlı döneminde sağlıkta yardımlaşmanın toplumun her kesimini kapsayan, geniş bir hayırseverlik ağı ile desteklendiğini göstermektedir. Sağlık hizmetlerinin vakıflar aracılığıyla sunulması, ihtiyaç sahiplerinin tedavi masraflarının karşılanması ve sağlık çalışanlarının desteklenmesi gibi pek çok konuda önemli katkılar sağlamıştır. Bu yardımlaşma kültürü, modern sağlık sistemlerinin bazı yönleriyle benzerlikler taşımaktadır.

Günümüzde sağlıkta yardımlaşma, devlet destekli sağlık sigortaları, sosyal güvenlik sistemleri ve özel yardım kuruluşları aracılığıyla gerçekleştirilmektedir. Örneğin, Türkiye'de Sosyal Güvenlik Kurumu (SGK) aracılığıyla vatandaşların sağlık hizmetlerine erişimi sağlanmakta ve tedavi masrafları karşılanmaktadır. Ayrıca, pek çok sivil toplum kuruluşu ve dernek, ihtiyaç sahiplerine yönelik sağlık yardımları düzenlemektedir (18).

Modern sağlık sistemleri ile Osmanlı dönemindeki vakıf sistemi karşılaştırıldığında, her iki yapının da toplumun sağlık ihtiyaçlarını karşılamak için benzer hedeflere sahip olduğu görülmektedir. Ancak, Osmanlı döneminde vakıfların gönüllülük esasına dayanarak faaliyet göstermesi, modern sağlık sistemlerinde ise devletin daha aktif bir rol oynaması önemli bir farklılıktır. Ayrıca, günümüzde teknoloji ve tıp alanındaki ilerlemeler, sağlık hizmetlerinin kalitesini ve erişilebilirliğini artırmıştır (19).

Günümüzde sağlıkta yardımlaşma örneklerinden biri de küresel sağlık yardımlarıdır. Dünya Sağlık Örgütü (WHO) ve çeşitli uluslararası kuruluşlar, dünya genelinde sağlık hizmetlerinin yaygınlaştırılması ve iyileştirilmesi için çeşitli projeler yürütmektedir. Özellikle salgın hastalıklarla mücadele, aşı kampanyaları ve temel sağlık hizmetlerinin sağlanması konularında önemli yardımlar yapılmaktadır (20).

Sonuç olarak, Osmanlı dönemindeki sağlık vakıfları ve modern sağlık sistemleri arasındaki karşılaştırma, sağlık hizmetlerinin tarihsel gelişimini ve toplumsal dayanışmanın önemini ortaya koymaktadır. Bu çalışma, geçmişten günümüze sağlıkta yardımlaşmanın nasıl evrildiğini ve günümüz uygulamalarına nasıl ilham verdiğini göstermektedir. Gelecekte de sağlık hizmetlerinin daha kapsayıcı ve erişilebilir olması için tarihsel deneyimlerden faydalanmak önemlidir.

Kadı sicillerindeki kayıtlar, sağlık ve yardımlaşmaya dair doğrudan bilgiler içermemekle birlikte, davaların satır aralarında bu konuda önemli ipuçları bulunmaktadır. Vakıfların ve vakfiye kayıtlarının incelenmesi, sağlıkta yardımlaşma konusunda hayırseverlik duygusunun etkisini göstermektedir. Hem vakıf kayıtlarının hem de sicillerin yeni belge ve bilgilerle incelenmeye devam etmesi, konuya dair farklı bakış açıları getirecektir.

Bilgilendirme

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Çocuklarda D vitamini ile migren arasındaki ilişkinin değerlendirilmesi

Evaluation of the relationship between vitamin D and migraine in children

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Öz

Amaç: Migrende inflamasyon önemli bir rol oynar, bu nedenle vitamin D'nin anti-enflamatuar rolü migren baş ağrılarını önlemede önemli bir rol oynayabilir. Çocuklarda vitamin D eksikliği ile migren arasında bir ilişki olabileceğini düşünüp bu çalışmada bunu göstermeyi amaçladık.

Yöntemler: Bu retrospektif çalışmada, kliniğe migren şikayetiyle başvuran çocuklarla genel muayeneyle başvuran çocuklar karşılaştırıldı. Çocukların hasta dosyalarından alınan demografik verileri, vitamin D düzeyleri, kalsiyum, fosfor, alkalen fosfataz ve albümin değerleri kaydedildi.

Bulgular: Çalışmaya 80'i migren olmak üzere 182 vaka dâhil edildi. Migren grubunun %66,3'ü, kontrol grubunun %67,6'sı kız idi. Hastaların vitamin D düzeylerinin düşük ve normal olarak 2 gruba ayrıldığında migren grubunda %86,3'ü düşük iken, kontrol grubunda %11,8'i düşük olup istatistiksel olarak anlamlı fark saptandı (p<0,001). Migrenli hastalarda bakılan ortalama laboratuvar değerleri vitamin D; 3,15 ng/ml, kalsiyum; 9,5 mg/dl iken kontrol grubunda vitamin D; 32,95 ng/ml, kalsiyum; 9,7 mg/dl saptanmış olup istatistiksel olarak aralarında anlamlı fark bulunmuştur (Sırayla; p<0,001, p=0,015).

Sonuçlar: Çalışmamızda migrenli hastalarda vitamin D düzeyini anlamlı derecede düşük saptadık. Baş ağrısı ile başvuran ve migren tanısı alan hastalara bakılan tetkikler arasında vitamin D ve kalsiyum düzeyinin de olması gerektiğini düşünüyoruz.

Anahtar Sözcükler: Başağrısı; çocuk; vitamin D

Abstract

Aim: Since inflammation is crucial in migraines, vitamin D's anti-inflammatory role may help prevent migraine headaches. We hypothesized a link between vitamin D deficiency and migraines in children and aimed to demonstrate this in our study.

Methods: In this retrospective study, children presenting to the clinic with migraine complaints were compared with children presenting for a general examination. Demographic data, vitamin D levels, calcium, phosphorus, alkaline phosphatase, and albumin levels were recorded from patient records.

Results: The study included 182 cases, with 80 in the migraine group. Females comprised 66.3% of the migraine group and 67.6% of the control group. When vitamin D levels were categorized as low and normal, 86.3% of the migraine group had low levels compared to 11.8% of the control group, showing a statistically significant difference (p<0.001). The mean laboratory values for migraine patients were: vitamin D: 13.15 ng/ml, calcium: 9.5 mg/dl, whereas for the control group, the values were: vitamin D: 32.95 ng/ml, calcium: 9.7 mg/dl, showing a statistically significant difference between them(respectively; p<0.001, p=0.015).

Conclusions: We found significantly lower vitamin D levels in migraine patients in our study. We recommend including vitamin D and calcium levels among the tests for patients presenting with headaches and diagnosed with migraines.

Keywords: Child; headache; vitamin D

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GİRİŞ

Baş ağrısı hem çocukluk hem de ergenlik döneminde sıkça karşılaşılan bir durumdur. Migren tipi baş ağrısı ve gerilim tipi baş ağrısı, dünya genelinde insanların %80 kadarını etkileyen en yaygın primer baş ağrısı bozukluklarıdır. Migren, ilerleyici ve kronik bir nörolojik bozukluktur. (1) Migren, merkezi sinir sisteminin artmış uyarılabilirliğine bağlı olarak gelişen, yaygın ve işlevsellikte ciddi kısıtlılığa yol açabilen nörovasküler ve multifaktöriyel bir primer baş ağrısı bozukluğudur. Migrenin patogenezi çok yönlü ve karmaşıktır. Reaktif vazodilatasyon, merkezi ağrı yollarının aşırı duyarlılığı, plazma proteinlerinin damar dışına çıkışı ve steril inflamasyon nedeniyle serebral kan akışında azalma önemli rol oynar (2). Migrenin en yaygın nedenleri arasında açlık veya yeterli beslenmeme gelir, bu özellikle genç insanlar için önemlidir (1). Migren, çocuklar ve ergenler arasında çok yaygın bir şekilde görülür ve ilkokul çağındaki çocukların yaklaşık %4-11'ini ve ergenlerin %8-23'ünü etkiler. Uluslararası Baş Ağrısı Bozuklukları Sınıflandırması kriterlerine göre, çocuklarda migren baş ağrıları genellikle nabız atan, tek taraflı veya çift taraflı baş ağrısı atakları, ışık ve sese duyarlılık ile birlikte bulantı veya kusma şeklinde karakterize edilir (3). Bu baş ağrıları genellikle 2-72 saat sürer ve çocukların davranışı genellikle baş ağrısı sırasında değişir.

Migren baş ağrıları, çocukların ve ailelerinin yaşam kalitesi üzerinde büyük bir olumsuz etkiye sahiptir. Yeterli uyku, uygun ve zamanında beslenme gibi biyodavranışsal önlemler baş ağrılarının yönetimine yardımcı olabilir, ancak sık (haftada 2'den fazla atak) veya şiddetli migren ataklarına sahip birçok çocuk ilaçlara ihtiyaç duyar. Amerika Birleşik Devletleri Gıda ve İlaç Dairesi (FDA) tarafından çocuklarda migren tedavisi için onaylanmış ilaçlar sınırlıdır. Valproat, levetirasetam gibi antiepileptik ilaçlar, flunarizin, sinnarizin, siproheptadin gibi kalsiyum kanal blokerleri, propranolol gibi beta blokerleri ve amitriptilin gibi trisiklik antidepresanlar gibi farklı ilaç sınıfları kullanılmıştır (4).

Vitamin D, kemik gelişimi ve bağışıklık sistemi için gereken ve yağda çözünen bir vitamindir. Vitamin D'ye "güneş vitamini" denir çünkü ultraviyole güneş ışığı cildimizde vitamin D sentezini tetikler. Ayrıca besinlerden balık, et ve yumurta yüksek miktarda vitamin D içerir (5). Vitamin D, kemikler, böbrekler, bağırsaklar ve paratiroid bezleri üzerinde fizyolojik etkiler göstererek fosfor (P) ve kalsiyum (Ca) metabolizmasını düzenler (6). Vitamin D, bağışıklık sistemi, kemik sağlığı ve sinir sistemi gibi birçok fonksiyonda önemli rol oynayan bir vitamindir. Vitamin D eksikliği, kemik hastalıklarının yanı sıra bağışıklık sistemi sorunları, depresyon, kardiyovasküler hastalıklar ve migren gibi çeşitli sağlık sorunlarıyla ilişkilendirilebilir (7). Vitamin D, migren baş ağrılarında çeşitli yollarla etkili olabilir. Migrende inflamasyon önemli bir rol oynar, bu nedenle vitamin D'nin antiinflamatuar rolü migren baş ağrılarını önlemede önemli bir rol oynayabilir (8). Ayrıca, vitamin D takviyesi, güçlü bir enflamatuar aracı olan C reaktif protein gibi enflamasyon faktörlerini azaltabilir (9). Vitamin D eksikliği, magnezyum eksikliğine yol açabilir. Magnezyum, aşırı uyarıyı önlemede merkezi bir rol oynar ve magnezyum eksikliği ile migren arasında güçlü bir bağ olduğunu gösteren çalışmalar bulunmaktadır (10). Nitrik oksit (NO), migrende önemli bir aracı olarak bilinir ve vitamin D, NO üretimini azaltır (11). Dopamin ve serotonin salınımının vitamin D tarafından etkilendiği ve bu faktörlerin migren patogenezinde rol aldıkları gösterilmiştir (12). Melatonin seviyelerinin düşük olduğu migren hastalarında, vitamin D eksikliğinin bu düşüklüğe neden olabileceği gösterilmiştir (13). Tüm bu önerilen mekanizmalar, migrenin patofizyolojisinde vitamin D'nin önemini göstermektedir.

Normal bir çocukta vitamin D düzeylerinin normal olması beklenmektedir. Migren ile başvuran çocuk hastalarda vitamin D düzeylerinin normal olup olmadığı bilinmemektedir. Bu çalışmada hasta dosyalarından alınan veriler kıyaslanacak olup migreni olan çocuklar ile genel muayene ile başvuran çocukların Vitamin D düzeyleri karşılaştırılacaktır. Böylece migreni olan çocuklarda vitamin D eksikliği varlığı sorgulanması amaçlanmaktadır.

GEREÇ VE YÖNTEMLER

Çalışma protokolü

Çalışmamız retrospektif bir çalışmadır. Çalışmaya 01.01.2022-01.01.2023 tarihleri arasında Adıyaman

Üniversitesi Eğitim ve Araştırma Hastanesi çocuk nöroloji bölümüne migren tanısı ile başvuran çocuk hastalar ile çocuk sağlığı ve hastalıkları polikliniğine genel muayene için başvurup tetkik alınmış hastalar alındı.

Etik kurul onayı

Fırat Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu'ndan etik kurul onayı alındı (tarih: 06.06.2024, karar no: 2024/09-20).

Dâhil edilme ve dışlanma kriterleri

0-18 yaş arası vitamin D bakılan 80 migren ve 102 kontrol grubu çocukların hasta dosyasından alınan demografik verileri, vitamin D düzeyleri, fosfor (P), kalsiyum, albümin ve alkalen fosfataz (ALP) gibi değerler excel dosyasına kaydedildi. Çalışmamızda dosyasında kronik hastalığı tanısı bulunan (epilepsi, konjenital kalp hastalığı, kronik böbrek yetmezliği vb.) hastalar ve yabancı uyruklu hastalar çalışma dışı bırakıldı.

Veri toplama

Veriler hastaneye migren tanısı ile başvuran çocuk hastalar ile genel muayane için başvuran çocuk hastaların hasta dosyalarından alındı.

Çocuklarda Amerikan Çocuk Endokrin Birliği'nin önerilerine göre değerlendirilen vitamin D düzeyleri; >20 ng/ml normal, 15- 20 ng/ml yetersizlik, <5-15 ng/ml eksiklik, <5 ng/ml şiddetli eksiklik, olarak değerlendirildi (14).

Birincil ve ikincil çıktılar

Hastaların demografik verileri (cinsiyet, yaş), vitamin D düzeyleri (>20 ng/ml normal, 15- 20 ng/ml yetersizlik, <5-15 ng/ml eksiklik, <5 ng/ml şiddetli eksiklik), fosfor düzeyleri (2,8-4 mg/dL), kalsiyum düzeyleri (8,6 – 10,2 mg/dL), albümin düzeyleri (3,5 – 5,5 g/dl) ve alkalen fosfataz düzeyleri (44-147 U/l) tek tek hasta dosyasından alınıp excel ortamına kaydedildi.

Örneklem sayısı

Çalışmamız retrospektif bir çalışmadır. Çalışmaya 01.01.2022-01.01.2023 tarihleri arasında çocuk nöroloji polikliniğine dâhil edilme kriterlerini sağlayan (18 yaş altı vitamin D bakılan ve kronik hastalığı olmayan tüm hastalar) tüm hastalar alındığı için örneklem yapılamamış olup örneklem tüm evrendir.

İstatistiksel analiz

Analizler SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) 25 paket programında değerlendirildi. Nominal bulgular, sayı (n) ve yüzde (%) olarak raporlandı. Devamlı verilerin dağılımı Shapiro wilk testi ile incelendi. Normal dağılıma uymadığından Man Whitney U testi ile devamlı veriler karşılaştırıldı. Bağımsız gruplardaki kategorik değişkenlerin analizinde Ki-kare testi uygulandı. İstatistiksel anlamlılık düzeyi p<0,05 olarak belirlendi.

