e-ISSN: 2687-2781

akdeniz tıp dergisi
akdeniz medical journal

Akdeniz Üniversitesi Tıp Fakültesi Yayım Organıdır / Official Journal of Akdeniz University Medical School

Cilt / Volume : 9, Sayı / Number : 3, Eylül / September 2023

https://dergipark.org.tr/tr/pub/akd

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Akdeniz Tıp Dergisi (Akd Tıp Derg) / Akdeniz Medical Journal (Akd Med J)

Akdeniz Üniversitesi Tıp Fakültesi'nin Hakemli Yayım Organıdır
The peer-reviewed Journal of the Akdeniz University Faculty of Medicine

Yılda üç kez yayımlanır (Ocak, Mayıs, Eylül)
Akdeniz Medical Journal is published three times per year (January,May,September).

Yayın Türü : Ulusal süreli yayın
Publication type : National periodical

Grafik Tasarım : Özden ÖZ

AMAÇ ve KAPSAM

Derginin amacı, sağlık bilimleri ile ilgili alanlarda Akdeniz Tıp Fakültesi ve Türkiye'de yapılan araştırmaları ulusal ve uluslararası bilim çevrelerine sunarak, duyurulması ve paylaşılmasına katkı sağlamak, bu bağlamda Türkiye'nin tanıtılmasına katkıda bulunmaktır. Akdeniz Tıp Dergisi, öncelikle Türkiye ve dünyada konuyla ilgili tüm tıbbi kurum ve bilgi merkezlerine ücretsiz olarak basılı ya da elektronik ortamda dergiye kolayca erişilmeyi sağlamanın yanı sıra, ulusal ve uluslararası dizinlerde de yer almayı hedeflemektedir. Akdeniz Tıp Dergisi, Akdeniz Üniversitesi Tıp Fakültesi'nin bilimsel yayın organı olup, etik ilke ve kurallara bağlı olarak yılda üç kez olmak üzere (Ocak, Mayıs, Eylül) dört ayda bir yayınlanan bilimsel ve hakemli, disiplinlerarası bir tıp dergisidir.
Akdeniz Tıp Dergisi, TÜBİTAK-ULAKBİM Türk Tıp Dizini, Türk Medline, Sobiad, İndex Copernicus ve Academindex Türkiye tarafından dizinlemektedir. Derginin amacı, sağlık bilimleri ile ilgili alanlarda Akdeniz Tıp Fakültesi ve Türkiye'de yapılan araştırmaları ulusal ve uluslararası bilim çevrelerine sunarak, duyurulması ve paylaşılmasına katkı sağlamak, bu bağlamda Türkiye'nin tanıtılmasına katkıda bulunmaktır. Akdeniz Tıp Dergisi, öncelikle Türkiye ve dünyada konuyla ilgili tüm tıbbi kurum ve bilgi merkezlerine ücretsiz olarak basılı ya da açık erişim ile elektronik ortamda dergiye kolayca erişilmeyi sağlamanın yanı sıra, ulusal ve uluslararası dizinlerde de yer almayı hedeflemektedir. Bu hedefler doğrultusunda, Akdeniz Tıp Dergisi'nde yayınlanması istenilen makalelerin daha çok özgün araştırmaları (temel, klinik ve epidemiyolojik) içermesi gerekmektedir. Ayrıca editör görüşü, derleme, olgu sunumu, editöre mektup, teknik notlar, tıp eğitimi ile ilgili yazılar, tıp tarihçesi ile ilgili yazılar, biyografi yazıları da kabul edilmektedir. Gönderilen yazıların, daha önce yazılı olarak veya elektronik bir formatta yayınlanmamış veya yayınlanma amacıyla bir başka dergiye veya elektronik ortama gönderilmemiş olması gerekmektedir. Gönderilecek yazılarda, Türk dergilerinde yayınlanmış makalelere de atıf yapılması özellikle aranmaktadır. Daha önceden basılı olarak yayınlanan Akdeniz Tıp Dergisi yayın hayatına elektronik olarak devam ettiğinden daha önceden 1300-1779 olan ISSN numarası 08.08.2019 tarihinden itibaren 2687-2781 şeklinde değişmiştir. Derginin yayın dili Türkçe ve İngilizce'dir. Türkçe yazılarda, Türk dilinin bütünlüğünün korunmasına dikkat edilmeli ve Türk Dil Kurumu'nun güncel baskı Yazım Kılavuzu ve Türkçe Sözlüğü esas alınmalıdır.
Tıp terimlerinin kullanılmasında olabildiğince "Türkçe Bilim Terimleri" nin kullanımına özen gösterilmelidir. Bunun için yazarlar Türk Dil Kurumu'nun "Hekimlik Terimleri Kılavuzu" veya diğer Tıp Terimleri Sözlüklerinden yararlanabilir.

YAYIN POLİTİKASI

Açık Erişim ve Makale İşleme

Akdeniz Tıp Dergisi, bilimsel yayınlara açık erişim sağlar. Yayımlanan sayıya ve içeriğinde yer alan yazıların tam metinlerine ücretsiz ulaşılabilir. Yazar(lar)dan yazılarının yayımı için herhangi bir ücret talep edilmez.

Okuyucular dergi içeriğini akademik veya eğitsel kullanım amaçlı olarak ücretsiz indirebilirler. Dergi herkese, ücretsizdir. Bunu sağlayabilmek için dergi Akdeniz Üniversitesi'nin mali kaynaklarından, editörlerin ve hakemlerin süregelen gönüllü çabalarından yararlanmaktadır.

Yazıların tüm bilimsel sorumluluğu yazarlara aittir. Gönderilen yazılarda isim sıralaması ortak verilen bir karar olmalıdır. Sorumlu yazar, yazar sıralamasını "Yazar sorumluluk ve Yayın Hakkı Devir Formu"nu doldurup imzalayarak, tüm yazarlar adına kabul etmiş sayılır. Yazarlık için gerekli ölçütleri karşılamayan, ancak çalışmaya katkısı olan kişiler "Teşekkür" bölümünde sıralanabilir. Yazarlar, yayının özgün bir yazı olduğunu, daha önce herhangi bir yerde yayınlanmadığını ve değerlendirme süreci içerisinde başka herhangi bir yerde yayınlama girişiminde bulunmayacaklarına yönelik imzalı bir beyanda bulunmalıdırlar.

Yazarlar, bilimsel içerikte değişiklik yapılmaması koşuluyla, editörlük tarafından yapılacak değişiklik ve düzeltmeleri önceden kabul etmiş sayılırlar. Gönderilen yazılar yayınlansın veya yayınlanmasın iade edilmez, yalnız yayınlanmayan resimler ve şekiller istek üzerine yazarına gönderilebilir.

Gönderilen yazıların, dergi kurallarına göre hazırlanmış ve eksiksiz olarak sayfa düzenlemesine hazır duruma getirilmiş olması gerekir. Yayın kurulu yazım kurallarına uymayan yazıları yayınlamamak, düzeltilmek üzere yazara iade etmek ya da şekil açısından yeniden düzenlemek yetkisine sahiptir. Editör ve dil editörleri, yazım dili, imla düzeltmeleri ve kaynakların yazım kurallarına uygunluğunun denetimi ve ilgili diğer konularda değişiklik ve düzeltmelerin yapılmasında tam yetkilidir. Makalede daha önce yayınlanmış alıntı yazı, tablo, resim vb. var ise, makalenin sorumlu yazarı, ilgili yayın hakkı sahibinden ve yazarlarından yazılı izin almak, ayrıca bunu makalede belirtmek zorundadır.

Yayın Süreci ve Makale Değerlendirme Süresi

Akdeniz Tıp Dergisi'ne gönderilen makaleler öncelikle Editörler Kurulu tarafından nesnel bir değerlendirmeye alınarak gözden geçirilir. Editörler yazıları doğrudan doğruya reddetme veya yeniden düzenlenmesi için geri gönderme hakkına sahiptir. Bu aşamada yazının reddini gerektirecek bir neden yoksa, yazı konu ile ilgili iki ayrı danışmana gönderilir. Makale değerlendirmesi için davet edilen hakemlerin azami 7 gün içerisinde daveti kabul etmesi istenir. Alan değerlendirmesinden iki olumlu hakem raporu alan makale yayınlanmaya hak kazanır. Bir olumlu bir olumsuz hakem raporu alan makale, üçüncü bir hakeme gönderilir ve makalenin yayınlanıp yayınlanmaması üçüncü hakemin raporu ve/veya editör kararı doğrultusunda belirlenir. Daveti kabul eden hakemlerin değerlendirme süreleri azami 30 gündür. Hakemlerin değerlendirmeyi kabul etmemesi veya gün sonunda değerlendirme raporunu göndermemesi durumunda makale değerlendirilmek üzere yeni bir hakeme gönderilir. Hakemler, makaleyi değerlendirdikten sonra yorum ve önerilerini içeren değerlendirme formunu editöre gönderirler. Editör tarafından hakem yorum ve önerileri yazarlara iletilerek düzeltilmiş makaleyi tekrar sisteme yüklemeleri istenir. Yazarların düzeltme süresi azami 60 gündür. Hakemler düzeltme sonrası makaleyi tekrar görmek istemişse makale değerlendirilmek üzere hakemlere tekrar gönderilir. Bu süreç hakemlerin makalenin kabulü veya reddi yönünde görüşünü bildirmelerine kadar devam eder. Hakemlerden gelen görüşler, editör/ler tarafından en geç 15 gün içerisinde değerlendirilir**.** Bu inceleme sonucunda nihai kararını yazar(lar)a iletir.

Son yayın onayı kararını editörler verir. Yapılacak olan sayfa düzenlemeleri ve düzeltilerden sonra, sorumlu yazarlardan son kontrol istenecek ve yazılı olarak "yayım onayı" alınacaktır. Yayıma kabul edilen makaleler, kabul tarihi sırasına göre Erken Çevrim İçi makaleler kısmında yayımlanmaktadır. Bir makalenin erken görünümde olması bir sonraki sayıya dahil edileceğini göstermez. Erken görünüm sırasında yazarların makalelerini gözden geçirmeleri ve dergi yazım kuralları ve mizanpaj açısından düzeltme önerilerini yayın kuruluna bildirmeleri gerekmektedir. Yayımlanmak üzere kabul edilen makalelerin basımı 12-18 ay arasındadır. Bununla birlikte makalenin güncelliği, özgünlüğü, yayım için bekleyen makale sayısı gibi faktörlere bağlı olarak bu süre daha erken veya daha geç olabilmektedir. Dergi yayımlandıktan sonra makalelerde değişiklik yapılamamaktadır.

Yazılar körleme danışmanlık (peer-review) sistemi uyarınca, yazarların isimleri yazı metninden çıkartılarak danışmanlara gönderilir. Yazarlara da, yazının hangi danışmanlara gönderildiği ile ilgili bilgi verilmez. Danışmanlar ve Yayın Kurulu üyeleri, yazıları topluma açık bir şekilde tartışamaz. Bazı durumlarda, danışmanların bir yazıya ait yorumları, aynı yazıyı inceleyen diğer danışmanlara editör tarafından gönderilerek, danışmanların bu süreçte aydınlatılmaları sağlanabilir. Gönderilen yazıyı, verilen süre içerisinde değerlendirmeyen danışmanın yerine, başka bir danışmana da görev verilebilir.

ETİK İLKELER

Akdeniz Tıp Dergisi, yazarlardan araştırma ve yayın etiğine uyumlu olunmasını istemektedir. İnsanlarda veya hayvanlarda gerçekleştirilen araştırmalarda ulusal ve uluslararası etik kılavuzlara uyum ve ilgili etik kurul-

lardan izin esastır. Alınan "Etik Kurul Onayı" çevrimiçi olarak, https://dergipark.org.tr/tr/pub/akd adresine gönderilmelidir. Makalelerin etik kurallara uygunluğu yazarların sorumluluğundadır.

İnsanlar üzerinde yapılan araştırmalar: Dergi, "İnsan" öğesinin içinde bulunduğu tüm çalışmalarda WMA"Helsinki Bildirgesi", "İyi Klinik Uygulamalar Kılavuzu" ve "İyi Laboratuvar Uygulamaları Kılavuzu"'nda belirtilen esaslara ve T.C. Sağlık Bakanlığı'nın ilgili yönetmeliklerine uygunluk ilkesini kabul eder. İnsanlar üzerinde yapılan araştırmalarda, "Klinik Araştırmalar Etik Kurul"undan izin alınması ve ilgili belgenin dergiye gönderilmesi zorunludur. Yazarlar, makalenin Gereç ve Yöntem bölümünde ilgili etik kuruldan ve çalışmaya katılmış insanlardan imzalı "Bilgilendirilmiş onam" (informed consent) belgesini aldıklarını belirtmek zorundadır. Olgu sunumlarında hastanın kimliğinin ortaya çıkmasına bakılmaksızın hastalardan veya gereği durumunda yasal temsilcisinden "Bilgilendirilmiş onam" (informed consent) belgesi alınmalı ve makalenin olgu sunumu başlığı altında yazılı olarak ifade edilmelidir. Hastadan veya yasal temsilcisinden alınan "Bilgilendirilmiş onam" belgesi dergiye yollanmalıdır.

Hayvanlar üzerinde yapılan araştırmalar: Hayvanlar üzerinde yapılan araştırmalarda, "Deney Hayvanları Etik Kurul"undan izin alınması ve ilgili belgenin bir kopyasının dergiye gönderilmesi zorunludur. Araştırmanın Gereç ve Yöntem bölümünde, deneysel çalışmalarda tüm hayvanların "Laboratuvar Hayvanlarının Bakım ve Kullanımı Kılavuzu"na **(Guide for the Care and Use of Laboratory Animals, www.nap.edu/catalog/5140.html)** uygun olarak insancıl bir muameleye tabi tutulduğu ve Deney Hayvanları Etik Kurul onay raporu alındığı belirtilmelidir. Hayvanlar üzerinde yapılan çalışmalarda ağrı, acı ve rahatsızlık verilmemesi için neler yapıldığı açık bir şekilde belirtilmelidir. Etik Kurul onayının bir kopyasının dergiye gönderilmemesi durumunda yazı yayınlanmayacaktır.

İzinler: Akdeniz Tıp Dergisi, makalelerin Atıf-Gayri Ticari-Aynı Lisansla Paylaş 4.0 Uluslararası (CC BY) lisansına uygun bir şekilde paylaşılmasına izin verir. Buna göre yazarlar ve okurlar; uygun biçimde atıf vermek, materyali ticari amaçlarla kullanmamak ve uyarladıklarını aynı lisansla paylaşmak koşullarına uymaları halinde eserleri kopyalayabilir, çoğaltabilir ve uyarlayabilirler. Dergide yayımlanan yazılar için telif hakkı ödenmez.

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Çıkar çatışmaları: Yazarlar, makaleleriyle ilgili çıkar çatışmalarını (varsa) bildirmelidirler. Eğer makalede dolaylı veya dolaysız ticari bağlantı (istihdam edilme, doğrudan ödemeler, hisse senedine sahip olma, firma danışmanlığı, patent lisans ayarlamaları, veya hizmet bedeli gibi) veya çalışma için maddi destek veren kurum mevcut ise yazarlar; kullanılan ticari ürün, ilaç, firma v.b ile ticari hiçbir ilişkisinin olmadığını ve varsa nasıl bir ilişkisinin olduğunu, editöre sunum sayfasında ve ayrıca makalede kaynaklar bölümünden önce "Çıkar çatışması" başlığı altında bildirmek zorundadır. http://icmje.org/conflicts-of-interest/

Yazarlık katkısı: Çok yazarlı makalelerde yazarların araştırmaya katkıları (fikir oluşturma, çalışma tasarımı, deneysel uygulamalar, istatistik, makalenin yazımı, v.b) açıklanmalı ve imzalı olarak editöre (yayın hakkı devir formu kapsamı içinde) sunulmalıdır. Yazarlık katkısı bilgisi, kaynaklar bölümünden önce makalede bildirilmek zorundadır.

Maddi destek: Araştırma için alınmış finansal destek, bağış ve diğer bütün faaliyetler (istatistiksel analiz, İngilizce/Türkçe değerlendirme) ve/veya teknik yardım varsa açıkça makalenin kaynaklar bölümünden önce bildirilmek zorundadır. Ayrıca yazarlar aşağıda belirtilen alanlarda, varsa çalışmaya sponsorluk edenlerin rollerini beyan etmelidirler: 1) Çalışmanın tasarımı, 2) Veri toplanması, analizi ve sonuçların yorumlanması, 3) Raporun yazılması, 4) Yayın için gönderilmesine karar verilmesi.

İntihal: Dergiye gönderilen tüm yazılar, değerlendirme sürecine alınmadan önce iThenticate veya Turnitin programından geçirilerek benzerlik raporu alınır. Benzerlik oranı %20'den fazla olan makaleler intihal olarak kabul edilir ve ret edilir. Akdeniz Tıp Dergisi Yayın Kurulu dergiye gönderilen çalışmalarla ilgili aşırma, atıf manipülasyonu ve veri sahteciliği iddia ve şüpheleri karşısında COPE kurallarına uygun olarak hareket edebilmektedir.

ETİK SORUMLULUKLAR

Bilimsel bir çalışma ortaya koyan tüm paydaşların (yazar, editör ve hakem), bilimin doğru bir şekilde ilerlemesine katkı sağlaması hedeflenir. Bu hedef gereğince hazırlanan bilimsel çalışmalarda bilimsel etik ilkelere uygunluk önemlidir.

Bu ilkeler, tarafımızca kabul edilmiştir ve paydaşlar tarafından da benimsenmesi önerilerek, bir kısmı aşağıda sunulmuştur.

Derginin editörlük ve yayın süreçleri International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE) ve National Information Standards Organization (NISO) yönergelerine uygun olarak şekillenmektedir. Dergi, Principles of Transparaency and Best Practice in Scholarly Publishing (doaj.org./bestpractice) ilkelerini benimsemiştir.

Yazarların Etik Sorumlulukları

- Çalışmayla ilişkili verilerin doğruluğundan emin olmak, araştırmasına ilişkin kayıtlarını düzenli tutmak ve olası bir talep üzerine bu verilere erişim verebilmek.
- Gönderdiği makalenin başka bir yerde yayınlanmadığından veya kabul edilmediğinden emin olmak.
- Sunduğu içerik yayınlanmış veya sunulan başka içerikle eşleşirse, bu çakışmayı kabul etmek ve alıntı yapmak. Gerektiğinde, çalışmasıyla ilgili benzer içeriğe sahip olabilecek herhangi bir çalışma varsa bunun bir kopyasını editöre sunmak. Başka kaynaklardan herhangi bir içeriği çoğaltmak ya da kullanmak için izin almak, atıf göstermek.
- İnsan veya hayvan denek içeren tüm çalışmalar için ulusal ve uluslararası yasalara ve yönergelere uygun olmasını sağlamak, (örneğin, WMA Helsinki Bildirgesi, NIH Laboratuvar Hayvanlarının Kullanımına İlişkin Politika, Hayvanların Kullanımına İlişkin AB Direktifi) gerekli onayların alındığını belirtmek, denek mahremiyete saygı göstermek. Çalışmasına dair ilgili etik kurul onaylarını ve araştırma detaylarını çalışmanın "Gereç ve Yöntem" kısmında belirtmek.
- Herhangi bir çıkar çatışması durumunda, makalesiyle ilgili etik bir ihlal tespit ettiğinde bunu editör ve yayıncı ile paylaşmak, hata beyanı, zeyilname, tazminat bildirimi yayınlamak veya gerekli görüldüğü durumlarda çalışmayı geri çekmek.

Editörlerin Etik Görev ve Sorumlulukları

- Yazarların cinsiyet, dinî veya politik inançlar, etnik veya coğrafi kökenleri üzerine ayrım yapılmaksızın görevlerini yerine getirirken dengeli, objektif ve adil bir şekilde hareket etmek.
- Dergiye gönderilen çalışmaları içeriğine göre değerlendirmek, hiçbir yazara ayrıcalık göstermemek.
- Olası çıkar çatışmalarını önlemek adına gerekli önlemleri almak ve varsa mevcut beyanları değerlendirmek.
- Sponsorlu çalışmaları veya özel konulardaki çalışmaları diğer çalışmalarla aynı şekilde ele almak.
- Etik ihlali niteliğinde bir şikâyet olması durumunda, derginin politika ve kurallarına bağlı kalarak gerekli işlemleri uygulamak. Yazarlara, gelen şikayete cevap vermek için bir fırsat vermek, çalışma kime ait olursa olsun gerekli yaptırımları uygulamaktan kaçınmamak.
- Derginin amaç ve kapsamına uygun olmaması durumunda gelen çalışmayı reddetmek.

Hakemlerin Etik Sorumlulukları

- Editörün karar verme sürecine katkıda bulunmak için makaleyi objektif olarak zamanında incelemek ve sadece uzmanlık alanı ile ilgili çalışma değerlendirmeyi kabul etmek.

- Değerlendirmeyi nesnel bir şekilde sadece çalışmanın içeriği ile ilgili olarak yapmak. Dinî, siyasi ve ekonomik çıkarlar gözetmeden çalışmayı değerlendirmek.
- Yayınlanacak makalenin kalitesini yükseltmeye yardımcı olacak yönlendirmelerde bulunmak ve çalışmayı titizlikle incelemek. Yorumlarını yapıcı ve nâzik bir dille yazara iletmek.
- Editör ve yazar tarafından sağlanan bilgilerin gizliliğini korumak, gizlilik ilkesi gereği incelediği çalışmayı değerlendirme sürecinden sonra yok etmek, kör hakemliğe aykırı bir durum varsa editöre bildirmek ve çalışmayı değerlendirmemek.
- Olası çıkar çatışmalarının (mali, kurumsal, işbirlikçi ya da yazarlar arasındaki diğer ilişkiler) farkında olmak ve gerekirse bu yazı için yardımlarını geri çekmek konusunda editörü uyarmak.

Bilimsel araştırma ve yayın etiğine aykırı olduğu düşünülen eylemlerden bazıları:

- İntihal: Başkalarının özgün fikirlerini, metotlarını, verilerini veya eserlerini bilimsel kurallara uygun biçimde atıf yapmadan kısmen veya tamamen kendi eseri gibi göstermek.
- Sahtecilik: Bilimsel araştırmalarda gerçekte var olmayan veya tahrif edilmiş verileri kullanmak.
- Çarpıtma: Araştırma kayıtları veya elde edilen verileri tahrif etmek, araştırmada kullanılmayan cihaz veya materyalleri kullanılmış gibi göstermek, destek alınan kişi ve kuruluşların çıkarları doğrultusunda araştırma sonuçlarını tahrif etmek veya şekillendirmek.
- Tekrar yayım: Mükerrer yayınlarını akademik atama ve yükselmelerde ayrı yayınlar olarak sunmak.
- Dilimleme: Bir araştırmanın sonuçlarını, araştırmanın bütünlüğünü bozacak şekilde ve uygun olmayan biçimde parçalara ayırıp birden fazla sayıda yayımlayarak bu yayınları akademik atama ve yükselmelerde ayrı yayınlar olarak sunmak.
- Haksız yazarlık: Aktif katkısı olmayan kişileri yazarlar arasına dâhil etmek veya olan kişileri dâhil etmemek, yazar sıralamasını gerekçesiz ve uygun olmayan bir biçimde değiştirmek, aktif katkısı olanların isimlerini sonraki baskılarda eserden çıkartmak, aktif katkısı olmadığı halde nüfuzunu kullanarak ismini yazarlar arasına dâhil ettirmek.
- Destek alınarak yürütülen araştırmalar sonucu yapılan yayınlarda destek veren kişi, kurum veya kuruluşlar ile bunların katkılarını belirtmemek.
- Henüz sunulmamış veya savunularak kabul edilmemiş tez veya çalışmaları, sahibinin izni olmadan kaynak olarak kullanmak.
- İnsan ve hayvanlar üzerinde yapılan araştırmalarda etik kurallara uymamak, yayınlarında hasta haklarına saygı göstermemek, hayvan sağlığına ve ekolojik dengeye zarar vermek, gerekli izinleri almamak.
- Bilimsel araştırma için sağlanan veya ayrılan kaynakları, mekânları, imkânları ve cihazları amaç dışı kullanmak.
- Akademik atama ve yükseltmelerde bilimsel araştırma ve yayınlara ilişkin yanlış veya yanıltıcı beyanda bulunmak.

YAZIM KURALLARI

Dergide yayınlanmak üzere editöre gönderilen yazılar A4 sayfasının bir yüzüne 12 punto, çift aralıkla ve kenarlarda 3'er cm boşluk bırakılarak Times Newroman karakterinde yazılmalıdır. Kullanılan kısaltmalar yazı içerisinde ilk geçtikleri yerde, parantez içinde, açık olarak yazılmalı, özel kısaltmalar yapılmamalıdır. Yazı içindeki 1-10 arası sayısal veriler yazıyla (Her iki tedavi grubunda, ... ikinci gün .....), 10 ve üstü rakamla belirtilmelidir. Ancak, yanında tanımlayıcı bir takısı olan 1-10 arası sayılar rakamla (.... 1 yıl) cümle başındaki rakamlar da (On beş yaşında bir kız hasta.....) yazıyla yazılmalıdır. Özgün araştırma makaleleri ve derleme yazılarında özel bir kelime sayısı sınırlandırılması yoktur. Olgu sunumları Öz/Abstract hariç 1000 sözcük ile sınırlandırılmalı ve en az sayıda şekil, tablo ve kaynak içermelidir. Editöre çeşitli konularda ve dergide yayınlanan yazılarla ilgili görüşler yazılabilir ve yazarlarından cevaplandırılması istenebilir. Editöre mektuplar (en fazla 1000 sözcük, tablosuz ve şekilsiz) olmalı ve mektup, tüm yazarlar tarafından imzalanmış olmalıdır. Bunların dergide yayınlanıp yayınlanmaması editörün yetkisindedir. Ayrıca dergide tıp alanındaki bilimsel toplantılar, tarih, konu ve konuşmacıları duyurmak amacı ile yayınlanabilir. Yazılar aşağıda belirtilen sıra izlenerek düzenlenmelidir.

Başlık Sayfası:

Yazının Türkçe ve İngilizce başlığı, yazarların adları, görevleri (akademik unvanları) ve iletişim bilgileri (e-mail, telefon) ile, hangi kuruluştan gönderildiği, varsa çalışmayı destekleyen kurum yazılmalıdır. Tüm yazarların uluslararası geçerliliği bulunan "ORCID" bilgisine yer verilmelidir. Yazı daha önce herhangi bir toplantıda bildiri olarak sunulmuşsa, yeri ve tarihi belirtilmelidir. Ayrıca bu sayfada yazışma yapılacak yazarın adı, soyadı, adresi, telefon ve faks numaraları, e-posta adresi açıkça yazılmalıdır.

Öz:

Ayrı bir sayfaya Türkçe ve İngilizce olarak hazırlanmalı, başlıklar dahil her biri 250 sözcüğü aşmamalıdır. Öz, makaleyi yansıtacak nitelikte olmalı, önemli sonuçlar verilmeli ve bunların kısaca yorumu yapılmalıdır. Özde açıklanmayan kısaltmalar kullanılmamalı, kaynak gösterilmemelidir. Türkçe ve İngilizce özler, bölümlü olmalı ve aşağıdaki gibi yapılandırılmalıdır: Amaç/Objective; Gereç ve Yöntem(ler)/Material and Method(s); Bulgular/Results; Sonuç /Conclusion.

Anahtar Sözcükler:

"Index Medicus: Medical Subject Headings" standartlarına uygun Türkçe ve İngilizce anahtar sözcükler verilmelidir. (http://www.nlm.nih.gov/mesh/authors.html) Tüm yazıların Türkçe ve İngilizce özlerinin altında, 3-10 adet anahtar sözcük yer almalıdır. Anahtar sözcüklerin belgeye erişimde en önemli öge olduğu gözönünde tutulmalıdır.

Bölümler:

Özgün araştırma makalelerinde giriş, gereç ve yöntem (çalışma tasarımı, olguların seçimi ve tanımlanması, teknik bilgi, istatistik vs), bulgular, tartışma ve sonuç bölümleri yer almalı, olgu sunumlarında ise giriş, olgu(ların) sunumu ve tartışma bölümleri yer almalıdır. Bu bölümlerden sonra, varsa araştırmaya veya makalenin hazırlanmasına katkıda bulunanlara "teşekkür" yazılabilir. Teşekkürlere yazının sonunda kaynaklardan önce yer verilir. Bu bölümde kişisel, teknik ve gereç yardımı gibi nedenlerle yapılacak teşekkür ifadeleri yer alır.

Kaynaklar:

Kaynaklar yazının sonunda (Kaynaklar/References) başlığı altında metindeki geçiş sırasına göre numaralandırılıp dizilmelidir. Metin içinde ise parantez içinde yazılmalıdır. Kaynakların listesiyle metin içinde yer alış sırası arasında bir uyumsuzluk bulunmamalıdır. Aslı görünmeden diğer bir kaynak aracılığı ile bilgi edinilen kaynaklar numaralandırılmaz, zorunlu hallerde parantez içinde verilir. Kaynakların doğruluğundan yazar(lar) sorumludur. Tüm kaynaklar metinde belirtilmelidir. Kaynaklar aşağıdaki örneklerdeki gibi gösterilmelidir. Tüm yazarlar belirtilmeli, "ve ark. - et al." ibaresi kullanılmamalıdır. Dergilerin isimleri Index Medicus'a uygun olarak kısaltılmış biçimde verilir. Index'e girmeyen dergi isimlerinde kısaltma yapılmamalıdır.

Kaynakların Yazımı İçin Örnekler:

Dergiler için

Muzaale AD, Massie AB, Wang MC, Montgomery RA, McBride MA, Wainright JL, Segev DL. Risk of end-stage renal disease following live kidney donation. JAMA 2014; 311:579-86.

Kitaplar için

Chabner BA, Longo DL. Cancer Chemotherapy and Biotherapy: Principles and Practice, 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2011.

Kitaptan alınan bölümler için

Goadsby PJ. Pathophysiology of headache. In: Silberstein SD, Lipton RB,

Dalessio DJ, eds. Wolff's headache and other head pain. 7th ed. Oxford: Oxford University Press, 2001:57-72.

Toplantı bildirileri için

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002:182-91.

Çevrim-içi makaleler için

U.S. Renal Data System. USRDS 2007 annual data report. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2007 (http://www.usrds.org/atlas07.aspx).

Dergi ekleri için

Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int 2012;24 Suppl 2:1-138.

Index Medicus'ta yer almayan Türkçe kaynaklarda yukardaki örneklere uyulur, ancak dergi isimleri kısaltılmadan yazılır.

Tablolar:

Tablolar, kaynaklar sayfasından sonra gelmeli, her bir tablo ayrı bir sayfada olacak şekilde yazılmalıdır. Tablolar, yazı içinde geçiş sırasına göre Romen rakamları ile numaralandırılmalıdır. Tablo başlıkları kısa, öz olmalı ve bu başlık tablonun üstünde yer almalıdır. Tablo açıklamaları ve kısaltmaları ise, tablonun altında yer almalıdır. Metin içinde her tabloya değinilmelidir.

Şekiller:

Metinden ayrı sayfaya yerleştirilmelidir. Şekiller ya profesyonel olarak çizilmeli ve fotoğraflanmalı ya da fotoğraf kalitesinde dijital olarak gönderilmelidir. Şekillerin basıma uygun versiyonlarının yanı sıra, JPEG ya da GIF gibi elektronik versiyonlarda yüksek çözünürlükte görüntü oluşturacak biçimlerde elektronik dosyaları gönderilmeli ve yazarlar göndermeden önce bu dosyaların görüntü kalitelerini bilgisayar ekranında kontrol etmelidir. Semboller, oklar ya da harfler fonla kontrast oluşturmalıdır. Mikroskopik resimlerde büyütme oranı ve kullanılan boyama tekniği belirtilmelidir. Eğer insan fotoğrafı kullanılacaksa ya bu kişiler fotoğraftan tanınmamalıdır ya da yazılı izin alınmalıdır. (Etik bölümüne bakınız) Şekil ve resimlerin yazıları altta, (1,2,3,....) arabik rakamlar ile birlikte yazılmalıdır. Şekiller metinde geçiş sıralarına göre numaralandırılmalıdır. Şekillerin metin içindeki yerleri belirtilmelidir. Metin içinde her şekle değinilmelidir. Renkli şekiller Editör gerekli gördüğünde ya da sadece yazar ek masrafı karşılarsa basılabilir.

Makalelerin Dergiye Gönderilmesi:

Makaleler, yazının yayınlanmak üzere gönderildiğini ve Akdeniz Tıp Dergisi'nin hangi bölümü (özgün araştırma, olgu sunumu, derleme) için başvurulduğunu belirten bir mektup, yazının elektronik formunu içeren Microsoft Word 2003 ve üzerindeki versiyonları ile yazılmış elektronik dosyası ile tüm yazarların imzaladığı "Telif Hakkı Devri Formu" eklenerek gönderilmelidir. Yazıların alınmasının ardından yazarlara makalenin alındığı, bir makale numarası ile bildirilecektir. Tüm yazışmalarda bu makale numarası kullanılacaktır. Makalelerde aşağıdaki sıra takip edilmelidir ve her bölüm yeni bir sayfa ile başlamalıdır:

1. Başlık sayfası
2. Öz
3. Metin
4. Teşekkür
5. Kaynaklar
6. Tablo ve Şekiller.

Tüm sayfalar sırayla numaralandırılmalıdır. Akdeniz Tıp Dergisi, kendisine gönderilen yazıları, hem üç nüsha halinde, yazıcı çıktısı olarak ve hem de CD ve/veya E-posta uzantısı olarak elektronik makale gönderisi şeklinde kabul etmektedir. Elektronik gönderi, hem zaman kazandırıp posta ücretinden kurtarmakta, hem de değerlendirme süreci sırasında makalenin elektronik biçimi gönderildiğinden üstünlük sağlamaktadır. Çevrimiçi gönderim (on-line submission) ile birlikte Akdeniz Tıp Dergisi web sitesi (https://dergipark.org.tr/tr/pub/akd) nin ilgili kısımlarındaki talimatlarına uyarak da makale gönderilip, hakem süreçleri de bu yolla değerlendirilmektedir. Yazarların makalelerini göndermeden önce bir eksiklik olmadığından emin olmaları için aşağıda bir kontrol listesi bulunmaktadır.

Son Kontrol Listesi:

1. Editöre sunum sayfası; a) Makalenin kategorisi b) Başka bir dergiye gönderilmemiş olduğu bilgisi c) Sponsor veya ticari bir firma ile ilişkisi (varsa belirtiniz) d) İstatistik kontrolünün yapıldığı (araştırma makaleleri için) e) İngilizce yönünden kontrolünün yapıldığı
2. Telif hakları devri formu
3. Daha önce basılmış belge (yazı, resim, tablo) kullanılmış ise izin belgesi
4. İnsan ögesi bulunan çalışmalarda "gereç ve yöntemler" bölümünde HELSİNKİ Deklarasyonu ilkelerine uygunluk, etik kurul onayı ve hastalardan "bilgilendirilmiş olur" alındığının belirtilmesi.
5. Hayvan ögesi kullanılmış ise "gereç ve yöntemler" bölümünde "*Guide for the Care and Use of Laboratory Animals*" ilkelerine uygunluğunun belirtilmesi.
6. Kapak sayfası a) Makalenin Türkçe ve İngilizce başlığı (tercihen birer satır) b) Yazarlar ve kurumları c) Tüm yazarların yazışma adresi, iş telefonu, GSM numarası, E-posta adresleri (bu bilgiler yalnızca makalenin orijinal nüshasında olmalı, diğer üç kopyada bulunmamalıdır.)
7. Özler: 250 sözcük (Türkçe ve İngilizce)
8. Anahtar sözcükler: 3-10 arası (Türkçe ve İngilizce)
9. Teşekkür
10. Kaynaklar
11. Tablolar – Şekiller

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AIMS and SCOPE

The Akdeniz Medical Journal is the scientific publication of Akdeniz University Faculty of Medicine and is a peer-reviewed, interdisciplinary medical journal published every four months (January, May, September) according to ethical principles and rules.
The abbreviation of Akdeniz Medical Journal is Akd Med J / Akd Tıp D.
The Akdeniz Medical Journal is the scientific publication of Akdeniz University Faculty of Medicine and is a peer-reviewed, interdisciplinary medical journal published every four months (January, May, September) according to ethical principles and rules. The abbreviation of Akdeniz Medical Journal is Akd Med J / Akd Tıp D. The Akdeniz Medical Journal is indexed by Turkish Medical Index of TÜBİTAK-ULAKBİM, Turk Medline, Sobiad, Index Copernicus and Academindex Turkey. The aim of the journal is to present the studies conducted at the Akdeniz Faculty of Medicine and in Turkey in the fields of health sciences and related areas to the national and international science environment and contribute to their announcement and sharing and therefore to the promotion of Turkey in this context. The Akdeniz Medical Journal is targeting to provide free and easy access to the journal in printed or electronic form for all relevant medical institutions and information centers in Turkey and globally and also to be included in national and international indexes.

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All scientific responsibility for the articles belongs to the authors. The name order of the submitted articles should be a joint decision. The responsible author is considered to accept the author order in the name of all authors by signing the "Author responsibility and Copyright Transfer Form". Anyone who does not meet the criteria for authoring but has contributed to the study can be listed in "Acknowledgements". The authors should declare in writing that the article is an original paper that has not been published before and that they will not attempt to publish it somewhere else during the evaluation process.

The authors are considered to have accepted any changes and corrections made by the editor as long as the scientific content is not changed. The articles sent are not returned whether published or not, and only images and figures that are not published can be returned to the author upon request.

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The articles sent to the Akdeniz Medical Journal first undergo an objective review by the Editorial Board. The editors have the right to reject the articles directly or to send them back for re-editing. If there is no reason to reject the article in this stage, it is sent to two separate reviewers familiar with the article subject. Referees invited for article evaluation are asked to accept the invitation within a maximum of 7 days. An article that receives two positive referee reports from the field assessment is entitled to be published. An article that receives a positive and a negative referee's report is sent to a third referee, and whether the article is published or not is determined in accordance with the third referee's report and/or the editorial decision. The evaluation period of the referees accepting the invitation is a maximum of 30 days. If the referees do not agree to the evaluation or do not submit the evaluation report at the end of the period, the article is sent to a new referee for evaluation. After evaluating the article, the referees send the evaluation form with their comments and suggestions to the editor. The editor then submits the editor comments and suggestions to the authors and asks them to upload the revised article back to the system. The authors' revision period is a maximum of 60 days. If the referees have asked to see the article again after the revision, the article is sent back to the referees for evaluation. This process continues until the referees provide their opinion as regards the acceptance or rejection of the article. The opinions of the referees are evaluated by the editors within 15 days at the latest. The final decision is declared to the author(s) as a result of this review.

The final decision for publication belongs to the editors. Once the page layout is prepared and corrections are made, the responsible authors will be asked for a final check and "publishing approval" to be provided in writing. Articles accepted for publication are published in the early online articles section in order of the date of acceptance. The presence of an article in early view does not indicate that it will be included in the next issue. During this early view period, the authors are required to review their articles and report their recommendations for revision according to the Journal writing rules and layout to the editorial board. The time to publication of the articles accepted for publication is 12-18 months. However, depending on factors such as the timeliness of the article, its originality, and the number of articles waiting for publication, this period may be shorter or longer. No changes can be made to the articles once the Journal is published.

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The aim is to have all stakeholders (authors, editors and reviewers) who put forward a scientific study to contribute to the appropriate advancement of science. Compliance with the scientific ethical principles is important in scientific studies prepared in accordance with this goal.

These principles have been adopted by us and their adoption has also been proposed by various stakeholders, some of which are presented below.

The editorial and publication processes of the Journal have been developed according to the directives of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE) and the National Information Standards Organization (NISO). The Journal has adopted the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org./bestpractice).

Ethical Responsibilities of the Authors

- To ensure the accuracy of data related to the study, to keep regular records of the research, and to be able to provide access to this data upon a possible request.
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For chapters taken from books

Goadsby PJ. Pathophysiology of headache. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. Wolff's headache and other head pain. 7th ed. Oxford, England: Oxford University Press, 2001:57-72.

For conference papers

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

For online articles

U.S. Renal Data System. USRDS 2007 annual data report. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2007 (http://www.usrds.org/atlas07.aspx).

For journal annexes

Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl 2012;2:1-138.

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5. References
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Geliş Tarihi : 29 November 2021
Received
Kabul Tarihi : 25 October 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Akgun M, Akpinar A, Yangın H, Boz I.
The Effect of Birth Types on Postpartum Comfort Level in Pregnant Women
Akd Med J 2023; 9(3): 232 - 240

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DOI: 10.53394/akd.1030089

The Effect of Birth Types on Postpartum Comfort Level in Pregnant Women

Gebe Kadınların Postpartum Konfor Düzeyi Üzerine Doğum Şekillerinin Etkisi

ABSTRACT

Objective:

It is known that the birth type has important effects on women's postpartum comfort level. The aim of this study is to determine the effects of birth types on postpartum comfort levels, and to determine whether any of these birth types is superior to the others.

Material and Methods:

The data for this descriptive study were obtained through a public hospital and a social media platform for 150 women (50 with vaginal birth, 50 with cesarean section, and 50 with vaginal birth after cesarean) between November 2017 and February 2018. The data were collected using a Personal Information Form and the Postpartum Comfort Scale. The data were analyzed via frequency, mean, standard deviation, chi square, Cronbach Alpha analysis, multivariate linear regression, and t test.

Results:

The women with vaginal birth after cesarean had significantly higher mean scores of Postpartum Comfort Scale total and subscales compared to women with vaginal birth or cesarean section ($p<0.001$). This study indicated that women with vaginal birth after cesarean had the highest postpartum comfort levels compared to vaginal birth or cesarean section.

Conclusion:

It was determined that the postpartum comfort levels of women, who had a vaginal delivery after cesarean section, were higher than women who had a vaginal birth or cesarean section.

Key Words:

Cesarean birth, Postpartum comfort, Vaginal birth, Vaginal birth after cesarean

ÖZ

Amaç:

Doğum şeklinin kadınların doğum sonu konfor düzeyi üzerinde önemli etkileri olduğu bilinmektedir. Bu çalışmanın amacı, doğum şekillerinin doğum sonu konfor düzeyi üzerine etkisini belirlemek ve bu doğum şekillerinin herhangi birinin etkisinin diğerine göre üstün olup olmadığını incelemektir.

Gereç ve Yöntemler:
Tanımlayıcı tipteki bu çalışmanın verileri Kasım 2017-Şubat 2018 tarihleri arasında bir devlet hastanesi ve bir sosyal medya platformu üzerinden Kişisel Bilgi Formu ve Doğum Sonu Konfor Ölçeği kullanılarak 150 kadından (50 vajinal doğum, 50 sezaryen ve 50 sezaryen sonrası vajinal doğum) elde edilmiştir. Veriler frekans, ortalama, standart sapma, ki-kare, Cronbach alpha analizi, çok değişkenli doğrusal regresyon ve t testi ile analiz edilmiştir.

Bulgular:
Sezaryen sonrası vajinal doğum yapan kadınların doğum sonu konfor ölçeği toplam ve alt ölçek puan ortalamaları vajinal doğum veya sezaryen olan kadınlara göre anlamlı olarak daha yüksekti ($p<0.001$). Bu çalışma, vajinal doğum veya sezaryen ile karşılaştırıldığında sezaryen sonrası vajinal doğum yapan kadınların en yüksek doğum sonrası konfor seviyelerine sahip olduğunu göstermiştir.

Sonuç:
Bu çalışmada, sezaryen sonrası vajinal doğum yapan kadınların doğum sonu konfor düzeylerinin vajinal doğum veya sezaryen olan kadınlara göre daha yüksek olduğu belirlendi.

Anahtar Sözcükler:
Sezaryen doğum, Doğum sonu konfor, Vajinal doğum, Sezaryen sonrası vajinal doğum

INTRODUCTION

It is known that women experience many physical and psychological problems together in the postpartum period such as pain, fatigue, breast problems such as engorgement, mastitis, small and inverted nipple at an early phase, infection, stress incontinence, constipation, feeling of inadequacy in self and newborn care (1-7). Postpartum comfort means woman's quality of life regarding these problems. Birth type is known to affect a woman's adaptation to the postpartum period; the problems that women experience in the postpartum period may vary according to the birth type (8,9). It is known that Comfort Theory is used in the evaluation and development of postpartum comfort (10). The theoretical structure of this theory is based on the concept of holism and human needs. Kolcaba states that when basic human needs, which are biological, psychological and social needs, are met, the comfort of the individual will be in relief phase (10). Lima et al., (2017) summarized the compliance of comfort theory for postpartum women in three aspects. First, it was observed that Kolcaba's comfort theory supports the systematization of nursing care for a postpartum woman with acute pain related to harmful physical agents (operative wound) characterized by verbal report of pain. Moreover, this theory takes into account sleep deprivation related to maternal practices that do not favor sleep characterized by anxiety, tiredness and sleepiness during the day. The comfort theory is appropriate for evaluating psychological problems as well as physical problems of postpartum women. Finally, this theory emphasizes that impaired comfort characterized by anxiety, fear, and reports of feeling uncomfortable is important in the postpartum women (11).

It is known that women who experience caesarean section have many more major and minor problems after vaginal birth (VB) and therefore their comforts are negatively affected (12,13). In a study conducted in Taiwan, it was determined that following CS compared to VB, women's discharge period is longer and their urinary tract infection and surgical wound complications are at a higher level (14). Besides, current studies revealed that women who experience CS compared to VB have higher levels of after pain, a lower level of physical activity, a lower level of success in breastfeeding in the first hour, and a lower level of newborn and maternal attachment (15-18). Likewise, the studies conducted in Turkey revealed that women who experience CS compared to VB experience a higher level of after pain, that the lactation process is delayed, and women have a lower level of breastfeeding success and a lower level of breastfeeding self-sufficiency (19-21). Postpartum comfort is crucial in detecting and efficiently managing these problems that occur in the postpartum period.

Although we did not find any study on examining postpartum comfort in the international literature review, we identified six studies in this field in Turkey were carried out. The first study reported that postpartum comfort levels were higher in women with VB than in those with CS under general and regional anesthesia (22). Çapık et al., (2014) detected that the physical and sociocultural comfort and postpartum comfort levels were higher in women with VB compared to those with CS (8). With regards to CS, another study found that general anesthesia had a negative impact on postpartum comfort and adaptation compared to regional anesthesia (23). Akgün (2016) found that the physical and psychospiritual comfort levels of women with VB were higher than those of women with CS (24). In contrast, only one study reported no difference between the postpartum comfort levels of different birth types (25).

Based on recent studies, the comfort levels of women with VB are generally higher than those of women with CS; however, to our knowledge, there has been no study investigating the comfort levels of women following vaginal birth after cesarean (VBAC). Therefore, the aim of the current study is to determine the effects of birth types on postpartum comfort levels, and to determine whether one method is superior to the others.

MATERIAL and METHODS

Study Design

This descriptive study was conducted between November 2017 and February 2018 through Akdeniz University Hospital Gynecology and Postpartum Services and a social media platform with members throughout Turkey .

Ethics Approval

This study was approved by the Akdeniz University Clinical Research Ethics Committee (No: 565, Date: 20.09.2017), and application approval was obtained from the institution. Approval was also obtained from the administrators of the social media platform used in this study. The participants were informed about the purpose of the study prior to providing informed consent with forms prepared according to the Helsinki Declaration.

Population and Sample

In the calculation of the sample size, initially the parameters of the power, confidence interval, effect size of the study was determined. In this study, the confidence interval was determined as 95 %, the power of the research as 80% and effect size as 0.8 in the calculation of the sample size. In line with these values, the priori calculated sample size, performed using G Power 3.1 packaged software was determined as 150. The previous studies were also considered in the calculation of the sample size (8,25). This study included a total of 150 women (50 with VB, 50 with CS, and 50 with VBAC).

Inclusion and exclusion criteria of the study were determined as follows. All of the participants who agreed to participate in the study were literate, gave birth to a single baby after 37 gestational weeks, had a healthy baby, and were in the postpartum period. Women were excluded from the study, if they gave birth before 37 weeks, or if had complications associated with themselves and/or their babies at birth or during the postpartum period.

Data Collection

Data of women who underwent VB and CS were collected by face-to-face interviews in postpartum clinics within 24-48 hours after birth. It is known that an average of 650 women give birth annually, including VB and CS in Akdeniz University Hospital. During the data collection process, 120 women were invited to the study, but 20 women refused to participate because of afterpain, because they looked after their baby or did not feel well. The data collection process was completed when 50 VB and 50 CS women who agreed to participate in the study were reached according to the sample size calculation.

Since the study was conducted in a country with a low level of VBAC and VBAC did not become widespread in public hospitals, the data of these women were obtained through social media. Data for women with VBAC were gathered through an online survey developed with the 'Survey monkey' program on social media. The data regarding VBAC group were collected from a single social media site. The participants were members of a social media platform called "VBAC (Turkey's first and only mothers' group)" having more than 40.000 members. In this social media group, there were women who wanted to do VBAC or had experience with VBAC. These women shared their experiences about pregnancy and childbirth experiences with each other. This study was announced on social media platform. In the announcement made on social media, it was especially emphasized that this study is aimed at women in the first 24-48 hours following VBAC.

Variables and Assessment Tools

Data were collected using the Personel Information Form and Postpartum Comfort Scale. The personal information form was prepared based on the relevant literature by the researchers.

The Personal Information Form

The form consisted of 20 questions, including sociodemographic (such as age, gender, educational status, employment status, income status) and obstetric characteristics (such as number of pregnancies, number of deliveries, number of living children, miscarriage, curettage, pregnancy intendedness, place of last birth, evaluation of the last birth and suggestion of the last birth type to other pregnant women) of women. Also, this form includes six questions to examine the environmental comfort of women in the postpartum period.

Postpartum Comfort Scale

The "Postpartum Comfort Scale (PCS)" consists of 34 items and was developed by Karakaplan and Yıldız (2010) using a Turkish version of General Comfort Scale (22). As a result of factor analysis, subscales of the PCS include physical, psychospiritual, and sociocultural comforts. The environmental comfort subscale of the PCS was removed from this scale by the original author of this scale. However, the original author suggested that this subscale can be used as binary data (yes-no) if requested by the researchers. In this study, items related to environmental comfort were used as binary data (yes-no) in line with the author's suggestion. The PCS scale is a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). The lowest possible score is 34, and the highest possible score is 170. The mean score is obtained by dividing the total score by the total number of items, and it ranges from 1 to 5. Higher PCS scores indicate increased postpartum comfort level. The Cronbach's Alpha value of the scale was 0.78, and the scale was found to be reliable in terms of internal consistency (22). In current study, the PCS Cronbach Alpha value was 0.90.

Data Analysis

All of the data were evaluated using the Statistical Package for Social Sciences (SPSS 23.0) for Windows. An expert statistician contributed to the data analysis. The scale scores were normally distributed according to Kurtosis and Skewness Coefficients. The frequency, mean, standard deviation, and chi square were used for descriptive analyses; the Cronbach Alpha analysis was used to determine the reliability of the scale items; and multivariate linear regression and t test were used to compare the mean scale scores with other parameters. $p<0.05$ were considered significant.

RESULTS

There was no significant difference among the groups in terms of distribution of sociodemographic characteristics ($p>0.05$) (Table I). However, related to obstetric characteristics, there was a significant difference among the groups in terms of number of pregnancies, deliveries, and living children. This difference is most likely due to the fact that the women in the VBAC group in this study had to have had at least two deliveries in order for VBAC to occur (Table I).

Table I. Distribution of descriptive and obstetric characteristics according to birth type (N=150)

	CS* n=50 (%)	VB** n=50 (%)	VBAC*** n=50 (%)	Total n=150 (%)
Age				
20-25	10 (20)	6 (12)	4 (8)	20 (13.3)
26-30	18 (36)	19 (38)	21 (42)	58 (38.7)
31-35	15 (30)	16 (32)	22 (44)	53 (35.3)
36 and ↑	7 (14)	9 (18)	3 (6)	19 (12.7)
		χ^2=7.611, p=0.268		
Age $\overline{X}$±SD (min-max)	30.40±5.47 (21-47)	30.72±4.87 (20-43)	30.54±3.73 (23-40)	30.55±4.71 (20-47)
		F=0.057, p=0.944		
Education Level				
Primary school to High school	12 (24)	12 (24)	17 (34)	41 (27.3)
Graduate degree or higher	38 (76)	38 (76)	33 (66)	109 (72.7)
		χ^2=1.678, p=0.432		
Employment Status				
Employed	24 (48)	29 (58)	20 (40)	73 (48.7)
Unemployed	26 (52)	21 (42)	30 (60)	77 (51.3)
		χ^2=3.256, p=0.196		
Income Status				
Income is less than expense	10 (20)	7 (14)	7 (14)	24 (16)
Income is equal to expense	29 (58)	29 (58)	32 (64)	90 (60)
Income is greater than expense	11 (22)	14 (28)	11 (22)	36 (24)
		χ^2=1.450, p=0.835		
Number of Pregnancies				
1	20 (40)	22 (44)	0 (0)	42 (28)
2	15 (30)	17 (34)	36 (72)	68 (45.3)
3 or more	15 (30)	11 (22)	14 (28)	25 (16.7)
		χ^2=33.716, **p<0.001**		
Number of Deliveries				
1	30 (60)	29 (58)	0 (0)	59 (39.3)
2	16 (32)	16 (32)	45 (90)	77 (51.3)
3 or more	4 (8)	5 (10)	5 (10)	14 (9.4)
		χ^2=51.512, **p<0.001**		
Number of Living Children				
1	30 (60)	30 (60)	1 (2)	61 (40.7)
2	17 (34)	15 (30)	44 (88)	76 (50.7)
3 or more	3 (6)	5 (10)	5 (10)	13 (8.7)
		χ^2=48.900 **p<0.001**		
Miscarriage				
Yes	15 (30)	7 (14)	10 (20)	32 (21.3)
No	35 (70)	43 (86)	40 (80)	118 (78.7)
		χ^2=3.893, p=0.143		
Curettage				
Yes	9 (18)	6 (12)	6 (12)	21 (14)
No	41 (82)	44 (88)	44 (88)	129 (86)
		χ^2=0.997, p=0.608		
Pregnancy intendedness				
Planned pregnancy	39 (78)	34 (68)	39 (78)	112 (74.7)
Unplanned pregnancy	9 (18)	13 (26)	11 (22)	33 (22)
Unwanted pregnancy	2 (4)	3 (6)	0 (0)	5 (3.3)
		χ^2=3.974, p=0.410		
Place of Last Birth				
Private Hospital	35 (70)	40 (80)	43 (86)	118 (78.7)
Public Hospital	15 (30)	10 (20)	7 (14)	32 (21.3)
		χ^2=3.893, p=0.143		

*CS: Cesarean Section, **VB: Vaginal Birth, ***VBAC: Vaginal Birth After Cesarean

A total of 60.7% of women identified their last birth as an "easy birth," and 64% would 'probably' suggest their birth type to other pregnant women. There was a significant difference among the groups in terms of 'easiness' of last birth (x^2=6.929, p=0.031) and suggestion of the last birth type to other pregnant women (x^2=80.441, p<0.001). The VBAC group had significantly more positive evaluations of their births than the other groups. The women in the VBAC group perceived their birth type as an easy birth with the highest rate (70%) and stated with the highest rate (92%) that they would suggest their birth type to other pregnant women (Table II).

According to the multiple linear regression analysis conducted by considering CS point averages as fixed, compared to CS the postpartum comfort scale total scores of women who gave VB (Beta=0.372, t=4.465, p<0.001) and VBAC (Beta=0.548, t=6.571, p<0.001) respectively. Birth type explains 24% of this variability (Adjusted R2=0.224) in the postpartum comfort scale total score (F=22.515, p<0.001). It was found that in physical comfort subscale, women who gave VB (Beta=0.424, t=5.060, p<0.001) and VBAC (Beta=0.513, t=6.127, p<0.001) respectively had higher comfort levels compared to CS. Birth type explains 21.5 % (Adjusted R2=0.215) of this change in the physical comfort subscale score (F=21.429, p<0.001). Regarding psychospiritual comfort, which is another sub-dimension, the comfort levels of women who gave VB (Beta=0.195, t=2.245, p=0.026) and VBAC (Beta=0.470, t=5.401, p<0.001) were found to be higher than caesarean respectively and it may be asserted that 15.6 % (Adjusted R2=0.156) of this difference stems from birth type (F=14.726, p<0.001). Finally, for sociocultural comfort subscale, when the point average of women who have experienced CS is kept fixed as in the other sub-dimensions, it is found that women who give VB (Beta=0.252, t=2.828, p<0.001) and VBAC (Beta=0.400, t=4.488, p<0.001) respectively have higher comfort levels compared to CS and 11.1% (Adjusted R2=0.111) of this difference is explained with birth type (F=10.299, p<0.001) (Table III).

Table II. Women's difficulty perception of the last birth and their suggestion to other pregnant women

	CS* n=50 (%)	VB** n=50 (%)	VBAC*** n=50 (%)	Total n=150 (%)
Evaluation of the Last Birth				
Easy	23 (46)	33 (66)	35 (70)	91 (60.7)
Hard	27 (54)	17 (34)	15 (30)	59 (39.3)
		χ^2=6.929, **p=0.031**		
Suggestion of the Last Birth Type to Other Pregnant Women				
Yes	8 (16)	42 (84)	46 (92)	96 (64)
No	33 (66)	4 (8)	1 (2)	38 (25.3)
Partly	9 (18)	4 (8)	3 (6)	16 (10.7)
		χ^2=80.441, **p<0.001**		

*CS: Cesarean Section, **VB: Vaginal Birth, ***VBAC: Vaginal Birth After Cesarean

Table III. Regression results of the mean PCS total score and the mean subscale scores according to birth type

	Unstandardized Coefficients Beta	Std. Error	Standardized Coefficients Beta	t	Sig.
PCS Total Score (F=22.515, Adjusted R^2= 0.224, **p=0.000)**					
CS*(Constant)	109.020	2.331		46.770	**0.000**
VB**	14.720	3.296	0.372	4.465	**0.000**
VBAC***	21.660	3.296	0.548	6.571	**0.000**
Physical Comfort Subscale Score (F=21.429, Adjusted R^2= 0.215, **p<0.001)**					
CS*(Constant)	40.760	1.246		32.702	**0.000**
VB**	8.920	1.763	0.424	5.060	**0.000**
VBAC***	10.800	1.763	0.513	6.127	**0.000**
Psychospiritual Comfort Subscale Score (F=14.726, Adjusted R^2= 0.156, **p<0.001)**					
CS*(Constant)	39.180	.636		61.580	**0.000**
VB**	2.020	.900	0.195	2.245	**0.026**
VBAC***	4.860	.900	0.470	5.401	**0.000**
Sociocultural Comfort Subscale Score (F=10.299, Adjusted R^2= 0.111, **p<0.001)**					
CS*(Constant)	29.080	.945		30.764	**0.000**
VB**	3.780	1.337	0.252	2.828	**0.005**
VBAC***	6.000	1.337	0.400	4.488	**0.000**

*CS: Cesarean Section, **VB: Vaginal Birth, ***VBAC: Vaginal Birth After Cesarean

There were no significant differences among groups in terms of finding the room quiet, the temperature adequate, the bed comfortable, and feeling safe in the postpartum period (respectively, p=0.092, p=0.318, p=0.268, p=0.168). However, there were significant differences among groups in terms of room ventilation and opportunity for relatives/friends to visit in the postpartum period (respectively, p=0.004 and p=0.014). These environmental comfort levels were higher in women with VBAC and VB compared to women with CS (Table IV).

