DÜZCE TIP FAKÜLTESİ DERGİSİ
DUZCE MEDICAL JOURNAL

e-ISSN: 1307-671X

Yıl Year 2019 Cilt Volume 21 Sayı Issue 3

Düzce Tıp Fakültesi Dergisi (Düzce Tıp Fak Derg) / Duzce Medical Journal (Duzce Med J)
e-ISSN: 1307-671X

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Yılda üç kez yayınlanan uluslararası hakemli bir dergidir. / An international peer-reviewed journal published three times a year.
Yayın dili Türkçe ve İngilizcedir. / Publication languages are Turkish and English.
Makalelerin sorumluluğu yazarlarına aittir. / The authors are responsible for their articles.

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Davetli Derleme / Invited Review
doi: 10.18678/dtfd.662776

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2019;21(3):151-155

Ağız Mukozası Epitelinde Psödoepitelyomatöz Hiperplazi

Pseudoepitheliomatous Hyperplasia in Oral Mucosa Epithelium

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ÖZ

Ağız mukozasını örten çok katlı yassı epitel irritasyonlara açıktır ve anormal reaktif proliferasyonlar gösterebilir. Bu değişiklikler anormal bir klinik kitle yaratabilir ve histolojik olarak neoplastik lezyonları taklit edebilir. Bu reaksiyonlar psödoepitelyomatöz hiperplazi veya psödokarsinomatöz değişiklik olarak adlandırılmaktadır. Epitelin rejeneratif amaçla gösterdiği bu tür anormal proliferasyonlar oral patolojide deneyimsiz hekimlerin yanlışlıkla ağız kanseri tanısı koymalarına neden olabilir. Diğer yandan histolojik benzerliklerden dolayı oral kanserler de reaktif lezyon olarak yanlış tanı alabilirler ve bu da hastaların doğru tedavi almalarında gecikmelere neden olacaktır. Bu makalede ağız ve çevre dokularında psödoepitelyomatöz hiperplaziye yol açabilen nedenlere ve ilişkili olduğu spesifik hastalıklara değinilecektir. Aynı zamanda bu lezyonun morfolojik özellikleri ile histolojik benzerlik gösterebilen oral kanserlerle ayırıcı tanısı işlenecektir. Klinik özelliklerin iyi bilinmesi ve histolojik bulguların dikkatli değerlendirilmesi ileride gelişebilecek istenmeyen sorunları önleyecektir. Bu yazıda verilen bilgiler daha çok patologların kullanımına yönelik olmakla birlikte, klinisyenlerin de tanı sürecindeki sorunları ve güçlükleri bilmeleri doğru tanıyı koymada yol gösterici olacaktır.
Keywords: Psödoepitelyomatöz hiperplazi; psödokarsinomatöz değişiklik; ağız mukozası.

ABSTRACT

Squamous epithelium covering the oral mucosa is open to a variety of irritations and may show aberrant reactive proliferations. These changes may create an abnormal clinical mass and histologically mimic neoplastic lesions. These reactions are called pseudoepitheliomatous hyperplasia or pseudocarcinomatous change. Exaggerated abnormal reactive changes may cause misdiagnosis of oral cancer in the mouth by inexperienced persons in oral pathology. On the other hand, due to histological similarities, also oral cancers may underdiagnosed wrongly as reactive lesions and lead to delays in cancer diagnosis and treatment. In this article, the causes of pseudoepitheliomatous hyperplasia and related specific diseases will be discussed. Additionally, the differential diagnosis of oral cancers from reactive lesions will be covered. The well knowing of the clinical features and a careful histological evaluation will prevent undesirable problems in the future. The information of the article is more useful for the pathologists; however, it will be helpful for the clinicians to know the problems and difficulties in the accurate diagnostic process.
Anahtar kelimeler: Pseudoepitheliomatous hyperplasia; pseudocarcinomatous change; oral mucosa.

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Geliş Tarihi / Received : 06.11.2019
Kabul Tarihi / Accepted : 17.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 22.12.2019

GİRİŞ

Psödoepitelyomatöz veya psödokarsinomatöz hiperplazi olarak bilinen reaktif değişiklik, başta inflamasyon olmak üzere, dermatozlar, neoplaziler ve diğer değişik etkenlere bağlı olarak mukozalar ve deride epitelin rejeneratif amaçla gösterdiği anormal proliferasyondur (1-3). Yaralanma bölgelerinde yabancı olarak kabul edilen maddelerin epitel yolu ile atılımını sağlamaya yönelik (transepidermal eliminasyon) bir fonksiyon olarak da karşılaşılır. Psödoepitelyomatöz hiperplazi rejeneratif sürecin devam ettiği ve tamamlanamadığının göstergesidir. Bütün epitellerde görülebilir, ancak irritasyonların daha yoğun olduğu ağız ve çevre dokuları mukozalarında daha sık görülmektedir. Mukozalarda psödoepitelyomatöz hiperplazi yüzey epiteli yanı sıra minör tükürük bezi duktus ve asini epitellerinde de belirgin olarak görülebilir (2).

Psödoepitelyomatöz hiperplazi histolojik görünümü nedeni ile yassı epitel hücreli karsinoma başta olmak üzere epitelyal tümörlere benzerlik gösterebilmekte ve ayırıcı tanılarda yer almaktadır. Benzerlik nedeni ile ağız kanserleri ile psödoepitelyomatöz hiperplazi ayrımı zorluğu ağız kanserlerine geç tanı konulmasına yol açabilmektedir. Yine aynı nedenle psödoepitelyomatöz hiperplazinin yanlış kanser tanısı alabilmesi mümkün olmaktadır. Psödoepitelyomatöz hiperplazi ve ağız karsinomları ayrımı özellikle yüzeyel, küçük ve kötü oryante olmuş dokularda daha zordur. Ağız kanserlerinin önemli bir kısmı diferansiye tip yassı epitel hücreli karsinomlardır ve bunlar histolojik olarak reaktif lezyonlara benzediği için ayırıcı tanıları güç olabilmektedir (4,5). Diferansiye tip karsinomlar özellikle dudak ve dilde daha sıktır. Psödoepitelyomatöz hiperplazi ile ağız karsinomu ayırımında karmaşaya diferansiye tip displazi ve diferansiye tip karsinomun iyi anlaşılmamış olması da sebep olmaktadır.

Tecrübe, klinik özelliklerin iyi bilinmesi ve histolojik bulguların dikkatli değerlendirilmesi sorunları önleyici olabilmektedir. Reaktif ve neoplastik lezyonların tedavilerinin farklılığı ve birbirlerinden ayrımının önemi iyi bilinmektedir.

Bu makalede ağız ve çevre dokularında psödoepitelyomatöz hiperplaziye yol açabilen nedenler, bu lezyonun morfolojik özellikleri ile histolojik benzerlik gösterebilen ağız karsinomundan bahsedilecek ve örnekler verilecektir. Verilen bilgiler esas olarak patologların kullanımına yönelik olmasına rağmen, klinisyenlerin de tanı sürecinin sorunları ve güçlüğünü bilmelerini sağlayabilir.

PSÖDOEPİTELYOMATÖZ HİPERPLAZİ MORFOLOJİSİ

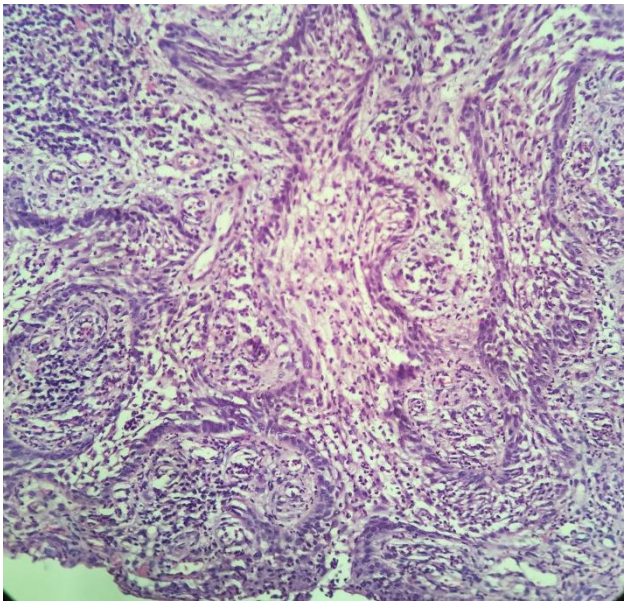
Psödoepitelyomatöz hiperplazi sıklıkla çok katlı yassı epitelde görülen, benign abartılı epitel proliferasyonudur. Abartılı epitel proliferasyonu makroskopik olarak kitle görüntüsü oluşturabilir ve histolojik olarak yassı epitel hücreli karsinoma benzeyebilir. Bu lezyona benzer reaktif değişiklikler diğer tip epitellerde de görülebilir ancak daha seyrektir. Psödoepitelyomatöz hiperplazi lümene doğru gelişen papillomatöz hiperplazi ve aşağı yönde prolifere olan sivri uçlu invajinasyonlar içerir (Resim 1). Mukozalar gibi çok katlı yassı epitel ile örtülü dokularda, beraberinde subepitelyal alanda bulunan minör bezlerde asini ve duktus epitellerinde de reaktif, abartılı hiperplastik değişiklikler izlenebilir. Psödoepitelyomatöz hiperplazi proliferasyon yeteneği fazla olan minör tükürük bezi duktus epitellerinde de gelişebilir (2). Klinik olarak bu tür lezyonlar, genellikle küçük boyutlu, plak, nodül, verrükoid keratotik kabarıklık veya kısmen ülsere lezyon halinde olabilir (1,3). Lezyonlar özgün bir makroskopik yapı veya renk göstermez.

Psödoepitelyomatöz hiperplazi ile yassı epitel hücreli karsinom ayrımı bazen gerçekten zor olabilir (2). Psödoepitelyomatöz hiperplazi özelliklerinin iyi bilinmesi yanı sıra dikkatli klinik değerlendirme ayırım zorluğunu azaltır. Bu tür lezyonların ve ağız kanserinin doğru ayrımı, neoplastik olmayan bir lezyona yanlış kanser tanısı konulmasını veya tam tersine kanser tanısının atlanılması ve gecikilmesini önleyecektir. Tedavileri ve seyirleri çok farklı olduğu için bu ayırım çok önemlidir.

Histolojik olarak, psödoepitelyomatöz hiperplazi de hiperplastik yassı epitelde hücre içi ve hücreler arası belirgin ödem ile epitel içinde yoğun polimorfonükleer lökosit infiltrasyonu en önemli bulgudur (1-3,6,7). Nötrofil ve beraberinde eozinofil lökositlerden oluşur. Ancak her olguda bu değişiklik belirgin olmayabilir veya karsinomlar içinde de inflamatuar hücreler bulunabilir.

Psödoepitelyomatöz hiperplazide epitel hücrelerinde nükleer irileşme bulunabilir, ancak bu hücrelerin sitoplazmaları da genişlemiştir. Ancak nükleer/sitoplazmik oran korunmuştur. Diskeratoz, kompakt parakeratoz, keratinosit nekrozu ve apopitoz beklenen değişiklik değildir. Belirgin nükleer atipi, atipik mitoz, keratinositlerde tek hücre nekrozu daha çok yassı epitel hücreli karsinomlarda görülmesi beklenen bulgulardır.

Ağız mukozasındaki psödoepitelyomatöz hiperplazide subepitelyal bağ dokusu ödemli, gevşek yapıdadır ve granülasyon dokusu görünümündedir. Deri dokusundaki PEH'de dermal desmoplazi bulunabilir (3). Submukozal



Resim 1. Mukoza epitelinde psödoepitelyomatöz hiperplazi olan alanda intraepitelyal ödem, aşağı yönde proliferasyon ile epitel içi yoğun PMN lökosit ekzositozu, HEx200

bağ dokusu içinde apse oluşumu, granülomatöz reaksiyon, yabancı cisim tipi dev hücre reaksiyonu, yoğun eozinofil lökosit ve plazma hücre infiltrasyonu enfeksiyöz bir etyoloji ve buna bağlı bir reaksiyonu akla getirmelidir (8). Bu tabloda öncelikle PAS, GMS ve Ziehl-Nielsen ve Giemsa gibi histokimyasal boyamalar kullanarak ve polarize ışıkta yabancı cisim aranarak etken bulunmaya çalışılmalıdır. Psödoepitelyomatöz hiperplazi değerlendirmesinde hastanın yaşı, mesleği, yaşadığı bölge, lezyonun gelişim şekli ve süresi gibi verileri içeren klinik hikâye dikkatle değerlendirilmelidir.