Şekil 1. D vitamini düzeylerinin gruplar arasında dağılımı

Tablo 1. Gruplar arasında demografik verilerin dağılımı

	Migren	Kontrol	*p*
Sayı (n)	80	102	
Cinsiyet (K)	53 (%66,3)	69 (%67,6)	0,84
(E)	27	33	
Yaş (yıl)	12 (9-15)	16 (13-17)	0,9

p<0,05 anlamlı kabul edildi. K: Kız, E: Erkek, n: Sayı, %: Yüzde

Tablo 2. Gruplar arasında laboratuvar değerlerinin dağılımı

	Migren	Kontrol	#*p*
Vitamin D Düzeyi (ng/ml)	13,15 (9,41-17,55)	32,95 (23,66-41,79)	***<0,001***
Ca (mg/dl)	9,5 (9,3-9,8)	9,7(9,47-9,9)	***0,015***
P (mg/dl)	4 (3,62-4,7)	4,4 (4-4,8)	***0,001***
ALP U/L	148 (81,25-209,25)	298,5 (263-355,25)	***<0,001***
Alb (g/dl)	4,4 (4,1-4,5)	4,7 (4,3-4,9)	***<0,001***

#*p*<0,05: Anlamlı, değerler median (çeyrekler arası aralık) olarak ifade edilmiştir.
Ca: Kalsiyum, P: Fosfor, ALP: Alkalen fosfataz, Alb: Albümin
ng/ml: nanogram/mililitre, mg/dl: miligram/desilitre, g/dl: gram/desilitre, U/L: Ünite/litre

BULGULAR

Çalışmaya 80 migrenli çocuk hasta ve 102 kontrol hastası olmak üzere toplam 182 vaka dâhil edildi. Migrenli hastaların yaş ortalaması 12 (9-15) yıl iken, kontrol grubunun yaş ortalaması 16 (13-17) yıl olup, bu iki grup arasında istatistiki olarak anlamlı bir fark saptanmadı (p=0,9). Migren grubunun %66,3'ü kız iken, kontrol grubunun %67,6'sı kız idi. Cinsiyet açısından iki grup arasında anlamlı bir fark bulunmadı (p=0,84) (Tablo 1).

Hastaları vitamin D düzeyleri düşük (<20 ng/ml) ve normal (>20 ng/ml) olarak 2 gruba ayırdığımızda migren grubunda %86,3'ü düşük iken, kontrol grubunda %11,8'i düşük olup istatistiki olarak anlamlı fark saptandı (p<0.001) (Şekil 1).

Migren hastalarında ortalama median değerlerine bakıldığında yaş; 14,5 yıl (11-16), vitamin D düzeyi; 13,15 (9,41-17,55) ng/ml olarak saptanmışken, kontrol grubunda, yaş; 15 yıl (11-16), vitamin D düzeyi; 32,95 (23,66-41,79) ng/ml olarak saptanmıştır. Bakılan laboratuvar değerleri (D vit, Ca, P, ALP, Alb) migrenli hastalarda daha düşük bulunmuştur (Tablo 2).

TARTIŞMA VE SONUÇ

Çalışmamızda migrenli çocuk hastaların vitamin D, Ca, P, ALP ve albümin değerleri kontrol grubuna oranla daha düşük saptandı. Çalışmamızın ana bulgusu olan vitamin D düzeyi de anlamlı derecede düşük saptandı. İki grup arasında yaş ve cinsiyet açısından ise anlamlı fark saptanmadı.

Momen ve arkadaşlarının (15) yaptığı çalışmada migrenli hastaların %56,4'ü, Çıplak ve ark.'ın (2) yaptığı çalışmada ise %76'sı kız idi. Bizim çalışmamızda da migrenlilerin %66,3'ü kız idi. Migren, kızlarda literatüre benzer olarak daha yüksek saptanmıştır.

Hanci ve ark. (16) ile Momen ve ark. (15) vitamin D düzeyi ile migren arasında istatistiksel olarak anlamlı fark bulamamışken, Dönmez ve ark. tarafından çocuklar üzerinde yapılan bir vaka-kontrol çalışmasında, migrenli çocuklarda vitamin D düzeylerinin sağlıklı kontrol grubundan önemli ölçüde düşük olduğu gösterilmiştir (17). Çıplak ve ark. ise migrenli hastalarda vitamin D düzeyini yüksek bulmuşlardır (2). Çayır ve ekibinin yaptığı araştırmada, 8-16 yaş arası migren tanısı konulmuş 53 çocuk hastada amitripti-

lin tedavisine ek olarak vitamin D tedavisinin migren ataklarının sıklığı üzerindeki etkisi değerlendirilmiştir. Araştırma sonuçları, vitamin D tedavisinin antimigren tedaviye ek olarak migren ataklarının sayısını azaltmada potansiyel bir rol oynayabileceğini göstermiştir (18). Farklı çalışmalarda farklı sonuçlar çıkmış olmasına rağmen bizim çalışmamızda migreni olan çocukların %86,3'ünde vitamin D düzeyi düşük idi. Kontrol grubu ile kıyaslandığında aralarında istatistiksel olarak anlamlı fark saptandı (*p<0,001*). Bizim çalışmamızda literatürün çoğunluğuyla benzer sonuçlar elde edilmiştir.

Çıplak ve ekibinin (2) gerçekleştirdiği çalışmada, hasta ve kontrol gruplarının karşılaştırılması sonucunda kalsiyum (*p=0.001*) ve albümin (*p=0.03*) değerlerinde hasta grubunun lehine istatistiksel olarak anlamlı farklar bulunmuştur. Buna karşılık, fosfor düzeylerinde istatistiksel olarak anlamlı bir fark tespit edilmemiştir (p=0,544). Bizim çalışmamızda ise Ca, P ve alb düzeyleri migreni olan çocuklarda daha düşük saptanmıştır. Bu da literatürle benzer saptanmıştır.

2007-2008 yılları arasında yapılan bir başka araştırmada, genel popülasyonda serum 25-hidroksi D vitamin düzeyleri [25(OH)D3] ile baş ağrısı arasındaki ilişki incelenmiştir. Araştırma, migren dışı baş ağrıları ile 25(OH)D3 düzeyleri arasında bir bağlantı bulmuş, ancak migren ve serum 25(OH)D3 düzeyleri arasında anlamlı bir ilişki saptayamamıştır (19).

Çalışmamız retrospektif olduğundan hastaların ilaç kullanma öykülerinin sorgulanamaması, tek merkez olması ve vaka azlığı çalışmamızın kısıtlılıklarıdır.

Sonuç olarak, literatürde vitamin D ve migren ilişkisiyle ilgili farklı sonuçlar paylaşılmış olup bizim çalışmamızda migrenli hastalarda vitamin D düzeyini anlamlı derecede düşük saptadık. Baş ağrısı ile başvuran ve migren tanısı alan hastalara bakılan tetkikler arasında vitamin D ve Ca düzeyinin de olması gerektiğini düşünüyoruz. Yapılacak ileri çalışmalarla migren hastalarına vitamin D takviyesinin verilebileceğini düşünmekteyiz.

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Impact of pediatric nutritional syrups on the color stability of glass ionomer restorations

Pediatrik besin takviye şuruplarının cam iyonomer restorasyonların renk stabilitesine etkisi

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Abstract

Aim: The purpose of this study was to evaluate the effects of different pediatric nutritional syrups' formulations on the color changes of glass ionomer-based restorative materials (GICs) used in pediatric dentistry.

Methods: Three types of GICs—compomer (Dyract XP, Dentsply), conventional glass ionomer (Equia Forte, GC), and glass carbomer (Glass Fill, GCP Dental)—were tested. 120 disc-shaped specimens (5 mm diameter, 2 mm deep) were prepared. Each type was divided into four groups (n=30). Specimens were stored in distilled water for 24 hours, then immersed in three different pediatric pediatric nutritional syrups (iron-Fe+3 [Ferifer, Berko], iron-Fe+2 [Ferro Sanol B, Adeka], and multivitamin [Polivit, Abdi İbrahim]) and distilled water. Color measurements were taken before and after immersion using a spectrophotometer (VITA Easyshade V, VITA Zahnfabrik). Color changes (ΔE00) were calculated at 30 and 90 days using the CIEDE2000 formula. Data were analyzed using two-way ANOVA and post-hoc Tukey's test ($p < 0.05$).

Results: After 30 days, the highest ΔE00 was observed in the glass carbomer group immersed in multivitamins (7.13 ± 0.77), while the lowest was in the compomer group immersed in distilled water (0.26 ± 0.13). ΔE00 values were significantly higher in the glass carbomer groups compared to the conventional glass ionomer and compomer groups ($p < 0.05$). At 90 days, no significant differences were found between the conventional glass ionomer and compomer groups ($p > 0.05$). The highest ΔE00 at 90 days was in the glass carbomer group immersed in multivitamins (9.15 ± 0.93), and the lowest was in the compomer group immersed in distilled water (0.38 ± 0.11).

Conclusion: Pediatric syrups, frequently used to treat malnutrition, caused more color changes in glass carbomers. Results indicated that as the resin content increased, the amount of coloration decreased.

Keywords: Color; discoloration; glass ionomer; iron; staining

Öz

Amaç: Bu çalışmanın amacı, pediatrik diş hekimliğinde kullanılan cam iyonomer bazlı restoratif materyallerin (GIC'ler) renk değişiklikleri üzerindeki farklı pediatrik besleyici şurup formülasyonlarının etkilerini değerlendirmekti.

Yöntemler: Üç tür GIC—kompomer (Dyract XP, Dentsply), konvansiyonel cam iyonomer (Equia Forte, GC) ve cam karbomer (Glass Fill, GCP Dental)—test edildi. 120 disk şeklinde örnek (5 mm çapında, 2 mm derinliğinde) hazırlandı. Her tür dört gruba ayrıldı (n=30). Örnekler 24 saat boyunca distile suda bekletildikten sonra üç farklı pediatrik ilaç (demir-Fe+3 [Ferifer, Berko], demir-Fe+2 [Ferro Sanol B, Adeka] ve multivitamin [Polivit, Abdi İbrahim]) ve distile suya daldırıldı. Renk ölçümleri, daldırma öncesi ve sonrası bir spektrofotometre (VITA Easyshade V, VITA Zahnfabrik) kullanılarak alındı. Renk değişiklikleri (ΔE00) CIEDE2000 formülü kullanılarak 30 ve 90 günün sonunda hesaplandı. Veriler two-way ANOVA ve post-hoc Tukey testi ile analiz edildi ($p < 0.05$).

Bulgular: 30 gün sonra, en yüksek ΔE00 multivitamin içine daldırılan cam karbomer grubunda (7.13 ± 0.77) gözlenirken, en düşük kompomer grubunda distile suya daldırıldığında (0.26 ± 0.13) gözlendi. ΔE00 değerleri cam karbomer gruplarında konvansiyonel cam iyonomer ve kompomer gruplarına göre anlamlı derecede yüksekti ($p < 0.05$). 90 gün sonunda, konvansiyonel cam iyonomer ve kompomer grupları arasında anlamlı bir fark bulunamadı ($p > 0.05$). 90 gün sonunda en yüksek ΔE00 multivitamin içine daldırılan cam karbomer grubunda (9.15 ± 0.93), en düşük ise distile suya daldırılan kompomer grubunda (0.38 ± 0.11) bulundu.

Sonuç: Malnütrisyon tedavisinde sıkça kullanılan pediatrik şuruplar, cam karbomerlerde daha fazla renk değişikliğine neden oldu. Sonuçlar, reçine içeriği arttıkça renklenmenin azaldığını gösterdi.

Anahtar Sözcükler: Cam iyonomer; demir; renk; renklenme; renk değişimi

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INTRODUCTION

Pediatric dentistry, a specialized field focused on the oral health and well-being of young patients, demands meticulous consideration of various factors, including the choice of restorative dental materials. Among these critical aspects is the impact of pediatric nutritional syrups, often administered in syrup form, on the color stability of dental restorations. Children with malnutrition or specific health conditions frequently require prolonged exposure to these medications, potentially leading to unintended consequences such as alterations in tooth color and the appearance of dental restorative materials (1).

Glass ionomer-based restorative materials (GICs) are widely used in pediatric dentistry due to their favorable characteristics, including adhesion to tooth structure, fluoride release, and biocompatibility (2). However, concerns exist within the dental community regarding the susceptibility of these materials to color changes when exposed to various environmental factors, especially pediatric nutritional syrups. This study aims to comprehensively evaluate the effects of different pediatric drug formulations on the color stability of three distinct GICs: compomer (Dyract XP, Dentsply), conventional glass ionomer (Equia Forte, GC), and glass carbomer (Glass Fill, GCP Dental).

Iron, a substantial nutrient for the human body, plays a significant role in many metabolic processes, such as electron transport, oxygen transport, and DNA synthesis. Iron deficiency is a major global public health problem and is commonly seen as a nutritional deficiency worldwide (3). Treatment typically includes nutritional improvement, iron supplementation, and enhancing awareness of the patient and family. Children often consume iron supplements in drop or syrup form (4). One basic drawback of these supplements is the potential for black discoloration on teeth, due to an insoluble ferric compound formed by the interaction between iron ions or gingival fluid composition and hydrogen sulfide produced by bacteria (5).

Previous research has shown that iron syrups can significantly stain primary teeth. There is limited literature on the staining effects of pediatric nutritional syrups, including iron syrups, on restorative materials. The highest color change values have been reported in iron syrups, often exceeding acceptable thresholds. Surface sealants have been suggested as a means to minimize color changes related to pediatric liquid nutritional syrups on restorative materials by saturating the material surface, correcting irregularities, and increasing stain resistance (6-8).

This study extends beyond restorative materials to consider the staining effects of pediatric nutritional syrups, including iron syrup, and the potential benefits of surface sealants on color stability. This study aims to investigate whether the use of surface sealant can mitigate the susceptibility of restorative materials to staining, whether exposure to different forms of iron syrups and the duration of exposure impact the staining resistance of restorative materials, and whether the type of restorative material affects staining resistance. In our study, two null hypotheses were determined, respectively: 'The waiting time of the restorations in solutions and in the control group should not affect the color change.' and 'The nutritional supplement syrups used should not cause color change in the restorations.'

MATERIAL AND METHODS

Specimen Preparation

In this study, no materials derived from animals or humans were used. The solutions applied in the experimental groups were also not derived from any animal or human materials. In our study, where we evaluated the potential color changes of restorative materials used in dentistry when immersed in tea, coffee, and water, ethical committee approval is not required.

Sample size calculation was performed with the G*Power 3.1 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) and the sample size was calculated as 10 per group with alpha-type error of 0.05, a power (1-beta) of 0.95, an effect size of 0.712 obtained from a previous study (9). A total of 120 specimens (n=40) were prepared according to the manufacturer's recommendations. (Table 1.)

Restorative material resins were placed in stainless steel molds with dimensions of 2 mm in depth and 5 mm in diameter. To avoid air bubbles and achieve a smooth surface, Mylar strips and glass slides were placed on each specimen, and pressure was applied to

remove any excess material. The specimens were then polymerized for 20 seconds using an LED light source (Elipar Freelight II, 3M ESPE, AG, Germany, 1150 mW/cm²). The power of the light source was verified to be above 1000 mW/cm² before polymerizing every five specimens. After curing, the specimens were removed from the molds, and their thickness was standardized using a digital caliper (Ultra-Cal V, Fowler Corp., Sylvac, Switzerland). Finally, the surfaces of the polymerized specimens were polished with aluminum oxide-coated discs (Sof-Lex XT; 3M/ESPE, St. Paul, MN, USA).

Color measurements

In this study, color values were measured using the Commission International de l'Eclairage (CIE) L*a*b* system with a spectrophotometer (VitaEasyshade V, Vita Zahnfabrik, Bad Sackingen, Germany) against a neutral gray background (L*=64.1; a*=0.3; b*=−3.4). Measurements were conducted under D65 standard lighting conditions, and the spectrophotometer was calibrated according to the manufacturer's instructions before each measurement. Specimens were dried with tissue paper, and three measurements were taken on each surface, with the average L, a, and b values calculated.

The CIELAB system is based on the sensitivities of three types of cone cells in the eye to red, green, and blue light. Each color is represented by L* (lightness), a* (red-green axis), and b* (blue-yellow axis). The L* value ranges from 0 to 100, indicating lightness or darkness, while a* and b* represent the color's hue.

Initial color measurements (L0, a0, b0) of the specimens were taken after they were stored in distilled water at 37°C for 24 hours. The specimens were divided into four groups based on the type of restorative materials (n=40). Ten randomly selected specimens were immersed in iron syrup (Ferifer, Berko), ten in Iron + Multivitamin Syrup (Ferro Sanol B, Adeka), and ten in Multivitamin Syrup (Polivit, Abdi İbrahim). The control group consisted of ten specimens immersed in distilled water and kept in an incubator at 37°C for 90 days. The samples were immersed in the test solutions for 2 minutes daily, then removed, dried, and stored in distilled water. The second color measurement was taken on the 30th day, and the final measurement on the 90th day.