Table IV. Distribution of responses of women to environmental comfort variables according to birth type

Postpartum	CS* n=50 (%)	VB** n=50 (%)	VBAC*** n=50 (%)
Finding the room quiet	38 (76)	42 (84)	46 (92)
		χ^2=4.762, p=0.092	
Finding the room temperature adequate	46 (92)	44 (88)	41 (82)
		χ^2=2.290, p=0.318	
Finding the room ventilation adequate	30 (60)	32 (64)	44 (88)
		χ^2=11.063, **p=0.004**	
Finding the bed comfortable	36 (72)	36 (72)	42 (84)
		χ^2=2.632, p=0.268	
Feeling safe	40 (80)	40 (80)	46 (92)
		χ^2=3.571, p=0.168	
Opportunity for relatives/friends to visit after birth	45 (90)	40 (80)	49 (98)
		χ^2=8.535, **p=0.014**	

*CS: Cesarean Section, **VB: Vaginal Birth, ***VBAC: Vaginal Birth After Cesarean

DISCUSSION

This study is unique in investigating the effects of birth types, including VB, CS, and VBAC, on postpartum comfort. In current study, postpartum comfort level was highest in VBAC, followed by VB and finally CS. One study has supported that birth types affect postpartum comfort levels, and that the postpartum comfort levels of women with VB are higher than those of women with CS (26). This study included women who underwent VBAC; these women are able to compare factors affecting postpartum comfort with their prior experiences with CS and VB. It has been reported that women delivering via VBAC experience less pain and less postpartum complications, such as delayed mobilization, constipation, and engorgement (27). Previous studies have also shown that mother-baby interaction and bonding are achieved in a shorter period with VBAC compared to CS, and that this enhanced the adaptation to maternity and the postpartum period (27-29). The results of qualitative studies emphasize that women with VBAC have a readiness for with VBAC have a readiness for with VBAC had a readiness for delivery and postpartum satisfaction experiences (27,29,30).

Results of the current study revealed a significant difference in terms of the mean physical comfort scores and the physical comfort level of the three groups. The VBAC group had the highest scores, followed by the VB group, and finally, the CS group. The first subscale of comfort theory (physical comfort associated with bodily perceptions) consists of physiological factors such as rest and relaxation, which are known to affect an individual's physical condition, responses to disease, nutrition and homeostasis, and bowel function continuity (10). The results of the current study were similar to those of other Turkish studies, in particular, that the physical comfort levels of women with VB were higher than those of women with CS (8,9). Women experiencing VBAC and VB are known to mobilize faster and be more independent than women with CS. Further, women undergoing VBAC and VB also experience less postpartum complications than those with CS. That women who have experienced VB have these problems, which affect physical comfort in a less ratio and severity compared to women who have experienced CS is also supported by international literature. It was also found that women who experience VB have less severe afterpain, less risk of surgical complication, less gastrointestinal problems, higher level of physical activity and that they get discharged in a shorter span of time compared to CS (14,16,17). The results of current study support the literature, which suggests that these factors improve postpartum comfort.

The psychospiritual comfort sub-dimension of the scale involves postpartum woman's psychological well-being, positive relationship with the newborn and perceived social support. In this study, women's psychospiritual comfort levels were respectively found to be the highest for VBAC, VB and CS. Similarly, the qualitative studies on the experiences of women after VBAC indicate that women psychologically feel better and stronger and that newborn-maternal relationship is more positive compared to CS (27-30). Additionally, in a current study, it was found that women's maternal well-being level is affected by the birth type in the postpartum period, that the well-being level of women who experience VB is higher than that of those who experience CS and that the risk of postpartum depression is less for women who experience VB (31). It is observed that women who gave VB have a more positive birth experience and that their perceptions regarding

the care provided by healthcare professionals, themselves and the newborn is more positive (32-34).

In the current study, there was a significant difference among birth types in terms of environmental comfort (i.e., room ventilation and opportunities for relatives/friends to visit). Women with VBAC reported that they were more satisfied with these parameters compared to those with VB and CS. Environmental comfort is the last subscale of postpartum comfort. It positively contributes to the recovery process and makes women feel good, which can be considered a sign of postpartum healthcare and social support (10). It was reported that the environmental comfort level of women with VB was higher than that of women with CS, whereas no difference was detected in the environmental comfort levels among women with different birth types (9,25). However, these studies had no data associated with the type of hospital where the deliveries took place. In our current study, the majority of women gave birth in private hospitals. We suggest that the difference in the women's perceptions about environmental comfort in our current study is due to the more flexible visiting hours and special care for room ventilation in private hospitals.

Limitations

The current study has several limitations. According to our data analysis, the PCS scale was divided into three factors, and the items on the environmental comfort scale were included in the sociocultural subscale. Therefore, the PCS could only measure environmental comfort in a limited sense. Data collection on the online platform has enabled access to women with higher education levels. Therefore, the findings of the study can be generalized to women with a high level of education. Also in the current study, we did not examine the postpartum comfort levels of women with or without episiotomy in VB and VBAC, because vaginal births mostly involve intervention and the rate of episiotomy in our country is 87.5% (35). Moreover, we did not examine the anesthesia type in CS. Further, the evaluation of hospital type (i.e., public and private) on comfort level may not be accurate, as the majority of participants gave birth in private hospitals.

CONCLUSION

Current study indicates that women with VBAC had higher postpartum comfort levels than those experiencing VB and CS. The highest postpartum comfort level achieved in the VBAC group is an important finding for healthcare professionals. It should be suggested that women's postpartum comfort should be periodically evaluated, and that regulations should be made based on the results. Measurement tools used in the current study should be used for this purpose. We also propose that future studies compare the postpartum comfort levels of women from different sampling groups (e.g., public hospitals). In addition, qualitative studies investigating postpartum comfort levels are also recommended.

Acknowledgement

We would like to express our gratitude to Prof. Dr. Mehmet Ziya Fırat, an expert statistician, for his contribution to data analysis. Also, we would like to thank to all of the women involved in this study for sharing their private and valuable experiences, as they have made important contributions to nursing science.

Informed Consent:

Approval was also obtained from the administrators of the social media platform used in this study. The participants were informed about the purpose of the study prior to providing informed consent with forms prepared according to the Helsinki Declaration.

Author Contributions:

Concept - İB, MA; Design - İB, HY, MA, AA; Supervision - İB, HY; Resources - İB, HY, MA, AA; Materials - İB, HY, MA, AA; Data Collection - MA, AA; Analysis and Interpretation - AA, İB; Literature Search - İB, HY, MA, AA; Writing Manuscript - MA, AA; Critical Review - İB, HY.

Conflict of Interest:

The authors have no conflict of interest to declare.

Financial Disclosure:

The authors declared that this study has received no financial support.

Presented Congress:

Only, a brief abstract of this study was presented verbally at 1st International 3rd National Childbirth Education and Educators Congress on 18-21 October 2018 in Turkey.

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ORIGINAL ARTICLE
Özgün Araştırma

The Reference Diameters of the Three Great Vessels in the Fetuses Between 20-24 Weeks by Sonography

Sonografide 20-24 Hafta Arasındaki Fetüslerde Üç Büyük Damarın Referans Çapları

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Geliş Tarihi : October 22, 2021
Received
Kabul Tarihi : May 16, 2022
Accepted
E Yayın Tarihi : September 01, 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Aksoy C, Simsek A, Ozgur O, Durmaz E, Apaydın A, Sindel H.T.
The Reference Diameters of the Three Great Vessels in the Fetuses Between 20-24 Weeks by Sonography
Akd Med J 2023; 9(3): 241-246

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DOI: 10.53394/akd.1009966

ABSTRACT

Objective:

We aimed to obtain reference values of three major vessels [Pulmonary artery (PA), aorta, superior vena cava (SVC)] diameters in fetuses between 20-24 weeks of gestation in the Turkish population and to evaluate the fetal heart anatomy.

Material and Methods:

Pregnant women who were evaluated in the Radiology Department were scanned by sonography in order to obtain fetal cardiac nomograms of the great vessels. Cardiac axis, size and three great vessels in addition to the four chamber view of the heart were evaluated. The cases were followed up postnatally with echocardiography and clinical evaluation. We calculated both the sensitivity and specificity of sonographic screening at the 20-24th gestational weeks. Also, we found the frequency of congenital cardiac disease. Nomograms were obtained by calculating average vascular diameter for each gestational week.

Results:

A total of 371 fetuses were evaluated in the sudy. The mean gestational age was 29.2±5.2. The mean diameters of PA, aorta and SVC were found as 4.28±0.51 mm, 3.70±0.54 mm, 2.45±0.45 mm, res- pectively. The ratio of PA/aorta was 1.17±0.14. The mean diameters of PA, aorta and SVC increased gradually between 20 and 24 gestational weeks (p values 0.001, 0.007 and 0.001; repeated measures ANOVA). In five cases a cardiac anomaly was detected (tetralogy of Fallot, one atrium one ventricle anomaly, ASD, PA wider than normal, aorta wider than normal,) sonographically. Of these five, three cases were confirmed by postnatal fetal echocardiography performed by pediatric cardiologists.

Conclusions:
This study represents the reference values for diameters of three great vessels of fetuses between 20 and 24 weeks in the Turkish population. The data obtained from our study will be a reference for future studies from our country.

Key Words:
Congenital heart disease, Ultrasonography, Prenatal screening

ÖZ
Amaç:
Fetal kalp anatomisini değerlendirmek ve Türk popülasyonunda 20-24 hafta arasındaki fetüslerde üç ana damar [Pulmoner arter (PA), aorta, vena kava süperior (VKS)] çaplarının referans değerlerini saptamayı amaçladık.

Gereç ve Yöntemler:
Radyoloji Bölümünde değerlendirilen gebelere fetal kardiyak büyük damarların nomogramlarının elde edilmesi için sonografik tarama yapıldı. Kalbin dört odacık görünümüne ek olarak kardiyak aks, boyut ve üç büyük damar değerlendirildi. Olgular postnatal olarak ekokardiyografi ve klinik değerlendirme ile takip edildi. Postnatal değerlendirme sonuçları temel alınarak 20-24. gebelik haftalarında yapılan sonografik taramanın duyarlılığı ve özgüllüğü hesaplandı. Ayrıca konjenital kalp hastalığı sıklığı araştırıldı. Her gebelik haftası için ortalama damar çapı hesaplanarak nomogramlar elde edildi.

Bulgular:
Çalışma kapsamında toplam 371 fetüs değerlendirildi. Ortalama gebelik yaşı 29,2±5,2 yıldı. PA, aorta ve VKS ortalama çapları sırasıyla 4,28±0,51 mm, 3,70±0,54 mm ve 2,45±0,45 mm olarak bulundu. PA/aort oranı 1,17±0,14 idi. PA, aort ve VKS'nin ortalama çaplarının 20 ila 24 gebelik haftaları arasında kademeli olarak arttığı gözlendi (p değerleri 0,001, 0,007 ve 0,001). Sonografik olarak antenatal dönemde beş olguda kardiyak anomali (Fallot tetralojisi, tek atriyum tek ventrikül anomalisi, ASD, normalden geniş PA, normalden geniş aorta) tespit edildi. Beş vakadan üçünün tanısı doğum sonrası dönemde pediatrik kardiyologlar tarafından yapılan fetal ekokardiyografi ile doğrulandı.

Sonuç:
Bu çalışma, 20-24 gestasyon haftasındaki fetüslerde üç büyük damar çapı için Türk popülasyonuna ait referans değerleri sunmaktadır. Çalışmamızdan elde edilen veriler ülkemizden yapılacak çalışmalar için referans oluşturacaktır.

Anahtar Sözcükler:
Konjenital kalp hastalığı, Ultrasonografi, Prenatal tarama

INTRODUCTION
Second trimester sonographic examination is very important in preventing neonatal morbidity and mortality due to congenital cardiac anomalies (1). Congenital heart disease (CHD) is the most common congenital anomaly, the incidence of CHD range from 4 / 1,000 to 50 / 1,000 live births in different studies (2). One fourth of newborns with congenital heart disease have an increased morbidity and mortality rate (3). Detection of congenital cardiac anomalies in the fetal period will provide a chance for treatment and intervention for these patients (4). Current screening technique includes four-chamber, right ventricular outflow tract, and left ventricular outflow tract views. The three-vessel view is also often used in screening. These views are essential for a complete evaluation of the fetal heart (5,6). Previous studies claimed that four-chamber view was sufficient for detecting fetal congenital structural abnormalities (6-9). Using four-chamber view, the rate of CHD diagnosis was about 60%, which was less than expected (7-10). In some CHD, such as Tetralogy of Fallot and transposition of the great vessels, it cannot be detected by the four-chamber view (9,10).
Wong et al., explained that 86% CHD can be detected using the three-vessel viewing plane of the main vessels [pulmonary artery (PA), aorta, superior vena cava (SVC)] and the PA/aorta ratio (11). In the second trimester fetal cardiac screening, it is recommended to add the measurement of anatomical structures in addition to subjective assessments in cardiac examination. The nomograms of the diameters of three vessels in the second trimeste are very important because abnormal measurements are a clue in the diagnosis of heart diseases. In our unit, we perform fetal cardiac examinations between 20 and 24 weeks of gestation. Thus, we aimed to conduct a prospective study to reveal the nomograms of the three great vessels corresponding to each week in the fetuses between 20-24 gestational weeks by sonography.

MATERIAL and METHODS
Study design
Four hundred thirty-nine pregnant women who applied to our Radiology department for routine fetal organ screening were included in the study. Among these patients, those who were followed up during the fetal and postpartum periods and those who stated in written form they participated in the study were included in the study. Exclusion criteria were as follows: etuses with cardiac anomaly, fetuses with chromosomal anomaly, fetuses with extra cardiac anomaly, fetuses whose mothers had cardiac disease history, fetuses whose brothers had fetal cardiac anomaly history and multi-parity. Also, pregnant women who had an inconsistency between the gestational age calculated according to the last menstrual period and the gestational age obtained according to ultrasound measurements were excluded from the study. Approval was obtained from the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (Decision Number: 01/22, date:08.01.2013). The study was conducted in accordance with the Helsinki Declaration. All pregnant women included in the study were informed and signed voluntary consent forms were obtained.

After excluding 33 pregnant women without regular follow-up, were included in the study. In five cases a cardiac anomaly was detected (tetralogy of Fallot, one atrium one ventricle anomaly, ASD, PA wider than normal, aorta wider than normal,) sonographically. Of these five, three cases were confirmed by postnatal fetal echocardiography performed by pediatric cardiologists. These 5 patients with cardiac anomaly were excluded from the study.

The study was continued with 371 pregnant women. The pregnant women were evaluated in 20-24 weeks of gestation according to their menstruation age. All patients were re-evaluated with clinic and echocardiographic indings in the postnatal period.

Imaging method

Ultrasonography (US) images were obtained in three-vessel view. Technically we found first four-chamber view in transaxial plane which is perpendicular to the long axis of the fetus. From four-chamber view, we moved slightly the transducer on the patient without changing angle toward the fetal head. When we saw three-vessels in line with each other in the order of largest PA to smallest SVC, we froze the image to take measurements of vessel diameter parallel to the anterior thoracic wall or perpendicular to the fetal ribs. In addition, PA/aorta ratio was calculated (Figure 1).

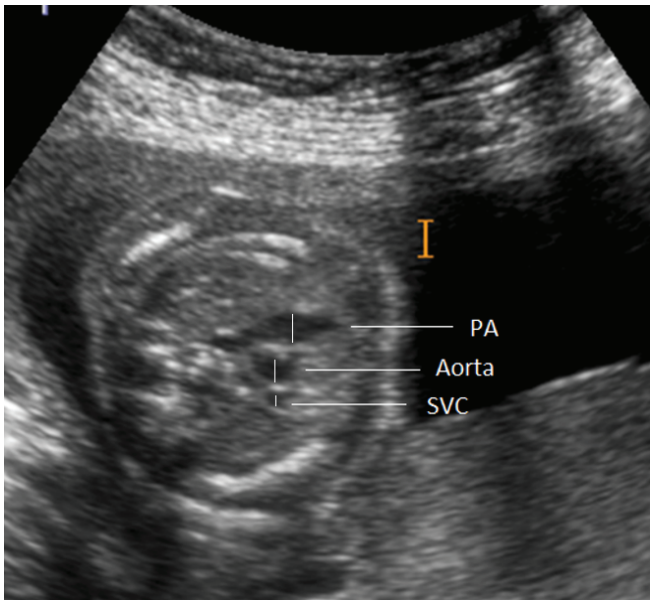

Figure 1: Pulmonary artery (P) and aorta (A) and SVC measurement, showing the appearance of three-vessels view in the transverse plane of the fetal thorax.

One of the radiologists had ten years of experience for fetal imaging. The other radiologist had 5 years of experience for general radiology. The US reports and images of all patients were enrolled for follow-up by the same radiologists to our digital US archive (Tomtec Imaging Systems, version 2.7, Munich, Germany).

Statistical Evaluation

Linear regression analyses was used to generate nomograms. Descriptive statistics were presented as frequency, percentage, mean, standard deviation (SD) and 95% CI. The Shapiro Wilk test, histogram and Q-Q graphics were used for evaluation of normality of distribution. The Fisher's Exact Test was used in the analysis of relationships between categorical variables. Diameters of PA, aorta, SVC and PA/aorta ratio were compared between gestational weeks using repeated measures ANOVA. Comparison between two different groups was performed through two independent samples T-Test and comparison between more than two groups was performed with Kruskal-Wallis analysis. The statistical analyses were performed by using the SPSS version 21.0 package program for Windows (IBM, Armonk, NY). $p<0.05$ were accepted significant to show statistical significance.

RESULTS

A total of 371 pregnant women with mean age of 29.2±5.2 years were included in the study. In 371 fetuses between 20-24 weeks, the mean diameters of PA, aorta and SVC were found as 4.28±0.51mm (95% CI: 4.23-4.34; range 2.6–5.6); 3.70±0.54 mm (95% CI: 3.64-3.76; range 2.0-5.2); 2.45±0.45 mm (95% CI: 2.41-2.50; range 1.6-3.8) respectively (Table I).

Table I: The mean diameters of PA, aorta and SVC and PA/aorta ratio in the fetuses between 20-24 gestational weeks (n: 371).

Variable	Min.	Max.	Mean and SD	95% CI
PA	2.60	5.60	4.28 (±0.51)	4.23-4.34
Aorta	2.00	5.20	3.70 (±0.54)	3.64-3.76
SVC	1.60	3.80	2.45 (±0.45)	2.41-2.50
PA / aorta	0.98	1.95	1.17 (±0.14)	1.15 – 1.18

PA: Pulmonary artery SVC: Superior vena cava. The ratio of PA/aorta was 1.17±0.14 (95% CI: 1.15 – 1.18; range 0.98-1.95). In each screening week between 20 and 24, you can find the diameters of PA, aorta, SVC and PA/aorta ratio in Figure 2-5 and Table II.

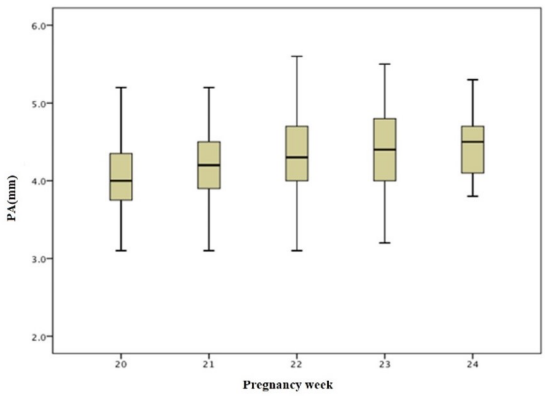

Figure 2: The values of PA according to gestational age in normal 371 cases (p: 0.001).

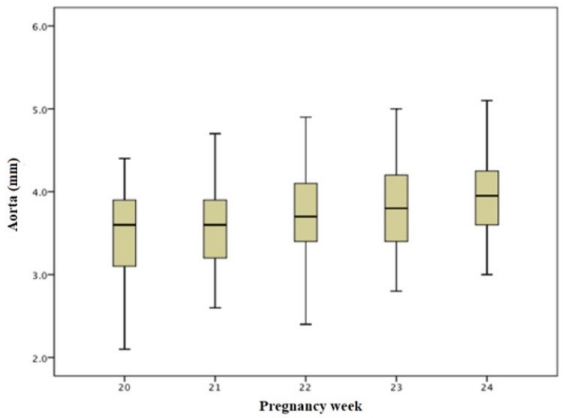

Figure 3: The values of aorta according to gestational age in 371 normal cases (p: 0.007).

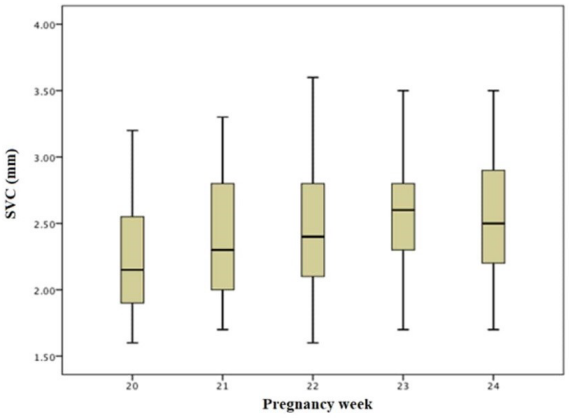

Figure 4: The values of SVC according to gestational age in 371 normal cases (p: 0.001).

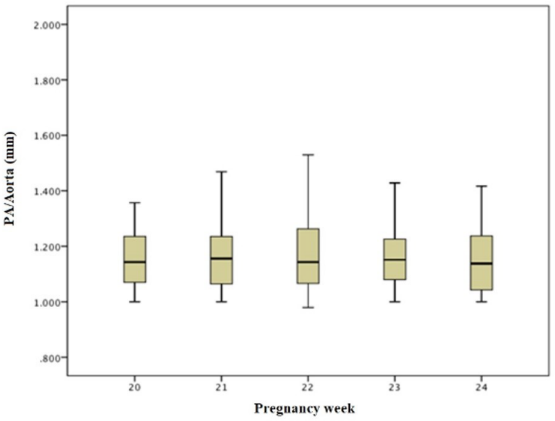

Figure 5: The values of Pa/aorta according to gestational age in normal 371 cases (p: 0.961).

Table II. The mean diameters of PA, aorta and SVC, and PA/aorta ratio of 371 fetuses with regular follow-up according to gestational age.

——	Gestational age (weeks)	n (371)	Min.	Max.	Mean and SD	95% CI	P
PA	20	40	2.6	5.2.	4.00 ±0.53	3.83-4.17	0.001
	21	65	2.7	5.2	4.19 ±0.50	4.07-4.32	
	22	143	2.6	5.6	4.30 ±0.50	4.22-4.39	
	23	79	3.2	5.5	4.38 ±0.49	4.27-4.49	
	24	44	2.7	5.3	4.44 ±0.47	4.29-4.58	
Aorta	20	40	2.1	4.4	3.48 ±0.54	3.31-3.66	0.007
	21	65	2.6	4.7	3.61 ±0.53	3.48-3.74	
	22	143	2.0	5.2	3.70 ±0.53	3.61-3.79	
	23	79	2.8	5.0	3.79 ±0.53	3.67-3.91	
	24	44	2.6	5.1	3.88 ±0.54	3.71-4.04	
SVC	20	40	1.6	3.2	2.26 ±0.42	2.12-2.40	0.001
	21	65	1.7	3.3	2.37 ±0.41	2.27-2.47	
	22	143	1.6	3.6	2.45 ±0.45	2.37-2.52	
	23	79	1.7	3.6	2.57 ±0.44	2.49-2.68	
	24	44	1.7	3.5	2.54 ±0.47	2.39-2.68	
PA/ aorta	20	40	1.16	1.53	1.16 ±0.12	1.12-1.19	0.961
	21	65	1.00	1.65	1.17 ±0.13	1.14-1.20	
	22	143	0.98	1.95	1.17 ±0.15	1.15-1.20	
	23	79	1.00	1.50	1.16 ±0.11	1.14-1.19	
	24	45	1.00	1.58	1.15 ±0.13	1.11-1.19	

The mean diameters of PA, aorta and SVC were increasing gradually between 20 and 24 gestational weeks (p values 0.001, 0.007 and 0.001; repeated measures ANOVA). But PA/aorta ratio was stable between 20-24 gestational weeks (p: 0.961, repeated measures ANOVA).

The great vessel diameters in fetuses of mothers older than 35 years were similar to those of mothers younger than 35 years (p: 0.559 for PA, p: 0.940 for aorta, p: 0.695 for SVC, samples T-Test).

DISCUSSION

During second trimester, screening US should include a comprehensive examination of fetal organs. When it comes to fetal heart, radiologists are not so eager to perform detailed screening. Because in many centers, radiologists think cardiac evaluation is not so easy and requires a special experience.

Because in many center, radiologists think cardiac evaluation is not so easy and requires a special experience: cardiac axis, size, rhythm, four chamber view and finally three vessel evaluation by size. Of course subjective evaluation under experience is a part of cardiac examination of fetal screening. Adding three vessel view evaluation to screening will help to detect more CHD prenatally. In the study of Bromley et al, the frequency of CHD obtained using the four-chamber view was 63%, while the three-vessel view was added to the examination and the frequency increased to 83% (11).

In our study, we evaluated the nomograms of three-vessel diameters between 20-24 weeks of gestation. The mean diameters of PA, aorta and SVC was 4.28±0.51mm, 3.70±0.54mm and 2.45±0.45 mm, respectively. Kenny et al., revealed the nomograms of PA and aorta diameters at 19-40 weeks of gestation, and PA diameter was 12% larger than aorta diameter (12). Cartier et al., obtained nomograms of PA and aorta diameters at 16-40 weeks of gestation according to gestational week and biparietal diameter (13). Also, Achiron et al., obtained nomograms of PA and aorta diameters at 16-24 weeks of gestation according to gestational week (14).

We evaluated PA, aorta and SVC separately according to gestational weeks and it was found that the diameter of all three vessels increased as the gestational week increases. In 2004, Zalel et al., evaluated three vessel diameters at 14-38 weeks of gestation and formulated weekly increases for easy applicability after determining normal values separately for weeks; PA diameter (mm) = −2.275+0.273×gestation week, Aorta diameter (mm) = −1.77+0.227×gestation week and SVC diameter (mm) = −0.98 +0.142×gestation week (15).

In our study, we also calculated the PA/aorta ratio, and we noticed that this ratio did not change between 20 and 24 weeks. The ratio of PA/aorta was 1.17±0.14 (95% CI: 1.15–1.18; range 0.98-1.95). Similarly, Wong et al., found the PA/aorta ratio as 1.16±0.18, and stated that this rate was stable at 16-24 weeks of gestation (11). Determining the normal reference values for three vessel diameters will set a reference for other studies to be conducted in our country. In our point of view, the most useful value that can be helpful in cardiac sonography, is the stable PA/aorta ratio during second trimester. Because the nomograms of great vessel diameters may result in different values in different nations.

We included only 20 to 24 weeks pregnant women in our study in order to see better cardiac anatomical structures. However cardiac screening is most appropriately performed between 18 and 22 weeks (16). It should be kept in mind that especially valvular anomalies can be detected in the following gestational weeks (17). Therefore, in Japan, in addition to the second trimerster evaluation, a cardiac examination is repeated at the 30th gestational week (17).

This study has some limitations. Since the number of the study population was limited and our cases were not randomized, our results didn't reflect whole national population.

CONCLUSION

Our results will be a reference in the fetuses between 20 and 24 weeks during cardiac sonography. Also we found that the ratio PA/aorta was stable between 20-24 gestational weeks with the value of 1.17. We think that this ratio can be used as a reference value, if the radiologist finds very questionable diameters in PA or aorta.

Ethics Committee Approval:

Ethics commitee approval was received from the Ethics Committee of Akdeniz University Medical Faculty for this study (Decision Number: 01/22, date:08.01.2013). The study was conducted in accordance with the Helsinki Declaration.

Informed Consent:

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:

Concept– C.A.; Design – A.A.; Supervision – E.D.; Funding-Akdeniz university scientific research Project; Materials – C.A.; Data Collection and/or Processing-C.A.; Analysis and/or Interpretation – Ö.Ö.; Literature Review – A.A.; Writing – C.A.; Critical Review – T.S.

Conflict of Interest:

The authors have no conflicts of interest to declare.

Financial Disclosure:

Akdeniz University Scientific Research Projects Coordination Unit. Project number: 2011.04.0103.030

Presented Congress:

European Congress of Radiology ECR 2015, Vienna, Austria, 4 -08 March 2015. Presented as a poster presentation.

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ORIGINAL ARTICLE
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Geliş Tarihi : October 20, 2021
Received
Kabul Tarihi : February 13, 2022
Accepted
E Yayın Tarihi : September 01, 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Evlice B, Duyan H, Guner Akgul I, Uri A.
Use of Cone-Beam Computed Tomography in Pediatric Patients in a Turkish Dental School
Akd Med J 2023; 9(3): 247-252

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DOI: 10.53394/akd.1012417

Use of Cone-Beam Computed Tomography in Pediatric Patients in a Turkish Dental School

Bir Türk Diş Hekimliği Fakültesinde Çocuk Hastalarda Konik-Işınlı Bilgisayarlı Tomografi Kullanımı

ABSTRACT

Objective:

The purpose of the present study was to provide information that might help in planning cone-beam computed tomography (CBCT) imaging in pediatric patients. This study focused on the evaluation of indications for CBCT in pediatric patients in a Turkish dental school.

Material and Methods:

Six-hundred-seven CBCT scans belonging to patients under the age of 16 were included in this study. The following data were recorded from an electronic patient database: Age, gender, indication for referral (impacted teeth, supernumerary teeth, trauma, cysts/tumors, clefts, temporomandibular joint, and other reasons), dispersion of referrals by departments, external or internal referral.

Results:

Mean age was 12.39 years [range: 4-16; 260 females (42.8%) and 347 males (57.2%)]. The most frequent and largest age group (54.2%) was 13- to 16-years old. The most frequent request was to assess an impacted tooth and its localization (38.2%). Examining the FOVs, the maxilla was the most frequently imaged area (27.2%). Four-hundred sixty-six patients (76.8%) had been referred from departments of the dental school while 141 (23.2%) patients were referred from external clinics. Re-exposure was required in 52 cases (8.6%) due to patient-motion artefacts.

Conclusion:

The results of the present study can help dental professionals make the decision to refer for CBCT when extra three dimensional imaging is necessary for a pediatric patient. It is proper that an oral and maxillofacial radiologist decides when CBCT is necessary and then supervises the CBCT scanning protocol to minimize the radiation dose to pediatric patients.

Key Words:

Cone-beam computed tomography, Indication, Maxillofacial radiology, Pediatric dentistry

ÖZ

Amaç:

Bu çalışmanın amacı, çocuk hastalarda konik-ışınlı bilgisayarlı tomografi (KIBT) görüntülemenin planlanmasına yardımcı olabilecek bilgiler sağlamaktır. Bu çalışma, bir Türk diş hekimliği fakültesindeki çocuk hastalarda KIBT endikasyonlarının değerlendirilmesini amaçlamaktadır.

Gereç ve Yöntemler:
Bu çalışmaya 16 yaş altı hastalara ait 607 KIBT taraması dahil edildi. Aşağıda sıralanan veriler, elektronik hasta veri tabanından kaydedildi: Yaş, cinsiyet, sevk endikasyonu (gömülü dişler, süpernümere dişler, travma, kistler/tümörler, yarıklar, temporomandibular eklem ve diğer nedenler), sevklerin bölümlere göre dağılımı, dış veya iç sevkler.

Bulgular:
Ortalama yaş 12,39 idi [Yaş aralığı: 4-16; 260 kadın (%42,8) ve 347 erkek (%57,2)]. En sık ve en büyük yaş grubu (%54,2) 13-16 yaş aralığıydı. En sık talep nedeni gömülü diş ve lokalizasyonunun değerlendirilmesiydi (%38,2).
FOV'lar incelendiğinde en sık görüntülenen alan maksillaydı (%27,2). Dört yüz altmış altı hasta (%76,8) diş hekimliği fakültesi bölümlerinden, 141 hasta (%23,2) dış kliniklerden sevk edilmişti. Hasta hareket artefaktları nedeniyle 52 olguda (%8,6) yeniden çekim yapılmıştı.

Sonuç:
Bu çalışmanın sonuçları, diş hekimlerinin çocuk hastada ekstra üç boyutlu görüntüleme gerektiğinde KIBT'ye başvurma kararını vermelerine yardımcı olabilir. Bir oral ve maksillofasiyal radyoloğun KIBT'nin ne zaman gerekli olduğuna karar vermesi ve ardından çocuk hastalarda radyasyon dozunu en aza indirmek için KIBT tarama protokolünü denetlemesi uygun olacaktır.

Anahtar Sözcükler:
Konik-ışınlı bilgisayarlı tomografi, Endikasyon, Maksillofasiyal radyoloji, Çocuk diş hekimliği

INTRODUCTION
Cone-Beam Computed Tomography (CBCT) is an advanced imaging technique that provides three-dimensional imaging of dental and maxillofacial tissues. CBCT, which ensures a lower dose and a lower-cost alternative to conventional computed tomography (CT), is increasingly used in oral and maxillofacial radiology practice, especially in dental schools (1-3).
Paediatric patients refer to the dental clinics with various complaints and in specific conditions radiological examinations are needed to diagnose the source of the problems. To avoid unnecessary radiological applications, the radiological examination should not be requested without taking the patient's anamnesis and detailed clinical examination. In some cases where a complete diagnosis cannot be made with conventional x-ray techniques, it may be necessary to resort to advanced imaging methods such as CBCT.
Children are more susceptible to ionizing radiation risks because their tissues grow at a faster rate. Therefore they are more undefended to DNA damage and other changes (4,5). The European DIMITRA Project (dentomaxillofacial paediatric imaging: an investigation toward low-dose radiation induced risks- www.dimitra.be) is part of a project for the development of patient-specific and indication-oriented recommendations for the use of CBCT in pediatric dentistry. DIMITRA project is focused on optimizing pediatric doses. The DIMITRA consortium has recently proposed to move from ALARA (As Low as Reasonably Achievable) and ALADA principles (As Low as Diagnostically Acceptable) to ALADAIP principle (As Low as Diagnostically Acceptable being Indication-oriented and Patient-specific) (6). So a convenient CBCT-scanning protocol must be developed to minimize the radiation dose to pediatric patients. In turn to do this, it is important to determine why CBCT is currently being used.
In the literature, there are many studies on the reasons for the requests of CBCT including all age groups (7-10). However, only a few studies were found related to indications of CBCT utilization in paediatric dentistry (11-13). The main aim of the present study was to investigate the indications being used for recommending a CBCT examination of pediatric patients in a Turkish dental school. Other aims were to determine the dispersions of departments sending referrals for CBCT imaging, the ages and genders of the patients, fields of view (FOV) size of the CBCT scans, and presence of a repeated x-ray exposure.

MATERIAL and METHODS
The Ethical Committee of Cukurova University's Medical School approved the study (approval number: 89/14.06.2019-77). CBCT scans of 607 patients under the age of 16 who underwent CBCT imaging in the Oral and Maxillofacial Radiology Department of Cukurova University's Dental School during May 2015- December 2019 composed the study sample.
CBCT unit was a Planmeca® ProMax 3D Mid (Helsinki, Finland). Pediatric patients' CBCT images were scanned at six sets of FOV (width x height in mm): For face (200 x 170); for jaws (maxilla and mandible) (200 x 100); for maxilla (200 x 60); for mandible (200 x 60); for teeth (100 x 60) and for tooth (40 x 80). All of CBCT scans were archieved in the Romexis® database, and there was no possibility for missing/lost data.
Referrals (internal-from the departments of dental school or external-outer special clinics) and tomography reports written by an oral and maxillofacial radiologist were obtained from the Hospital Information Management System (Enlil, Eroglu Information Systems LLC, Eskisehir, Turkey). The following data were retrieved from the Romexis® database and the general electronic patient database: Age, gender, indication for referral (impacted teeth, supernumerary teeth, trauma, cysts/tumors, clefts, temporomandibular joint, and other reasons), and CBCT FOVs. Repeated exposures due to patient-motion artefacts which were written to patients' charts by radiology technicians were recorded.
The study inclusion criteria were fine visibility of all structures, including abnormalities or pathologies, with no imaging-artefacts due to patient movement or metal objects. In case of multiple CBCT scans per patient, only the first CBCT scan was included.
One author (BE) with 12 years experience analysed all data. After data collection, the patients were divided into three age groups, similar to the Isman et al.'s study: 4–6, 7–12, and 13–16 years based on primary, mixed, and permanent dentition, respectively (13).

IBM® SPSS 25.0 (Armonk, NY, USA) version was used for the statistical analysis. The significance level was set at 5% ($p<0.05$). The chi-square test was performed to determine the relationship between age groups, gender, CBCT indications, and FOV dimensions.

RESULTS

Mean participant age was 12.39 (SD=2.63) years [range: 4-16; 260 females (42.8%) and 347 males (57.2%)]. A hundred CBCT scans (16.5%) were taken in children aged between 4 to 6 year olds, 178 scans (29.3%) in children aged between 7 to 12 year olds and 329 scans (54.2%) in children aged between 13 to 16 year olds.

CBCT indications for referral were recorded, which could afterwards be subdivided into 7 categories, based on the represented cases (Table I). Two-hundred thirty-two reasons (38.2%) were for impacted teeth, 100 (16.5%) for pathological findings such as cyst/tumors, 88 (14.5%) for alveolar clefts, 76 (12.5%) for supernumerary teeth, 52 (8.5%) for other reasons (dental anomalies (2.0%), syndromes (1.6%), orthognathic surgery (1.2%), delayed eruption (1.1%), undetermined swelling (0.7%), external resorption (0.6%), sialolithiasis (0.5%), soft tissue calcification (0.5%), follow-up autotransplant (0.3%)); 41 (6.8%) for dentoalveolar trauma, and 18 (3.0%) were for the visualization of the temporomandibular joint (TMJ).

A significant relationship was found between age groups and CBCT indications (p=0.003) (Table I).

According to the referrals the most frequent and the largest age group was 13 to 16 year olds (54.2%). In all age groups, the most frequent request was to assess an impacted teeth and its localization. In the 4-6 and 7-12 age groups, the second most common reason was the supernumerary tooth (17%, 16.3%) respectively, while in the 13-16 age group that was cyst/tumor (19.2%). In the 4-6 age group, the third most frequent reason was trauma (15.0%), while that was clefts in the 7-12 (15.7%) and 13-16 age (14.3%) groups.

The distribution for the FOVs was listed as: 165 CBCT scans (27.2%) had a FOV of 200 x 60 mm (maxilla), 156 (25.7%) a FOV of 200 x 100 mm, 124 (20.4%) a FOV of 200 × 60 mm (mandible), 82 (13.5%) a FOV of 100 x 60 mm, 69 (11.4%) a FOV of 200 X 170 mm, and 11 CBCT scans (1.8%) were taken with a FOV of 40 × 80 mm (Table II). The maxilla was the most frequently imaged area in both 4-6 (49.0%) and 7-12 (35.4%) aged groups. In the 13-16 aged group, the most commonly imaged area was the mandible (25.5%) (Table II).

Table I. Distribution of indications for CBCT by age groups.

	IT	ST	PF	AC	DT	TMJ	OR	Total
4-6	32	17	11	13	15	3	9	100
	32%	17%	11%	13%	15%	3%	9%	100%
	13.8%	22.4%	11%	14.8%	36.6%	16.7%	17.3%	16.5%
7-12	61	29	26	28	13	3	18	178
	34.3%	16.3%	14.6%	15.7%	7.3%	1.7%	10.1%	100%
	26.3%	38.2%	26%	31.8%	31.7%	16.7%	34.6%	29.3%
13-16	139	30	63	47	13	12	25	329
	42.2%	9.1%	19.1%	14.3%	4%	3.6%	7.6%	100%
	59.9%	39.5%	63%	53.4%	31.7%	66.7%	48.1%	54.2%
Total	232	76	100	88	41	18	52	607
	38.2%	12.5%	16.5%	14.5%	6.8%	3%	8.6%	100%
	100%	100%	100%	100%	100%	100%	100%	100%
				p*=0.003				

IT: Impacted teeth, ST: Supernumerary teeth, PF: Pathological findings, AC: Alveolarcleft, DT: Dentoalveolar trauma, TMJ: Temporomandibular joint, OR: Other reasons. The results are expressed as the frequency (%). Chi-square test (*$p< 0.05$).

Table II. Distribution of FOV dimensions by age groups.

	200X170 (Face)	200X100 (M-M)	200X60 (Max)	200X60 (Mand)	100X60 (Teeth)	40X80 (Tooth)	Total
4-6	25	26	49				100
	25%	26%	49%	-	-	-	100%
	36.2%	16.7%	29.7%				16.5%
7-12	20	49	63	40	6		178
	11.2%	27.5%	35.4%	22.5%	3.4%	-	100%
	29%	31.4%	38.2%	32.3%	7.3%		29.3%
13-16	24	81	53	84	76	11	329
	7.3%	24.6%	16.1%	25.5%	23.1%	3.3%	100%
	34.8%	51.9%	32.1%	67.7%	92.7%	100%	54.2%
Total	69	156	165	124	82	11	607
	11.4%	25.7%	27.2%	20.4%	13.5%	1.8%	100%
	100%	100%	100%	100%	100%	100%	100%
				p*=0.000			

The results are expressed as the frequency (%). Chi-square test (*$p< 0.05$). FOV: Field of view; FOV dimensions are presented as width x height in mm. M-M: maxilla and mandible; Max: maxilla; Mand: mandible.

There was no significant difference between gender and CBCT indications (p=0.140) (Table III). The most frequent request was to assess an impacted teeth in both females (37.7%) and males (38.6%). While the second most common reason of CBCT requests in females was cyst/tumor (18.1%); in males, supernumerary teeth (15.3%) and cyst/tumor (15.3%) ranked second with the same rate (Table III).

Table III. Distribution of indications for CBCT by gender.

	IT	ST	PF	AC	DT	TMJ	OR	Total
Female	98	23	47	38	16	10	28	260
	37.7%	8.8%	18.1%	14.6%	6.2%	3.8%	10.8%	100%
	42.2%	30.3%	47%	43.2%	39%	55.6%	53.8%	42.8%
Male	134	53	53	50	25	8	24	347
	38.6%	15.3%	15.3%	14.4%	7.2%	2.3%	6.9%	100%
	57.8%	69.7%	53%	56.8%	61%	44.4%	46.2%	57.2%
Total	232	76	100	88	41	18	52	607
	38.2%	12.5%	16.5%	14.5%	6.8%	3%	8.6%	100%
	100%	100%	100%	100%	100%	100%	100%	100%
					p=0.140			

IT: Impacted teeth, ST: Supernumerary teeth, PF: Pathological findings, AC: Alveolar cleft, DT: Dentoalveolar trauma, TMJ: Temporomandibular joint, OR: Other reasons. The results are expressed as the frequency (%). Chi-square test (*p< 0.05).

Fifty-two (8.6%) of the CBCT scans were re-taken due to patient-motion artefacts.

Four-hundred sixty-six patients (76.8%) were referred from various departments (orthodontics (51.9%), paediatric dentistry (27.5%), and oral and maxillofacial surgery (20.6%)) of the dental school, while 141 (23.2%) patients were referred from the external clinics. The dispersion of these 141 patients was as follows: private dental clinics (63.8%) and medical clinics (36.2%) (Figure 1).

DISCUSSION

For decision of maxillofacial imaging in pediatric patients it should be taken into consideration how much it is really required and which structures need to be visualized. CBCT technology which has been available for about 20 years in dentistry became a convenient method for oral and maxillofacial diagnostic imaging. CBCT allows images to be acquired using a low dose of radiation, shorter patient examination time and lower costs than conventional computerized tomography (CT), which makes its usage preferable for specific indications of oral and maxillofacial imaging (3,14-16). However, a few studies have appointed that CBCT applications are not always necessary for a high benefit for the patients (17,18). This study focused on the evaluation of indications for CBCT in oral and maxillofacial imaging in pediatric patients. The purpose was to provide information that might help in planning CBCT imaging in pediatric patients.

Mean age was 12.39 years, this is similar with the age distribution in previous studies (11,19,20). A lower mean age of 8.3 years was shown in the study of Suzuki et al. (21). According to the referrals the most frequent and the largest age group was the 13- to 16-year olds (54.2%) in the present study. Hajem et al. reported 58% of the investigations were made in 11- to 15- year olds age group in their study on Swedish children and adolescents (11). There were more males (57.2%) than females in this sample, in similar with the study by Van Acker et al. (19) and in contrast to the study by Hidalgo-Rivas et al. (20).

There are several studies in the literature regarding the use of CBCT in pediatric patients. In the study of M. Marcu et al. the most common indication for CBCT scans in children was the evaluation of dental anomalies (12). The main clinical indication was for tooth localisation and assessment of resorption of adjacent tooth roots, typically concerning ectopic maxillary canine impaction in previous studies (11,20). In a Japanese survey, Suzuki et al. reported 51% of CBCT examinations were performed for impacted supernumerary teeth and 28% for disorders of tooth eruption (21).

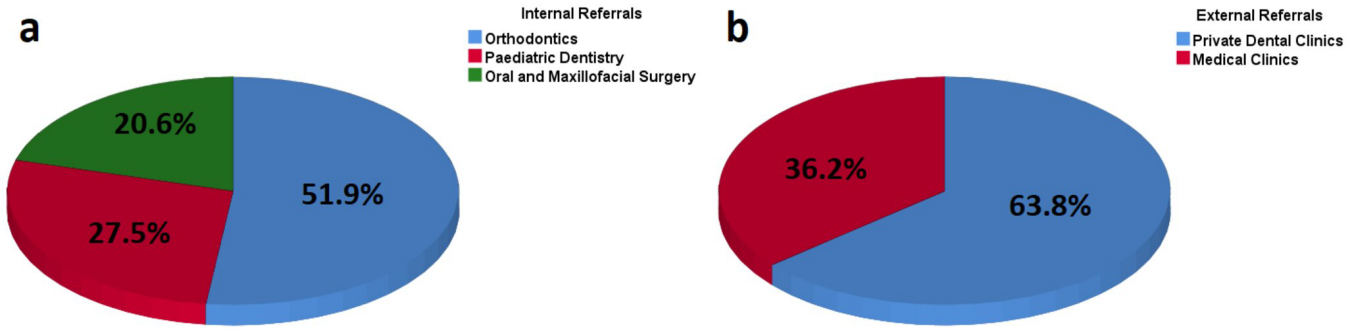

Figure 1. Distribution of internal and external referrals for CBCT scans.

The same study also reported that 9.2% of examinations were made for the TMJ. In our study, 3.0% of CBCT scans were for the visualization of TMJ. Thirty-six % of reasons were for developing dentition-localized and 1.0% was for TMJ in the study of Van Acker et al. (19). In accordance with the literature, the most frequent request was to assess an impacted tooth and its localization (38.2%) in our study. Since it is not possible to determine the positions of impacted or/and supernumerary teeth with conventional x-ray techniques that offer a two-dimensional view, CBCT is favored as much more beneficial method for the evaluation of impacted teeth. It is also clear that there is a variety in the presence and reaches to CBCT imaging and it should be taken into account in terms of culture and ethnicity while evaluating the literature from different regions of the world.

Field of view (FOV) is a parameter that determines the scan volume of the CBCT device. FOV limits the radiation exposure to a specific region of interest. In the present study, the distribution of different FOVs were investigated. Since larger FOVs results with higher radiation doses, it is crucial to choose the appropriate FOV for the area of interest. It would be appropriate to use a smaller FOV to examine one or two teeth (22). In the study of Isman et al., the most frequently used FOV was the face, because of the most common CBCT indication in their study was malocclusion and dentomaxillofacial anomalies (13). Examining the CBCT FOVs in this study, the maxilla was the most frequently imaged area (27.2%), followed by the jaws (maxilla and mandible; 25.7%), the mandible (20.4%), teeth (13.5%), face (11.4%) and tooth (1.8%). The CBCT scans with the two smallest FOV values specified in the study (100 x 60 and 40 x 80) accounted for only 15.3% of all scans. When making a CBCT request in a pediatric patient, the area to be examined is usually specified by a general or pediatric dentist. According to our findings, general dentists and paediatric dentists should be informed about the use of suitable FOVs to avoid the higher radiation doses. It might be proper that an oral and maxillofacial radiologist decides when CBCT is necessary and then supervises the examination.

Spin-Neto and Wenzel found that prevalence of movement during CBCT investigations could be approximately 20% in a systematic review (23). Movements and motion artefacts of patients underwent CBCT is more common in pediatric patients (11,24-26). In present study 52 (8.6%) of the CBCT scans were re-taken due to patient-motion artefacts. For avoiding image repetition it is important to provide that pediatric patient can cooperate for the radiological practice remaining motionless for a prolonged period.

In the current study, internal referrals (76.8%) from departments of dental school were much more common. Departments of orthodontics (51.9%), paediatric dentistry (27.5%), and oral and maxillofacial surgery (20.6%) referred the pediatric patients for CBCT imaging. In Hajem et al.'s study the largest group of referrals came from general practice dentists (43%) (11). In the study of Van Acker et al., 48.1% of patients received treatment in the local university dental out-patient hospital, while 49.4% of CBCT scans were external referrals (19).

A limitation of this retrospective survey was that patients from only a dental school were included in the study. In further studies, it will be interesting to perform a full analysis of all referrals of pediatric patients from various dentistry fields.

CBCT should be performed with following the ALADAIP principle and be used where the pediatric patient's benefit would outweigh potential risks. It may be recommended that an oral and maxillofacial radiologist decides when CBCT is necessary and then supervises the CBCT-scanning protocol to minimize the radiation dose in pediatric patients.

CONCLUSIONS

The results of the present study can help dental professionals make the decision to refer for CBCT when extra three dimensional imaging is necessary for a pediatric patient. The most frequent and the largest age group was the 13- to 16-year olds in the present study. The most frequent CBCT request was to assess an impacted tooth and its localization, and the maxilla was the most frequently imaged area. 8.6% of the CBCT scans were re-taken due to patient-motion artefacts. The majority of CBCT scans were consisted of requests from the dental school's departments.

Ethics Committee Approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (approval number: 89/14062019-77) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent:

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:

Concept – B.E., H.D., I.G.A, A.U.; Design – B.E., H.D., Supervision – B.E.; Resources – B.E.; Materials – B.E.; Data Collection and/or Processing – H.D., I.G.A, A.U.; Analysis and/ or Interpretation – H.D., I.G.A, A.U.; Literature Search – I.G.A, A.U.; Writing Manuscript – B.E., H.D., Critical Review – B.E.

Conflict of Interest:

The authors have no conflict of interest to declare.

Financial Disclosure:

The authors declare that this study has received no financial support.

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ÖZGÜN ARAŞTIRMA
Original Article

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Geliş Tarihi : 27 Kasım 2021
Received
Kabul Tarihi : 24 Mart 2022
Accepted
E Yayın Tarihi : 01 Eylül 2023
Online published

Bu makalede yapılacak atıf
Cite this article as
Sarıdemir Ünal D, Doğru V, Avanaz A, Yaprak M, Gürer S. Covid-19'un Karın Duvarı Fıtığı Cerrahi Eğitimine Etkisi
Akd Tıp D 2023; 9(3): 253-258

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DOI: 10.53394/akd.1029006

Covid-19'un Karın Duvarı Fıtığı Cerrahi Eğitimine Etkisi

The Effect of Covid-19 on Surgical Training for Abdominal Wall Hernia

ÖZ

Amaç:
Covid-19, geleneksel genel cerrahi asistan eğitim programlarında alışılagelmedik değişikliklerin yaşanmasına sebep olmuştur. Akdeniz Üniversitesi Hastanesi Genel Cerrahi Kliniği'nin altı yıllık asistan eğitimi geçmişinin incelendiği bu çalışma, pandemi sonrası karın duvarı fıtıkları için yapılan eğitimsel işlemlerin trendlerindeki değişiklikleri ortaya koymayı amaçlamaktadır.

Gereç ve Yöntemler:
Batın duvarı fıtığı endikasyonu ile 18 Eylül 2014 ve 17 Eylül 2020 tarihleri arasında kliniğimizde gerçekleştirilen cerrahi prosedürlerin kayıtları incelenmiş Covid-19 etkisindeki dönem, geçmiş yılların trendleri ile karşılaştırılmıştır.

Bulgular:
Toplamda gerçekleştirilen 2587 prosedürün 2330'unda (%90) cerrahi ekipte en az bir asistan katılımı olduğu görülmektedir. Umblikal fıtıklar dışında asistan katılımı olan prosedür sayılarında Covid-19 sonrası anlamlı bir düşüş olmamış; beklenen aylık medyan umblikal prosedür sayısı 5,6 iken, gerçek değerin 1,0 olduğu anlaşılmıştır (Çeyrekler Arası Aralık 5,3-6,0 ve 0,0-3,0; p=0,041). İnguinal fıtıklarda operatörlük (sırasıyla, 16,9 ±2,1 ve 9,8 ±5,6; p=0,017) ve eğitici asistan görevi üstlenen asistanların sayısında (sırasıyla, 4,0 ±0,8 ve 1,8 ±1,8; p=0,025) belirgin düşüşler olmuştur.

Sonuç:
Covid-19 pandemisi daha çok cerrahi ekipteki görev dağılımını etkilemiştir. Bu dönemde eskiye göre daha kıdemsiz asistanlar batın duvarı fıtıklarında yardımcı cerrah pozisyonunda görevlendirilmişlerdir. Fıtık cerrahisine giriş niteliği taşıyan umblikal fıtıkların Covid-19'dan en çok etkilenen eğitsel prosedürler olduğu ve telafi edilmeleri gerektiği anlaşılmıştır.

Anahtar Sözcükler:
Karın duvarı fıtığı, Cerrahi eğitim, Genel cerrahi, Asistanlık

ABSTRACT

Objective:
Covid-19 has caused unusual changes in traditional general surgery resident training programs. This study, which examines the six year residency training history of Akdeniz University Hospital General Surgery Clinic, aims to reveal the changes in the trends of educational procedures for abdominal wall hernias after the pandemic.

Material and Methods:
Records of surgical procedures performed in our clinic between 18 September 2014 and 17 September 2020 with the indication of abdominal wall hernia were examined and the period under the influence of Covid-19 was compared with the trends of the past years.

Results:
In 2330 (90%) of the 2587 procedures performed in total, at least one assistant participated in the surgical team. Except for umbilical hernias, there was no significant decrease in the number of procedures with assistant participation after Covid-19; the expected median number of umbilical procedures per month was 5.6, while the true value was 1.0 (Interquartile range 5.3-6.0 and 0.0-3.0, respectively; p=0.041). There were significant decreases in the number of residents who served as the operator (16.9 ±2.1 and 9.8 ±5.6, respectively; p=0.017; p=0.017, respectively) and the teaching resident (4.0 ±0.8 and 1.8 ±1.8; p=0.025, respectively) in inguinal hernias.

Conclusion:
The Covid-19 pandemic mostly affected the distribution of tasks in the surgical team. In this period, more junior residents were assigned as assisting surgeons in abdominal wall hernias compared to the past. It has been understood that umbilical hernias, which are seen as an introduction to hernia surgery, are the educational procedures most affected by Covid-19 and should be compensated.

Key Words:
Abdominal wall hernia, Surgical training, General surgery, Residency

GİRİŞ

Covid-19 pandemisine karşı alınan önlemler kapsamında sosyal mesafenin korunması, hasta ve temaslıların karantinayla izolasyonu gibi politikaların yanı sıra hastanelerin yatak kapasitelerini dengede tutabilmek, sağlık sisteminin aşırı başvurular karşısında çökmesini önlemek adına elektif vakaların mümkün olduğunca ertelenmesi yoluna gidildi. Bu doğrultuda, sağlık bakanlığı da 17 Mart 2020 tarihinde bir genelge yayınladı. Tüm bu gelişmeler geleneksel genel cerrahi asistan eğitim programlarında alışılagelmedik değişikliklerin yaşanmasına sebep oldu. Dünya genelinde tıbbi çevreler içinden birçok topluluk, durumun aciliyeti nedeniyle pandemiye hızlı bir reaksiyon vererek alınacak önlemlere dair görüş ve önerilerini henüz daha pandeminin ilk zamanlarında bildirmeye başladı (1,2). Zamanla, kanıt düzeyi daha yüksek araştırmalarla uluslararası boyutlarda sağlık sisteminin temellerinin nasıl sarsıldığı bir bir ortaya çıkmaya başladı (3,4). Söz konusu görüş ve önerilerden biri de karın duvarı fıtığı olan hastaların acilse ameliyat edilmesi, elektif bekleme listelerindeki hastaların ameliyatlarının ise kontrollü bir şekilde ertelenmesi üzerineydi (5). Ancak, kısıtlamaların Covid-19 vaka sayılarının azalma eğilimi göstermesi ile birlikte hafifletilmesi üzerine karın duvarı fıtıklarında ciddi bir geri sıçrama etkisi görüldü (6).

Öte yandan, eğitim veren gerek ekiplerin seyreltilmesi gerekse de vaka sayılarının azaltılması gibi önlemler asistan eğitimini derinden sarsmıştı. Bu sarsıntının yarattığı eğitsel eksikliğin telafisini konu alan, eğitimi alan ve veren tarafların üzerinde uzlaştığı bir manifesto özelliği taşıyan önerilerin yayınlanması hastalığın triaj önerilerinin yayınlanmasından çok sonra oldu (5,7). Bu bağlamda, her programın, kendi ihtiyaçlarına, kapasitesine ve pandeminin üzerinde bıraktığı izlere göre bir denge tutturmaya çalıştığı bir döneme girilmiş oldu. Akdeniz Üniversitesi Hastanesi de bölgesinin en büyük üçüncü basamak sağlık merkezlerinden biri olarak, bir yandan pandeminin yükünü sırtlamaya çalışırken bir yandan da sevk zincirinin son basamağında bulunması gerçeği ile yüzleşerek kapasitesi azaltılan kuruluşlar nedeniyle tarafına yönlendirilen hastaların yönetimini kontrol etmeye çalışıyordu.
Neticede bir denge kuruldu. Bir fotoğraf ortaya çıktı. Biz de gelecek nesiller için bir uyarı mahiyetinde ortaya çıkan bu sonucu, karın duvarı fıtıkları özelinde araştırmak ve asistanlarımızın eğitimlerinin olan bitenlerden nasıl etkilendiklerini anlayabilmek düşüncesi ile bu araştırmayı başlattık. Bu nedenle araştırmamızın temel amacı, kliniğimizin son bölümü pandeminin etkisi altında geçen altı yıllık eğitsel geçmişini mercek altına almak ve pandemi ile birlikte karın duvarı fıtıkları için yapılan prosedürlerin trendlerindeki değişiklikleri ortaya koymaktı.

GEREÇ ve YÖNTEMLER

Çalışmada, batın duvarı fıtığı endikasyonu ile 18 Eylül 2014 ve 17 Eylül 2020 tarihleri arasında kliniğimizde gerçekleştirilen cerrahi prosedürlerin kayıtları incelenmiştir. Prosedürler kasık fıtığı, umlikal fıtık, insizyonel fıtık ve diğer fıtıklar şeklinde sınıflandırılarak analiz edilmiştir. Diafragma/hiatus fıtıkları ve meş enfeksiyonu/reaksiyonu için yapılan eksizyon prosedürleri çalışma dışı bırakılmıştır. Çalışmanın altı yıllık süresi içinde bölümümüzde istihdam edilen 32 Genel Cerrahi Asistanının (GCA) bu prosedürlere iştirakı aldıkları görevlere göre ayrıca gruplandırılarak analiz edilmiştir; operatörlük, otonom operatörlük ve eğitici asistanlık. Operatör ve yardımcı cerrahın her ikisinin de asistan olduğu prosedürlerin operatörü "otonom operatör" kapsamına alınırken, yardımcı cerrahın daha kıdemli olduğu prosedürlerin yardımcı cerrahları "eğitici asistanlık" kapsamında değerlendirilmiştir. Buradaki otonomluk ve eğiticilikten kasıt cerrahlığın tam bağımsız olarak icrası değil her iki durumda da bir öğretim üyesinin dikkatli gözetimi altında gerçekleştirdiği ve genel cerrahi asistanlık programının bir parçası kapsamında kabul edilen cerrahide liderlik eğitimi için yapılan yetkilendirmelerdir. Sonuç olarak çalışmadaki tüm prosedürler bir öğretim üyesinin dikkatli gözetimi altında gerçekleştirilmiştir. Covid-19 etkisinin görülmeye başladığı tarih olarak sağlık bakanlığımızın 17 Mart 2020 tarihinde yayınladığı genelge kabul edildi. Genelgeden önceki 5,5 yıllık dönemin yıllar içindeki trendlerinden yola çıkılarak Covid-19 etkisi altında geçen altı ay için öngörüde bulunuldu ve beklenen aylık ortalama (veya medyan) değerler gerçek değerlerle kıyaslandı. Bu çalışma Helsinki Bildirgesi'ne göre Araştırma ve Yayın Etiğine uygun olarak tasarlandı ve Akdeniz Üniversitesi Klinik Araştırmalar Etik Kurulu (Karar no: KAEK-961/23.12.2020) ile birlikte Sağlık Bakanlığı Bilimsel Araştırma onayı (Karar no: 2020-11-17T11_30_07) alındı.