AĞIZDA PSÖDOEPİTELYOMATÖZ HİPERPLAZİ SEBEPLERİ

Psödoepitelyomatöz hiperplazi, ağızda klinik olarak nodüler kabarıklık oluşturuyor ise mukoza epiteli sıklıkla ülseredir veya tamamlanmamış kronik bir iyileşme süreci vardır. Boyutu nadiren iki santimin üzerine çıkar. Diş çekimi kaviteleri, odontojenik kist epitelleri (Resim 2), greft uygulama ve periodontal inflamasyon alanları, sekestre-nekrotik kemik trabekülleri (Resim 3) etrafında nodüler lezyon olarak görülür. Progresif büyümesi olmaz, çok derine inmez, sıklıkla boyutu görüldüğü kadar kalır. Odontojenik lezyonlarda yaralanma bölgesinin temizlenmesi, yara bakımı ve granülasyon dokularının çıkarıldığı işlemler sıklıkla tedavi edicidir ve nüks etmesi beklenmez. Nüks eden lezyonlarda spesifik bir enfeksiyonun eşlik etmesi olasılığı düşünülmelidir.

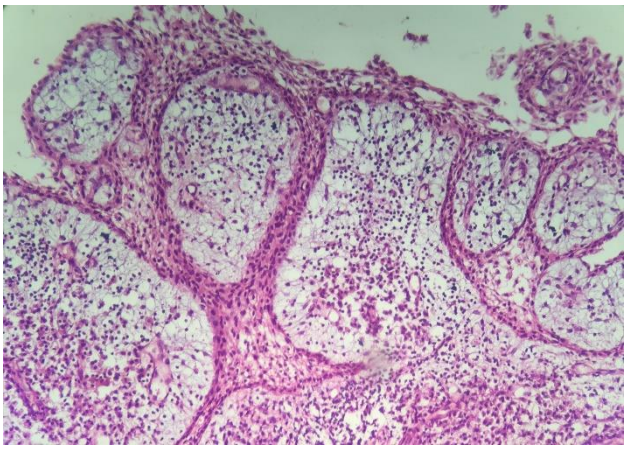
Epulis fissuratum, median romboid glosssit, oral submuköz fibrozis ağızda psödoepitelyomatöz hiperplaziye sebep olabilen ağız lezyonlarıdır (2). Yanık, lazer uygulama skarları da psödoepitelyomatöz hiperplazi oluşturan sebeplerdendir. İnflamasyon ağız mukozası ve dişetlerinde sık olduğu için kronik inflamatuar fibröz hiperplazilerde mukoza epiteli de psödoepitelyomatöz hiperplazi gösterecektir. İnflamasyonun eşlik ettiği psödoepitelyomatöz hiperplazi olan alanlarda matriks metalloproteaz miktarları da artmaktadır. Matriks metalloproteaz artışı, eşlik eden rejeneratif değişiklikler ve yüksek sitokin salınımları metastatik tümörler için psödoepitelyomatöz hiperplazi olan bölgeye gelme (homing) olasılığını artırabilmektedir. Bu nedenle inflamasyon olan bölgelerde metastazlar da daha sık olmaktadır.

Psödoepitelyomatöz hiperplazi ağız bölgesinde odontojenik tümörler olan skuamöz odontojenik tümör, akantomatöz ameloblastoma ve Pindborg tümörü ile benzerlikler gösterebilir (6). İmmünohistokimyasal olarak psödoepitelyomatöz hiperplazi ve yassı epitel hücreli karsinom ayırımında yoğun ve epitelin bütün tabakalarında yaygın P53 yüksek pozitifliği yassı epitel hücreli karsinoma tanısını desteklemek için kullanılabilir (4).

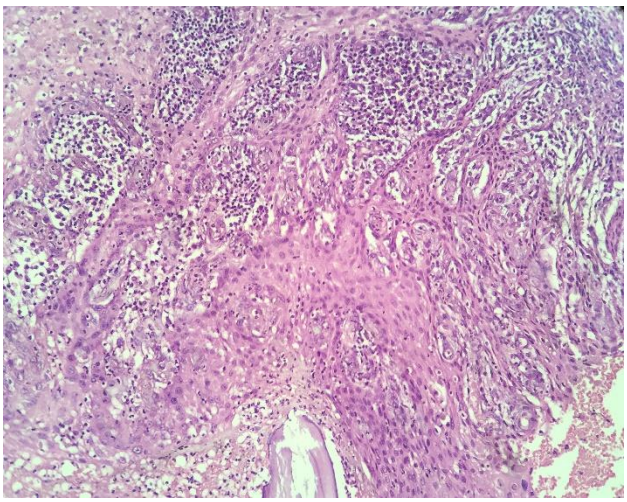
Odontojenik inflamatuar kist (radiküler veya rezidüel) epitellerinde psödoepitelyomatöz hiperplazi bulunabilir ve özellikle inflamasyonun akut olduğu dönemde daha belirgindir. Benzer şekilde mukus ekstravazasyon kistlerinde mukoza epitelinde psödoepitelyomatöz hiperplazi izlenebilir. Osteomiyelit, radyoterapi sonrası gelişen nekroz ve bifosfanat nekrozlarında, sekestre trabekülleri vücut dışına atmaya yönelik olarak nekroz çevresini demarke etmeye çalışan epitel subepitelyal invajinasyon ve psödoepitelyomatöz hiperplazi gösterir (7,9-11). Piyojenik granülom ve yabancı cisim reaksiyonlarında ülsere yüzey epitellerinde bu lezyon kaçınılmaz olarak bulunur. Ayrıca iskemik nekroza bağlı olarak tükürük bezi asini ve duktuslarında görülen skuamoz metaplazi (nekrotizan sialometaplazi) tümörlerle karışabilen histolojik bir bulgudur ve psödoepitelyomatöz hiperplazi örneği bir değişikliktir.

SPESİFİK HASTALIKLARLA İLİŞKİLİ PSÖDOEPİTELYOMATÖZ HİPERPLAZİ

Submukozal granülomatöz reaksiyon bulunan olgularda yüzey epitelinde hiperplastik değişiklik de bulunuyor ise tüberküloz gibi mikobakteriel ve mantar enfeksiyonu olasılığı aranmalıdır (8). Benzer şekilde Basiller angiomatözde, Aktinomikozis ve Leishmaniazisde (Donovonazis) psödoepitelyomatöz hiperplazi oluşabilir (2). Wegener granülomatozu gibi etyolojisi tam belli olmayan



Resim 2. İnflamatuar odontojenik kist epitelinde psödoepitelyomatöz hiperplazi ile uyumlu proliferasyon, subepitelyal alanda ödemli gevşek bağ dokusu ve yoğun inflamatuar hücre infiltrasyonu, HEx200



Resim 3. Nekrotik diş-kemik görünümündeki sert dokuyu vücut dışına çıkarmaya (transepidermal eliminasyon) yönelik olarak mukoza epitelinde psödoepitelyomatöz hiperplazi ile uyumlu proliferasyon, ödem ve subepitelyal aktif-kronik yoğun inflamatuar hücre infiltrasyonu, HEx200

hastalıklarda da subepitelyal granülomatöz reaksiyon ile yüzey epitelinde psödoepitelyomatöz hiperplazi bulunabilir. Viral lezyonlarda da bu tür değişiklikler olabileceğinden de bahsedilmektedir. Özellikle AIDS başta olmak üzere immünsupresif hastalarda hiperplastik herpes ve hiperplastik zoster enfeksiyonları ile birlikte psödoepitelyomatöz hiperplazi tanımlanmıştır (12).

Fungal enfeksiyonların da bu tür lezyonlar oluşturabileceğine ait çok sayıda yayın mevcuttur (5). Hiperplastik kandida, tümöre sebep mi, tümörle birlikte bir bulgu mu sorusu tam yanıt bulamamıştır ve epitelde belirgin rejenerasyon yaratabilir (5,8). Blastomikoz, Aspergillozis, Mukormikozis gibi fungal enfeksiyonlarda da mukoza epitellerinde hiperplastik değişiklikler belirgin olabilir (2).

DERMATOLOJİK MUKOZAL LEZYONLARDA PSÖDOEPİTELYOMATÖZ HİPERPLAZİ

Ağız mukozasını tutan hipertrofik lupus eritematozus ve hipertrofik liken planusta rejenere epitel immüno-inflamatuar reaksiyona bağlı olarak hiperplazi gösterir (Resim 4). Kronik lezyonlarda epiteldeki yapısal değişiklikler karsinom benzeri bulgu yaratabilir. Ayrıca lupus eritematozus ve liken planus gibi kronik, dermatolojik mukozal lezyonlarda ağız karsinomu riski de artmıştır. Dermatolojik hastalığın uzun yıllardır bulunması, yaşlı hastada görülmesi, uzun süredir sigara kullanımının olması ile dil-retromolar bölge gibi riskli bölgelerde lezyon bulunması durumunda ağız karsinomu riski daha da artmaktadır. Prekanseröz lezyon olarak kabul edilen liken planusta yüzey epitelinde psödoepitelyomatöz hiperplazi belirgin olabilir ve epitel aşağı yönde proliferasyon gösterebilir (13). Bu lezyonlarda klinikopatolojik değerlendirme önemlidir. Nekrotik-apoptotik keratinosit saptanması liken tanısını destekleyen bulgu olarak kullanılmamalıdır, çünkü tümörlerde de görülebilir. Benzer şekilde pemfigus grubu hastalıkların ağızda uzun süredir bulunması ağızda psödoepitelyomatöz hiperplaziye sebep olurken, bu hastalarda ağız karsinomu riski de artmıştır. Dermatolojik lezyonlarda ağız karsinomu geliştiği durumda genellikle daha agresiv davranış beklenir ve histolojik olarak sitolojik atipi belirgindir.

Sweet sendromda submukozal alanda PMN lökosit zengin yoğun inflamasyon bulunur, yüzeyde ise ciddi psödoepitelyomatöz hiperplazi görülebilmektedir (14). Bu görünüm lignöz mukozal hastalık benzeri görünüme yol açabilmektedir. Mukozal lignöz periodontit olgularında erken ve geç evre lezyonlarında yüzey epitelinde psödoepitelyomatöz hiperplazi benzeri değişiklikler izlenir (15).

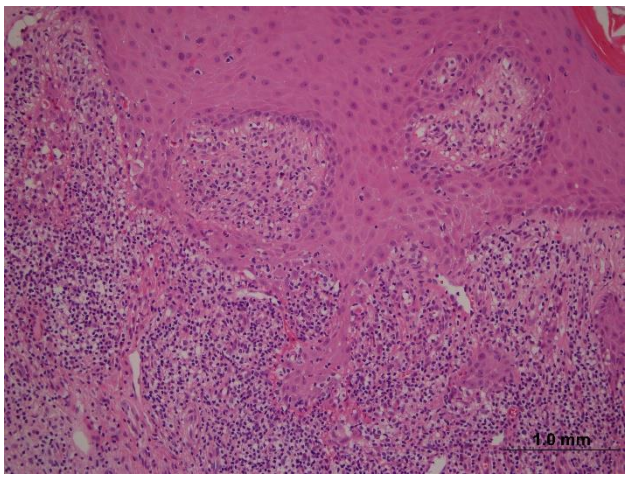
Ağız ve çevre dokularında yapılan döğme (tatto) veya ağızda kullanılan metaller ve amalgam pigmentasyonu bulunan bölgelerde mukoza epitelinde de bu tür lezyonlar oluşabilir (16). Psödoepitelyomatöz hiperplazi benzeri lezyonlar döğme yapma sonrası kısa sürede gelişir ve bu bulgu ağız karsinomu olasılığını dışlamada kullanılabilir.

Dudakta erken evre kanserlerde, yanlış olarak psödoepitelyomatöz hiperplazi olarak değerlendirilen, bromoderma ve sifiliz gibi hastalıklara bağlanmaya çalışılan değişiklikler tanı gecikmelerine yol açmıştır.