The color change levels in the specimens were calculated using the CIEDE2000 formula as follows: (Figure 1)

- $\Delta L'$ is the lightness difference
- $\Delta C'$ is the chroma difference
- $\Delta H'$ is the hue difference
- R_T is the rotation term that accounts for the interaction between chroma and hue differences
- S_L, S_C, and S_H are the weighting functions for the lightness, chroma, and hue components, respectively
- K_L, K_C, and K_H are the parametric factors for the lightness, chroma, and hue components, respectively

$$\Delta E_{00} = \left[\left(\frac{\Delta L'}{K_L S_L}\right)^2 + \left(\frac{\Delta C'}{K_C S_C}\right)^2 + \left(\frac{\Delta H'}{K_H S_H}\right)^2 + R_T\left(\frac{\Delta C'}{K_C S_C}\right)\left(\frac{\Delta H'}{K_H S_H}\right)\right]^{\frac{1}{2}}$$

Figure 1. CIEDE2000 formula used to determine color change in our study

The ΔE00 (color change value) value measured 0.8, referencing perceptibility (PT) and acceptability (AT) threshold values of 1.8. These thresholds serve as benchmarks to assess whether the color change is noticeable or acceptable based on perceptual sensitivity (10).

Statistical analyses

Statistical Package for the Social Sciences package program version 26.0 (SPSS Inc., Chicago, IL, USA) was employed for statistical analyses. A paired-sample t-test ($p<0.05$) was utilized to assess significant differences. The effects of composites and solutions on ΔE00 over time were analyzed using two-way ANOVA., followed by post-hoc Tukey tests for multiple comparisons. Changes in ΔE00, values within the same solution over time were analyzed using paired-sample t-tests.

RESULTS

A two-way ANOVA test was applied to compare the 30-day groups, revealing a significant difference in the color change of restorative materials in pediatric nutritional syrup groups after 30 days ($p<0.05$). Table 2 presents the mean and standard deviation (Std. Dev.) of color changes across different time points. At both 30 and 90 days, the control group exhibited the lowest color change in all restorative materials. Among the

Table 1. Materials used in the study.

	Product Name	Type	Ingredients	Manufacturer
Restorative Materials	Dyract XP	Polyacid Modified Glass Ionomer	Strontium-fluoro-silicate glass, strontium fluoride, TCB resin, UDMA, photoinitiator and stabilizers	Dentsply DeTrey, GmbH, Germany
	GCP Glass Fill	Glass Carbomer	Fluoroaluminosilicate glass, nano fluoro/ hydroxyapatite, olyacids	GCP Dental, Vianen,Holland
	Equia Forte	Glass Hybrid	Strontium fluoroaluminosilicate glass, polyacrylic acid and aqueous polyacrylic acid	GC Corporation, Tokyo, Japan
Pediatric Nutritional Syrups	Ferifer	Iron syrup	100 mg iron (ferrous III hydroxide polymaltose complex), Sorbitol (E420), methyl paraben sodium (E219), propyl paraben sodium (E217), citric acid monohydrate, vanilla flavor, glycerin, propylene glycol and deionized water.	Berko İlaç ve Kimya Sanayi Anonim Şirketi, İstanbul, Türkiye
	Ferro Sanol B	Iron + Multivitamin Syrup	112.50 mg iron (II)-glycine-sulfate-complex (equivalent to 20 mg Fe^{+2}), 0.43 mg riboflavin -5-sodium phosphate, 0.32 mg vitamin B1 (thiamine hydrochloride), 0.63 mg vitamin B6 (pyridoxine hydrochloride), Ascorbic acid , once refined sugar, glucose monohydrate, sorbitol, sulfuric acid 95-98%, orange essence, pear essence, deionized water	ADEKA İlaç Sanayi ve Ticaret Anonim Şirketi, Samsun, Türkiye
	Polivit	Multivitamin Syrup	1500 IU Vitamin A, 1 mg Vitamin B, 1.2 mg Vitamin B2, 2 mg Vitamin B6, 7 mg Nicotinamide (PP), 3 mg D-Panthenol, 25 mg Vitamin C, 400 IU Vitamin D3, 5 mg Vitamin E, : 3.75 mg Sodium saccharin, 5.00 mg Sodium benzoate	Abdi İbrahim İlaç Sanayi ve Ticaret Anonim Şirketi, İstanbul, Türkiye

TCB: A reaction product of butane tetracarboxylic acid and hydroxymethyl methacrylate, UDMA: Urethane dimethacrylate, Fe+2: Ferrous ion, San: Sanayi, Tic: Ticaret, A.Ş: Anonim şirketi, mg: Miligram, %: Percentage, IU: International unit

Table 2. Mean ΔE00 values ± standard deviations of composites after 30 days and 90 days of immersion in solutions.

Restorative Materials	Time	Ferifer (Mean±Std.Dev.)	Ferro Sanol (Mean±Std.Dev.)	Polivit (Mean±Std.Dev.)	Distillized Water (Mean±Std.Dev.)
Glass Carbomer	30 day	4.063±1.8021 aA	6.09±1.0938 bF	7.134±0.7732 bJ	0.561±0.3212 cN
	90 day	4.83±2.3739 dC	8.655±1.348 eH	9.149±0.9302 eL	0.773±0.4222 fP
Glass Hybrid	30 day	0.818±0.3823 gB	0.744±0.42 g,hF	0.577±0.4482 g,hK	0.349±0.2643 hN,O
	90 day	1.046±0.4647 ıD	1.221±0.8193 ı,iI	0.594±0.4237 iM	0.413±0.2717 iR
Polyacid Modified Glass Ionomer	30 day	0.753±0.2891 j,kB	1.238±0.3706 jG	0.658±0.2203 k,lK	0.264±0.1318 lO
	90 day	0.914±0.5612 mD	1.728±0.3706 nI	1.148±0.2957 oM	0.383±0.1049 pR

*Lowercase letters indicate differences in rows, uppercase letters indicate differences in columns. ($p < 0.05$) Std. Dev.: standard deviation

experimental groups, Ferifer showed the least color change, while Polivit showed the most.

On the 30th day, the control group again exhibited the least color change. When comparing the 30- and 90-day immersion periods in terms of ΔE00, polyacid-modified glass ionomer specimens immersed in water showed the lowest color change, while the highest color change was observed in glass carbomer specimens kept in multivitamin syrup (Figures 2 and 3). The mean (SD) color change of restorative materials indicated that the color in the control group remained within acceptable limits at all time points.

The results demonstrated that prolonged use of pediatric nutritional supplements led to a greater color change in the Ferifer, Ferro Sanol, and Polivit groups at all time points, considering the normal data distribution and mean color change over time (Table 2). The two-way ANOVA indicated a significant color difference at 30 and 90 days in the Ferifer, Ferro Sanol, and Polivit groups ($P<0.05$). Additionally, pairwise comparisons using the LSD test showed significant differences at different time points ($P=0.0001$).

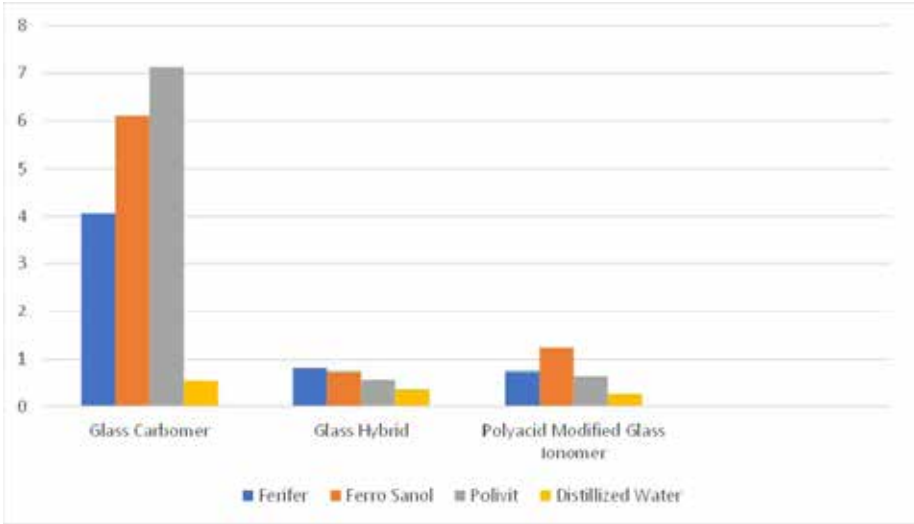

Figure 2. Changes in ΔE00 color difference values of the restorative materials used in our study after 30 days

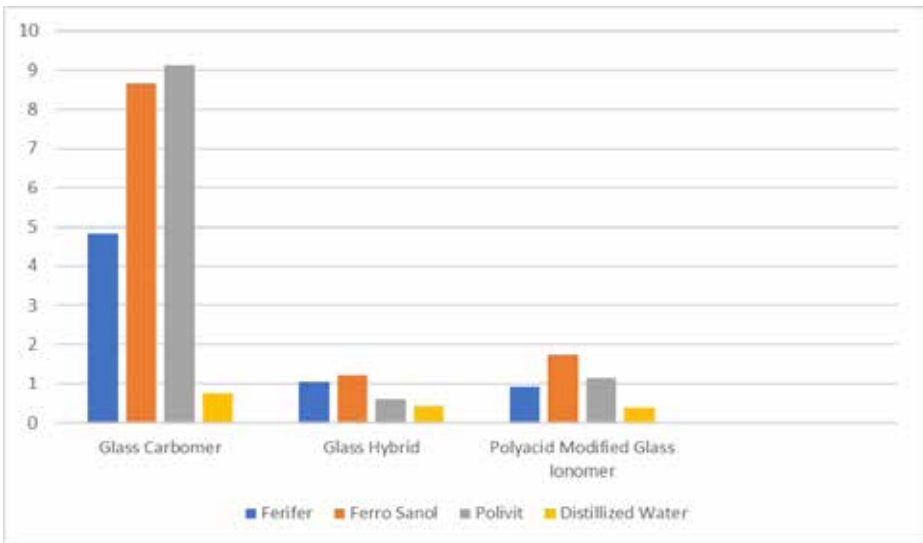

Figure 3. Changes in ΔE00 color difference values of the restorative materials used in our study after 90 days.

DISCUSSION AND CONCLUSION

The findings of this study provide valuable insights into how pediatric nutritional syrups impact the color stability of glass ionomer-based restorative materials (GICs) in pediatric dentistry. Understanding these effects is crucial for clinicians when selecting appropriate restorative materials and managing the oral health of their patients. According to the data obtained in our study, our first hypothesis, 'The waiting time of the restorations in solutions and in the control group should not affect the color change.' was rejected. Additionally, our second hypothesis, 'The nutritional supplement syrups used should not cause color change in the restorations', was rejected.

Yıldırım and Uslu (11) did not find a correlation between the degree of color change in glass carbomer and glass hybrid restorations after immersion in nutritional syrups and subsequent tooth brushing. In our study, after removing the samples from the syrups, they were rinsed and measured.

Pani et al. (6) and Yıldırım and Kaya (12) demonstrated in their studies that iron syrups cause significant discoloration in teeth and restorations over

time. In our research, a noticeable increase in color change was observed in all groups during the 90-day period compared to the 30-day period. Color change (ΔE00) was assessed at two intervals (30 days and 90 days) after immersion in various pediatric drug formulations and distilled water. The results revealed that the glass carbomer group exhibited the highest ΔE00 values when immersed in multivitamin syrup at both time points, suggesting greater susceptibility to color changes compared to compomers and conventional glass ionomers. Interestingly, no significant differences in color change were found between compomers and conventional glass ionomers after 90 days of immersion. However, at 30 days, compomers exhibited significantly lower ΔE00 values than conventional glass ionomers, particularly when immersed in distilled water, indicating superior initial color stability.

Numerous studies have reported that nutritional syrups and nutritional supplements in syrup form can induce color changes in restorations. (13 -15) The amount of discoloration may vary depending on the iron composition present in iron syrups. Tayebi et al. (16) demonstrated that Vitamin C, found in multivitamins, can cause considerable color change. In our study, the greatest color change was observed in glass carbomer specimens immersed in multivitamin syrup. However, the most significant color changes were observed in the groups immersed in Ferifer (containing iron III hydroxide polymaltose) after 30 days for Cam hybrid and in Ferro Sanol B (containing iron (II)-glycine-sulfate and a multivitamin complex) after 90 days. In the compomer group, the most pronounced color change occurred with Ferro Sanol B. These differences in color stability among GICs can be attributed to their distinct compositions. Compomers, which contain resin components, exhibited greater resistance to color change, especially in the absence of pediatric nutritional syrups, suggesting that resin content may enhance color stability. (17) Conversely, the composition of glass carbomers made them more susceptible to coloration induced by pediatric nutritional syrups.

These findings underscore the importance of carefully selecting GIC materials in pediatric dentistry, particularly considering potential long-term exposure to pediatric nutritional syrups. Clinicians are advised to choose restorative materials that offer optimal color stability alongside other desirable clinical properties. In their study, Yıldırım and Uslu (11) found that glass carbomers demonstrated superior color stability under the influence of pediatric nutritional syrups. According to Tüzüner et al. (18), glass ionomer cements exhibit superior resistance to color change. In our research, the least color change occurred in the compomer group immersed in distilled water. Its UDMA content provided greater color stability compared to TEDGMA and Bis-GMA. Conversely, glass carbomers exhibited the most significant color change across all groups, while glass hybrid materials showed resistance to color change.

In conclusion, this study highlights that pediatric nutritional supplements in syrup form can lead to color changes in GIC-based restorative materials, with glass carbomers being particularly susceptible. It also emphasizes the role of resin content in mitigating color change, with compomers demonstrating better initial color stability. These insights can assist clinicians in making informed decisions regarding restorative materials for pediatric patients and advocate for further research to enhance GIC color stability in pediatric dentistry. However, our study could be further improved by comparing syrup and drop forms through in vivo experiments.

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Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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Biyo-tıp Etiği ve Hukuk

Sevtap Metin

Biyo-tıp etiği, muhtaç olanlara gerektiği şekilde yardım etme biçimindeki genel ahlaki yükümün, doktorun faaliyetinde somutlaştırılması olarak görülür. Bu durumda yardıma gereksinim duyanlar hastalardır ve onlara yapılması gereken yardım esas olarak tıbbidir. Yine de hekimlik etkinliği sadece teknik gerekleri yerine getirmekle yetinemez; öyle ki eğer ahlak boyutu eksikse hekim tıbbı uygulayan bir teknisyen olmaktan öteye geçemeyecektir. Ancak bunun da ötesinde, içinde yaşadığımız 21. yüzyıla dair nitelendirmelerden biri de biyoteknoloji yüzyılı olacağı öngörüsüdür. Bir kısmı şu an için pratiğe geçirilemese de tasavvur ötesi olmayan birçok biyoteknolojik atılım ve bunun insan hayatı ve sağlığına etkisi, görmezden gelinemeyecek aşamaya gelmiştir. İşte bu dönemde tıbbi işlemlerin sadece ahlaki tarafına vakıf olmanın da ötesine geçilerek felsefi bir tartışma ve yaklaşıma her zamankinden daha fazla ihtiyaç vardır.

Türkiye'nin ilk ve tek tıp ve insani bilimler merkezi Beşikçizade Tıp ve İnsani Bilimler Merkezi—BETİM tarafından yayımlanan bu önemli eser tıbbın felsefi yönü ile de ilgilenen okurlar için vazgeçilemez bir başvuru kaynağı olacaktır.

Betim Kitaplığı

Exploring the relationship between berberine and the gut microbiome: A closer look at recent studies

Berberin ve bağırsak mikrobiyomu arasındaki ilişkinin araştırılması: Son çalışmalara yakından bir bakış

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Abstract

Aim: Berberine, known for regulating blood glucose and reducing inflammation, also enhances gut microbiota diversity and repairs microbial profiles. However, comprehensive reviews on its disease-specific impacts are limited. This study aims to explore berberine's influence on microbiota diversity in various diseases, offering a novel perspective.

Methods: A literature review was conducted using PubMed, Web of Science, ScienceDirect, and Google Scholar, focusing on studies from 2018-2023. Keywords related to berberine and gut microbiota were used, excluding irrelevant topics. A total of 84 titles and abstracts were screened, with 33 articles meeting inclusion criteria for detailed review.

Results: Berberine promotes beneficial species like Bacteroidetes and Akkermansia, shows antimicrobial properties, and targets specific pathogens. Studies, particularly in obese and Type 2 diabetic mice, suggest it can improve gut microbiota and diversity. However, the optimal dosage remains unclear, and individual microbial responses can vary, sometimes leading to dysbiotic profiles.