İstatistik

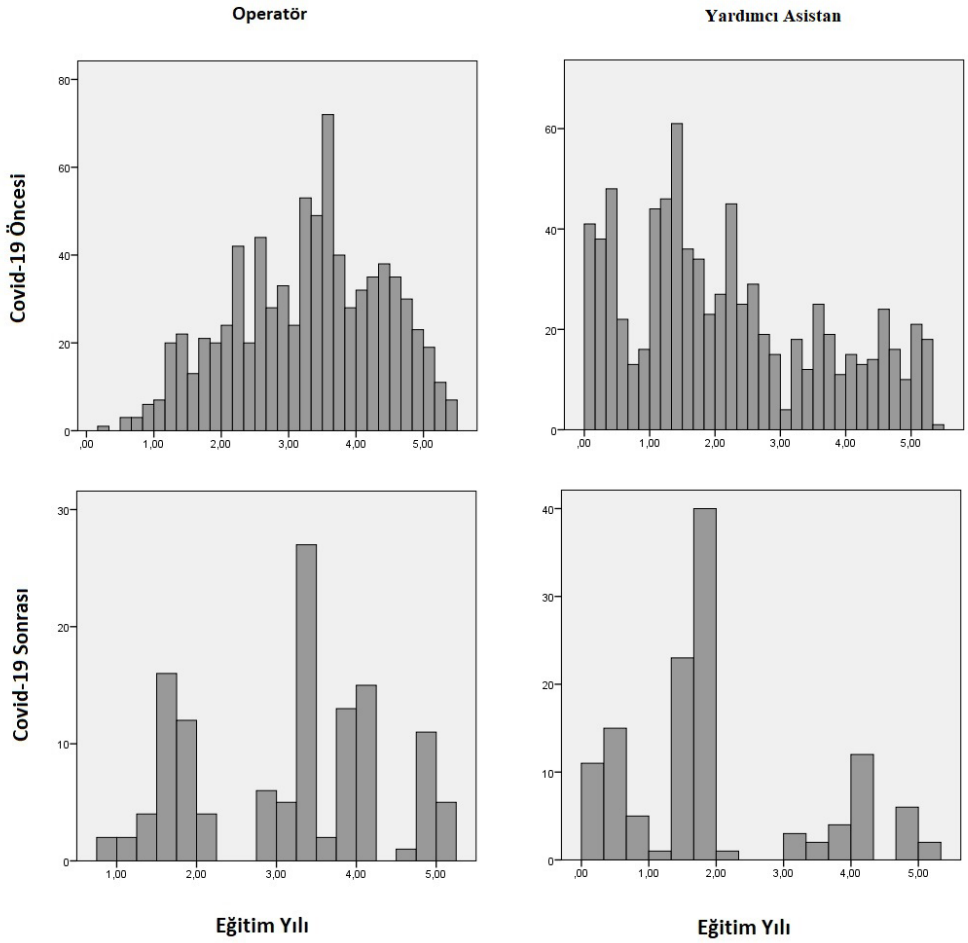
İstatistiksel analizlerde, Statistical Package for Social Sciences (SPSS) sürüm 23.0 programı (IBM, NY, ABD kullanılmıştır. Verilerin dağılımını belirlemek için Shapiro-Wilk veya Kolmogorov-Smirnov testi kullanılmış, ardından test varsayımlarına göre Student t testi veya Mann-Whitney U testi yapılmıştır. Parametrik veriler ortalama ve standart sapma (SD) ile, parametrik olmayan veriler ise medyan ve çeyrekler arası aralık (ÇAA) ile sunulmuştur. Kategorik değişkenlerin analizinde dağılımlarına göre Pearson Ki-kare veya Fisher testi kullanılmıştır. Geçmiş yılların trendlerini baz alan beklentilerin istatistiksel olarak hesaplanmasında SPSS'in "expert modeler" fonksiyonu literatürdeki benzer epidemiyolojik tahmin/beklenti çalışmalarına uygun olarak kullanıldı (8). İstatistiksel anlamlılık düzeyi p<0,05 olarak belirlendi.

BULGULAR

Çalışma aralığında kliniğimizde toplamda karın duvarı fıtığı endikasyonu nedeniyle 2587 cerrahi prosedür gerçekleştirilmiştir. Bunların 2282'si (%88) elektif, 305'i (%12) acildi. Prosedürlerin 1249'u (%48) inguinal, 188'i (%7) umblikal, 805'i (%31) insizyonel ve 345'i (%13) diğer karın duvarı fıtıkları için gerçekleştirilmiştir. Topografik bölgelere göre acil prosedürlerin oranı, inguinallerde %6 (n=74), umblikallerde %4 (n=13), insizyonellerde %23 (n=187), diğer fıtıklarda ise %9'dur (n=31).

Toplamda gerçekleştirilen 2587 prosedürün 2330'unda (%90) cerrahi ekipte en az bir asistan katılımı olduğu görülmektedir. Her iki prosedürden birinde yardımcı cerrahın, her dört prosedürün üçünde ise operatörün bir GCA olduğu görülmüştür. Bu oranlar topografik bölgelere göre yardımcı cerrahlık için inguinal fıtıkta %52 (n=652), umblikal fıtıkta %49 (n=92), insizyonel fıtıkta %49 (n=395), diğer fıtıkta %47 (n=162); operatörlük için ise, sırasıyla, %77 (n=967), %80 (n=151), %68 (n=551) ve %75'tir (n=259).

Asistanların operasyona katılım anındaki eğitim yıllarına bakıldığında, operatörlük görevini üstlenen asistanların cerrahi deneyim dağılımları Covid-19 öncesi ve sonrasında benzerlik gösteriyordu. Covid-19 öncesi operatörlük görevini üstlenen asistanların medyan cerrahi deneyimi 3,3 yıl (ÇAA 2,7-4,0) iken sonrasında bu asistanların deneyimi 3,3 yıldı (ÇAA 1,8-4,0) (p=0,050). Yardımcı cerrahlarda ise bu değerler, sırasıyla, 2,4 yıl (ÇAA 1,3-3,6) ve 1,7 yıl (ÇAA 1,4-3,3) ile istatistiksel olarak farklıydı (p=0,001). Operatörlük ile yardımcı cerrahlık görevlerini üstlenen genel cerrahi asistanlarının Covid-19 öncesi ve sonrası dönemlerinin cerrahi deneyimleri açısından karşılaştırılması Figür 1'de gösterilmektedir.



Figür 1. Covid-19 öncesi ve sonrası genel cerrahi asistanlarının operatörlük ve yardımcı cerrahlık görevlerinin karşılaştırması.

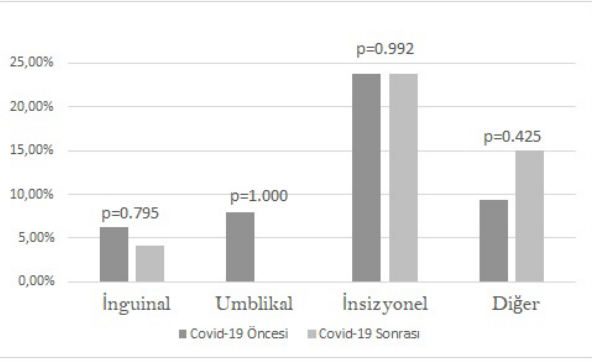
Covid-19'un öncesi, GCA'ların katıldığı prosedürlerin aylık ortalamasının 33±10 olduğu görülmüştür. Covid-19'dan sonra bu ortalama 27±17'ye düşmüş olsa da aradaki fark istatistiksel olarak anlamlı değildir (p=0,409). Covid-19 öncesi ve sonrası kıyaslandığında, operatör GCA'ların aylık medyan prosedür sayılarının 27 ve 24 (ÇAA 21-32 ve 9-34; p=0,431), otonom GCA'ların 9 ve 21 (ÇAA 6-17 ve 6-29; p=0,187), eğitmen GCA'ların ise 3 ve 7 (ÇAA 1-5 ve 3-8; p=0,085) olduğu saptandı. Kliniğimizin 5,5 yıllık trendlerine göre beklenen aylık ortalama veya medyan karın duvarı fıtığı prosedürlerinin Covid-19 etkisi altındaki gerçek değerlerle kıyaslaması ise Tablo I'de gösterilmektedir.

Tablo I: Kliniğimizin 5,5 yıllık trendlerine göre beklenen aylık ortalama veya medyan karın duvarı fıtığı prosedürlerinin Covid-19 etkisi altındaki gerçek değerlerle kıyaslaması.

		Beklenen Değer	Gerçek Değer	p
Toplam	GCA katılımı olanlar	35,7 ±3,6	27 ±17	0,248
	Operatör GCA'lar	31,2 ±3,4	23 ±15	0,246
	Otonom operatör GCA'lar	23,0 ±2,8	20 ±14	0,595
	Eğitici GCA'lar	6,9 ±1,5	5,5 ±2,9	0,328
İnguinal	GCA katılımı olanlar	17,2 ±2,0	11,8 ±7,5	0,121
	Operatör GCA'lar	16,9 ±2,1	9,8 ±5,6	0,017*
	Otonom operatör GCA'lar	11,9 ±1,6	8,2 ±5,5	0,158
	Eğitici GCA'lar	4,0 ±0,8	1,8 ±1,8	0,025*
Umblikal	GCA katılımı olanlar	5,6 (5,3-6,0)	1,0 (0,0-3,0)	0,041*
	Operatör GCA'lar	4,1 (3,8-4,4)	1,0 (0,0-3,0)	0,065
	Otonom operatör GCA'lar	4,5 (4,1-4,7)	0,5 (0,0-3,0)	0,065
	Eğitici GCA'lar	1,2 (1,0-1,5)	0,0 (0,0-1,3)	0,093
İnsizyonel	GCA katılımı olanlar	9,2 ±1,8	9,8 ±8,0	0,854
	Operatör GCA'lar	7,0 ±1,7	8,5 ±7,2	0,643
	Otonom operatör GCA'lar	6,5 ±1,4	7,3 ±6,5	0,773
	Eğitici GCA'lar	1,2 ±0,5	1,3 ±1,0	0,832
Diğer	GCA katılımı olanlar	3,1 ±1,3	3,3 ±1,9	0,800
	Operatör GCA'lar	2,6 ±0,7	3,3 ±1,9	0,161
	Otonom operatör GCA'lar	1,8 ±0,5	2,8 ±1,6	0,410
	Eğitici GCA'lar	0,5 ±0,3	1,8 ±1,2	0,156

GCA, genel cerrahi asistanı; * p<0,05

Asistan katılımı olan 2330 prosedür içinde acil olan prosedürlerin oranı Covid-19 öncesinde %11,8'di. Etki sonrasında %12,5 ile bir miktar artış gözlense de arada istatistiksel olarak anlamlı bir fark olmadığı görülmüştür (p=0,777). Topografik bölge dağılımlarına göre acil fıtık prosedürlerinin oranının Covid-19 öncesi ve sonrası kıyaslaması Figür 2'de gösterilmektedir.



Figür 2. Acil fıtık prosedürlerinin oranının Covid-19 öncesi ve sonrası kıyaslaması.

TARTIŞMA

Fıtık prosedürlerinin kimi serilerde tüm ameliyatlar içinde %7,5'a kadar geniş bir yer tutabildiği ve karın duvarı fıtıklarının prevalansının %20,9'u bulabildiği bilinmektedir (9,10). İki binli yılların ilk dekatında acil fıtık prosedürlerinin insidansında 100,000 kişide 16'dan 19'a doğru trajik bir yükseliş yaşandığını gösteren çalışmalar da mevcuttur (11). Öte yandan, Covid-19 pandemisi nedeniyle elektif cerrahi prosedürlerde kısıtlamaya gidilmiştir (5). Kliniğimizdeki GCA'larının eğitimi açısından bu kısıtlamanın en belirgin etkisi umblikal fıtıklarda tespit edilmiştir. Asistan katılımı olan prosedür sayılarında aylık medyan 5,6'lık (ÇAA 5,3-6,0) bir beklenti olmasına karşın 17 Mart'taki genelge sonrasında bu değer 1,0'a (ÇAA 0,0-3,0) kadar düşmüştür (p=0,041). Umblikal fıtık için onarımlar defektin büyük olması ve eşlik eden batın içi yapışıklıklarla daha kompleks hale gelebilse de bu gibi faktörler olmadığında çoğunlukla diğer batın duvarı fıtıkları içinde en az kompleks olanıdır ve çoğunlukla kliniğimizdeki asistanlarımızın ilk tecrübe ettiği fıtık onarımı prosedürüdür. Burada edinilen tecrübe daha kompleks onarımlar için bir temel niteliğindedir. Fıtık cerrahisine giriş niteliği taşıyan bu eğitimin eksikliği, bu nedenle çok büyük önem arz eder ve mutlaka telafi edilmelidir. İkinci en belirgin etki inguinal fıtıklarda saptanmıştır. Her ne kadar GCA katılımlı toplam prosedür sayılarındaki azalma beklenenden istatistiksel olarak anlamlı bir fark yaratmamış olsa da (gerçek 11,8 ±7,5, beklenen 17,2 ±2,0; p=0,121) operatörlük görevi üstlenen GCA'ların aylık ortalamasında, hemen hemen yarı yarıya bir düşüş göze çarpmıştır (sırasıyla, 9,8 ±5,6 ve 16,9 ±2,1; p=0,017). Bundan daha derin bir düşüş ise inguinal fıtık prosedürlerindeki eğitici asistanlık yapanların sayısında görülmüştür (sırasıyla, 1,8 ±1,8 ve 4,0 ±0,8; p=0,025). Bir cerrahi asistanının ameliyat sürelerinde stabil bir seyre ulaşabilmesi için gözetim altında yapması gereken operasyon sayısının Lichtenstein prosedürü için 37 ila 42 prosedür olduğu tahmin edilmektedir (12). Altı yılda 32 asistanın tam ya da kısmen eğitimini geçirdiği bir genel cerrahi kliniğinde tüm asistanların toplamda ayda 10'dan az inguinal fıtık prosedürü yapması eğitim programının sürdürülebilirliğini şüphesiz ki gölgede bırakmaktadır.

İlk bakışta Covid-19'a bağlı elektif fıtıkların ertelenmesinin, inkarserasyon ve strangülasyonlu fıtıkları sayısal olarak artıracağına ihtimal verilse de çalışmanın sonuçlarında böyle bir etki görülmemektedir. Literatürde, operasyonun haftalarca ertelenebilmesine imkan verdiği için, akut strangüle olmadığından emin olunan inguinal fıtık vakalarının redükte edilip takibe alınması ile uygun vakalarda hemen hemen %70 başarı sağlanabildiği ve bu strateji ile pandemi dönemindeki yükün önemli ölçüde azaltılabildiği bildirilmiştir (13). Bu strateji bizim kliniğimizde de oldukça sık tercih edildiğinden söz konusu etki belirgin hissedilmemiş olabilir.

Öte yandan, salgının zirvesi kabul edilen 11 Mart ile 10 Mayıs 2020 tarihleri arasında yapılan toplam acil fıtıkların, 2019'un aynı dönemine kıyasla %48 daha az olduğunu gösteren bir yayın, daha önceden acil sıfatıyla gerçekleştirilen ameliyatların ne kadarının gerçek acil olduğunun sorgulanması gerektiğini vurgulamaktadır (14). Bu ince nüansı açık bir şekilde ortaya koyabilmek ne yazık ki oldukça zordur.

Örneğin tekrar tekrar redükte edilen bir fıtığın, giderek zorlaşması, sancılı olması, hastanın sağlık hizmetine ulaşabilmesine engel olan durumların varlığı gibi birçok faktör hastanın elektif listeden ne zaman çıkartılıp, ne zaman acil programa alınması gerektiğini belirleyecektir. Yani diğer bir deyişle bu konuda keskin bir yorum yapabilmek için, acil karın duvarı fıtıklarının kavramsal olarak net bir şekilde tarif edilmesi ve tüm cerrahların bu tanıma uyduğundan emin olunması gerekir. Sonuç olarak, manüel redüksüyonun da katkısının olduğunu düşündüğümüz multifaktöryel etkileşimler neticesinde acil prosedürlerin kliniğimizde istatistiksel olarak değişmediği ve bu doğrultuda, asistanlarımızın acil fıtık onarımı eğitiminde ciddi bir etkilenme olmadığı düşünülebilir.

Sonuçlarımızdaki anlamlı bir diğer bulgu yardımcı cerrahların kıdeminin eskiye göre daha az olmasıdır. Bu durum asistan ekibimizin özellikle üçüncü yıl kıdeminde daha önce yaşanan istifalar nedeniyle kimsenin olmayışı ile kısmen açıklanabilir. Covid-19 döneminde asistanların eğitiminde eksiklik olacağı kaygısı ile verilen reaksiyon da bu eğilime katkı sağlamış olabilir.

Hastalara uygulanan cerrahi prosedürlerin kapalı ya da açık olarak gruplandırılmasının araştırmamızın kapsamında olmayışı çalışmamızın bir kısıtlamasıdır. Araştırmamızın tek bir merkezin deneyimlerini analiz ediyor olması çalışmamızın bir diğer kısıtlaması olmuştur. Şüphesiz ki genel cerrahi eğitimi verilen tüm klinikler gerek eğitimi veren öğretim üyesi özellikleri açısından gerekse de eğitim alan asistanlar açısından farklı özellikler taşır. Ayrıca her ekipte kendi içinde dahi zaman zaman değişik etkileşimler yaşanabilmektedir. Bu nedenle çok merkezli çalışmaların konuya ciddi katkıları olacaktır. Öte yandan, trakeal entübasyonun, Covid-19 bulaşma riskini artırma ihtimali nedeniyle kasık fıtığı onarımlarında bu dönemde genel anestezi veya derin sedasyondan kaçınılıp kaçınılmadığı, lokal veya bölgesel anestezinin daha çok tercih edilip edilmediği; bu tercihlerin asistanların eğitimini nasıl etkilediği gelecek çalışmalar için güzel araştırma konuları olabilir.

SONUÇ

Genel cerrahide asistan eğitimi birçok cerrahi branşta olduğu gibi usta çırak ilişkisine dayanır. Hangi tür ameliyatların hangi senelik kıdemde yapıldığı geleneksel olarak yerleşmiş uygulamalar olsa da dış etkileşimler ile dengelerde değişiklikler yaşanabilir. Kliniğimizde redükte edilebilen karın duvarı fıtıkları, kontrollü bir izlem altında tutulmuş, acı verici veya redüksüyonun giderek zorlaştığı fıtıklara öncelik verilmiştir. Umblikal fıtıklar dışında asistan katılımı olan prosedür sayılarında anlamlı bir düşüş olmamıştır. Covid-19 pandemisi daha çok cerrahi ekipteki görev dağılımını etkilemiştir. Bu dönemde eskiye göre daha kıdemsiz asistanlar batın duvarı fıtıklarında yardımcı cerrah pozisyonunda görevlendirilmişlerdir. İnguinal fıtıklarda operatörlük ve eğitici asistan görevi üstlenen GCA'ların sayısında belirgin düşüşler olmuştur.

Etik Komite Onayı:
Bu çalışma Helsinki Bildirgesi'ne göre Araştırma ve Yayın Etiğine uygun olarak tasarlandı ve Akdeniz Üniversitesi Klinik Araştırmalar Etik Kurulu (Karar no: KAEK-961/23.12.2020) ile birlikte Sağlık Bakanlığı Bilimsel Araştırma onayı (Karar no: 2020-11-17T11_30_07) alındı.

Yazar Katkıları:
Fikir- V.D., D.S.Ü., A.A.; Tasarım- V.D.; Denetleme- M.Y., S.G.; Veri Toplanması ve/veya İşlenmesi- V.D.; Analiz ve/veya Yorum- V.D.; Literatür Taranması- D.S.Ü., A.A.; Makalenin Yazımı- V.D., D.S.Ü., A.A.; Eleştirel İnceleme- M.Y., S.G.

Çıkar Çatışması:
Yazarların beyan edecek çıkar çatışması yoktur.

Finansal Destek:
Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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ORIGINAL ARTICLE
Özgün Araştırma

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Geliş Tarihi : 01 December 2021
Received
Kabul Tarihi : 03 February 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Yarci E, Baldan E.
25-Hydroxyvitamin D Levels in Preterm Infants ≤32 Weeks Gestational Age and Respiratory Distress Syndrome
Akd Med J 2023; 9(3): 259-264

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DOI: 10.53394/akd.1031158

25-Hydroxyvitamin D Levels in Preterm Infants ≤32 Weeks Gestational Age and Respiratory Distress Syndrome

Gebelik Yaşı ≤32 Hafta Olan Preterm Bebeklerde 25-Hidroksivitamin D Düzeyleri ve Respiratuvar Distres Sendromu Arasındaki İlişki

ABSTRACT

Objective:

This study aimed to evaluate effect of vitamin D levels on the development of respiratory distress syndrome (RDS) in preterm infants with a gestational age of ≤ 32 weeks. The association between RDS and severity of vitamin D deficiency was secondary outcome of this study.

Material and Methods:

Newborns having a gestational age of ≤32 weeks with RDS constituted the study group, while newborns hospitalized in the neonatal intensive care unit having ≤32 weeks of gestational age with no signs of RDS were the control group.

Results:

During the study period, 122 preterm infants having a gestational age of ≤ 32 weeks were included. From these, 56 (46%) had RDS (study group), while 66 (54%) newborns (control group) did not have RDS. The groups were similar in terms of maternal age, multiple pregnancy, use of antenatal steroid, mode of delivery, sex accompanying maternal diseases and birth season. Median 25-OHD levels of study group and control group were similar (12.3 ng/ml vs 15.6 ng/ml; p=0.38). The rates of preterm infants having low vitamin D levels (25-OHD level<15 ng/ml) did not differ between the groups (38/56, 68% vs 35/66, 53%; p=0.09).

Conclusions:

There is no established optimal 25-OHD level for both term and premature infants. Besides, taking into account possible unfavorable both maternal and neonatal effects of vitamin D deficiency, adequate vitamin D supplementation should be provided in countries where vitamin D deficiency is common.

Key Words:

25-hydroxyvitamin D, Preterm infant, Respiratory distress syndrome

ÖZ

Amaç:

Bu çalışmanın amacı, gebelik yaşı ≤ 32 hafta olan prematüre bebeklerde D vitamini durumunu ve D vitamini düzeylerinin respiratuvar distres sendromu (RDS) gelişimine etkisini değerlendirmektir. RDS ile D vitamini eksikliğinin şiddeti arasındaki ilişki bu çalışmanın ikincil sonucunu oluşturmaktadır.

Gereç ve Yöntemler:
RDS'li gebelik yaşı ≤32 hafta olan yenidoğanlar çalışma grubunu oluştururken, yenidoğan yoğun bakım ünitesinde yatan ve RDS bulgusu olmayan ≤32 hafta olan yenidoğanlar kontrol grubunu oluşturmakta idi.

Bulgular:
Çalışma süresi boyunca gebelik yaşı ≤ 32 hafta olan 122 erken doğmuş bebek dahil edildi. Bunlardan 56'sında (%46) RDS (çalışma grubu) varken, 66 yenidoğanda (%54) (kontrol grubu) RDS saptanmadı. Gruplar arasında anne yaşı, çoğul gebelik, antenatal steroid kullanımı, cinsiyet, doğum şekli, anne yaşı, antenatal steroid kullanımı, eşlik eden anne hastalıkları ve doğum mevsimi açısından anlamlı fark yoktu. Çalışma grubu ve kontrol grubunun medyan 25-OHD seviyeleri benzerdi (12,3 ng/ml'ye karşı 15,6 ng/ml; p=0.38).
Gruplar arasında D vitamini düzeyi düşük olan (25-OHD düzeyi <15 ng/ml) erken doğmuş bebeklerin oranları açısından farklılık saptanmadı (38/56, %68'e karşı 35/66, %53; p=0,09).

Sonuç:
Hem zamanında doğan hem de prematüre bebekler için belirlenmiş bir optimal 25-OHD seviyesi yoktur. Buna karşın, D vitamini eksikliğinin hem maternal hem de neonatal olası olumsuz etkileri göz önünde bulundurularak, D vitamini eksikliğinin yaygın olduğu ülkelerde yeterli D vitamini desteği sağlanmalıdır.

Anahtar Sözcükler:
25-hidroksivitamin D, Preterm bebek, Respiratuvar distres sendromu

INTRODUCTION

Vitamin D is the key regulator of calcium and phosphate homeostasis. Also, it acts on induction of cell differentiation and inhibition of cancer cells, regulation of cardiovascular function and the innate and adaptive immune responses (1). Development of the lung is an ongoing process which begins as soon as third week of gestational age and continues until early adulthood. Vitamin D plays a prominent role in lung development in branching morphogenesis, proliferation of alveolar type-2 cells, surfactant phospholipid secretion and lung maturation (2).
In the premature newborns, the most common respiratory problem is respiratory distress syndrome (RDS). Especially, surfactant deficiency and lung immaturity are foremost factors causing RDS (3). The relationship between vitamin D levels and many common neonatal morbidities especially encountered in the premature infants such as; RDS, sepsis, necrotizing enterocolitis and bronchopulmonary dysplasia have been investigated in the last few years (4). There is limited data on the effect of vitamin D deficiency and development of RDS in preterm newborns (5,6). This study aimed to evaluate effect of vitamin D levels on the development of RDS in preterm infants with a gestational age of ≤ 32 weeks. The association between RDS and severity of vitamin D deficiency was secondary outcome of this study.

MATERIAL and METHODS

This single center retrospective study was performed between April 2019 and April 2021 at Dortcelik Children's Hospital. The research has been complied with all the relevant national regulations, institutional policies and in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee. Parental informed consent was obtained from each patient included in the study. The present study was approved by the Ethics Committee of Uludag University Medical School. The Ethics committee certificate date and no was 11.08.2021: 2021-11/17.
Newborns with a gestational age of ≤32 weeks were included in the study. Gestational age was determined primarily by ultrasonographic evaluation performed in the first trimester and by calculation based on the last menstrual period in follow-up of pregnancies or by clinical evaluation after delivery. Newborns having a gestational age of ≤32 weeks with RDS consisted the study group, while newborns hospitalized in the NICU having ≤ 32 weeks of gestational age with no signs of RDS were the control group. The diagnosis of RDS was considered by x-ray and clinical findings. Nasal continuous positive airway pressure with a mean airway pressure of 7 cm H2O was applied to all newborns. Infants aged ≤26 weeks needed an inspired oxygen fraction (FiO2) of 0.3 and infants aged >26 weeks needed a FiO2 of 0.4, for a target of of arterial oxygen pressure > 60 mm Hg. Beractant alfa (Survanta, Abbvie Inc, North Chicago/ABD) at a dose of 200 mg/kg was used for the infants who needed FiO2 above 0.4. Six hours after the first dose, surfactant treatment were administered to those infants who had no improvement in the clinical course and needing a FiO2 ≥0.4.
Blood sampling for alkaline phosphatase (ALP), calcium (Ca), magnesium (Mg), phosphorus (P), parathyroid hormone (PTH) and 25-hydroxyvitamin D (25-OHD), have been performed from all participants at postnatal six hours of life in the NICU. Serum levels of PTH and 25-OHD were measured by chemiluminescent immunoassay analyzer (Abbott i2000, Abbott Laboratories, USA). The photometry method was used for measuring Ca, Mg, P and ALP levels on the Beckman Coulter AU680 analyzer (Danaher Corporation, Brea, CA, USA). Render BC64 device (Render Biotech Co. Ltd. Shenzen, China) was used for analyzing blood cultures. Maternal demographic data were obtained from medical records. Accompanying maternal diseases, multiple pregnancies, maternal age at the time of delivery and medications used were recorded. Newborns' characteristics such as mode of delivery, birth weight, gestational age, sex, Apgar scores, antenatal steroid use, duration of total parenteral nutrition (TPN), non-invasive and invasive mechanical ventilation (MV) and body weight at discharge and duration of hospitalization were recorded. Also, microorganisms that grew in the blood culture were recorded in the study group. The classification of birth season was; spring (March, April, May), summer (June, July, August), fall (September, October, November) and winter (December, January, February). According to neonatal 25-OHD levels, preterm infants were classified into three groups: Severe vitamin D deficiency (25-OHD levels ≤5 ng/ml), Vitamin D insufficiency (25-OHD levels 5-15 ng/ml) and normal vitamin D (25-OHD levels>15 ng/ml). 25-OHD level ≤ 15 ng/ml was defined as low vitamin D level (6,7).

RESULTS

During the study period, 122 preterm infants having a gestational age of ≤ 32 weeks were included. From these, 56 (46%) had RDS (study group), while 66 (54%) newborns (control group) did not have RDS. The groups did not differ in terms of maternal age, multiple pregnancy, use of antenatal steroid, mode of delivery, sex, maternal age, accompanying maternal diseases, small for gestational age (SGA) infants and body weight at discharge and birth season. In contrast to that, control group had higher gestational age, birth weight, first minute and fifth minute Apgar scores compared to the study group. The study group had longer duration of invasive MV, non-invasive MV and TPN compared to control group. Also, study group was found to have a significantly longer length of hospital stay compared to control group (Table I).

Table I. The maternal and neonatal characteristics of the study and control groups

	Control Group n=66	Study Group n=56	p
Maternal age, year Median(min-max)	28 (16-44)	30 (15-38)	0.13
GA, week Median (min-max)	31 (28-32)	30 (24-32)	0.001
Birth weight, gr Median (min-max)	1670 (740-2200)	1222 (730-1860)	0.001
SGA, n %	22 (33)	10 (18)	0.05
Multiple pregnancy, n %	17 (26)	11 (20)	0.42
Male sex, n %	29 (44)	31 (55)	0.20
Use of antenatal steroid, n %	26 (39)	22 (39)	0.99
Delivery with CS, n%	57 (86)	51 (91)	0.41
1st min Apgar, median (IQR)	8 (4-10)	6 (4-9)	0.001
5th min Apgar, median (IQR)	9 (6-10)	8 (6-10)	0.001
Birth season, n%			0.20
Summer	9 (13)	7 (13)	
Fall	21 (32)	10 (18)	
Winter	13 (20)	19 (34)	
Spring	23 (35)	20 (35)	
Duration of invasive MV, day Median (min-max)	1 (0-5)	4 (0-42)	0.0001
Duration of non-invasive MV, day Median (min-max)	1 (0-18)	4.5 (0-45)	0.0001
Duration of oxygen treatment, day Median (min-max)	1 (0-15)	3 (0-40)	0.001
Length of hospital stay, day Median (min-max)	30 (11-115)	48.5(2-280)	0.0001
Body weight at discharge, gr Median (min-max)	2342 (1600-3480)	2400 (1200-4220)	0.76
Maternal disease, n (%)	31 (47)	36 (64)	0.05
Preeclampsia	8 (12)	22 (39)	
Gestational Diabetes	8 (12)	3 (5)	

p: < 0.05 statistically significant

CS: Cesarean section, GA: Gestational age, IQR: Interquartile range, MV: Mechanical ventilation, SGA: Small for gestational age,

When the groups were compared for laboratory parameters; Ca levels were found to be higher in the control group, while levels of P and Mg were higher in the study group. In contrast to that, median 25-OHD levels of study group and control group were similar (12.3 ng/ml vs 15.6 ng/ml; p=0.38). Also, median ALP and PTH levels were similar between the groups. The rates of preterm infants having low vitamin D levels (25-OHD level<15 ng/ml) did not differ between the groups (38/56, 68% vs 35/66, 53%; p=0.09). In the study group, 5 (9%) preterm infants had severe vitamin D deficiency, 33 (%59) had vitamin D insufficiency and 18 (32%) had normal vitamin D levels. In the control group, 5 (8%) preterm infants had severe vitamin D deficiency, 30 (45%) had vitamin D insufficiency and 31 (47%) had normal vitamin D levels (Table II).

Table II. Comparison of laboratory findings of the study and control groups

Variables	Control group n=66	Study Group n=56	p
Ca (mg/dl), mean ± SD	8.6 ± 0.78	8.2 ± 0.89	0.003
P (mg/dl), Median (min-max)	5.5 (3.4-7.2)	5.6 (2-8.5)	0.02
Mg (mg/dl), Median (min-max)	1.95 (1.4-4.5)	2.1 (1.4-4.7)	0.02
ALP (U/L), Median (min-max)	193 (81- 491)	191 (87-395)	0.95
PTH (pg/ml), Median (min-max)	48 (10-333)	43.5 (15-367)	0.55
25-OHD (ng/ml), Median (min-max)	15.6 (4.4-47.2)	12.3 (4.2-38)	0.38
25-OHD levels, n (%)			0.09
Low (<15 ng/ml)	35 (53)	38 (68)	
Normal (≥15 ng/ml)	31 (47)	18 (32)	
25-OHD levels, n (%)			0.25
Severe deficiency	5 (8)	5 (9)	
Insufficiency	30 (45)	33 (59)	
Normal	31(47)	18 (32)	

p: < 0.05 statistically significant.

Ca: Calcium, P: Phosphorus, Mg: Magnesium, ALP: Alkaline phosphatase, PTH: Parathyroid hormone, 25-OHD: 25-hydroxyvitamin D.

When groups were compared for vitamin D levels in terms of birth season, control group had significantly lower vitamin D levels compared to study group in the winter (10.2 ng/ml vs 16.2 ng/ml; p=0.003), but there was no difference between the groups for other seasons (Table III).

Table III. Comparison of neonatal 25-hydroxyvitamin D levels in terms of season and group at birth

Season	25-hydroxyvitamin D level (ng/ml)		p
	Control Group n=66	Study Group n=56	
	Median (min-max)	Median (min-max)	
Spring	16.4 (6.2-47.2)	11.5 (4.2-18.8)	0.05
Summer	15.7 (4.4-26)	8.8 (4.2-38)	0.25
Fall	16.9 (4.7-20.5)	9.9 (7-17.6)	0.09
Winter	10.2 (5.7-32.3)	16.2 (9.6-29.9)	0.003

P: < 0.05 statistically significant

DISCUSSION

Preterm delivery is the most common cause of surfactant deficiency. In the premature newborns, decreased quantity and quality of surfactant results in RDS (8). Also, the surfactant produced in preterm infants compared with surfactant from term infants has reduced activity because of differences in lipid and protein compositions (9). Experimental animal studies suggested the role of inflammation in the pathogenesis of RDS related to the rapid accumulation of neutrophils in the lung and pulmonary edema. Atelectasis related to surfactant deficiency may result in respiratory epithelial and alveolar capillary endothelial injury, which can trigger a cytokine-mediated inflammatory response (10). Also synthesis of a less active surfactant, reduced surfactant production, and surfactant inactivation decreases the effective surfactant pool size.

Some key hormones have an important role in the development and maturation of organs such as thyroid hormones, glucocorti-

coids and insulin. Growth factors and many other hormones interact with each other in this development process. Recently, new hormones including ghrelin, leptin, glucagon like peptid-1 and gene regulating-hormones such as cholecalciferols and retinoids were found to have a key role in the development of several organs, including the lung (2).
The key regulator of calcium homeostasis is Vitamin D. Calcitriol (1,25-dihydroxyvitamin D) is the active form of vitamin D and produced first by hepatic 25-hydroxylation with the cytochrome P450 2R1 and other enzymes, followed by peripheral tissue 1α-hydroxylation with CYP27B1 enzyme (11). Calcitriol interacts with vitamin D receptor. After binding, it requires a heterodimer formation with retinoid X receptor to interact with vitamin D response elements presenting in the DNA to regulate gene expression (2). The lung is one of the main target tissues of calcitriol during fetal development. Vitamin D receptor is expressed in fetal alveolar type II cells, where its activation induces proliferation and the synthesis and secretion of surfactant.

In animal studies, maternal calcitriol deficiency during lung development was found to have negative effects on development of many organs including the lung which may affect the normal lung physiology (12). Calcitriol supplementation during lactation in rodents with previous deficiency during gestation improves alveolar septation and lung function (13).
Compared to past few years, survival rates of preterm infants have evidently raised with advances in perinatal and neonatal care (14). As a result, rates of extremely low birth (ELBW) and very low birth weight (VLBW) infants have increased. These resulted in an increase of prematurity related morbidities and complications. Therefore, more effort has been given for the prevention rather than the treatment of these morbidities and complications. The incidence of RDS increases with decreasing gestational age. A recent study from Turkey reported the incidence of RDS 95% in the same gestational age group (14). Stoll et al., reported the incidence of RDS as 93% having a gestational age of 28 weeks or below (15).

Vitamin D can be synthesized from the fetal tissues, but maternal vitamin D status is the most important factor on the neonatal 25-OHD levels until neonates are supported for vitamin D from external sources (16). As vitamin D has many important functions in many systems in the human body, supplementation of vitamin D is given during pregnancy all over the world. In Turkey, regardless of blood 25-OHD levels vitamin D supplementation is given beginning from the 12th week of pregnancy to end of pregnancy and continued for six months after delivery. The dose of vitamin D is 1200 IU per day given orally (17).
In this study, premature infants with a gestational age of ≤32 weeks with RDS were found to have lower 25-OHD levels compared to premature infants at the same gestational age without RDS but this was not statistically significant. In contrast to our finding, Dogan et al., reported lower vitamin D levels in RDS patients, but RDS patients had lower gestational age and birth weight compared to control patients (5). Also, RDS patients had higher rates of cesarean section in this study, and cesarean section was reported to be an independent predictor of RDS (5,18,19). In our study, RDS patients had lower birth weight and gestational age compared to control group, but there was no difference for mode of delivery between the groups. In the literature, there are few studies evaluating the association of vitamin D deficiency and its effect on RDS development. These studies concluded vitamin D deficiency as an independent risk factor for RDS development, contrary to our findings (8,19,20). The duration of oxygen treatment, non-invasive and invasive MV were shorter in the control group compared to RDS group, similar to reported in the literature (4,5). In contrast to that, there were no difference in terms of duration of oxygenation and MV in a study examining the association between deficient serum 25-OHD levels at birth and respiratory morbidity which evolved during hospitalization among very low birth weight (VLBW) infants (20). Duration of hospitalization was found to be longer in RDS patients compared to control group, similar to reported in the literature (4-6,21). The RDS patients had lower gestational age and birth weight in the present study. In our opinion, the most important factors for longer duration of oxygen treatment, non-invasive and invasive MV were low gestational age and birth weight, which also caused longer duration of hospital stay. Dogan et al., reported a significant effect of bronchopulmonary dysplasia on the duration of hospitalization and the rate of bronchopulmonary dysplasia was found significantly higher in severe vitamin D deficiency group in that study (5). Similarly Cetinkaya et al. reported a severe vitamin D deficiency in all premature BPD patients (22). In the present study, BPD was not evaluated.

A study including VLBW infants reported higher ALP concentrations in patients with severe vitamin D deficiency compared to vitamin D deficiency and insufficiency groups but in that study, cut-off vitamin D levels were different from the present study (4). ALP levels were similar between the groups in this study.
In the present study, there was no difference between the groups in terms of birth season, but Dogan et al. reported higher birth rates in summer and spring in RDS patients compared to patients without RDS (5).

The present study focused on the relation between neonatal 25-OHD levels and the development of RDS. This study has several limitations. Firstly, due to its retrospective nature, the maternal 25-OHD levels at the time of delivery were not evaluated. Secondly, pregnant women are given vitamin D supplementation beginning from the 12th week of gestation. In the present study, the use of vitamin D supplementation (no usage, irregular use, regular use) was not included. As exposure to sunlight is the most important factor for vitamin D synthesis and use of sun-protective clothing is a major factor in this process, these were not included in the study. Another limitation was the small sample size of the study population. Lastly, the primary focus of this study was the relationship between neonatal 25-OHD levels and development of LOS; maternal 25-OHD levels and use of vitamin D supplementation were not recorded. This was another limitation of the study.

CONCLUSION

In conclusion, the present study found no correlation between 25-OHD deficiency and RDS development. This is the first study declaring no association between vitamin D deficiency and development of RDS having similar sample size with studies declaring contrary results. Up to now, there is no established optimal 25-OHD level for both term and premature infants. Further studies with larger sample size are needed to achieve precise results. Besides, taking into account possible unfavorable both maternal and neonatal effects of vitamin D deficiency, adequate vitamin D supplementation should be provided in countries where vitamin D deficiency is common.

Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Ethics Committee Approval:

The present study was approved by the Ethics Committee of Uludag University Medical School. The Ethics committee certificate date and no was 11.08.2021: 2021-11/17.

Author Contributions:

Erbu Yarci and Emre Baldan were responsible for the conception, design, analysis, and interpretation of data, data collection, writing the draft of the manuscript, and final approval of the manuscript. All authors have read and approved the final version of the article. All authors contributed to the study conception and design.

Financial Disclosure:

The authors received no financial support for the authorship and publication of this article.

Conflict of Interest:

EY and EB declare that they have no conflict of interest.

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ORIGINAL ARTICLE
Özgün Araştırma

The Value Of Ultra-Sensitive Troponin-I In Determining Mortality In Patients With Suspected Acute Coronary Syndrome

Akut Koroner Sendrom Şüpheli Hastalarda Mortalitenin Belirlenmesinde Ultra-Duyarlı Troponin-I'in Değeri

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Geliş Tarihi : 03 December 2021
Received
Kabul Tarihi : 03 March 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Araci C.E, Duyan M, Kartal M, Goksu E.
The Value Of Ultra-Sensitive Troponin-I In Determining Mortality In Patients With Suspected Acute Coronary Syndrome
Akd Med J 2023; 9(3): 265-270

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DOI: 10.53394/akd.1032104

ABSTRACT

Objective:
This study investigated the role of the reference value of ultra-sensitive troponin kits used in daily practice in determining mortality.

Material and Methods:
This study was conducted in the emergency department (ED) of Akdeniz University Hospital between January 1 2018 and June 30 2019. All patients admitted to the emergency department within a period of eighteen months and who had the result of the ultra-sensitive troponin level in the range of 0.06-0.1 ng/mL were included in the study. The recurrent admissions of the patients to the ED were included, and only the first troponin values of the patients were taken as s reference for the study.

Results:
It was determined that 1029 troponin values of 591 patients with initial troponin I value in the range 0.06-0.1 ng/mL were measured. It was found that 332 of these patients were discharged from the emergency department, and the others were hospitalized. It was found that 168 (28.43%) of the patients died. Considering the gender distribution of the patients who died, it was observed that 101 (60.11%) patients were male, and 67 (39.89%) patients were female. A statistically significant difference was found between the ages of the patients who died (mean 71.38±12.25) and the age of patients alive (mean 61.78 ± 15.89) ($p < 0.019$). In univariate analysis, in addition to the positive troponin value, DM ($p<0.022$) and hyperlipidemia ($p<0.018$) were found to be statistically significant.

Conclusion:
For high-sensitive troponin worked in the ED, the upper value of 0.06 ng/mL effectively determines mortality.

Key Words:
Ultra-Sensitive Troponin-I, Mortality, Acute coronary syndrome

ÖZ

Amaç:
Bu çalışmada, günlük pratikte kullanılan ultra-duyarlı troponin kitlerinin referans değerinin mortaliteyi belirlemedeki rolü araştırıldı.

Gereç ve Yöntemler:
Bu çalışma 1 Ocak 2018-30 Haziran 2019 tarihleri arasında Akdeniz Üniversitesi Hastanesi acil servisinde (AS) yapılmıştır. On sekiz ay içinde acil servise başvuran ve ultrasensitif troponin sonucu 0,06-0,1 ng/mL aralığında olan tüm hastalar çalışmaya dahil edildi. Hastaların acil servise tekrarlayan başvuruları dahil edildi ve hastaların sadece ilk troponin değerleri çalışma için referans olarak alındı.

Bulgular:
Başlangıç troponin I değeri 0,06-0,1 ng/mL aralığında olan 591 hastanın 1029 troponin değerinin ölçüldüğü belirlendi. Bu hastalardan 332'sinin acil servisten taburcu edildiği, diğerlerinin ise hastaneye kaldırıldığı öğrenildi. Hastaların 168'inin (%28,43) öldüğü belirlendi. Ölen hastaların cinsiyet dağılımına bakıldığında 101 (%60,11) hastanın erkek, 67 (%39,89) hastanın kadın olduğu görüldü. Ölen hastaların yaşları (ortalama 71,38±12,25) ile yaşayan hastaların yaşları (ortalama 61,78±15,89) arasında istatistiksel olarak anlamlı fark bulundu (p<0,019). Tek değişkenli analizde pozitif troponin değerine ek olarak DM (p<0,022) ve hiperlipidemi (p<0,018) istatistiksel olarak anlamlı bulundu.

Sonuç:
Acil serviste çalışılan yüksek duyarlı troponin için 0,06 ng/mL'lik üst değer etkin bir şekilde mortaliteyi belirler.

Anahtar Sözcükler:
Ultra-Sensitive Troponin-I, Mortalite, Akut koroner sendrom

INTRODUCTION
Despite the recent increase in published research on the diagnosis and treatment of acute chest pain in the emergency department (ED), evaluation of these patients in the ED is compeller. Chest pain is the main complaint in 3-6% of all patients admitted to the ED. The patients with the acute coronary syndrome (ACS), including acute myocardial infarction (AMI) and other high-risk conditions, should be timely and effectively recognized by the emergency physician to initiate specific clinical actions (1,2). In the ED, the risk level of the individual patient is determined by demographic characteristics, history, physical examination, ECG, and the laboratory markers for myocardial necrosis. However, despite all these efforts, 2-8% of the patients are discharged from the ED without a different definitive diagnosis for their chest pain (3).

Globally preferred biomarkers for myocardial damage are cTNs (I or T) with almost absolute myocardial tissue specificity as well as high sensitivity. This means that the microscopic areas of myocardial necrosis can be detected by new assays (4). These measurement kits can measure the troponin levels as low as 1/10 of the old troponin kits. However, while high sensitivity kits have increased sensitivity, their specificity is low, and these assays cause more ACS diagnoses, thus causing more invasive procedures with longer hospitalization periods without any effect on 6-month survival (5,6).

Studies conducted in EDs on high sensitivity troponin tests are generally conducted with cTnT, with fewer studies on cTnI. Lower and upper limits set as normal limits in troponin kits, which have been used as golden standard tests to determine myocardial damage in the world for a long time, are determined against the 99% reference range studied in the normal population. With the introduction of the newer generation hsTn-I kits into daily practice, in the management of patients presenting to the ED with symptoms suggestive of the ACS, there is serious confusion due to the difference between the reference ranges of the hsTn-I kits and the standard kits used in the past. The accepted normal range for older generation standard measuring kits falls in the high troponin level range for hsTn-I kits, and this causes patients discharged from the emergency department to be accepted as acute myocardial infarction (AMI) in the past, assuming that there was no myocardial necrosis. Many patients in this range bring the risk of keeping emergency department and cardiology services busy, patient care beyond the capacity, extra intervention on patients, unnecessary medical expenses, and a large loss of workforce with it. However, high diagnostic sensitivity prevents mortality in more patients.

In this study, the role of the reference value of ultra-sensitive troponin kits used in daily practice in determining mortality was investigated. On the other hand, by examining additional risk factors in patients with troponin values above the reference value and died, properties that may increase specificity in determining mortality with troponin were investigated.

MATERIAL and METHODS
Study Design
This retrospective study was conducted in the ED of Akdeniz University Hospital between January 1 2018 and June 30 2019. The study was approved, and the requirement for informed consent was waived by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (Decision number:773 Date:28th August 2019). The present study was conducted in line with the Declaration of Helsinki.

Sample Selection
All patients admitted to the emergency department within a period of eighteen months and who had the result of the ultra-sensitive troponin level in the range of 0.06-0.1 ng/mL were included in the study. The recurrent admissions of the patients to the ED were included, and only the first troponin values of the patients were taken as a reference for the study. The role of ultra-sensitive troponin kits used in daily practice in the range of 0.06-0.1 ng/mL in determining mortality was investigated.

Data Collection
The records of comorbidities, smoking status (diabetes mellitus, hypertension, hyperlipidemia, history of coronary artery disease) and ultra-sensitive were collected. Troponin I values was obtained from the Hospital Information Management System (MiaMed®) records. Patients who died and their dates of death were identified in the Ministry of Health, Turkey Public Health Institution, Death Reporting System.

High-Sensitive Troponin Kit

High-sensitive cTnI (Siemens, ADVIA Centaur® TnI-Ultra® Assay) kit was used, and the values between 6 ng/L and 50.000 ng/L can be measured in blood. The reference value was 0.06 ng/mL.

Dependent Variable

According to the cardiac risk scoring system, a decision was made for discharge and hospitalization. Mortality within a month was determined through the hospital information management system and the national death reporting system. How the hospital admissions of dying and not dying patients result in terms of discharge and hospitalization were determined.

The patients were classified in terms of their comorbid factors (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, smoking, presence of the tumor, elevated serum creatinine).

Statistical Analysis

The data collected for the study were recorded in SPSS® (IBM Statistical Package for the Social Sciences) and MedCalc® programs. For statistical analysis, Chi-Square and Mann-Whitney U tests were used. Logistic regression analysis was performed for the association between comorbidities and deaths.

RESULTS

A total of 154.589 patients were presented to the ED during the study period, and it was found that troponin analysis was conducted in 16.927 of these patients with suspicion of ACS. It was determined that 1029 troponin values of 591 patients with initial troponin I value in the range of 0.06-0.1 ng/mL were measured.

Three hundred sixty eight of the 591 patients were male (62.26%). The average age was determined as 64.51±15.55. It was found that 332 of these patients were discharged from the emergency department, and the others were hospitalized. It was found that 168 (28.43%) of the patients died. Considering the gender distribution of the patients who died, it was observed that 101 (60.11%) patients were male, and 67 (39.89%) patients were female. It was understood that 51 (30.35%) of the patients who died were discharged from the ED (Table I).

Table I: Demographic and hospitalization data of patients.

Number of Patients Died	101 (60.11%)	67 (39.89%)	51 (30.35%)	117 (69.65%)	168
Number of Patients Alive	267 (63.12%)	156 (36.88%)	281 (66.40%)	142 (33.60%)	423
Total Number of Patients	368	223	332	259	591

Two hundred twenty-eight of the patients had DM, 379 had HT, 101 had HPL (according to the raised LDL level), and 340 had a history of late CAD. Smoking and family history parameters of all patients were not included in the analysis because they could not be reached (Table II).

Table II: Presence of CAD risk factors in patients.

Number of Patients Died	77 (33.77%)	108 (28.49%)	19 (18.81%)	99 (29.12%)
Number of Patients Alive	151 (66.23%)	271 (71.51%)	82 (81.19%)	241 (70.88%)
Total	**228**	**379**	**101**	**340**

Abbreviations: **DM**: Diabetes Mellitus; **HT**: Hypertension; **HPL**: Hyperlipidemia; **CAD**: Coronary Artery Disease

A statistically significant difference was found between the ages of the patients who died (mean 71.38±12.25) and the ages of patients alive (mean 61.78 ± 15.89) (p <0.019).

In univariate analysis, in addition to the positive troponin value, DM (p<0.022) and hyperlipidemia (p<0.018) were found to be statistically significant.

According to the multivariate (regression) analysis, the history of DM, HT, and HPL was found to be statistically significant in terms of determining death (Table III).

Table III: Logistic regression analysis.

DM	,016
HT	,026
HPL	,030
Late CAD	,643
Gender	,479
Age	,000
Constant	,000

Abbreviations: **DM**: Diabetes Mellitus; **HT**: Hypertension; **HPL**: Hyperlipidemia; **CAD**: Coronary Artery Disease

DISCUSSION

According to the results of our study, it was found that mortality was high (28.43%) in patients with high-sensitive troponin I levels (in the range of 0.06-0.1 ng/mL) compared to the current values. On the other hand, even if the troponin is slightly increased, it was determined that patients exceeding the reference value are at high risk for major cardiac events.

Several studies on the value of high-sensitivity troponin levels were conducted in previous years. Kavasoğlu et al., in their study, tested the effectiveness of the 14 pg/ml threshold value of high-sensitive troponin T in determining mortality. They found the sensitivity of the present value of troponin T to be 87% and the selectivity to be 69%. Their study found that the sensitivity of high-sensitivity troponin increased at low values and its selectivity increased at high values (7). Our study determined that the next generation high-sensitive troponin level is highly effective in predicting mortality at values above the reference value. It was determined that 168 of the total 591 troponin-positive patients died. Still, similarly, as the reference value increases, the selectivity of the test increases. From this point forth, it can be said that the high-sensitive troponin reference value is effective in determining mortality. On the other hand, our patient group in the study started from the lowest reference value of 0.06 ng/mL. In this case, it may be difficult to interpret in terms of determining the death of patients at values below the current reference value. In other saying, a study to determine a new lower threshold value may be helpful in terms of the value of the current threshold in determining the measurement. Indeed, in their article, Lippi, and Sanchez-Comar investigated the high-sensitivity troponins and stated that new threshold value studies would be useful in this regard (8).

The value of high-sensitivity cardiac troponin measurement in determining myocardial infarction has been recently investigated (9). Accordingly, it is stated that the diagnostic algorithms used safely in Europe can safely diagnose AMI, and these diagnostic algorithms can be applied in the USA. One of the algorithms used in this study is the Siemens ADVIA Centaur® TnI-Ultra® kit that we used in our study. According to the results of our study, it can be interpreted that the aforementioned high-sensitivity kit can be used safely in the diagnosis of AMI.

The value of cardiac troponins in predicting major adverse events, including death, is known (10). The relationship between high troponin levels and death has also been confirmed in our study. The use of risk scoring in terms of ACS evaluation in the ED is a class 1 recommendation (11). Accordingly, a positive cardiac troponin level is used in HEART and TIMI scores used for these patients (12). In the HEART scoring system, 1 point is given for an increase of 1-3 times the normal level of troponin, and 2 points are given for an increase of 3 times and above. According to our study, it was found that mortality increases significantly even with troponin levels increasing up to 70% of normal. Although the Heart score study determined risk factors with a very high number of patients and related regression analyses, it should be noted that troponin levels can currently be considered as an independent risk factor. High troponin value is an exclusively effective parameter in determining mortality. It may be useful to be more weighted when using risk scores. Besides, if a lower threshold value is determined, more patients can be identified in the ED. New studies to be conducted on this subject can be enlightening.

One of the most important factors in our study is the association between DM and cardiac adverse events. Hyperglycemia and insulin resistance seen in diabetes and prediabetes causes an increase in oxygen radicals that trigger intracellular molecular signaling. The increase in the resulting prothrombotic process and inflammatory mediators also accelerates atherosclerotic changes and the development of macrovascular complications. It has been shown that prediabetic states characterized by impaired fasting glycemia (IFG) or impaired glucose tolerance (IGT) are directly related to cardiac morbidity and mortality (13). In our study, DM was determined as an exclusively important risk factor in the occurrence of cardiac adverse events. DM is not the only parameter among the parameters used for ACS risk scoring in EDs (14). However, according to the results of our study, DM was identified as a parameter that can be used to determine death. Although risk evaluation of diabetes in patients with normal troponin levels has not been performed, it can be said that mortality will be high in patients with low troponin positivity who are considered to have diabetes and ACS. New risk assessment studies to be conducted can be a guide in this regard.

According to the results of our study, HPL is also seen as an independent risk factor. Although the retrospective nature of our research allows these patients to have their HPL evaluated, this information is not always available in the ED. Even so, HPL, if present, can be taken into account when performing risk evaluation. The absence of previously requested lipid panels in patients with suspected ACS may be requested from the ED.

Limitations

Due to the retrospective nature of the study, there may be question marks regarding data reliability. On the other hand, the fact that the hospitalization and discharge procedures of the patients in our hospital are conducted according to the current guidelines (AHA and ESC), also, the major parameter of the study, the measurement of which is done through the Death Reporting System (DRS) minimizes the importance of this problem. The cause of death was determined from the Ministry of Health, Turkey Public Health Institution, Death Reporting System (DRS). In this system, the exact cause of death of the patients may not be understood. On the other hand, although there is a possibility that patients might die from another cause, the death rate of 28.43% is a very high rate. While determining the number of patients who died, a certain time limitation for death was not taken into account. The duration of death in these patients is unclear. This situation does not meet the criteria for serious cardiac events and death generally accepted in the literature. On the other hand, there is a high mortality rate even when time is not taken into account. It should also be noted that the troponin value for these patients is sent with the prediagnosis of ACS. This study only provides information about the first high-sensitive troponin value studied at the time of admission. Consequently, it does not provide enough information about other troponin values that were studied repeatedly. Besides, since the troponin values of the patients at the time of applica-

tion were included in the study, it does not provide any information about the time of symptom onset. Troponin values in the range of 0.06 - 0.10 ng/mL were included in the study, and it would be possible to reach different results in a study to be conducted on all positive values. Studies to be conducted on this subject are needed. Besides, it is also thought that different practices varying from physician to physician and different preferences in sending troponin may affect the results.

CONCLUSION

For high-sensitive troponin measured in the ED, the upper value of 0.06 ng/mL is effective in determining mortality. However, studies to be conducted to lower the upper threshold value may be suitable for the reduction of false-negative patients. On the other hand, DM was determined as a parameter that can be used alone in determining mortality, and this may be a guide in the risk evaluation of patients.

Ethics Committee Approval:
The study was approved, and the requirement for informed consent was waived by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (Decision number:773 Date:28th August 2019). The present study was conducted in line with the Declaration of Helsinki.

Informed Consent:
Informed consent was not obtained as it was a retrospective clinical study.

Author Contributions:
Concept – C.E.A., M.K.; Design - CEA., M.K.; Supervision - C.E.A., M.K., M.D., E.G.; Resources - C.E.A., M.K., M.D., E.G; Materials C.E.A., M.K., M.D., E.G; Data Collection and/or Processing C.E.A., M.K., M.D., E.G; Analysis and/ or Interpretation - C.E.A., M.K., M.D., E.G; Literature Search - C.E.A., M.K., M.D., E.G; Writing Manuscript - C.E.A., M.K., M.D., E.G; Critical Review - C.E.A., M.K., M.D., E.G.

Conflict of Interest:
The authors have no conflict of interest to declare.

Financial Disclosure:
The authors declared that this study has received no financial support.

Presented in:
On 27 November 2021, as an emergency report at the 7th Eurasian Medical Congress and the 17th Turkey Medical Congress.

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ÖZGÜN ARAŞTIRMA
Original Article

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Geliş Tarihi : 07 Aralık 2021
Received
Kabul Tarihi : 26 Şubat 2022
Accepted
E Yayın Tarihi : 01 Eylül 2023
Online published

Bu makalede yapılacak atıf
Cite this article as
Perk O, Çakmak FN, Aliefendioğlu D.
Yenidoğan Dönemi Hastalıklarında Kan Basıncı Değerlerinin Belirlenmesi
Akd Tıp D 2023;9(3): 271-276

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DOI: 10.53394/akd.1033418

Yenidoğan Dönemi Hastalıklarında Kan Basıncı Değerlerinin Belirlenmesi

Determination Of Blood Pressure In Newborn Diseases

ÖZ

Amaç:
Bu çalışmada, yenidoğan yoğun bakım ünitesinde farklı tanılarla izlenen bebeklerin kan basınçlarının sağlıklı bebeklerle karşılaştırılması, doğum şekli, gebelik yaşı, kilo, cinsiyet ve postnatal yaşa göre değerlendirilmesi ve hipertansiyon sıklığının belirlenmesi amaçlanmıştır.