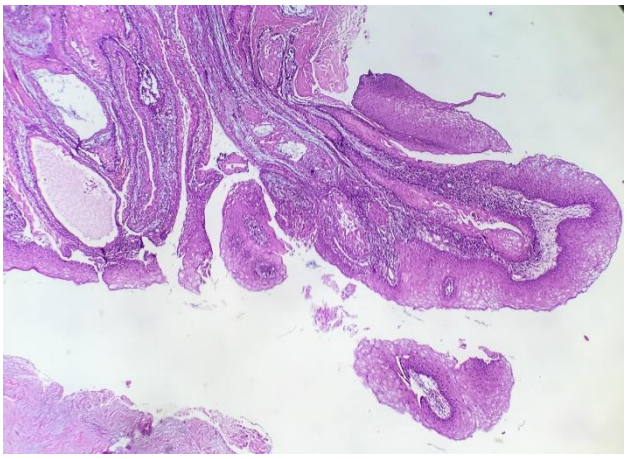
NEOPLASTİK LEZYONLARIN ÜZERİNDE GELİŞEN PSÖDOEPİTELYOMATÖZ HİPERPLAZİ

Bazı neoplastik lezyonlar üzerinde psödoepitelyomatöz hiperplazi görülmesi bilinen bir değişikliktir. Mukozal granular hücreli tümör ve üzerindeki epitelde yassı epitel hücreli karsinom benzeri değişiklik buna iyi bir örnektir (1,2,4). Bu hiperplazi bazen çok belirgin ve dikkat çekici olabilir ve granüler hücreli tümör tanısı fark edilemeyebilir. Özellikle yüzeyel alınan biyopsilerde yanlışlıkla yassı epitel hücreli karsinom tanısı verilebilir. Benzer şekilde bazı non-Hodgkin lenfoma infiltrasyonlarında yüzey epitelinde hiperplastik değişiklikler abartılı olabilir (17,18). Non-Hodgkin lenfoma tutulumlarında mukozada ülsere olmayan nodüler kabarıklık ve bölgesel lenf nodlarında büyüme bulunması lenfoma düşündürücü bir bulgudur. Lenfoid neoplazilerde neoplastik hücrelerin sitokin salgılamaları ile psödoepitelyomatöz hiperplazi geliştiği düşünülmektedir (18).

Mukoepidermoid karsinom, periferal yerleşimli odontojenik tümörler veya metastatik karsinom gibi malign tümörlerin yüzeyinde verrüköz veya papillomatöz yapıda hiperplazi oluşabilir. Periferal ameloblastomalarda yüzey epiteli tutulumunda psödoepitelyomatöz hiperplazi tümörle devamlılık gösterir (Resim 5). Dermatofibroma



Resim 4. Liken planusta, kronik otoimmün inflamasyona bağlı olarak mukoza epiteli subepitelyal alana doğru psödoepitelyomatöz hiperplazi göstermektedir. HEx200



Resim 5. Periferal yerleşimli odontojenik tümör yüzeyinde mukoza epitelinde papilliform hiperplazi, HEx100

ağızda az görülen bir lezyondur, ancak üzerinde epitel hiperplazisi bulunması önemli tanısal bir bulgudur. Nevüsler ve melanom gibi melanositik lezyonların üzerindeki yassı epitelde belirgin hiperplazi bulunabilir. Akciğer ve kolon adenokarsinomları ile melanomlarda hedefe yönelik tedavi olarak kullanılan anti-braf antikorlar deri ve mukozalarda psödoepitelyomatöz hiperplazi benzeri lezyonlara ve hiperkeratoz oluşumuna sebep olabilir.

Çocuk ve gençlerde ağız karsinomu az görüldüğü için, yassı epitel hücreli karsinomun erken evrelerinde morfolojik değişiklikler psödoepitelyomatöz hiperplazi olarak değerlendirilebilir. Karsinoma kunikulatum gibi diferansiye tip karsinomlarda subepitelyal alana oyuklar açar gibi ilerleme olduğu için psödoepitelyomatöz hiperplazi benzeri yanlış bir değerlendirmeye yol açabilir.

SONUÇ

Sonuç olarak, psödoepitelyomatöz hiperplazi tanısı ve ağız karsinomu ayırımında bir kontrol listesi yapılmalıdır. Epitel içinde ödem, PMN lökosit veya eozinofilik apse oluşumu, epidermotropizm, ara yüz mukoziti bulguları, epitelde ayrılma, bazal membran kalınlaşması, subepitelyal granülasyon dokusu benzeri görünüm, granülomatöz reaksiyon, yabancı cisim veya neoplastik bir lezyon bulunması psödoepitelyomatöz hiperplaziyi destekleyen bulgular olarak düşünülür. Kompakt parakeratoz, diskeratoz, epitelde sitoplazmik eozinofili artması, nukleus/sitoplazma oranında nukleus lehine artma, bazal tabakaya yakın keratin yumağı oluşumu, dezmoplastik bağ dokusu, diferansiye tip ağız kanseri ihtimalini desteklemektedir. Halen ayırıcı tanıda kullanılabilecek kesin moleküler bir veri de yoktur (19). Bu nedenle kesin tanı sürecinde klinik bulguların da dikkatle değerlendirilmesi önem kazanmaktadır.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.570027

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):156-161

Evaluation of Sonoelastography Compatibility on the Achilles Tendon Between Different Devices and Observers

Aşil Tendonunun Sonoelastografisinde Farklı Cihazlar ve Gözleyiciler Arasındaki Uyumluluğun Değerlendirilmesi

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Geliş Tarihi / Received : 07.07.2019
Kabul Tarihi / Accepted : 17.10.2019
Çevrimiçi Yayın Tarihi / Available Online : 04.11.2019

ABSTRACT

Aim: To investigate the reliability of sonoelastography by comparing the Achilles tendon strain ratio obtained in healthy volunteers by different observers with different sonoelastography devices working on the same principle.
Material and Methods: A total of 80 Achilles tendons in 40 volunteers without chronic disease were evaluated using Toshiba and Hitachi devices using real-time elastography principle. The Kager fat pad was selected for strain ratio measurement. Each tendon was evaluated with both devices twice by both observers. The intraobserver and interobserver agreement were examined by intraclass correlation coefficient (ICC) obtained by two-way mixed ANOVA model for absolute agreement and interpreted as Ko and Li (11) suggested.
Results: Interobserver agreement in the first and second measurements of the Hitachi device and in the second measurements of the Toshiba device was found to be good (average ICC>0.75). The interobserver agreement in the first measurements made on the Toshiba device was found to be lower (average ICC=0.729, p<0.001). The intraobserver agreement was found to be excellent (ICC>0.90) for both device. The interobserver agreement for the Toshiba device was found lower than for the Hitachi device. Mean strain ratio was 2.96±1.07 for the Hitachi device and 3.54±1.03 for the Toshiba device. Measurements obtained from the Toshiba device were determined as significantly higher than those from the Hitachi device.
Conclusion: There may be differences in strain rates depending on the compression application limits of the devices, in studies carried out using different devices. Therefore, intraobserver and interobserver agreement should be evaluated separately for each device.
Keywords: Sonoelastography; strain ratio; achilles tendon.

ÖZ

Amaç: Aynı prensiple çalışan farklı sonoelastografi cihazlarında, farklı gözleyiciler tarafından sağlıklı gönüllülerden elde edilen aşil tendonu gerinim oranlarını karşılaştırarak sonoelastografinin güvenilirliğini araştırmak.
Gereç ve Yöntemler: Kronik hastalığı olmayan 40 gönüllüde toplam 80 aşil tendonu, real-time elastografi prensibi ile çalışan Toshiba ve Hitachi marka cihazlar kullanılarak değerlendirildi. Gerinim oranı ölçümü için Kager yağ planı seçildi. Her bir tendon, her iki cihazda her iki gözleyici tarafından iki kez değerlendirildi. Gözleyici içi ve gözleyiciler arası uyum, iki yönlü ANOVA modelinden mutlak uyum için elde edilen sınıf içi korelasyon katsayısı (SKK) ile incelenerek Ko ve Li'nin (11) önerdiği sınıflandırmaya göre yorumlandı.
Bulgular: Hitachi marka cihazda yapılan birinci ve ikinci ölçümlerde, Toshiba marka cihazda yapılan ikinci ölçümde gözleyiciler arası uyumun iyi seviyede olduğu tespit edildi. (ortalama SKK>0,75). Toshiba marka cihazda yapılan birinci ölçümde ise gözleyiciler arası uyumun daha düşük olduğu saptandı (ortalama SKK=0,729, p<0,001). Her iki cihazda da gözleyiciler içi uyumun mükemmel seviyede olduğu izlendi (SKK>0,90). Toshiba marka cihaz için gözleyiciler arası uyumun Hitachi marka cihaza göre daha düşük olduğu görüldü. Gerinim oranlarının ortalaması Hitachi marka cihaz için 2.96±1.07 ve Toshiba marka cihaz için 3.54±1.03 idi. Toshiba marka cihazdan elde edilen ölçümlerin, Hitachi marka cihazdan elde edilen ölçümlere göre anlamlı düzeyde yüksek olduğu belirlendi.
Sonuç: Farklı cihazlarla yapılan çalışmalarda cihazların kompresyon uygulama sınırlarına bağlı olarak gerinim oranlarında farklılıklar olabilir. Bu nedenle her cihaz için gözleyici içi ve gözleyiciler arası uyum ayrı ayrı değerlendirilmelidir.
Anahtar kelimeler: Sonoelastografi; gerinim oranı; aşil tendonu.

Presented as an abstract at European Congress of Radiology, ECR 2016 (March 02-06, 2016, Vienna, Austria).

INTRODUCTION

Sonoelastography is an imaging method based on ultrasonography (US), which uses conventional US devices to semi-quantitatively measure the degree of localisation change according to the deformation characteristic proportional to the hardness of the tissue on which pressure is applied (1-6).

That tissue elasticity can be revealed with elastography has been known since the beginning of the 1980s. Rapid developments in computer and US technology in recent years has enabled the widespread use of sonoelastography. With studies showing that sonoelastography can be successfully applied in the diagnosis of breast, prostate, thyroid, lymph node, muscle and tendon lesions, it has become more frequently used in current routine practice (4,5,7,8).

In addition to the evaluation of tumoral lesions in various organs, there is increasing application of sonoelastography in the musculoskeletal system. There are studies in literature that have described it for the evaluation of the Achilles tendon in particular. Elasticity patterns have been defined and findings of tendinitis and similar pathologies have been reported in healthy individuals with elastography of the Achilles tendon (9).

Although many clinicians currently prefer magnetic resonance imaging (MRI) for the evaluation of the musculoskeletal system following physical examination, US is an alternative imaging method to MRI in several situations. Especially in the evaluation of superficially located structures in the musculoskeletal system, US examination can be made comfortably using linear high-frequency probes. Furthermore, as US is inexpensive, repeatable and easily available, it can be superior to MRI in daily practice.

There are currently different sonoelastography devices available and different methods are used. To the best of our knowledge, there is no study in literature that has investigated the compatibility between devices and between the practitioners examining and interpreting the sonoelastography, which is a subjective method.

Therefore, the aim of this study was to determine the intra and interobserver compatibility of Achilles tendon strain ratio using sonoelastography devices with similar mechanisms produced by different firms.

MATERIAL AND METHODS

Patients and Study Protocol

By evaluating normal Achilles tendon strain ratios (SR) on 2 different devices by 2 different researchers at 2 different times, it was investigated whether or not the same values were given by the researchers and the devices at different times.

Volunteers included in this study were selected by random sampling method. The sample size was calculated using GPower 3.1 software (10). The sample of the study was calculated as 80 with a 95% confidence interval and an expected interobserver agreement of 0.7. The study included 42 volunteers selected from staff and their relatives at Ankara Atatürk Training and Research Hospital. Informed consent was obtained from all participants and approval for the study was granted by the Clinical Research Ethics Committee of Ankara Atatürk Training and Research Hospital (decision no: 27, dated: 14.01.2015). All procedures were conducted in compliance with the principles of the Helsinki Declaration. Two volunteers were excluded from the study because there was little Kager fat tissue and a negative effect of compression. Thus, the study was applied to 80 tendons of the remaining 40 volunteers. The study participants comprised 16 males with a mean age of 28.69±7.09 years and 24 females with a mean age of 31.88±6.00 years.