Conclusion: Berberine shows promise in enhancing gut microbiota diversity and combating pathogens. Nevertheless, further studies are needed to confirm its therapeutic potential and establish optimal treatment protocols with long-term clinical outcomes.

Keywords: Berberine; microbiota; microbial; microbiome

Öz

Amaç: Berberin, kan şekeri düzenleme ve iltihap azaltma özellikleriyle bilinir ve ayrıca bağırsak mikrobiyota çeşitliliğini artırır ve mikrobiyal profilleri onarır. Ancak, hastalıklara özgü etkileri üzerine kapsamlı incelemeler sınırlıdır. Bu çalışma, berberinin çeşitli hastalıklardaki mikrobiyota çeşitliliği üzerindeki etkisini araştırmayı ve bu konuda yeni bir bakış açısı sunmayı amaçlamaktadır.

Yöntem: 2018-2023 yılları arasında PubMed, Web of Science, ScienceDirect ve Google Scholar gibi veritabanlarında, berberin ve bağırsak mikrobiyotası ile ilgili anahtar kelimeler kullanılarak bir literatür taraması yapılmıştır. İlgisiz konular hariç tutularak 84 başlık ve özet incelenmiş, 33 makale belirlenen kriterlere göre detaylı olarak gözden geçirilmiştir.

Bulgular: Berberin, Bacteroidetes ve Akkermansia gibi yararlı türleri destekler, antimikrobiyal özellikler gösterir ve belirli patojenleri hedef alır. Özellikle obez ve Tip 2 diyabetik farelerde yapılan çalışmalar, bağırsak mikrobiyotası ve çeşitliliğinde iyileşme potansiyeline işaret etmektedir. Ancak, optimal dozaj belirsizdir ve bireysel mikrobiyal yanıtlar farklılık gösterebilir, bazen disbiyotik profillere yol açabilir.

Sonuç: Berberin, bağırsak mikrobiyota çeşitliliğini artırma ve patojenlerle mücadelede umut vadetmektedir. Bununla birlikte, terapötik potansiyelini doğrulamak ve uzun vadeli klinik sonuçlar elde etmek için daha fazla araştırma gereklidir.

Anahtar Sözcükler: Berberin; mikrobiyota; mikrobiyal; mikrobiyom

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INTRODUCTION

Berberine (BBR) is a distinctive molecule belonging to the protoberberine group of isoquinoline alkaloids. Classified as a quaternary ammonium salt, it is characterized by the molecular formula $C_{20}H_{18}NO_4$ (1, 2). It is a bioactive compound found in many plants such as *B. Petiolaris*, *B. aristate*, *B. darwinii*, and *B. vulgaris* (3-6) (Figure 1). The stems and roots of *Berberis aristata, B. darwinii, B. petiolaris,* and *B. vulgaris* have been extensively studied for their high berberine content. Additionally, many other medicinal plants with high berberine content have been reported, including *Coptis chinensis* (Chinese goldthread) and *Hydrastis canadensis* (goldenseal) (7). Berberine is found in various plant families, such as *Annonaceae, Berberidaceae, Menispermaceae, Papaveraceae, Ranunculaceae,* and *Rutaceae.* Within the genus *Berberis, B. vulgaris* is particularly significant, with its bark containing over 8% alkaloids, of which approximately 5% is berberine. This compound is prevalent in the barks, leaves, twigs, rhizomes, roots, and stems of numerous medicinal plants like *Argemone mexicana, Berberis aristata,* and *Hydrastis canadensis*. Research indicates that the highest concentrations of berberine are typically found in the bark and roots of these plants (8).

Berberine, with its multi-target mechanism, has demonstrated positive pharmacological effects in diverse diseases, including inflammation, atherosclerosis, hyperlipidemia, mental disorders, liver diseases, intestinal diseases, autoimmune and cardiovascular diseases, and non-alcoholic fatty liver disease (NAFLD), notably reducing blood lipids and glucose in health issues like Type 2 diabetes and hyperlipidemia (9-14). Berberine supplementation significantly reduced the levels of polysaccharide lyases and carbohydrate esterases compared to the control group, while stimulating key pathways from the Kyoto Encyclopedia of Genes and Genomes (KEGG), including carbohydrate metabolism and microbial metabolism, by altering microbial enzyme activities. In vivo studies further demonstrated that while berberine did not affect *Enterobacteriaceae*, it inhibited some butyrate-producing bacteria and, at high doses, improved chicken gut morphology and reduced inflammation independently of gut microbiota changes (15).

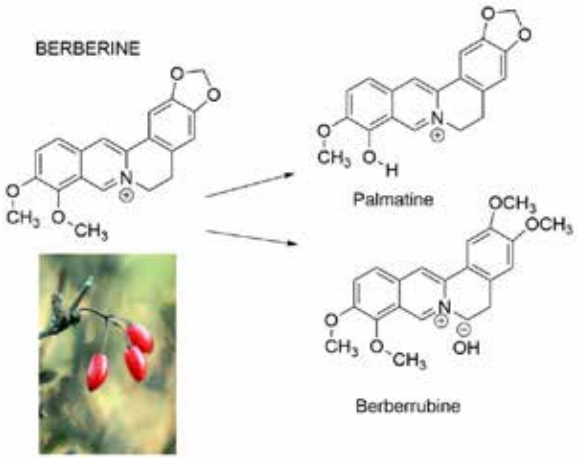

Figure 1. Molecular structures of berberine, berberrubine and palmatine

The intestinal microbiota, consisting of trillions of microorganisms, serves as the primary endocrine organ and plays a crucial role in essential physiological processes, including macronutrient digestion and vitamin synthesis, contributing to the preservation of host homeostasis. Therefore, it is evident that alterations in the balance of the intestinal flora can potentially contribute to the onset of various chronic and autoimmune diseases, such as obesity, diabetes, and other metabolic syndromes (16). It has also been discussed in previous studies that the low oral bioavailability of berberine and its effects may be due to intestinal microbiota interaction (10, 17). Studies have suggested that berberine may improve insulin resistance by modulating the gut microbiota and may also help treat cardiovascular diseases that accompany dyslipidemia and obesity (18). Although there has been increasing evidence in recent years that berberine can regulate the dysbiotic intestinal microbiome composition, there are also studies showing that it reduces the overall intestinal microbial diversity (19-21). While some studies suggest that berberine contributes to microbial balance by replacing dominant gut bacteria, other studies have emphasized the importance of berberine dosage and have shown that high doses taken as a dietary supplement may lead to dysbiosis-like changes in the intestinal microbiota (22). However, it's worth noting that, despite various studies addressing and discussing BBR and gut microbiota interactions from different perspectives, there has not yet been a com-

prehensive discussion regarding berberine's effects on the overall diversity of the gut microbiota, including both the positive and negative aspects of these effects (1, 2, 10, 23).

METHODS

In this narrative review article, a comprehensive literature search was conducted to evaluate the effects of berberine on the gut microbiota. Scientific studies published between 2018 and 2023 were sourced from various electronic databases, including PubMed, Web of Science, Science Direct, and Google Scholar (Figure 2). The search strategy employed the following keywords and combinations: ("Berberine" OR "Gut Microbiota" OR "Gut Microbiome") OR ("Gut Bacteria and Berberine" OR "Berberine and SCFA (short chain fatty acid)" OR "Gut Microbiota Richness" OR "Gut Microbiota Diversity" OR "Berberine and diseases") AND NOT ("review" [Title/Abstract] OR "Berberine and Cancer" OR "Berberine and Neurology"). This extensive search yielded a total of 84 titles and abstracts for initial screening, out of which 33 articles were thoroughly reviewed based on the inclusion criteria.

The selected studies prioritized those involving 16S rRNA and metagenomic analyses. The included articles comprised review articles, clinical and experimental intervention studies, observational studies, and systematic reviews. These studies commonly explored berberine's impact on gut microbiota alterations, microbial diversity and richness, short-chain fatty acids (SCFA), and berberine's potential therapeutic effects mediated by gut microbiota on various diseases. Additionally, studies investigating the effects of berberine on health issues such as metabolic diseases, inflammatory bowel diseases, and obesity were included.

This methodological approach facilitated a comprehensive evaluation of the existing literature, enabling a better understanding of the interactions between berberine and gut microbiota.

RESULTS

Berberine and gut microbiota interaction

While berberine is known to have beneficial health effects, its significantly low bioavailability has attracted attention and has been extensively investigated. Studies suggest that the interaction of berberine with the gut microbiota may contribute to potential health benefits. BBR has poor oral bioavailability; therefore, the ability to regulate gut microbiota and gut metabolites may be present (24). It has the potential to contribute to disease management. In human pharmacokinetic studies, less than 5% of orally administered berberine enters systemic circulation. Berberine is rapidly distributed and filtered by the liver, resulting in low circulation levels, and undergoes phase I demethylation followed by phase II conjugation processes. Its accu-

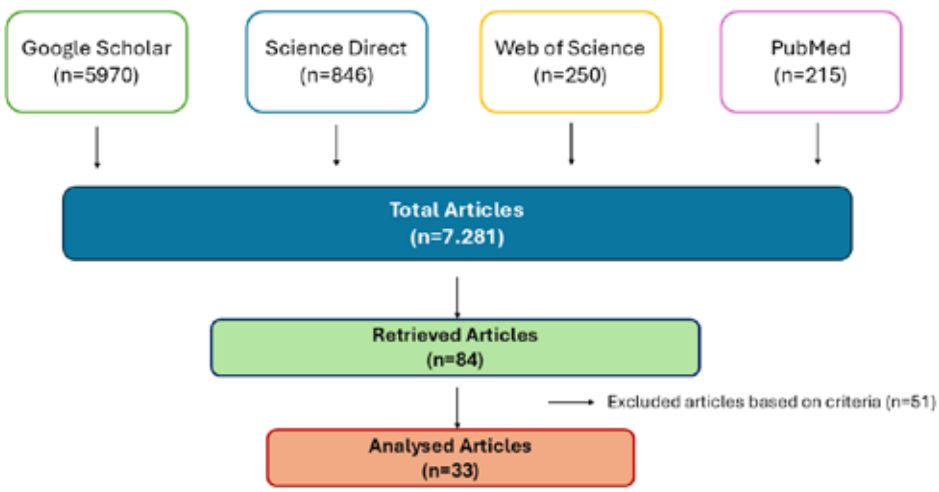

Figure 2. Flow diagram

mulation in tissues (e.g., liver, kidneys, muscle, brain) explains the pharmacological effects observed in clinical studies (e.g., cholesterol and blood glucose reduction) despite low plasma levels (25). Several studies have shown that berberine exhibits positive effects on various diseases such as cancer, inflammation, bacterial infections, and non-alcoholic fatty liver disease. In a study conducted in rats, the absolute bioavailability of orally administered 100 mg/kg berberine was measured at 0.68%. In dogs, the maximum concentration of berberine in the blood was found to be 36.88 ng/mL when administered at a dose of 50 mg/kg. This discrepancy between the low bioavailability and the potent pharmacological effects of berberine has puzzled researchers for some time (2, 23). It has been proposed that the bioavailability of berberine, which is markedly below 1%, is estimated to result in a peak plasma concentration of around 0.4 ng/ml following the administration of a 400 mg oral dose, thus reinforcing this suggestion (23). Additionally, a report highlights a specific finding on the interaction between berberine and the gut microbiota, indicating that approximately 43.5% of berberine undergoes metabolism in the intestines. Furthermore, nitroreductases within the gut microbiota have been documented to transform berberine into dihydroberberine (dhBBR), a more readily absorbable form that boasts a fivefold increase in intestinal absorption compared to berberine (26). Moreover, recent research has revealed that berberine modulates the gut microbiota, promoting microbial balance in rats subjected to a high-fat diet, and manifests therapeutic effects in metabolic diseases, particularly impacting the phylum-level composition (11, 27).

Health effects of berberine on intestinal microbiota

Berberine takes center stage as a potential adjunct in the management of various diseases, particularly by revealing its biological effects through interactions with the intestinal microbiota. Its ability to modulate the balance of gut microbiota positions berberine as a promising compound for therapeutic research, emphasizing its significance in promoting overall health. The antidepressant effect of BBR is linked to its regulation of the brain-gut axis via gut microbiota and SCFAs, increasing levels of serotonin, norepinephrine, dopamine, and BDNF. This mechanism alleviates depression-like behaviors (28). In a study, the effects of Diane-35, probiotics, and berberine were compared in a dihydrotestosterone (DHT)-induced polycystic ovary syndrome (PCOS) rat model. Diane-35 and probiotics improved reproductive and metabolic functions in PCOS rats by restoring gut microbiota diversity (29). It has been observed that berberine intervention significantly alters the gut microbiota in mice with glucose and lipid metabolism disorders, enriching bacteria such as *Akkermansia, Eubacterium*, and *Ruminococcus* (30). The use of berberine for therapeutic purposes has been observed to significantly increase the richness and diversity of the microbial community, alleviating symptoms of Type 2 diabetes in diabetic rats (24). Additionally, in another study aiming to compare the effects of berberine in combination with probiotics and berberine alone in Type 2 diabetes (T2D) patients, it was observed that they shared similar changes in terms of microbial alterations and functions. As a result of the study, the use of berberine for correcting intestinal microbiota dysbiosis in T2D patients was recommended (31). In other research evaluating the combination of BBR with a probiotic, it was found that the combination did not provide any additional benefit in improving postprandial plasma triglycerides (pTG) compared to berberine alone (32). In a study conducted on chickens, the impact of low (0.1 g/kg feed), medium (0.5 g/kg feed), and high (1 g/kg feed) doses of berberine intervention on the microbiome composition was investigated. Analysis of 16S rRNA gene sequences revealed that low and medium doses of berberine promoted beneficial bacteria from the *Lachnospiraceae* family in the chicken's cecum, while medium and high doses tended to increase villus length in the small intestine. The highest concentration of berberine significantly increased microbial diversity in the ileum. These findings suggest that berberine dosages can influence microbiome composition, with effects varying depending on the dose (33). However, berberine has been shown to have beneficial effects, like probiotics and antibiotics, in creating the microbial composition targeting the increase in *lactobacilli* and *bifidobacteria* in inflammatory bowel disease (IBD) patients (34). It can also be seen that the cholesterol-lowering effect of berberine is due to its

Table 1. Berberine's interactions with gut microbiota.