Gereçler ve Yöntemler:
Bu prospektif, gözlemsel, kohort bir çalışmada, Ankara Dışkapı Çocuk Hastanesi Yenidoğan Servisinde altı ay süreyle izlenen 465 bebeğin kan basıncı değerleri değerlendirildi. Kan basıncı değerlerinin cinsiyet, postnatal yaş, doğum şekli, doğum ağırlığı, annedeki hipertansiyon ve diyabet öyküsü gibi parametreler ile ilişkisi değerlendirildi. Değişik tanı gruplarındaki respiratuar distres sendromu (RDS), neonatal pnömoni, sepsis, indirekt hiperbilirubinemili (İHB) hasta bebekler, gestasyonel yaşları dikkate alınarak kontrol grubuyla sistolik, diastolik, nabız ve ortalama arteryel kan basınçları (OAKB) açısından karşılaştırıldı.

Bulgular:
Çalışmamıza 465 yenidoğan bebek dahil edildi. Bunlardan 217'si kız idi (%46,7). Doğum ağırlığı ve gebelik yaşı arttıkça kan basıncının da paralel olarak arttığı görüldü ($p<0,05$). Term ve preterm sepsis, RDS, neonatal pnömoni tanısı olan bebeklerin kontrol grubuna göre sistolik kan basınçları düşük ($p<0,05$), diastolik kan basınçları ise yüksek bulundu ($p<0,05$). Altı bebekte hipertansiyon saptandı (%1,3). Bu bebeklerin tanıları bilateral renal displazi (n=1), akut böbrek yetmezliği (dehidratasyona bağlı) (n=1), hipoksik iskemik ensefalopatiye bağlı böbrek yetmezliği (n=1), aort koarktasyonu (n=1), konjenital adrenal hiperplazi (tuz kaybettiren form) (n=1) ve pnömotoraks (n=1) idi.

Sonuç:
Yenidoğan yoğun bakım ünitesinde yatan hastaların takip ve tedavisinde tansiyon ölçümü son derece önemlidir. Kan basıncı ölçümü tanı koydurucudur. Bu yüzden ölçüm dikkatli yapılmalıdır. Direkt ölçüm standart olsa da noninvaziv metotlar klinik olarak daha kullanışlıdır.

Anahtar Kelimeler:
Yenidoğan, Kan basıncı, Yenidoğan yoğun bakım, Hipertansiyon

ABSTRACT

Objective:

In this study, we aimed to compare the blood pressures of babies followed up with different diagnoses in the neonatal intensive care unit with healthy babies, to evaluate them according to delivery type, gestational age, weight, gender and postnatal age, and to determine the frequency of hypertension.

Material and Methods:

A prospective, observational and cohort study was conducted on blood pressures of 465 infants for a year in Ankara Pediatrics Training Hospital Neonatal Service. The relationship between blood pressure values and parameters such as gender, postnatal age, type of delivery, birth weight, maternal hypertension and diabetes history were evaluated. İll babies in different diagnosis groups of respiratory distress syndrome (RDS), neonatal pneumonia, sepsis, indirect hyperbilirubinemia (İHB) were compared with the control group in terms of systolic, diastolic, arterial pulse and mean blood pressures, taking into account their gestational age.

Results:

A total of 465 newborns, of whom 217 (46.7%) were female, were included in our study. It was observed that blood pressure increased in parallel with increasing birth weight and gestational age ($p<0.05$). Compared to the control group, infants diagnosed with early and late neonatal sepsis, RDS and neonatal pneumonia had lower systolic blood pressures ($p<0.05$) and higher diastolic blood pressures ($p<0.05$). Hypertension was found in six infants (1.3%). The diagnoses of these babies were as follows; Bilateral Renal Dysplasia (n=1), Acute Prerenal Kidney Failure (Due to Dehydration) (n=1), Hypoxic Ischemic Encephalopathy and Intrinsic Renal Kidney Failure (n=1), Aortic Coarctation (n=1), Congenital Adrenal Hyperplasia (salt-losing form) (n=1) and Pneumothorax (n=1).

Conclusion:

Blood pressure measurement is extremely important in the follow-up and treatment of patients hospitalized in the neonatal intensive care unit. Blood pressure measurement is diagnostic. Although direct measurement is standard, noninvasive methods are more clinically useful.

Key Words:

Neonatal, Blood pressure, Neonatal intensive care, Hypertension

GİRİŞ

Hipertansiyon, 1970'li yıllarda yenidoğanın önemli bir klinik problemi olarak değer1endirilmiştir (1). Bundan sonraki dönemde araştırmalar yenidoğan yoğun bakım ünitelerinde kan basıncı ölçümü üzerine yoğunlaşmıştır. Kan basıncını daha invaziv teknikler ile ölçme daha doğru ve kesin tanı koymaya yardımcı olmasına karşın, umbilikal artere kateter yerleştirmenin getirdiği komplikasyonlar (renal arter veya dallarında tromboz veya hipertansiyon gelişme riski gibi) görülebilir (2).

Son zamanlarda hipertansiyonun tanı ve tedavisine yönelik çalışmalar hız kazanmıştır (3). Hipertansiyon teriminin kullanılması normal tansiyon değerinin çok iyi belirlenmiş olmasını gerektirir. Renal, vasküler, endokrin ve ilaç kullanımı gibi sebepler hipertansiyon etyolojisinde rol alabilir (2). Yenidoğanlarda çoğunlukla hipertansiyon nedeni renovasküler ve renal parankimal hastalığa bağlı olduğu için pediatrik nefroloji uzmanlarıyla birlikte çalışmak gerekebilir (4,5).

Hastaneye yatırılan yenidoğanların kan basıncı en az bir kez tüm ekstremitelerden ölçülmelidir (6). Yenidoğan döneminde kan basıncı yüksek saptanan bebeklerin hayatının sonraki döneminde kan basıncının yüksek seyrettiği bildirilmiştir (7). Bu nedenle hipertansiyonlu yenidoğanların uzun süreli izlemi gereklidir.

Bu çalışmanın amacı, yenidoğan yoğun bakım ünitesinde takip edilen bebeklerin tanı gruplarına göre kan basınçlarının izlemi ile doğum şekli, gebelik yaşı, kilo, cinsiyet ve postnatal yaşa göre sağlıklı infantlarla kan basınçlarını karşılaştırmaktır.

GEREÇ ve YÖNTEMLER

Bu çalışma, Doç. Dr. Fatma Nur Çakmak ve Prof. Dr. Didem Aliefendioğlu danışmanlığında 2004 tarihinde sunduğumuz prospektif bir çalışma olan "Yenidoğan Dönemi Hastalıklarında Kan Basıncı Değerlerinin Belirlenmesi" başlıklı tıpta uzmanlık tezi esas alınarak hazırlanmıştır. Etik kurul onayı İnsan katılımcıları içeren çalışmalarda gerçekleştirilen tüm prosedürler, kurumsal ve/veya ulusal araştırma komitesinin etik standartlarına ve 1964 Helsinki deklarasyonuna ve daha sonraki değişikliklere veya karşılaştırılabilir etik standartlara uygun şekilde yapılmıştır. Bu çalışma için etik kurul onayı Ankara Dışkapı Çocuk Hastanesi etik kurulundan alınmıştır (10.04.2003; E. Kurul -E 218).

Ankara Dışkapı Çocuk Hastanesi Yenidoğan Servisi'nde 1 Aralık 2002 ile 1 Haziran 2003 tarihleri arasında altı ay süresince izlenen bebeklerin (n=465) sağ üst ekstremiteden ölçülen kan basınçları ölçümü benzer gebelik yaşında ve ağırlığında sağlıklı (n=118) term ve preterm bebeklerle karşılaştırıldı. Ölçümler, yattığı anından itibaren beş gün boyunca sabah dokuzda olmak üzere osilometrik yöntemle yapıldı. Ölçüm sırasında tüm bebekler beslenmiş ve uyanıktı.

Manşon seçimi "American Heart Association" tarafından önerilen genişliği ekstremitenin orta noktasını çevreleyen mesafenin en azından %40'nı, uzunluğu ekstremitenin 2/3'ünü kapsayacak şekilde sağ üst ekstremiteden ölçüldü. Her hastanın femoral nabzı kontrol edildi. Ölçümler yatar pozisyonda ve ekstremite kalp düzeyinde iken yapıldı. Sistolik ve diastolik kan basınçları Athena (SunTech, ABD) monitörde kaydedildi. Aynı hastaların kan basınçları ölçümleri aynı hemşireler tarafından alındı.

Kan basıncı değerleri tanı gruplarına göre sınıflandırıldı. Ayrıca, kan basıncı değerlerinin cinsiyet, postnatal yaş, doğum şekli, doğum ağırlığı, annedeki hipertansiyon ve diyabet öyküsü gibi parametreler ile ilişkisi değerlendirildi. Kan basınçları tanı gruplarına göre yüksek, normal ve düşük olarak değerlendirildi. Değerlendirmede gebelik yaşı ve postnatal yaşa göre belirlenmiş kan basıncı eğrileri kullanıldı. İstatistiksel derecede karşılaştırma tanı grupları gestasyonel yaş dikkate alınarak sağlıklı kontrol grubuyla sistolik, diastolik, nabız ve ortalama kan basıncı arasında karşılaştırma yapıldı.

Yenidoğan yoğun bakım ünitemizde en sık görülen respiratuvar distres sendromu, neonatal pnömoni, sepsis, indirekt hiperbilirubinemili hastalar çalışmaya dahil edildi. Sürfaktan ve/veya ventilatör destek tedavisi alan veya almayan bütün RDS'li bebekler ile exchange transfüzyon ve/veya fototerapi tedavisi alan veya almayan bütün İHB'li hastalar araştırmaya dahil edildi. Hastalar gestasyonel yaşlarına göre aşırı preterm, preterm, term ve postterm olarak sınıflandırıldı. Doğum ağırlıklarına göre ise, 1000 gram altı, 1001-1500 gram, 1501-2500 gram, 2501-4000 gram ve 4001 gram üzeri olarak sınıflandırıldı. Hastaların sistolik, diastolik nabız ve ortalama arteryel basınçları kaydedildi.

İstatistiksel analiz ve yöntem

İlk olarak değişkenlerin tanımlayıcı özellikleri (ortalama, ortanca, sayı ve yüzde) bulundu. Sayısal değişkenlerin normal dağılıma uyup uymadıkları kontrol edildi. İki grup karşılaştırılırken normal dağılım gösteren sayısal değişkenler için Student t testi kullanıldı. Normal dağılmayan sayısal değişkenler için Mann-Whitney U testi kullanıldı. Kategorik değişkenleri karşılaştırmak için ki-kare testi yapıldı. Bir p-değeri <0,05 istatistiksel olarak anlamlı kabul edildi. Sonuçları değerlendirmek için Statistical Package for Social Sciences (SPSS) sürüm 17 (Chicago, Illinois, ABD) kullanıldı.

BULGULAR

Çalışmamız 465 yenidoğan bebek ile gerçekleştirildi. Bunlardan 217'si kız (%46,7), 248'i (%53,3) erkekti. Bebeklerin cinsiyetlerine göre sistolik, diastolik, nabız ve ortalama arteryel kan basınçları arasında anlamlı fark saptanmadı (p>0,05). Doğumların 320'si normal spontan doğum, 145'i sezaryan doğumla gerçekleşmişti ve doğum şekli ile kan basınçları arasında anlamlı bir fark görülmedi (p>0,05).

Bebekler doğum ağırlığına göre gruplandırıldığında 1000-1500 gram arasında 37 bebek, 1500-2500 gram arasında 112 bebek ve 2500 gramın üzerinde 316 bebek mevcuttu. Kan basınçları ile doğum ağırlığı arasında anlamlı bir ilişki bulundu (p<0,05). Doğum ağırlığı arttıkça sistolik, diastolik, nabız basıncı ve ortalama arteryel kan basıncı artış göstermektedir.

Çalışmadaki bebeklerin 131'i preterm, 334'ü term idi ve gebelik yaşı ile kan basınçları arasında istatistiksel olarak anlamlı bir ilişki bulundu (p<0,05). Gebelik yaşı arttıkça kan basınçları da artmaktadır.

Kontrol grubundaki preterm bebeklerin kan basıncı ortalama ± SD değerleri: Sistolik 71,2 ± 6,1 mmHg, diastolik 38,3 ± 5,9 mmHg, nabız basıncı 33,0 ± 4,7 mmHg ve OAKB 49,3 ± 5,6 mmHg olarak ölçüldü. Kontrol grubundaki term bebeklerin kan basıncı ortalama ± SD değerleri: Sistolik 76,2 ± 7,3 mmHg, diastolik 39,3 ± 6,2 mmHg, nabız basıncı 36,9 ± 7,6 mmHg ve Ortalama arteryel kan basıncı (OAKB) 51,3 ± 5,5 mmHg olarak ölçüldü.

RDS'li preterm bebeklerin arteryel kan basıncı ortalama ± SD değerleri: Sistolik 62,4 ± 8,7 mmHg, diastolik 38,8 ± 8,1 mmHg, nabız basıncı 23,8 ± 8,3 mmHg, ortalama arteryel kan basıncı 46,7 ± 7,5 mmHg olarak ölçüldü. Bu bebekler preterm kontrol grubu ile karşılaştırıldığında, RDS'li bebeklerin sistolik ve nabız basınçları daha düşük bulundu.

Ayrıca, bu grupta sistolik kan basınçları ile nabız basınçları arasında anlamlı bir ilişki bulunurken (p<0,05) diastolik kan basınçları ve ortalama arteryel kan basınçları arasında anlamlı bir ilişki bulunmadı (p>0,05).

Annede gestasyonel diyabet öyküsü olan yedi yenidoğan bebeğimiz vardı. Bu bebeklerin hepsi makrozomikti. Annede hipertansiyon hikayesi olan 27 yenidoğan vardı. Annede hipertansiyon öyküsü olanlar ile olmayanlar arasında kan basıncında anlamlı bir ilişki saptanmadı (p>0,05).

Vakaların tanılarına göre dağılımı Tablo I'de verilmiştir.

Tablo I: Bebeklerin tanılarına göre dağılımı

Tanı	Vaka	%
RDS	43	9,2
Neonatal Pnömoni	70	15,1
Islak Akciğer	2	0,4
Pnömotoraks	3	0,6
Mekanik Ventilatör desteği	4	0,9
Aort Koarktasyonu	1	0,2
PDA	2	0,4
Diğer Konjenital Kalp Hastalıkları	14	3,0
ABY	3	0,6
Konjenital Renal Anomaliler	2	0,4
HİE	11	2,4
Neonatal konvülziyon	3	0,6
İntra kranial kanamalar	3	0,6
SSS gelişimsel anomaliler	3	0,6
Sepsis	53	11,4
Menenjit	1	0,2
Cilt enfeksiyonu	7	1,5
Metabolik Hastalık	3	0,6
Dehidratasyon	10	2,1
Hipoglisemi	3	0,6
İUGG	17	3,7
Polisitemi	2	0,4
Anemi	3	0,6
Kan değişimi Gerektiren Sarılık	6	1,3
İndirekt Hiperbilirubinemi (Preterm)	21	4,5
İndirekt Hiperbilirubinemi (Term)	53	11,4
MAS	4	0,8
Preterm sağlıklı kontrol grubu	31	6,7
Term sağlıklı kontrol grubu	87	18,7
Toplam	**465**	**100**

RDS: Respiratuvar Distres Sendromu, PDA: Patent Ductus Arteriozis, ABY: Akut Böbrek Yetmezliği, HİE: Hipoksik İskemik Ensefolopati, SSS: Santral Sinir Sistemi, İUGG: İntra Uterin Gelişme Geriliği, MAS: Mekonyum Aspirasyon Sendromu

Neonatal pnömoni (%15,1), Sepsis (%11,4), İHB (%11,4) ve RDS (%9,2) sık görülen hastalıklardı. Bu nedenle çalışmaya, istatistiksel açıdan karşılaştırma yapılabilecek tanı gruplarından RDS, neonatal pnömoni ve sepsis tanısı olan hastalar alındı. Bunlar term ve preterm olarak gruplandırıldı ve sağlıklı kontrol grupları ile karşılaştırıldı. Tanılarına göre kan basınçlarının ortalama ± SD değerleri (mmHg) Tablo II'de verilmiştir.

Tablo II: Tanılarına göre kan basınçlarının ortalama ± SD değerleri (mmHg)

Tanı	Sistolik KB	Diastolik KB	Nabız B	Ortalama KB
RDS	62,4 ± 8,7	38,8 ± 8,1	23,8 ± 8,3	46,7 ± 7,5
Neonatal Pnömoni (Preterm)	70,5 ± 12,1	45,2 ± 5,7	25,2 ± 8,4	54,0 ± 7,5
Neonatal Pnömoni (Term)	69,6 ± 9,9	47,2 ± 6,6	22,3 ± 6,9	54,8 ± 7,2
Sepsis (Preterm)	63,2 ± 6,4	43,0 ± 5,8	20,1 ± 6,7	49,7 ± 5,1
Sepsis (Term)	69,8 ± 7,6	46,5 ± 6,9	22,9 ± 5,5	54,3 ± 6,8
İndirekt Hiperbilirubinemi (Preterm)	59,9 ± 10,4	38,8 ± 6,3	21,0 ± 7,6	45,9 ± 7,1
İndirekt Hiperbilirubinemi (Term)	69,6 ± 9,9	45,5 ± 6,2	23,7 ± 7,5	53,1 ± 6,6
Sağlıklı kontrol grubu (Preterm)	71,2 ± 6,1	38,3 ± 5,9	33,0 ± 4,7	49,3 ±5,6
Sağlıklı kontrol grubu (Term)	76,2 ± 7,3	39,3 ± 6,2	36,9 ± 7,6	51,3 ±5,5

KB: Kan Basıncı

Neonatal pnömonili bebekler (n=70) gebelik yaşlarına göre preterm ve term olarak gruplandırıldı. Neonatal pnömonili preterm bebeklerin (n=27) arteryel kan basınç ortalama ± SD değerleri: Sistolik 70,5 ± 12,1 mmHg, diastolik 45,2 ± 5,7 mmHg, nabız basıncı 25,2 ± 8,4 mmHg, ortalama arteryel kan basıncı 54,0 ± 7,5 mmHg olarak ölçüldü. Bu bebekler ile preterm kontrol grubu ile karşılaştırıldığında aralarında diastolik ve nabız basıncı açısından anlamlı fark bulunurken (p<0,05), sistolik ve (OAKB) açısından fark bulunmadı (p> 0,05). Neonatal pnömonili preterm bebeklerde diastolik kan basıncı daha yüksek iken nabız basıncı ise daha düşük idi.

Neonatal pnömonili term bebeklerin kan basıncı ortalama ± SD değerleri: Sistolik 69,6 ± 9,9 mmHg, diastolik 47,2 ± 6,6 mmHg, nabız basıncı 22,3 ± 6,9 mmHg, OAKB 54,8 ± 7,2 mmHg olarak ölçüldü. Bu bebeklerin sistolik, nabız ve OAK basınçları pnömonisi olmayan term bebeklere göre daha düşük iken, diastolik kan basıncı daha yüksek bulundu. Sistolik, diastolik, nabız ve OAKB' ları arasında istatistiksel olarak anlamlı ilişki bulunmuştur (p <0,05).

Sepsisli preterm bebeklerin kan basıncı ortalama ± SD değer leri: Sistolik 63,2 ± 6,4 mmHg, diastolik 43,0 ± 5,8 mmHg, nabız basıncı 20,1 ± 6,7 mmHg, OAKB 49,7 ± 5,1 mmHg olarak ölçüldü. Bu bebekler ile preterm kontrol grubu arasında sistolik, diastolik ve nabız basıncı açısından anlamlı fark saptanırken (p<0,05), OAKB açısından anlamlı fark bulunmadı. Sistolik ve nabız basınçları kontrol grubuna göre daha düşük bulunurken, diastolik kan basınçarı daha yüksek bulundu.

Sepsisli term bebeklerin kan basıncı ortalama ± SD değerleri: Sistolik 69,8 ± 7,6 mmHg, diastolik 46,5 ± 6,9 mmHg, nabız basıncı 22,9 ± 5,5 mmHg, OAKB basıncı ise 54,3 ± 6,8 mmHg olarak ölçüldü. Bu bebekler ile sağlıklı term bebekler arasında arasında sistolik, diastolik, nabız basınçları ve OAKB açısından anlamlı fark bulundu (p<0,05). Sistolik ve nabız basınçları düşük, diastolik ve OAKB ise daha yüksek idi.

İHB'li preterm bebeklerin kan basınç ortalama ± SD değerleri: Sistolik 59,9 ± 10,4 mmHg, diastolik 38,8 ± 6,3 mmHg, nabız basıncı 21,7 ± 7,6 mmHg, OAKB 45,9 ± 7,1 mmHg ölçüldü. İHB'li preterm bebeklerle sağlıklı preterm bebekler arasında sistolik, nabız basıncı ve OAKB açısından anlamlı fark bulunurken (p<0,05), diastolik kan basıncı açısından anlamlı fark bulunmadı (p> 0,05). Sistolik ve nabız basınçları ile OAKB kontrol grubuna göre anlamlı olarak düşüktü.

İndirekt hiperbilirübinemili term bebeklerin kan basıncı ortalama ± SD değerleri: Sistolik 69,6 ± 9,9 mmHg, diastolik 45,5 ± 6,2 mmHg, nabız basıncı 23,7 ± 7,5 mmHg, OAKB 53,1 ± 6,6 mmHg olarak ölçüldü ve sağlıklı term bebekler ile karşılaştırıldığında sistolik, diastolik, nabız basınçları ve OAKB açısından anlamlı fark saptandı (p <0,05). İlk grupta diastolik kan basıncı daha yüksek iken sistolik ve nabız basıncı ile OAKB daha düşük bulundu.

Çalışmamızda, altı yenidoğan bebekte hipertansiyon tanımlandı. Hipertansiyon saptanan bebeklerin tanıları: Bilateral renal displazi (n=1), prerenal böbrek yetmezliği (dehidratasyona bağlı) (n=1), hipoksik iskemik ensefolopati + renal zedelenme (n=1), aort koarktasyonu (n=1), konjenital adrenal hiperplazi (tuz kaybettiren form) (n=1) ve pnömotoraks (n=1) idi. İlk üç yenidoğanın kan basınçları antihipertansif ilaçlarla regüle edildi. Çalışmamızda üç pnömotorakslı bebekten diğer ikisinin kan basıncı normaldi.

TARTIŞMA

Yenidoğanlarda hipertansiyon insidansı, %0,2 ile %3 aralığında yer almaktadır. İnsidansın farklı oranlarda bulunması, ölçümlerdeki teknik farklılıktan olabileceği gibi, çalışma yapılan ünitelerde izlenen hasta popülasyonunun farklılığından da kaynaklanıyor olabilir. Yoğun bakıma kabul edilen hipertansif hastaların %25'ini doğum ağırlığı 1500 gramdan az olan yenidoğanların oluşturduğu bildirilmektedir (4,8). Bu çalışmada, hasta bebeklerde kontrol grubuna göre kan basınçları daha düşük bulundu. Hipertansiyon saptanan sadece altı hastamız vardı.

Kan basıncının umbilikal veya radiyal kateterde ölçülmesi en doğru yöntemdir. Ayrıca bu kateter hipertansiyonun düzeltilmesinde tedavi amaçlı olarak ta kullanılabilir. Çalışmamızda, kan basıncı ölçümleri osilometrik yöntemle yapılmıştır. Frisen ve arkadaşları, osilometrik yöntemle Doppler tekniğini karşılaştırmışlar ve sonuçta hem prematürelerde ve hem de zamanında doğan bebeklerde istatistiksel açıdan anlamlı bir korelasyon olduğunu göstermişlerdir (9). Osilometrik ölçümlerde direk arteryel basınç ölçümüne yakın sonuçlar elde edilmektedir, ancak ekstremite ödemi veya hipertansiyon varlığında metod geçerliliğini yitirmektedir. Uygun manşon uzunluğunun kol çevresine oranının 0,45-0,70 arasında olduğu bildirilmektedir. Direkt yöntemlerle elde edilen kan basıncı ile osilometrik yöntemle elde edilen kan basıncı arasında fark olmasının nedeni uygun olmayan manşonun kullanılmasıdır.

Postnatal ilk 48 saatte osilometrik teknikle belirlenen ortalama arteryel kan basıncının direkt yöntemle ölçülen kan basıncından 3 mmHg daha yüksektir. Hastaların 391'inde, bu değerlerin 5-7. haftalarda ölçülen kan basıncıyla ilişkili olduğunu saptamışlardır. Bu bilgiler ışığında 4-6. günlerde ölçülen kan basınçlarıyla hipertansiyon eğiliminin belirleneceğini öne sürmüşlerdir (10). Bir başka çalışmada ise 219 bebeğin kan basıncı değerleri sistolik 62 ± 6,9 mmHg, diastolik 38 ± 5,7 mmHg bulunmuştur (11). Çalışmamızda belirtilen osilometrik sonuçlar, yukarıda belirtilen çalışmalar ile benzerdir.

Philadelphia neonatal kan basıncı çalışma grubu tarafından yönetilen çok merkezli bir çalışma bulgularında, istatistiksel olarak sistolik ve diastolik kan basıncıyla doğum ağırlığı arasında pozitif ilişki saptamışlardır (12). Çalışmamızda da doğum ağırlığı ile sistolik ve diastolik kan basınçları pozitif korelasyon göstermiştir. Vajinal ve sezaryenle doğan bebeklerde sempa-

toadrenal aktivite ve periferik kan akımını karşılaştırmışlar, vajinal yolla doğan bebeklerde daha yüksek katekolamin konsantrasyonuna bağlı olarak periferik vasküler direnç doğumda ve postnatal 2. saatte yüksek bulunmuş ve 24 bebek üzerinde yapılan bu çalışmada kan basınçlarını iki grup arasında benzer bulmuşlardır (13). Araştırmamızda, normal doğumlar ile sezaryen doğumların kan basıncı arasındaki fark istatistiksel olarak anlamlı değildi.

Bir çalışmada, üç ay boyunca büyük bir hastanenin yenidoğan yoğun bakım ünitesine başvuran 695 bebeği araştırmışlar. Bu çalışmada kan basıncının alt ve üst limitleri tanımlanmış. Gestasyonel yaş artıkça kan basıncının artığı bu araştırmada saptanmış (12). Benzer bir çalışmada da sağlıklı 162 term yenidoğanda sistolik kan basıncı 48 saat süresince ölçülmüş ve kan basıncıyla gebelik yaşı arasında önemli ilişki bulunmamıştır (14). Çalışmamızda gestasyonel yaş ile kan basıncı arasında istatistiksel olarak anlamlı ilişki olduğu ve gestasyonel yaş artıkça kan basıncınında artığı gösterilmiştir ($p<0,05$).

Montoring ve arkadaşlarının yapmış olduğu bir çalışmada kan basıncının yüksek seyretmesinde annede hipertansiyon öyküsünün önemli olduğunu ortaya koydular (15). Çalışmamızda annede hipertansiyon hikayesi bulunan bebeklerin kan basınçlarında istatistiksel olarak önemli bir fark saptamadı.

Ağır RDS'li infantlarda kan basıncı, sağlıklı prematür yenidoğanlara göre daha düşük olduğunu gösteren çalışmalar vardır (16). Çalışmamızda da RDS'li hastalar ile sağlıklı preterm hastalar arasında kan basıncı arasında anlamlı fark saptandı ($p<0,05$). RDS'li hastalarımızda kontrol grubuna göre kan basıncı düşük idi.

Yirmi bir yenidoğanla yapılan bir çalışmada septik şokta vasküler rezistansın artığını ve sistemik kan basıncında ise azalma saptandı (17). Çalışmamızda term ve preterm sepsisli hastalarımızda istatistiksel yönden anlamlı olarak sistolik kan basıncı düşük, diastolik kan basıncı ise yüksek bulundu. Yenidoğanda hiperbilirubinemili 963 hastayı değerlendirdikleri çalışmalarında fototerapi alan hastalarında hipotansiyon saptadılar (18).

Pnömoni tanısı alan bebeklerde pulmoner hipertansiyon geliştiği, sağ ventrükül yükünü basınç ve volüm yönünden artırarak periferik vasküler direncin artmasına neden olup diastolik kan basıncının artığı bulunmuş (19). Çalışmamızda neonatal pnömonili hastaların diastolik kan basıncı istatistiksel olarak anlamlı yüksek bulundu. Sistolik kan basıncı ise term neonatal pnömonili hastalarda düşük bulundu ve kan basıncı değerleri hastalık gruplarına göre değişebileceği saptandı. Doğum ağırlığı ve gestasyon yaşıyla kan basıncı arasında önemli ilişki saptanırken cinsiyet, doğum şekli ve annede hipertansiyon hikayesinin olması kan basınçlarında istatistiksel olarak önemli fark saptanmadı. Altı bebekte hipertansiyon saptamamız, yenidoğan bakım ünitemizde kan basınç ölçümünün standart hale getirilmesiyle ilişkilidir.

SONUÇ

Kan basıncı ölçümü tanı koydurucudur. Bu yüzden ölçüm dikkatli yapılmalıdır. Ölçüm tekniğinin seçimi bu nedenle çok önemlidir. Kan basıncı doğru ölçülürse hipertansiyon doğru tanımlanır. Osilometrik cihazlar kullanıldığından manşon uygun olmalıdır. Çoğu zaman normal kan basıncı sağ koldan ölçülür. Ölçmede mümkün olduğunca aynı ekstremiteyi kullanmak gerekir. Sıklıkla doğrudan invaziv arteryel kan basıncı ölçümleri önerilir fakat bütün infantlarda bu mümkün olmayabilir. Direkt ölçüm standart olsa da noninvaziv metotlar klinik olarak daha kullanışlıdır.

Etik Komite Onayı:
Bu araştırma, ilgili tüm ulusal düzenlemelere, kurumsal politikalara ve Helsinki Bildirgesinin ilkelerine uygundur ve Bu çalışma için etik kurul onayı Ankara Dışkapı Çocuk Hastanesi etik kurulundan alınmıştır (10.04.2003; E. Kurul -E 218).

Hasta Onamı:
Tüm katılımcıların hakları korunmuş ve Helsinki Deklarasyonuna göre prosedürlerden önce yazılı bilgilendirilmiş onam alınmıştır.

Yazar Katkıları:
Fikir – O. P., F. N. Ç.; Tasarım – O. P.., F. N. Ç. D. A.; Denetleme – F. N. Ç. D. A..; Kaynaklar – O. P.., F. N. Ç. D. A.; Malzemeler – O. P., F. N. Ç. D. A.; Veri Toplanması ve/veya İşlemesi – O. P.; Analiz ve/veya Yorum – F. N. Ç. D. A.; Literatür Taraması – O.P.; Yazıyı Yazan – O.P.; Eleştirel İnceleme – F. N. Ç., D. A.

Çıkar Çatışması:
Yazarların beyan edecek çıkar çatışması yoktur.

Finansal Destek:
Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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ORIGINAL ARTICLE
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Geliş Tarihi : 14 December 2021
Received
Kabul Tarihi : 08 April 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Abdullayeva G, Ozen N, Ulker P, Basralı F.
The Effect of P2X1 Receptor on Vascular Responses in the Diabetic Rat Model
Akd Med J 2023;9(3): 277-283

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DOI: 10.53394/akd.1034657

The Effect of P2X1 Receptor on Vascular Responses in the Diabetic Rat Model

Diyabetik Sıçan Modelinde Damar Yanıtları Üzerine P2X1 Reseptörünün Etkisi

ABSTRACT

Objective:
Although it is known that there are changes in the vascular purinergic system in diabetes, it is unknown whether P2X1-mediated vascular responses are affected. We aimed to investigate the vascular responses mediated by P2X1 receptor activation in the streptozotocin-induced diabetes model, in this study.

Method:
Animals were divided into two groups: diabetes and control. Diabetes was induced by 65 mg/kg single dose of streptozotocin. After 12 weeks, second branches of the mesenteric artery were isolated and placed into the wire myograph to evaluate the vascular responses to (ATP) and P2X1 receptor agonist. Vascular responses were also examined in the presence of endothelial nitric oxide synthase, cyclooxygenase, or K+ channel inhibitors, to determine the possible mechanism/s of relaxation responses.

Results:
In the diabetes group relaxation responses to ATP and P2X1 receptor agonists were lower compared to the control group. Vascular relaxation responses to P2X1 receptor agonists were significantly decreased in both groups in the presence of endothelial nitric oxide synthase inhibitor. Cyclooxygenase inhibitor and K+ channels inhibitors significantly blocked vascular relaxation responses in the diabetes group but not in control animals.

Conclusion:
The results of this study revealed that vascular P2X1 receptor-mediated relaxation responses are decreased in diabetes and the pathways mediating these responses were changed.

Key Words:
Diabetes, Purinergic signaling, Vasodilatation

ÖZ

Amaç:
Diyabette vasküler pürinerjik sinyalizasyonun değiştiği bilinmesine rağmen, P2X1 aracılı vasküler yanıtların etkilenip etkilenmediği bilinmemektedir. Bu çalışmada, streptozotosin ile oluşturulan diyabetik sıçan modelinde P2X1 reseptör aracılı vasküler yanıtları incelemeyi amaçladık.

Yöntem:
Hayvanlar kontrol ve diyabet olmak üzere iki gruba ayrıldı. Diyabet grubundaki sıçanlara 65 mg/kg streptozotosin, intraperitoneal yolla tek doz uygulandı. On iki hafta sonra mezenter arterin ikinci dalı alınarak, (ATP) ve P2X1 reseptör agonistine cevaben oluşan damar yanıtları, telli miyograf düzeneği kullanılarak değerlendirildi. Vasküler gevşeme yanıtlarına aracılık edebilecek olası mekanizmaların açığa çılarılması amacıyla, vasküler yanıtlar aynı zamanda endotelial nitrik oksit sentaz, siklooksijenaz ve K+ kanal inhibitörlerinin varlığında da incelendi.

Bulgular:
Diyabet grubunda ATP ve P2X1 reseptör agonistine verilen gevşeme yanıtları kontrol grubuna kıyasla önemli düzeyde düşük bulundu. P2X1 reseptör agonistine cevaben oluşan gevşeme yanıtları her iki grupta endotelial nitrik oksit sentaz inhibitörü varlığında önemli derecede azalma gösterdi. Siklooksijenaz inhibitörü ve K+ kanal inhibitörleri ise diyabet grubunda vasküler gevşeme yanıtlarını önemli düzeyde baskılarken, kontrol grubunda etkili bulunmadı.

Sonuç:
Bu çalışmanın sonuçları, diyabette vasküler P2X1 reseptör aracılı gevşeme yanıtlarının azaldığını ve bu yanıtlara aracılık eden yolakların değiştiğini ortaya koymuştur.

Anahtar Sözcükler:
Diyabet, Pürinerjik sinyalizasyon, Vazodilatasyon

INTRODUCTION

ATP and its metabolites are potent mediators of vasomotor tone in several vascular beds. Purinergic receptors, that can bind ATP and ATP degradation products, are present in many tissues in animals and humans. It is known that purinergic signaling has significant effects on vascular tonus and remodeling and plays important roles in various physiological and pathophysiological conditions in the cardiovascular system (1,2). Purinergic receptors are divided into two groups as P1 and P2 receptors and can cause contraction or relaxation of the vessel depending on the location in the vascular tissue and the signaling pathway they are paired with. Although P2 receptors are classified as P2X and P2Y, many subtypes have also been shown. The vasodilator actions of ATP are mediated mainly by P2Y receptors located on the endothelium. P2X receptors, which have seven subtypes, are ligand-gated cation channels and activated by ATP causing membrane depolarization (3). Arterial P2X receptors are usually described as smooth muscle receptors and mediate vasoconstriction (4-6). However, it's suggested by several studies that P2X receptors are also expressed on the endothelium, depending on vascular bed types (7-10). Previous studies have shown endothelial expression of P2X1 receptor in healthy rat mesenteric arteries and its activation with a specific ligand causes vasodilation of isolated mesenteric arteries (11). However, few and insufficient studies examine the role of P2X1 receptors in physiological and pathophysiological conditions compared to other purinergic receptors (1,6,8).

The chronic metabolic disorder diabetes mellitus (DM) is a disease characterized by chronic hyperglycemia. Progressive vascular dysfunction is inevitable as a result of chronic metabolic changes occurring in diabetes. On the other hand, DM contributes to the development of cardiovascular diseases such as hypertension, cardiomyopathy, and atherosclerosis. These complications accompanying diabetes are largely due to micro-and macro-vascular dysfunction. Although the underlying causes of vascular dysfunction are multifactorial, purinergic signaling is also altered in diabetes and contributes to vascular dysfunction development (12). Although studies examining how vascular signaling changes in diabetes have mostly focused on P2X7, P2X4, and P2Y1 receptor-mediated pathways, it is not yet clear whether P2X1 receptor-mediated signaling is affected (12-14). Therefore, the aim of the present study was to investigate whether P2X1 receptor-mediated purinergic signaling alters the vascular response in DM. Second, we examined the vasodilator factors that may mediate the P2X1 induced vascular responses. For this purpose, we blocked endothelial-derived vasoactive mediators, including nitric oxide (NO), prostacyclin (PGI2), or endothelium-derived hyperpolarizing factor (EDHF), independently.

MATERIAL and METHODS

Animals

Local Ethics Committee on Experimental Animal Research of Akdeniz University approved all animal procedures and experiments (ID: 628/ 2017.02.05). This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration. Forty Wistar male rats (8 weeks old) were used in this study. The rats were housed in stainless steel cages with a constant room temperature at 23±2°C and on a 12:12-h light-dark cycle and had free access to rat chow and drinking water.

Grouping and induction of experimental diabetes model

The rats were randomly divided into two groups as follows: Group 1, Control (C, n=20) rats; Group 2, Streptozotocin (STZ)-induced diabetic rats (DM, n=20). Diabetes was induced in the diabetic group with a single dose of 65 mg/kg STZ in 0.1 mol/L freshly prepared citrate buffer (pH 4.5), intra-peritoneally. One week after injection of STZ, blood glucose level was measured and rats with blood glucose levels above 250 mg/dL were considered diabetic. C rats were given citrate buffer alone (pH = 4.5).

Body weights were assessed at the beginning and at the end of the experiment, fluid-food consumption and blood glucose levels were monitored regularly (daily and weekly, respectively). Blood sampling was performed from the tail vein and blood glucose was measured with the use of a glucometer.

The blood pressure (BP) of rats was measured by using a noninvasive tail-cuff method. Measurements were performed at the start and end of the experiment. Data were obtained with a MAY-BPHR 9610-PC unit and MP 150 data-acquisition system (BIOPAC Systems; Santa Barbara, CA).

Termination of the experiment

At the end of 12 weeks, all rats were killed by withdrawing the blood from the abdominal aorta under thiopental sodium (80 mg·kg−1, i.p.) anesthesia. The mesenteric vascular bed was excised and transferred to the dissecting dishes filled with ice-cold physiological saline solution (PSS) containing (in mM) 110 NaCl, 5 KCl, 24 NaHCO3, 1 KH2PO4, 1 MgSO4, 2.5 CaCl2, 0.02 EDTA, and 10 glucose.

Vascular ring preparation

A second-order branch of the superior mesenteric artery, approximately 230-250 µm in diameter, was isolated from the mesenteric vascular bed, cleaned off surrounding connective tissue, and cut into 2-mm-long segments under a dissecting microscope (SZ61, Olympus, Japan). Vessel rings were mounted in a wire myograph (Model 620M, Danish Myo Technology, Aarhus N, Denmark) with two tungsten wires (25 µm in diameter). Myograph bath solution (PSS) was maintained at 37°C and gassed continuously with 95% O2/5% CO_2 (pH 7.4). The vessel segments were rested for 15 min. prior to the normalization procedure. In the normalization procedure, the vessels were stretched to a length that yielded a circumference equivalent to 90% of that given by internal pressure of 90 mmHg. The isometric tension generated by the vessels was recorded using isometric force transducers (Danish Myo Technology, Aarhus, Denmark). Also, the diameter–tension graph was drawn and basal tension calculated with the help of computer software (LabChart Pro V7, ADInstruments, Bella Vista, Australia). After that arteries were left to rest for an hour at its calculated basal tension. The bath solution was changed every 15 min. during the resting period. After resting, the period vitalization procedure was performed by adding KCl (20 mM) and phenylephrine (Phe 10−7 M) to the bath solution, and this procedure was repeated three times, sequentially.

Three resistance arteries were obtained from each experimental animal and different protocols were applied simultaneously. The number of vessels used for each experimental protocol was between 8 and 10 (n= 8-10, each experimental protocol).

Determination of Vasodilator Responses

Dose-Response Curve to ATP and P2X1 Receptor Agonist

The dose–relaxation curve in response to ATP (10–6-10−4 M) and α,β-methylene ATP (α,β-meATP; 10–6-10−4 M), a highly selective agonist of P2X1 receptor was obtained in rings pre-contracted with Phe (10–6 M). Then 4,4',4",4"'-[Carbonyl-bis(imino-5,1,3-benzenetriyl-bis(carbonylimino))] tetrakis-1,3-benzenedisulfonic acid, octasodium salt (NF 449), a highly selective P2X1 receptor antagonist was added in the organ bath at the dose of 50 µM and after 20 min. the incubation period, the dose-response curve to ATP and α,β-meATP reevaluated. The dose–relaxation curve in response to ATP was performed at the presence of an ecto-ATPase inhibitor, 6-N, N-diethyl-D-beta, gamma-dibromomethylene ATP (ARL 67156; 10-4 M), to prevent degradation of ATP.

Assessment of Endothelium-dependent dilation

Vascular responses were also examined under four different conditions to reveal factors that may mediate vascular relaxation responses to α,β-meATP: (a) vasodilator responses were assessed in the presence of Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME; 10-4 M) in order to inhibit nitric oxide synthase (NOS). (b) vasodilator responses were assessed in the presence of indomethacin (INDO; 10-5 M) in order to inhibit cyclooxygenase (COX) and (c), vasodilator responses were assessed in the presence of apamin (APA, a calcium-activated K+ channel (KCa) blocker; (10-6 M) and (d) Tetraethylammonium (TEA, a non-specific K+ channel inhibitor; 10-6 M). Prior to obtaining the vascular responses vessels were incubated for 30 min. with inhibitors separately. In between all the consecutive protocols applied, the vascular segments were left to rest for 30 min.

All doses–relaxation curves were obtained in rings pre-contracted with Phe (10–6 M). The Phe-induced steady state of contraction was considered to be 100%, and the relaxation responses were calculated as percentages of this contraction response.

Statistical Analysis

All results are expressed as mean±SEM. Statistical analysis was performed by Paired t or unpaired Student t-test for observations between two groups. Two-way ANOVA for repeated measurements followed by the Dunnett test was used for comparison of the response curves (GraphPad Prism. 5 Software Inc, SanDiego, CA, USA). A value of $P<0.05$ was considered statistically significant.

RESULTS

Characteristics of experimental animals

Initial levels of blood glucose, body weight, food, and water intake were not different between the groups. Diabetic animals had higher blood glucose levels ($p<0.001$), food and water intake ($p<0.001$) but lower body weight than those of control rats at the final of the study ($p<0.001$). Blood glucose level, food, and water intake were higher ($p<0.001$), whereas body weight was lower ($p<0.01$) in diabetic animals at the end of the study compared to their initial values. Blood pressure levels were not different between the groups at the initial or end of the study (Table I).

Table I. Changes in blood glucose, body weight, food-water intake, and blood pressure during the experimental period

	C		DM	
	Initial	Final	Initial	Final
Blood glucose (mg/dl)	133.1±5.1	163.5±14.30	129.8±4.6	483.1±31.0***###
Body weight (g)	221.9±2.5	414.9±12.0	242.8±8.4	202.5±11.6***##
Food intake (g/day)	30.34±2.8	33.94±4.5	32.34±5.0	81.38±2.5***###
Water intake (ml/day)	51.02±3.4	48.52±5.9	52.45±4.9	128.8±6.7***###
Blood pressure (mm Hg)	136.6±4.3	142.8±3.7	145.9±3.5	144.8±4.5

C, Control; DM, Diabetes.
'Initial' and 'Final' represent the observation times of the first and twelve weeks of the experimental period, respectively.
Values are expressed as means ± SE.
***P<0.001 vs control; ##P<0.01, ###P<0.001 vs initial.

Dose-Response Curves of Small Mesenteric Arteries

The concentration-response curves to ATP and α,β-meATP in mesenteric resistance arteries from experimental groups have been shown in Figures 1a and 1b, respectively.

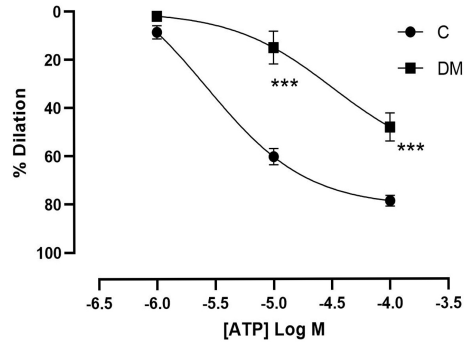

Figure 1. a. ATP-induced dilation in small mesenteric arteries of C and DM animals. C, Control; DM, diabetes. ***P<0.001 vs control.

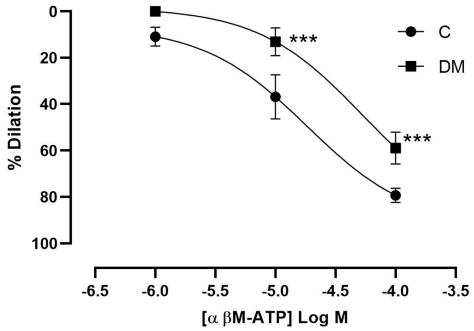

Figure 1. b. αβ-methylene ATP-induced dilation in small mesenteric arteries of C and DM animals. C, Control; DM, diabetes. ***P<0.001 vs control.

The relaxation responses to both agents significantly decreased in DM groups compared to C animals (p<0.001, p<0.001). Dilation responses to ATP (Figure 2a) and α,β-meATP (Figure 2b), were markedly blunted by the selective P2X1 receptor antagonist NF 449 (NF; 10−5 M) in both groups (p<0.001; p<0.001).

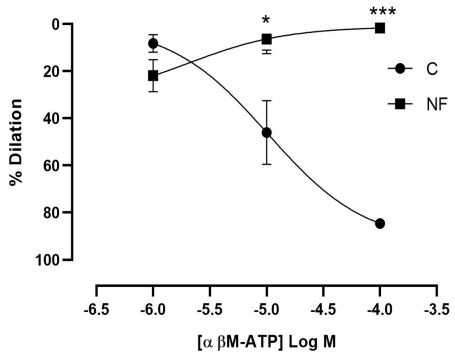

Figure 2. a. ATP-induced dilation responses in small mesenteric arteries of C and DM animals in the absence and presence of selective P2X1 receptor blocker (NF 449). C, Control; DM, diabetes; NF, NF 449. *P<0.05, *** P<0.001, vs control.

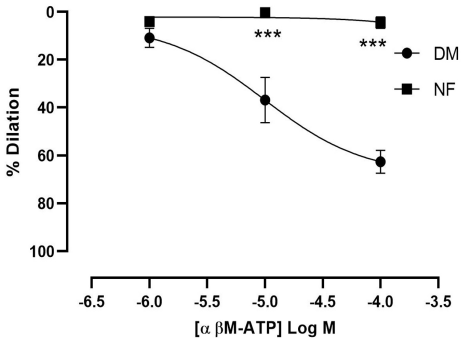

Figure 2. b. αβ-methylene ATP-induced dilation responses in small mesenteric arteries of C and DM animals in the absence and presence of selective P2X1 receptor blocker (NF 449). C, Control; DM, diabetes; NF, NF 449. ***P<0.001 vs diabetes.

Endothelium-dependent dilation

In order to examine the contribution of eNOS, COX, and EDHF pathways to the vascular responses, we also obtained dose-response curves in response to the selective P2X1 receptor agonist, in the presence of L-NAME, INDO, APA, and TEA in the organ bath. In C animals L-NAME significantly depressed the dilation responses to α,β-meATP (p<0.001), whereas INDO, TEA, and APA did not affect it (Figure 3).

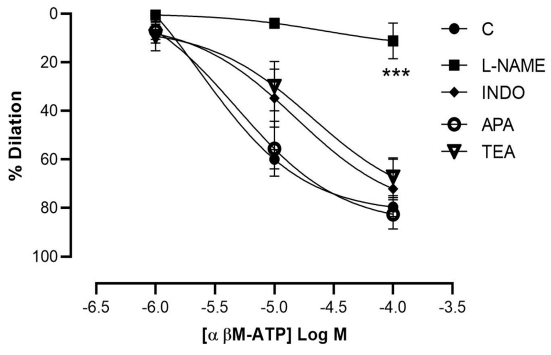

Figure 3. αβ-methylene ATP -induced dilation responses in small mesenteric arteries of C animals in the absence and presence of L-NAME, INDO, APA or TEA. C, Control; L-NAME, NOS blocker; INDO, Indomethasin; APA, Apamin; TEA, Tetraethylammonium ***P<0.001 vs control.

On the other hand, α,β-meATP -induced vascular dilation responses were significantly suppressed by all of the inhibitors excluding TEA in the DM group (p<0.001), (Figure 4).

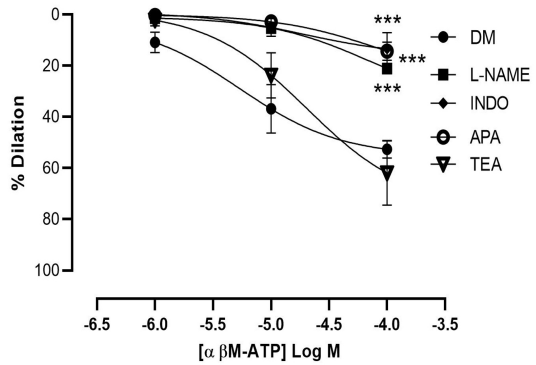

Figure 4. αβ-methylene ATP -induced dilation responses in small mesenteric arteries of DM animals in the absence and presence of L-NAME, INDO, APA or TEA. DM, diabetes. L-NAME, NOS blocker; INDO, Indomethasin; APA, Apamin; TEA, Tetraethylammonium. ***P<0.001 vs diabetes.

DISCUSSION

The relationship between diabetes and vascular complications in humans has been investigated in detail in numerous studies. It's well known that purinergic receptors are common in the vascular system and contribute to the regulation of vascular tone. The present study has investigated whether P2X1 receptors contribute to impaired vascular responses in the experimental diabetes model. According to the results of our study vascular dilation responses to ATP and a strong selective P2X1 receptor agonists, α,β-meATP, are impaired in the diabetes group. These relaxation responses were completely abolished in the presence of the specific P2X1 receptor antagonist. While ATP exerts its relaxant effect through the NOS pathway, it has been demonstrated that α,β-meATP achieves its relaxant effect primarily by NOS and partially by PGI2, a product of the COX pathway, and EDHF pathway.

In our study, STZ was used for induction of the diabetes model, and the blood glucose levels of STZ animals were found to be an average of 480 mg/dl at the end of the study. Additionally, increased food and water consumption and weight loss were detected in diabetic animals. All of these findings are in accordance with the literature that demonstrates the successful induction of the experimental diabetes model (15). Although hypertension would be expected to contribute to diabetes, measured blood pressure levels were found to be similar in C and DM groups in our study. This issue is controversial in the literature. Although some studies demonstrated the development of hypertension in STZ-induced diabetes model; other studies indicated that there is no change in blood pressure, in accordance with our findings (16,17). These different results may arise from the species and sex of the used experimental animals, the dose of STZ administered, and /or the duration of diabetes.

Besides being a neurotransmitter, ATP is an important extracellular signaling molecule and plays an important role in the regulation of purinergic signaling and vascular tone. The effects of ATP on vascular tone are mediated by purinergic receptors located on vascular smooth muscle cells and endothelium. The binding of ATP to purinergic receptors on the endothelium generally causes vasodilation mediated by NO, PGI2, or EDHF, while it is binding to its receptors in smooth muscle cells causes vasoconstriction. The common opinion is that ATP has a permanent and pronounced vasodilator effect after temporary vasoconstriction (1), in in-vitro conditions. We found a similar vasoactive pattern in mesenteric arteries in response to ATP (data not shown).

ATP exerts its effects via P2X and P2Y receptors found on vascular endothelium and smooth muscle cells. Studies investigating the effects of ATP on vascular tonus focused on endothelial P2X4, P2Y1, and P2Y2 receptors and several P2X receptors on smooth muscle cells. Although there are considerable evidence showing the expression of P2X mRNA and protein in endothelial cells, little is known about their functions. While the P2X1 receptor is expressed primarily in vascular smooth muscle cells, some studies identified its expression in some vascular endothelial cells including human mammary arteries, saphenous veins, rat mesenteric arteries, etc. Whether there are numerous studies investigating the role of P2X1 receptors found on smooth muscle, there is no study investigating the possible roles of P2X1 receptors expressed on endothelial cells.

In our study, both ATP and P2X1 agonists caused a permanent relaxation response followed by a transient and mild contraction response (data not shown) in the vessels obtained from C and DM group animals. On the other hand, it has been shown that P2X1 receptors are mostly located on vascular smooth muscle cells and cause vasoconstriction as a result of their activation (18). However, it was also shown that P2X1 receptors were also present on the endothelium of mesenteric arteries and when stimulated, they first caused temporary vasoconstriction and then permanent vasodilation (11,19). These findings coincide with the results of our study. In addition to these findings, our study has been demonstrated P2X1 receptor-mediated relaxation of small mesenteric arteries in diabetic animals for the first time. On the other hand, although both ATP and α,β-meATP generate dose-dependent relaxation responses in both groups, these responses were found to be lower in the DM group than those of C animals. In addition, these relaxation responses to both ATP and α,β-meATP were completely abolished in the presence of the P2X1 receptor antagonist. This finding confirms that relaxation responses to both ATP and α,β-meATP are predominantly mediated P2X1 receptor (20).

In our study, lower relaxation responses to ATP and α,β-meATP occurred in the diabetes group compared to the control group may be due to endothelial dysfunction common in diabetes (21). Hyperglycemia, insulin resistance, oxidant stress, decreased eNOS activity and NO bioavailability are the main factors in the development of endothelial dysfunction in diabetes (21-23). By stimulation of P2X1 receptors on endothelial cells release of endothelial-derived relaxant factors such as NO, PGI2, EDHF, has been shown before. Hence, diminished relaxation response in the DM group may cause by the decrement of these vasodilator mediators (18). Another aim of this study was to investigate the pathways involved in the relaxation responses elicited by P2X1. For this purpose, we examined the vascular relaxation responses to α,β-meATP, a P2X1 receptor agonist, in the presence of the endothelium-derived relaxant factor inhibitors in the organ bath. As a result of these experiments, it was determined that the relaxation responses to α,β-meATP

completely disappeared in the C group in the presence of L-NAME. However, inhibitors of other endothelium-derived relaxant factors, PGI2 and EDHF, did not cause any changes in the C group. In contrast to our results, another study supported that P2X1-related relaxation response is mediated mostly by EDHF in the mesenteric vascular bed of control animals (11). We demonstrated in the present study no contribution of EDHF to α,β-meATP mediated relaxation responses by using non-specific potassium channel blocker, TEA or KCa channel blocker, APA. It has been shown that the expression of P2X1 receptors decreases with age in vascular tissues (24). Therefore, these conflicting results may arise from the age differences of the rats that might cause altered receptor expression or signaling of vascular tissues in these studies. In the DM group, the vasodilation response created by α,β-meATP was inhibited not only with L-NAME but also in the presence of INDO and APA. The effect of TEA may not have been observed since it was a nonspecific potassium channel inhibitor. These results, which we obtained using K+ channel inhibitors, are compatible with the literature, and it has been reported that changes in vascular KCa activation occur in diabetes (25).

These results show that the NO, PGI2, and KCa pathways, all contribute to the P2X1 receptor-mediated dilation response in the STZ-induced diabetes rat model.

Although there is no similar study to compare the results of our study, the differences in relaxation responses to ATP and α,β-meATP, and the pathways they use, may be the cause of the changes in the vascular purinergic signaling in DM. It has even been suggested that these changes may contribute to diabetes induced vascular disorders (12,26). Impairment of purinergic receptor-NO signaling, altered purinergic receptor expression, and/or changes in purinergic receptor sensitivity are among the factors mediating endothelial dysfunction that occurs in diabetes (26).

CONCLUSION

In our study using the second branch of the mesenteric artery, α,β-meATP, the P2X1 receptor agonist caused relaxation in both healthy and diabetic animals, but this relaxation response was significantly reduced in diabetic conditions. Besides, the endothelium-derived factors that mediate the relaxation response were different in control and diabetic animals. While only the NOS pathway contributes to the relaxation response in control animals, in diabetic animals all three of the NO, PGI2, and KCa channels have been shown to contribute to the P2X1 receptor-mediated dilatation responses. Considering all the results of our study, it can be suggested that P2X1-mediated vascular purinergic signaling changes in diabetes. However, considering severe vascular complications accompany diabetes, further studies are needed to elucidate vascular purinergic signaling.

Ethics Committee Approval:

This research complies with all the relevant national regulations, institutional policies and in accodance with the tenets of the Helsinki Declaration. Local Ethics Committee on Experimental Animal Research of Akdeniz University approved all animal procedures and experiments (ID: 628/ 2017.02.05).

Author Contributions:

Concept - G.A., N.Ö., P.Ü., F.B.; Design - G.A., N.Ö., P.Ü., F.B.; Supervision - P.Ü., F.B.; Resources – Akdeniz University BAP; Materials - G.A., N.Ö., F.B.; Data Collection and/or Processing - G.A., N.Ö.; Analysis and/ or Interpretation - F.B.; Literature Search - G.A., F.B.; Writing Manuscript - F.B.; Critical Review - P.Ü., F.B.

Conflict of Interest:

The authors have no conflict of interest to declare.

Financial Disclosure:

This study was supported by the Akdeniz University Research Projects Unit (Project cod. TYL-2017-2676).

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ORIGINAL ARTICLE
Özgün Araştırma

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Geliş Tarihi : 30 December 2021
Received
Kabul Tarihi : 13 March 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Onturk Akyuz H, Alkan S.
The Complementary and Alternative Medicine use of Health Services Vocational School Students During Covid-19
Akd Med J 2023;9(3): 284-289

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DOI: 10.53394/akd.1051378

The Complementary and Alternative Medicine use of Health Services Vocational School Students During Covid-19

Covid-19 Döneminde Sağlık Hizmetleri Meslek Yüksekokulu Öğrencilerinin Tamamlayıcı ve Alternatif Tıp Kullanımı

ABSTRACT

Objective:
This research was conducted to evaluate Health Services Vocational School Students use of complementary and alternative medicine (CAM) methods against Covid-19.

Material and Methods:
This research was designed as a descriptive study. Data were collected from October 1st to October 30th, 2021. A questionnaire form developed by the researchers following the literature was used for data collection. The questionnaire was converted into an online form and delivered to the participants. The IBM SPSS Statistics 22 program was used for data evaluation.

Results:
78% of the students participating in the study were female, and 22% were male. The mean age was 20.81, and the standard deviation was 3.02. It was identified that the participants' monthly income was between 1500-2000 YTL at a rate of 71%. 25% of the participants had Covid-19, 95% were vaccinated, 16% used CAM when they had Covid-19, 35% heard the of CAM on the internet, complementary and alternative medicine use among those who took CAM training was 41%, vitamin D usage ranked first at a 59.1% rate, and those who received CAM training were 41%.

Conclusion:
The use of CAM of the participants during Covid-19 was 16%. It was observed that CAM use was low, there was a positive change in the behaviors of those trained in CAM, and there was no gender difference regarding CAM use.

Key Words:
CAM, University student, Covid-19

ÖZ

Amaç:
Bu çalışma, Covid-19 enfeksiyonundan korunmak için Tamamlayıcı ve Alternatif Tıp (TAT) yöntemleri kullanımı açısından, Sağlık Hizmetleri Meslek Yüksekokulu öğrencilerinin yaklaşımlarını değerlendirmek amacıyla yapıldı.

Gereç ve Yöntemler:
Çalışma, tanımlayıcı tipte planlandı. Veriler 1 Ekim-30 Ekim 2021 tarihleri arasında toplandı. Veri toplamada, araştırmacılar tarafından literatür doğrultusunda geliştirilen anket formu kullanıldı. Anket formu internet üzerinden katılımcılara ulaştırıldı. Verilerin değerlendirilmesinde IBM SPSS Statistics 22 programı kullanıldı.