All the participants had no history of trauma to the Achilles tendon, no surgery and no episodes of pain. In all cases, systemic inflammatory diseases such as rheumatoid arthritis, spondyloarthropathy and hypercholesterolemia, which could be associated with tendon abnormalities, were discounted.

Imaging

The Applio 500 (Toshiba Medical Systems, Co Ltd Otowara, Japan) and Hitachi Vision Preirus Colour Doppler US devices (Hitachi Medical Systems, Tokyo, Japan) were used for imaging.

For the acquisition of the images on both devices, the subject was positioned prone with the ankles at the lower end of the gurney (Figure 1). Evaluation was made from the mid level 2-6 cm proximal to the attachment point of the Achilles tendon to the calcaneus.

The tendons were imaged twice on both devices by both researchers at an interval of approximately 10 days. On the Hitachi device, an EUB-54 MA 13x6 Mhz microcomposite linear probe was used at 13 MHz frequency, and on the Toshiba device, a Toshiba PLT-1204 BX linear probe at 12 MHz frequency. The musculoskeletal pre-settings were fixed by the devices and the elastograpy evaluation and measurements of the SR were taken using the integrated software (Figures 2, 3).

To avoid anisotropy, care was taken that the probe was placed vertically on the tendon and the compression ratios were symmetrical on consecutive images. For the strain ratio (SR) measurement, the region of interest (ROI) was standardised at a dimension of 20x5 mm. The ROI was first placed on the centre of the Achilles tendon (A), then on the Kager fat pad (B), which was accepted as reference tissue. The SR was automatically calculated by the devices as B/A values.

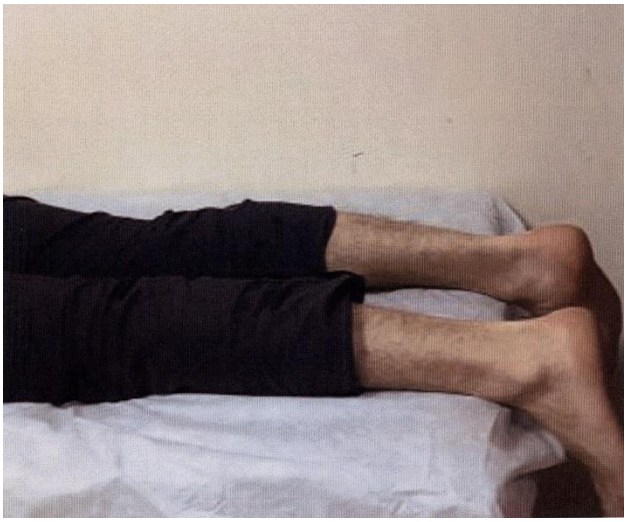

Figure 1. Positioning of the subject on the examination table

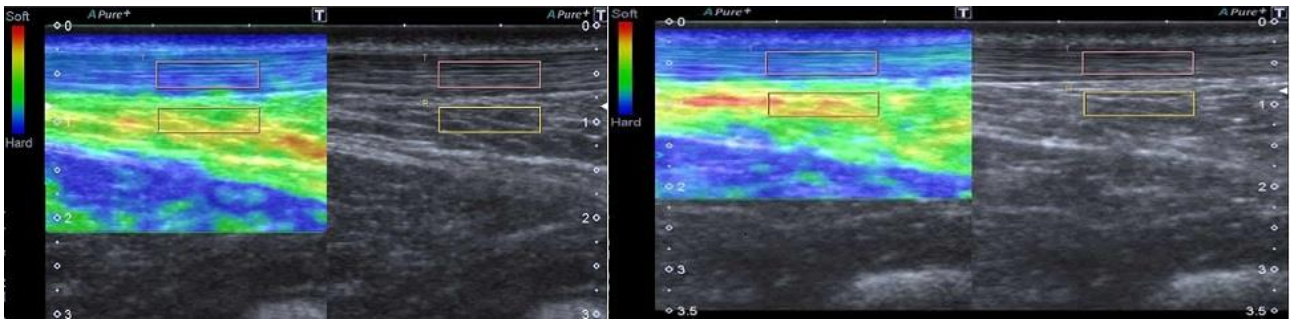

Figure 2. Images of the 1st and 2nd examinations of the same subject by Observer 1 on the Toshiba device

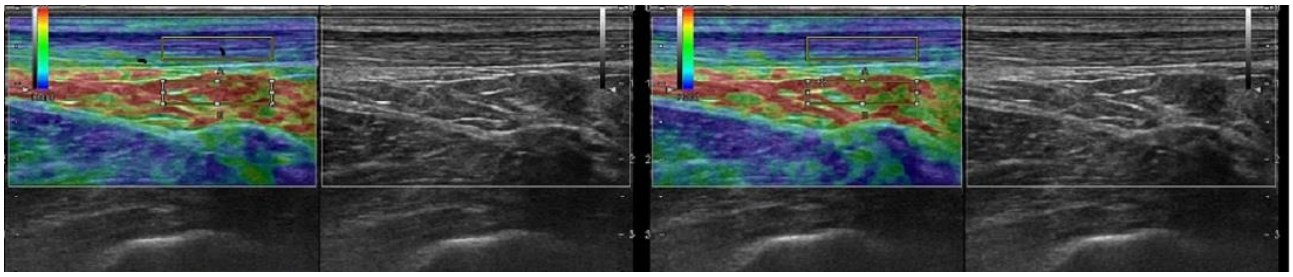

Figure 3. Images of the 1st and 2nd examinations of the same subject by Observer 2 on the Hitachi device

Statistical Analysis

Data obtained in this study were analyzed via IBM SPSS Statistics 21.0 software. The distribution of age, height, weight and SR values were examined by the Shapiro Wilks test. Variables with normal distribution were stated as mean±standard deviation (SD) and those not showing normal distribution as median and interquartile range (IQR) values. Gender was summarized as frequency and percentage. The males and females were compared with respect to the age, height and weight values by the Independent Samples t test, and the device measurements were compared by the Wilcoxon test. The intraobserver and interobserver agreement was assessed by Intraclass Correlation Coefficient (ICC) obtained by two-way mixed ANOVA model for absolute agreement, and its 95% confidence interval (CI). Since the intraobserver agreement was extremely high (ICC>0.90), the mean of each pair of measurements for each observer was calculated and the interobserver agreement was re-evaluated for each device. As the interobserver agreement was good (average ICC>0.75), the mean of the measurements of each observer was calculated and one measurement was obtained for each device. To evaluate the agreement of the measurements obtained from the devices, the ICC value was calculated using two-way mixed ANOVA model. The ICC was interpreted as suggested by Ko and Li (11): <0.5 as poor, 0.50-0.74 as fair, 0.75-0.90 as good and >0.90 as excellent. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The 40 subjects included in the study comprised 16 (40%) males with a mean age of 28.69±7.09 years and 24 (60%) females with a mean age of 31.88±6.00 years (Table 1). The age of the male and female subjects was seen to be similar (p=0.134). The height and weight values of the male subjects were statistically significantly higher than those of the females ($p<0.001$ and p=0.015, respectively).

The interobserver agreement was observed to be good for the first and second measurements on the Hitachi device and for the second measurement on the Toshiba device (average ICC>0.75, Table 2). The interobserver agreement for the first measurement on the Toshiba device was determined to be lower (average ICC=0.729, $p<0.001$).

When the repeated measurements of each observer were evaluated, the intraobserver agreement was determined as excellent for both devices (ICC>0.90, Table 3).

As the intraobserver agreement was high, the mean of the repeated measurements made by each observer for each device was taken and the interobserver agreement was re-evaluated for each device separately. The interobserver agreement was seen to be good for each device, with a slightly lower level for the Toshiba device than the Hitachi (Table 4).

As the interobserver agreeement was good, a single measurement value was obtained for each device by calculating the mean of the measurements of the observers. The agreement between the devices was determined at a good level (average ICC=0.852), but at 95%CI, the ICC fell to 0.258 (Table 5).

The SR values were determined to range 1.22-5.51 for the Hitachi device and 1.74-5.97 for the Toshiba device (Table 6). The mean SR values were calculated as 2.96±1.07 for the Hitachi device and 3.54±1.03 for the Toshiba device, and the difference was statistically significant (Z=6.884, $p<0.001$, Figure 4).

Table 1. Demographic characteristics

	Male (n=16)	Female (n=24)	p
Age (years)	28.69±7.09	31.88±6.00	0.134
Height (cm)	178.50±6.02	164.46±6.05	**<0.001**
Weight (kg)	73.75±13.55	63.88±7.42	**0.015**

cm: centimeter, kg: kilogram

Table 2. Interobserver agreement

Device	ICC type	1st Measurement ICC (95% CI)	2nd Measurement ICC (95% CI)
Hitachi	Single	0.716 (0.590-0.808)	0.680 (0.541-0.782)
	Average	0.835 (0.742-0.894)	0.809 (0.703-0.878)
Toshiba	Single	0.573 (0.395-0.708)	0.602 (0.438-0.727)
	Average	0.729 (0.567-0.829)	0.752 (0.609-0.842)

ICC: Intraclass correlation coefficient, CI: Confidence interval, p<0.001 for all ICC

Table 3. Intraobserver agreement

Observer	ICC type	Hitachi ICC (95% CI)	Toshiba ICC (95% CI)
1	Single	0.958 (0.909-0.978)	0.942 (0.848-0.972)
	Average	0.979 (0.952-0.989)	0.970 (0.917-0.986)
2	Single	0.954 (0.915-0.973)	0.923 (0.868-0.954)
	Average	0.976 (0.955-0.986)	0.960 (0.929-0.976)

ICC: Intraclass correlation coefficient, CI: Confidence interval, p<0.001 for all ICC

Table 4. Interobserver agreement of the mean of the repeated measurements

Observer	ICC type	Hitachi ICC (95% CI)	Toshiba ICC (95% CI)
1 - 2	Single	0.710 (0.582-0.804)	0.604 (0.435-0.730)
	Average	0.830 (0.735-0.891)	0.753 (0.607-0.844)

ICC: Intraclass correlation coefficient, CI: Confidence interval, p<0.001 for all ICC

Table 5. Compatibility between devices

Devices	ICC type	ICC (95% CI)
Hitachi - Toshiba	Single	0.742 (0.148-0.897)
	Average	0.852 (0.258-0.946)

ICC: Intraclass correlation coefficient, CI: Confidence interval, p<0.001 for all ICC

Table 6. Comparison of the measurements obtained from the devices

Device	Min - Max	Mean±SD	Median (IQR)	p
Hitachi	1.22 - 5.51	2.96±1.07	2.85 (1.55)	**<0.001**
Toshiba	1.74 - 5.97	3.54±1.03	3.31 (1.54)	

Min: minimum, Max: maximum, SD: Standard deviation, IQR: Interquartile range

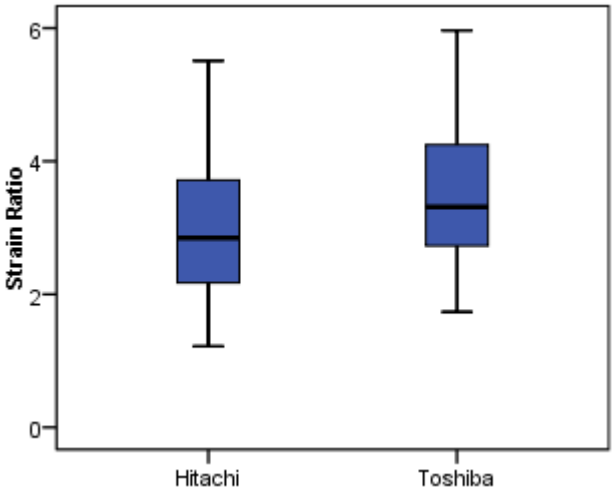

Figure 4. Strain ratio values obtained from the devices

DISCUSSION

This is the first study to have been conducted to determine the compatibility of elastography SR measurements on different sonoelastography devices. In the study, the Achilles tendon, which is the thickest and most superficially located tendon in the body, was evaluated in respect of strain ratio (SR) with separate inter and intraobserver evaluations and on different devices. While the excellent compatibility was determined in the intraobserver evaluations, the compatibility between the researchers was good but showed a lower correlation. The intraobserver evaluation showed excellent for both devices, while the interobserver agreement was good for both devices. However, the first measurement of the Toshiba device showed lower interobserver agreement. In the comparison of the devices, generally higher numerical SR values were provided by the Toshiba device.