Animal/ human models	Dosage of BBR	Key findings	Refs.
Healthy Sprague-Dawley rats	150 mg/kg daily for 4 weeks	Hepatic inflammation↑ *Bacteroidetes*↑ *Firmicutes*↓ Diversity↓	(20)
Sprague-Dawley rat	200 mg/kg daily for 6 weeks	T2D symptoms↓ The community richness↑ Diversity↑ *Lactobacillaceae*↑ *Bacteroidetes*↓ *Proteobacteria*¯ *Verrucomicrobia*↓	(24)
Human, diagnosed with T2D	BBR; 0.6 g (6 pills) twice daily before meals Probiotics; 4 g (2 strips of powder) once daily at bedtime for 12 weeks	78 species changed BBR alone or in combination with probiotics altered the gut microbiome	(31)
Human, diagnosed with T2D	BBR; 0.6 g (6 pills) twice daily before meals Probiotics;4 g (2 strips of powder) once daily at bedtime for 12 weeks	Prob + BBR group did not show added benefits in improving pTG compared to BBR alone.	(32)
Hyperlipidemic human patient	0.5 g twice daily for 3 months	*Blautia*↑ *Akkermansia*↑ *Clostridium XI*↑ *Robinsoniella*↑ *Cronobacter*↑ *Anaerostipes*↑ *Coprobacillus*↑ *Alistipes*↓ *Helicobacter*↓ *Enterorhabdus*↓ *Desulfovibrio*↓	(35)
C57BL/6 mice	200 mg/kg daily for 56 days	Anti-hyperlipidemic effect of BBR *Blautia producta*↑ *Clostridiales*↑ *Akkermansia muciniphila*↑ In the HFD + BBR group; Blautia↑	(36)
Specific pathogen-free ICR mice	100-200-300 mg/kg daily for 5 weeks	*Akkermansia*↑ Too high dose of BBR may act as a weak antibiotic.	(38)
Sprague-Dawley and hamsters	100 mg/kg daily 10 days	Treatment of HFD-hamsters with BBR increased the butyrate content	(37)
Apoe −/− mice (SPF class)	0.5 g/L in water daily for 14 weeks	Berberine in HFD-fed Apoe −/− mice; Restored intestinal barrier HFD-induced inflammation↓ Akkermansia spp. ↑	(40)
BKS-Leprdb (*db/db*, T2DM model) and C57BLKS/JNju mice	136.5 mg/kg BRB 113.75 mg/kg metformin daily 19 weeks	In the berberine and metformin groups; *Butyricimonas*↑ *Lactobacilli*↑ *Coprococcus*↑ *Ruminococcus*↑ *Akkermansia*↑ *Prevotella*↓ *Proteus*↓	(41)
Sprague-Dawley rats	150 mg/kg berberine chloride daily for 4 months	HDF-induced metabolic disorders ameliorated *Bactriodetes* phylum↑	(42)

Human, diagnosed with hyperglycemia	0.5 g oral BBR tablets twice daily 0.70 g live *Bifidobacterium* capsules twice daily for 16 weeks	HbA1c↓ Bifidobacterium enhances the hypoglycemic effect of berberine	(43)
db/db mice and wild type mice	6 groups of *db/db* mice (*db*, M250, B250, B125, B250 + M250, and B125 + M250) with wild type (WT) as control for 14 days	Combination metformin and berberine; *Proteobacteria*↑ *Verrucomicrobia*↑ B125 + M250; insulin sensitivity↑ distinct changes in intestinal microbial communities	(44)
Specific pathogen-free (SPF) Wistar rat	200 mg/kg BBR 100 mg/kg BBR 200 mg/kg MET once a day for 18 weeks	Metformin more dominant effect on Lactobacillus and Klebsiella↑ Berberine more dominant effect on Allobaculum, Blautia, Bacteroides and Butyricicoccus↑ HDF-induced changes were reversed in both	(45)
HDF- Sprague Dawley rats	150 mg/kg daily for 4 weeks	BBR altered the intestinal microbiota in rats with MS. *A. muciniphila*↑ *Bacteroides*↑ *Ruminococcus*↑ *Candidatus arthromitus*↓ *Prevotella*↓ *Phascolarctobacterium*↓	(46)
Male apoE-/- mice; Mice are coprophagic (feces-eating)	Intragastric administration twice a week 50 mg/kg for 12 weeks	BBR may ameliorate HFD-induced atherosclerosis via gut microbiota modulation. BBR-treated gut microbiota transferred between mice.	(47)
C57BL/6J mice	100 mg/kg oral daily for 4 weeks	HDF-induced intestinal dysbiosis↓ Bacteroidetes↑ Clostridiales↑ Lactobacillaceae↑ Bacteroidale↑	(48)
Sprague-Dawley rats	150 mg/kg via gavage daily for 6 weeks	Inhibit the synthesis of trimethylamine N-oxide remodeled the intestinal microbiota Lactobacillus genus↑	(49)
C57BL/6J mice	100 μg/kg/d for 15 weeks	It may improve chronic HFD-induced metabolic syndrome. Its combination with antibiotics is no different from its effect alone in preventing HDF-induced weight gain.	(50)
Goto-Kakizaki (GK) rats	200 mg/kg BBR 100 mg/kg Metformine intragastricly once daily for 8 weeks	In two groups; *Bacteroidetes*↓ *Bacteroidetes/Firmicutes*↓ *Muribaculaceae*↓ *Allobaculum*↑ Berberine can modulate gut microbiota in T2DM rats	(51)
C57BL/6J-Apc min/+ mice and wild-type C57BL/6	500 ppm berberine for 12 weeks	Restored the enteric microbiome community in HFD-fed mice. Verrucomicrobia↓ Akkermansia↓ SCFA↑	(52)
C57BL/6 J mice	150 mg/kg/day BBR chloride via intragastric for 4 weeks	Protective effect in hypertension *Firmicutes/Bacteroidetes*↓ *Lactobacillus*↑	(53)
Balb/c mice	40 mg/kg BBR, once a day for 10 days	The results showed that BBR could modulate the intestinal microbiota composition in ulcerative colitis model mice.	(54)

Syrian golden hamsters	HFD group, LB group (HFD+75 mg/kg/day BBR), HB group (HFD+150 mg/kg/day BBR), LM group (HFD+75 mg/kg/day MTF), HM group (HFD+150 mg/kg/day MTF	The α-diversity of the gut microbiota, which was for 8 weeks significantly reduced by HFD nutrition, was significantly reversed by MTF and BBR; A relatively milder effect of berberine than MTF was detected on bacterial diversity.	(55)

* BBR: Berberine, T2D: Type 2 Diabetes, Prob: Probiotic, HDF: High fat diet, MS: Metabolic syndrome

Table 2. Effect of berberine on intestinal diversity.

Animal/ human models	Dosage of BBR	Key findings	Refs.
Broiler Chickens	1 g berberine/kg supplemented diet for 21 days	*Proteobacteria*↑ *Firmicutes*↓ High doses of BBR have dysbiosis-like effects.	(15)
C57BL/6J mice	10 mg/kg BBR 50 mg/kg BBR 100 mg/kg BBR for 33 days	There is no significant dose-response relationship for BBR between 10 – 100 mg/kg. Richness and diversity↓ A. muciniphila It may reduce alcoholic fatty liver.	(21)
Healthy Duorc × (Landrace × Large White) weaned piglet	0.1% for 21 days	Beneficial bacteria like; *S. variabile*↑ *L. johnsonii*↑ *P. distasonis*↑ Richness and diversity↑	(22)
Sprague-Dawley rat	150 mg/kg oral daily for 6 weeks	Richness↑ Alleviated HFD-induced hepatic steatosis and damage.	(27)
Wistar rats	50 mg/kg BBR 100 mg/kg BBR intragastrically once daily for 14 consecutive days	Richness↓ BBR can reduce depression in rats.	(28)
Wistar rats	150 mg/kg via intragastric for 1 month	Species diversity↓ The amount of intestinal microbiota↓ It did not show any improvement in PCOS.	(29)
C57BL/6J mice	200 mg/kg for 14 weeks	Akkermansia↑ Eubacterium↑ Ruminococcus↑ Microbial richness and diversity↓ BBR may improve glucose and lipid metabolism disorders.	(30)
C57BL/6 mice	0, 3, 10, 30, 100, 300 mg/kg of BBR via gavage for 2 weeks	BBR is a broad spectrum antibiotic. *Bacteroide*↑ *Ruminococcus*↓	(57)
ApoE−/− mice and C57BL/6J mice	100 mg/kg BBR hydrochloride 50 mg/kg BBR by gavage once a day for 13 weeks	Both high and low doses *Turicibacter*↑ High dose BBR; Alistipes↑ Roseburia↑ Bacteroidetes↓ Low dose BBR; Allobaculum↑ Blautia↑ Both high and low doses of BBR can alleviate HFD-induced atherosclerosis.	(74)

* PCOS: Polycystic ovary syndrome

association with the intestinal microbiota, as the effect of berberine is significantly reduced in the absence of *Blautia* and in metagenomic analysis, the key species most enriched by berberine was found to be the *Blautia* genus of *B. producta* (35, 36).

In a study, 83 hyperlipidemic patients were administered 1 g of oral berberine or a placebo daily for three months, and it was found that berberine significantly reduced serum levels of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-c) compared to the placebo group (35). Another study demonstrated that oral administration of berberine (BBR) promotes butyrate production in the gut microbiota, which subsequently leads to berberine entering the bloodstream and reducing blood lipid and glucose levels (37).

Modern pharmacological studies emphasize the importance of gut microbiota in the development stages of type 2 diabetes mellitus (T2DM), akin to genetic, environmental, and dietary factors. Berberine, when administered intragastrically at a dose of 136.5 mg/kg in db/db mice, increases the ratio of *Butyricimonas*, *Coprococcus*, and *Ruminococcus* bacteria, which produce short-chain fatty acids. These short-chain fatty acids lead to increased secretion of glucagon-like peptide-1 (GLP-1), improve insulin secretion, and suppress glucagon secretion to improve blood sugar levels. Gegen Qinlian decoction (containing BBR as the main component) and BBR alone enrich bacteria producing butyrate, such as *Faecalibacterium* and *Roseburia*, and increase SCFA levels in feces (2).

Exploring berberine's impact on restoring gut diversity and bacterial abundance

Berberine's effect on intestinal microbiota composition is known not only by increasing SCFA-producing bacteria but also by selectively inhibiting harmful bacteria (39). In a corroborative study, it is highlighted that berberine facilitates the growth of *Akkermansia* by triggering increased mucin secretion in the colon (25). As shown in Table 1, some human and animal studies have revealed that BBR can regulate gut microbiota composition, promote the increase of beneficial bacteria such as SCFA, reduce disease symptoms, and provide microbial restoration(20, 24, 31, 32, 35, 36, 38-55). Furthermore, BBR can regulate intestinal microbiota-associated metabolites (such as LPS, SCFAs, BAs) and reverse metabolic disorders by reversing the changes in the amount, structure, and composition of the intestinal microbiota (17). Among these studies, the three most commonly used models are the high-fat diet (HFD) induced disease model, the type 2 diabetes model, and the models compared to metformin or probiotics. Dietary berberine was observed in this study to increase the abundance of beneficial bacteria such as *S. variabile*, which inhibits food allergy in mice, and *L. johnsonii*, which can be considered as probiotics, by improving the intestinal mucosal immune response. In contrast, it has also been noted that dietary berberine may cause systemic autoimmunity because it promotes decreased interleukin-18 production by reducing the abundance of *P. Copri* (22).

In examining some animal studies, it was seen that berberine could improve intestinal microbiota dysbiosis and restore the intestinal barrier by enriching SCFA-producing bacteria such as *Bacteroides* and *Blautia* in rats with obesity induced by a high-fat diet (11). Berberine intervention in rats with HFD-induced metabolic syndrome (MS) has been shown to cause positive microbial changes by increasing the abundance of beneficial microflora such as *Akkermansia muciniphila* (*A. muciniphila*), *Bacteroides*, and selectively reducing the abundance of harmful microflora, and it has been suggested that it may have benefits in the treatments of obesity and insulin resistance (46). Despite this, some studies observed that berberine did not have any impact on the prevalence of the *Bacteroidetes phylum*, which is known for its beneficial effects (27) while other studies reported a significant increase in the number of *Bacteroides* after berberine treatment (54).

Looking at the changes observed in another High-fat diet (HFD) + BBR (150 mg/kg/day, 4 months) group, the enriching effect of berberine intervention on the *Bacteroides phylum* confirmed to produce SCFA was clearly seen ($p < 0.05$). Moreover, the abundance of several genera within the *Firmicutes phylum,* including *Roseburia, Dorea*, and *Blautia*, which experienced an increase due to the high-fat diet, was reversed with the administration of berberine (42). Intragastric administration of 200 mg/kg berberine for 6 weeks on diabetic rats was found to reduce the rela-

tive abundance of the *phylum Proteobacteria* and *Verrucomicrobia* while increasing the relative abundance of *Bacteroides* and probiotic *Lactobacillaceae*, which is negatively correlated with the risk of T2DM(10). Moreover, upon comparing the impact of BBR and metformin (MTF) in ApoE (-/-) mice subjected to a high-fat diet, similar alterations in intestinal microbial composition were noted. This included a notable reversal of reduced gut microbiota α-diversity, mitigating the dysbiosis induced by the high-fat diet (55). In a study on db/db mice comparing metformin and berberine, it was observed that both the diversity and richness of the gut microbiome were reduced by berberine intervention, unlike metformin. Intervention with metformin or berberine has been shown to positively affect the gut microbiota by increasing the abundance of probiotic bacteria, including *Lactobacillus* and *Akkermansia*, in db/db mice (41). Additionally, in a study investigating the combination of metformin at a dosage of 250 mg/kg and berberine at 125 mg/kg in db/db mice, it was observed that significant changes occurred in the intestinal microbial communities, especially *Verrucomicrobia*, and insulin sensitivity increased in these mice compared to individual mice (44).

Berberine intervention at 150 mg/kg/day for a month in NASH mice alleviated HDF-induced intestinal dysbiosis by increasing *Bacteroidetes* and *Lactobacillaceae,* and modulated gut microbiota associated with bile acid de-conjugation and transformation. This modulation was evidenced by changes in bile acid species, such as deoxycholic acid and ursodeoxycholic acid (48). Moreover, in a study investigating its relationship with NAFLD, berberine was shown to significantly reduce bacterial diversity in the intestinal flora (OTUs) and promote the increase of SCFAs by increasing *Bacteroidetes* which may have protective effects on NAFLD. Notably, berberine increased *Bacteroidetes* and decreased *Firmicutes* compared to previous results (20). In addition, the *Firmicutes/Bacteroidetes* ratio has a higher *Firmicutes* content. At a dose of 150 mg/kg, berberine intervention appeared to reduce the abundance of *Firmicutes* and restore balance with a slight increase in *Bacteroidetes* (56). In summary, BBR can increase microbial diversity by regulating the composition of both animal and human gut microbiota, have probiotic-like effects by supporting the growth of beneficial bacteria, and alleviate T2D and other diseases by reshaping the disrupted microbiota caused by HFD.

Berberine may positively influence gut microbiota by regulating bacterial abundance and diversity. In this context, it is suggested that berberine could contribute to maintaining a healthy intestinal environment, potentially offering health benefits. Therefore, the interactions between berberine and gut microbiota play a significant role in understanding crucial biological effects on health. In a group of HFD-fed Apoe-/- mice, berberine intervention has been reported to contribute to a healthy intestinal environment by increasing the relative abundance of *Bacteroides* and *Akkermansia* (40, 46). A study observed correlations between berberine concentrations and the composition of gut flora, highlighting negative correlations with bacteria such as *Ruminococcus gnavus, Ruminococcus schinkii, Lactobacillus acidophilus, Lactobacillus murinus,* and *Lactococcus lactis* (57). As shown in Table 2, some studies on animal models have found data that berberine reduces overall microbial diversity and causes dysbiotic microbiota formation. When alpha diversity analysis was examined in this study, it was seen that berberine; consistent with previous reports, it was observed that it significantly reduced the variety and diversity of the intestinal microbiota. The emphasized feature of berberine at this stage is that it acts as a broad-spectrum antimicrobial agent against pathogens in the microbiota (40).

In another research examining the effect of berberine alone in combination with antibiotics on microbial diversity, ob/ob mice receiving oral antibiotics for 3 days were simultaneously treated with berberine or antibiotics for 10 days. The study revealed that treatment with both berberine and antibiotics reduced the bacterial colony by 57% compared to berberine alone (37). Subsequent to the intervention of berberine hydrochloride, suggested to regulate intestinal microbial functions in Parkinson's patients, microbial diversity decreased in the berberine group compared to the control group (58). Similarly, intervention of berberine (200 mg/kg, e.g.) in normal rats showed that the number of species decreased and imbalance in the gut microbiota developed with the concentration of

SCFAs (short-chain fatty acids) in berberine-induced rats (59).

In a different study on rats, it was reported that berberine and metformin showed high similarity in enriching short-chain fatty acid-producing bacteria and inhibiting various intestinal microbes. The study also highlighted that high doses of berberine reduced the abundance of *Bacteroidetes*, whereas low doses of berberine and metformin did not have such an effect (45). Echoing these findings, in vivo results of another study on chickens also showed that increasing berberine dosage inhibited the growth of butyrate-producing bacterial strains (15).