Bulgular:
Araştırmaya katılan öğrencilerin %78'i kadın, %22'si erkektir. Yaş ortalaması 20,81 ve standart sapması 3,02 bulunmuştur. Katılımcıların aylık gelir durumu %71 oranında 1500-2000 YTL arası olduğu görüldü. Öğrencilerin %25'inin Covid-19 geçirdiği, %95'inin aşı olduğu, % 16 sının Covid-19 geçirdiğinde TAT kullandığı, %35 inin TAT kavramını internetten duyduğu, TAT eğitimi alanların içinde tamamlayıcı ve alternatif ilaç kullanımı % 41 olduğu, D vitamini kullanımının %59,1 oranıyla ilk sırada yer aldığı, TAT eğitimi alanların %41 olduğu bulundu.

Sonuç:
Katılımcıların Covid-19 hastalığında TAT kullanım oranı %16 olarak bulundu. TAT kullanım oranı oldukça düşük olduğu, tat kullanımı konusunda eğitim alanların davranışlarında olumlu yönde değişim olduğu, TAT kullanımı bakımından cinsiyete göre bir farklılık olmadığı görüldü.

Anahtar Sözcükler:
TAT, Üniversite öğrencileri, Covid-19

INTRODUCTION

There is no denying the increase in using traditional methods to protect health and reduce signs of disease in recent years. There are many different traditional medicine practices and different treatment methods related to them worldwide. These methods, which have existed throughout the history of humanity, keep strengthening and becoming more widespread (1).

Alternative medicine is used instead of scientific medicine applications. On the other hand, complementary medicine uses alternative medicine products and methods and the treatment protocols of modern medicine. According to the World Health Organization's (WHO) definition of traditional medicine, it is the whole of knowledge, skills, and practices based on theories, beliefs, and experiences specific to different cultures, which are used in the maintenance of health and the prevention, diagnosis, improvement or treatment of physical and mental diseases (1-4). The most preferred CAM methods are massage, acupuncture, herbal products, cupping, acupressure (Shiatsu), yoga, therapeutic touch, hydrotherapy, reflexology, bioenergy, music, relaxation, imagination, and vitamin supplements (3-6).

Although alternative and complementary medicine concepts differ, they are often used together. Complementary-Alternative Medicine (CAM) consists of special medicine methods that use natural substances and special solutions, different treatment and exercise techniques to protect physical and mental health, reconcile the person with themselves, their family, and their environment to get to know themselves better. There is currently no proven cure for Covid-19, although it has affected our country and the whole world for approximately 1.5 years (6-8). While the efficacy, safety, mode of action, quantity, and desired physiological response expected from a drug are the most important features in the modern treatment and drug concept, "herbal medicines" are becoming increasingly popular worldwide. More than 80% of the world's population uses Complementary and Alternative Medicines (CAM). CAM is becoming an increasing component in the US healthcare system, with 70% of the population using it at least once and costing $34 billion a year. Since the National CAM Center establishment, basic science and therapeutic-based clinical studies on CAM have significantly increased. The worldwide herbal medicine market, including herbal products and raw materials, is projected to grow by 5% to 15% per year. The world herbal medicine market is estimated at $62 billion, and it is estimated to grow to $5 trillion by 2050. The global pharmaceutical market was valued at $550 billion in 2004 and grew to $900 billion in 2008. Herbal sources of immune-enhancing substances are consumed in many countries to promote health, increase the body's normal resistance to infectious agents, and prevent and treat various diseases. However, these drugs are sometimes sold under inappropriate conditions without a license or approval. There is not enough scientific evidence about the effectiveness of some of these drugs (7-11).

This study was conducted to evaluate the approach of Health Services Vocational School Students in using CAM to prevent Covid-19.

MATERIAL and METHODS

This research was designed as a descriptive study. The universe and sample of the study were made up of all of the students at Bitlis Eren University Vocational School of Health Services. Without selecting the study sample, volunteers were included in the study. The population of the study consisted of 1200 students studying at Vocational School of Health Services. The sample consisted of 550 students. Data were collected from October 1st to October 30th, 2021. The "Survey Form" prepared by the researcher in line with the literature was used for data collection. The socio-demographic questions in the first part of the questionnaire included the health vocational school students' age, gender, department, and monthly income. The second part consisted of whether the students had chronic diseases and whether they had Covid-19 or not. The third part asked whether the students received training on complementary and alternative medicines, if they heard about it (if so, from what source), if they used this type of medicine (if so, which one, why, and how frequently?), how much they spend on these types of drugs monthly. The final section of the questionnaire aimed to identify students views on descriptive and alternative drug use. Participant answers were evaluated based on their answers given on a 5-point Likert-type scale. The lowest score that could be obtained is 0, and the highest is 5. An online form was created via Google forms and sent to the participants online. The incomplete answers were excluded from the evaluation. This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration. Consent was obtained from

the participants, and has been approved by the Bitlis Eren University Ethics Committee (approval number: 21/9-3 1064).

Statistical Evaluation

SPSS programs were used to evaluate the data obtained from the research, and frequency distribution, average, and comparative analyses were made. Chi-square tests were used to examine whether there was a difference between students' CAM use, depending on their gender, department, and whether they were trained in CAM methods. An independent sample t-test investigated the differences between complementary and alternative drug use between those who had Covid-19 and those who did not. Although the Kolmogorov-Smirnov normality test results indicate that the variables are not distributed normally, because of the Central Limit Theorem, the distribution of sample means converges to a normal distribution as the sample size is sufficiently large in both groups (sample size of those who had Covid-19 is 136 and the sample size of those did not have Covid-19 is 414). The t-test also investigated the differences between students views who received and did not receive CAM training on whether complementary and alternative drugs protected Covid-19. The $p<0.05$ was considered statistically significant in the comparisons.

RESULTS

78% of the students participating in the study were female, and 22% were male. The mean age was 20.81, and the standard deviation was 3.02 (Table I).

Table I. Demographics of participants

Age	
Average	20.81
Standard deviation	3.02
Gender	**%**
Female	78%
Male	22%

The participants' distribution according to the departments they attend is given in the Table II. Table III shows the participants' monthly income distribution and in Table IV the distribution of the answers given by participants to various questions is given. Table V and Table VI provide joint frequencies and relative joint frequencies of CAM Training and Cam Usage variables.

Table II: Participants distribution according to the departments they attend

Department	Number	%
Anesthesia	51	11%
Child Development	88	19%
Disables Care and Rehabilitation	27	6%
Nursing	49	11%
First Aid and Emergency Aid	54	12%
Optician	24	5%
Pathology Laboratory Techniques	51	11%
Social Services	24	5%
Medical Imaging Techniques	30	6%
Elderly Care	64	14%

Table III: The participants' monthly income distribution

Monthly Income	Number	%
1500-2000	252	71%
2001-2500	27	8%
2501-3000	29	8%
3001-3500	11	3%
3501-4000	5	1%
4001-4500	8	2%
4501-5000	8	2%
5001 and over	16	5%

Table IV. The distribution of the answers given by participants to various questions

Which CAM medicines did you use?		
Vitamin D	110	59.10%
Black cumin	38	20.40%
Calcium	15	8.10%
Zinc	6	3.20%
Propolis	6	3.20%
B12	3	1.60%
Quercetin	3	1.60%
Herbal teas	1	0.50%
Ginkgo biloba	1	0.50%
Spraydin	1	0.50%
Vitamins	1	0.50%
Adder's tongue	1	0.50%
If you use complementary and alternative medicines, what is the reason:		
I didn't think about it	146	56.20%
To be healthy	96	36.90%
Habit	13	5.00%
To prevent cramps	1	0.40%
To cure my illness	1	0.40%
I use B12 because I am vegan	1	0.40%
Due to my vitamin deficiency	2	0.80%
How often do you use complementary and alternative medicines?		
Once a year	104	47%
Once a month	48	22%
Once a week	22	10%
Every day	24	11%
Twice a week or more	21	10%
How much do you spend on complementary and alternative medicines monthly?		
Less than 50 YTL	160	73%
51-100 YTL	32	15%
101-150 YTL	8	4%
151-200 YTL	5	2%
201-250 YTL	3	1%
More than 251 YTL	12	5%

Table IV. Continued

Have you had Covid-19?			
	Yes	136	25%
	No	413	75%
If you had Covid-19, how did you recover?			
I was treated at home.		103	73%
I didn't notice it.		27	19%
I was treated at the hospital.		9	6%
I was in intensive care.		3	2%
Have you had the Covid-19 vaccination?			
Yes	521	95%	
No	29	5%	
Have you received training on complementary and alternative medicine?			
Yes	34	6%	
No	511	94%	
If you had Covid, did you use any complementary and alternative medicine?			
Yes	32	16%	
No	164	84%	
Did you hear about complementary and alternative medicine?			
Yes	233	43%	
No	312	57%	
Where did you hear about complementary and alternative medicine?			
Internet	122	35.30%	
Television	69	19.90%	
Social media	58	16.80%	
School	51	14.70%	
Family	16	4.60%	
Friend	13	3.80%	
Hospital	5	1.40%	
Newspaper	3	0.90%	
Workplace	3	0.90%	
Radio	2	0.60%	
Health worker	2	0.60%	
Books	1	0.30%	
Phone notification	1	0.30%	

Table V: CAM Training * CAM Usage Joint Frequency Table

		CAM Usage		
		Yes	No	Total
CAM Training	Yes	14	20	34
	No	37	474	511
Total		51	494	545

Table VI: CAM Training *CAM Usage Relative Freguengrey Table

	CAM Usage		
CAM Training	Yes	No	Total
Yes	41%	59%	100%
No	7%	93%	100%

While complementary and alternative drug use was 41% among those who received CAM training, this rate was 7% in the group who did not receive training. This shows the importance of receiving CAM training to increase the use of CAM.

There was no statistically significant difference at the 0.05 level between the students' views who received and did not receive CAM training on whether complementary and alternative medicine use protects from Covid-19 (z-value = -1,2271, p-value = 0.2198).

A t-test was used for independent groups to determine whether there was a difference between the frequency of complementary and alternative drug use in the group that had Covid-19 and the group that did not. In the analysis of the answers given to the question "I Yfrequently use complementary and alternative medicines" according to the Likert scale, no statistically significant difference was found between the groups.Cohen's d effect size value of the t-test was 0.328. This is a small effect size. When the effect size was 0.3, the statistical significance level was 0.05, the power of the test was 0.90, and the required sample size was 469. The sample size in this study, 550, satisfies this requirement. As a result of the t-test, a statistically significant difference at the level of 0.05 was found between the frequency of using complementary and alternative drugs among students who had and did not have Covid-19 (z-value = 1.979, p-value = 0.0478). Cohen's d effect size of this difference was small (Cohen's d = 0.328).

DISCUSSION

In addition to scientific and modern medicine, there has been an increase in traditional medicine, alternative medicine or complementary medicine applications. In addition to being widely used worldwide, their usage rate is higher in some world countries (1,10). Many studies are conducted with various groups on the subject in this context. In our study with university students, 78% were female, and 22% were male. The mean age was 20.81, and the standard deviation was 3.02. When the income status of the participants is examined, it is seen that the rate of students with 1500-2000 YTL income is 71%. When the participation rates were examined according to their departments, it was identified that 19% were in child development and 14% in elderly care. 25% of the participants had Covid-19, 95% had the Covid-19 vaccine, and 16% used CAM when they had Covid-19.

The mean age in the study was 20.81. When similar studies are examined, a positive relationship was found between age and CAM use in students, and that CAM use increases with age. Studies report that the age range of CAM use is 39-65 years. Many studies show that CAM use is more common among middle-aged and elderly groups. This situation supports the directly proportional relationship between age and CAM use (12-14).

In this study, the CAM usage rate was 16%. The usage rate of complementary and alternative medicine for our country was 12.60% - 86.30% in similar studies when the literature was examined. Oğlakçı Ilhan et al.'s study with university students in 2018 determined that participants rate of using TCME (Traditional and Complementary Medicine Education) was 29%. However, when the literature is examined, the rate of CAM use

was moderate or high in similar studies. In the study conducted by Solmaz and Altay with university students in 2019, the rate of CAM use was 89.5%. Similarly, the frequency of CAM use was 61.2% in Araz et al.'s 2012 study. In contrast, this was 50.0% in Sönmez et al.'s study (12, 15-18).

When the students were asked whether they had received CAM training before, it was identified that 94% of the participants did not receive any training. In a similar study, it was determined that the students did not have sufficient knowledge about CAM use, and in another study, 94.7% of the students reported that they did not receive training on CAM (19). In this study, in which the use of CAM was very low, the majority of the students did not receive training on CAM methods, and the rate of students CAM use was 59%. In the study, a statistically significant correlation at 0.05 was found between CAM drugs use and whether the student received training on CAM. This is the importance of CAM education and the low usage rate due to no CAM education.

When the source CAM knowledge was questioned, 35% of the participants heard of it from the internet. There are many studies in the literature with similar findings. Solmaz and Altay (2019) reported that 55.9% of students had access to CAM information via the internet. Similarly, Doğanay et al., reported that 52.4% of the students accessed CAM information via the internet. In the same way, Açıkgöz et al., suggested that 56.4% of the students found information on CAM methods via the internet (12,19,20).

To the question "Which CAM drug did you use most" 59.1% of the participants reported that they used vitamin D, 20.4% black cumin, and 8.1% used calcium-containing drugs. Similar studies have been found in the literature. Doğanay et al. found that the use of supplemental vitamins was 24.0% among participants, and the usage rate of herbal treatment products was 21.4%. Barutçu et al., found that iron and vitamin D usage was 60.7% and 83.3%, respectively (19-22).

As to why the participants used CAM, 56.22% of the participants answered, "I didn't think about it", and 36.9% said it was to be healthy. Similar studies have been found in the literature. Yıldırım et al., 2010 reported that most students found modern non-medical treatments beneficial (23). Solmaz and Altay (2019) stated that 67.6% of the participants reported using complementary and alternative therapies because they found them beneficial for health (12).

The study analyzed whether there is a relationship between complementary and alternative drug use and gender, but no statistically significant relationship was found between these two variables. There are similar studies in the literature. In Aktaş's study, no statistically significant difference was reported regarding the use of CAM by demographic characteristics such as gender, class, educational status of parents, place of residence, and the number of siblings (24-27).

Limitations of the study:

The study's generalization is limited to university students because it was conducted among a single unit of associate degree health students in the East.

CONCLUSION

The use of CAM of the participants during Covid-19 was 16%. It was observed that CAM use was low, there was a positive change in the behaviors of those trained in CAM. It is recommended that the study be carried out with larger student groups, whether regional or country-wide.

There are many studies on the use of CAM in the literature. However, there was no study on Covid-19 and students use of CAM. We believe that this study will contribute to the literature in this respect.

Ethics Committee Approval:

This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Bitlis Eren University Ethics Committee (approval number: 21/9-3 1064).

Informed Consent:

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:

Concept – S.A., H.Ö.A; Design – S.A., H.Ö.A; Supervision – S.A; Resources – H.Ö.A., S.A; Materials – S.A., H.Ö.A; Data Collection and/or Processing – H.Ö.A; Analysis and/ or Interpretation – S.A; Literature Search – H.Ö.A; Writing Manuscript – H.Ö.A; Critical Review – S.A.

Conflict of Interest:

The authors have no conflict of interest to declare.

Financial Disclosure:

The authors declared that this study has received no financial support.

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ORIGINAL ARTICLE
Özgün Araştırma

Anxiety and Depression Levels of Healthcare Professionals During the COVID-19 Pandemic and Related Factors

COVID-19 Pandemisi Sırasında Sağlık Çalışanlarının Anksiyete ve Depresyon Düzeyleri ve İlişkili Faktörler

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Geliş Tarihi : 04 January 2022
Received
Kabul Tarihi : 29 March 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Ozturk Atkaya N, Bilgin Kocak M, Oruc MA. Anxiety and Depression Levels of Healthcare Professionals during the COVID-19 Pandemic and Related Factors
Akd Med J 2023;9(3): 290-295

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DOI: 10.53394/akd.1052773

ABSTRACT

Objective:
The aim of this study is to investigate the anxiety and depression levels of healthcare professionals during the COVID-19 pandemic and related factors.

Material and Methods:
The study group involved the doctors and nurses working in hospitals where COVID-19 patients were treated. An online questionnaire was used to assess the anxiety and depression levels and associated factors. The questionnaire consisted of a socio-demographic section, Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAI).

Results:
A total of 446 healthcare professionals participated in the study. The depression, state, and trait anxiety scores were clinically significant in 18.6%, 60.5%, and 69% of the participants, respectively. Being a woman, a nurse, prolonged exposure to COVID-19 news, and lack of physical exercise were associated with higher anxiety scores. We also observed that younger age, lack of physical exercise, prolonged exposure to COVID-19 news and a history of mental illness prior to the pandemic increased the levels of depression and/or anxiety in healthcare professionals.

Conclusion:
Healthcare professionals face with high risk for impairment in psychological well-being during the COVID-19 pandemic. The low rate of admissions for mental illnesses despite high rates of anxiety and depression symptoms in our study suggests that the psychological support needs of healthcare professionals should be taken into account during the pandemic.

Key Words:
COVID-19 pandemic, Healthcare professionals, Anxiety, Depression

ÖZ

Amaç:
Bu çalışmanın amacı, COVID-19 pandemisinde sağlık çalışanlarının anksiyete ve depresyon düzeyleri ve ilişkili faktörleri araştırmaktır.

Gereç ve Yöntemler:
COVID-19 pandemisinde sağlık çalışanlarının anksiyete ve depresyon düzeylerini ve ilişkili faktörleri değerlendirmek için çevrimiçi bir anket kullanıldı. Çalışma, COVID-19 hastalarının tedavi edildiği hastanelerde çalışan doktor ve hemşireleri içeriyordu. Anket sosyo demografik veriler, Beck Depresyon Envanteri (BDE) ve Durumluk-Sürekli Kaygı Ölçeği'nden (DSKÖ) oluşuyordu.

Bulgular:
Çalışmaya toplam 446 sağlık çalışanı katıldı. Katılımcıların % 18,6' sı klinik olarak anlamlı sayılan depresyon puanlarına, % 60,5'i klinik olarak anlamlı sayılan durumluk anksiyete ve % 69,0' ı sürekli anksiyete puanlarına sahipti. Kadın olmak, hemşire olmak, COVID-19 yayınlarına uzun süreli maruz kalmak ve fiziksel egzersiz yapmamak, daha yüksek anksiyete puanları ile ilişkilendirildi. Bu çalışmada, COVID-19 pandemisinde daha genç yaşta olmanın, fiziksel egzersiz yapmamanın, uzun süreli COVID-19 yayınlarına maruz kalmanın ve pandemiden önce ruhsal bir hastalığa sahip olmanın, COVID-19 pandemisinde sağlık çalışanlarında depresyon ve / veya anksiyete riskini arttırdığı saptanmıştır.

Sonuç:
COVID-19 pandemisi sırasında sağlık çalışanları ruhsal iyilik hallerinin bozulması açısından risk altındadır. Çalışmamızdaki anksiyete ve depresyon belirtilerinin oranları ve bu oranlara rağmen ruhsal sıkıntı nedeniyle doktor başvurusundaki oranların azlığı pandemi sırasında sağlık çalışanlarının psikiyatrik destek ihtiyaçlarının dikkate alınması gerekliliğini kanıtlamaktadır.

Anahtar Kelimeler:
COVID-19 pandemisi, Sağlık çalışanları, Anksiyete, Depresyon

INTRODUCTION

In December 2019, many pneumonia-like cases of unknown cause emerged in Wuhan, China, and then the causative agent was determined to be a new type of coronavirus (1). The novel coronavirus has been named SARS-CoV-2, and the disease it caused as 'COVID-19' by the International Committee on Taxonomy of Viruses (2). COVID-19, which transmits as an airborne infection, has rapidly spread to other countries and has been declared a pandemic by the World Health Organization (3). It is predicted that the COVID-19 pandemic would continue to affect the mental health of society in the future as it is at present (4). Also, it has been reported that healthcare professionals working with probable or definite COVID-19 patients in the hospitals are more vulnerable to experiencing mental problems. Thus, this group of workers has a high risk for developing a stress response against being in close contact with the SARS-CoV-2, being exposed to traumatic situations such as death from COVID-19, and making difficult decisions during the disease (5,6).

Stress causes mental problems, such as anxiety, depressive symptoms, insomnia, denial, and anger, leading to disruptions in the fight against COVID-19. Stress may also affect attention and comprehension skills, as well as produce long-term effects on the general well-being of employees. Therefore, it is important to protect and support the mental health of healthcare professionals for both effective pandemic containment and the long-term well-being of the population (7).

Studies on the mental well-being of healthcare workers during the COVID-19 pandemic are still in progress (8,9).

The aim of this study was to investigate the effects of the COVID-19 pandemic on the mental well-being of healthcare workers and related factors.

MATERIAL and METHODS

Study sample:

This cross-sectional study was conducted with the doctors and nurses working in the city of Samsun hospitals, where COVID-19 patients were treated/followed up. The healthcare professionals were informed about the study and the voluntary basis of participation. The participants in the study remained anonymous. Institutional ethics committee approval from Ondokuz Mayıs University was obtained (OMU KAEK 2020/335, 12.05.2020).

Study protocol:

The questionnaire that consisted of three sections was sent to the healthcare professionals using online sources. The introduction part of the questionnaire form involved a detailed explanation of the study. The subjects volunteered to participate in the study, completed the rest of the questionnaire that consisted of three sections. The first section of the questionnaire included the socio-demographic data form. The second and third sections involved the Beck Depression Inventory (BDI) and State (STAI-I) and Trait Anxiety Inventory (STAI-II), respectively. A total of 446 volunteers participated in the study.

Tools for Data Collection

Beck Depression Inventory (BDI):

The scale developed by Beck et al. was used to evaluate the presence and severity of depressive symptoms (10). It is a self-report scale including 21 items. The score may change between 0-63. The cut-off score of the scale is 17, and higher scores indicate the presence of clinically significant depressive symptoms. The Turkish validity and reliability study for BDI was conducted by Hisli et al. (11).

State and Trait Anxiety Inventory (STAI):

It was developed by Spielberger et al. in 1970 (12). It consists of two scales, namely the State Anxiety Inventory (STAI-I) and Trait Anxiety Inventory (STAI-II), each having 20 items. All of the items are scored from 1-4, and higher scores indicate high levels of anxiety. The validity and reliability study of its Turkish translation was conducted by Oner et al. (13). Scores on both scales range between 20 and 80. High scores indicate high anxiety levels, and low scores indicate low anxiety levels. The cut-off score of 40 is commonly recommended for determining clinically relevant anxiety levels (14,15).

Statistical analysis

All statistical analyses were performed with SPSS 25.0 package program. The Kolmogorov-Smirnov and the Shapiro-Wilk test were used to evaluate the normal distribution of the data. Continuous variables were defined as mean ± standard deviation, median (minimum-maximum values), and categorical variables were defined as number and percentage. Independent samples t-test was used for independent group comparisons when parametric test conditions were met, and the Mann-Whitney U test was used otherwise. We used the Spearman correlation analysis to analyze the relationships between continuous variables. We used Binary Logistic Regression models to determine risk factors. Statistical significance was accepted to be $p<0.05$.

RESULTS

Our study was conducted with 190 doctors and 256 nurses (total number: 446). The number of female and male participants was 271 (60.8%) and 175 (39.2%), respectively, and the mean age was 36.94 ± 8.7 years. The number of participants who worked in close contact with COVID-19 patients was 302 (67.7%) (Table I). Descriptive information for psychiatric symptoms in the general sample is presented in Table II.

When the mean depression scores of the participants in our study were examined, we found that 198 (44.4%) participants had depressive symptoms (BDI score 10≤), while 83 (18.6%) had clinically significant depression (BDI 17≤). There was no statistically significant difference according to gender ($p>0.05$). The mean BDI scores of nurses were found to be statistically significantly higher than that of the doctors ($p = 0.001$). The other groups with significantly higher mean BDI scores were those who received mental treatment before the pandemic ($p = 0.001$), those who did not exercise regularly ($p = 0.0001$), and those who were exposed to COVID-19 news for more than 1 hour a day ($p = 0.0001$) (Table I).

Table I. Relationship between sociodemographic/occupational characteristics of participants and scores of BDI, STAI-I, and STAI-II.

		BDI	STAI-I	STAI-II
Gender	Woman (n=271)	10.63 ± 8.52	43.83 ± 10.62	44.33 ± 8.22
	Man (n=175)	9.44 ± 8.75	41.61 ± 11.41	41.97 ± 8.25
	Inter group p	0.061 (z=-1.871)	0.036(t=2.101)	0.0001 (z=-3.615)
Occupation	Physician (n=190)	8.61 ± 7.66	41.43 ± 10.7	42.44 ± 8.87
	Nurse (n=256)	11.32 ± 9.11	44.1 ± 11.06	44.12 ± 7.8
	Inter group p	0.001 (z=-3.244)	0.011 (t=-2.557)	0.002 (z=-3.048)
Working in close contact with COVID-19 patients	No (n=144)	10.24 ± 8.49	42.53 ± 10.63	43.52 ± 8.29
	Yes (n=302)	10.13 ± 8.7	43.17 ± 11.15	43.35 ± 8.32
	Inter group p	0.768 (z=-0.295)	0.567 (t=-0.573)	0.692 (z=-0.397)
Doing physical exercise at home or not	No (n=281)	11.6 ± 9.09	44.52 ± 11.13	44.55 ± 8.42
	Yes (n=165)	7.72 ± 7.14	40.3 ± 10.21	41.45 ± 7.74
	Inter group p	0.0001(z=-4.858)	0.0001 (t=3.991)	0.0001 (z=-3.706)
Exposure time to COVID-19 publications	Less than 1 hour	7.98 ± 7.96	39.99 ± 10.84	42.01 ± 8.3
	More than 1 hour	11.56 ± 8.75	44.86 ± 10.65	44.29 ± 8.2
	Inter group p	0.0001 (z=-4.929)	0.0001(z=-4.597)	0.006 (z=-2.725)
Having psychiatric disorder prior pandemic	No (n=398)	9.63 ± 8.16	42.61 ± 10.71	42.85 ± 8.02
	Yes (n=48)	14.63 ± 10.85	45.83 ± 12.74	47.96 ± 9.22
	Inter group p	0.001 (z=-3.188)	0.144 (z=-1.459)	0.0001 (z=-3.552)
With mental distress during a pandemic	No (n=431)	10.11 ± 8.72	42.93 ± 11.04	43.36 ± 8.38
	Yes (n=15)	11.8 ± 4.74	43.87 ± 9.21	44.67 ± 5.47
	Inter group p	0.096 (z=-1.665)	0.592 (z=-0.536)	0.297 (z=-1.042)

SD: Standard Deviation; Med: Median; Min – max: Minimum – maximum values, STAI-I: State-Trait Anxiety Inventory-I STAI-II: State-Trait Anxiety Inventory-II BDI: Beck Depression Inventory

Considering the STAI mean scores of the participants, 60.5% (n = 270) had state anxiety scores considered to be clinically significant and 69% (n = 309) had trait anxiety scores considered to be clinically significant. Although there were clinically significant trait and state anxiety, mean scores in all variables, women ($p = 0.036$ for STAI-I, and $p = 0.0001$ for STAI-II), nurses ($p = 0.011$ for STAI-I, and $p=0.002$ for STAI-II), those who didn't exercise regularly ($p = 0.0001$), and who were exposed to COVID-19 news longer than an hour a day ($p =$

0.0001 for STAI-I, and p = 0.006 for STAI-II) had statistically significantly higher scores.

The trait anxiety level was found to be significantly higher in those with mental illness before the pandemic compared to those without prior mental illness (p = 0.0001) (Table I).

Table II. Mean scores of STAI-I, STAI-II and BDI scales in the general sample.

	Mean ± SD	Med (min - max)
STAI-I	42.96 ±10.98	43 (20 - 79)
STAI-II	43.4 ±8.3	43 (22 - 79)
BDI	10.17 ±8.62	8 (0 - 47)

SD: Standard Deviation; Med: Median; Min – max: Minimum – maximum values. STAI-I: State-Trait Anxiety Inventory-I STAI-II: State-Trait Anxiety Inventory-II BDI: Beck Depression Inventory

When the multivariate model, which was obtained from univariate models in logistic regression was examined, it was found that young age, long exposure times to COVID-19 news, lack of regular exercise, and mental illness prior to the pandemic were significant risk factors. Exposure to COVID-19 news for long hours and lack of regular exercise were risk factors for clinically significant state anxiety scores. Young age, lack of regular exercise, and a mental illness prior to the pandemic were significant risk factors for clinically significant trait anxiety scores (Table III).

Table III. Risk Factors for Depression and Anxiety Identified by Multivariable Logistic Regression Analysis.

		Univariate Models				Multiple Models			
		p	O.R.	95% C.I.for O.R.		p	O.R.	95% C.I.for O.R.	
Dependent Variable	Independent Variable			Lower	Upper			Lower	Upper
BDI (17 and more)	Age	0.003	0.96	0.93	0.986	0.108	0.97	0.938	1.006
	Gender (Woman)	0.034	1.75	1.043	2.94	0.47	1.25	0.682	2.293
	Marital status (Married)	0.312	0.77	0.459	1.283	-	-	-	-
	Living with children or elderly person	0.619	1.14	0.687	1.878	-	-	-	-
	Occupation (Nurse)	0.006	2.07	1.235	3.476	0.072	1.76	0.952	3.263
	Working in close contact with COVID-19 patients (Yes)	0.835	1.06	0.632	1.764	-	-	-	-
	Having a diagnosis of COVID-19	0.936	1.1	0.121	9.922	-	-	-	-
	Exposure time to COVID-19 publications (more than 1 hour)	0.001	2.51	1.444	4.362	0,001	2.78	1.497	5.163
	Doing physical exercise at home (No)	0.008	2.1	1.215	3.614	0.071	1.76	0.953	3.251
	With mental distress during a pandemic to apply for a doctor (Yes)	0.888	1.1	0.302	3.978	-	-	-	-
	Psychiatric disorder prior to pandemic (Yes)	0.001	3.07	1.618	5.841	0,023	2.38	1.128	5.029
STAI-I (40 and more)	Age	0.611	0.99	0.973	1.016	-	-	-	-
	Gender (Woman)	0.049	1.48	1.002	2.175	0.216	1.32	0.85	2.056
	Marital status (Married)	0.222	1.3	0.854	1.975	-	-	-	-
	Living with children or elderly person	0.035	1.53	1.03	2.261	0.117	1.41	0.918	2.165
	Occupation (Nurse)	0.05	1.47	1	2.154	0.755	1.07	0.69	1.666
	Working in close contact with COVID-19 patients (Yes)	0.808	1.05	0.701	1.577	-	-	-	-
	Having a diagnosis of COVID-19	0.98	0.98	0.162	5.91	-	-	-	-
	Exposure time to COVID-19 publications (more than 1 hour)	0.001	1.98	1.338	2.919	0.0001	1.99	1.311	3.032
	Doing physical exercise at home (No)	0.029	1.55	1.045	2.286	0.18	1.34	0.874	2.046
	With mental distress during a pandemic to apply for a doctor (Yes)	0.622	1.32	0.442	3.915	-	-	-	-
	Psychiatric disorder prior to pandemic (Yes)	0.769	1.1	0.591	2.035	-	-	-	-
STAI-II (40 and more)	Age	0.001	0.96	0.933	0.979	0.127	0.97	0.942	1.007
	Gender (Woman)	0.032	1.56	1.04	2.352	0.804	1.08	0.6	1.935
	Marital status (Married)	0.714	1.09	0.696	1.696	-	-	-	-
	Living with children or elderly person	0.042	1.54	1.016	2.32	0.092	1.7	0.917	3.164
	Occupation (Nurse)	0.005	1.79	1.194	2.692	0.882	1.05	0.57	1.925
	Working in close contact with COVID-19 patients (Yes)	0.296	1.25	0.82	1.918	-	-	-	-
	Having a diagnosis of COVID-19	0.653	0.66	0.109	4.006	-	-	-	-
	Exposure time to COVID-19 publications (more than 1 hour)	0.243	1.28	0.847	1.921	-	-	-	-
	Doing physical exercise at home (No)	0.009	1.73	1.145	2.607	0.318	1.34	0.757	2.353
	With mental distress during a pandemic to apply for a doctor (Yes)	0.367	1.81	0.501	6.501	-	-	-	-
	Psychiatric disorder prior to pandemic (Yes)	0.003	4.27	1.652	11.027	0.014	5.52	1.416	21.473

p<0.05 statistically significant effect; O.R: Odds Ratio; C.I: Confidence Interval; Binary Logistic Regression STAI-I: State-Trait Anxiety Inventory-I STAI-II: State-Trait Anxiety Inventory-II BDI: Beck Depression Inventory

DISCUSSION

The first COVID-19 case in Turkey was detected on March 11. Many measures have been taken by the Ministry of Health to prevent the spread of the COVID-19 outbreak. In addition, measures to protect and improve mental health, such as the establishment of psychological support lines, have also been established (16).

A study conducted on the effects of COVID-19 on the mood of healthcare workers in China with doctors and nurses working in hospitals with a COVID-19 clinic showed that 50.4% and 44.6% of the participants had depression and anxiety symptoms, respectively (17). A study conducted in Turkey showed that 64.7% of the physicians had depressive symptoms, 51.6% had anxiety, and 41.2% had stress-related symptoms (9).

The rates of depressive and anxiety symptoms in our study that indicated the importance of the possible effects of the COVID-19 pandemic on the mental well-being of healthcare workers were in line with other studies. In our study, despite of the clinically significant depression and anxiety rates (based on the BDI and STAI scores), the rate of the people who visited a doctor for mental distress complaints during the pandemic is only 3.36%. The observed low rate of healthcare workers who visited a doctor for mental distress reveals the critical need for psychiatric support to healthcare workers during the pandemic.

In a study conducted during the previous SARS epidemic, it was stated that anxiety and fear prevailed in the early stages of the pandemic, and depression and post-traumatic stress symptoms prevailed in the long term (18). We found higher levels of anxiety than depression which might be due to the fact that our study was conducted at an earlier period of the pandemic.

The fact that the depression and anxiety scores of nurses were found to be significantly higher than physicians in our study is consistent with the literature (17). However, the logistic regression analysis demonstrated that being a nurse did not have an increasing effect on the risk of depression and anxiety while being younger increased the risk, which might be due to the significantly younger mean age of nurses in the study compared to that of the physicians ($p = 0.0001$). This might be attributed to less duration of professional experience.

During a pandemic, people seek fast and reliable information. The media can have a positive and an adaptive effect on mental health; on the other hand, it can increase anxiety by disseminating news filled with risk messages and negativity (19). Anxiety and uncertainty can increase media exposure and stress, resulting in a vicious cycle that is difficult to break (20).

In this paper a relationship was found between longer periods of exposure to COVID-19 news and high depression and anxiety scores. Prolonged exposure to the news of COVID-19 may cause increased symptoms of depression and anxiety in healthcare professionals, on the other hand healthcare professionals who already have high anxiety levels may follow news sources more closely in order to reduce their anxiety.

It has been reported that physical activities, which are exercise-based interventions, were effective as independent or adjunctive treatments to reduce anxiety symptoms and reduce symptoms in trauma and stress-related disorders such as in patients with post-traumatic stress disorder (21-23).

A meta-analysis conducted to determine the effectiveness of exercise in treating depression reported that exercise had a moderate effect in reducing depressive symptoms in adults (24). These findings are consistent with the significantly lower depression and anxiety scale scores of those who exercise regularly than those who do not. These findings suggest that physical exercise is one of the protective factors for mental health in the pandemic.

There are advantages and disadvantages of our study being conducted through an online survey. Since it is a self-report scale, there are no results for the clinical evaluation by the clinician. However, it has provided the opportunity to reach more people than might be available through face-to-face interviews. One of the limitations of our study is the limited data on working conditions and hours of occupational groups. Since our study is a cross-sectional study, the long-term psychological effects of the pandemic on healthcare workers couldn't be evaluated.

CONCLUSION

In this study, considering the anxiety and depression levels of healthcare workers, they were at risk for anxiety and depression during the pandemic process. However, we found that being at a younger age, long periods of exposure to COVID news, having mental illness prior to the pandemic, and lack of regular physical exercise increased the risk of depression and / or anxiety.

Ethics Committee Approval:

This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Ondokuz Mayıs University Medical Faculty Ethical Committee, Ondokuz Mayıs University (approval number: KAEK 2020/335).

Author Contributions:

Concept - N.Ö.A, M.B.K., M.A.O.; Design - N.Ö.A, M.B.K., M.A.O; Supervision - N.Ö.A, M.B.K., M.A.O.; Resources - N.Ö.A, M.B.K., M.A.O; Materials - N.Ö.A, M.B.K., M.A.O.; Data Collection and/or Processing - N.Ö.A, M.B.K., M.A.O; Analysis and/ or Interpretation - N.Ö.A, M.B.K., M.A.O.; Literature Search - N.Ö.A, M.B.K., M.A.O; Writing Manuscript - N.Ö.A, M.B.K., M.A.O; Critical Review - N.Ö.A, M.B.K., M.A.O.

Conflict of Interest:

The authors have no conflict of interest to declare.

Financial Disclosure:

The authors declared that this study has received no financial support.

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Original Article

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Geliş Tarihi : 03 Ocak 2022
Received
Kabul Tarihi : 13 Mart 2022
Accepted
E Yayın Tarihi : 01 Eylül 2023
Online published

Bu makalede yapılacak atıf
Cite this article as
Çelik G, Öztürk Rİ.
Tip 1 Diyabetli Adölesanlarda Diyete Uyum Durumu ile Diyabulimia Riskinin HbA1c Düzeyine Etkisi
Akd Tıp D 2023;9(3): 296-301

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DOI: 10.53394/akd.1053081

Tip 1 Diyabetli Adölesanlarda Diyete Uyum Durumu ile Diyabulimia Riskinin HbA1c Düzeyine Etkisi

The Effect of Diet Compliance and Diabulimia Risk on HbA1c Levels in Adolescents with Type-1 Diabetes

ÖZ

Amaç:
Diyabulimia riski yüksek olan ve diyabetik diyet tedavisine uymayan bireylerin metabolik kontrolün önemli bir göstergesi olan HbA1c değerinin yüksek seyrettiği düşünülmektedir. Çalışmamızda Tip 1 diyabetli adölesan bireylerin diyete uyum durumunun ve diyabulimia riskinin saptanması ve bunların HbA1c düzeyine etkisinin incelenmesi amaçlanmıştır.

Gereç ve Yöntemler:
Çalışma; 9-18 yaş arası Tip 1 diyabetli, 54'ü kız ve 22'si erkek olmak üzere toplam 76 adölesan ile yürütülmüştür. Katılımcılara; genel bilgiler, antropometrik ölçümler, beslenme durumu ve diyabulimia riskine (Diyabette Yeme Sorunları Anketi) dair soruları içeren anket çevrimiçi yöntemle uygulanmıştır. Elde edilen veriler SPSS 26.0 programı ile analiz edilmiştir.

Bulgular:
Araştırmada HbA1c düzeyi %7 ve altında olan bireylerin %50'si diyetine daima uymakta, %25'i bazen uymakta, kalanı da uymamaktadır. HbA1c düzeyi %9 ve üzeri olan bireylerin ise yarısı diyabetik diyetlerine uymamakta ve diğer yarısı ise diyete bazen uymaktadır. Diyabetik diyet uyumu ile HbA1c düzeyleri arasında istatistiksel olarak negatif yönde anlamlı bir ilişki saptanmıştır (p=0,039). HbA1c düzeyi %9 ve üzerinde olan katılımcıların Diyabette Yeme Sorunları Anketi ortalama puanı (33,7±13,1) anlamlı olarak HbA1c düzeyi %8 ve altında olan katılımcıların ortalama puanından yüksektir.

Sonuç:
Tip 1 diyabetli adölesan bireylerde diyete uyumun zayıf olması ve diyabulimia riskinin yüksek olması HbA1c seviyesinin yüksek seyretmesine sebep olmaktadır.

Anahtar Sözcükler:
Tip 1 diyabet, Diyabulimia, Diyet, HbA1c

ABSTRACT

Objective:
It is proposed that individuals with a high risk of diabulimia and who do not comply with diabetic diet treatment have a high HbA1c value, which is an important indicator of metabolic control. In our study, it was aimed to determine the diet compliance status and diabulimia risk of adolescents with Type 1 diabetes and to examine their effects on HbA1c levels.

Material and Methods:
Study was conducted with a total of 76 adolescents (54 girls and 22 boys) aged 9-18 with Type 1 diabetes. To the participants; the questionnaire, which included questions about general information, anthropometric measurements, nutritional status and diabulimia risk (Diabetes Eating Problem Survey-Revised) was applied online. The obtained data were analyzed with the SPSS 26.0 program.

Results:
In the study, 50% of individuals with HbA1c level 7% and below always, 25% sometimes and the rest never adhered to their diet. While half of individuals with HbA1c level of 9% and above did not follow their diabetic diet the other half seldom did. A statistically significant negative correlation was found between diabetic diet adherence and HbA1c levels (p=0.039). The Diabetes Eating Problems Questionnaire mean scores were significantly higher (33.67±13.31) in the subjects with an HbA1c level of 9% and above than those with HbA1c levels of 8% and lower.

Conclusion:
Poor dietary compliance and high risk of diabulimia in adolescents with Type 1 diabetes is related with high HbA1c levels.

Key Words:
Type 1 diabetes, Diabulimia, Diet, HbA1c

GİRİŞ
Tip 1 diyabet, pankreasın insülin üreten beta hücrelerinin yıkımına bağlı olarak mutlak insülin yokluğu ve buna bağlı hiperglisemi ile seyreden, otoimmün veya otoimmün dışı etmenlerden kaynaklanan kronik bir hastalıktır. Yaşamın devamı için ömür boyu eksojen insüline ihtiyaç duyulması Tip 1 diyabeti diğer diyabet türlerinden ayıran en temel faktördür. Her yaşta tanı konulsa da çoğunlukla ergenlik döneminde ortaya çıkmaktadır (1). Başlıca tedavisini insülin replasmanı, egzersiz ve tıbbi beslenme tedavisi oluşturmakta ve tedaviye uyumun kötü olması metabolik kontrolün göstergesi olan HbA1c düzeyinin yüksek seyretmesine neden olmaktadır (2,3). Başlı başına kritik fizyolojik ve psikolojik değişimlerin yaşandığı bir süreç olan adölesan dönemde diyabet tanısı almak, bu dönemi daha karmaşık hale getirmekte ve zorunlu diyabet yönetimi bireylerde yük oluşturmaktadır (4). Doğru bir diyabet yönetimi için bireyler; ömür boyu beslenme alışkanlıklarını düzenlemek, diyet listelerine uymak, uygun besin seçimi yapmak, besin etiketlerini okumak, öğünlerin zamanına ve miktarına dikkat etmek, karbonhidrat sayımı yapmak ve kan şekerini izlemek zorundadır. Tüm bunlar diyabetli bireylerin sürekli yiyeceklere odaklanmasına ve zihinsel olarak beslenmeyle ve kilo kontrolü ile meşgul olmasına sebep olmaktadır. Bununla beraber diyabetin kronik bir hastalık olması ve ömür boyu insülin tedavisi ve yaşam tarzı değişikliği gerektirmesi de bireylerin kaygı düzeyinin artmasına ve bozulmuş yeme davranışları geliştirmesine neden olmaktadır (5-7). Tip 1 diyabetli bireylerin genellikle tanı öncesi idrarla glukoz kaybı, lipoliz ve protein katabolizmasının artışına bağlı olarak hızla kilo kaybettiği görülmektedir. Tanı sonrasında insülin tedavisiyle birlikte bireylerin kilo almaya başlamasının endişeye yol açtığı ve yeme bozuklukları ya da bozulmuş yeme davranışlarına neden olabileceği bildirilmiştir (8). Bir kilo verme stratejisi olarak insülin dozunu azaltma veya atlama, diyabete özgü bozulmuş yeme davranışı olarak kabul edilir ve bu durumun görülme sıklığı %5-%40 arasındadır. Henüz DSM-5 (Ruhsal Bozuklukların Tanısal ve İstatistiksel El Kitabı)'te tanımlanan bir yeme bozukluğu olmasa da 1970'li yıllardan itibaren diyabet ve bozulmuş yeme davranışı arasında ilişki fark edilmiş ve bu şekilde "diyabulimia" terimi kullanılmaya başlanmıştır (6). Bozulmuş yeme davranışına sahip olan Tip 1 diyabetlilerde; kötüleşmiş metabolik kontrol ve buna bağlı komplikasyonların bozulmuş yeme davranışına sahip olmayanlara göre daha erken başladığı bildirilmiştir (9,10). Diyabulimia, diyabetliler arasında yaygın olan bir bozulmuş yeme davranışı olsa da bu konuda yapılan çalışmalar yetersizdir. Tip 1 diyabetli bireylerde sağlıklı akranlarına göre bozulmuş yeme davranışı riskinin daha fazla olması ve bu riskin diyabetli bireylerde ciddi komplikasyonlara yol açması endişe vericidir (8,11).
Bu çalışmanın amacı Tip 1 diyabetli adölesanların diyabetik diyete uyum durumunun ve diyabulimiya riskinin HbA1c düzeyine etkisinin incelenmesidir.

GEREÇ ve YÖNTEMLER
Bu çalışmada 15.06.2021-15.07.2021 tarihleri arasında Tip 1 diyabet tanılı 9-18 yaş arasında 54'ü kız, 22'si erkek olmak üzere çalışmaya katılmayı kabul eden toplam 76 adölesan birey sosyal medyada bulunmuş, anket formları aynı platformda uygulanmıştır. Adölesanların genel özellikleri, antropometrik ölçümleri, diyabulimia riskini gösteren Diyabette Yeme Sorunları Anketi (Diabetes Eating Problem Survey-Revised, DEPS-R) çevrimiçi anket yöntemiyle elde edilmiştir. Uygulanan anket formu adölesanların sosyodemografik özellikleri (yaş, cinsiyet, diyabet tanı yaşı), sosyoekonomik durumları (anne ve babanın çalışma durumu, gelir düzeyi) ile ilgili verileri içermektedir. Uygulanan anket formu adölesanların vücut ağırlığı (kg), boy uzunluğu (cm), vücut kütle indeksi (VKİ) (kg/m²) değerlerine ait bilgileri içermektedir. Yaşa göre boy ve VKİ persentil değerlerinin sınıflaması Neyzi ve ark., persentil referans değerleri tablosuna göre yapılmıştır (12). Markowitz ve ark., tarafından ergen bireyler için 16 soru olarak revize edilen DEPS-R diyabette bozulmuş yeme davranışlarını saptamak için kullanılmaktadır (13). Bu anketin kesme puanı 20'dir ve alınan puanın 20 ve üzeri olması durumunda diyabetli bireyde bozulmuş yeme davranışı olduğunu gösterir. Altılı likert skalasına (0=hiçbir zaman, 1=nadiren, 2=bazen, 3=sık, 4=çok sık, 5=daima) göre değerlendirilen anket 10 dakikadan daha kısa sürmektedir. Türk çocuk ve ergenler için bu ölçeğin geçerlilik ve güvenilirliği Altınok ve ark., tarafından yapılmıştır (14).

İstatistiksel Analiz
Çalışmada istatistiksel programlardan olan SPSS 26.0 (Statistical Package for the Social Sciences) kullanılmıştır. Verilerin çözümlenmesinde frekans, yüzde, aritmetik ortalama, standart sapma, minimum ve maksimum gibi tanımlayıcı istatistiklerden faydalanılmıştır. Verilerin analizinde parametrik testlerden faydalanılmıştır. Kategorik iki grubun ilişki analizinde ki-kare

ilişki testi, bağımsız iki grubun ortalamaları karşılaştırılmasında bağımsız örneklem t testi, ikiden fazla bağımsız grubun karşılaştırılmasında One-way ANOVA testi sonucu kullanılmıştır. ANOVA testi için varyans homojenliği için Levene testi ve grup farklılıkları için ise varyans homojenliği sağlanıyorsa (p≥0,05) Tukey HSD, varyans homojenliği sağlanmıyor ise (p<0,05) Tamhane çoklu karşılaştırma testi kullanılmıştır. Tüm test sonuçları 0,05 anlamlılık düzeyinde değerlendirilmiştir.

Etik Onam:
İstanbul Medipol Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu tarafından 17.06.2021 tarihinde yazılı izin alınmıştır (Çalışma sayısı: E-10840098-772.02-2863, Karar numarası: 638). Tüm katılımcılardan Helsinki Deklarasyonuna göre prosedürlerden önce yazılı bilgilendirilmiş onam alınmıştır. Çalışma, Araştırma ve Yayın Etiğine uygun olarak yapılmıştır.

BULGULAR

Çalışmaya dahil edilen ve yaşları 9 ile 18 arasında değişen toplam 76 Tip 1 diyabetli bireyin 54'ü kız, 22'si ise erkektir. Katılımcıların %14,5'i 9-10, %42,1'i 11-14, %30,2'si 15-17, %13,2'si ise 18 yaş grubundadır. Adölesanların yarıdan fazlasının annelerinin ev hanımı olduğu (%60,5), babalarının %26,4'ünün işçi, %22,3'ünün memur, %9,4'ünün emekli, %5,3'ünün işsiz ve %26,8 diğer meslek gruplarına dahil olduğu görülmektedir. Ailelerin aylık gelir düzeyleri %3,9'unun 2000 TL ve altı, %44,7'sinin ise 5000 TL ve üzeridir. Adölesanların %5,3'ünün diyabet tanı yaşı 1-2 yıl, %7,9'unun 3-5 yıl arasında, %40,7'sinin 6-10 yıl arasında ve %46,1'inin ise 10 yıl üzerinde olduğu görülmektedir.
Katılımcıların yaşa göre VKİ değerlerine bakıldığında; %9,2'sinin çok zayıf, %10,5'inin zayıf, %50'sinin normal, %25'inin hafif şişman, %5,3'ünün ise obez olduğu görülmektedir. Katılımcıların %5,3'ünün yaşa göre boyu çok kısa (bodur), %5,3'ünün kısa, %63,2'sinin normal, %13,2'sinin uzun ve %13,2'sinin yaşa göre boyunun çok uzun olduğu görülmektedir.
Araştırmada katılımcıların toplam %42,1'inin diyabetik diyetine daima uydukları, %35,5'inin bazen uydukları, %22,4'ünün ise diyabetik diyet uygulamadıkları görülmüştür. Yaş grupları ile diyabetik diyete uyum durumu arasında anlamlı bir ilişki saptanmamıştır (p=0,929) (Tablo I).

Tablo I: Adölesanların yaş gruplarına göre diyabetik diyete uyum durumlarının dağılımı.

		Yaş grupları										X²	p
		9-10 (n=11)		11-14 (n=32)		15-17 (n=23)		18 (n=10)		Toplam (n=76)			
		n	%	n	%	n	%	n	%	n	%		
Diyabetik diyete uyum durumu	Hiç	1	9,1	8	25,0	5	21,7	3	30,0	17	22,4	1,894	**0,929**
	Bazen	4	36,4	11	34,4	9	39,1	3	30,0	27	35,5		
	Daima	6	54,5	13	40,6	9	39,1	4	40,0	32	42,1		

Araştırmada katılımcıların %57,9'unun HbA1c düzeyi %7 ve altı, %34,2'sinin %8, %7,9'unun ise %9 ve üzeridir. Yaş grupları ile HbA1c düzeyleri arasında anlamlı bir ilişki saptanmamıştır (Tablo II).

Tablo II: Adölesanların yaş gruplarına göre HbA1c dağılımı.

		Yaş grupları										X²	p
		9-10 (n=11)		11-14 (n=32)		15-17 (n=23)		18 (n=10)		Toplam (n=76)			
		n	%	n	%	n	%	n	%	n	%		
HbA1c (%)	7 ve altı	6	54,5	20	62,5	12	52,2	6	60,0	44	57,9	1,815	**0,936**
	8	4	36,4	9	28,1	9	39,1	4	40,0	26	34,2		
	9 ve üzeri	1	9,1	3	9,4	2	8,7	0	0,0	6	7,9		

Araştırmada HbA1c düzeyi %7 ve altında olan bireylerin %50'sinin diyetine daima uydukları ve %25'inin ise bazen uydukları görülmüştür. HbA1c düzeyi %8 olan katılımcıların ise %50'sinin diyabetik diyetlerine bazen uydukları, HbA1c düzeyi %9 ve üzeri olan bireylerin ise %50'sinin diyabetik diyetlerine uymadıkları ve %50'sinin ise diyete bazen uydukları görülmektedir. Diyabetik diyet uyumu ile HbA1c düzeyleri arasında istatistiksel olarak anlamlı bir ilişki saptanmıştır (p=0,039) (Tablo III).

Tablo III: Adölesanların diyabetik diyete uyumu ile HbA1c düzeyi arasındaki ilişki.

Diyabetik diyete uyum durumu	HbA1c seviyesi (%)						χ^2	p
	7 ve altı (n=44)		8 (n=26)		9 ve üzerinde (n=6)			
	n	%	n	%	n	%		
Uymam.	11	25,0	3	11,5	3	50,0		
Bazen uyarım.	11	25,0	13	50,0	3	50,0	10,066	**0,039***
Daima uyarım.	22	50,0	10	38,5	0	0,0		

*p≤0,05

Araştırmada, adölesanların DEPS-R puanlarının yaş gruplarına göre tek yönlü varyans analizi ile değerlendirildiğinde, DEPS-R ortalama puanları kız (p=0,304) ve erkek (p=0,203) bireylerin yaş grupları arasında anlamlı farklılık göstermemektedir (Tablo IV).

Tablo IV: Yaş ve cinsiyete göre DEPS-R puan dağılımı.

Yaş grupları	DEPS-R puanı sınıflaması							
	≥20 puan				<20 puan			
	Erkek		Kız		Erkek		Kız	
	n	%	n	%	n	%	n	%
9-10	0	0,0	1	4,0	4	28,6	6	20,7
11-14	7	87,5	8	32,0	9	64,3	8	27,6
15-17	1	12,5	13	52,0	0	0,0	9	31
18	0	0,0	3	12,0	1	7,1	6	20,7
Toplam	8	100	25	100	14	100	29	100
X²	7,616				8,878			
P	**0,055**				**0,031***			

*p≤0,05

Araştırmada DEPS-R puanı 20 ve üzerinde olan adölesanların cinsiyetleri ile yaş grupları arasında anlamlı bir ilişki saptanmamıştır (p=0,055). DEPS-R puanı 20 altında olan adölesanların cinsiyetleri ile yaş grupları arasında anlamlı bir ilişki saptanmıştır (p=0,031). Yirmi puan altında en fazla kişi sayısı oranı 11-14 yaş erkek grubunda görülmektedir (Tablo V).

Tablo V: Adölesanların yaş ve cinsiyete göre DEPS-R puan dağılımı.

DEPS-R puanı sınıflaması								
Yaş grupları	≥20 puan				<20 puan			
	Erkek		Kız		Erkek		Kız	
	n	%	n	%	n	%	n	%
9-10	0	0,0	1	4,0	4	28,6	6	20,7
11-14	7	87,5	8	32,0	9	64,3	8	27,6
15-17	1	12,5	13	52,0	0	0,0	9	31
18	0	0,0	3	12,0	1	7,1	6	20,7
Toplam	8	100	25	100	14	100	29	100
X^2	7,616				8,878			
P	**0,055**				**0,031***			

*p≤0,05

Araştırmada DEPS-R ortalama puanları ile HbA1c grupları arasında anlamlı bir farklılık görülmüştür (F(2, 73): 4,756). Grup varyanslarının homojenliği Levene testi ile test edilmiş ve varyansların homojen dağıldığı tespit edilmiştir. Gruplar arası farklılığın hangi HbA1c düzeyi arasında olduğunu tespit etmek için yapılan Tukey HSD testi sonuçlarına göre, HbA1c düzeyi %9 ve üzerinde olan çocukların DEPS-R ortalama puanı (33,67±13,31) anlamlı olarak HbA1c düzeyi %7 ve altında ve %8 düzeyinde olan adölesanların ortalama puanından yüksek olduğu görülmektedir (Tablo VI).

Tablo VI: Adölesanların DEPS-R puanı ile HbA1c düzeyi arasındaki ilişki.

		DEPS-R		F	p
		N	Ort.±SS		
HbA1c seviyesi (%)	7 ve altı	44	18,09±12,51	4,756	**0,011***
	8	26	20,65±9,55		
	9 üzerinde	6	33,67±13,31		

*p≤0,05

TARTIŞMA

Bu çalışmada Tip 1 diyabetli adölesanların diyete uyum durumunun ve diyabulimia riskinin metabolik kontrolün önemli bir göstergesi olan HbA1c düzeyine etkisinin incelenmesi amaçlanmıştır.

Çalışmamızda adölesanların diyabetik diyete uyum durumu arttıkça HbA1c düzeyleri daha iyiye gitmiştir. Gruplar arasındaki fark istatistiksel olarak anlamlı bulunmuştur (Tablo III). Brezilya'da Tip 1 diyabetli hastalarda yüksek HbA1c düzeyi ile ilişkili faktörlerin incelendiği çok merkezli bir çalışmada diyete zayıf uyum ile daha yüksek HbA1c düzeyi arasında güçlü bir ilişki olduğu ve diyete zayıf uyum bildiren Tip 1 diyabetli bireylerin HbA1c seviyelerinde ortalama %0,88'lik bir artış saptanmıştır (15). Glisemik hedeflerine ulaşan Tip 1 diyabetli çocukların diyet alımının incelendiği bir başka çalışmada ise kendisine önerilen beslenme programını takip eden çocukların düzensiz bir şekilde beslenen çocuklara kıyasla HbA1c düzeyinin anlamlı olarak daha düşük olduğu bulunmuştur (%7,7'ye karşı %6,1) (16). Diyetisyenler tarafından uygulanan tıbbi beslenme tedavisinin sağlığa etkisini değerlendirilen bir meta-analiz çalışmasına 1227 diyabetli hasta dahil edilmiştir. Buna göre tıbbi beslenme tedavisine uyan hastaların HbA1c düzeyi, uymayanlara göre önemli bir düşüş göstermiştir (17).

Yapılan bazı çalışmalarda diyabulimia riski taşıyanların HbA1c düzeyinin anlamlı olarak daha yüksek olduğu saptanmıştır (18,19). Doyle ve ark., toplam 27 kadın ve 33 erkek diyabetli birey ile yaptığı bir çalışmada DEPS-R puanı yüksek olan hastaların HbA1c seviyesinin düşük olanlara göre anlamlı olarak daha yüksek olduğu bulunmuştur (%10,4±2,1'e karşı %7,8±1,3) (20). Hindistan'da 100 diyabetli ergen ile yapılan bir çalışmada diyabete özgü bozulmuş yeme davranışı ile glisemik kontrol arasındaki ilişki incelenmiştir. DEPS-R puanına göre bozulmuş yeme davranışına sahip olan diyabetli bireylerin bozulmuş yeme davranışı riski olmayanlara göre ortalama HbA1c düzeyi anlamlı olarak yüksek bulunmuştur (21). Ülkemizde beslenme durumunun ve diyabulimia riskinin HbA1c düzeyine etkisinin birlikte incelendiği bir çalışmaya rastlanmamıştır. Bununla birlikte Altınok ve ark., tarafından DEPS-R Türkçe versiyonunun güvenilirliği ve geçerliliği incelenmiştir (14). Çalışmaya yaşları 9-18 arasında değişen toplam 200 Tip 1 diyabetli birey katılmıştır. DEPS-R kesme puanının üzerinde puan alan hastalarda HbA1c düzeyleri her iki cinsiyette de anlamlı olarak yüksek bulunmuştur. Literatürle uyumlu olarak çalışmamızda da bireylerin HbA1c düzeyi ile DEPS-R ortalama puanları arasında anlamlı bir ilişki saptanmıştır (Tablo VI). HbA1c düzeyi %9 ve üzerinde olan adölesanların DEPS-R ortalama puanı (33,67±13,31) anlamlı olarak HbA1c düzeyi %7 ve altında (18,09±12,51) ve %8 düzeyinde (20,65±9,55) olan çocukların ortalama puanından yüksek olduğu bulunmuştur. DEPS-R puanları yüksek olan adölesanların insülin dozunu atlamaları sebebiyle HbA1c seviyelerinde artış yaşanmış ve glisemik kontrolleri bozulmuş olabilir. Ayrıca literatürde kızlarda zayıflamak amacıyla insülin ihmalinin daha sık gözlendiği ve DEPS-R ortalama puanının daha yüksek olduğu belirtilmektedir (22-24). Bununla birlikte diyabulimia riskinin erkeklerde de giderek yaygınlaştığı ve hem erkek hem de kadın cinsiyetinde önemli bir sorun olduğu düşünülmektedir (20,25). Çalışmamızda erkeklerin ortalama DEPS-R puanı kızlardan düşük olsa da birbirine yakındır ve cinsiyetler arası anlamlı bir farklılık bulunmamıştır (Tablo IV). Ancak DEPS-R puanı 20 altında olan adölesanların cinsiyetleri ile yaş grupları arasında anlamlı bir ilişki saptanmıştır. Buna göre 11-14 yaş grubu erkek bireylerde diyabulimia riski en düşük görülmektedir (Tablo V).