Using sonoelastography devices produced by different companies but working on the same principle, the compatibility was investigated of interobserver and intraobserver elastography examinations of the strain ratio (SR) between the Kager fat pad and the Achilles tendon, which is easy to examine because of its superficial localisation. When the repeated measurements of each observer were evaluated, the intraobserver agreement was determined to be excellent for both devices. The interobserver agreement was found to be good for each device and slightly lower for the Toshiba device than for Hitachi.

Elastography is a technique based on the hypothesis that under external force, there is greater deformation of soft tissues than hard tissues, and the strain of the deformation is stated numerically (12,5).

Several researchers have reported the benefits of elastography according to the elasticity points, colour map and SR. In the colour map method, sub-groups, which are dependent on the user and therefore not objective, are coded according to the effect of the compression applied associated with the examined tissue. Therefore, although the sonoelastography colour scoring system is widely used in clinics, it does not provide an objective evaluation as it is practitioner dependent. In a study evaluating thyroid nodules, Wang et al. (13) reported that semi-quantitative analysis was provided with SR and this method was less user dependent. In the same study, in the tissue hardness evaluation between SR and the elastography scoring system, a statistically significant correlation was observed. With the colour scoring system, 15 thyroid nodules with deep localisation gave a false positive result and the pathological results of benign for the same nodules were found to be consistent with the SR values.

In literature, interobserver studies have been conducted previously with a single device using colour scoring in elastography for different pathologies. In a study which evaluated malignant thyroid nodules, although significant agreement was found between 3 researchers using B mode US, the same agreement could not be determined with sonoelastography colour scoring (14).

Sonoelastography cannot provide correct information about calcified benign lesions. Wang et al. (15) reported that with blue colour coding in the colour scale on sonoelastography, follicular adenoma containing calcifications could mimic thyroid cancer. Ning et al. (3)

reported that in nodules with SR>4.2, malignancy could be determined with 81% sensitivity and 83% specificity.

Although a change is seen depending on whether or not the stress applied is homogenous, SR is an important parameter showing tissue stiffness. However, there are studies showing that the addition of SR to colour coding did not increase the diagnostic performance compared to colour coding only (16).

In the current study, as it was considered that the objectivity of the colour scoring system could be low between users, it was decided to compare SRs with the aim of being more quantitative, taking into consideration whether different devices could be used in the future for the differentiation of benign and malignant lesions. Achilles tendon elasticity studies have been previously conducted on experimental models in the laboratory, or in vivo when excised from animals (17,18). Just as studies have been conducted in many areas with sonoelastography, it also has the advantage of low cost and ease of application in Achilles tendon elasticity evaluation. In the current study, a wide range of Achilles tendon SR values were determined; 1.22-5.51 on the Hitachi device and 1.74-5.97 on the Toshiba device. The difference between the SRs could be related to the fact that the mid third of the tendon was examined. This level is known as the critical zone, as it is the most defenceless section of the tendon (19). Therefore, there may not be homogeneity in asymptomatic individuals.

A difference in mechanical characteristics between various tissue components within a normal tendon may be an early indication of disease for which no clinical or sonographic signs have yet emerged. Babic et al. (20) demonstrated that the soleus and gastrocnemius components of the triceps surae complex have different viscoelasticity.

To date, no standard values have been defined in literature for SR of the Achilles tendon. In a study by Drokonaki et al. (21), no significant correlation was determined between Achilles tendon appearance and age or gender. However, in biomechanical studies, differences between individuals have been determined in the viscoelastic properties of the Achilles tendon depending on age, gender and the level of physical activity (20,22). Turan et al. (23) compared a young population with an elderly population, and as a result of colour scoring, the tendons in the elderly group were determined to have been coded as harder. In the currrent study, the subjects were not separated into subgroups according to age, gender or body mass index.

The ROI used in the current study to evaluate the SR was placed over the longitudinal axis. Previous studies that have investigated tendon strain in the axial plane have determined higher SRs compared to longitudinal measurements (24). It was decided to examine the SR in the longitudinal axis in the current study as it is difficult to apply stable, repeated pressure to the Achilles tendon surface in the axial axis and the compressions may not be standardised, especially in the peripheral sections of the tendon.

Although real-time sonoelastography is a less expensive and more widely used technique than “shear wave” technology, the fact that it is user-dependent is a limiting factor. As there is no standard for the pressure applied with the probe, elasticity values can show great variability. Therefore, in some devices, scales have been established warning the user to standardise the amount of compression applied (25).

The mean SR values obtained from the Hitachi and Toshiba devices used in this study were calculated as 2.96±1.07 and 3.54±1.03 respectively. The measurements obtained from the Toshiba device were significantly higher than those obtained from the Hitachi device. For standardization of the compressions, there are upper and lower limit lines on the Hitachi device, and so during application, less compression force is applied to avoid going outside these limits. However, on the Toshiba device there are no limit lines and it was seen that more evident compression force was applied to avoid colour confusion. If the rule is followed during application that at least 3 consecutive waves are homogenous on the compression graph, then the intraobserver agreement was found to be lower, related to the experience of the observer, especially in the first examinations.

The Kager fat pad, used as the reference tissue, is a heterogenous tissue secondary to the vascular structures, fibrous septa and fatty lobules it contains, and it shows differences between individuals depending on the body mass index, as was the case for the two subjects excluded from the study. With an increase in compression force, it is normal for more movement and deformation to develop in the Kager fat pad than in the tendon, which is a harder structure, and in parallel, the SR will be higher.

There were some limitations to this study. The healthy volunteers were only evaluated according to oral statements about chronic diseases, trauma anamnesis, and levels of activity, no patients were excluded from additional laboratory tests, and the tendons were not evaluated with MRI. Previous studies in literature using MRI have reported that on sagittal T1W examinations of the normal Achilles tendon, the reason for a non-homogenous appearance in the distal part of the tendon in 45% of cases is septations between collagen bundles forming linear and focal high signals (26).

CONCLUSION

Sonoelastography is an imaging method based on ultrasonography, which shows tissue elasticity and is being increasingly used in clinics. The results of the current study showed that in applications made by the same person at different times, the SRs showed excellent agreement. When a standard was established in compressions, the results in the evaluations made by the different researchers showed significant agreement. In studies made on different devices, there may be a difference in SRs associated with the compression application limits of the device. Therefore, intra and interobserver agreement should be evaluated separately for each device.

Finance

The study received no financial suppot from any individual or institution.

Conflict of Interests

The authors have no conflict of interests to declare.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.559329

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):162-165

A Glance into Botulinum Toxin Outpatient Clinic in Movement Disorders Practice: Self Experience

Hareket Bozuklukları Pratiğinde Botulinum Toksin Polikliniğine Bakış: Kişisel Deneyim

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Geliş Tarihi / Received : 30.04.2019
Kabul Tarihi / Accepted : 21.10.2019
Çevrimiçi Yayın Tarihi / Available Online : 07.11.2019

ABSTRACT

Aim: Aim of this study is to determine socio-demographic and disease features of patients who underwent Botulinum toxin injections, and to present our clinical experience via documenting intervals of Botulinum toxin injections and effect-side effect profiles.
Material and Methods: Socio-demographic features of patients and characteristic features of Botulinum toxin treatment were recorded. The diagnosis of the patients who underwent Botulinum toxin injections, disease durations and the onset of Botulinum toxin treatments were investigated. Possible side-effects were recorded.
Results: Thirty-two patients (20 men, 12 women) with the diagnosis of various types of movement disorders were enrolled the study. Mean age of patients was 60.65±14.40 years (range= 22-83 years). Diagnosis of the patients who underwent Botulinum toxin injections were cervical dystonia, blepharospasm, clonic hemifacial spasm, focal hand dystonia/writer's cramp, oromandibular dystonia, and dystonic tremor. All patients had repetitive Botulinum toxin injections. There were no remarkable adverse effects, other than mild temporary bruises in injection site in two patients with blepharospasm.
Conclusion: Botulinum toxin is an important treatment option in patients with focal dystonia. Botulinum toxin as a neurotoxin of *Clostridium botulinum* bacteria, suppresses muscle contractions via inhibiting acetylcholine release to the synaptic gap. This reversible effect lasts three to four months due to the neuronal sprouting. It is important to share clinical experiences, data of Botulinum toxin outpatient clinics or clinics from the movement disorders perspective to increase awareness of Botulinum toxin effectivity in patients with movement disorders, focal dystonia particularly.
Keywords: Botulinum toxin; movement disorders; focal distonia.

ÖZ

Amaç: Bu çalışmanın amacı Botulinum toksin enjeksiyonu uygulanan hastaların sosyodemografik özellikleri ve hastalık özelliklerinin belirlenmesi, ve Botulinum toksin uygulama aralıkları ile etki ve yan etki profillerini dokümante ederek klinik deneyimimizin sunulmasıdır.
Gereç ve Yöntemler: Hastaların sosyodemografik özellikleri ve Botulinum toksin tedavisinin karakteristik özellikleri kaydedilmiştir. Botulinum toksin enjeksiyonu yapılan hastaların hastalık tanıları, hastalık süreleri ve Botulinum toksin tedavisine başlama süreleri incelenmiştir. Olası yan etkiler kaydedilmiştir.
Bulgular: Çeşitli hareket hastalıkları tanısı almış otuz iki hasta (20 erkek, 12 kadın) çalışmaya dahil edilmiştir. Hastaların yaş ortalaması 60.65±14.40 yaştır (aralık= 22-83 yaş). Botulinum toksin enjeksiyonu uygulanan hastaların tanıları servikal distoni, blefarospazm, klonik hemifasiyal spazm, fokal el distonisi/yazıcı krampı, oromandibular distoni ve distonik tremordur. Tüm hastalara tekrarlayan Botulinum nörotoksin enjeksiyonları yapılmıştır. İki blefarospazm hastasında enjeksiyon bölgesinde izlenen hafif morluklar dışında, hastalarda belirgin yan etki görülmemiştir.
Sonuç: Botulinum toksin fokal distonili hastalarda önemli bir tedavi seçeneğidir. *Clostridium botulinum* bakterisinin nörotoksini olan Botulinum nörotoksin, sinaptik aralığa asetilkolin salınımını engelleyerek kas kasılmasını baskılamak üzere çalışır. Geri dönüşümlü olan bir etki ile nöronal filizlenmenin süresiyle ilişkili olarak yaklaşık üç ila dört ay kadar sürmektedir. Özellikle fokal distoni gibi hareket bozuklukları hastalarında Botulinum toksin etkinliğine ilişkin farkındalığı arttırmak amacıyla ve hareket hastalıkları perspektifinden Botulinum toksin poliklinik veya kliniklerinin klinik deneyimlerini ve verilerini paylaşmak önem arz etmektedir.
Anahtar kelimeler: Botulinum toksin; hareket bozuklukları; fokal distoni.

INTRODUCTION

Botulinum toxin (BoNT) is the most potent neurotoxin that is produced by gram-positive anaerobic bacteria known a *Clostridium botulinum*. It contains a peptide composed of a 100-kDa heavy chain and a 50-kDa light chain, which shows a mechanism of action in the terminals of cholinergic neurons at the neuromuscular junction via blocking the release of acetylcholine at the nerve terminals, and leading to a reversible paralysis in the skeletal muscle (1).

Since the effect of BoNT is reversible due to the reestablishment of the axonal sprouting on the nerve terminals of neuromuscular junction leading to acetylcholine release, and restore muscle contraction, periodic administrations of BONT is needed in order to maintain therapeutic effect (2,3). Although there are eight different serotypes as A to H, currently type A and B are the ones in market with the Food Drug Administration (FDA) approval in clinical use (1,4). These are commercially known as onabotulinum toxin-A (®Botox), abobotulinum toxin-A (®Dysport), incobotulinum toxin-A (®Xeomin), and rimabotulinum toxin-B (®Myobloc) in markets (5,6).