Microbial diversity as an indicator of health

The microbial profiling approach, based on the 16S rRNA gene, has played a crucial role in systematically characterizing microbial communities. This method has provided valuable insights into the microbiome of healthy individuals, establishing connections between microbial changes and various diseases and health conditions. Our understanding in this field has expanded significantly, thanks to research on the human gut microbiota, which houses several hundred different bacterial species. Conducted across continents, extensive population-based studies have contributed valuable information. Sequencing techniques can currently identify between 100 and 200 different species of bacteria in a single sample, and phylogenetic classification is still unable to account for the physiological variations that species-level diversity causes among individuals (60). The gut microbiota is highly diverse, with each healthy adult human typically harboring more than 1,000 species of bacteria belonging to the dominant phyla *Bacteroidetes* and *Firmicutes* and relatively few other known bacterial phyla (61). Infections and inflammatory illnesses are caused by dysbiosis, a shift in the composition of gut microbes. Immune, metabolic, and neurobehavioral aspects of human health are all significantly influenced by gut microbes (62). Researchers discovered in a study that T2DM patients had a GM imbalance and had fewer *Lactobacillus* and *Bifidobacterium* than controls. The study also found a possible link between decreased microbial diversity and an increased risk of developing diabetes mellitus and developing insulin resistance (56). Dysbiosis in the gut microbiota has been associated with a range of human diseases, including diabetes, inflammatory bowel disease, anxiety, hypertension, cardiovascular diseases, liver disease, heart disease, obesity, and depression (63, 64). It has been reported that the alpha diversity of the gut microbiome is associated with human health, and lower diversity levels have been found to be linked to various acute and chronic diseases. When previous analyses of gut community composition and alpha diversity are examined, a negative relationship is often observed with the *Bacteroidetes phylum*. However, comparisons of gut microbiomes between rural Africans and urban Europeans have revealed the opposite, showing higher diversity and corresponding *Bacteroidetes* richness in rural Africans. Therefore, a single measurement such as the *Firmicutes/Bacteroidetes* (F/B) ratio, *Bacteroidetes* ratio, or microbial diversity may not allow us to reach a comprehensive and accurate conclusion for overall health (65). While a decrease in metagenomic richness is identified as an indicator of metabolic syndrome, the concept of dysbiosis lacks a precise definition due to the absence of a universally accepted norm for healthy microbiota. In adults, the diversity of the microbiota is considered a potential indicator linked to states of health or disease. Diminished microbial diversity, quantified through measures like Simpson, Shannon, Chao1, or phylogenetic diversity, has been documented in various disease states. Due to the absence of a precise definition of a healthy or normal microbiota, the concept of dysbiosis remains controversial. However, analyses in infants have reported that certain factors, like diminished microbial diversity or abnormal microbial composition, are associated with diseases such as asthma, intestinal diseases, inflammatory bowel disease, and metabolic disorders that occur in later stages of life, including in the infant. It has also been reported that the gut microbiota in breastfed infants exhibits lower diversity than in bottle-fed babies (19). Diversity analyses of the gut microbiome have associated the gut microbiome of people with large social networks with higher diversity, while the gut microbial diversity of people experiencing, stress, and anxiety is associated with a lower diversity and an altered microbiome (66). Recent research has implicated gut microorganisms in various human diseases such

as psoriasis, obesity, autism, and mood disorders (67). Unlikely, obesity, type 2 diabetes, and inflammatory bowel diseases, whose prevalence has increased sharply in recent years, have been associated with a reduction in gastrointestinal microbiome biodiversity. Loss of dietary biodiversity, one of the most important factors affecting microbial diversity, has been implicated as a critical factor in the development of obesity linked to reduced gastrointestinal microbiome diversity (68). Although there is ongoing disagreement regarding the relative importance of different intestinal taxa, it is generally agreed that having a diverse gut microbiome is beneficial. Studies that assess the functions that bacteria contribute, as opposed to variety, are also available. According to the study, this is because a diverse community appears to have a stronger correlation with health as it encompasses a wider range of functional domains. The investigation also noted that complex connections between shared species offer advantages that no single species can provide (60).

The therapeutic role of berberine in clinical diseases in the future

Since the introduction of the microbiome concept to the scientific community, we have been navigating a process that not only uncovers more profound insights into health and disease but also allows us to gain deeper knowledge through analyses, thanks to technological advancements. Although we know a lot about the microbiome thanks to valuable studies, the microbiome is an area that has not yet been fully elucidated and needs deeper and long-term observations. Healthy microbiota and dysbiosis do not yet have a precise profile definition. In addition to the many benefits of berberine, the fact that it reduces intestinal microbial diversity and causes the formation of a dysbiotic environment with its broad-spectrum antibiotic effect is an issue that needs to be further researched and clarified. Berberine is considered a promising compound in the treatment of diseases, as it enhances the growth of beneficial bacteria that produce health-related metabolites, especially SCFA and butyrate. It also modulates the disrupted microbial composition in metabolic diseases, promoting beneficial bacteria while reducing harmful ones, effectively acting as a probiotic. A meta-analysis of 21 clinical studies found that berberine had therapeutic effects comparable to other therapeutic regimens on T2DM, hyperlipidemia, and hypertension (69). The pro-inflammatory condition that dysbiosis induces in the gut damages the intestinal barrier's ability to function, which allows bacterial endotoxins to translocate and triggers a systemic immune response, which could be one reason why NAFLD occurs. Studies on humans and animals that connect microbial dysbiosis with gut inflammation provide credence to this theory (56). As a result of a study investigating the intestinal barrier protective effect of berberine against NAFLD in rats, it was observed that berberine reduced serum lipids and improved intestinal mucosal barrier dysfunction (70). In addition to these data, the examination of whether microbial diversity was restored in the long term as a result of the berberine intervention, optimal dose rates, and dose-dependent personalized microbial responses was not undertaken. To the best of our knowledge, one of the first analyses of the microbiome profiles of functional constipation patients individually and a study using a personalized diet modulation intervention based on the literature was conducted by us. In our study, it was determined that symptoms and quality of life of functional constipation patients were improved through personalized microbiome modulation with dietary intervention based on artificial intelligence-supported fecal microbiome profiling (71). The importance of personalized microbial responses is emphasized by our study, which is the first in the literature to compare the therapeutic effect of an AI-based personalized diet for irritable bowel patients. In our study, machine learning was utilized to identify a personalized diet to modulate the microbiota of an irritable bowel syndrome patient population to a similar "healthy" state. Consequently, it was demonstrated in our study that the score improvement for the personalized diet group was significantly higher than the standard irritable bowel syndrome diet group, highlighting the importance of personalized microbial responses (72). Both high (100 mg/kg) and low (50 mg/kg) doses of Berberine (BBR) administered alleviate atherosclerosis induced by a high-fat diet (HFD) in ApoE-/- and C57BL/6J mouse models, and may impact different components of gut microbiota (73). Therefore, the proposed berberine intervention for the treatment

of complex and multifactorial metabolic and chronic diseases necessitates more detailed studies, the assessment of individual microbial responses, and long-term follow-up studies of microbiome effects.

CONCLUSIONS

The interaction between berberine and the gut microbiota has significant health implications. Our literature review elucidates the multifaceted effects of berberine on the composition and diversity of the gut microbiota, shedding light on its therapeutic potential. Berberine promotes the growth of beneficial bacteria while targeting specific pathogens and exhibiting antimicrobial properties. Studies, particularly in obese or Type 2 Diabetic models, suggest potential benefits in improving gut microbiota and diversity (20, 24, 31, 32, 35, 36). However, the lack of a defined optimal dosage and unassessed individual microbial responses have been linked to the formation of dysbiotic microbiota profiles (15, 38, 57).

It is apparent that berberine may have benefits arising from its interaction with the gut microbiota. Throughout various studies, the variety of the gut microbiota was significantly enhanced by berberine intervention, although some studies observed the opposite. Understanding the impact of berberine on the composition of the gut microbiota will improve the efficacy of this compound in the treatment of metabolic and chronic diseases by elucidating its long-term efficacy, elucidating individual microbiota-dependent responses, and determining optimal dosage.

Further research into the long-term effects, individual microbial responses, optimal dosage rates, and personalized interventions based on microbial profiles will enhance our understanding of berberine's therapeutic role in complex metabolic and chronic diseases. Such research will pave the way for more tailored and effective treatments.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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ANADOLU KLİNİĞİ TIP BİLİMLERİ DERGİSİ YAZIM KURALLARI

1. GENEL BİLGİLER

- Dergilerin, uluslararası standartları göz önüne alarak, bir makalenin hazırlanması sırasında uyulması gereken ilkeleri belirlemeleri ve değerlendirmeye alacakları makalelerde bu kurallara uygunluğu kontrol etmeleri, bilimsel yayıncılık standartlarımızın yükseltilmesi açısından önem taşımaktadır.
- Bilimsel dergilere gönderilecek bir makalenin hazırlığı sırasında uyulması gereken, uluslararası tıp dergilerinin de kabul ettiği ve uyguladığı en önemli standartlar şu şekildedir:
  - Yayımlanmak için gönderilen çalışmaların daha önce başka bir yerde yayımlanmamış veya başka bir yere yayımlanmak üzere gönderilmemiş olması gerekir.
  - Makale daha önce yayımlanmışsa ve(ya) alıntı yazı, tablo, fotoğraf gibi ögeler içeriyorsa evvelki yayın hakkı sahibinden ve(ya) bu ögelerin telif hakkı sahiplerinden yazılı izin alınması ve bunun makalede belirtilmesi gerekir.
  - Bilimsel toplantılarda sunulan yazılar, bu sunumun dipnot olarak belirtilmesi koşuluyla, değerlendirmeye alınır.
  - Türkçe yazılarda Türk Dil Kurumu'nun güncel ve bilimsel sözlüklerinde geçen yazımlar esas alınmalıdır. İngilizce yazılar Amerikan İngilizcesi ile yazılmalıdır.

2. BİLİMSEL SORUMLULUK

- Gönderilen bilimsel yazıda, tüm yazarların akademik–bilimsel olarak doğrudan katkısı olmalıdır.
- Dergi ile iletişim görevini yapan yazar (yazışma yazarı), tüm yazarlar adına yazının son halinin sorumluluğunu taşır.

3. ETİK SORUMLULUK

- "İnsan" ögesi içeren tüm orijinal araştırmalarda Helsinki Bildirgesi prensiplerine uygunluk şarttır. Bu tip araştırmalarda yazarların, yazılarının GEREÇ VE YÖNTEMLER bölümünde, araştırmaları sırasında bu prensiplere uyduklarını ve ayrıca kurumlarının etik kurullarından ve çalışmaya katılmış insanlardan "bilgilendirilmiş onam" (*informed consent*) aldıklarını belirtmeleri gerekmektedir.
- "Hayvan" ögesi içeren orijinal araştırmalarda ise yazarlar, yazılarının GEREÇ VE YÖNTEMLER bölümünde, araştırmaları sırasında *Guide for the Care and Use of Laboratory Animals* prensipleri doğrultusunda hayvan haklarını koruduklarını ve hayvan etik kurullarından onay aldıklarını belirtmelidirler.
- Vaka sunumlarında sunulan kişi ya da kişilerin kimliğinin açığa çıkıp çıkmadığına bakılmaksızın "bilgilendirilmiş onam" (*informed consent*) alınmalıdır.
- Çalışmaları ile ilgili direkt–endirekt bir ticari bağlantıları veya çalışmalarına maddi destek veren bir destekçileri varsa, yazarlar bunları ve bu ilişkilerinin doğasını (konsültan, diğer anlaşmalar) Editöre Sunum sayfasında belirtmelidirler.
- Makalede "etik kurul onayı" alınması gerekli ise; yazarlar, yazılı etik kurul izni / onayı aldıklarını "Gereç ve Yöntemler" bölümünde "……..etik kurulundan …….tarih ve…… sayı ile etik kurul onayı alınmıştır" şeklinde beyan etmelidir. "Sözlü etik onay alınmıştır" ifadesi kullanılmamalıdır.

4. YAYIN/TELİF HAKKI

- Yayımlanmak üzere kabul edilen yazıların her türlü yayın/telif hakları dergimize aittir. Yazılardaki düşünce ve öneriler tümüyle yazarların sorumluluğundadır.

5. YAZI TÜRLERİNE GÖRE YAZIM KURALLARI

- Derginin yayın dili Türkçe ve İngilizcedir.
- Her tür bilimsel yazı için, *Word* dosyası halinde ayrı ayrı "Editöre Sunum Sayfası" ve "Kapak Sayfası" hazırlanmalı ve dergiye başvuru esnasında ayrı birer dosya halinde gönderilmelidir. Dergimiz İnternet sitesinden "Editore Sunum Sayfası" ve "Kapak Sayfası"na dair örnek şablonlar indirilebilir. Yazım dili Türkçe olan yazılar için sadece Türkçe şablonun, yazım dili İngilizce olan yazılar için ise sadece İngilizce şablonun doldurulup gönderilmesi yeterlidir.
- Her makale için yazarlar "TELİF HAKKI DEVİR FORMU" nu, bilimsel yazılarını dergiye başvuru esnasında doldurup imzalayarak, yazıları ile birlikte dergiye göndermelidirler. Türkçe ve İngilizce form İnternet sayfamızdan indirilebilir. Yazım dili Türkçe olan yazılar için sadece Türkçe formun, yazım dili İngilizce olan yazılar için ise sadece İngilizce formun doldurulup gönderilmesi yeterlidir.
- Bilimsel yazı kabul edildikten sonra baskı öncesi kopyanın her sayfasının ve Telif Hakkı Devir Formu'nun tüm yazarlar tarafından ıslak imza ile imzalanması ve tüm bu evrakın BETİM Hasekisultan Mah., Topçu Emin Bey Çıkmazı, no. 4, 34096 İstanbul adresine posta yoluyla gönderilmesi gerekmektedir (tel. 0212 632 0369; faks 0212 632 0328). İlk başvuruda bunların elektronik olarak yüklenmesi yeterlidir.
- Dergilere yayımlanmak üzere gönderilecek yazıların türlerine göre yazım kuralları aşağıda tanımlanmıştır.

5.1. ORİJİNAL ARAŞTIRMA MAKALESİ

- Yazılar *Microsoft Word*® belgesi olarak hazırlanmalı ve 1,5 aralıklı, 12 punto, iki yana yaslı ve *Times New Roman* karakteri kullanılarak yazılmalıdır. Sayfa kenarlarında 2,5 cm boşluk bırakılmalı ve sayfa numaraları sayfanın sağ üst köşesine yerleştirilmelidir.
- Kör hakemlik ilkesi gereğince, "Editöre Sunum Sayfası" ve "Kapak Sayfası" sisteme ayrı birer dosya halinde yüklenmelidir. Editöre sunum sayfasında olması gereken bilgiler, yazının türü, daha önce başka bir dergiye gönderilmemiş olduğu ve varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve bu özel ve tüzel kişilerin yazarlarla olan ilişkileri belirtilmelidir. Kapak sayfasında ise Türkçe ve İngilizce olarak alt alta olacak şekilde yazının uzun başlığı ve 40 karakteri geçmeyen kısa başlığı, yazar bilgileri ve sorumlu yazar bilgileri ve önerilen hakem bilgileri yer alır. İnternet sitemizdeki örnek şablonlarda bu bilgilerin nerede ve nasıl verileceğine dair yönlendirmeler mevcuttur. Yazarlara, izin alınan etik kurullara ve kurumlara ait bilgiler yazının ana metninde yer almamalıdır. GEREÇ VE YÖNTEMLER bölümünde bu ibareler XXXXXXX şeklinde yazılmalıdır.
- Yazıya ait ana metnin ilk sayfasında çalışmanın uzun başlığı Türkçe ve İngilizce olarak yer almalı, başlık büyük harflerle yazılmalı ve sayfanın geri kalan kısmı boş bırakılmalıdır. Başlıkta kısaltma kullanılmamalıdır.
- Daha sonra önce "ÖZ" (çalışmanın yazım dili İngilizce ise *ABSTRACT*) bölümü yazılmalıdır. Bu bölüm en fazla 300 kelimeden oluşmalıdır. Türkçe ve İngilizce yazılmalıdır. Bu sayfa da ayrı bir sayfa olmalı ve anahtar sözcüklerden başka yazı bölümü içermemelidir.
- Yazının ana metni Türkçe ise önce ilk sayfaya Türkçe ÖZ, ikinci sayfaya İngilizce *ABSTRACT* yazılmalıdır. Yazının ana metni İngilizce ise önce ilk sayfaya İngilizce *ABSTRACT*, ikinci sayfaya Türkçe ÖZ yazılmalıdır.
- ÖZ veya *ABSTRACT* yapılandırılmış olmalıdır. Yapılandırılmış ÖZ (*ABSTRACT*) bölümünde

- "Amaç (*Aim*),"
- "Gereç ve Yöntemler (*Materials and Methods*),"
- "Bulgular (*Results*),"
- "Tartışma ve Sonuç (*Discussion and Conclusion*)"

olmak üzere dört alt başlık yer almalıdır. ÖZ'de paragraflar içeriden başlamamalıdır.