SONUÇ

Bu çalışmada kendisine önerilen beslenme tedavisine uymayan ve diyabulimia riski taşıyan Tip 1 diyabetli adölesan bireylerin metabolik kontrolünün kötüleştiği gözlenmiştir. Özellikle risk grubunda olan Tip 1 diyabetli adölesan bireyler DEPS-R gibi güvenilir bir ölçekle diyabulimia açısından değerlendirilmelidir. Gelecekte bununla ilgili multidisipliner bir çalışma ile farklı alt gruplarda çok yönlü bir çalışma yapılabilir. Anketin çevrimiçi ortamda uygulanması çalışmamızın sınırlılıkları arasında gösterilebilir. Yüz yüze anket yöntemiyle katılımcıların beslenme durumuna ilişkin daha güvenilir bilgiler alınabilir.

Etik Komite Onayı:
Bu araştırma, ilgili tüm ulusal düzenlemelere, kurumsal politikalara ve Helsinki Bildirgesinin ilkelerine uygundur ve İstanbul Medipol Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu tarafından 17.06.2021 tarihinde onaylanmıştır (Çalışma sayısı: E-10840098-772.02-2863, Onay numarası: 638).

Hasta Onamı:
Tüm katılımcıların hakları korunmuş ve Helsinki Deklarasyonuna göre prosedürlerden önce yazılı bilgilendirilmiş onam alınmıştır.

Yazar Katkıları:
Fikir-G.Ç.; Tasarım-R.İ.Ö., G.Ç.; Denetleme/Danışmanlık-R.İ.Ö., Veri Toplama ve/veya İşleme-G.Ç.; Analiz/Yorum-G.Ç., R.İ.Ö.; Literatür taraması-G.Ç., R.İ.Ö.; Makalenin Yazımı-G.Ç., R.İ.Ö.; Eleştirel İnceleme-R.İ.Ö.

Çıkar Çatışması:
Yazarların beyan edecek çıkar çatışması yoktur.

Finansal Destek:
Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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ORIGINAL ARTICLE

Özgün Araştırma

Comparing Individual and Family Member Assisted Peritoneal Dialysis In Elderly End-Stage Renal Disease Patients

Yaşlı Son Dönem Böbrek Hastalarında Asiste Periton Diyalizinin Karşılaştırılması

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Geliş Tarihi : 07 January 2022
Received
Kabul Tarihi : 08 April 2022
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Koyuncu S, Uysal C, Akın S, Gundogdu A, Kocyigit I, Sipahioglu MH, Oymak O, Tokgoz B. Comparing Individual and Family Member Assisted Peritoneal Dialysis In Elderly End-Stage Renal Disease Patients
Akd Med J 2023;9(3): 302-308

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ABSTRACT

Objective:

With the increase in the elderly population, the number of patients in end-stage renal disease (ESRD) and in correlation with renal replacement therapy (RRT) has increased. We aimed to compare the efficiency and complications between individual and family member-assisted peritoneal dialysis (APD) in a patient group with geriatric ESRD.

Material and Methods:

This retrospective study included 50 patients > 65 years of age who received continuous ambulatory peritoneal dialysis treatment between 2017-2019 in the peritoneal dialysis unit. In the daily routine dialysis method, pre-observational evaluation was evaluated with the 6-item activity of life and 8-item daily activities of life. Their three years' follow-up results were evaluated in terms of dialysis efficiency parameters and dialysis complications.

Results:

There was no statistical difference in terms of gender, age, and biochemical data between the two groups compared. There was also no difference between edema, exit-site infection, and leakage; however, a significant difference was observed between the total number of peritonitis and the time until the first peritonitis attack. The time until the first peritonitis attack was shorter in the APD group than in the other group. Besides, the number of total peritonitis attacks was higher in the assisted PD group.

Conclusion:

Despite the increase in end-stage renal disease in the elderly population, the number of patients undergoing peritoneal dialysis is decreasing. However, if APD is not done well, it may not be an effective strategy to reverse this decline and provide safe and successful treatment to many frail, elderly patients.

DOI: 10.53394/akd.1054948

Key Words:
Assisted, Elderly, Peritoneal Dialysis

ÖZ

Amaç:
Renal replasman tedavisi (RRT) alan son dönem böbrek yetmezliği (SDBY) olan yaşlı hastaların sayısında sürekli bir artış olmuştur. Geriatrik SDBY'li bir hasta grubunda birey ve aile üyesi destekli periton diyalizi (APD) arasındaki etkinlik ve komplikasyonları karşılaştırmayı amaçladık.

Gereç ve Yöntemler:
Bu retrospektif çalışmaya 2017-2019 yılları arasında periton diyalizi ünitesinde SAPD tedavisi gören 65 yaş üstü 50 hasta dahil edildi. Diyaliz yöntemi seçiminden önce hastaların fonksiyonel durumları altı maddelik günlük yaşam aktiviteleri ve sekiz maddelik enstrümantal günlük yaşam aktiviteleri ile değerlendirildi. Üç yıllık takip sonuçları, diyaliz etkinlik parametreleri ve diyaliz komplikasyonları kayıt altına alındı.

Bulgular:
Karşılaştırılan iki grup arasında cinsiyet, yaş ve biyokimyasal verilerde istatistiksel olarak anlamlı bir fark saptanmadı. Ödem, çıkış yeri enfeksiyonu ve sızıntı arasında da fark yoktu; ancak toplam peritonit sayısı ile ilk peritonit atağına kadar geçen süre arasında anlamlı bir fark gözlendi. APD grubunda ilk peritonit atağına kadar geçen süre diğer gruba göre daha kısaydı. Ayrıca asiste PD grubunda total peritonit atak sayısı daha fazlaydı.

Sonuç:
Yaşlı SDBY popülasyonu artmasına ragmen, PD uygulanan hasta sayısı dünya çapında azalmaktadır. Bununla birlikte, APD iyi yapılmazsa, bu düşüşü tersine çevirmek ve birçok zayıf, yaşlı hastaya güvenli ve başarılı tedavi sağlamak için etkili bir strateji olmayabilir.

Anahtar Sözcükler:
Yardımlı, Yaşlılık, Periton dializi

INTRODUCTION
The incidence of chronic diseases increases with increasing age. One of the most common among these chronic diseases is chronic kidney disease (CKD). With GFR estimated by the CKD-EPI equation, data from the NHANES database showed that the overall prevalence of CKD stages 3 to 4 increased from 4.8 percent in 1988 to 6.9 percent in 1994. Thereafter, it remained stable with a prevalence of 6.9 percent from 2011 to 2012, showing the prevalence was 21.7 percent in individuals aged 65 to 79 years (1).

In many developed countries, the number of elderly patients with end-stage renal disease (ESRD) receiving renal replacement therapy (RRT) has been increasing in recent years.

The RRT treatment rate more than doubled from 1995 to 2004 in patients ≥75 years of age in ESRD cases in the Canadian Organ Replacement Registry 2006 annual report (2). The average age of patients receiving RRT therapy has increased to 60 in most European countries (3).

The elderly constitute the most extensive and fastest-growing patient group starting dialysis.

Although there has been an increase in the number of patients receiving RRT, there has been no increase in the number of patients undergoing PD. The choice of dialysis methods may differ between countries. While 5.23% of patients aged 65-74 years received PD treatment in the USA, only 3.9% of patients aged over 75 years were treated for PD (4). The European Kidney Association/European Society for Dialysis and Transplantation (ERA-EDTA) registries have shown that the older the patients, the more likely they are to start treatment with hemodialysis (HD) (5). According to the 2018 data of the Turkish Nephrology Association Registry, the ratio of patients who underwent PD in RRT was 3.94%. Approximately 28.85% of this patient group consisted of patients ≥65 years (6).

PD has the advantage of being done at home. For the fit elderly, this means they can travel, enjoy their retirement, and have an active social life.

Many elderly patients can be trained to do their PD, although this may take longer than younger patients.

More than 80% of these patients need assistance (7). Assisted PD (APD) is defined as PD treatment performed at the patient's home and with the help of a health care technician, a family member, or a community nurse (8).

With family members willing to assist with all or part of the procedure, the use of community nurses increasingly allows frail patients to have PD in their homes. Therefore, assisting with PD will increase the proportion of patients who start PD treatment (9). Physical and cognitive dysfunction, depression, social isolation, and decreased vision and hearing functions can create a barrier to selecting PD in elderly patients (10).

The role of assistive modalities (family or nurse-assisted PD) on technical failure and peritonitis occurrence should also be explored. The disease burden for family members may prevent the technique from being more effective and increase peritoneal infection risk in assisted PD (11). The present study compares the efficiency and complications between individual and family member-assisted PD in a patient group with geriatric ESRD.

MATERIAL and METHODS
This retrospective study included 50 patients > 65 years of age who received PD treatment between 2017-2019 in the Continuous Peritoneal Dialysis Unit.

The demographical information and clinical data such as the 4-hour peritoneal equilibration test (D/P Cr), total Kt/V, normalized protein catabolic rate (nPCR), and peritoneal ultrafiltration were recorded for each patient. The study was performed after the approval of Erciyes University Scientific Research Ethical Committee (Number: 2020/619). Three years follow up data of the patients with Ambulatory Peritoneal Dialysis were recorded on study form. The research was carried out by the publication of ethics and the Declaration of Helsinki. Patients who were receiving PD treatment before and continuing were also included in the study. Twenty-five of these patients were undergoing dialysis themselves, and 25 were doing it with their family members' help. Since there are not enough PD training and follow-up nurses in our center, nurse-assisted PD cannot be provided. The relatives of the patients come to the hospital at

regular intervals and receive support. Therefore, when the patient decides on assisted PD, the patient's relative is subjected to the training process. When the patient decides on assisted PD, the relatives of the patient are subjected to the education process and their experiences are checked at regular intervals. The decision of which patient to help is made according to Lawton's scale. These patients were followed up for three years.

In the daily routine dialysis method, pre-observational evaluation was evaluated with the 6-item activity of life (ADL) and 8-item daily activities of life (IADL). The ADL scale is based on six levels, including carrying out personal toileting, bathing or showering dressing, eating and moving from bed to chair, and bowel or urine continence. The (IADL) scale is based on eight levels, including the telephone, shopping, cooking, housekeeping, laundry, transportation, ability to take his/her medications, and financial management. Each item is evaluated on a three-point scale (1=unable, 2= needs assistance, 3=independent). An ADL score of ≤ 12 points is considered a dependent, IADL score of 17 points is regarded as a dependent (12). Validation of Katz index of independence in activities of daily living in Turkish older adults was also performed (13).

Hemoglobin (Hb), leukocyte, transferrin saturation, ferritin, blood urea nitrogen (BUN), creatinine (Cr), calcium (Ca), phosphorus (P), uric acid, alkaline phosphatase (ALP), albumin, C-reactive protein (CRP), parathormone (PTH), total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, vitamin B12, and folic acid levels were obtained from patient records. Information about the medications they used was also obtained from their records. The blood chemistry values are obtained from the beginning of the period. All patients included in the study were in a standard PD treatment program with four or five cycles per day and 2000- or 2500-ml volume changes, and were evaluated for dialysis efficacy parameters and dialysis complications.

Statistical Analysis

Statistical analysis of the study data was made with SPSS 15.0 (Statistical Packages for Social Sciences; SPSS Inc. Chicago, Illinois, USA). Measurable data suitable for parametric analysis were given as arithmetic mean±standard deviation (x ± ss). The distribution was defined as median (25% -75%) for the data measured and not suitable for parametric analysis. Suitability to normal distribution was evaluated with the Kolmogorov-Smirnov test. The Kruskal-Wallis test was used for nonparametric testing.

RESULTS

The study included 50 patients aged >65 years followed up regularly in the Peritoneal Dialysis Unit, Medical Faculty, Erciyes University. They were a group of patients who chose the PD method after being diagnosed with ESRD. They were divided into two groups: those who performed PD treatment themselves (n=25) and those who received help from their family members. Their demographic, biochemical, and PD-related parameters were compared with each other (Table I).

Table I: Comparison of demographic and laboratory parameters between the patient groups.

Variables	Individual PD (*n*=25)	Assisted PD (*n*=25)	p
Age (years)	69.76±5.43	68.92±4.83	0.571
Body surface area (m^2)	1.80±0.19	1.78±0.21	0.670
Body mass index (kg/m^2)	27.57±5.49	27.10±4.72	0.750
Diabetes mellitus (present)	8 (32.0)	12 (48.0)	0.248
Hypertension (present)	18 (72.0)	19 (76.0)	0.747
Duration of PD (month)	65 (37.5-121.5)	48 (30.0-102.0)	0.322
BUN (mg/dL)	49.10±16.98	49.51±12.63	0.923
Creatinine (mg/dL)	7.34±2.44	8.33±2.77	0.185
Sodium (mmol/l)	135.56±4.95	137.28±4.69	0.213
Calcium (mg/dL)	9.03±0.85	8.96±0.61	0.731
Phosporus (mg/dL)	4.53±1.16	4.55±0.93	0.954
Total cholesterol (mg/dL)	187.87±45.35	186.52±51.82	0.924
LDL cholesterol (mg/dL)	105.85±38.39	114.96±42.83	0.443
Albumin (g/dL)	3.60±0.54	3.68±0.49	0.595
Hemoglobin (g/dL)	11.87±1.90	11.79±1.74	0.877
Ferritin (ng/ml)	228 (97.3-415.0)	209 (133.0-580.5)	0.614
PTH (pg/ml)	377 (168.5-510.5)	361 (244.0-581.5)	0.541
Total Kt/V	1.91 (1.76-2.30)	2.01 (1.82-2.49)	0.491
nPCR	0.81±0.20	0.81±0.15	0.976

PD: peritoneal dialysis. Values are expressed as *n* (%),

There was no statistical difference between the two groups regarding their gender, age, and biochemical data. At the same time, no significant difference was found in dialysis efficiency (Kt/V). Besides, PD-related complications patients experienced during the treatment process were also compared (Table II).

Table II: Comparison of peritoneal dialysis- related complications between patient groups.

Variables	Individual PD (*n*=25)	Assisted PD (*n*=25)	P
Edema	4(16.0)	9 (36.0)	0.107
Leakage	3(12.0)	2 (8.0)	0.999
Exit-site infection	0 (0-1)	0 (0-2)	0.974
Hernia	5(20.0)	5 (20.0)	0.999
Time to first peritonitis attack*	15 (9-50)	9 (2-35)	0.042
Number of peritonitis attacks	1(0-2)	2 (1-5)	0.001

PD: peritoneal dialysis. Values are expressed as *n*(%), mean±SD or median(1^{st}-3^{rd} quartiles).
*month

There was no difference between edema, exit-site infection, and leakage; however, a significant difference was observed between the total number of peritonitis infections and the time until the first peritonitis attack. The time until the first peritonitis attack was shorter in the group with APD than in the other group. Also, the number of total peritonitis attacks was higher in the APD group (Figure 1).

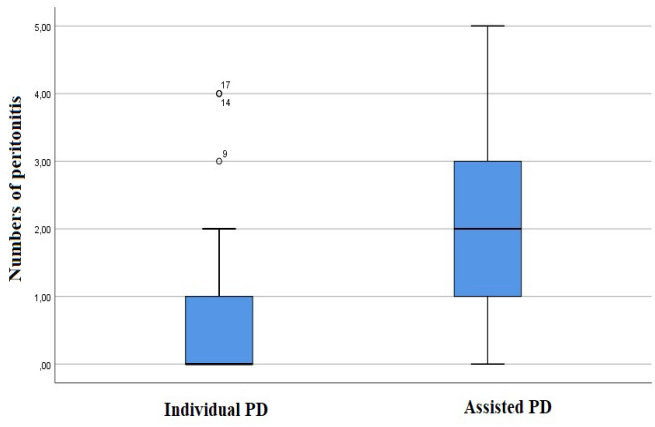

Figure 1: Comparing number of peritonitis between the groups.

Five of the patients with assisted PD and one from the other group switched to HD. One person in each group died. The patients in the assisted PD group had more comorbidity. Of fifteen patients who made assisted PD, ten individual PD patients; required at least one hospitalization within 3 years (Table III).

Table III: Comparision of comorbidity and hospitalization between patient. groups

Variables	Individual PD (*n*=25)	Assisted PD (*n*=25)	P
Diabetes mellitus (present)	8 (32.0)	12 (48.0)	0.24
Hypertension (present)	18 (72.0)	19 (76.0)	0.74
Heart failure	3(12.0)	7(28.0)	0.02
Malignancy	-	1(4.0)	-
Cerebral vascular disease	2(8.0)	7(28.0)	0.03
Hospitalisation	10(40)	15(60)	0.045

PD: peritoneal dialysis. Values are expressed as *n* (%)

DISCUSSION

The rate of ESRD in elderly patients is increasing worldwide. Immobile and physically disabled patients are not eligible for central hemodialysis in cases where vascular access is poor. CAPD may be the only treatment option in this specific patient group (14).

Physical and cognitive dysfunction, depression, social isolation, and decreased vision and hearing functions in elderly patients can create a barrier to selecting PD. However, at the same time, these factors may offer the dialysis option in their homes where they feel independent. Besides, factors that prevent patients from choosing PD may cause difficulties in adapting hemodialysis to their lives (9).

It has been shown that the quality of life of patients aged ≥65 years undergoing PD is superior to those <65 years of age (15). It was emphasized that PD treatment could be more successful in elderly individuals who receive family- and nurse-assisted care. Again, the annual cost of PD was found to be lower than hemodialysis, easing the economic burden (16).

PD treatment at home can offer several advantages compared to in-center hemodialysis (HD). That may be particularly important for elderly patients with severe comorbidity. Most importantly, it means avoiding commuting to and from the dialysis unit, the associated bacteremia and access failure, vascular access for HD, the risk of post-treatment fatigue, and hemodynamic instability during HD sessions (17,18).

Considering the challenges of running an APD program, its success relies critically on a well-organized multidisciplinary team of dedicated kidney nurses, nephrologists, surgeons, assistants, social workers, dieticians, and others. APD should be considered a safe and viable better alternative to in-center HD for the growing group of dependent elderly patients with ESRD (19).

APD treatment is carried out in the patient's home with the assistance of a healthcare technician, a community nurse, a family member, or a spouse (7). Although PD complications are similar between young and older patients, several studies have shown that the risk of peritonitis is higher in the elderly (20-23). The risk of malnutrition is also higher in elderly patients, but this can be overcome with adequate nutritional counseling and amino acid-based dialysis solutions (24). Exit site infection, malposition, and other catheter-related complications occur at similar rates in younger patients (25,26). Some studies report that hernia and leakage occur more frequently or at similar rates (27,28).

The survival rates of elderly patients with chronic PD are shorter than those of younger patients, as expected (29). Several reports have shown that rates of peritonitis and exit site infection are not significantly different between home care nurse-assisted dialysis patients and those receiving self-dialysis treatment (30). The home-care nurse can help treat peritonitis episodes and other complications and reduce hospitalization rates (31). Lobbedez et al., demonstrated that even the assistance of a family member or a private nurse could provide safe CAPD treatment in elderly patients. This study clearly shows that APD is an appropriate method for patients who cannot perform their PD replacement. The risk of peritonitis was relatively high in the assisted group; however, the PD modality may affect the rate of peritonitis. In addition, diverticulosis is more common in elderly patients (32).

In a study by Solene et al., APD was not associated with a higher risk of peritonitis in automated PD patients (33). This observation is consistent with data from a recent Australian study in PD patients where CAPD was not associated with an increased risk of peritonitis (34). The results of a UK study showed that PD modality did not affect peritonitis-free survival (35).

Cheng et al., compared those patients who performed PD themselves and those who underwent APD. The results demonstrated that APD patients had a worse outcome in patient survival and technical failure, but there was no increase in peritonitis incidence (36). Similar results were found in other studies, which suggested no relationship between technical survival and adjunct method (37). Finally, it has been shown that assisted care by non-professional staff leads to worse outcomes in both patient and technical survival in PD (38). Similarly, we found worse outcomes in the APD group compared with self-care PD. In our study, like other previous studies, we found that hospitalization rates were higher in patients with APD. Because, as in other studies, comorbidity was higher in patients in this group. APD evaluation should be done in order not to make these patients completely dependent on dialysis centers (32).

As the number of peritoneal dialysis decreases in Turkey and worldwide, the number of patients is correspondingly low. However, the complication rate can be high in relative-assisted peritoneal treatment. In recent years, pandemics have taught us that we need to reduce the arrival and departure of elderly patients in hospitals and their presence in crowded environments such as dialysis centers. For this, we should increase the training of relatives in countries that do not have adequate nurse support and facilitate patient follow-up by expanding telemedicine.

CONCLUSION

As a result, the elderly ESRD population is increasing and PD use is declining worldwide. However, in the elderly patient group with high comorbidity, assisted PD may be an appropriate approach due to both socioeconomic reasons and the problems experienced in the transfer of these patients. In addition, we may have protected these patients from public environments with a high risk of infection.

Ethics Committee Approval:
This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Erciyes Medical Faculty Ethical Committee, Erciyes University (approval number: 2020/619).

Informed Consent:
All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:
Concept – S.K., İ.K.; Design – S.K., S.A.; Supervision – B.T., S.A.; Resources – C.U.A.G.; Materials - S.K., İ.K, Data Collection and/or Processing – S.K, İ.K., A.G Analysis and/ or Interpretation – S.K., O.O., İ.K..; Literature Search – S.K., A.A., C.U; Writing Manuscript – M.H.S., C.U.; Critical Review – S.K., İ.K, C.U.

Conflict of Interest:
The authors have no conflict of interest to declare.

Financial Disclosure:
No support was received from any institution in the realization of this study. The necessary resources for the study were provided by the authors. There is no financial conflict between the authors.

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Original Article

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Geliş Tarihi : 21 Ocak 2022
Received
Kabul Tarihi : 03 Mart 2022
Accepted
E Yayın Tarihi : 01 Eylül 2023
Online published

Bu makalede yapılacak atıf
Cite this article as
Efil S, Parlak E, Türen S.
Yoğun Bakım Hemşirelerinin Organ Bağışı Tutumlarının Belirlenmesi
Akd Tıp D 2023; 9(3): 309-316

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DOI: 10.53394/akd.1061100

Yoğun Bakım Hemşirelerinin Organ Bağışı Tutumlarının Belirlenmesi

Determination of Organ Donation Attitudes of Intensive Care Nurses

ÖZ

Amaç:
Bu çalışma, yoğun bakım hemşirelerinin organ bağışı hakkındaki tutumlarını belirlemek amacıyla yapılmıştır.

Yöntem:
Araştırma tanımlayıcı nitelikte olup, 04.06.2021 ile 30.07.2021 tarihleri arasında, çevrim içi google anket formu kullanılarak çok merkezli yürütülmüştür. Araştırmaya 105 hemşire katılmıştır. Araştırmanın verileri "Hemşire Tanıtım Formu" ve "Organ Bağışı Tutum Ölçeği" ile toplanmıştır. Veriler, tanımlayıcı istatistikler, student t testi ve tek yönlü varyans analizi (ANOVA) ile değerlendirilmiştir.

Bulgular:
Hemşirelerin yaş ortalaması 28,22±6,6, toplam mesleki deneyim 6,11±6,57, toplam yoğun bakım deneyimi 3,54±4,58 ve haftalık ortalama çalışma saati 53,23±14,10 olarak belirlendi. Katılımcıların çoğu kadın (%80), lisans mezunu (%68,6), bekar (%69,5), vardiyalı çalışan (%81,9), dahili yoğun bakım ünitesinde çalışandı (%79,1). Organ bağışı ile ilgili eğitim aldığını (%22,9) ve organ bağışı kartı olduğunu ifade eden (%18,1) hemşire oranı düşük bulundu. Hemşirelerin Organ bağışı tutum ölçeği'ne göre pozitif tutum skoru yüksek (106,36±13,9), negatif tutum skoru ise (43,53±19,40) düşüktü. Hemşirelerin organ bağışı tutumları ile yaş, toplam mesleki ve yoğun bakım deneyim, haftalık ortalama çalışma saati, cinsiyet, medeni durum, çocuk sahibi olma, çalışma düzeni, statü, çalıştığı yoğun bakım ünitesi, organ bağışı eğitimi alma durumu ve organ bağışı kartı bulunma durumları arasında istatiksel olarak anlamda bir farklılık olmadığı görüldü (p>0,05).

Sonuç:
Yoğun bakım hemşirelerinin organ bağışı konusunda gönüllü tutumlarının güçlü olduğu fakat organ bağışı kartı olanların çok az olduğu belirlendi.

Anahtar Kelimeler:
Yoğun Bakım Üniteleri, Hemşire, Organ Bağışı, Tutum

ABSTRACT

Objective:

This study was conducted to determine the attitudes of intensive care nurses about organ donation.

Methods:

This is a descriptive research, and was carried out in multi-center using the online google questionnaire between 01.06.2021 and 30.07.2021. 105 nurses participated in the study. The data of the research were collected with the "Nurse Information Form" and "Organ Donation Attitude Scale". Data were evaluated with descriptive statistics, student t test and one-way analysis of variance (ANOVA).

Results:

The mean age of the nurses was 28.22±6.6, the total professional experience was 6.11±6.57, the total intensive care experience was 3.54±4.58, and the average weekly working hours were 53.23±14.10. Most of the participants were female (80%), undergraduate (68.6%), single (69.5%), shift worker (81.9%), and working in the medical intensive care unit (79.1%). The proportion of nurses (22.9%) who stated that they had received education on organ donation and had an organ donation card (18.1%) was found to be low. According to the organ donation attitude scale of nurses, positive attitude score was high (106.36±13.9) and negative attitude score was low (43.53±19.40). It was seen that there was no statistically significant difference ($p>0.05$) between the nurses' attitudes towards organ donation and age, total professional and intensive care experience, average weekly working hours, gender, marital status, having a child, working order, status, intensive care unit, organ donation education and organ donation card status.

Conclusion:

It was determined that the volunteer attitudes of intensive care nurses about organ donation were strong, but those who had organ donation cards were very few.

Key Words:

Intensive Care Units, Nurse, Organ Donation, Attitude

GİRİŞ

Organ bağışı, bir kişinin kendisine ait bir organı yasal olarak, hayatta iken veya tıbbi olarak ölü ilan edilmesinden sonra başka hastaların tedavisi için kullanılmasına rıza göstermesi ve bunu belgelendirmesini içerir (1,2). Son dönem organ yetmezliği olan bireylerde daha uzun sağkalım ve daha iyi yaşam kalitesi için organ nakli hayat kurtarıcı bir tedavi yaklaşımıdır (3). Organ bağışı bekleyen hasta sayısı her geçen yıl artmakta, ihtiyaç duyulan organ bağışı yetersiz kalmaktadır. Dünya Sağlık Örgütü (DSÖ), GODT (Global Observatory on Donation and Transplantation) 2019 verilerine göre; 2018 yılında organ bağışı ihtiyacında %4,8 oranında artış olduğu ve küresel ihtiyacın bir önceki yılda olduğu gibi ≤ %10 karşılandığı raporlandırmıştır (4). Ülkemizde, 2021 yılı organ bekleme listesinde 24490 hasta bulunduğu buna karşın organ nakli yapılan toplam hasta sayısının 3703 olduğu bildirilmiştir (5). Ulusal ve uluslararası verilere bakıldığında yeterli sayıda organ bağışı yapılmasının, gereken organ nakilleri için kritik öneme sahip olduğu görülmektedir. Yeterli sayıda organ bağışına ulaşmak için toplumun teşvik edilmesi ve bu konudaki engellerin iyileştirilmesi gereklidir. Organ bağışına yönelik tutumun organ nakli için belirleyici bir faktör olduğu unutulmamalıdır (6).

Literatürde dini inanç, bilgi eksikliği, sağlık hizmetlerine güven eksikliği, hukuk sistemindeki eksiklikler, sosyokültürel yapı ve aile ilişkileri gibi birçok faktör nedeni ile organ bağışında bulunma istekliliğinin az olduğu saptanmıştır (6-8). Toplumun organ bağışına yönelik tutum ve davranışları, sağlık profesyonellerinin organ bağışına yönelik tutumlarından etkilenebilir. Bu nedenle sağlık profesyonellerinin organ bağışına yönelik karar almalarında, bu konudaki tutumları ve bilgi düzeyleri önemlidir (9). Literatürde organ bağışı ile ilgili istekliliğin sağlık çalışanlarında düşük oranda olduğu görülmektedir (10-15). Özellikle yoğun bakım hemşireleri, potansiyel organ donörlerinin belirlenmesi ve organ bağış sayısının artırılmasında önemli bir rol oynar (12). Ayrıca, donör bakımı, organ nakli koordinasyonu, donör ailesiyle iletişim ve organ bağışı farkındalığı hakkında eğitim programlarının düzenlenmesi gibi birçok önemli rolleri de yerine getirmektedir (16). Bu nedenle yoğun bakım hemşirelerinin organ bağışına yönelik bilgi ve tutumları organ bağışı sayısını etkileyen önemli faktörlerden biridir (7,17,18).

Bilgi ve olumlu tutum, insanların organ bağışına tepkilerini iyileştirebilir ve organ bağışına karşı dirençleri önleyebilir (19). Bu nedenle yoğun bakım hemşirelerinin olumlu bir tutum ve uygulamaya sahip olmaları önemlidir. Literatürde hemşirelerin organ bağışına yönelik tutumlarının olumlu olduğunu gösteren çalışmalar bulunmaktadır (7,17,20,21). Xie ve ark. (2017) ise, hemşirelerin organ bağışına yönelik iyimser bir tutum sergilemediklerini belirlemişlerdir (13). Yoğun bakımda çalışan sağlık profesyonellerinin bağışa yönelik olumlu tutumları, organ bağışında artan başarı ile ilişkilidir. Abbasi ve ark. (2018) çalışmasında; yaş, eğitim, mesleki deneyim, dini inanç ve tutumlar, ölen kişinin ailesiyle olan ilişki, beyin ölümü gerçekleşen hastalara bakma öyküsü ve kişisel deneyimler gibi çeşitli faktörlerin hemşirelerin organ bağışına yönelik tutumlarını etkilediği saptanmıştır (22). Sağlık profesyonellerinde organ nakli ve transplantasyonu süreci ile ilgili yeterlilik ve güvenin yaygınlaştırılması, ailelerin organ bağışı konusundaki kararlarını olumlu yönde etkilemede önemlidir. Bu durum, organ bağışı bekleyen bireyin hayatta kalması ve yaşam kalitesinin iyileştirilmesi için önemli bir adım olurken, yakınını kaybetmiş ailenin yaşadığı büyük acıyı da bir dayanışma fırsatına dönüştürmek konusunda etkili olacaktır (21). Doku ve organ bağışına yönelik sergilenen tutum, doku ve organ bağışı yapılmasında belirleyicidir (23). Türkiye'de yoğun bakım hemşirelerinin organ bağışı ile ilgili tutumları ve bilgi düzeylerini değerlendiren sınırlı sayıda çalışma bulunmaktadır (10,12,24). Bu çalışma ile yoğun bakım hemşirelerinin organ bağışı ile ilgili tutumlarını ve bu tutumları etkileyen faktörleri belirlemek amaçlanmıştır.

YÖNTEM

Araştırmanın tipi:
Bu araştırma, tanımlayıcı niteliktedir.

Araştırma Soruları
• Yoğun bakım hemşirelerinin organ bağışı tutumları nasıldır?
• Yoğun bakım hemşirelerinin organ bağışı tutumunu etkileyen faktörler nelerdir?

Araştırmanın evreni ve örneklemi

Türkiye genelindeki kamu ve özel hastanelerde çalışan yoğun bakım hemşireleri araştırmanın evrenini oluşturmuştur. Evrendeki minimum örneklem büyüklüğü G*Power (v3.1.9.7) programı ile güç analizi yapılarak belirlenmiştir. Analiz 0,05 anlamlılık düzeyi (α), %80 istatistiksel test gücü (1-β) elde etmek için yapılan hesaplamada etki büyüklüğü 0,30 olarak hesaplanmış ve standart sapma (SS) değerine göre minimum örneklem büyüklüğü en az 82 bulunmuştur. Türkiye'nin farklı bölgelerinden çalışmaya katılmayı kabul eden 105 yoğun bakım hemşiresi araştırmaya dahil edilmiştir. Araştırmanın yapıldığı tarihlerde izinli ya da raporlu olan, araştırmaya katılmayı kabul etmeyen hemşireler araştırmanın dışlanma kriterleri olarak belirlenmiştir.

Veri Toplama Araçları

Araştırmanın verileri "Hemşire Tanıtım Formu" ve "Organ Bağışı Tutum Ölçeği" ile toplanmıştır.

Hemşire Tanıtım Formu:
Araştırmacılar tarafından literatür araştırması yapılarak oluşturulmuştur (9,10,12,24). Formda, hemşirelerin tanımlayıcı özelliklerini (cinsiyet, yaş, eğitim, medeni durum, çalıştığı klinik, toplam mesleki deneyim, yoğun bakım deneyimi gibi) ve organ bağışına yönelik düşüncelerini belirlemeye yönelik 14 soru yer almıştır.

Organ Bağışı Tutum Ölçeği:
Parisi ve Katz tarafından 1986 yılında geliştirilmiştir. Ölçeğin Türkçe geçerlilik ve güvenirliği Sayın tarafından (2015) yapılmıştır. Ölçekte her bir boyutu 20'şer madde olmak üzere iki boyut yer almaktadır. Birinci boyut, insanların organ bağışı konusundaki "yardımseverlik ve ahlaki değerleri/inançlarını" gösteren pozitif söylemleri içermektedir. İkinci boyut ise negatif söylemlerden oluşmakta ve 10'ar madde olan, "tıbbi olarak ihmal edilme korkusu" ve "bedensel yaralanma korkusunu" içermektedir. Ölçekte her bir maddenin puanı toplanarak hesaplanmaktadır. Pozitif tutum skoru 20 ile 120 arasındadır. Negatif tutumları içeren "tıbbi olarak ihmal edilme korkusu" ve "bedensel yaralanma korkusu" puanları ise 10 ile 60 arasında değişmekte olup, toplam negatif tutum skoru 20 ile 120 arasındadır. Pozitif tutumun yüksek, negatif tutumun düşük skorda olması organ bağışı konusunda gönüllü tutumların güçlü olması şeklinde yorumlanmaktadır. Ölçeğin toplam, pozitif ve negatif tutum için Cronbach alfa değeri sırasıyla 0,857, 0,925, 0,914'tür (25). Bu çalışmada ise, ölçeğin Cronbach alfa değeri geneli için 0,784, pozitif tutum için 0,910, negatif tutum için 0,858'dir.

Verilerin toplanması

Veriler 4 Haziran-30 Temmuz 2021 tarihleri arasında, çevrim içi google anket formu kullanılarak gerçekleştirilmiştir. Türkiye genelindeki kamu ve özel hastanelerde çalışan yoğun bakım hemşirelerine ulaşabilmek amacıyla çevrim içi anket bağlantısı e-posta ve sosyal ağlar aracılığıyla dağıtılmıştır. Araştırmacılar kendi sosyal ağlarını kullanarak dernek ve hemşirelere ulaşmıştır. Ayrıca bir üniversitenin mezun izlem komisyonu ile görüşülmüş, araştırmanın amacı ve prosedürü açıklanarak anket bağlantısını mezun üyeleri ile paylaşmaları istenmiştir. İlgili komisyonda kaydı olan Türkiye'nin birçok farklı sağlık kurumunda çalışan 540 hemşire bulunmaktadır. Ulaşılan hemşirelerden anket bağlantısını çalıştıkları kurumlardaki yoğun bakım hemşirelerinin yer aldığı sosyal gruplardan paylaşmaları istenmiştir. Gönüllü olanlar araştırmaya katılmaya davet edilmiştir. Katılımcılara haftada iki kez hatırlatma yapılmıştır. Sosyal ağlarda da anket linki veri toplama sürecinde paylaşılmıştır. Araştırmayı kabul eden katılımcılar anket sorularını görebilmişlerdir. Anket formunun yanıtlanması her bir katılımcı için ortalama 10 dakika sürmüştür.

İstatistiksel analiz

Çalışmadan elde edilen veriler, Statistical Package for Social Science (SPSS) 20.0 paket programı kullanılarak değerlendirilmiştir. Sürekli değişkenler ortalama±SS olarak, kategorik değişkenler ise yüzde olarak ifade edilmiştir. Verilerin normal dağılıma uygunlukları Kolmogorov-Smirnov testi ile bakılmıştır. Sürekli değişkenler için student t testi ve tek yönlü varyans analizi (ANOVA) ile karşılaştırılmıştır. İstatistiksel anlamlılık düzeyi $p<0,05$ olarak kabul edilmiştir.

Etik İlkeler

Araştırmaya başlamadan önce Çanakkale Onsekiz Mart Üniversitesi Lisansüstü Eğitim Enstitüsü Etik Kurulu 03.06.2021 tarihli ve 10/07 sayılı karar (2021-YÖNP-0468 nolu) ile etik izin alınmıştır. Ölçeğin kullanılabilmesi için sorumlu yazardan izin alınmıştır. Veri güvenliğini sağlamak için çevrim içi google anket formu düzenlenirken, bir kez gönderme butonu seçilerek veri girişlerinin tekrarlanması önlenmiştir. Çevrim içi google anket formunda katılımcıları bilgilendirmek ve yazılı onamlarını almak amacıyla sorulardan önce bilgilendirilmiş onam formu eklenmiştir. Katılımcılar anket linkine tıkladıklarında bilgilendirilmiş onam formuna yönlendirilmiştir. Bu formda araştırmanın amacı, içeriği, süresi, elde edilen verilerin nerede kullanılacağı ilgili yazılı metin yer almıştır. Katılımcılar, bilgilendirilmiş onam formunu okuduktan sonra isteklilik ve gönüllük ilkeleri doğrultusunda, "Bu çalışmaya katılmayı tamamen kabul ediyorum" kutusunu işaretleyerek çalışmaya katılmışlardır. Anketin uygulanması süresinde araştırmayı tamamlamak istemeyenler sistemden çıktıklarında kayıt alınmamıştır. Katılımcılardan alınan bilgilerin araştırma amacı dışında kullanılmayacağı konusunda bilgi verilerek "sadakat ve gizlilik ilkelerine" bağlı kalınmıştır. Araştırma Helsinki Bildirgesine uygun olarak yürütülmüş olup, araştırma ve yayın etiğine uyulmuştur.

BULGULAR

Hemşirelerin yaş ortalaması 28,22±6,66 yıl, toplam mesleki deneyim 6,11±6,57 yıl ve toplam yoğun bakım deneyimi 3,54±4,58 yıl olarak belirlendi. Katılımcıların çoğu kadın (%80), lisans mezunu (%68,6), bekar (%69,5), vardiyalı (%81,9) ve dahili yoğun bakım ünitesinde çalışandı (%79,1). Organ bağışı ile ilgili eğitim aldığını (%22,9) ve organ bağışı kartı olduğunu ifade eden (%18,1) yoğun bakım hemşiresi düşük iken, organ bağışı bekleyen yakını olan hemşire oranı %4,8'di (Tablo I).

Tablo I: Yoğun Bakım Hemşirelerinin Tanıtıcı Özellikleri.

Yaş, yıl		28,22±6,66 (min.20-mak.50)	
Toplam mesleki deneyim, yıl		6,11±6,57 (min.1-mak.31)	
YBÜ'de toplam deneyim, yıl		3,54±4,58 (min.6 ay-mak.24)	
Haftalık ortalama çalışma saati		53,23±14,10 (min.40-mak.96)	
		n	**%**
Cinsiyet	Kadın	84	80,0
	Erkek	21	20,0
Eğitim Durumu	Sağlık Meslek Lisesi	6	5,7
	Ön Lisans	11	10,5
	Lisans	72	68,6
	Lisansüstü (Yüksek Lisans/Doktora)	16	15,2
Medeni durum	Evli	32	30,5
	Bekar	73	69,5
Çocuk sahibi olma	Evet	25	23,8
	Hayır	80	76,2
Çalışma düzeni	Sürekli gündüz	14	13,3
	Gece/Gündüz	86	81,9
	Sürekli gece	5	4,8
Statü	Klinisyen/Yoğun bakım hemşiresi	91	86,7
	Sorumlu hemşire	14	13,3
Çalıştığı YBÜ	Dahili YBÜ	82	78,1
	Cerrahi YBÜ	23	21,9
Organ bağışı eğitimi	Evet	24	22,9
	Hayır	81	77,1
Organ bağışı kartı	Evet	19	18,1
	Hayır	86	81,9
Organ bağışı bekleyen yakını	Evet	5	4,8
	Hayır	100	95,2

Hemşirelerin Organ bağışı tutum ölçeği'ne göre pozitif tutum skorları 106,36±13,99 (min.50-mak.120) iken, negatif tutum skorları 43,53±19,40 (min.20-mak.103)'dı. Negatif tutumun alt boyutları olan "Tıbbi Olarak İhmal Edilme Korkusu" skoru 21,48±10,68 (min.10-mak.53), "Bedensel Yaralanma Korkusu" skoru 22,15±10,06 (min.10-mak.54) olduğu saptandı. Hemşirelerin organ bağışı konusunda gönüllü tutumlarının güçlü olduğu belirlendi (Tablo II).

Tablo II: Yoğun Bakım Hemşirelerinin Organ Bağışı Tutum Ölçeği Puan Ortalamaları.

	Ort ± SS	**Min-Mak**
OBTÖ, Yardımseverlik ve Ahlaki Değerleri Total Pozitif Tutum (20-120 puan)	106,36±13,99	min.50-mak.120
OBTÖ, Tıbbi Olarak İhmal Edilme Korkusu (10-60 puan)	21,48±10,68	min.10-mak.53
OBTÖ, Bedensel Yaralanma Korkusu (10-60 puan)	22,15±10,06	min.10-mak.54
OBTÖ, Toplam Negatif Tutum (20-120 puan)	43,53±19,40	min.20-mak.103

[1]Ort ± SS; [2]Min-mak; OBTÖ, Organ Bağışı Tutum Ölçeği

Hemşirelerin organ bağışı tutumları ile yaş, toplam mesleki ve yoğun bakım deneyim, haftalık ortalama çalışma saati, cinsiyet, medeni durum, çocuk sahibi olma, çalışma düzeni, statü, çalıştığı yoğun bakım ünitesi arasında anlamlı bir ilişki saptanmadı (p>0,05). Ayrıca hemşirelerin organ bağışı eğitimi alma durumu, organ bağışı kartı bulunma durumları ve organ bağışı bekleyen yakını olma durumları ile organ bağışı tutumları arasında ilişki yoktu (p>0,05) (Tablo III).

Tablo III: Yoğun Bakım Hemşirelerinin Organ Bağışı Tutumunu Etkileyen Faktörler.

		Toplam Pozitif Tutum	t, F	p	Negatif Tutum 1	t, F	p	Negatif Tutum 2	t, F	p	Toplam Negatif Tutum	t, F	p
Yaş	20-25	104,92±16,54	*-1,02	0,30	20,45±11,26	*-0,96	0,33	22,35±10,52	*0,19	0,84	42,80±20,38	*-0,37	0,71
	25 ve üzeri	107,72±11,05			22,46±10,12			21,96±9,70			44,22±18,60		
Toplam mesleki deneyim	1-5 yıl	104,51±16,00			21,69±11,49			23,25±10,79			44,92±20,03		
	6-10 yıl	109,70±9,98	**1,14	0,33	21,90±9,63	**0,41	0,74	18,95±6,38	**1,35	0,26	40,35±14,46	**0,73	0,53
	11-15 yıl	107,86±6,31			17,14±1,95			18,43±8,16			35,57±9,54		
	≥ 16 yıl	110,64±13,99			22,27±11,05			23,64±11,22			45,91±21,45		
YBÜ'de toplam deneyim	≤ 5 yıl	106,00±15,02			21,34±11,00			22,12±10,02			43,33±19,71		
	6-10 yıl	106,33±10,57	**0,24	0,86	23,93±10,98	**0,53	0,66	24,40±11,77	**0,73	0,53	48,33±21,14	**0,71	0,54
	11-15 yıl	109,17±7,47			19,17±5,98			19,33±6,80			38,50±10,63		
	16 yıl ve üzeri	113,00±9,90			16,00±4,24			15,00±1,41			31,00±5,66		
Haftalık ortalama çalışma saati	≤ 40 saat	107,08±13,02	*0,29	0,76	21,00±10,90	*-0,26	0,79	21,00±10,60	*-0,67	0,50	42,00±20,49	*-0,46	0,64
	> 40 saat	106,13±14,37			21,64±10,68			22,53±9,92			44,04±19,14		
Cinsiyet	Kadın	107,26±14,12	*1,32	0,18	20,90±10,44	*-1,11	0,26	21,55±9,99	*-1,23	0,22	42,56±18,96	*-1,02	0,30
	Erkek	102,76±13,16			23,81±11,59			24,57±10,20			47,43±21,09		
Eğitim Durumu	Sağlık meslek lisesi	106,83±9,54	**0,82		24,83±11,62	**0,59		26,83±10,80	**1,80		51,67±21,48	**1,22	
	Ön lisans	112,54±4,91		0,48	19,45±8,16		0,61	17,4±4,80		0,15	37,00±11,81		0,30
	Lisans	105,69±15,40			22,00±11,22			23,05±10,87			44,92±20,83		
	Lisansüstü (Yüksek Lisans/Doktora)	104,94±12,50			19,31±9,61			19,50±7,24			38,75±14,79		
Medeni durum	Evli	107,19±10,15	*0,39	0,69	22,03±10,29	*0,34	0,73	22,12±8,82	*-0,01	0,98	44,12±17,81	*-0,20	0,83
	Bekar	106,00±15,42			21,25±10,91			22,16±10,61			43,27±20,17		
Çocuk sahibi olma	Evet	109,92±7,41	*1,46	0,14	19,28±8,24	*-1,18	0,23	20,40±9,23	*-0,99	0,32	39,68±16,20	*-1,13	0,25
	Hayır	105,25±15,35			22,17±11,30			22,70±10,30			44,74±20,24		
Çalışma düzeni	Sürekli gündüz	109,64±7,14	**0,69		21,28±10,83	**0,28		20,57±10,57	**0,21		41,86±20,70	**0,09	
	Gece/Gündüz	105,60±15,03		0,50	21,31±10,91		0,75	22,35±10,02		0,80	43,65±19,46		0,90
	Sürekli gece	110,20±7,26			25,00±6,40			23,20±11,17			46,20±18,16		
Statü	Klinisyen/Yoğun bakım hemşiresi	106,13±14,78	*-0,42	0,67	21,38±10,78	*-0,24	0,80	22,05±10,16	*-0,25	0,80	43,32±19,52	*-0,28	0,77
	Sorumlu hemşire	107,86±7,16			22,14±10,43			22,78±9,74			44,93±19,23		
Çalıştığı YBÜ	Dahili YBÜ	106,40±14,09	*0,05	0,95	21,10±10,60	*-0,70	0,48	22,08±10,06	*-0,12	0,89	43,05±19,28	*-0,48	0,63
	Cerrahi YBÜ	106,22±13,95			22,87±11,10			22,39±10,27			45,26±20,18		
Organ bağışı eğitimi	Evet	109,33±8,81	*1,18	0,23	22,08±12,19	*0,31	0,75	22,21±11,85	*0,03	0,97	44,71±22,99	*0,33	0,73
	Hayır	105,48±15,12			21,31±10,27			22,13±9,55			43,18±18,35		
Organ bağışı kartı	Evet	112,00±5,31	*1,96	0,06	21,21±9,32	*-0,12	0,90	19,37±9,35	*-1,33	0,18	40,05±18,17	*-0,86	0,39
	Hayır	105,12±15,00			21,55±11,01			22,77±10,16			44,30±19,68		
Organ bağışı bekleyen yakını	Evet	113,00±3,39	*1,08	0,27	22,20±7,79	*0,15	0,87	23,00±4,95	*0,19	0,84	45,20±9,98	*0,19	0,84
	Hayır	106,03±14,24			21,45±10,84			21,11±10,26			43,45±19,78		

Ort ± SS; Significant difference at (p<0,05); *Students t test (t), **ANOVA (F); OBTO, Örgan Bağışı Tutum Ölçeği; Toplam Pozitif Tutum, Yardımseverlik ve Ahlakı Değerleri; Negatif Tutum 1, Tıbbi Olarak İhmal Edilme Korkusu; Negatif Tutum 2, Bedensel Yaralanma Korkusu

TARTIŞMA

Bu çalışmada yoğun bakım hemşirelerinin organ bağışına yönelik tutumları incelenmiştir. Çalışmada yoğun bakım hemşirelerinin organ bağışı konusunda pozitif tutumlarının yüksek düzeyde (106,36±13,99) olduğu belirlenmiştir. Yoğun bakım hemşireleri, verimli bir organ bağış süreciyle ilgili diğer temel görevlerin yanı sıra ailenin karar verme sürecine destek olma, potansiyel bağışçıların belirlenmesi, bildirilmesi ve sürecin sorunsuz bir şekilde sürdürülmesinde önemli bir yere sahiptir. Dolayısıyla yoğun bakım hemşirelerinin organ bağışı konusunda bilgi ve tutumları, toplumun organ bağışına yönelik karar vermesini desteklemek için önemlidir. Bu nedenle hemşirelerin organ bağışı konusunda yeterli bilgi ve olumlu tutuma sahip olmaları gereklidir (26,27). Fernández-Alonso ve ark. (2020), yoğun bakım hemşirelerinin organ bağışına yönelik olumlu tutum sergilediklerini saptamışlardır (7). Farklı çalışmalarda da, hemşirelerin organ bağışına yönelik tutumları olumludur (17,20). Yoğun bakım hemşirelerinin organ bağışı tutumları ile ilgili bu çalışmanın sonuçları da literatür ile benzerlik göstermektedir.

Organ bağışı kartı olan hemşirelerin organ bağışına yönelik tutumlarının olumlu olduğu ve bu konuda farkındalıklarının iyi düzeyde olduğu bilinmektedir. Organ bağışı süreci hakkında yeterli bilgiye sahip olan hemşireler organ bağış kartı sahibi olmaya ikna etmede önemli bir faktördür (28). Organ nakli sürecinde yer alan yoğun bakım hemşirelerinin organ bağışı konusunda olumlu tutum sergilemeleri istenen bir durumdur. Çalışmada yoğun bakım hemşirelerinin organ bağışına yönelik olumlu tutum puanları yüksek olmasına rağmen, organ bağış kartına sahip hemşirelerin çok az olduğu (%18,1) belirlenmiştir. Organ bağış kartına sahip hemşirelerin düşük oranda olduğunu gösteren farklı çalışmalarda bulunmaktadır (10-12,26,29,30). Fırıncıoğlu ve ark. (2020) çalışmasında da, yoğun bakım hemşirelerinde organ bağışı yapmayı düşünenlere kıyasla organ bağış kartı olanların daha az oranda (%20,22) olduğu belirlenmiştir (24). Organ bağışı kartına sahip olma oranının düşük olması, organ bağışı konusunda farkındalığın eksikliği ile ilgili olabilir.

Organ bağışı ve nakli konusunda hemşire eğitimi, hemşirelerin olumlu bir tutum sergilemesi için gerekli ve belirleyicidir (26,27). Çalıkoğlu ve ark. (2018), bilgi düzeyi yeterli olan yoğun bakım hemşirelerinde organ bağışını yüksek bulunmuştur. Aynı çalışmada kendi kendine organ nakli talebinde bulunma ile organ bağışı arasında ilişki olduğu saptanmıştır (10). Literatürde hemşirelerde organ bağışı yapma konusunda isteklilik olmakla birlikte; organ bağışı yapmayı düşünmeyenler veya bu konuda kararsız olan hemşirelerin azımsanmayacak sayıda olduğu dikkat çekmektedir (8,10,11,26,31). Çalışmada da organ bağışı kartı sahibi olmayanların çoğunlukta olması, organ bağışı yapma ile ilgili kendilerini hazır hissetmemeleri veya isteksiz olmaları ile ilgili olabilir. Bu nedenle organ bağışına yönelik kararsızlığın veya olumsuz tutumun iyileştirilmesi gereklidir. Mekkodathil ve ark. (2020) çalışmasında; organ bağışında bulunma isteğinin organ bağışı hakkında bilgi sahibi olmakla ilişkili olduğu bulunmuştur (6). Hu ve Huang (2015) ise, sağlık çalışanlarının %17,4'ünün organ bağışı ile ilgili bazı eğitim

kurslarına veya konferanslara katıldığını belirlemişlerdir (14). Bu çalışmada da, organ bağışı ile ilgili eğitim alanların oranı düşük (%22,9) bulunmuştur. Organ bağışına yönelik tutumlar olumlu olsa da, tutumların eyleme geçmesi için yoğun bakım hemşirelerinde farkındalık arttırılmalı ve yeterli bilgiye sahip olmaları sağlanmalıdır.

Bireylerin birinci derece yakınlarında veya çevresinde organ nakli bekleyen veya bu süreci yaşayanların olması organ bağışının önemini anlama, organ bağışına yönelik empatik yaklaşabilme ve duyarlı olmalarında etkili olabilmektedir (32). Çalışmada hemşirelerin organ bağışı bekleyen yakınlarının olması ile organ bağışı tutumları arasında bir ilişki bulunmamıştır. Ayrıca yoğun bakım hemşirelerinin sosyo-demografik özellikleri, mesleki deneyimleri, çalışma koşulları gibi faktörlere göre organ bağışı tutumlarının değişmediği belirlenmemiştir (Tablo III). Araujo ve Siqueira'nın (2016) çalışmasında da benzer şekilde medeni durum ve organ bağışı tutumu arasında ilişki saptanmamıştır (21). Bu sonuçların aksine Janatolmakan ve ark. (2020), evli olma ve organ bağış kartına sahip olmanın organ bağışına yönelik tutumu etkilediğini belirlemişlerdir (19). Damar ve ark. (2019) çalışmasında da, organ bağışına yönelik olumsuz tutumların yaş arttıkça azaldığı saptanmıştır (26). Tutum, insanları belirli bir davranışı yapmaya hazır hale getirebilir. Daha olumlu bir tutuma sahip olma, davranışı yapma olasılığını arttırmada önemlidir (19). Literatürde organ bağışı tutumunu etkileyen birçok faktör olduğu bilinmekle birlikte, organ bağışına yönelik olumlu tutumların davranışa dönüşmesinin önemli olduğuna vurgu yapılmıştır (6,8,10,11,26,31,32). Bu bağlamda organ bağışına yönelik olumlu tutumun davranışa aktarılmasına teşvik eden, motivasyonu arttıran girişimlere ihtiyaç olduğu düşünülmektedir. Hemşirelerin organ bağışına yönelik tutumları kişisel görüş ve değerlerden etkilenebilir (7). Olumlu organ bağışı tutumunun davranışa aktarılmasını engelleyen faktörleri ve olası nedenleri ortaya koymak için nitel çalışmaların yapılması önerilmektedir.

Araştırmanın sınırlılığı

Bu çalışmada anket kullanılması nedeni ile seçim yanlılığının olması bir sınırlılıktır. Çok merkezli yürütülmesine rağmen verilerin pandemi döneminde toplanması nedeni ile katılımcı sayısında çoğunluk sağlanamamakla birlikte, belirlenen örneklem sayısına ulaşılmıştır. Tükenmişlik, bilgi düzeyi gibi organ bağışı tutumunu etkileyebilecek durumlar analiz edilmemiştir.

SONUÇ

Yoğun bakım hemşirelerinin organ bağışı konusunda gönüllü tutumlarının güçlü olduğu fakat organ bağışı kartına sahip olanların düşük oranda olduğu belirlenmiştir. Bu sonuçlar doğrultusunda yoğun bakım hemşireleri organ bağışına karşı olmamakla birlikte, bağış yapmaya hazır olmamış olabilir. Organ bağışı konusunda olumsuz tutumların iyileştirilmesi, uygun eğitim ve motivasyonun sağlanması önemlidir. Ayrıca yoğun bakım hemşirelerinin organ bağışı ile ilgili yapılan etkinliklerde görev almaları sağlanabilir.

Etik Komite Onayı:
Bu araştırma, ilgili tüm ulusal düzenlemelere, kurumsal politikalara ve Helsinki Bildirgesinin ilkelerine uygundur ve Çanakkale Onsekiz Mart Üniversitesi Lisansüstü Eğitim Enstitüsü Etik Kurulu tarafından onaylanmıştır (onay numarası: 2021-YÖNP-0468 nolu).

Bilgilendirilmiş Onam:
Tüm katılımcıların hakları korunmuş ve Helsinki Deklarasyonuna göre prosedürlerden önce yazılı bilgilendirilmiş onam alınmıştır.

Yazar Katkıları:
Fikir – S.E., E.P., S.T.; Tasarım - S.E., E.P., S.T.; Denetleme - S.E., E.P., S.T.; Kaynaklar - S.E., E.P., S.T.; Malzemeler - S.E., E.P., S.T.; Veri Toplanması ve/veya İşlemesi - S.E., E.P., S.T.; Analiz ve/veya Yorum - S.E., E.P., S.T.; Literatür Taraması - S.E., E.P., S.T.; Yazıyı Yazan - S.E., E.P., S.T.; Eleştirel İnceleme - S.E., E.P., S.T.

Çıkar Çatışması:
Yazarların beyan edecek çıkar çatışması yoktur.

Finansal Destek:
Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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Geliş Tarihi : 19 Temmuz 2022
Received
Kabul Tarihi : 10 Nisan 2023
Accepted
E Yayın Tarihi : 01 Eylül 2023
Online published

Bu makalede yapılacak atıf
Cite this article as
Ünal A, Önal MZ.
Geçici Serebral İskemi Modelinde Fokal Hipotermik Tedavi
Akd Tıp D 2023; 9(3): 317-324

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Geçici Serebral İskemi Modelinde Fokal Hipotermik Tedavi

Focal Hypothermic Treatment in Temporary Cerebral Ischemia Model

ÖZ

Amaç:
İskemik inme tedavisinde reperfüzyon yöntemleri ile iyi sonuçlar elde edilmektedir. Reperfüzyonun faydasının yanında inflamasyon ve beyin ödemini içerecek şekilde istenmeyen etkileri de vardır. Reperfüze olan bölgenin fokal olarak ısısının düşürülmesi istenmeyen etkileri azaltarak nöron hasarını azaltabilir. Bu çalışmada deneysel geçici serebral iskemi modelinde, iskemik dallara soğuk serum fizyolojik enjeksiyonu ile lokal olarak sağlanacak beyin ısısındaki düşüşün infarkt alanına ve klinik sonlanıma etkisini göstermeyi amaçladık.

Gereç ve Yöntemler:
Çalışmada 28 adet rat kullanılarak intralüminal sütür tekniği ile 90 dakikalık geçici orta serebral arter oklüzyonu yapıldı. Rekanalizasyon sonrası kontrol grubunda işlem sonlandırıldı, diğer gruplarda ise internal karotis arter yoluyla sırasıyla 15ºC, 23ºC ve 37ºC ısısında serum fizyolojik infüzyonu yapıldı. Çalışma sırasında 15ºC salin infüzyonu yapılan grupta erken dönem ölümler görülmesi üzerine çalışmanın bu ayağı sonlandırıldı. Diğer gruplar 24. saat sonunda infarkt hacmi ve nörolojik sonlanım açısından karşılaştırıldı.