It has a wide range of use in ophthalmological, gastrointestinal, urological, orthopedic, dermatological, secretory, and painful disorders, as well as neurological diseases (7). In terms of neurological disorders, BoNT is a well-known treatment option in dystonia, which is a movement disorder syndrome characterized with sustained muscle contractions, frequently causing twisted and repetitive movements, or abnormal postures (8). Moreover in movement disorders practice, it is considered as an effective treatment in focal dystonia such as cervical dystonia, blepharospasm, clonic hemifacial spasm, task specific/focal hand dystonia and more (9-12).

Since BoNT has emerged as a powerful, multipurpose therapeutic agent leading to a dramatic improvement with an increase in the quality of life of patients with dystonia in movement disorders practice of neurology, in particular, the aim of this study was to present and document our self-experience of BoNT injections in our BoNT outpatient clinic, and discuss in the light of literature knowledge from the movement disorders perspective.

MATERIAL AND METHODS

In this retrospective study, patients with the diagnosis of dystonia who underwent BoNT injections in Duzce University Medical Faculty Hospital BoNT outpatient clinic of the Neurology Department by the same examiner between 1 January 2018 and 30 April 2019 were enrolled the study. The patients who underwent BoNT injections apart from the diagnosis dystonia and movement disorders were excluded. All participants were informed about the content of the procedure and gave their written approval before BoNT injections. The study was approved with the local ethical committee of Duzce University with the date and number as 27/05/2019 and 2019/114, respectively.

Socio-demographic features of the patients including age, gender, occupation, dominant-hand, marital status from retrospective analysis of the patients' data were recorded, as well as the type of movement disorders diagnosis that needed BoNT injections, and the disease durations. The characteristics of the BoNT injections including the duration of treatment, the number of injections, dilution parameters and side effects, if any, were also documented.

Statistical Analysis

Data were organized in an SPSS Version 15.0 (Statistical Package for Social Sciences for Windows) database. Statistical analyses were performed with the descriptive analysis, and the comparison of the groups was performed with parametric and non-parametric tests. Descriptive statistics calculated as mean ± SD or median (mean-max); and frequency and percentage as appropriate.

RESULTS

Thirty-two patients (20 men, 12 women) with the diagnosis of various types of movement disorders were enrolled the study. Mean age of the patients was 60.65±14.40 years (range= 22-83 years).

All were right-handed. Socio-demographic features of the patients are shown in Table 1. The types of movement disorders were focal dystonia including blepharospasm, clonic hemifacial spasm, oromandibular dystonia, and task specific dystonia which was called writer's cramp. Dystonic tremor was another diagnosis and one patient had a combined clinical manifestation of blepharospasm and cervical dystonia. The diagnosis of the patients in terms of movement disorders can be seen in Table 2.

Table 1. Socio-demographic features of the patients

	n (%)
Gender	
Male	20 (62.5)
Female	12 (37.5)
Marital status	
Single	31 (96.9)
Married	1 (3.1)
Education	
Not literate	5 (15.6)
Literate	3 (9.4)
Primary school (5 years)	19 (59.4)
Middle school (+3 years)	0 (0.0)
High school (+3 years)	2 (6.3)
College	3 (9.4)
Occupation	
Housewife	18 (56.3)
Retired	7 (21.9)
Tradesman	1 (3.1)
Teacher	1 (3.1)
Farmer	1 (3.1)
Officer	2 (6.3)
Worker	2 (6.3)

Table 2. Diagnosis of the patients

Diagnosis	**n (%)**
Cervical dystonia	4 (12.5)
Blepharospasm	3 (9.4)
Blepharospasm and cervical dystonia	1 (3.1)
Clonic hemifasial spasm	20 (62.5)
Task spesiphic dystonia/writer's cramp	1 (3.1)
Oromandibular dystonia	1 (3.1)
Dystonic tremor	2 (6.3)

Mean duration of disease was 6.35±4.95 years (range= 1-22 years). Mean duration of BoNT treatment among the patients was 3.48±2.70 years (range= 1-13 years). Within this period, they underwent repetitive BoNT treatments. Median number of BoNT injections was 3 (range= 1-7 injections).

In our clinic onabotulinum toxin-A (®Botox, Allergan) was used with the dilution of 2 ml of saline solution. Commonly injected muscles with the appropriate dosages, based on the diagnosis, indications and clinical needs were orbicularis oculi, stenocleidomastoid, splenius capitis, levator scapula, and the flexor muscles of the hand in the patient with writer's cramp, and masseter in the patient with jaw closing oromandibular dystonia. None of the patients reported any remarkable side-effects, other than mild temporary bruises in the injection site in 2 patients with blepharospasm.

DISCUSSION

BoNT is a favourable therapeutic agent in movement disorders clinics and outpatient clinics for focal dystonia, in particular (13). The term "focal dystonia" includes a wide range of disorders such as blepharospasm, cervical dystonia, clonic hemifacial spasm, focal hand dystonia, and there are several drugs like benzodiazepines, anticholinergic, and baclofen that are commonly used in the pharmacological treatment of dystonia. However, BoNT injections are the gold standard treatment options in focal dystonia, so far (14).

Targeting the acetylcholine release with consequently reduced overactive muscle contraction in the dystonic muscles at the site of injection is the main mechanism of action of BoNT leading to a reversible improvement, which makes BoNT most effective and widely used treatment in focal dystonia (13,14). The success of treatment depends on accurate diagnosis and injections that depends on the precise determination of the involved muscles, and the experience and the skills of the clinician applying the injections with appropriate doses and techniques, in which BoNT dosing and muscle targeting are mainly based on consensus and experience (15).

Thus the aim of this study was to document our clinical experience in BoNT injections from the perspective of movement disorders practice in the patients with the diagnosis of focal dystonia in various types. Similar to our data and results, previous studies reveal that the type of dystonia is commonly focal in patients who underwent BoNT injections such as blepharopasm, cervical dystonia, focal hand dystonia, and clonic hemifacial spasm (8-10,12).

As a well-known entity, BoNT has a reversible functional denervation lasting up to 3 months due to the sprouting of nerve terminals and formation of new synaptic contacts (16). Thus, similar to our data, patients need repetitive injections as the function of the injected muscles recover (12,15-17).

Most common adverse effects reported in the previous studies for BoNT injections in the movement disorders practice are mild pain and/or bruises in the injection side, as we two of our patients with blepharospasm experienced. The most unwanted adverse effect is the paralysis of the adjacent muscle caused by the spread of toxin which is also temporary. In patients with cervical dystonia, dysphagia is a frightening side-effect when injecting the neck muscles. Moreover, pitosis may be seen in 1-3% of the patients as a result of paralysis due to ocular musculature injections via migration of toxin to the levator palpebrae superioris muscle in the treatment of clonic hemifacial spasm and/or blepharospasm in movement disorders practice (16-17). However it usually resolves within several weeks or months. Infrequently, adverse effects such as brachial plexopathy, and influenza-like illness are also reported. However, it is generally a well-tolerated therapy with few side effects when performed accurately by experienced clinicians (17).

CONCLUSIONS

Owing to its well-known therapeutic effects in focal dystonia, BoNT is an important treatment option in preventing the involuntary, disabling muscle contractions in dystonia, which can often deteriorate the daily living activities of patients, and lead them to be socially isolated. On this aspect, it is important to share clinical experiences, and data of BoNT outpatient clinics from the movement disorders perspective in order to increase the utility, and awareness of BoNT affectivity in patients with movement disorders, focal dystonia in particular.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.507400

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):166-171

Serebral Venöz Trombozlu Erişkinlerde Etiyoloji ve Genetik Polimorfizm İlişkisi

The Relationship Between Etiology and Genetic Polymorphism in Adults with Cerebral Venous Thrombosis

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Geliş Tarihi / Received : 03.01.2019
Kabul Tarihi / Accepted : 24.10.2019
Çevrimiçi Yayın Tarihi / Available Online : 07.11.2019

ÖZ

Amaç: Serebral ven trombozu (SVT) nadir bir inme nedeni olup etiyolojisinde birçok faktör yer almaktadır. Olguların en az 1/4'ü trombofiliye bağlıdır. Tromboembolizm için en yaygın risk faktörleri metilen-tetra-hidro-folat redüktaz (MTHFR) C677T, faktör 5 (FV) G1691A (Leiden), faktör 2 (FII) GA20210 ve mutasyonlarıdır. Farklı genetik polimorfizmleri ve yüksek homosistein düzeyleri ile ilişkisi de araştırılmıştır. Bu çalışmada SVT'li olgularda genetik polimorfizm varlığı ve homosistein düzeylerinin SVT etiyolojisindeki rolünün araştırılması amaçlanmıştır.
Gereç ve Yöntemler: Ocak 2010-Haziran 2018 yılları arasında merkezimizde geliş tanısı SVT olan hastaların demografik özellikleri, klinik, radyolojik ve laboratuvar verileri geriye dönük olarak incelendi. SVT için etiyolojik risk faktörleri ve bu risk faktörleri içinde genetik polimorfizmin rolü araştırıldı.
Bulgular: Çalışmada 92 (73 kadın ve 19 erkek) hasta ve 52 (44 kadın ve 8 erkek) kontrol birey değerlendirildi. SVT'li hastalarda en sık başvuru semptomu baş ağrısı idi. MTHFR, Faktör 13 (F13) V34L, plazminojen aktivatör inhibitörü (PAI) ve β-fibrinojen mutasyonları kontrol grubunda daha yüksek idi. FV Leiden, FII, Glikoprotein 3a mutasyonu ve homosistein düzeyi açısından her iki grup arasında anlamlı istatistiksel fark tespit edilmedi.
Sonuç: Bu çalışmada literatür ile uyumlu olan sonuçlar yanında bazı farklı sonuçlarda tespit edilmiştir. MTHFR (C677T, A1289C), FV Leiden, FII G20210, β-fibrinojen 455 G-A, PAI-1 4G/5G polimorfizmleri SVT için risk oluşturmamaktadır. F13 V34L polimorfizminin SVT'ye karşı koruyucu rolü vardır.
Anahtar kelimeler: Serebral venöz tromboz; trombofili; genetik polimorfizm.

ABSTRACT

Aim: Cerebral venous thrombosis (CVT) is a rare cause of stroke, and there are many factors in its etiology. At least 1/4 of cases is based on thrombophilia. The most common risk factors for thromboembolism were methyl-tetra-hydro-folate reductase (MTHFR) C677T, factor V (FV) G1691A (Leiden), factor II (FII) GA20210 and their mutations. Its relationship with different genetic polymorphisms and high homocysteine levels were also investigated. In this study, it was aimed to investigate the existence of genetic polymorphism and the role of homocysteine levels in CVT etiology.
Material and Methods: Demographic characteristics, clinical, radiological and laboratory data of patients diagnosed with CVT between January 2010 and June 2018 were reviewed retrospectively. Etiologic risk factors for CVT and the role of genetic polymorphism in these risk factors were investigated.
Results: In this study, 92 (73 female and 19 male) patients and 52 (44 female and 8 male) control subjects were evaluated. The most frequent admission symptom was headache in patients with CVT. MTFHR, factor 13 (F13) V34L, plasminogen activator inhibitory (PAI) and β-fibrinogen mutations were higher in control group. No statistically significant difference was found between the two groups in terms of FV Leiden, FII, Glycoprotein 3a mutation and homocysteine level.
Conclusion: In this study, in addition to the results consistent with the literature, some different results were determined. MTHFR (C677T, A1289C), FV Leiden, FII G20210, β-fibrinogen 455 G-A, PAI-1 4G/5G polymorphisms do not pose a risk for CVT. F13 V34L polymorphism has a protective role against CVT.
Keywords: Cerebral venous thrombosis; thrombophilia; genetic polymorphism.

GİRİŞ

Serebral ven trombozu (SVT), iskemik inmenin nadir görülen nedenlerinden biridir. İnsidansı yılda 0,2-1,2/100000 olgudur (1). Her yaş grubunda görülmekle birlikte en çok genç yetişkinleri, doğurganlık çağındaki kadınları ve çocukları etkilemektedir. Kadınlar, erkeklerden daha fazla etkilenmektedir. Çocuklar ve ileri yaş olgularda cinsiyetler arasında fark yok iken, genç erişkin yaş grubundaki kadınlarda, erkeklerden üç kat daha fazla rastlanmaktadır (2).