- Türkçe ve İngilizce özetin sonunda yer alacak olan anahtar sözcüklerin sayısı en az iki, en fazla altı olmalıdır. Bunlar birbirinden noktalı virgül (;) ile ayrılmalı ve alfabetik sıraya göre sıralanmalıdır. Örneğin: **Anahtar Sözcükler:** insan denekler; klinik araştırmalar; kontrollü deney; randomize kontrollü deney. İngilizce anahtar sözcükler *Medical Subject Headings* (*MeSH*) doğrultusunda verilmelidir. Anahtar sözcük seçimi için, izleyen bağlantı tıklanarak açılan sayfada, ilgili konuya dair uygun sözcük girilerek anahtar sözcüklere ulaşılabilir: www.nlm.nih.gov/mesh/MBrowser.html. Türkçe anahtar sözcükler Türkiye Bilim Terimleri (TBT) doğrultusunda verilmelidir: www.bilimterimleri.com.
- ÖZ ve *ABSTRACT* bölümlerinden sonra ana metne yeni bir sayfada GİRİŞ bölümü ile başlanmalıdır. Yazıda GİRİŞ, GEREÇ VE YÖNTEMLER, BULGULAR, TARTIŞMA VE SONUÇ, gerekli ise TEŞEKKÜR ve KAYNAKLAR ana bölümleri yer almalıdır. Ana bölümlerin başlığı büyük harflerle ve **kalın** olarak yazılmalıdır. Ana başlıklar sola yaslı olmalıdır.
- GİRİŞ bölümünün son paragrafı çalışmanın amacını açıklamalıdır.
- Kaynaklar, ilgili cümlenin sonunda parantez içinde numaralarla, metin içinde geçtiği sıraya göre verilmelidir. Örneğin; …… (1). veya …… (1,2). veya …… (3–5).
- Ana metinde paragraflar *Word* programında yer alan cetvel yardımıyla 1 cm içeriden başlamalıdır.
- Yazıda yer alan tüm alt başlıkların sadece ilk harfi büyük olmalıdır. Yalnızca alt bölümler içindeki alt bölümlerin (alt-alt bölümlerin) başlıkları *italik* yazılmalıdır.
- GEREÇ VE YÖNTEMLER bölümü ile BULGULAR bölümünde verilmesi düşünülen Tablo ve Görsel yazılarının ilk harfi büyük olmalı ve **kalın** yazılmalıdır. Örneğin **Tablo 1., Görsel 1.** Tablo yazıları ilgili tablonun üzerinde, görsel yazıları ise ilgili görselin altında yer almalıdır.
- Tablo ve şekiller metin içerisinde nerede geçiyor ise o bölümde ilgili cümlenin sonuna parantez içinde **Tablo 1.** veya **Görsel 1.** gibi yazılmalı, ancak ilgili tablo ve görseller başlıklarıyla birlikte kaynaklardan sonra ve her biri bir sayfada olacak şekilde ayrı ayrı verilmelidir. Görsel ve tablo üzerinde kısaltma ve/veya sembol kullanılmış ise tablo/görsel altında 8 punto ile yazılarak açıklanmalıdır.
- Görseller (örneğin fotoğraflar) metne eklenmemeli, ayrı bir dosya olarak (görüntü kalitesi 300 dpi olacak şekilde ve .jpeg, .bmp, .tif vb. formatta) sisteme yüklenmelidir. Görsel alt yazıları, son tablonun olduğu sayfadan hemen sonra, ayrı bir sayfada sırasıyla, ilk harfleri büyük olacak biçimde (**Görsel 1.** Açıklayıcı metin) yazılmalıdır.
- Daha önce basılmış görsel, tablo ve grafik kullanılmış ise yazılı izin alınmalı ve bu izin açıklama olarak görsel, tablo ve grafik açıklamasında parantez içinde belirtilmelidir.
- Çalışmada veri analizi yapılmış ise GEREÇ VE YÖNTEMLER bölümünün son alt başlığı olarak "İstatistiksel analiz" başlığı tanımlanmalı ve bu bölümde hangi amaç için hangi istatistiksel yöntemlerin kullanıldığı ve ilgili paket programlar yazılmalıdır.
- BULGULAR bölümünde yöntem adları verilmemelidir.
- Çalışmada TEŞEKKÜR bölümü gerekli ise bu bölümde, çıkar çatışması, finansal destek, bağış ve diğer bütün editöryal (İngilizce/Türkçe değerlendirme) ve/veya teknik yardım belirtilmelidir.
- KAYNAKLAR bölümü aşağıda belirtilen kurallara uygun olarak yazılmalıdır.

5.2. DERLEME TÜRÜ YAZILAR

Orijinal araştırma yazıları için yukarıda tanımlanan yazım kuralları derleme türü yazılar için de geçerlidir. Sadece aşağıda tanımlanan birkaç maddede değişiklikler söz konusudur:

- Derleme türü yazılarda ana başlıklarda değişiklikler yapılabilir.
- Derleme türü yazılarda ÖZ en fazla 250 kelimeden oluşmalıdır.

5.3. VAKA SUNUMU / VAKA SERİLERİ VE DİĞER TÜRDEN YAZILAR

Orijinal araştırma yazıları için yukarıda tanımlanan yazım kuralları vaka sunumu veya vaka serileri türünde hazırlanan yazılar için de geçerlidir. Sadece aşağıda tanımlanan birkaç maddede değişiklikler söz konusudur:

- Vaka sunumu türündeki yazılarda ana başlıklarda değişiklikler yapılabilir.
- Derleme türü yazılarda ÖZ en fazla 150 kelimeden oluşmalıdır.
- Bu tür yazılarda kaynak sayısı 15'i aşmamalıdır.

Bu üç ana yazı türünden başka;

- Editöryel Yorum/Tartışma türünde (yayımlanan orijinal araştırma makalelerinin, araştırmanın yazarları dışında konunun uzmanı tarafından değerlendirilmesi) veya
- Editöre Mektup türünde (son bir yıl içinde dergide yayımlanan makaleler ile ilgili okuyucuların değişik görüş, tecrübe ve sorularını içeren, en fazla 500 kelimeden oluşan yazı türü) yazılar da gönderilebilir. Bu yazıların hazırlanmasında da genel yazım kuralları geçerlidir. Bu yazı türlerinde,
  - Başlık ve özet bölümleri yoktur.
  - Kaynak sayısı beş ile sınırlıdır.
  - Sayı ve tarih verilerek hangi makaleye atıf yapıldığı belirtilmeli ve sonunda yazarın ismi, kurumu ve adresi bulunmalıdır. Mektuba cevap, editör veya makalenin yazar(lar)ı tarafından, yine dergide yayımlanarak verilir.

KAYNAK YAZIM KURALLARI

- Dergilerin atıf sayılarının sağlıklı olarak tespit edilebilmesi, kaynakların düzgün yazılmasıyla doğrudan ilişkilidir. Dergimizde Vancouver kaynak yazım stilinin bir varyantı kullanılmaktadır.
- Dergiye başvuru sırasında kaynakların ayrıştırılması, atıflar açısından büyük önem taşımaktadır. Bu ayrıştırmanın sağlıklı bir şekilde yapılabilmesi için kaynakların Vancouver kaynak yazım stiline göre yazılması büyük önem arzetmektedir. Dergimiz kaynak yazım kuralları, kaynak yazının türüne göre aşağıda tanımlanmıştır.

Dergi Makaleleri İçin Yazım Kuralları

[Her yazar için] yazarın soyadı, yazarın adının baş harf[ler]i. Makalenin başlığı [yalnızca ilk kelimenin ilk harfi büyük, geri kalanlar özel isim değilse küçük olarak]. Derginin adı [italik, kısaltılmış ve her harf öbeğinin ilk harfi büyük olarak]. Yıl;cilt(sayı):başlangıç sayfa numarası–bitiş sf. no. [mükerrer rakamlar çıkarılmış olarak].

Örnek:
Abaraogu UO, Tabansi-Ochuogu CS. As acupressure decreases pain, acupuncture may improve some aspects of quality of life for women with primary dysmenorrhea: a systematic review with meta-analist. J Acupunct Meridian Stud. 2015;8(5):220–8.

Kitaplar İçin Yazım Kuralları
[Her yazar için] yazarın soyadı, yazarın adının baş harf[ler]i. Kitabın Adı [bağlaç, soru eki vb. hariç, tüm sözcüklerin ilk harfleri büyük olarak], [varsa] ed. [her editör için] editörün soyadı, editörün adının baş harf[ler]i, [ya da varsa] çev. çevirmenin soyadı, çevirmenin adının baş harf[ler]i, X. ed. [ilk edisyon/baskı değilse X. edisyon/baskı olduğu bilgisi]. Yayınevinin kenti: Yayınevinin ismi; yayımlanma tarihi:göstermek istenirse kaynak gösterilen sayfa[lar].

Örnek:
Ankaralı H, Cangür Ş, Sungur MA. Formülsüz Biyoistatistik. İstanbul: BETİM; 2015.

Beauchamp TL, Childress JF. Biyomedikal Etik Prensipleri, çev. Temel MK, 7. ed. İstanbul: BETİM: 2017:263.

Kitaplar Bölümleri İçin Yazım Kuralları
[Her yazar için] yazarın soyadı, yazarın adının baş harf[ler]i. Kitabın bölümünün adı [yalnızca ilk kelimenin ilk harfi büyük, geri kalanlar özel isim değilse küçük olarak]. In: [varsa, her editör için] editörün soyadı, editörün adının baş harf[ler]i, (ed.), [ya da varsa] çevirmenin soyadı, çevirmenin adının baş harf[ler]i (çev.), Kitabın Adı [tüm esas sözcüklerin ilk harfleri büyük olarak], X. ed. [ilk edisyon/baskı değilse X. edisyon/baskı olduğu bilgisi]. Yayınevinin kenti: Yayınevinin ismi; yayımlanma tarihi:bölümün başladığı–bittiği sayfa.

Örnek:
Beauchamp TL, Childress JF. Özerkliğe saygı. In: Temel MK (çev.), Biyomedikal Etik Prensipleri, 7. ed. İstanbul: BETİM: 2017:153–226.

İnternet Kaynakları İçin Yazım Kuralları
İnternet girisini giren kişinin soyadı, adının baş harf[ler]i, ya da, kurumun tam ve açık adı (varsa giri tarihi). Giri başlığı [özel isim olmadığı sürece sadece ilk kelimenin ilk harfi büyük olarak]. Erişim: adresi (erişildi: son erişildiği tarih).

Örnek:
T.C. Resmî Gazete (29.6.2019). Eczacılar ve Eczaneler Hakkında Yönetmelikte Değişiklik Yapılmasına Dair Yönetmelik. Erişim: www.resmigazete.gov.tr/eskiler/2019/06/20190629-8.htm (erişildi: 12.9.2020).

Türk Dil Kurumu. Kesme işareti (’). Erişim: www.tdk.gov.tr/icerik/yazim-kurallari/kesme-isareti (erişildi: 8.8.2020).

Yayımlanmamış Yüksek Lisans/Doktora Tezleri İçin Yazım Kuralları
Yazarın soyadı, yazarın adının baş harf[ler]i. Tezin adı [kitap adı gibi yazılmış şekilde] (yayımlanmamış yüksek lisans/doktora tezi). Yükseköğretim kurumunun kenti: kurumun ismi: yıl [kitapların yayımlandığı yer, yayınevi ve tarih bilgileri gibi].

Örnek:
Barış M. Down Sendromu Bağlamında Seçici Kürtaj Hakkındaki Etik Argümanların Normatif Analizi (yayımlanmamış yüksek lisans tezi). İstanbul: T.C. İstanbul Üniversitesi, İstanbul Tıp Fakültesi, Tıp Tarihi ve Etik Anabilim Dalı; 2017.

6. GENEL AÇIKLAMALAR

Medical Subject Headings (MeSH) nedir?
- Uluslararası başlıca makale tarama dizinleri ve veri tabanlarında, makalelerin sınıflandırılması için kullanılmakta olan, tıbbi–biyolojik terminolojiye standart getirmeyi amaçlayan ve sürekli güncellenen, İngilizce makalelerin anahtar sözcüklerinin seçilebileceği, geniş bir tıbbi–biyolojik terimler dizinidir.

Türkiye Bilim Terimleri (TBT) nedir?
Ulusal düzeyde tıbbi–biyolojik terminolojiye standart getirmeyi amaçlayan, şimdilik 186.000 tıbbi–biyolojik terim içeren ve sürekli güncellenen, Türkçe makalelerin anahtar sözcüklerinin seçilebileceği tıbbi–biyolojik terimler dizinidir.

Anahtar Sözcükler Neden *MeSH* ya da TBT Arasından Seçilmelidir?
- *MeSH* ve TBT terimleri, ana başlıklar ve alt başlıklardan oluşan, birbiri ile ilişkilendirilmiş hiyerarşik bir yapı ile kodlanmışlardır.
- Böylece tek bir terim ile yapılan aramada, ana başlıklar yanında terimin ilişkilendirildiği tüm alt başlıklar da otomatik olarak aramaya dahil edilir.
- Aynı terim, birden çok terminoloji ile tanımlanmış olduğundan, araştırmacının az veriyle, kolay ve hızlı bir şekilde mümkün olduğunca çok makaleye ulaşabilmesini sağlar.

KISALTMA VE AKRONİMLER
Kısaltılacak sözcüğün ya da sözcük öbeğinin ilk geçtiği yerde parantez içinde verilmelidirler. Aynı sözcük(ler) için tüm metin boyunca aynı kısaltma/akronim kullanılmalıdır. Uluslararası kullanılan kısaltmalar için “Bilimsel Yazım Kuralları” (*Scientific Style and Format: the CBE Manual for Authors, Editors, and Publishers)* kaynağına başvurulabilir.

7. YAZININ GÖNDERİM AŞAMASINDA DİKKAT EDİLECEK NOKTALAR

- Sorumlu yazar, “TELİF HAKKI DEVİR FORMU”nu doldurup, çalışma ile birlikte dergiye göndermelidir.
- Yazarlar, makaleyi değerlendirmek üzere potansiyel iki hakemin ismini ve güncel iletişim bilgilerini (e-posta, telefon, faks) Editöre Sunum sayfasında bildirmelidirler. Bununla birlikte editörlerin hakemleri bizzat seçme hakkı mahfuzdur.
- Gönderiler, yazılar TÜBİTAK ULAKBİM DergiPark sistemine (http://dergipark.gov.tr/anadoluklin) yüklenerek gerçekleştirilmelidir.
- Gönderi sırasında Editöre Sunum sayfası, kapak sayfası, yazının ana metni, Telif Hakkı Devir Formu ve varsa görseller ayrı dosyalar halinde yüklenmelidir.
- Yazarlar İnternet sitemizdeki hakem değerlendirme formlarını inceleyerek hakemlerin incelediği konulara özellikle dikkat ederlerse yazımdaki eksikliklerini hakem sürecinden dönmeden gidermiş olurlar. Yine de hakemler her türlü eleştiriyi yapma hakkına sahiptir.

S. 10 ANADOLU KLİNİĞİ, Haziran 1935 Yıl 3 : No. 1

Bu günün canlı mevzuları üzerinde

MÜCMEL YAZILAR.

Asrî bir çocuk hastanesinin vazifeleri.

Prof. Dr. İhsan Hilmi Alantar
İstanbul.

Şimdiki çocuk hastahanelerinin artık yalnız hastaları kabul ve tedaviden başka vazifeleri de vardır; bu vazifeler, bilhassa hastalığın sirayetine mani olmak, yani o hastalığı başka hastalara geçirmiyecek tedbirlere riayet etmektir; memleketin esenliği noktayi nazarından bu işin ne kadar mühim olduğunu ise uzun uzadıya anlatmak istemez.

Orta çağda, çocuklara ait hastaneler yoktu; hatta onlar için hususi koğuşlar bile yoktu; o zamanlarda her hangi bir büyük adamlar koğuşuna bir çocuk hastası alındığı zaman oldukça düşünülür, eğer o çocuğun hastalığı yüz güldürecek gibi değilde içinden çıkılmayacak ciddî bir hastalıksa o hasta çocuk istemiye istemiye içeriye alınır ve kısa bir müddet sonra da taburcu edilirdi; yani hasta kabulünde bir nevi seçme «*triage*» yapılmakta idi.

Zaman geçtikçe bu yanlış fikirler değiştirildi: çocuklara mahsus koğuşlar açıldı; fakat kabul edilen çocuklar iç hastalığı hekiminin nezareti altında ve en genç bir asistan ve en işe yaramaz bir hademe ceza kabilinden olarak, hasta bakıcı vazifesile çocuk koğuşuna verilirdi; yani bu suretle çocuk koğuşları üvey evlat muamelesi görürlerdi.