Bulgular:
Salin infüzyonu yapılan iki grupta (23 ve 37 ºC) da kontrol grubuna göre infarkt hacimlerinde küçülme saptandı (p=0,012). Salin infüzyonu yapılan gruplar arasında toplam (kortikal ve subkortikal) infarkt hacmi arasında fark yoktu. Kortikal infarkt hacmi açısından yapılan karşılaştırmada 23ºC grupta kontrole kıyasla anlamlı küçülme gösterildi (p=0,011), 37 ºC grup kontrolle kıyaslandığında anlamlı küçülme görülmedi ve sadece fark eğilimi vardı (p=0,063). Nörolojik skor açısından kıyaslama yapıldığında 23ºC'lik infüzyon yapılan grubun skoru diğer gruplara göre daha iyi bulundu (p=0,010).

Sonuç:
Reperfüzyon sırasında salin infüzyonu ile infarkt hacminde azalma sağlanmıştır. Bu etki soğuk uygulama ile birlikte daha belirgindir. Ayrıca soğuk uygulama yapılan deneklerin nörolojik skorları daha iyidir.

Anahtar Kelimeler:
Serebral iskemi, İnfarkt, Hipodermi, Reperfüzyon hasarı

DOI: 10.53394/akd.1145360

ABSTRACT

Objective:

Positive results have been attained in ischemic stroke treatment by reperfusion. Despite the benefits of reperfusion there are also certain side effects consisting of inflammation and brain edema. Decreasing the temperature of the reperfused region locally may diminish the unwanted impact and mitigate the neuron damage. In this study, we aimed to show the effect of the decrease in cerebral temperature, which will be provided locally by the injection of cold saline into the ischemic branches, on the infarct area and clinical outcome in the experimental temporary cerebral ischemia model.

Material and Methods:

Using the 28 rats, 90-minute temporary middle cerebral artery occlusion has been done by using intraluminal suture technique. Following the recanalization the process was terminated for the control group. In the other groups, serum physiologic infusion via internal carotid artery was done in temperatures of 15ºC, 23ºC and 37ºC consecutively. During the study early deaths were observed in the group which 15ºC saline infusion was done therefore, this pillar of the study was terminated. Other groups were compared in terms of infarct volume and neurological outcome after 24 hours.

Results:

In both groups which saline infusion was administered (23 and 37 ºC) shrinkage was identified in infarct volumes compared to the control group (p=0,012). There was no difference in total cortical and subcortical infarct volumes between the groups subject to saline infusion. In terms of cortical infarct volume 23ºC group has shown a meaningful shrinkage compared to the control group (p=0,011) whereas 37-ºC group did not have meaningful shrinkage compared to the control and had only a tendency of difference (p=0,063). In comparison of neurological score, the score of the group infused with 23ºC saline was better compared to the other groups (p=0,010).

Conclusion:

During the reperfusion shrinkage in infarct volume was attained by the help of saline infusion and the impact is more evident paired with cold administration. Additionally, the neurological scores of cold administered subjects are better.

Key Words:

Cerebral ischemia, Infarct, Hypothermia, Reperfusion damage

GİRİŞ ve AMAÇ

İskemik inme ciddi ve önlenebilir bir toplumsal sağlık sorunudur. Koruyucu hekimlik uygulamaları, risk faktörlerinin tedavisi ile görülme sıklığı azaltılabilir (1). İskemik inme geçiren hastada intravenöz tromboliz ve/veya mekanik trombektomi ile iyi sonuçlar elde edilmektedir (2-7). Trombüse yönelik tedavilerde tedavinin tipine göre belirlenen, hasta ya da görüntüleme özelliklerine göre de değişebilen süre sınırlamaları vardır (2,3,7-9). Bu sınırlama günlerle değil, saat, hatta dakikalarla ölçülmektedir.

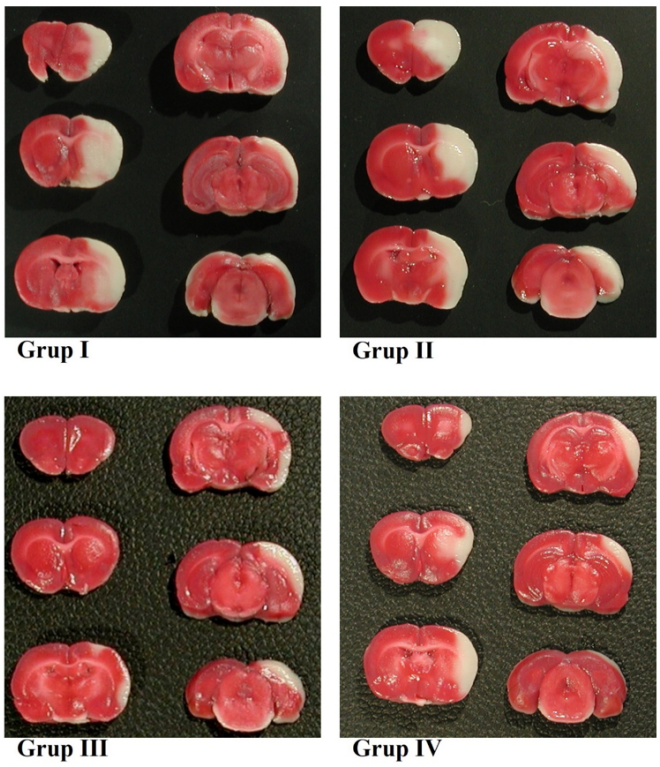
İskemik inmenin tedavisinde diğer bir alan da nöroproteksiyondur. Nöroproteksiyon iskemi direncini arttırarak zaman kazanma ve ortaya çıkan serbest oksijen radikalleri, adezyon molekülleri ve inflamasyonu azaltmayı ve apopitozu engellemeyi hedef almaktadır. Ayrıca tüm bu süreçleri tetikleyen reperfüzyon hasarından korunmak da önemlidir. Özellikle trombüse yönelik tedavideki gelişmeler, reperfüzyona bağlı olabilecek nöronal hasarın önlenmesini gerekli kılmaktadır. İskemik beynin reperfüzyonunun, yaygın hücre hasarı ve ölümüne yol açtığı bilinmektedir (10,11). İskemide sitokin üretimi ve moleküler adeziv olaylar erken dönemde oluşur ve arkasından gelişen reperfüzyon sırasında lökosit göçü inflamatuar cevabı arttırır (12-15). Nöroproteksiyonu hedefleyen farklı farmakolojik ajanlarla gerçekleştirilen preklinik çalışmalar, henüz klinik kullanılabilecek bir ilaçla sonuçlanmamıştır. Vücut ısısının düşürülerek inflamatuar cevabın azaltılması ve nöron metabolizmasının yavaşlatılması doku hasarını azaltabilir. Hayvan çalışmalarında beyin ısısının hafif ya da orta derecede düşürülmesiyle hem iskemik hem de travmatik hasarın azaldığı gösterilmiştir (14,16-19). Kardiyak arrest sonrası hipotermi uygulamasının nörolojik sonlanıma faydası gösterilmiş, fakat iskemik inmede tüm vücut soğutması şeklinde hipotermi uygulamasının faydası gösterilememiştir (20-24). Tedavi edici hipotermi için tüm vücut soğutması sık çalışılmıştır, bununla birlikte lokal uygulama açısından bilgiler sınırlıdır (17-19,25). Günümüzde akut inmenin intraarteriyel tedavisinde giderek artan gelişmeler lokal soğuk uygulamanın araştırılması için önem arz etmektedir (26-28).

Bu çalışmada deneysel, geçici serebral iskemi modelinde, iskemik dallara soğuk serum fizyolojik enjeksiyonu ile lokal olarak sağlanacak beyin ısısındaki düşüşün infarkt alanına ve klinik sonlanıma etkisini göstermeyi amaçladık.

GEREÇ ve YÖNTEMLER

Çalışmamızda yetişkin, 260-330 gr ağırlığında, 28 adet rat kullanıldı. Hayvanlar Akdeniz Üniversitesi hayvan laboratuvarından temin edildi ve çalışma "Guide for the Care and Use of Laboratory Animals" ilkelerine, ilgili tüm ulusal düzenlemelere ve kurumsal politikalara uygun şekilde yürütülmüş olup, Akdeniz Üniversitesi Hayvan Etik Kurulu tarafından onaylanmıştır (Karar No: E-74568308-020-479190). Ratlar rastgele dört gruba ayrıldı. Anestezi, kloral hidratın serum fizyolojik ile hazırlanan çözeltisinin intraperitoneal olarak, 400 mg/kg dozunda uygulanması ile elde edildi. İdame dozlarda ise 100 mg/kg dozdan intraperitoneal enjeksiyonlar yapıldı. Vücut ısısı, sirkulatuar ısı battaniyesi (Harvard apparatus. Hemaothermic blanket control unit) ve masa lambası ile rektal ısı 36-37ºC olacak şekilde ayarlandı. Rektal ısı takibine cerrahi işlem öncesinde başlandı ve prosedür bittikten sonraki 20. dakikaya kadar devam edildi (Electromedics inc. Dual display thermometer). Cerrahi öncesinde sağ femoral arterden kanülasyonla (Braun Introcan-W 24G) sürekli arteriyel basınç monitörizasyonu (Astro-med. Inc Grass Instrument division) yapıldı. Bu şekilde cerrahi ve tedavi uygulandığı sırada arteriyel basınçlar kaydedildi (polyVIEW Reviewer). Kanülasyon alanından elde edilen arteriyel kanla, iskemi gerçekleştirildiği anda ve iskeminin birinci saatinde arteriyel kan gazları çalışıldı (Nova Biomedical. Stat profile M). Aynı örneklerden hema-

tokrit, kan glukoz ve elektrolit düzeyleri de bakılıp kaydedildi. Tüm gruplarda intralüminal sütür kullanılarak geçici orta serebral arter (OSA) oklüzyonu yapıldı. Fokal serebral iskemi (FSİ) ilk kez 1986'da Koizumi tarafından tanımlanan intralüminal sütür tekniği kullanılarak OSA'in dolaşımının kesilmesi ile gerçekleştirildi (29-31). OSA akımı kesildikten 90 dakika sonra sütür geri çekilerek rekanalizasyon sağlandı ve internal karotis arterden (İKA) ters akım görülerek teyit edildi. Rekanalizasyon sonrası kontrol grubunda (I. Grup) İKA bağlanıp hemostaz sağlandı. Diğer gruplarda ise sütürün geri çıkarılmasını takiben, aynı insizyon yerinden branül yerleştirilip İKA'e doğru ilerletildi ve FSİ'nin uygulandığı karotis sisteme, guruplara göre sırasıyla 15ºC (II. Grup), 23ºC (III. Grup) ve 37ºC (IV. Grup) ısıdaki serum fizyolojik, 2 ml/dakika hızla, toplam 6 ml olmak üzere enjekte edildi. Enjeksiyon sonrası branül geri çıkarıldı ve İKA bağlanarak hemostaz sağlandı.



Ortalama hacim değerleri standart sapma ile verilmiştir. Veriler Kruskal-Wallis test ile değerlendirildi. Gruplar arası farklılıklar Post Hoc testle analiz edildi. p<0,050 anlamlı fark olarak kabul edilip ' < ' ile 0,050-0,750 fark eğilimi olarak kabul edilip ' ≤ ' ile 0,750 den büyük değerlerde fark olmadığı kabul edilip ' = ' işareti ile gösterilmiştir.

Şekil 1. Kesitlerden çekilen fotoğraflara, her grup için birer örnek. İnfarkt alanları beyaz renkte görülüyor.

Nörolojik değerlendirme Menzies SA. ve arkadaşlarının geliştirdiği muayene skalasına göre FSİ başlangıcından sonraki 24. saatte yapıldı (31,32). Nörolojik derecelendirme skalası Tablo I'de özetlenmiştir.

Tablo I. Nörolojik durum derecelendirme skalası.

Nörolojik muayene bulgusu	Nörolojik skor
Defisit yok	0
Ön bacağı uzatmada yetersizlik	1
Ön bacağın çekmeye direncinin azalması	2
Kuyruktan çekmeye yanıt olarak sola dönme	3
Spontan dönme	4
Ölüm	5

Operasyondan sonra 24. saatte ratlar yüksek dozda kloral hidrat çözeltisi ile uyutulup, dekapite edildi. Beyinler koronal düzlemde, önden arkaya doğru 2 mm kalınlığında olacak şekilde altı kesite ayrıldı. Alınan kesitler 30 dakika boyunca, 37ºC'de, serum fizyolojikle hazırlanan %2'lik 2.3.5-trifeniltetrazolium klorid (TTC, Sigma) solüsyonunda bekletildi. İnfarkt alanının saptanmasında TTC hemotoksilen eozine benzer sonuç vermektedir (33). Boyama işlemi sonrasında kesitler %10'luk formalin solüsyonu (Merck) ile fikse edildi ve 24 saat bekletildikten sonra fotoğrafları çekildi. Fotoğraflardan bazı örnekler Şekil 1'de gösterilmiştir. Bu fotoğraflar kişisel bilgisayara yüklendikten sonra bir görüntü analiz programı kullanılarak (UTHSCSA Image Tool, Version 3.00) analiz edildi. Analiz sırasında her bir kesit için sağ, sol hemisfer alanları, infarkt alanı, kortikal ve subkortikal infarkt alan değerleri hesaplandı. Bu değerler kesit kalınlığı ile çarpılarak hacim değerleri elde edildi. İnfarkt hacmi koronal kesitlerde lezyon alanlarının toplam hacmi ile elde edildi. Düzeltilmiş infarkt hacmi ise, karşı hemisfer hacminden aynı taraf hemisferin etkilenmemiş hacminin çıkarılmasıyla hesaplandı. Bu iki metot arasındaki fark beyin ödemini dışlamak ve düzeltilmiş lezyon hacmini bulmaktır (34).
Düzeltilmiş infarkt hacmi = sol hemisfer hacmi - (sağ hemisfer hacmi- infarkt hacmi)

İstatistiksel Analiz

Elde edilen verilerin değerlendirilmesinde Kruskal-Wallis test kullanıldı. Post-Hoc Man Witney U test kullanılarak farkın hangi gruplardan kaynaklandığı incelendi. Tüm testlerde p<0,05 anlamlı değer olarak kabul edildi.
Grup II (15ºC salin infüzyon grubu) sonuçlarda tartışılacağı üzere analizden çıkarıldı ve tüm analizler grup I, III, IV den elde edilen veriler üzerinden gerçekleştirildi.

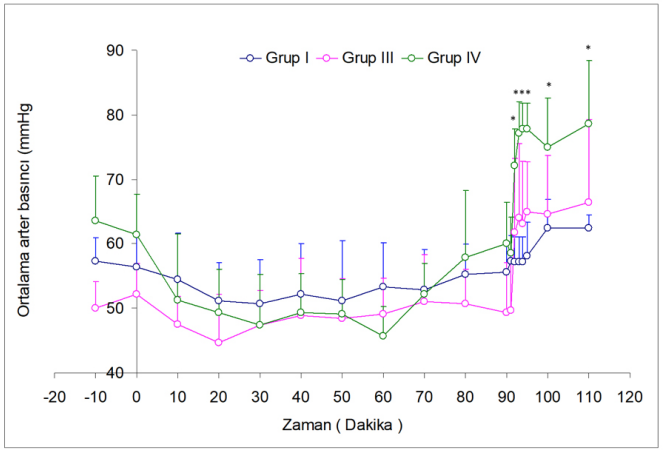
BULGULAR

Grup II'de (15ºC infüzyonu) çalışılan ilk dört ratta erken ölüm görüldü. İkisi işlem sonrası anestezi etkisi geçip bilinç açılmaya başlarken, epileptik nöbetler geçirmeye başladılar ve bilinçleri düzelmeden nöbet geçirerek altıncı ve on ikinci saatte öldüler. Diğer ikisinde benzer tarzda nöbeti oldu, fakat şiddeti ve süresi daha az olup arada bilincin açık olduğu dönemler mevcuttu. Bu ratların ölüm saatleri net belirlenememekle birlikte 24. saatte ölü olarak bulundular. Hepsinin beyinleri çıkartılarak incelendi ve tümünde OSA arter sulama alanında infarkt dışında bulgu yoktu. Dört ratta da benzer şekilde nöbetler ve erken ölüm olması kötü sonuç olarak değerlendirildi.

Çalışma bu grup için sonlandırıldı ve denek sayısındaki azlık nedeniyle grup değerlendirmeden çıkarıldı.

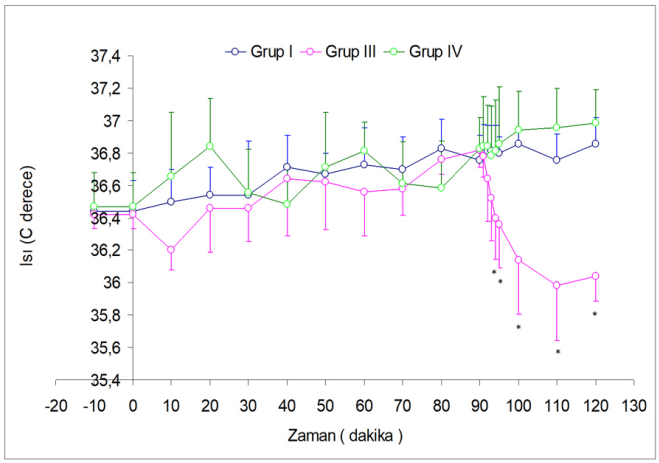
İnfarkt başlangıcında ve birinci saatin sonunda alınan arteriyel kandan çalışılan, pH, pO2, pCO2, HCO3 ve hematokrit (Htc) değerlerinin ortalamaları hesaplandı. Gruplar arasında hem başlangıç hem de birinci saat değerleri arasında fark yoktu.

Ölçülen ortalama arter basınçları karşılaştırıldı. Oklüzyon öncesi ve süresinde ortalama arter basınçları arasında fark yoktu. Bununla birlikte salin infüzyonu ile başlayan sonrasında da devam eden arteriyel basınç farkı bulundu. Salin infüzyonunun arteriyel basınç yükselmesine yol açması beklenen bir bulgudur. Ortalama arter basıncı ortalamaları ve standart sapma değerlerinin zaman içindeki değişimi Şekil 2'deki grafikte gösterilmiştir.



Şekil 2. İnfüzyon sonrası basınç artışları dikkati çekiyor, IV. gruptaki artış grup I ve III'e oranla daha fazla ve istatistiksel olarak anlamlı (*p<0,050).

Vücut ısıları karşılaştırıldı. Oklüzyon öncesi ve sonrasında gruplar arasında fark yoktu. Salin infüzyonu sonrasında üçüncü dakikada başlayan ve infüzyonun sonlanmasından sonraki 20. dakikaya kadar devam eden, gruplar arasında anlamlı ısı farkı saptandı (İnfüzyon sonrası üçüncü dakika p=0,016, 5-20. dakikalarda p=0,001). Post-Hoc değerlendirmede üçüncü dakikadaki fark, III. grubun I ve IV. gruplara göre farkından kaynaklanıyordu (III vs I p=0,008, III vs IV p=0,023). I ve IV. grup arasında ise anlamlı fark saptanmadı. Fokal hipotermi grubu diğerlerine göre istatistiksel olarak anlamlı şekilde soğutulmuş oldu. Isı düşüşü infüzyon sonrası 20. dakika da tekrar yükselme eğilimine girmiştir. Bu durum, düşük ısıdaki infüzyonun bitiminden sonra vücut ısısının tekrar regüle edilmeye başladığını düşündürür. Ortalama vücut ısı değerlerinin zamansal değişimi Şekil 3'te grafik üzerinde gösterilmiştir.



Şekil 3. İnfüzyon sonrası III. gruptaki ısı düşüşü dikkat çekmektedir ve infüzyonun 3. dakikasından itibaren izlem sonuna kadar düşüş istatistiksel olarak anlamlıdır (*p<0,050).

Düzeltilmemiş ve düzeltilmiş infarkt hacimleri açısından gruplar karşılaştırıldığında toplam infarkt hacminde istatistiksel olarak anlamlı fark bulundu (Düzeltilmemiş p=0,007, düzeltilmiş p=0,012). Her iki toplam infarkt hacminin gruplar arasındaki farkı grup I'in toplam hacminin diğer iki gruba göre büyük olmasından kaynaklandı. Grup III ile IV arasında infarkt hacimleri arasında fark olmakla birlikte istatistiksel olarak anlamlı bulunmadı.

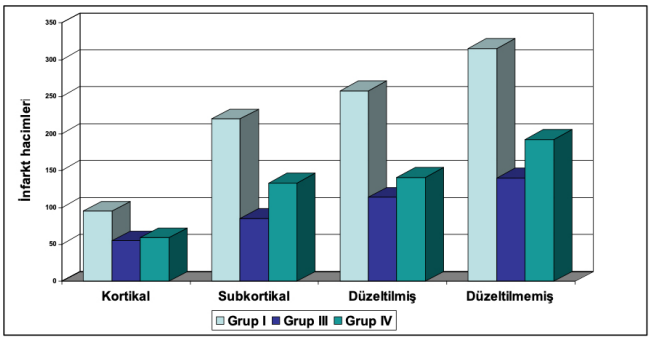
Gruplar kortikal ve subkortikal infarkt hacimleri açısından karşılaştırıldı. Kortikal infarkt hacmi için p=0,038, subkortikal infarkt hacmi için p=0,006 olarak bulundu. Post-Hoc değerlendirmede kortikal infarkt hacmi açısından, grup I'le III. gruplar birbirinden farklı bulundu ve I'le IV grup arasında fark eğilimi vardı fakat istatistiksel olarak anlamlı değildi (p=0,063). III ile IV. grup arasında ise istatistiksel anlamlı fark bulunmadı. Fark grup I'deki toplam kortikal infarkt hacminin III. gruptakinden büyük olmasından kaynaklanıyordu. Serum fizyolojiğin 23ºC olması, 37ºC olana göre toplam kortikal infarkt hacmini daha etkili bir şekilde azaltmıştır. İnfarkt hacim ortalamaları ve istatistiksel değerlendirme Tablo II'de özetlenmiştir ve Şekil 4'deki grafikte şematize edilmiştir.

Yirmi dördüncü saatte yapılan nörolojik muayene skorunda gruplar arasında fark bulundu (p=0,010). Bu fark III. grubun muayene bulgularının diğer iki gruba göre daha iyi olmasından kaynaklanıyordu. Grup IV'le I. grup arasında muayene skoru açısından fark saptanmadı. Bu sonuç nörolojik sonlanım açısından 23ºC salin verilmesinin, 37ºC saline göre daha iyi sonuç verdiğini göstermiştir (Tablo II).

Tablo II. Toplam infarkt hacimlerinin ve nörolojik muayene skorlarının gruplara dağılımı ve istatiksel değerlendirilmesi.

		GRUPLAR				
		I (n=7)	III (n=7)	IV (n=7)	p	Post-Hoc
TOPLAM İNFARKT HACİMLERİ	Kortikal mm^3	94,67± 21,94	55,72± 18,71	59,34± 34,78	**0,038**	I<III, I≤IV, III=IV
	Subkortikal mm^3	220,58± 48,98	85,20± 26,17	133,29± 81,14	**0,006**	I<III, I<IV, III=IV
	Düzeltilmiş mm^3	258,48± 74,68	114,15± 31,21	141,97± 88,92	**0,012**	I<III, I<IV, III=IV
	Düzeltilmemiş mm^3	315,26± 69,41	140,93± 39,80	192,63± 115,13	**0,007**	I<III, I<IV, III=IV
	NÖROLOJİK SKOR	3,7± 0,4	2,2± 0,7	3± 0,8	**0,010**	I<III, I=IV, III=IV

Ortalama hacim değerleri standart sapma ile verilmiştir. Veriler Kruskal-Wallis test ile değerlendirildi. Gruplar arası farklılıklar Post Hoc testle analiz edildi. p<0,050 anlamlı fark olarak kabul edilip ' < ' ile 0,050-0,750 fark eğilimi olarak kabul edilip ' ≤ ' ile 0,750 den büyük değerlerde fark olmadığı kabul edilip ' = ' işareti ile gösterilmiştir.



Şekil 4. İnfarkt hacminin gruplara dağılımını gösteren grafik.

Sonuç olarak geçici FSİ'de iskemik dallara serum fizyolojik infüzyonu infarkt hacmini azaltmaktadır ve serum fizyolojik ısısı 23ºC olursa kortikal infarkt hacmi azalması daha belirgindir. Benzer şekilde düşük ısıda verilen serum fizyolojik nörolojik sonlanım içinde iyi sonuç vermiştir.

TARTIŞMA

Bu çalışmada; deneysel olarak oluşturulan geçici FSİ sonrası, iskemik dallara uygulanan salin tedavisi ile infarkt hacminde küçülme ve daha iyi bir nörolojik sonlanım sağladık. Daha düşük derecede (23ºC) salin verilen grupta kortikal infarkt hacmindeki küçülme ve nörolojik durum 37ºC'lik gruba göre daha iyiydi. Toplam düzeltilmiş infarkt hacminde, 37ºC'lik grupta %46'lık bir azalma varken, 23ºC'lik grupta %66'lık bir azalma sağlandı. Elde edilen bu bulgular literatürle benzerlik göstermektedir (22,23,35).

OSA oklüzyonu sonrası serebral infarkt alanında inflamasyonun olduğu birçok çalışma ile gösterilmiştir. Başlangıçta sitokinlerin salınımı iskemiyi tetikler, inflamatuar mediatörlerin artışı reperfüzyon sırasında kan kaynaklı inflamatuar hücre adezyon ve infiltrasyonuna katkıda bulunur. Sonuç olarak lökositler; iskemi sonrasında, reperfüzyon sırasında fiziksel olarak kapillerin tıkanması ve beyin parankimine geçtikten sonra sitotoksik ürünlerin salınımı ile nöron hasarını arttırırlar (13,14,18,35). İnfarkt alanındaki azalma sıvı infüzyonunu ve hipotermi nedeniyle inflamatuar hücre, sitokinlerdeki dilüsyon ve mikrosirkülasyondaki düzelme ile ilgili olabilir, fakat kesin bir şey söylenemez. Çalışmamız özgül olarak nedeni belirlemekten ziyade tüm patofizyolojik sürecin bir sonucunu yansıtmaktadır.

Serebral iskemide iskemi sonrasında uygulanan hipoterminin nöroprotektif etkisi genel olarak global serebral iskemi modellerinde çalışılmıştır. Ratlarda global iskemi sonrası 5. ve 30. dakikada başlayan hipoterminin nöropatolojiye etkisi araştırılmıştır. Olay sonrası 5. dakikada başlayan soğutma ile hipokampal CA1 nöronlarında %50 korunma saptanmış, fakat 30. dakikada başlayan hipotermide koruyuculuk bulunmamıştır (36). Başka bir çalışma da ise hipotermi uygulanan hayvanlar üçüncü, yedinci günlerde ve iki ay sonra incelendi. Üç gün yaşatılan hayvanların CA1 bölgesindeki nöronlarda anlamlı korunma görülürken, yedi gün yaşatılanlarda korunma azalmış ve iki ayın sonunda ise kaybolmuştur (37). Global serebral iskeminin yaygın nedenlerinden olan kardiyak arrest ve canlandırma sırasında ve sonrasında gelişebilecek hasarın önlenmesi açısından uygulanan global hipoterminin faydası gösterilmiş ve önerilen bir tedavidir (21). Beyin dolaşımının fokal kesildiği iskemik inme benzeri durumlarda ise global hipotermi uygulaması arrest sonrası uygulama gibi etkili bulunamamıştır (20,22,38).

FSİ modellerinde selektif beyin ısısını düşürmeye yönelik çalışmalar az sayıdadır. FSİ'de tüm vücuda uygulanan hipotermik tedavinin tedavi etkinliği iskeminin başlangıcında başlatılan ve birkaç saat devam eden geçici iskemi modellerinde gösterilmiştir (39-41). Kalıcı vasküler oklüzyon modelleri hipotermik nöroproteksiyona daha dirençlidir, fakat iskemi sonrası derin soğutmalı modellerde infarkt hacminde azalma bildirilmiştir (41). Bir çalışmada, proksimal OSA klips oklüzyonu ile iki saatlik geçici FSİ oluşturulan ratlarda, beyin ısısı 30ºC'ye düşürüldü ve anlamlı nöroproteksiyon saptandı. İskemi sırasında soğutma ile kortikal infarkt hacminde %70, striatal infarkt hacminde ise %50 azalma bulundu (42). Başka bir çalışmada geçici iskemi 1,5, 2, 2,5 saatlerde iken yapılan lokal soğuk salin uygulaması infarkt alanında anlamlı azalmaya yol açarken daha geç saatlerde anlamlı bir kortikal infarkt alanı azalmasına yol açmamıştır (19). Bizim çalışmamızda da 1,5 saatlik geçici iskemi sonrası hipotermi uygulanan grupta kortikal infarkt hacminde benzer şekilde küçülme saptandı ve bu istatistiksel olarak anlamlıydı.

SONUÇ

Bu modelle geçici FSİ oluşturulan alana reperfüzyon sırasında salin infüzyonu ile infarkt hacminde azalma sağlanmıştır ve bu etki soğuk uygulama ile birlikte daha belirgindir. Lokal soğuk uygulamanın günümüzde giderek artan ve standart tedavilerden biri olan trombüse yönelik intraarteriyel girişimlerle kombine edilmesi düşünülebilir ve buna yönelik cihaz geliştirme, klinik çalışmalara ihtiyaç vardır.

Etik Komite Onayı:
Bu araştırma, ilgili tüm ulusal düzenlemelere, kurumsal politikalara ve "Deney ve Diğer Bilimsel Amaçlı Kullanılan Hayvanların Korunmasına İlişkin Konsey Direktiflerine" ve "Guide for the Care and Use of Laboratory Animals" ilkelerine uygundur ve Akdeniz Üniversitesi Hayvan Etik Kurulu tarafından onaylanmıştır (Karar No: E-74568308-020-479190).

Yazar Katkıları:
Fikir - A.Ü., MZ.Ö.; Tasarım – A.Ü.; Denetleme – MZ.Ü; Kaynaklar – A.Ü.; Modelin uygulanması – A.Ü.; Veri Toplanması ve/veya İşlemesi - A.Ü.; Analiz ve/veya Yorum - A.Ü., MZ.Ö.; Literatür Taraması - Yazıyı Yazan - A.Ü.;

Çıkar Çatışması:
Yazarların beyan edecek çıkar çatışması yoktur.

Finansal Destek:
Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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ORIGINAL ARTICLE
Özgün Araştırma

The Habits of Using Painkiller In Adult Inpatients With Burn Injury

Yanık Yaralanması Olan, Hastaneye Yatırılan Erişkin Hastalarda Ağrı Kesici Kullanma Alışkanlıkları

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Geliş Tarihi : 23 July 2023
Received
Kabul Tarihi : 04 August 2023
Accepted
E Yayın Tarihi : 01 September 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Tapan M, Ayaz T, Kece I, Cengiz M, Ozkan O, Ozkan O.
The Habits of Using Painkiller In Adult InpatientsWith Burn Injury
Akd Med J 2023; 9(3): 325-330

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ABSTRACT

Objective:
Modern burn care is dependent on the effective management of burn pain. Although opioids remain the cornerstone of treatment, their adverse effects remain serious. In this study, we investigated non-opioid painkillers, including acetaminophen and dexketoprofen, which are commonly used in the clinical practice for adult burn inpatients who do not require admission to an intensive care unit.

Methods:
Thirteen consecutive inpatients with burns were included in this study. During the six-day period, the patients self-administered painkillers as needed. The time of medication intake was recorded, and a visual analog scale was used to assess pain. Thereafter, statistical analyses were performed.

Results:
No significant differences were observed between age and sex groups. As the percentage of burns increased, the number of painkillers used also increased. It was found that the patients took painkillers most frequently at 11 o'clock (when the wound dressing was changed) and least frequently at 14 o'clock. No significant difference was observed between the effects of dexketoprofen and paracetamol in reducing pain.

Conclusions:
The need for painkillers in patients with burns varies throughout the day. The effectiveness of acetaminophen and dexketoprofen during the day was higher than that during dressing changes. The total body surface area should be considered with regards to the amount and frequency of painkiller administered.

Key Words:
Acetaminophen, Adult inpatient with burn, Burn injury, Dexketoprofen, Painkiller

DOI: 10.53394/akd.1333575

ÖZ

Amaç:

Modern yanık bakımı, yanık ağrısının etkili yönetimine bağlıdır. Opioidler tedavinin temel taşı olmaya devam etse de, yan etkileri ciddiyetini koruyor. Bu çalışmada, yoğun bakım ünitesine yatış gerektirmeyen erişkin yanık hastalarında klinik uygulamada yaygın olarak kullanılan asetaminofen ve deksketoprofen gibi opioid olmayan ağrı kesicileri araştırdık.

Yöntemler:

Bu çalışmaya ardışık 13 yanıklı yatan hasta dahil edildi. Altı günlük süre boyunca, hastalar gerektiği kadar ağrı kesici kullandılar. İlaç alma zamanı kaydedildi ve ağrıyı değerlendirmek için "visual analog scale" kullanıldı. Daha sonra istatistiksel analizler yapıldı.

Bulgular:

Yaş ve cinsiyet grupları arasında anlamlı bir fark gözlenmedi. Yanık yüzdesi arttıkça kullanılan ağrı kesici sayısı da arttı. Hastaların ağrı kesici ilaçlarını en sık saat 11:00'de (pansuman değiştirilirken), en az saat 14:00'te aldıkları saptandı. Ağrıyı azaltmada deksketoprofen ve asetominofen etkileri arasında anlamlı bir fark gözlenmedi.

Sonuç:

Yanık hastalarında ağrı kesici ihtiyacı gün boyunca değişkenlik gösterir. Asetominofen ve deksketoprofen'in gün içindeki etkinliği pansuman değişimlerine göre daha yüksekti. Uygulanan ağrı kesici miktarı ve sıklığı ile ilgili olarak toplam vücut yüzey alanı dikkate alınmalıdır.

Anahtar Kelimeler:

Asetominofen, Erişkin hastaneye yatırılan yanık hastası, Yanık yaralanması, Deksketoprofen, Ağrı Kesici

INTRODUCTION

Modern burn care is fundamentally dependent on the effective management of burn pain. However, pain management in patients with burn injuries is complex. Opioids are the cornerstone of treatment, especially in the acute stage of burn, pain and are the most effective drugs for the management of moderate-to-severe perioperative pain. However, opioid use is associated with serious adverse effects. The Center for Disease Control have released guidelines encouraging the use of opioid-sparing therapies for acute pain management (1-4).

Patients with burns may experience extreme pain due to injuries, mobilization, wound care, and surgery. Burn injuries cause two types of pain: Evoked (procedural) and background pain. Background pain is less intense but is constant. Burn injury pain is typically categorized temporally, first as pain during the acute phase and then as pain during the chronic phase, when the majority of tissue healing has taken place (5).
In this study, we investigated the non-opioid painkiller habits of adult inpatients with burns who did not require admission to an intensive care unit. The primary aims of this single center study were to: 1) Determine the painkiller need of the patients according to sex, age, and total burn surface area; 2) Determine the effect of acetaminophen versus dexketoprofen; 3) Determine the efficacy of the drugs during wound dressing and daily activity in the hospital; and 4) Determine the painkiller habits of patients before and after surgery.

MATERIAL and METHODS

This study was conducted between July 2022 and November 2022. The study was planned as a cross-sectional type and ethical approval was obtained from the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (20.07.2022 KAEK-439). The study was carried out in accordance with the Research and Publication Ethics and the Principles of the Declaration of Helsinki; Permission was obtained from the relevant institutions where the study would be conducted, and consent was obtained by explaining the purpose and scope of the study to the participants.

Thirteen consecutive patients were included in this study. The inclusion criteria were: 1) Patients ≥ 18 years; 2) not requiring admission to an intensive care unit; 3) Partial thickness burn injury between 10 and 30 % total body surface area; 4) Burns that involve the face, hands, perineum, genitalia, feet, or major joints; 5) Full thickness burns; 6) Patients only used painkillers when they experienced pain: 7) the pain killers used were acetaminophen or dexketoprofen which are commonly used in Turkey; and 8) At least 6 d hospital stay. Painkillers were randomly selected when required. The need for painkillers was recorded according to the length and hours of hospital stay. The wound dressing was always changed at 11 o'clock and on the day of the operation, there was no wound dressing at the service. For standardization, wound dressing and surgery were performed simultaneously (11 o'clock). Patients underwent surgery only once on the fourth or fifth day of the six-day period. Opioids are routinely used in these operations. Children with burns and adult patients with a history of burn admissions, polytrauma, or inhalation injuries were excluded.

A visual analog scale from 0 to 10 was used to assess the patient's pain scores when they experienced pain 30 min after medication administration. The reason for the 30-minute wait period was the intersection time of both maximum plasma concentration levels after the administration of the two drugs. Acetaminophen reached its maximum plasma concentration after 20–90 min after administration, and dexketoprofen reached its maximum concentration at 15–45 min after administration (6,7).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22 (IBM Corp., Armonk, NY, USA). Conformity of the data to normal distribution was evaluated using visual (probability and histogram graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The data distribution was nonparametric. Therefore, descriptive statistics are presented as medians (minimum-maximum). The Wilcoxon test was used to compare data from the same patients. The

Mann-Whitney U test was used to compare the data from different patients. The Spearman correlation test was used to determine whether there was a significant relationship between patient age and the number of painkillers used. The statistical significance was set at $p<0.05$ in all analyses.

RESULTS

Patients were aged between 18 and 70 years. Ten male and three female patients were included in this study. Patient characteristics are listed in Table I.

Table I. Patient characteristics

	Gender	Age	Etiology	Affected Region	Total burn surface area (%)
Patient 1	M	51	Flame	Right Forearm, Right Lumbar Region	15
Patient 2	M	34	Flame	Both Sides Forearm, Both Sides Thigh	15
Patient 3	M	48	Electric	Both Sides Palm, Left Foot	2
Patient 4	M	25	Electric	Left Foot	5
Patient 5	M	34	Electric	Head, Right Arm, Right Hand	8
Patient 6	F	20	Hot water	Both Sides Hand, Trunk, Both Sides Thigh	18
Patient 7	M	54	Thermal contact	Both Sides Leg, Both Sides Foot	8
Patient 8	M	70	Flame	Head, Neck, Left Arm	9
Patient 9	M	32	Flame	Both Sides Arm, Both Sides Hand	12
Patient 10	F	46	Hot water	Neck, Both Sides Arm	10
Patient 11	M	30	Flame	Head, Neck, Trunk, Left Arm, Right Foot	30
Patient 12	F	29	Hot water	Head, Trunk, Left Arm, Left Thigh	15
Patient 13	M	18	Hot water	Head, Neck, Right Arm	10

While no significant relationship was found between age and the number of painkillers used, there was a significant positive relationship between the percentage of burns and the number of painkillers used. As the percentage of burns increased, the number of painkillers used also increased ($r= 0.569$, $P =0.042$) (Table II).

Table II. Correlation of age and burn percentage with the amount of pain killer used. r: Correlation coefficient, p: Significance value, data showing significant correlations are marked in bold

		Pain Killer Quantity
Age	*r*	0,22
	p	0,47
Total Burn Surface Area	*r*	**0,569**
	p	**0,042**

It was found that patients took painkillers most frequently at 11 o'clock and least frequently at 2 pm (Table III).

Table III. The times at which each patient took painkillers during the 6 days.

	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
Patient 1	0	1	0	3	0	0	0	1	1	0	1	0	0	1	0	3	0	11
Patient 2	0	0	1	4	0	0	0	0	0	0	1	1	0	0	1	1	2	11
Patient 3	0	1	0	0	0	0	0	0	0	0	1	0	0	0	1	0	2	5
Patient 4	0	0	0	0	1	0	0	0	0	0	0	0	0	0	4	0	1	6
Patient 5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Patient 6	0	0	0	0	2	0	0	0	0	0	1	0	0	0	1	0	0	4
Patient 7	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	2
Patient 8	0	0	0	5	0	0	0	0	1	0	3	0	0	0	4	0	1	14
Patient 9	0	0	1	0	1	1	0	0	0	0	1	1	0	0	0	0	0	5
Patient 10	0	0	0	0	1	0	0	1	1	0	1	0	0	0	1	1	1	7
Patient 11	2	0	1	2	2	0	0	1	1	0	0	0	1	1	1	0	3	15
Patient 12	0	1	1	3	0	0	0	0	1	0	1	0	0	1	2	0	0	10
Patient 13	1	0	1	2	0	0	0	0	0	1	0	0	0	0	2	0	0	7
toplam	3	4	5	19	7	2	0	3	5	1	10	2	1	3	18	5	10	

When the total scores of female and male patients were compared, no significant differences were found (p=0.675). There was no significant difference between the painkiller habits of women after wound dressing, that is, at 11 o'clock, and men's habits of taking painkillers at 11 o'clock (p=0.692).

Taking pain killers at 11 o'clock was found to be significantly more frequent than that at 8, 9, 10, 13, 14, 15, 16, 17, 19, 20, 21, and 23 h. ($p<0.05$).

The number of analgesics administered before surgery (47) was found to be significantly lower than the number of painkillers administered after surgery (total 51) (p=0.027).

There was no significant difference between the number of painkillers used before (n = 10) and after surgery (n = 9) during wound dressing (p=0.098).

The reducing effect (52.55% reduction) of the pain killer given to the patients after dressing or surgery was found to be significantly lower than the reducing effect (60% reduction) of the pain killer given due to daytime pain ($p<0.001$).

There was no significant difference between the effect of dexketoprofen in reducing pain (58.37% reduction) and that of paracetamol (58.08% reduction) (p=0.372).

DISCUSSION

According to one study, parents of the patients with burn injuries tended to give painkillers as scheduled (8). This tendency may sometimes cause overtreatment of patients. However, burn mass-casualty incidents, such as explosions, accidents, and terror attacks, can occur at any time. When such incidents occur, burn centers can be better prepared by determining the required amount of analgesics (9). Our study design was based mainly on these hypotheses in adults. In this study, the patients were administered medication when needed.

Opioids, the cornerstone of treatment for burn injuries, can cause many side effects. Studies have shown that up to 92% of people who use opioids to treat acute pain experience adverse effects. At least one side effect is experienced by patients, and two or more side effects are experienced by 76% of patients (10). Patients should regularly review their pain with careful dose escalation to improve analgesic results and reduce the risk of side effects of opioids. This is crucial in the acute phase of an injury and in the first few days after surgery. Acetaminophen and nonsteroidal anti-inflammatory drugs are extensively used painkillers, that are considered much safer than opioids. As a result of their ability to work in conjunction with opioids, their use can reduce the quantity of opioids required by up to 20% to 30% (11). In our study, we used opioids only during the intraoperative period. Therefore, we aimed to avoid the adverse effects of opioids.

Burn center referral criteria are well defined (12). Our patients were selected based on this guideline, excluding patients who would not require admission to the intensive care unit. The operating dynamics of the intensive care unit differ from those of inpatients in the clinic.

This study was conducted without pediatric burns. Adequate pain control is very important in the pediatric burn population, and verbalizing complaints is lacking (8).

No significant difference was found between female and male patients in terms of pain scores or the need for painkillers during wound dressing. Age was also not a significant factor associated with the need for painkillers. However, the need for painkillers increased with an increase in the total burn surface area; this result is consistent with that of Laezar et al. (9).

According to our study, patients often felt the need for painkill-

ers at the time of wound dressing, while one of the times they needed painkillers the least was between 13 and 17 in the afternoon. Although our study showed that the need for painkillers increased after surgery, the need for painkillers during wound dressing did not.

According to a study on lower back pain, intravenous dexketoprofen, morphine, and acetaminophen are not superior to one another (13). In a dysmenorrhea study, dexketotoprofen was associated with a higher visual analog scale score, which was not clinically significant. (14). We found no statistically significant differences in visual analog scale changes between dexketoprofen and paracetamol in our burn inpatients. In addition, the efficacy of these painkillers during the day was higher than during dressing changes.

CONCLUSION

The need for painkillers in patients with burns varies throughout the day. The effectiveness of acetominophen and dexketoprofen during the day was higher than that during dressing changes. The patient's total body surface area should be considered when determining the amount and frequency of painkiller used.

Ethics Committee Approval:
This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Akdeniz Medical Faculty Ethical Committee, Akdeniz University (approval number: KAEK-439).

Informed Consent:
All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:
Concept –M. T.; Design – M. T. Supervision – Ö. Ö., Ö. Ö.; Resources – T. A., İ. K., M. C.; Materials -M. T., T. A., İ. K., M. C.; Data Collection and/or Processing – T. A., İ. K., M. C. Analysis and/ or Interpretation – M. T. Literature Search – M. T.; Writing Manuscript – M. T.; Critical Review – Ö. Ö., Ö. Ö.

Conflict of Interest:
The authors have no conflict of interest to declare.

Financial Disclosure:
The authors declared that this study has received no financial support.

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REVIEW
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Geliş Tarihi : April 27, 2022
Received
Kabul Tarihi : January 18, 2023
Accepted
E Yayın Tarihi : September 01, 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Sahin Z, Kalkan OF, Aktas O, Kalkan A.
Circadian Rhythm, Hypothalamo-Pituitary Adrenal Axis, and Immunity: Physiological and Pathological Examples
Akd Med J 2023; 9(3): 331-341

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DOI: 10.53394/akd.1110074

Circadian Rhythm, Hypothalamo-Pituitary Adrenal Axis, and Immunity: Physiological and Pathological Examples

Sirkadiyen Ritim, Hipotalamo-Hipofizer Adrenal Aks ve Bağışıklık: Fizyolojik ve Patolojik Örnekler

ABSTRACT
All living organisms, from single-celled microorganisms to humans, have to adapt to changing environmental conditions to maintain their survival processes. There are biological clocks in the body, which are related to the circadian rhythm and have a hierarchical organization. The master circadian clock is located in the suprachiasmatic nucleus (SCN) of hypothalamus. SCN maintain body rhythms in synchronous with the light-dark cycle in the external environment. There are also peripheral oscillators that work in coordination with SCN. Neurological, endocrinological, and immunological functions in the body are under the influence of circadian and seasonal rhythms. Melatonin and cortisol (corticosterone in animals) are among the most important hormones that show circadian rhythm in the body. The body adapts to daily and seasonal changes with biological rhythms regulated by biological clocks. It is well known that the immune system is affected by the external environment. Changes in endocrine system, hypothalamo-pituitary adrenal (HPA) axis, and immune system are marked, especially depending on the seasonal changes. Therefore, the immune system has close relationship with the circadian rhythm. Understanding relationship between physiological regulation of the circadian rhythm, HPA axis and immune activity is important for to keep our body in healthy conditions and struggle with the diseases as well. In current review, the interaction and relationship of genes and proteins related to the circadian rhythm with HPA axis and immune system parameters are discussed with both physiological and pathological examples.

Key Words:
Circadian rhythm, Immune system, Hypothalamo-pituitary adrenal axis, Health, Disease

ÖZ
Tek hücreli mikroorganizmalardan insanlara kadar, canlılar değişen çevre koşullarına uyum sağlamak zorundadır. Sirkadiyen ritim bu adaptasyonla ilişkili en önemli mekanizmadır. Vücutta sirkadiyen ritimle ilişkili, hiyerarşik organizasyona sahip, biyolojik saatler bulunmaktadır. Master sirkadiyen saat, hipotalamusun suprakiyazmatik nükleusunda (SCN) yer almaktadır. SCN, vücut ritimlerini dış ortamdaki aydınlık-karanlık döngüsüyle senkronize halde tutar. Merkezi saat olan SCN ile koordineli çalışan, periferal osilatörler de mevcuttur. Vücutta nörolojik, endokrinolojik ve immünolojik fonksiyonlar sirkadiyen ve mevsimsel ritimlerin etkisi altındadır. Vücutta sirkadiyen ritim gösteren hormonların başında melatonin ve kortizol (hayvanlarda kortikosteron) gelmektedir. Vücut, günlük ve mevsimsel değişikliklere biyolojik saatleri vasıtasıyla düzenlenen biyolojik ritimlerle uyum sağlamaktadır.

Bağışıklık sisteminin dış çevreden etkilendiği iyi bilinmektedir. Özellikle mevsimsel değişikliklere bağlı olarak endokrin sistemde, hipotalamo-hipofizer adrenal aksta ve immün sistemde değişiklikler kendini belli etmektedir. Bununla birlikte immün sistem sirkadiyen ritimle de sıkı ilişkiye sahiptir. Sirkadiyen ritmin fizyolojik regülasyonu ve immün aktivite arasındaki ilişkinin anlaşılması sağlıklı yaşam ve hastalıklarla mücadele bakımından önem arz etmektedir. Yazımızda sirkadiyen ritimle ilişkili gen ve proteinlerin immün sistem parametreleri ile etkileşimi ve ilişkisi güncel fizyolojik ve patolojik örneklerle ele alınmaktadır.

Anahtar Sözcükler:
Sirkadiyen ritim, İmmün sistem, Hipotalamo-hipofizer adrenal aks, Sağlık, Hastalık

INTRODUCTION

All living organisms, including humans have very close relationships with their environment. Since environmental conditions are dynamic factors, they constantly affect the body functions. Some events on the Earth occur cyclically such as day and night or they occur seasonally. Therefore, every organism must act in harmony with the environment in which they live. This is an indispensable condition for maintaining homeostasis and acquiring adaptation skills. There are specialized cell groups in the body that detect cyclical changes with the external environment and provide appropriate harmony. The most important regulator of this harmony is the suprachiasmatic nucleus (SCN), located in the hypothalamus. The SCN is to ensure the coordination of circadian rhythms in the body. This function of the SCN is supported by other circadian oscillators from the peripheral sections of the body. The circadian rhythm data is presented to the brain by the SCN. The brain, which is the control center of the body, communicates with all body cells with endocrine factors. This process is called neuroendocrine activity and it enables the body to act as a whole. Another factor with which the endocrine system interacts is the immune system. Thus, the integration of nervous stimuli with endocrine and immunological activity is ensured. This integration is known as the neuro-immunoendocrine system. Some hormones have special importance in the functionality of the neuro-immunoendocrine activity and its harmony with the circadian rhythm. Among the most important of these endocrine factors are melatonin produced from the pineal gland and glucocorticoids (cortisol in humans, corticosterone in animals) secreted from the adrenal gland. The hypothalamo-pituitary adrenal (HPA) axis must be activated in order to release cortisol from the adrenal gland. It is known that HPA axis activity has a circadian rhythm. However, the HPA axis might be activated by acute or chronic stress as well. Changes in HPA axis activity affect the immune system. In our review, important factors related to this interaction are discussed. Moreover, the effects of the circadian rhythm on the immune system physiology, as well as the pathophysiological conditions are discussed with current data.

CIRCADIAN RHYTHM

The concept of circadian rhythm was first defined by Franz Halberg using the Latin words “circa” (about) and “diem” (day) (1). Since then, this concept has been used to describe the cyclical, physiological, and behavioral effects of the light and dark cycle on the organism caused by the 24-hour rotation of the earth revolving around the sun on its axis. Such internal rhythms are valid in organisms from photosynthetic prokaryotes to mammals depending on the presence of endogenous circadian clocks, which regulate behavioral and physiological processes with their functions of adapting and coordinating the internal environment with external cues (2, 3). Thus, the organism can predict periodic changes to adapt to changing conditions and regulate its functions according to the time of day using circadian rhythms. The oscillators associated with the circadian rhythm consist of two main interrelated parts: the primary structure of these systems is the central clock located in the SCN of the hypothalamus and the others are peripheral clocks distributed throughout the body (4). The maintenance of circadian rhythms, formed by the alignment of internal circadian oscillators to external stimuli, relies on external cues such as light pattern, temperature, and food intake. The primary external synchronizer of circadian rhythms consists mainly of the daily light-dark cycle. In mammals, signals generated by light contact with the eyes are transmitted to the SCN via the retino-hypothalamic pathway. Thus, the SCN, a master oscillator, primarily uses the light-dark cycle to synchronize the body with the light signal (5). In order to maintain homeostasis, the circadian rhythms formed on the basis of the sleep-wake cycle must not be disturbed. In the coordination of the SCN, with the participation of peripheral oscillators, many physiological functions such as endocrine activity, immune activity, digestive system, body temperature, and blood pressure regulation, as well as psychophysiological functions such as sleep-wake, emotional state, learning-memory, feeding behavior are maintained in harmony (4, 6).

MOLECULAR PHYSIOLOGY OF THE CIRCADIAN RHYTHM

The mammalian circadian clock is a complex structure formed by a combination of feedback-feedforward mechanisms. In particular, transcription of BMAL1 (brain and muscle Arnt-like protein 1 (also called as ARNTL) and CLOCK (circadian locomotor output cycles kaput) genes, or its related gene NPAS2 (neuronal PAS domain-containing protein-2), leads to the heterodimerization in cytoplasm of the BMAL1 and CLOCK complex, which translocate into the nucleus where it binds to E-Boxes of clock-regulated genes (7). Clock genes and clock-related genes have a triple helix-loop-helix structure. The transcription factors are Clock, Bmal1, three Period genes Per1, Per2, and Per3, two Cryptochrome genes Cry1 and Cry2, three orphan nuclear receptors Nr1d1 (nuclear receptor family subclass group 1, member 1), Rev-Erb-α and Ror (retinoic acid-associated orphan nuclear receptors)-α. Transcription factors are thought to provide circadian regulation of gene expression (8) (Figure 1).

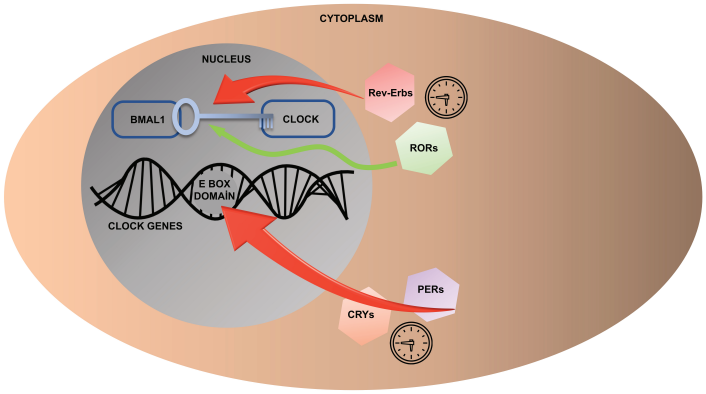

Figure 1. Schematic of BMAL1/CLOCK gene transcription and feedback mechanisms. (Modified from Ref. 8).

The transcriptional feedback pattern of circadian rhythm in mammals is mediated by the proteins Cry1, Cry2, and Per1, Per2. Clock and Bmal1 bind to the E-promoter region on the Per and Cry genes, inducing the expression of these genes. Per and Cry then heterodimerize and pass from the nucleus to the cytoplasm, inhibiting the gene expression induced by Clock/Bmal1 (9). Phosphorylation of related proteins occurs by casein kinases (CK1 ε and CK1δ) targeting Per proteins and adenosine monophosphate kinases (AMP kinase) targeting Cry proteins. In the following process, phosphorylated proteins are degraded by the ubiquitin ligase complex (10). With the breakdown of the Per/Cry complex, the cycle starts again. Besides the Per and Cry genes, BMAL1/CLOCK also activates the transcription of the Rev-Erb-α and Ror-α. This activation is inhibited by Rev-Erb-α, which binds to the retinoic acid-associated orphan nuclear receptor element of Bmal1, while it is activated by Ror-α (11). Other genes controlled by the circadian clock can also be regulated by the molecular clock since they contain an E-box in their promoter region (9). Regulation of clock genes with nuclear receptors such as Rev-Erb-α, Ror-α, and PPAR-α provides rhythmic realization of many hormones, nutritional signals (fatty acids and derivatives), and cellular redox status (12).

MASTER CLOCK SCN AND ITS LIGHT-MODIFIED CYTOKINE ACTIVITY

It is known that light is the most important zeitgeber. The melanopsin photopigments in the retina are activated by light stimuli, and this stimulation sets the internal clock's timer (13). The wheels begin to spin when the mainspring is wound, much like a mechanical clock. As a result, the clock spring is squeezed, activating the other component. While the interlocking gears continue to rotate exactly and the spring continues to discharge at the same rate, the spring starts to cycle down. When light stimuli reach the SCN in mammals, the primary wheel starts to turn. The central wheel attached to this circuitry is turned by the main circuit, which also causes the expression of the clock-related transcription factors BMAL1 and CLOCK. The clock-related Per and Cry genes' promoter region is located in this wheel. The second, minute, and hour circuits linked to the same vertical axis start spinning when the promoter is activated. Numerous clock-related genes are found throughout the body of mammals. One gear of the minute wheel is turned by one complete rotation of the second's wheel. A single gear on the clock wheel completes one full rotation of the minute hand gear. A 12-hour period is represented by one full rotation of the scorpion gear on the watch dial, while a 24-hour period is represented by two full revolutions (14, 15).

In mammals, SCN lesions cause sleep disturbance, and cause changes in melatonin production, primarily due to disruption of the circadian rhythm (16, 17). This situation affects many other body functions over time. The SCN network output has a sinusoidal pattern, but the relationship of this functioning to behavior varies depending on whether the organism has nocturnal or diurnal activity. In nocturnal animals such as rodents, the lowest level of SCN activity occurs in the active period, while in humans with diurnal rhythm, the peak in SCN activity occurs in the active period (18). A number of clock genes such as Per1 and Per2 in the SCN are light sensitive (19). It has been reported that dim light during the night affects the expression of per2 in the SCN of birds, leading to the loss of standard 24-hour cycles of Ror-α and Cry1 (20). In the same study, a decrease in interleukin (IL)-1β and Toll Like Receptor (TLR)-4 mRNA transcripts were also detected. In another study, it was determined that IL-1β and IL-10 levels were affected in birds exposed to dim light at night (21). The effect of clock gene changes on cytokine expression was also found to be valid in zebrafish (22). In the aforementioned study, it was determined that changes in Per1 and Per2 genes affect cytokine expression, and changes in per1b affect the neutrophil count. In a mammalian study of the photic effect of immunity, it was suggested that mice kept in constant-dark conditions showed a mortality rate three times higher than those in the normal light: dark cycle, but this was not associated with myeloid expression of BMAL-1 and CLOCK (23). Additionally, it was noted that when sepsis model mice with cecal ligation puncture were exposed to high-illumination blue light imitating early morning light, the rate of sepsis and organ damage decreased (24). The fact that other mammals have nocturnal rhythms like rodents and diurnal rhythms like humans is one of the most significant contrasts between them. The anti-phase expression of BMAL1 and Per2 in humans and mice is the most common illustration of this circumstance (25).

CIRCADIAN RHYTHM AND IMMUNE SYSTEM

It is known that the immune system, including innate and adaptive immunity, shows circadian variations (7). The first data on the relationship of the immune system with the circadian rhythm in humans date back to 75 years ago (26). In that study, it was reported that the amount of the circulating lymphocyte in healthy people showed variation during the day. An experimental animal study on the subject was carried out 60 years ago (27). In this study, in animals injected with endotoxin, toxin sensitivity was determined to be related to time-of-day. Recently, regulation of proinflammatory cytokine activity has attracted attention as one of the important links regarding the relationship between biological clocks and immune function. In macrophages stimulated by endotoxin, the increase in tumor necrosis factor (TNF)-α secretion may cause a change in the circadian rhythm depending on the endotoxin administration time (28). It is thought that there is a feedback mechanism between the formation of inflammation and the integration of the molecular

clock. Confirming this situation, BMAL1, CLOCK and Rev-Erb-α protein levels in cells decrease significantly after endotoxin injection, which is estimated to impair clock function (29-31). However, herpes virus infection induces BMAL1 promoter activity and results in a corresponding suppression of Cry1 and disruption in the feedback mechanism of the clock (32). All these data indicate that the circadian clock is affected in case of acute infection. However, the same is true for chronic infection as well. Significant changes occur in the immune system due to loss of function and mutations in genes associated with circadian rhythm (Table I).