SVT kliniği çeşitli semptomlardan oluşur. Farklı karakterlerde izlenebilen ve en sık semptom olan baş ağrısından, şiddetli bilinç bozukluğuna kadar değişen bir çok nörolojik semptom izlenebilir (3). Nörogörüntüleme tekniklerinde ve tedavideki gelişmelerle erken tanı ve tedavi sürecinin hızlanması mortalite oranlarını daha da azaltmıştır (4).

SVT etiyolojisinde gebelik, puerperium ve oral kontraseptif kullanımı haricinde sistemik inflamatuar hastalıklar, koagülopati tabloları, yüz, kulak, burun bölgesi enfeksiyonları, sistemik hastalıklar ve dehidratasyon gibi birçok nedenin yer aldığı bildirilmiştir (5). Trombofiliye bağlı SVT'nin, tüm olguların yaklaşık 1/4'ünden fazlasında tespit edildiği bildirilmiştir (6). Gelişmiş ülkelerde tromboembolizm için en yaygın risk faktörlerinin metilen-tetra-hidro-folat redüktaz (MTHFR) C677T, faktör 5 (FV) G1691A (Leiden) ve faktör 2 (FII) GA20210 mutasyonlarının olduğu bildirilmiştir (7). Yine yüksek homosistein düzeyleri ile tromboembolizm ilişkisi birçok çalışmada bildirilmiştir (8). Venöz tromboza yatkınlık sağlayan genetik polimorfizmlerin haricinde, Faktör 13 (F13) V34L polimorfizminin tromboza karşı koruduğu düşünülmektedir (9). İnme için önemli bir risk faktörü olan hiperfibrinojeneminin (10), β-fibrinojen genetik polimorfizmi ile gelişebileceği bildirilmiştir (11), fakat benzer risk venöz trombozlar için net değildir (12). Yine fibrinolitik sistemin aktivitesinde bir bozulmaya yol açtığı düşünülen plazminojen aktivatör inhibitörü tip-1 (PAI-1) 4G/5G polimorfizminin de trombotik etkisi tartışmalıdır (13). Benzer tartışmalar trombosit glikoprotein (GP) 3a polimorfizmi ile tromboembolik hastalık içinde geçerlidir (14,15).

Bu çalışmada SVT'li olguların klinik özellikleri ve genetik polimorfizm (MTHFR C677T, MTHFR A1298C, FV Leiden, FII (20210 G/A), F13a (V34L), PAI-1 (5G-4G), β-fibrinojen (455G>A), GP 3a (L33P)) varlığı ile homosistein düzeylerinin SVT etiyolojisindeki rolünü değerlendirmek amaçlanmıştır.

GEREÇ VE YÖNTEMLER

Hasta Seçimi

Ocak 2010 - Haziran 2018 yılları arasında Atatürk Üniversitesi Tıp Fakültesi Nöroloji ve Acil Servis Polikliniğine geliş tanısı SVT olan hastaların dosyaları retrospektif olarak incelendi. Takipleri SVT olarak devam edenler ve tanısı değişen hastalar iki gruba ayrıldı. SVT tanısı ile takip edilmiş hastalardan belirlenen nörogörüntüleme (manyetik rezonans görüntüleme-MRG) protokolüne uymayanlar, laboratuar tetkiklerinde ve dosyasında eksik veri olanlar çalışmaya dahil edilmedi. Kontrol grubu geliş tanısı SVT olup takiplerinde tanısı değişen (venöz hipoplazi, agenezi, araknoid granülasyon) olgulardan oluşturuldu. Bu grupta laboratuar tetkiklerinde ve dosyasında eksik veri olan olgular çalışmaya dahil edilmedi. Hastaların demografik verileri, klinik, radyolojik, laboratuar bulguları incelendi. MTHFR C677T, MTHFR A1298C, Faktör V (G1691A) Leiden, Faktör II (20210 G/A), Faktör 13a (V34L), PAI-1 (5G-4G), beta fibrinojen (455G>A), GP 3a (L33P) genetik polimorfizmleri, homosistein değerleri, geliş semptomları, etiyolojik nedenler ve trombüs tespit edilen sinüsler incelendi. SVT için etiyolojik risk faktörleri ve bu risk faktörleri içinde genetik polimorfizmin rolü araştırıldı. Bu çalışma Atatürk Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından onaylanmıştır (05/28/07.06.2018).

MRG Protokolü

SVT tanısıyla takip edilmiş, aksiyel FLAIR, aksiyel T1, aksiyel T2, koronal T2, sagittal T1 ve time of flight (TOF) venografi ve kontrastlı venografi görüntüleri ile trombüs tespit edilen hastalar çalışmaya dahil edildi. Geliş tanısı, beyin bilgisayarlı tomografi veya MRG ile SVT olup takiplerinde TOF MRG ve kontrastlı venografide dolum defekti alanı hipoplazi, aganezi veya agranülasyon lehine yorumlanan hastalar kontrol grubuna dahil edildi.

İstatistiksel Analiz

Analizler SPSS v.20 istatistik analiz programı ile yapıldı. Veriler medyan, minimum, maksimum, sayı ve yüzde olarak sunuldu. Sürekli değişkenin normal dağılıma uygunluğu Kolmogorov Smirnov testi ile incelendi. İki bağımsız grup arasındaki kıyaslamada normal dağılım şartı sağlanmadığı için Mann Whitney U testi kullanıldı. Kategorik değişkenler arasındaki 2x2'lik çapraz tablo kıyaslamalarında beklenen değer 5'ten büyük ise Pearson Ki-kare testi (hasta ve kontrol grubu arasında cinsiyet, GP3a, F13a, homosistein karşılaştırılmasında), beklenen değer 5'ten küçük ise Fisher's Exact testi (hasta ve kontrol grubu arasında F2 karşılaştırılmasında) yapıldı. Kategorik değişkenler arasındaki 2x2'den daha büyük çapraz tablo kıyaslamalarında beklenen değer 5'ten küçük olduğu durumda Fisher-Freeman-Halton testi (hasta ve kontrol grubu arasında PAI-1, beta fibrinojen, F5, MTHFR karşılaştırılmasında) uygulandı, anlamlı farklılık saptanan durumlarda post-hoc bonferroni test kullanıldı. İstatistiksel anlamlılık düzeyi $p<0,05$ olarak alındı.

BULGULAR

Ocak 2010 - Haziran 2018 yılları arasında 481 hastanın geliş tanısının SVT olduğu tespit edildi. Dahil edilme ve dışlama kriterleri ile 92 hasta ve 52 kontrol grubu çalışmada değerlendirildi. Hastaların yaş aralığı 18-76 arasında (medyan 33) ve kontrol grubunun yaş aralığı 18-72 arasında (medyan 36) olup gruplar arasında anlamlı istatistiksel fark yoktu (p=0,861). Hasta grubunda kadın olgu sayısı 73 (%79,3) iken kontrol grubunda 44 (%84,6) kadın vardı. Hasta grubunda 43 yaşında 1 (%1,6) kadın olgunun yatış takibinde öldüğü tespit edildi. Hasta grubunda başvuru semptomlarının dağılımı incelendi ve en sık başvuru sebebinin baş ağrısı (%90,2) olduğu görüldü. Hastaların %73,9'u (n=68) baş ağrılarını "migren benzeri ağrı", %6,5'i (n=6) "yanma" şeklinde, %19,6'sı (n=18) "sıkıştırıcı vasıfta" ağrı olarak tarif etmişti. Nöbet semptomu olguların %19,6'sında (n=18) tespit edildi. On sekiz hastanın %55,6'sında (n=10) jeneralize, %44,4'ünde (n=8) fokal nöbet olduğu görüldü. Nörolojik defisit olguların %20,7'sinde (n=19) tespit edildi. Hasta grubunun

%19,6'sında bilinç bozukluğu tespit edildi. Genetik polimorfizmleri ve homositein düzeyleri hasta ve kontrol gruplarında karşılaştırıldı. Hasta grubuna göre MTHFR mutasyon varlığı kontrol grubunda anlamlı düzeyde daha yüksek tespit edildi (p<0,001). FV Leiden ve FII mutasyonlarında her iki grup arasında istatistiksel olarak anlamlı bir fark tespit edilmedi (sırasıyla p=0,307 ve p=0,553). F13a, PAI-1 ve β-fibrinojen mutasyonları kontrol grubunda daha yüksek tespit edildi ve bu fark istatistiksel olarak da anlamlıydı (sırasıyla p=0,003; p<0,001 ve p<0,001). GP3a mutasyonu ve homosistein yüksekliği açısından gruplar arasında anlamlı istatistiksel fark tespit edilmedi (p=0,317 ve p=0,626). Hasta ve kontrol grubunda tespit edilen genetik polimorfizm oranları Tablo 1'de verilmiştir. Hastaların etiyolojileri incelendiğinde %32,6'sında trombofili tespit edildi. Trombüs tespit edilen sinüsler incelendiğinde %72,8 ile en sık transvers sinüste trombüs izlendi ve multiple sinüs etkileniminin %48,9 olduğu tespit edildi (Tablo 2).

TARTIŞMA

Bu çalışmada yaş ve cinsiyet dağılımı literatür ile uyumluydu. Olguların yaş ortalaması 30-40 yaş aralığında ve kadın olgu sayısı daha fazlaydı. İlk başvuruda baş ağrısı semptomu oranı daha fazlaydı, bilinç bozukluğu ise olguların yaklaşık 1/5'inde vardı. Etiyolojik nedenler arasında trombofiliye bağlı SVT, olguların %32,6'sında tespit edildi. En sık transvers sinüste trombüs tespit edildi. Bu çalışmada olgular ile kontrol grubu arasında genetik polimorfizm açısından literatürle uyumlu olan sonuçlar yanında bazı farklı sonuçlar da bulundu.

Bu çalışmada hasta grubunun yaş aralığı 18-76 arasında (medyan 33) ve kadın hasta oranı yaklaşık 4 kat daha fazlaydı (73 kadın, 19 erkek). En sık görülen semptom baş ağrısı olup SVT hastalarında hafif bir baş ağrısından, koma haline kadar değişebilen farklı semptomlar görülebilir. Yapılan bir çalışmada hastaların %46'sında akut nöbet öyküsünün olduğu ve nöbet öyküsünün bilinç bozukluğu seviyesi (GKS<8), fokal hasar, sagital sinüs trombozu ve yüksek D-Dimer seviyeleri ile ilişkili olduğu bildirilmiştir (16). Birçok çalışma bilinç değişikliklerinin %20-30 oranlarında görüldüğünü bildirmiştir (17). Farklı bir çalışmada bilinç bozukluğu olan olgularda hafif bilinç bozukluğu %28,6, orta derece ve şiddetli bilinç bozuklukları %63,3 ve %8,1 olarak bildirilmiştir (3). SVT'de en sık tromboz tespit edilen bölgeler %65 superior sagittal sinüs, %60,5 transvers sinüs, %71,2 çoklu venöz sinüs trombozu şeklindedir (3). Çok merkezli bir çalışmada, SVT'li hastaların %10,9'unda derin venöz tutulum, %17,1'inde kortikal ven tutulumu ve %11,9'unda juguler ven tutulumu olduğu bildirilmiştir. Serebellum ve kavernöz sinüs tutulumunun hastaların sadece %0,3 ve %1,3'ünde gözlendiği bildirilmiştir (17). Farklı bir çalışmada %57 ile transvers sinüs tutulumunun daha sık olduğu ve süperior sagital sinüs tutulumunun %49,4 olduğu bildirilmiştir (6). Bu çalışmada da en sık izlenen semptom baş ağrısı olup oranı %90,2 olarak tespit edildi. Migren benzeri ağrısı olan hasta oranı %73,9 ile en fazla, yanma şeklinde ağrı tarifleyen hasta oranı %6,5 ve sıkışma şeklinde ağrı tarifleyen hasta oranı %19,6 olarak tespit edildi ve tespit edilen bu oranlar literatür ile uyumluydu. En sık semptomun baş ağrısı olması ve ağrı karakterinin sık karşılaşılan primer baş ağrılarına benzemesi yanlış tanı