Son 50 — 60 senenin ilmî ilerlemeleridir ki bu noksanı bertaraf etmiş; yavaş yavaş çocuklara mahsus teşekküller de baş göstermiştir; bu arada evvelâ çocuk paviyonları ve sonra cocuk hastaneleri teşekkül etti; süt çocuklarına mahsus muayene yerleri, dispanserler, kreşler, irzahaneler..... gibi bir çok isimlerle anılan muhtelif tesisat meydana geldi ve bu gibi teşkilâtın çocuk korumasında mühim yeri olduğu gün geçtikçe daha iyi anlaşılmağa başlandı.

Zaten bütün Avrupa statistikleri bunu müeyyiddir; işte çocuk hastaneleri de bu terakkilerin bir örneğidir.

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Çocuk hastanelerine rağbet içten ve dıştan bir çok zorluklarla sarılmıştır; dış zorluklar arasında halkın hastaneye karşı olan itimadı mes'elesi mevzuubahistir; yanlış olarak bir çok yerlerde bu itimat elân teşekkül edememiştir ve bundan dolayı bir çok yerlerde halkın çocuk hastanelerine rağbeti yani hasta olan çocuklarından ayrılarak onları kendi evlerinden daha iyi bakılan bir müesseseye bırakmaları müşkül ve hatta muhal bir halde bulunmaktadır; bu ananeye uyuş; çocuk ne kadar körpe ise o kadarda köklüdür; buna sebep halkın yanlış itikadıdır: bu itiyadı, bu kötü fikri yerinden sarsacak tedbirlere tevessül edilmektedir; hakikaten bazı memleketlerde halk pek müztar bir hale gelmedikce meselâ çocuğu «granulie»gibi, «meningite tuberculeuse» gibi «croup» gibi, ağır bir kızıl gibi pek ciddi bir hastalığa yakalanmadıkca yani daha doğrusu ebeveyne çocuğu artık elinden çıkaracağı kanaati gelmedikçe hastaneye müracaat etmiyor ve netice olarak acınacak vak'alar meydana geliyor; işe evvelâ evden, komşulardan, hekim gibi geçinenlerin tedavi (?) lerinden başlıyarak pek geç olarak hekime ve ancak bunlardan sonra hastaneye gelen anne, çocuğun şifasını ancak o zeman hastaneden umuyor ve bu gecikmeden dolayı da ekseriya bu beklediği şifa, çok acıdır, husul bulamıyor; bu uzun yolu tahdit etmek yani hasta bir çocuk karşısında hastanenin yolunu kısaltmak ancak ebeveyin nezdinde müessir olmak sayesinde olacâktır; bazı yerlerde açılan dispanserlere, çocuk bakım yerlerine ve hastane polikliniklerine devam eden anneler hastaneye geliş yolunu kısaltmışlardır; fakat buralara uğramayan anneler elân hastalanan çocukları karşısında yukarıda saydığımız uzun kanallardan geçtikten ve tedavi için pek kıymettar olan zamanın kaybolmasına sebeb olduktan sonra ancak ve pek geç olarak hastane kapısını çalmaktadırlar. İşte bu itiyadı söküp atmak birinci vazifedir; bu fikrin sökülmesi bizim memlekette pek kolay olmuştur; çünkü bu hususta devlet sistemimiz hastanelerin fakirlere — hiç bir memlekette misli olmayacak surette — parasız olarak açık bulunmasını âmirdir; o halde memleketimizin çocukları mevzuubahis olduğu zaman ebeveyin hiç bir ekonomik zorluk karşısında kalmadan hasta bulunan çocuklarını hemen ve kolayca hastaneye kabul ettirmek imkânını bulmaktadırlar; o halde, eğer ihmal yoksa, hasta çocukların hastaneye hemen gelmelerinde hiç bir zorluk yoktur demektir neticesine varılır.

Bundan başka hastanelere hasta çocuklarla beraber annelerin de yatırılması hasta çocuğun hastalığı esnasında da annesinden ayrılmamasını mucip olur ve bu ise, gerek besleme —meme verme— ve gerek bakım noktai nazarından yazılmaya değer bir muvaffakiyettir. Yalnız hastaneye kabul edilenler için değil,, polikliniğe müracaat edenlerin bile hemen o gün aynı zamanda klinik muayenesinden başka eğer lâzım geliyorsa, şuaî ve kimyevî, hikemi teşhis vasıtalarından istifade edebilmesi imkân altındadır ve bu meyanda bir çok tedavi vasıtaları da halkın istifadesine vaz edilmiştir; bütün bu tesisatı cami

olan çocuk hastaneleri halkın yanlış itikatlarını kökünden silecek bir kudrettedir.

Çocuk hastanelerinin bir tekemmül ciheti de çocukların yaşları küçüldükçe onlara bakacak kimselerin artması noktai nazarındandır; büyücek çocuklara (8 — 12 yaşlarında) mahsus olan koğuşlarda her altı çocuğa bir hasta bakıcı kâfi gelebildiği halde bahusus ilk yaşlarda bulunan çocuklarda sütçocuklarında, her dört hastaya bir bakıcı iktiza eder; çünkü sütçocuğu koğuşlarında 24 saatte her çocuğa vasati olarak 5 defa yemek yedirmek ve 5 defada da altlarını temizlemek dolayısile beher yemek için 15 ve alt değişdirmek için de 5 dakika olarak her çocuğa bir saat 45 dakika zaman ister; bundan başka ilâç içirmek yemek hazırlamak, ve saire gibi daha bir çok vazifeler de vardır; bütün bunları hakkile yapabilmek için bir çocuğa günde en az 2 saat vakit gerektir o halde 12 çocuklu bir hasta koğuşu için çalışma saati 24 saat eder, bu 24 saat iş de ancak 3 hasta bakıcıdan beklenir.

Koğuş binasının işlerini hastabakıcıdan ziyade her hastanede bulunması lâzımgelen hizmetci görür; zaten her yerde hastabakıcı ile hizmetci ayrı ayrı vazifeler deruhde etmiş birer şahsiyettir; biri diğerinin vazifesine karışmaz; biri yalnız hasta ile onun beslenmesi ve tedavisi ile meşgul olduğu halde diğeri yani hizmetçi, ev, müessese, otel, pansiyon ve saire hizmetcileri gibi binanın temizliği ile mükelleftirler.

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Çocuk hastanelerinde büyük bir tehlike hôpitalisme dir. Bu her hangi bir hasta çocuğun hastane içinde başka bir hastalık daha kapabilmesi demektir; bu hal orta çağda ve orta çağa yakışan hastanelerde görülürdü; meselâ: bir çocuk kendi hastalığını savabildiği halde hastanede yakaladığı başka bir hastalıktan ölebilirdi; bu hale çare bulabilmek için son 20 — 30 yılların çocuk hastanelerinde bu gibi intanların sebebini bulmak ve onları men etmek ve onları men etmek düşünülmüştür; bunun için de çocuk hastanelerinde hıfzıssıhhat kaideleri çok sıkı olarak tatbik edilmiştir; çocuk hastanelerinde *cas interne* lere mani olabilmek için oraların temiz olması ihtimamın son derecede yolunda bulunmasından başka hususî bir takım tesisatda lâzımdır; işte bu tesisat box'lardır.

Bu box'lar, hepimizin bildiği gibi, bir kaç kısımdır; Grancher box'ları âdi birer paravanadan ibarettir; üç tarafları kapalı ve kapı tarafları açık bir takım box'ları da - yarım box - bu meyanda zikredebiliriz; bu gibi box'lar ancak sütçocukları salonlarında istimal edilebilir; umumiyetle sütçocukları salonu bu suretle onların birer birer tecrit edilebilmeleri esasına müpteni olmalıdır; burada yatan süt çocuklarının sâri bir hastalığı olmasa bile oraya hiçbir intanın girmemesi ve girse bile hemen bir yere münhasır ve mahdut kalabilmesini temin etmek için bu gibi yarım box'lar pek münasiptir.

Sâri hastalıklar için Hutinel veya Pasteur box'ları kullanılmalıdır; Hutinel box'ları yalnız tavan tarafları açık kalmış, dört tarafı kapalı boxlardır, cidarlar zeminden 2 metreye kadar yüksektir; burada sirayeti pek fazla olmayan hastalıklar (kızamık, boğmaca, çiçek, suçiçeği, veba, kolera, ruam müstesnadır) tedavi altına alınır; her box'a girip çıkarken ayrı gömlekler giyilir ve eller antiseptik bir mahlülle yıkanır.

Yukarıda sayılan hastalıklar için mutlaka ya ayrı bir pavion, veyahut bu kadar vasi bir teşkilât yoksa ayrı ayrı hücreler, odalar (Pasteur box'ları) lâzımdır; işte bu gibi tekayyüdatı şamil olan bir çocuk hastanesinde artık hôpitalisme meselesi yok demektir.

Görülüyor ki: bir çocuk hastanesi büyük adamlar hastanelerine nisbetle ne kadar çok hususî teşkilâtı havi olmak lâzımdır; yoksa bu gibi tesisatı havi olmayan alelâde bir çocuk hastanesi kendine terettüp eden vazifeleri görmekten pek uzak kalmış olur; oraya nezle ile giren bir çocuk ya bir bronkopnömoni den yahut herhangi bir umumî infection dan ölür; o halde, orta çağ geri gelmiş demektir; o çağın hastanelerinin kapısı üzerine (burada hükûmet hesabına çocuklar öldürülür) diye bir lavha konabilirdi.

Şimdiki çocuk hastaneleri birer şifa müesseseleridir; oralara herhangi bir hastalıktan girenler hôpitalisme'in zararlarına uğramıyacaklarına ve kendi hastalıklarının da er geç tamamen şifa bulacağına inanmalıdırlar.

Hôpitalisme'e mani olacak tedbirlerin başlıcası ne yalnız box'lardır ve ne de yalnız bu kadar fedakârlıkla yapılan tesisattır; buna mani olmak için en birinci sebep hastabakıcıların da öğrenmiş olmasıdır; hastabakıcılar, bulaşmanın ne demek olduğunu bilmezlerse ne kadar mükemmel tesis edilmiş olursa olsun öyle hastanelerde «*cas interne*» çıkmamasını beklemek abestir.

Çocuk hastanelerinde besleme meselesi de çok mühimdir, tabii çocuğun beslenmesi bile pek mühim telâkki edilen bu devrede hasta çocukların ve bu meyanda sıskalık, hypoplasie, toxicose, dizanteri şeklinde ishaller; rahitis, tétanie, anemiler ve saire gibi hastalıklarla mâlûl olan sütçocuklarının beslenme bahsinin ne kadar mühim olacağı nazarı dikkate alınmalıdır, bunun için çocuk hastanelerinde sütçocuklarına mahsus olan paviyonlarda birer süt mutbahının bulunması da lâzımdır; sütçocuklarının muhtelif gıdaları bu süt mutbahında, bilen, işi kavramış olan bir hemşire, bir hastabakıcı tarafından hazırlanır ve gıda temiz kaplara, şişelere konur buz dolabında saklanır her çocuğun baş ucunda çocuğun muhtelif saatlerde ne gibi mütenevvi gıdalar alacağı hekim tarafından yazılmıştır; bu cetvellere göre hazırlanmış olan yiyeceklere etiketleri ve kimlere mahsus olduğu yazılır ve bu suretle hasta çocukların yiyecekleri yekdiğerile karıştırılmamış olur; ha-

zırlanan yiyeceklerin temiz kalması ve bozulmaması için 24 saatta sarfedilmeleri lâzımdır.

Yeri, yapısı ve tesisatı, işlemesi yolunda olan bir çocuk hastanesinin rağbetsizliğe uğraması kabil değildir; netekim İstanbulun iyi havalı ve yüksek bir yerinde, güzel bir çam ormanı içinde yapılmış, bir çok paviyonlardan mürekkep olan Şişli çocuk hastanesi yalnız tesisat noktai nazarından değil, işleme noktasından da saydığımız iyilikleri câmidir; bu hastane hergün yüzlerce hastaya ayakta bakar, ayakta bakılanlarda bile lâzım olan teşhis ve tedavi vasıtalarına ait aramalar ve tedbirler hemen o gün yapılır, bu yapılanlar laboratuvar ve röntgen taharriyatı, ultra - violet, elektrik, diyatermi, küçük cerrahiye ait ameliyeler, kulak, boğaz, burun, göz ameliyeleri, birçok zerkler... ilâh gibi pek türlü türlüdür.

Bu suretle derdinin teşhis ve tedavi edildiğini ve birçok kezler hemen aynı gün derdinden kurtuluverdiğini de gören hastanın o müesseseye bağlanmaması kabilmidir? İşte bu bağlanış umumî sağlık ve esenlik noktasından kazanılmış bir sermayedir.

Biz, öyle çocuklar tanıyoruz ki doğduğundanberi oraya getirilmiş ve şimdi mektep yaşlarına gelmişlerdir. Bu gibi çocuklar fişlerinden de anlaşılacağı üzere polikliniğe muntazaman gelmişler ve halen de gelmekte bulunmuşlardır; işte bu hal, polikliniklerin gelip geçmeğe mahsus bir han kapısı olmaktan ziyade daimî rabıtayı temadi ettiren birer sıhhat yuvası olduğunu göstermeğe yeter; böyle olmasına sebep ise, çocuk hastanelerinin terakki ve tekemmülü kendilerine şiar edinmiş olmalarıdır; nizamsız işleyen bir yere rağbet olmaz.

Çocuk hastanelerinin bir vazifesi de bu hizmeti haricede teşmil edecek bir mahiyet alışı ve bu suretle de halkın rabıtasının bir kat daha artmasının teminidir; bu teşmil polikliniğe ve kliniğe müracaat eden hasta çocukların tedavisini hariçte, evlerinde de temadi ettirebilmektir: bir çocuğun klinikte uzun zaman yatması o hastanenin merbut olduğu makamca (hükûmet, belediye, idarei hususiye) oldukça masrafı muciptir; o çocuğun evde tedavi altına alınabilmesi ise çok ucuzdur; zaten bir çok ebeveyin çocuğu evinde alıkoymak, onu hastaneye vermemek, ana kucağından ayırmamak ister ve bunda bir dereceye kadar da hakkı vardır; işte bu gibi bazı hasta çocukların evde tedavisi hem masraf cihetinden ve hem de ebeveynin isteği cihetinden uygun bir hal olacaktır; ebeveynin evde kalan bir çocuğun tedavisini yaptıramadıkları her gün görülmektedir; buna sebep ekseriya kendilerinin ekonomik vaziyetleridir; çocuklarını ancak besleyebilen ebeveynin onlar hasta düştükleri zaman hekime koşmamalarının çocuk morbidité ve mortalité'si noktayı nazarından çok mühim bir yeri vardır; hastaneye kadar gelebilmek için belki çocuğun sıhhî hali müsait değildir; bu halde bir defa bize kadar gelebilmiş olan o çocuğun tedavisini evinde ikmal edebilmek bilhassa hertürlü vesaiti mükemmel olan çocuk hastanelerine düşen birvazife olmalıdır. Her ne kadar çocuk bakım evleri, dispanserler de bu işi deruhte etmişlerse de bunlar henuz bir çekirdek halinde bulunduklarından dolayı bu gibi soysal teşkilâtı daha iyi kavrayabilecek derecede bulunan hastanelerin de bu işe ehemmiyet vermeleri gerektir; bu gibi soysal yardım teşkilâtı hiç olmazsa bakım evleri ve dispanserlerle hastanelerin birleşik vazife görmelerini istilzam edeceği için de mühimdir.

Çocuk hastanelerinin bir vazifesi de muhitine istifade verici olmasıdır; meselâ civarda bulunan ebeveyne çocuk bakımına dair konferanslar vermek, çocuk ihtimamına dair projeksionlar, hatta filmler göstermek muhit için istifadeli olduğu gibi hastane için de materiel bulmak, halkın rabıta ve muhabbetini arttırmak noktai nazarından ehemmiyetlidir. Bununla beraber çocuk hastanesinde bir çocuk müzesi de bulunmalıdır; burası yalnız ana ve baba için değil, ana ve baba olacaklar için de faydalıdır; konferanslar burada ameli olarak verilir.

Artık sıhhî müesseselerin vazifesi hasta bakımı ve tedavisi diye bir tek değil, bunlarla beraber irşat, rabıtayı arttırma, sevgi kazanma, cehaleti azaltma gibi soysaldır da... işte bütün bunların ihtisas gözü ile tamamlandırılması iledir ki modern bir çocuk hastanesi kendisinden beklenen bütün vazifeleri görmüş olur.