Table I. Specific samples of altered adaptive immune phenotype in circadian mutant mice (Adapted from ref. 82)

Gene	Deletion	Adaptive immune phenotype	Ref.
Bmal1	Myeloid	Exacerbation of EAE symptoms	83
	CD4+ T cells	Loss of diurnal variation in EAE	84
Nr1d1	Global	Exacerbation of EAE symptoms	85
Ror-α$^{sg/sg}$	Global	Impaired Th17 cell development	28
Ror-γ	Global	Impaired Th17 cell development	36
Ror-α/γ	Global	No Th17 cell population Mice are resistant to EAE	28
Cry1/Cry2	Global	Mice are resistant to EAE	28
		Increased antibody-induced arthritis severity	86

The functioning of myeloid and lymphocyte subsets in both healthy humans and mice is another immune function related to the circadian rhythm (33). It is stated that variants of the clock gene Ror-γ and Ror-γt are important for the development of T helper (Th)17 cells, type 3 innate lymphoid cells, and lymphoid tissue inducer cells (34, 35). Ror-α, A canonical clock gene, is important for differentiation of the type 2 innate lymphoid cells (ILC2), which play a role in defense against allergy, type II inflammation, and parasitic infestations (35). Ror-α also has a role in the full development of Th17 cells (36). A disruption of molecular clock function can lead to abnormal Th17 cell development. Mice with impaired Th17 regulation become more susceptible to pathology in autoimmunity models such as experimental autoimmune encephalomyelitis (EAE, multiple sclerosis model) and colitis (37). Interestingly, Ror-γt mRNA expression is suppressed by melatonin, a hormone that is secreted from the pineal gland in a circadian rhythm and has a pleiotropic immunomodulatory effect (38). Recently, it has been discovered that circadian clocks also regulate neutrophil maturation (39).

In case of acute or chronic stress, the essential neuroendocrine response is activation of the HPA axis. Regardless of stress, the HPA axis also has a circadian rhythm governed daily by the SCN (40). In HPA activation, the brainstem and limbic forebrain stimulate corticotrophin-releasing hormone (CRH) and arginine vasopressin (AVP) secretion from neurosecretory neurons of the paraventricular nucleus of the hypothalamus (PVN) (41). As a result of the CRH secretion (partially with the involvement of AVP), adrenocorticotropin-releasing hormone (ACTH) is released from the anterior pituitary into the general circulation, leading to the secretion of glucocorticoids such as cortisol in humans and corticosterone in rodents from the cortex of the adrenal glands (42, 43). The circadian rhythms of glucocorticoids peak just before the onset of the active period, which is nocturnal for most rodent species and diurnal for humans (44). This rhythm encompasses a dynamic ultradian pattern for both ACTH and glucocorticoid secretion, driven by pituitary ACTH release and autocrine feedback of glucocorticoids (45-47). There is a bidirectional interaction between the HPA axis and the immune system (45) (Figure 2).

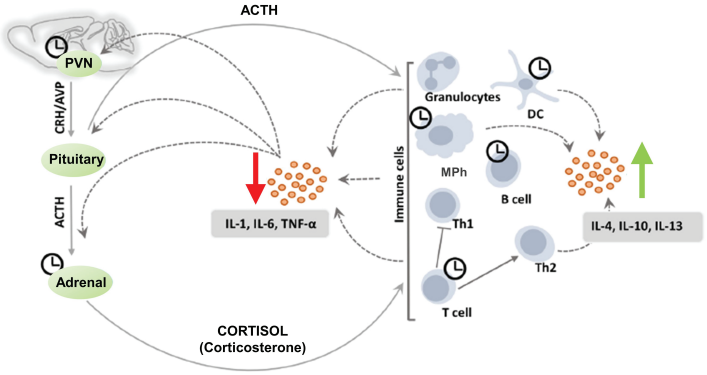

Figure 2. Circadian clocks in HPA axis-immune system crosstalk. Immune cells can activate the HPA axis via cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-1 and IL-6 at the level of the paraventricular nucleus (PVN) of the hypothalamus as well as at the pituitary and adrenal, stimulating the secretion of glucocorticoids. Glucocorticoids in turn act on the receptors on the surface or in the cytoplasm of immune cells to suppress the induction of pro-inflammatory responses, and to promote a shift from T helper cell type 1 (Th1) toward Th2-mediated humoral immunity. This inhibits the production of pro-inflammatory cytokines, while promoting the production of anti-inflammatory cytokines, such as IL-4, IL-10 and IL-13 by various immune cells. In addition, ACTH/cortisol exerts direct anti-inflammatory and immune-modulating effects via the melanocortin system. CRH: corticotropin-releasing hormone, AVP: arginine vasopressin, DC: dendritic cell, MPh: macrophage (Modified from Ref. 42).

It is well known that immune cells can activate the HPA axis through cytokines such as tumor necrosis factor-alpha (TNF-α), interleukins (IL-1, IL-6) and type I interferons (IFNs) (48-51). Moreover, some cytokines can activate the HPA axis through different mechanisms (52, 53). It can also affect the viability and function of many immune cell types, including glucocorticoids, T cells, B cells, monocytes, macrophages, and granulocytes (54,55). Glucocorticoids suppress the synthesis and release of proinflammatory cytokines, thereby protect the host organism from the harmful consequences of prolonged hyperactivity of the immune system. Glucocorticoids are still the most widely used and most effective treatment to control allergic, autoimmune, inflammatory, and hematological disorders (56). Glucocorticoid receptors are found in almost all immune cells and affect proinflammatory regulators such as NF-κB (Nuclear Factor kappa B) and activator protein 1 (AP-1) by activating anti-inflammatory molecules such as glucocorticoid-induced-leucine zipper (GILZ), annexin-1, mitogen-inducible gene-6 (Mig-6), MAPK phosphatase-1 (MKP-1) and SLAP1 (SRC-like adaptor protein 1) (56-63). In contrast to the well-defined immunosuppressive effects of glucocorticoids, recent studies indicate that these hormones can have permissive and even stimulating effects on immune processes (64-67). It is suggested that acute stress enhances, while chronic stress suppresses the peripheral immune response, but the mechanism

of this dual role is still unknown (64).

The immune system-related cytokines, the number of hematopoietic cells, and the hormones interacting with the immune system in the blood show a circadian rhythm (68). These parameters oscillate according to activity or resting phase, depending on whether the species is diurnal (humans) or nocturnal (rodents). Both cellular and humoral components of the immune system show opposite rhythms in the blood. Although amount of hematopoietic stem cells, progenitor cells (HSPCs) and most mature leukocytes (excluding effector CD8+ T cells) decrease during the active period, they peak in circulation during the resting phase (night-time in humans and during the daytime period in rodents) (68, 69). Moreover, there is an increase in the release of mature immune cells and HSPCs from the bone marrow to the blood at the beginning of the resting period (69). This release pattern is associated with local sympathetic innervation, which mediates rhythmic down-regulation of the expression of CXC-chemokine ligand 12 (CXCL12; formerly known as SDF1), an important attachment factor for hematopoietic cells in the bone marrow. This release is dependent on local sympathetic innervation, which mediates rhythmic down-regulation of the expression of CXC-chemokine ligand 12 (CXCL12; formerly known as SDF1), an important retention factor for hematopoietic cells in the bone marrow. Therefore, at the onset of the active period, there is an increase in the levels of glucocorticoids (cortisol in humans and corticosterone in mice), epinephrine, norepinephrine, and proinflammatory cytokines such as TNF- α and IL-1β (31, 68, 70).

IMMUNE SYSTEM-RELATED DISEASES WITH SYMPTOMS IN A CIRCADIAN RHYTHM

Changes related to the circadian rhythm in the symptoms of common immune system-related diseases are summarized in Table II.

Table II. Effects of circadian rhythm on symptoms of immune system-related diseases (Adapted from Ref. 87).

Species	Disease	Oscillating parameter	Acrophase	Ref.
Human	Allergic rhinitis	Sneezing, nasal congestion	CT6	88
	Bronchial asthma	Broncho- constriction	CT6	88
		Sputum eosinophils, IL-5	CT7	89
	Ischemic stroke	Hypertension	CT6-12	73
	Myocardial infarction	Pain	CT9	74
	Rheumatoid arthritis	Stiffness, Pain, TNF, IL-6	CT5-8	71
	Sickle cell vaso-occlusive crisis	Hospital admission	CT18	90
Note: CT: actual circadian time in hours (e.g. CT6 = 6AM).				

In patients with rheumatoid arthritis, pain and stiffness in the joint regions are common, especially during the early morning hours, associated with the increase in TNF and IL-6 in the blood (71). In this disease, symptoms that increase in the morning are positively correlated with high levels of circulating proinflammatory cytokines. In addition, circadian changes are observed in circulating inflammatory metabolites. Experimentally, animals lacking a functional clock gene (Cry1–/– Cry2–/– mice) have a more pronounced phenotype in a collagen antibody-driven model of inflammatory arthritis (72). The risk of stroke and myocardial infarction is again at the peak level in the early morning hours compared to other time periods of the day (73, 74). The increased activity of the sympathetic nervous system during the early morning hours and thus the increase in blood pressure, as well as the increase in blood viscosity and coagulation, and thus the tendency to thrombosis, are responsible for this increased risk (75). In our study on the subject, we determined that circadian rhythm proteins directly affect the brain damage that develops after cerebral ischemia. We observed an increase in the levels of Bmal1, Per1, CLOCK circadian rhythm proteins and p-AKT and p-Erk-1/2 mediated neuronal survival. We also observed a decrease in the number of apoptotic cells in mice with midnight ischemic stroke (Zeitgeber 18; 24:00) compared to mice with morning stroke (Zeitgeber 0, 06:00). As a result of our proteomic analysis, although GNAZ, NEGR1, IMPCT and PDE1B levels increased, CSKP, HBB1, HBB2 and HBA levels were significantly decreased in Zeitgeber 18 group compared to morning Zeitgeber 0. The results of our study showed that neuronal damage was less in those that had ischemic stroke at night, and this was provided by increased expression of survival kinases and circadian rhythm-related proteins (76). In addition, regarding stroke, it can be said that the process that started with the release of peroxiredoxins from the cytosolic antioxidant proteins of ischemic cells in the brain turned into a different situation. These antioxidant proteins are among the conserved markers of circadian rhythms that are vital for redox balance. Peroxiredoxins can bind to TLR2 and TLR4 on macrophages infiltrating the brain. This binding triggers the activity of T cells such as IL-17 and IL-23 and thus aggravates brain damage (77). It has been suggested that in addition to the increased risk of morning myocardial infarction, the infarct sizes are also larger, and rhythmic leukocyte infiltration may be responsible for this situation (78). It is well known that the symptoms of asthma, a pulmonary inflammatory disease, vary throughout the day (79). Asthma symptoms become more pronounced at night due to circadian variation in lung function. The cause of circadian oscillations in inflammatory cell numbers in the asthmatic lung is unclear. However, murine studies show that BMAL1 deletion in myeloid cells increases eosinophil release in the ovalbumin model of allergic asthma. This evidence indicates that the biological clock in myeloid cells plays a role in this process (80). The pathological course of multiple sclerosis may vary depending on circadian and seasonal cycles. It has been suggested that relapses of the disease occur more frequently in spring and summer, and this is due to lower levels of melatonin, a hormone associated with circadian rhythm (81). There are also circadian rhythm-related changes in the EAE model of multiple sclerosis and T cell-mediated autoimmune disease.

CONCLUSION

The immune system has an important function that controls all body cells. The cooperation of the immune system with the nervous system and endocrine system is important to maintain homeostasis. The most important factors that threaten homeostasis are the environmental factors. Therefore, the adaptation capacity of the organism to environmental conditions is critical. One of the important mechanisms that provide this is the biological clocks in the body. Thus, the adaptation of the organism to circadian and seasonal rhythms is ensured. It is well known that body functions and immune activity change, especially depending on seasonal changes. However, it is also same for the circadian rhythm, but the relationship among immune activity, HPA axis, and circadian rhythm is not well known. However, the immune system shows circadian variations, including innate and adaptive immune activity. A prominent link between the biological clocks and the immune system is the regulation of proinflammatory cytokine production. There is a feedback mechanism between inflammation and the integration of the molecular clock. In relation to this situation, BMAL1, Rev-Erb-α and CLOCK protein levels in cells decrease significantly after endotoxin injection, which is predicted to impair clock function. The immune system-related cytokines, the number of hematopoietic cells, and the hormones interacting with the immune system in the blood have a circadian rhythm.

Pain and stiffness in the joints are common in patients with rheumatoid arthritis, especially during the early morning hours. In this disease, symptoms that increase in the morning are positively correlated with increased levels of circulating proinflammatory cytokines. The risk of stroke and myocardial infarction is higher during the early morning hours than at other time periods of the day. In our previous study, we determined that circadian rhythm proteins directly affect the brain damage that develops after cerebral ischemia. Furthermore, we observed that neuronal damage was less in those who had ischemic stroke at night and that the expression of survival kinases and circadian rhythm-related proteins played a role regarding to this situation. It is a phenomenon that is considered to have a higher risk of morning myocardial infarction. There are several studies showing that asthma symptoms vary daily and are more severe, especially during the early morning hours. In addition, the pathological course of multiple sclerosis can vary depending on circadian and seasonal cycles, and it is an important data on the relationship with the circadian rhythm, where relapses of this disease occur more frequently in spring and summer. Data on circadian rhythm and immune system physiology are important in terms of understanding the pathophysiology of immune system-related diseases and producing effective treatment strategies.

Conflict of interest:
Authors declare that there is no conflict of interest.

Financial conflict of interest:
Authors declare that they did not receive any financial support in this study.

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REVIEW
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Geliş Tarihi : October 14, 2022
Received
Kabul Tarihi : December 24, 2022
Accepted
E Yayın Tarihi : September 01, 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Aycan IO, Dinc B.
Ambulatory Anaesthesia
Management for Obese
Patients
Akd Med J 2023;9(3) 342-350

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DOI: 10.53394/akd.1189245

Ambulatory Anaesthesia Management for Obese Patients

Obez Hastalar için Günübirlik Anestezi Uygulamaları

ABSTRACT
Standard operating room conditions may not be provided in areas where ambulatory anesthesia is applied. For this reason, the infrastructure of the center should be taken into account when evaluating obese patients. Obesity is not an independent risk factor. Accompanying comorbidities are decisive in the development of perioperative complications. Obese patients should be evaluated for cardiac, pulmonary, endocrine disorders, and Obstructive Sleep Apnea Syndrome. Particular attention should be paid when evaluating morbidly obese (Body Mass Index> 40 kg / m2) patients. Comorbidities, not Body Mass Index alone, should be decisive in terms of suitability for outpatient surgery. Super morbid obese patients with Body Mass Index> 50 kg / m2 can be taken to selected ambulatory surgery if there is no accompanying comorbidity. No relationship was found between Body Mass Index and difficult airway. However, it was stated that difficult mask ventilation and intubation were found in patients with a high mallampati score and neck circumference >50 cm. Therefore, it may be helpful to look at the neck circumference of obese patients preoperatively. The drugs to be used should be adjusted according to the ideal body weight and used by titration. It is recommended to use wakefulness (Bispectral Index Monitoring) monitoring methods when adjusting the anesthetic dose for obese patients. Non-opioid analgesia methods should be preferred. Opioids should be preferred as rescue analgesics. If possible, regional anesthesia and analgesia methods should be applied. Anatomical difficulties should be considered in regional anesthesia and analgesia applications. Hospitalization should be considered in surgeries longer than three hours. In surgeries longer than six hours, patients should be hospitalized.

Key Words:
Anesthesia, Ambulatory, Obesity, Outpatient

ÖZ
Günübirlik anestezi uygulanan alanlarda standart ameliyathane koşulları sağlanamayabilir. Bu nedenle obez hastaları değerlendirirken merkezin altyapısı da dikkate alınmalıdır. Obezite, bağımsız bir risk faktörü değildir. Eşlik eden komorbiditeler perioperatif komplikasyonların gelişiminde belirleyicidir. Obez hastalar kardiyak, pulmoner, endokrinolojik açıdan ve Obstrüktif Uyku Apne Sendromu açısından değerlendirilmelidir. Morbid obez (Vücut Kitle İndeks> 40 kg/m2) hastaları değerlendirirken özellikle dikkat edilmelidir. Ayaktan cerrahiye uygunluk açısından tek başına Vücut Kitle İndeks değil, komorbiditeler belirleyici olmalıdır. Vücut Kitle İndeks> 50 kg/m2 olan süper morbid obez hastalar eşlik eden bir komorbidite yoksa seçilmiş ayaktan cerrahiye alınabilir. Vücut Kitle İndeks ile zor hava yolu arasında ilişki bulunamamıştır.

Ancak mallampati skoru yüksek ve boyun çevresi >50 cm olan hastalarda zor maske ventilasyonu ve entübasyonuna rastlandığı belirtildi. Bu nedenle obez hastaların ameliyat öncesi boyun çevresine bakmak faydalı olabilir. Kullanılacak ilaçlar ideal vücut ağırlığına göre ayarlanmalı ve titrasyon ile kullanılmalıdır. Obez hastalarda anestezi dozu ayarlanırken uyanıklık (Bispektral İndeks Monitörizasyonu) izleme yöntemlerinin kullanılması önerilir. Opioid içermeyen analjezi yöntemleri tercih edilmelidir. Kurtarma analjezikleri olarak opioidler tercih edilmelidir. Mümkünse bölgesel anestezi ve analjezi yöntemleri uygulanmalıdır. Rejyonel anestezi ve analjezi uygulamalarında anatomik zorluklar göz önünde bulundurulmalıdır. Üç saatten uzun süren ameliyatlarda hastanede yatış düşünülmelidir. Altı saatten uzun süren ameliyatlarda hastaların hastaneye yatırılması gerekir.

Anahtar Kelimeler:
Anestezi, Ayakta tedavi, Obezite, Günübirlik

INTRODUCTION
Obesity is a disease characterized by excessive accumulation of fat in the body, the prevalence of which continues to increase every year (1,2). Obesity is defined as a body mass index greater than 30 kg m2 [BMI = weight (kg)/height2 (m2)]. Additional definitions of obesity are given in Table (I,II).

Table I. Shows additional definitions of obesity

BMI Range	Classification
25 < BMI < 30	Over-weight
30 < BMI < 35	Obesity class 1
35 < BMI < 40	Obesity class 2
40 < BMI < 50	Obesity class 3 / Morbid Obese
BMI > 50	Super Morbid Obese
BMI > 70	Ultra Obese

BMI: Body Mass Index

In 2016 there were 650 million people, about 12% of the estimated world population, classified as obese (3). Super morbid obese people (body mass index (BMI) >50 kg/m2) constitute the fastest-growing component of obese patients in the United States (2,4).

Heart disease, hypertension, coronary artery disease, obstructive sleep apnea (OSAS), diabetes, lung disorders, cancer, stroke risk, renal and thromboembolic complications, difficulty in glucose control, other endocrine and metabolic problems are accompanying obesity. Furthermore, they are associated with high morbidity and mortality during surgery (1,3,5). The incidence of anesthesia-related severe intraoperative events related to obesity is approximately 0.9%. The risk of death, venous thromboembolism, and long-term hospital stay increases linearly with the severity of obesity (6).

The increase in obesity prevalence every year presents a multifaceted problem in patient safety and rapid discharge home (1,3). Some of these problems indicate that obesity alone does not increase cardiovascular risk and that the increased risk may be related to comorbidities (5,6). The risk of both intraoperative and post-operative respiratory complications rises with obesity. In addition to hemodynamic instability, difficulties may be encountered in monitoring respiratory parameters, providing intravenous access, airway management leading to hypoxia, and the risk of position-related nerve damage may increase. Longer operation time, more blood loss, increased need for reoperation, impaired wound healing, and increased risk of wound infection are possible consequences (3-6).

Preoperative Evaluation
Obesity-related comorbidities can influence cardiovascular, respiratory, and metabolic systems (2). Patients should be evaluated for comorbidities, including high blood pressure, cardiovascular disease, coronary artery disease, respiratory disease, sleep apnea syndrome, endocrine disorders (especially diabetes mellitus), and an elevated risk of deep vein thrombosis (1,7). More careful evaluations should be made regarding potential comorbidities associated with a BMI greater than 40 kg/m2 (2). Obese patients with a BMI of 30-40 kg/m2 do not have an increased complication rate for ambulatory surgeries compared to regular patients. Although there is no definitive information regarding morbid obesity (BMI> 40 kg/m2), it is believed that patients may be prone to higher complication rates as BMI increases. Not only BMI but the presence of comorbidities should also be decisive in terms of suitability for ambulatory surgery (3).

Cardiovascular System
Considerations should be carried out regarding undiagnosed cardiopulmonary diseases due to obesity. Therefore a detailed history besides physical examination should be performed. Furthermore, cardiac function and functional capacity should be evaluated comprehensively (3,6). Depending on the severity of cardiovascular disease, patients may not be suitable candidates for ambulatory surgery due to the increased possibility of complications (3).

Obesity is primarily associated with hypertension (HT) due to increased plasma volume and cardiac output (2). The prevalence of HT can be caught around 50% in obese individuals and approximately 60% in severely obese (8). The most common change in cardiac morphology due to obesity is increased left ventricular (LV) mass, including LV hypertrophy (LVH). Bioactive mediators that result in atherosclerosis are released from adipose tissues, lipids, coagulation factors, fibrinolysis, and endothelial inflammatory dysfunction (9). However, HT is associated with activation of the adipocyte's renin-angiotensin-aldosterone system. This results in increased peripheral vascular resistance and sympathetic tone. Thus, through the direct effects of angiotensin II on the LV myocardium, it may contribute to left ventricular hypertrophy. Hyperleptinemia and leptin resistance were associated with left ventricular hypertrophy, while insulin resistance with hyperinsulinemia increased LV mass. A 50% increase in the risk of atrial fibrillation has been associated with sinoatrial node dysfunction and increased dysrhythmia due to fat infiltration of the conduction pathways (2,8).

Obesity cardiomyopathy is defined as heart failure that develops primarily due to severe obesity (8). Morbid obesity can lead to cardiomyopathy in the absence of coronary artery disease (7). Right heart pressures and pulmonary vascular resistance may be higher in class II-III obese patients compared to regular weight patients (8). Other considerable issues are; cardiovascular sequelae, congestive heart failure, dilated cardiomyopathy, pulmonary hypertension, high right heart pressures, and increased pulmonary vascular resistance. Left ventricular diastolic dysfunction is frequently seen in obese individuals, especially in extreme obese and hypertensive obese individuals (2,8). An increase of 5 kg/m2 in BMI increases the risk of cardiovascular death, a 10% increase in hemorrhagic stroke, and a 49% increase in hypertension. Furthermore, the increase in BMI; increases the risks of heart failure, coronary heart disease (CHD), atrial fibrillation, hemorrhagic stroke, ischemic stroke, hypertension, aortic valve stenosis, pulmonary embolism, and venous thromboembolism (9,10).

Ambulatory surgeries have a low perioperative risk for cardiac complications (< 1%). Therefore, the electrocardiogram should be evaluated in patients with limited functional capacity and few risk factors for perioperative cardiovascular morbidity (heart disease, congestive heart failure, cerebrovascular disease, insulin therapy, and serum creatinine >2 mg/dL). Cardiac enlargement or abnormal pulmonary vascularity should be evaluated on a chest X-ray. Left bundle branch block is not expected in uncomplicated obesity, and the underlying cause should be investigated. Stress tests and echocardiography may be indicated in patients with three or more risk factors (7). Non-invasive diagnostic cardiac techniques used to evaluate left ventricular diastolic function include Doppler echocardiography, tissue Doppler echocardiography, radionuclide left ventriculography, and cardiac magnetic resonance imaging (MRI) (8).

Respiratory system

Depending on obesity, the soft tissue weight increases, and lubrication occurs on the chest wall. Thus, compliance decreases due to increased pulmonary blood flow (2). While total lung capacity, functional residual capacity, expiratory reserve volume, and residual volume decrease with obesity, intra-abdominal pressure and the risk for atelectasis increases (2,11). Depending on the changes in smooth muscle structure, hyperreactivity increases, and airway diameter decreases (2). When moderate and deep sedation is applied with the prone position, the risk of hypoxia and apnea increases due to limited reserve, increased oxygen consumption, and pulmonary mechanical effects of the lungs (6).

The major comorbidity that can be seen in 70% of obese patients (over 40 kg/m2) is obstructive sleep apnea syndrome (OSAS), and it is undiagnosed in approximately 80% (2,6,7). OSAS is associated with adverse long-term health problems, perioperative risk, respiratory complications, and increased risk for ambulatory surgery (7,12). Predominantly respiratory complications can be seen in the coexistence of obesity and OSAS. Most patients can be treated safely on an ambulatory basis as long as the comorbidities are well controlled. All obese patients planning for surgery should be evaluated for OSAS by performing the STOP-BANG questionnaire (Table II).

Table II. STOP-BANG Questionnaire (2)

Snoring	Loud snoring (More noise than speaking or being heard through a closed door)
Tired	Do you feel tired, drowsy, exhausted all day long? Does he fall asleep during the day?
Observed	Has anyone observed you stop breathing or choke or gasp while you sleep?
Blood pressure	Do you have hypertension or are you receiving treatment for HT?
BMI	BMI ≥ 35 kg m^2
Age	≥ 50 years
Neck	Circumference (measured around Adam's apple) > 43 cm for Men, > 41 cm for Women
Sex	Male

BMI: Body Mass Index

A score of 0-2 indicates low probability, 3-4 indicates moderate risk, and 5-8 indicates high-risk patients for undiagnosed OSAS (2,6,7,11,12). Post-operative events (such as pulmonary complications, reintubation, and cardiac arrhythmias) were four times higher in patients with high-risk OSAS than those with low-risk OSAS (3). One factor that increases the risk in this group of patients is respiratory complications due to increasing the demand for narcotics post-operatively (12). Excessive opioid use should be avoided, and a non-opioid approach should be evaluated (6). Obese patients with OSAS scheduled for ambulatory surgery should be reviewed for other comorbidities and use a continuous positive airway pressure (CPAP) machine after post-operative discharge. When these conditions are established, suitable patients can receive ambulatory treatment (2,7).

Metabolic System

Metabolic syndrome consists of four features these are; hypertension, obesity, abnormal lipid levels (high triglyceride and low high-density lipoprotein), and hyperglycemia due to insulin resistance. Perioperative complications and mortality rates are higher in patients with untreated disorders (2). A 65% increase in the risk of acute kidney injury (AKI) has been noticed in obese patients within 30 days of surgery (11).

Obesity correlates with Type 2 diabetes mellitus (DM). Adults with a BMI ≥ 40 kg m2 are seven times more likely to have diabetes. It is estimated that 63% of obese people have Type 2 DM, and 90% have high blood sugar levels. DM causes tissue remodeling that affects elastin and collagen in the airways by increasing smooth muscle tone. 25% of the patients do not know their glycemic status. Therefore, glycemic levels should be monitored perioperatively (2,11). In their study, Sudy et al., showed that the intrinsic mechanical abnormalities caused by diabetes in the respiratory tract in obese individuals are balanced by hypoxic pulmonary vasoconstriction, which preserves the intrapulmonary shunt fraction and oxygenation ability of the lungs (13).

Airway management

The accumulation of adipose tissue causes changes in airway anatomy and respiratory function. It causes decreased pharyngeal area, obstructive sleep apnea, restriction in neck flexion, narrow jaw opening, tongue enlargement, reduction in functional residual capacity, decrease in alveolar oxygen reserve, and increase in O2 consumption (14). Although it is not an independent risk factor for difficult airway in obese patients, there is a correlation between high mallampati score and wide neck circumference and correspondingly difficult intubation (7). Preoxygenation is recommended in morbidly obese patients because of the possibility of a difficult airway and the increased risk of hypoxemia. As BMI increases, desaturation develops more quickly in the apneic condition. Preoxygenation can be improved with head-up position and continuous positive airway pressure (CPAP)/ Bi-level positive airway pressure (BIPAP) application. With the sniffing position, the difficulty in intubation can be reduced. In obese patients, video laryngoscopy is better than laryngoscopy in terms of success rate and intubation time and provides a better view of the glottis (7,14). However, despite the evidence showing the benefits of using video laryngoscopy, direct laryngoscopy is still more widely used (15).

Gill et al., conducted a study on the use of laryngeal mask airway (LMA) in obese patients (16). The study stated no increase in respiratory tract problems such as aspiration risk, laryngospasm, and inadequate ventilation compared to normal-weight patients. They also indicated that LMA could safely be used in obese patients.

Shaw et al., demonstrated that obesity was associated only with minor airway events (desaturation, inadequate ventilation with supraglottic airway devices), not major airway complications (difficult intubation, etc.) (15). Babayigit et al., reported that possible airway problems and complications in bariatric surgery are similar to non-bariatric surgeries (17). They found that an increase in neck circumference (>50 cm) was a more meaningful indicator than body mass index in predicting difficult intubation and ventilation.

The risk of atelectasis increases with obesity. There are no clear data on the optimal positive end expiratory pressure (PEEP) level in obesity. Recruiting maneuvers and PEEP applications can improve alveolar gas exchange and lung mechanics. Low tidal volume and personalized PEEP settings can reduce post-operative atelectasis. Obese patients may also need higher protective driving pressure (the difference between plateau pressure and PEEP) due to low lung capacity or intraoperative physiological changes (18).

The PEEP level for obese patients was much higher than that routinely used and not associated with BMI alone (19). Although individualized PEEP was found to be successful in intraoperative lung mechanics and oxygenation, it was observed that it did not improve post-operative oxygenation (19-21). With individualized PEEP, larger volumes of fluid and higher doses of vasopressors were required (19). However, general norepinephrine doses were low, so it may not cause a problem in most patients, but high PEEP values should be avoided in those with significant right heart failure (21).

Pressure-controlled ventilation can promote more homogeneous ventilation, reducing alveolar overswelling and improving oxygenation. Volume-controlled ventilation can reduce the risk of post-operative pulmonary complications by providing better tidal volume control during surgery that affects chest wall compliance (18).

Anesthetic Drugs

Anesthesia drug doses are calculated according to body weight. The drugs' pharmacokinetics (clearance, elimination, and distribution volumes) vary due to the more extensive vascular fat tissue in obese patients (2). There is uncertainty about appropriate dosing in obese patients (7). However, lean, ideal, and correct bodyweight should be calculated, and drug doses can be delivered by calculating weight according to the anesthesia drug scales given in Table III (2).

Table III. Calculations for Pharmacology (2)

Ideal Body Weight: Patient's normal lean fat mass ratio IBW= Height (cm) - 105 (Female) IBW= Height (cm) - 100 (Male)		
Lean Body Weight (LBW): Patient's lean body weight Male = 9270 x Total body weight (TBW) / 6680 + (216 x body mass index) Female = 9270 x TBW / 8780 + (244 x body mass index)		
Adjusted body weight (ABW): This allows for increased lean body weight and increased volume of distribution in obese individuals. ABW = IBW + 0.4 (TBW – IBW)		
DRUG SCALES FOR ANESTHESIA		
Lean Body Weight	**Ideal Body Weight**	**Total Body Weight**
Propofol (induction)	Propofol (Infusion for maintenance of anesthesia)	Succinylcholine
Thiopental	Antibiotics	
Fentanyl	Alfentanil	
Rocuronium	Low molecular weight heparin	
Atracurium	Neostigmine	
Vecuronium		
Morphine		
Paracetamol		
Bupivacaine		
Lidocaine		

Most ambulatory procedures can be performed with sedation/analgesia. The most commonly used agent is midazolam which should be used with caution in terms of respiratory depression (7). It is safer to perform induction in the operating room rather than the anesthesia room. In addition to standard monitoring, neuromuscular and bispectral index (BIS) monitoring is essential. Moreover, capnography follow-up should be performed to detect early apnea in patients receiving sedation (2,7). There is no ideal anesthesia technique for morbidly obese patients; the aim is to optimize oxygenation, ventilation, and

analgesia in the post-operative period (22). Propofol is preferred in procedures requiring deep sedation. However, the association of obesity with OSAS increases respiratory tract complications, and desaturation may ocur (7). The risk of respiratory depression increases with obesity, OSAS, male gender, American Society of Anesthesiologists (ASA) >3, and age. Therefore, drugs should be used by titration. Since ketamine does not reduce upper respiratory tract muscle activity, fewer respiratory tract complications develop; therefore, its combination with propofol is preferred. In addition, dexmedetomidine can be preferred due to the low incidence of respiratory tract complications. It has been found that the airway is better protected when dexmedetomidine and ketamine are used together (7).

Obesity studies have concluded that desflurane and sevoflurane have a faster recovery and early extubation than isoflurane and propofol. While some studies recommend propofol-based anesthesia, other studies remarkably suggest the use of desflurane (23). Some studies indicated that desflurane has faster recovery, while other findings did not show a difference in comparing desflurane and sevoflurane. Moreover, patients with propofol and dexmedetomidine had less post-operative nausea and vomiting (2,7). Demirel I. et al., compared desflurane and total intravenous anesthesia (TIVA), (propofol and remifentanil) infusion for morbidly obese patients (22). They found that cognitive functions improved more rapidly besides a faster post-operative recovery in the TIVA group. In a study comparing TIVA (propofol and dexmedetomidine together) and desflurane, lower heart rate and blood pressure were observed in the TIVA group.

In contrast, less pain, nausea, vomiting, and side effects were observed in the post-operative period (23). It has been observed that the potency and sensitivity of propofol are increased in morbidly obese patients. Therefore, administration of propofol induction dose based on lean body weight instead of total body weight has been shown to cause less cardiovascular depression and provide appropriate intubation. Accordingly, the induction dose was found to be 2.310-3.567 mg/kg based on lean body mass (24,25). The dosage administration of propofol according to lean body mass and the amount is given according to BIS monitoring were compared. It was seen that an additional amount of the drug should be administered to the drug dose given according to the lean body mass. For this reason, propofol induction and maintenance doses are controversial. It should be administered by monitoring the depth of anesthesia (BIS) in morbidly obese patients (2,26).

Intraoperative multimodal analgesia should be performed. The general recommendation is to use opioids as rescue analgesics. Opioid administration should be limited as it may increase post-operative respiratory complications. Therefore, paracetamol, non-steroidal anti- inflammatory drugs, and local anesthetic infiltrations can be used as alternatives. In addition, dexamethasone may benefit post-operative pain, nausea, and vomiting. However, intermittent hypoxia and sleep disruption was seen in OSAS may cause hyperalgesia and increase the need for analgesics. Non-opioid analgesia has been used more and more in recent years. Non-opioid drugs; lidocaine, dexmedetomidine, ketamine, and magnesium can be used alone or in combination. However, since the side effects of these drugs have not been adequately evaluated, their risks and benefits should be considered (2,7). In a study conducted on morbidly obese patients undergoing laparoscopic gastric bypass surgery, after induction, a bolus of 0.3 mg/kg of ketamine based on ideal body weight was administered, followed by 0.2 mg/kg/hour ketamine infusion continued for up to 24 hours. It has been shown that perioperatively ketamine infusions significantly reduce opioid consumption (27). Post-operative use of dexmedetomidine for post-operative analgesia in bariatric surgery has been shown to significantly reduce opioid consumption in 24 hours and cause less nausea and vomiting. Therefore, dexmedetomidine is a good alternative for multimodal analgesia in high-risk patients such as morbidly obese (28).

Intraoperative hyper- or hypovolemia administration in obese patients is associated with worse outcomes. Individualized targeted fluid therapy outcomes and tissue oxygenation are better in obese patients. Colloid fluids can stay in the intravascular space longer than crystalloid fluids, leading to hemodynamic stability, tissue perfusion, and oxygenation (18).

Neuromuscular Blockade

Since neuromuscular muscle relaxants (hydrophilic) and induction agents are distributed centrally without redistribution, dose adjustment should be made by calculating lean body mass. Unlike other drugs, succinylcholine is the only drug that should be administered according to total body weight due to increased plasma pseudocholinesterase and extracellular volume (2). Due to the risk of residual neuromuscular blockade, neuromuscular blockers should be reduced and avoided if possible. If used, it should be reversed at the end of surgery. According to ideal body weight, Rocuronium, vecuronium, and atracurium should be given according to ideal body weight. In a study comparing sugammadex and neostigmine in morbidly obese patients, residual blockade and the risk of post-operative nausea and vomiting were lower with sugammadex. Although it is suggested that the dose of sugammadex should be given according to total body weight (TBW) in obese patients, some studies show that the dose of sugammadex in morbidly obese patients can be TBW + 40% (2,7). However, in the study of Horrow et al., they showed that the sugammadex dose based on total body weight had a lower risk of decurarisation than the ideal body weight dose, regardless of the depth neuromuscular block or neuromuscular blocking agents (NMBA) used, and allowed faster extubation (29). In the study of Mostoller et al., sugammadex is recommended according to total body weight (30).

Regional Anesthesia for Obese Patients

Regional anesthesia techniques can be used in ambulatory anesthesia in upper and lower extremity surgeries. Thus, besides the airway problems that may occur, the side effects of anesthetic agents, neuromuscular blockade, and opioids are avoided. It also reduces the need for opioids by providing post-operative pain control. However, the block failure rate is 1.62 times higher due to anatomical difficulties. In morbidly obese patients, the intrathecal dose of bupivacaine (BMI >40) is similar to that of regular BMI patients (31). Sitting is recommended for obese patients in neuraxial anesthesia applications (2,7).

Post-operative Considerations

In the postanesthesia care unit (PACU), breathing activity increases in obese patients and should be considered regarding atelectasis and respiratory complications. It should be followed with pulse oximetry, and patients should lie in a semi-sitting position with their heads elevated to reduce airway obstruction (7,18). In the case of opioid use in patients with obesity and OSAS, airway obstruction due to pharyngeal laxity due to pharyngeal muscle weakness is the most common complication of PACU. Therefore, opioid-sparing analgesic approaches should be used (7,18,32). Oxygen support can be applied until the initial saturation value is reached in room air. However, there are concerns that it may suppress hypoxic arousal, increase the duration of apnea attacks, cause respiratory depression and increase carbon dioxide retention.

On the other hand, in the study conducted on OSAS patients, it was shown that the risk of apnea and hypercarbia did not increase. It has been reported that CPAP/BiPAP application is beneficial in patients with post-operative hypoxemia (oxygen saturation <90%). Use of high-flow nasal oxygen instead of CPAP/BiPAP may also be helpful. However, patients who need CPAP or high-flow nasal oxygen administration are not suitable for day-to-day procedures. It is recommended that they be treated as inpatients (7,18). In their study, Gabriel et al., found five conditions that increase the length of stay in PACU; morbid obesity, hypertension, type of surgery, type of anesthesia, and planned case duration (32).

Obesity alone is not a contraindication for outpatient surgery. The studies found the BMI value associated with the risk of readmission to the hospital after discharge as ≥45,7 kg/m2. In addition to BMI, patient comorbidity and surgical factors should also be considered (7). However, in the study by Hajmohamed et al., the probability of early rehospitalization was found to be the same in super morbidly obese patients (BMI ≥50 kg/m2) compared to morbidly obese patients (BMI ≥40 kg/m2) (4). In addition, they concluded that there is no increase in the risk of early post-operative complications at home after discharge in super morbidly obese patients who meet the discharge criteria. Similarly, Vertosick et al., conducted a study of 13957 patients (5). Although there was a slight difference between BMI and post-operative results, there was no significant difference between BMI and length of hospital stay, readmission, and complications. In another study examining 235 patients, there was no correlation between BMI and unplanned readmission. Although conflicting studies have been reported, appropriate selection of patients with high BMI, morbid or super-morbid obesity after considering other comorbidities may increase the success of ambulatory surgery (3,4).

There was no significant increased risk of complications with less than 3 hours of operation time. However, an increase in morbidity of 21% was observed for every hour of a surgery over 3 hours. Although there is no exact maximum time for outpatient surgery, hospitalization for more than 6 hours is recommended (12). Standard discharge criteria can determine the time to discharge from PACU (18). Enhanced recovery after surgery (ERAS) recommendations for post-operative care in bariatric surgery are given in Table IV.

Table IV. ERAS suggestions for post-operative care in bariatric surgery (18)

ELEMENTS	SUGGESTION	EVIDENCE LEVEL	RECOMMENDATION
Post-operative oxygenation	*Patients with OSAS with or without complications should be placed in a semi-sitting position with elevated heads and oxygen support.* *Follow-up of both groups after PACU should be done in a surgical ward.* *In the presence of signs of respiratory distress, it should be treated with non-invasive positive pressure ventilation and maintained oxygenation using a low threshold.*	Oxygen treatment: Low Post-operative position: High	Strong
	Patients with OSAS receiving CPAP treatment at home should use their equipment immediately after surgery.	Moderate	Strong
	Patients with obesity hypoventilation syndrome (OHS) are at higher risk for respiratory adverse events. *Post-operative BiPAP/NIV should be freely considered in the immediate post-operative period, especially in hypoxemia.*	Low	Strong
Thromboprophylaxis	*Thromboprophylaxis should include mechanical and pharmacological measures.* *Doses and duration of treatment should be individualized.*	High	Strong
Early post-operative nutritional care	*A clear liquid meal regimen can usually be started a few hours after surgery*	Moderate	Strong
	All patients should have access to a comprehensive dietetic assessment of the macronutrient and micronutrient content of the diet based on the surgical procedure and the patient's nutritional status, with the support of counseling.	Moderate	Strong
	Patients and healthcare professionals should be aware of thiamine deficiency, especially in the early post-operative period.	Low	Strong
Vitamin and mineral supplement	*It is necessary to monitor lifelong vitamin, mineral supplements, and nutritional habits with biochemical parameters.*	High	Strong
Proton pump inhibitor (PPI) prophylaxis	*PPI prophylaxis should be considered for at least 30 days after Roux-en-Y gastric bypass surgery.*	Roux-en-Y gastric bypass: Moderate	Strong
	There is insufficient evidence to recommend PPI prophylaxis for sleeve gastrectomy surgery, but reported a high incidence of gastroesophageal reflux after this procedure, it may be considered at least 30 days after surgery.	Sleeve gastrectomy: Very Low	Weak
Gallstone prevention	*Ursodeoxycholic acid should be considered six months after bariatric surgery in patients without intraoperative gallstones.*	Moderate	Strong

CONCLUSION

Standard operating room conditions may not be provided in areas where ambulatory anesthesia is applied. For this reason, the infrastructure of the center should be taken into account when evaluating obese patients. Obesity is not an independent risk factor. Accompanying comorbidities are decisive in the development of perioperative complications. Obese patients should be evaluated for cardiac, pulmonary, endocrine, and OSAS. Particular attention should be paid when evaluating morbidly obese (BMI> 40 kg / m2) patients. Comorbidities, not BMI alone, should be decisive in terms of suitability for outpatient surgery.

Super morbid obese patients with BMI> 50 kg / m2 can be taken to selected ambulatory surgery if there is no accompanying comorbidity. Although no relationship was found between BMI and difficult airway. However, it was stated that difficult mask ventilation and intubation were found in patients with a high mallampati score and neck circumference >50 cm. Therefore, it may be helpful to look at the neck circumference of obese patients preoperatively.

The drugs to be used should be adjusted according to the ideal body weight and used by titration. It is recommended to use wakefulness (BIS) monitoring methods when adjusting the anesthetic dose for obese patients. In addition to standard monitoring, BIS, Capnograph, and neuromuscular monitoring should be performed. Particularly muscle relaxants should not be used as much as possible; if necessary, sugammadex should be administered at the end of the operation. Sugammadex should be given by calculating the total body weight.

To avoid opioid use, non-opioid analgesia methods should be preferred. Opioids should be preferred as rescue analgesics. If possible, regional anesthesia and analgesia methods should be applied. Anatomical difficulties should be considered in regional anesthesia and analgesia applications.

Hospitalization should be considered in surgeries longer than three hours. In surgeries longer than 6 hours, patients should be hospitalized. If they are to be discharged, obese patients with OSAS using a CPAP/BIPAP device should be advised to use the CPAP/BIPAP device at home. Otherwise, hospitalization is recommended.

Conflict of interest

We have no commercial associations, contractual relations, financial support or proprietary considerations that might pose a conflict of interest related or unrelated to the submitted manuscript and have had no involvements that might raise the question of bias in work reported or in the conclusions, implications, or opinions stated.

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CASE REPORT
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Geliş Tarihi : July 28, 2021
Received
Kabul Tarihi : September 11, 2021
Accepted
E Yayın Tarihi : September 01, 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Dirol H, Aksu Yalcinkaya I.
Pneumomediastinum in an Asthmatic Patient with COVID-19
Akd Med J 2023; 9(3): 351-353

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DOI: 10.53394/akd.975554

Pneumomediastinum in an Asthmatic Patient with COVID-19

Astımlı COVID-19 Hastasında Pnömomediastinum

ABSTRACT
Spontaneous pneumomediastinum is a rare disease that develops due to alveolar rupture. Many cases with pneumomediastinum, related to Corona Virus Disease-19 (COVID-19) have been reported so far, but most of these patients had severe disease and extensive parenchymal damage. Pneumomediastinum with such a small lung infiltration is extremely rare in COVID-19 and may arise as a result of increased alveolar pressure caused by excessive coughing. Here, we present a patient with asthma and typical symptoms of COVID-19 and focal ground-glass opacity and pneumomediastinum on chest computerized tomography (CT).

Key Words:
COVID-19, Pneumomediastinum, Cough, Alveolus

ÖZ
Spontan pnömomediastinum alveol rüptürene bağlı gelişen nadir bir hastalıktır. Şimdiye kadar COVID-19 ile ilgili birçok pnömomediastinum vakası bildirilmiştir, ancak bu hastaların çoğunda ciddi hastalık ve yaygın parankim hasarı vardı. Pnömomediastinum, bu kadar küçük bir akciğer infiltrasyonu ile COVID-19'da oldukça nadirdir ve aşırı öksürüğün neden olduğu alveoler basıncın artması sonucu oluşabilir. Burada, tipik COVID-19 semptomları olan ve göğüs bilgisayarlı tomografisinde (BT) fokal buzlu cam opasitesi ve pnömomediastinumu olan astımlı bir hastayı sunuyoruz.

Anahtar Kelimeler:
COVID-19, Pnömomediastinum, Öksürük, Alveol

INTRODUCTION
Pneumomediastinum is a rare and life-threatening disease, defined as the presence of air in the mediastinum. The main cause of pneumomediastinum is the barotrauma arising during mechanical ventilation. Many COVID-19 patients with pneumomediastinum, following tracheal intubation have been reported so far (1-3). Besides the barotrauma provoked by mechanical ventilation, pneumomediastinum may also arise due to the barotrauma induced by persistent cough (2,3). Here, we present an asthmatic patient with typical symptoms of COVID-19 and pneumomediastinum with limited ground-glass opacity in the chest CT.

Case
A 36-year-old male patient presented with cough, sore throat, fever, chest and muscle pain for about a week. The most disturbing symptom was the cough, and the patient had never had such an intractable cough before. He had intermittent asthma that was under control and he was using a short-acting bronchodilator as he needed. There was no feature in his medical history other than asthma. He was an active smoker with a 10 packet year cigarette consumption history.

He did not either contact a COVID-19 positive patient or traveled to another country recently.

The patient's vital signs (heart rate was 98 beats/min, blood pressure was 110/55mmHg and respiratory rate was 20/min) were normal. He did not need oxygen supplementation (SpO2 was 98% at room air) either. Lung sounds were normal and there was no crackle or ronchus. The most prominent finding during the physical examination was the persistent cough, repeating with every breath. Leukocytosis (12400/µl) and mild thrombocytosis (378000/µl) were present in the complete blood count. All biochemical tests including serum electrolytes, kidney, and liver function tests, ferritin, d-dimer, troponin, C-Reactive Protein were normal, except there was a slight elevation in creatinine kinase (183 IU/L). In chest CT, there was a mild and limited ground-glass opacity in the right upper lobe and a pneumomediastinum (Figure 1).

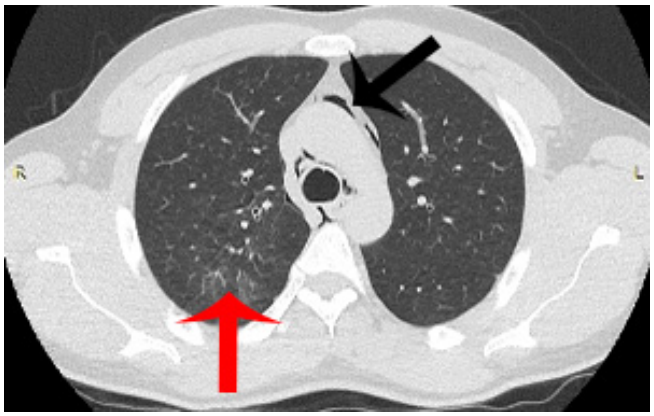

Figure 1: Chest CT showing a focal ground glass opacity (red arrow) and air in the mediastinum (black arrow).

The patient was started on hydroxychloroquine (2x200mg/day) and azithromycin (1x500mg/day) and he continued the asthma medication that he had been using. Both of the COVID-19 Polymerase Chain Reaction (PCR) tests performed two days apart, were negative. We completed the COVID-19 treatment regimen, as recommended by our medical science committee (hydroxychloroquine for 5 days and azithromycin for 3 days). We administered low molecular weight heparin and pain reliever (paracetamol, dexketoprofen) throughout the hospital stay. The patient was discharged on day 5. He had no cough by the 4th week of the diagnosis and pneumomediastinum had regressed spontaneously without causing any respiratory and circulatory complications.

DISCUSSION

Although many different symptoms have been reported in COVID 19 infection, the most common symptoms are fever, weakness, and extensive muscle pain. Especially during the pandemic, the patients with these symptoms should definitely be examined in terms of COVID-19. The reverse transcriptase-PCR test, used frequently for detection of the viral nucleic acid, has high specificity. However, false-negative test results may occur in up to 30% of the patients with COVID-19 (4). According to the results obtained from studies on PCR sensitivity, the sensitivity of PCR test ranges from 28% to 88% (5). In case of high clinical suspicion but a negative PCR test result, it is possible to benefit from chest CT findings of which the sensitivity was even higher than PCR (4).

Classical chest CT findings of COVID-19 pneumonia are bilateral, multifocal, basal, interstitial, and/or alveolar opacities (6). Extrapulmonary findings such as lymph node enlargement, pleural and pericardial effusion, are also possible. Although not often, spontaneous pneumomediastinum is one of the extrapulmonary complications of COVID-19 infection (1). The pathogenesis is not certain and it is thought to result from extensive alveolar damage or increased alveolar pressure. Most of the patients with pneumomediastinum related to COVID-19 had diffuse parenchymal changes. The patients with COVID-19 previously reported having pneumomediastinum were usually the ones with severe COVID pneumonia. So, the presence of pneumomediastinum has been suggested to be a poor prognostic factor (1,2). However, we have seen via this case that not all patients with pneumomediastinum developing during COVID-19 might have a bad prognosis. To our acknowledge, there is no such a report about pneumomediastinum in a patient with such a little parenchymal damage. The reason for pneumomediastinum in our patient was probably the persistent cough, increasing the alveolar pressure. We suppose that the most important factor in spontaneous and rapid recovery was the absence of severe parenchymal damage.

CONCLUSION

This case is important in two aspects. First of all, in this case, the diagnosis of COVID-19 was made clinically and radiologically despite PCR was negative. A negative PCR test result can't exclude the diagnosis in proper clinical and radiological findings. Second, pneumomediastinum developed in this case without serious parenchymal damage. Spontaneous pneumomediastinum, may arise in some patients with COVID-19, especially if they have severe parenchymal damage. Thus, it is presumed as a poor prognostic factor. However, it can also arise as a result of increased alveolar pressure induced by a persistent cough, in asthmatic patients without widespread parenchymal damage. Therefore the prognosis was better in this case than in patients with severe parenchymal damage.

Conflict of Interest:
There is no conflict of interest.

Patient Informed Consent:
Patient Informed consent was obtained.

Financial Disclosure:
The authors declared that this study has received no financial support.

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Geliş Tarihi : December 13, 2021
Received
Kabul Tarihi : April 29, 2021
Accepted
E Yayın Tarihi : September 01, 2023
Online published

Bu makalede yapılacak atıf
Cite this article as

Albeniz G.
Ileocaecal Intussusception Due To Inflammatory Fibroid Polyp: A Rare Case Report At District Hospital
Akd Med J 2023; 9(3): 354-356

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DOI: 10.53394/akd.1035920

Ileocaecal Intussusception Due To Inflammatory Fibroid Polyp: A Rare Case Report At District Hospital

Enflamatuar Fibroid Polibe Bağlı İleoçekal İnvajinasyon: İlçe Hastanesinde Nadir Bir Vaka

ABSTRACT
Inflammatory fibroid polyps are rare quasi tumor lesions that develop from the gastrointestinal tract's submucosa. We present an ileocecal intussusception case as due to IFP in a man aged 47 years who was admitted to a district hospital. Terminal ileum resection with right hemicolectomy was performed for this patient and the mass defined as an inflammatory fibroid polyp in pathological examination.

Key Words:
Intussusception, Inflammatory fibroid polyp, Terminal ileum

ÖZ
Enflamatuar fibroid polip, gastrointestinal sistemin submukozasından kaynaklanan nadir görülen tümör benzeri bir lezyondur. Yazımızda, terminal ileumda oluşan polipoid kütleye bağlı ileoçekal invajinasyon gelişen 47 yaşında bir erkek hastaya, kütle görünümünün kansere benzemesi nedeniyle terminal ileum rezeksiyonuyla beraber sağ hemikolektomi uygulandı. Ancak kütle patolojisinin enflamatuar fibroid polip olarak raporlanması üzerine olgu sunulmuştur.

Anahtar Sözcükler:
İnvajinasyon, Enflamatuar fibroid polip, Terminal ileum

INTRODUCTION
Intussusception is described as the invagination of a proximal segment of the intestine into a more distal segment of the bowel. When the distal section invaginates into the proximal segment, this is referred to as retrograde intussusception (1,2). Even though intussusception is a frequent malady in childhood due to lymphoid hyperplasia following viral infections, it is uncommon in adults. Clinical symptoms are cramping stomach pain, bloody diarrhea, and a tangible abdominal mass (2). Adult intussusception is different from pediatric intussusception in terms of clinical symptoms, its causes and in many ways (1-4).
Adult intussusception consists 5% of all intussusceptions, and 1%-5% of all cases of intestinal obstruction.
Inflammatory fibroid polyp (IFP) is an infrequent benign solitary tumor-like lesion that originate from the submucosa of the gastrointestinal tract (GIT) (5). They usually develop in the gastric antrum, yet may appear anywhere in the gastrointestinal tract. The most common place of development for these polyps is the ileal segment, where they trigger intussusception (6). The estimated incidence of IFP is 0.3 to 0.5% in the general population (7,8).

We present a rare ileo-cecal intussusception case due to IFP in a man aged 47 years who was admitted to a district hospital.

CASE REPORT

A man aged 47 years was admitted to the clinic as an emergency case with a history of increasing severity of colic, anorexia, nausea, and bilious vomiting for a month, with no history of abdominal distension. The physical examination revealed muscle defense and rebound pain. No blood or mucus were found on the digital rectal examination. His stools had small volume, were formed. In the last 3 months, he reported nausea, vomiting and intermittent abdominal pain. There was no significant gastric distension. Bowel sounds were hyperactive. The blood pressure was 90/70mmHg, pulse rate was 70 beats per minute, and body temperature was 37°C. Creatinine was 0.6 mg/dl (regular: 0.72-125 mg/dl) and protein of C-reactive was 130.20 mg/l (regular: 0-0.5 mg/l) in laboratory tests.19.89 ml of leukocyte count was revealed by counts of blood cells. (regular: 4.23-9.07 µl), the hemoglobin level was 12.6 g/dl (regular: 13.7-17.5 g/dl), and a platelet count was 538 µl (regular: 163-337 µl). The rest of the serum values were within regular ranges. X-rays of the abdomen and chest were also normal. The CT scans revealed intussusception due to a tumoral mass causing mechanical intestinal obstruction (Figure 1).

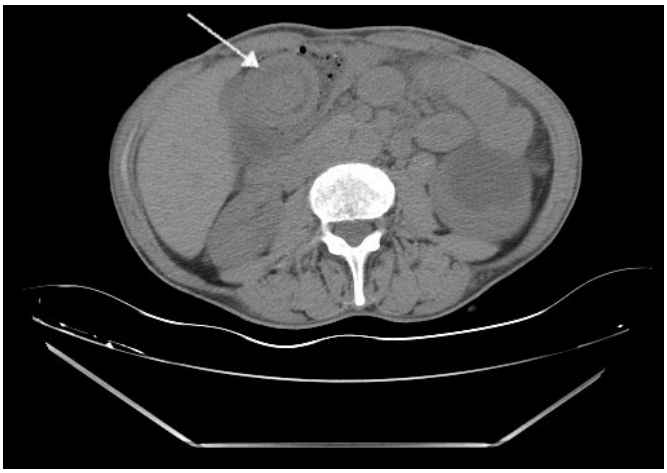

Figure 1: The CT scans revealed intussusception due to a tumoral mass causing mechanical intestinal obstruction

The patient was prepared and resuscitated for four hours in order to obtain a satisfactory urine output and laparotomy with a midline incision has been applied. The surgery revealed an ileo-cecal intussusception. The intussuscepted intestinal segment obstructed the intestinal lumen, which resulted with proximal intestinal segment dilatation. Segmental resection of intussuscepted ileocecal valve segment and end-to-end anastomosis have been realized. Resected ileum segment was 12 cm long and the resected colon segment was 28 cm long on macroscopic examination. Histopathological examination shows an IFP measuring 3.5x3x1.5 cm. Its lining mucosal surface was bleeding ulcers. On immunohistochemical analysis, Cytokeratin staining was positive. However, CD34 was negative, CD68 was negative and Ki67 was negative. There were no complications after the surgery. Five days following surgery, the patient was discharged. The eight-month follow-up period was uneventful.

DISCUSSION

Barbette was the first and Hunter was the second to describe intussusception in the literature. However, Sir Jonathan Hutchinson performed the first surgical intervention in 1871(9). Abdominal CT is currently considered the most sensitive radiological method for confirming intussusception, with a reported diagnostic accuracy of 58%-100%. On CT, a bowel-within-bowel configuration suggested by mesenteric fat and vessels compressed between the walls of the small bowel is pathognomonic of intussusception. In contrast to US, CT is unaffected by the presence of gas in the bowel lumen. Intussusception has always been thought as an illness that affects children and infants since its discovery. Intussusception has been classified according to location, i.e., enteric, colonic, ileo-caecal or ileocolic. Enteroenteric intussusception affects the small bowel, whereas colonic intussusception affects the large intestine. In ileocolic intussusception, the ileum invaginates towards the ileocaecal valve. Adult intussusceptions are more common in the small intestine (50%-88%) compared with the cases in the large intestine (12%-50%) (10). Intussusception may be grouped as primary (idiopathic) or secondary due to underlying etiological causes (benign or malignant lesion). Adult intussusceptions that occur due to a primary or idiopathic cause are most likely to arise in small intestine,accounting for roughly 10% of cases. Secondary intussusceptions are linked to a pathological disease that involves a lead point and is more common in adults. In published literatures, underlying etiology was malignant in ileocolonic and colocolonic intussusceptions meanwhile it was mostly benign in enteroenteric intussusceptions. Thus, the most crucial criteria is the type of the etiology to decide surgical process for an adult patient with no preoperative histological diagnosis. Adult intussusceptions are most commonly caused by benign tumors. IFPs are a rare cause of intussusception among adults (11,12).

CONCLUSION

The appropriate management that best fits to adult intussusception is controversial. Abstractly, surgical reduction prior to resection may allow for more limited resection; nevertheless, the possibility of intraluminal seeding or venous tumor diffusion during lesion manipulation should also be considered. The cause of small intestine intussusceptions, the frequency of malignancy varies between 1% to 47%, with the generality of lesions are metastatic. Recommendation is to perform resection without reduction for primary lesions which are the majority of these type of lesions.

Conflict of Interest Statement: None.

Funding: None.

Consent: The patient provided written informed consent for the publishing of this case report and associated pictures. A copy of the written consent is available for review from the Editor-in Chief of this journal.

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akdeniztıp dergisi
medicaljournal

Cilt/Vol.9, No. 3, 2023

Aşağıda isme göre alfabetik sırayla listelediğimiz hakemlere,
özenli değerlendirmeleri ve yol göstericilikleri için şükranlarımızı sunarız.

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Bumin DEĞİRENCİ
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