Tablo 1. Serebral ven trombozu olan ve olmayan hastaların genetik polimorfizm ilişkisi, n (%)

	SVT (n=92)	Kontrol (n=52)	p
Yaş (yıl) (medyan; min-maks)	33 (18-76)	36 (17-50)	0,861
Cinsiyet			
Erkek	19 (20,7)	8 (15,4)	0,473
Kadın	73 (79,3)	44 (84,6)	
MTHFR Polimorfizm			
C677T Heterozigot	12 (13,0)	12 (23,1)	
C677T Homozigot	6 (6,5)	2 (3,8)	
A1298C Heterozigot	3 (3,3)	17 (32,7)‡	
A1298C Homozigot	6 (6,5)	7 (13,5)	
C677T Heterozigot +A1298C Heterozigot	11 (12,0)	8 (15,4)	**<0,001**
C677T Heterozigot +A1298C Homozigot	0 (0,0)	1 (1,9)	
MTHFR Normal Genotip	54 (58,7)	5 (9,6)‡	
Factor 5 (G1691A)			
Homozigot	2 (2,2)	0 (0,0)	
Heterozigot	12 (13,0)	3 (5,8)	0,307
Normal Genotip	78 (84,8)	49 (94,2)	
Factor 2 (20210 G/A)			
Heterozigot	3 (3,3)	0 (0,0)	0,553
Normal Genotip	89 (96,7)	52 (100)	
Homosistein			
Yüksek	19 (20,7)	9 (17,3)	0,626
Normal	73 (79,3)	43 (82,7)	
Factor13a (V34L)			
Heterozigot	10 (10,9)	16 (30,8)	**0,003**
Normal Genotip	82 (89,1)	36 (69,2)	
B-fibrinojen (455G>A)			
Heterozigot	12 (13,0)	14 (26,9)‡	
Normal Genotip	80 (87,0)	33 (63,5)‡	**<0,001**
Homozigot	0 (0,0)	5 (9,6)‡	
PAI-1 (5G-4G)			
Homozigot	4 (4,3)	7 (13,5)	
Heterozigot	3 (3,3)	15 (28,8)	**<0,001**
Normal Genotip	85 (92,4)	30 (57,7)‡	
Glikoprotein 3a (L33P)			
Heterozigot	9 (9,8)	8 (15,4)	0,317
Normal Genotip	83 (90,2)	44 (84,6)	

MTHFR: Metilen Tetra Hidro Folat Redüktaz, PAI-1: Plazminojen Aktivatör İnhibitörü tip1, min: minimum, maks: maksimum, ‡ Post hoc bonferroni test

Tablo 2. Serebral ven trombozu nedenleri ve trombüs tespit edilen sinüsler

Etyoloji	**n (%)**
İdiyopatik	18 (19,6)
Gebelik / Postpartum	14 (15,2)
İlaç kullanımı (oral kontraseptif, hormon replasman tedavisi)	5 (5,4)
Trombofili	30 (32,6)
Sistemik Hastalıklar (Behçet hastalığı, Sistemik lupus eritematoz, Antifosfolipid sendromu)	5 (5,4)
Multifaktöryel	14 (15,2)
Enfeksiyon (Mastoidit...)	2 (2,2)
Malignite	4 (4,3)
Trombüs tespit edilen sinüs*	**n (%)**
Sagital Sinüs	30 (32,6)
Transvers Sinüs	67 (72,8)
Kavernöz Sinüs	1 (1,1)
Derin Venöz Sinüs	4 (4,3)
Çoklu	45 (48,9)

*Trombüs tesbit edilen sinüsler bazı hastalarda izole, bazı hastalarda iki sinüs, bazı hastalarda üç sinüs tutulumu şeklinde bir hastada birden fazla tutulum mevcuttur.

olasılığını akla getirmeli ve bu benzerlik akılda tutulmalıdır. Bu çalışmada 92 hastanın 18'inde (%19,6) epileptik nöbet olup, nöbetler 10 hastada jeneralize, 8 hastada fokal özellikte idi. Nörolojik defisit olan hasta oranı %20,7 (n=19) olarak tespit edildi. Nöbet oranının literatürde ki benzer çalışmalarda bildirilen oranlardan düşük olmasının nedeninin nörolojik defisitli hasta oranının daha düşük olmasından kaynaklandığını düşünüyoruz. Bu çalışmada hafif, orta ve ciddi bilinç bozukluğu oranları %55,6, %38,9 ve %5,5 şeklinde olup bu oranlar literatürden farklıydı. Hafif bilinç bozukluğu oranı daha yüksekti ve bununda hastalarda nörolojik defisit oranının düşük olması ile açıklanabileceğini düşünüyoruz. Bu çalışmada superior sagittal sinüsün %32,6, transvers sinüsün %72,8, kavernöz sinüsün %1,1, derin venlerin %4,3, multipl venöz tutulumun %48,9 oranlarında olduğu tespit edildi. Literatürdeki çoğu çalışmadan farklı olarak transvers sinüs tutulumu daha fazla olup superior sagittal sinüs tutulumunun yaklaşık iki katı kadardı. Bu tespitin, epileptik nöbet ve hafif bilinç bozukluğu oranlarının literatürde bildirilen diğer çalışmalardan daha düşük olmasını açıklayabileceğini düşünüyoruz.

SVT mortalitesinin %5-10 arasında olduğu bildirilmiştir (4). Bu çalışmada da mortalite oranı %1,6 (n=1) olarak tespit edildi. 43 yaşında kadın hasta yatış takibinde ölmüştü. SVT etiyolojisinde merkezi sinir sistemi enfeksiyonu, herhangi bir malign hastalık olması, kabul nörogörüntülemesinde intrakraniyal kanama, bilinç bozukluğu ve Glasgow Koma Skalası <9 olması, 37 yaşından büyük ve erkek cinsiyetin kötü prognozla ilişkili olabileceği bildirilmiştir (18). Bu çalışmada tespit edilen mortalite oranı literatürde bildirilenden görece düşüktü. Bu durumun kötü prognoz ile ilişkili olabileceği düşünülen etiyolojik, klinik ve demografik özelliklerin bu çalışmadaki hasta popülasyonunda daha az olmasıyla açıklanabileceğini düşünüyoruz.

SVT nedenleri karmaşık olup yaygın nedenler arasında tümör, travma, enfeksiyon, gebelik ve puerperium, genetik trombofili, sistemik hastalıklar, oral kontraseptifler, metabolik bozukluklar, dehidratasyon vs. vardır. Fakat hala SVT' nin %30'unda belirgin bir neden bulunamadığı bildirilmiştir (19). Trombofiliye bağlı SVT oranı %27,8 olarak bildirilmiştir (6). Farklı bir çalışmada bu oran %61,5 gibi daha yüksek tespit edilmiştir (20). Bu çalışmada trombofili etiyolojili SVT oranı %32,6 olarak tespit edildi. Batı ülkelerinde MTHFR C677T, FV Leiden, FII 20210G/A ve mutasyonlarının tromboembolizm için en yaygın risk faktörleri olduğu bildirilmiştir (21,22). MTHFR enzimi, folat metabolizmasında önemli bir enzimdir. MTHFR geninde meydana gelen bir mutasyon ile enzim aktivitesi azalmakta ve buna bağlı olarak da plazma homosistein düzeyi artmaktadır (21). Yüksek homosistein konsantrasyonunun trombojenezi arttırdığı bildirilmiştir (23,24). Hiperhomosisteinemi ile akut miyokard infarktüsü arasında ilişkinin araştırıldığı bir çalışmada sağlıklı bireylerde hastalardan daha sık MTHFR (C677T) homozigot mutasyonu tespit edildiği bildirilmiştir (25). Yine MTHFR C677T genotipin venöz trombozisde önemli bir risk faktörü olduğunun ileri sürülmesine rağmen, bu görüşün akside savunulmaktadır (26). MTHFR A1298C mutasyonunda MTHFR enzim aktivitesinde azalma olduğu ancak bu durumun homosistein düzeyinde önemli bir etki yapmadığı gösterilmiştir (27). Farklı çalışmalarda venöz trombozlu hastalarla sağlıklı kontrol grupları arasında homosistein seviyeleri arasında fark tespit edilmediği bildirilmiştir (28,29). FII 20210 G/A ve FV Leiden mutasyonlarının venöz tromboembolizm üzerindeki etkisi yaygın olarak kabul edilmesine rağmen (30), geleneksel trombofili parametrelerine (anti-trombin-3 ve protein C-S eksikliği) dahil edilmelerini tavsiye etmek için yeterli veri olmadığı da savunulmuştur (31). Farklı bir çalışmada SVT'li hastalarda FV Leiden mutasyonunun olguların %16,7'sinde tespit edildiği, fakat FII 20210G/A ve MTHFR C677T mutasyonunun SVT için risk faktörü olmadığı bildirilmiştir (32). SVT hastalarında FV Leiden mutasyonu sıklığı %3,7 ile %25 arasında değişirken, FII 20210 G/A sıklığının %0 ile %20 ve MTHFR C677T sıklığının %0 ile %36 arasında olduğu bildirilmiştir (33). FV Leiden, kalıtsal trombofilinin en yaygın kalıtsal formudur ve vakaların %40-50'sini oluşturur. Prevalansı popülasyona göre değişmektedir (34). Bu çalışmada FV Leiden, FII, Gp3a mutasyonları ve homosistein düzeyleri açısından hasta ve kontrol grubu arasında anlamlı istatistiksel farklılık tespit edilmedi. MTHFR mutasyonu kontrol grubunda daha yüksekti. Bu çalışmanın sonuçlarının literatürde benzer metodoloji ile yapılmış çalışmalardan farklı olmasının, mutasyonların bölgesel farklılıklar gösterebilmesi ve görece olgu sayısının az olması ile açıklanabileceğini düşünüyoruz.

Literatürde F13 V34L polimorfizminin miyokard enfarktüsüne karşı koruyucu olabileceği bildirilmiştir (35). Farklı bir çalışmada F13 V34L polimorfizminin venöz tromboemboliye karşı koruyucu etkisi olduğu tanımlanmıştır (9). F13a, bitişik fibrin monomeri molekülleri arasındaki peptit bağlarının oluşumunu katalize eder, böylece pıhtıya kimyasal ve mekanik stabilite kazandırır (36). F13a ve 13b genetik mutasyonları kan pıhtılarının zayıf ve kararsız hale gelmesine neden olan fonksiyonel F13 yetersizliğine yol açarlar. Bu çalışmada F13 V34L polimorfizmi açısından SVT'li hastalar ve kontrol grubu arasında istatistiksel olarak anlamlı fark olup, kontrol grubunda daha yüksekti. SVT'li hastalarda polimorfizm oranı %10,9 iken kontrol grubunda %30,8 olarak tespit edildi. Yani F13 V34L polimorfizm varlığının SVT için koruyucu olduğu düşünülmektedir.

Kardiyovasküler hastalık ve inme için diğer bir önemli risk faktörü hiperfibrinojenemidir (37). β-fibrinojen geni veya bunun transkripsiyonu ile ilgili herhangi bir mutasyonun plazma fibrinojen seviyeleri üzerinde bir etkisi olabileceği bildirilmiş (11), fakat β-fibrinojen genetik polimorfizmi ile venöz tromboz arasındaki ilişki hala aydınlatılamamıştır ve venöz tromboz riski ile ilişkisinin olmadığı bildirilmiştir (12,28). Bu çalışmada SVT ile kontrol grupları arasında kontrol grubu lehine fark tespit edildi. Kontrol grubunda polimorfizm oranı daha yüksekti. Yani β-fibrinojen polimorfizm varlığı SVT riskinde bir artışa neden olmuyordu.

PAI-1 4G/5G polimorfizminin iskemik inme olaylarıyla bağlantısı olduğuna dair deliller mevcuttur (38). PAI-1 doku plazminojen aktivatörü ve ürokinaz adı verilen proteazları inhibe eden bir serin proteaz inhibitörüdür (39). PAI-1'in aşırı ekspresyonunun fibrinolitik sistemin aktivitesinde bir bozulmaya yol açarak trombotik olaylar için riski artırdığı bildirilmiştir (40). Fakat daha güncel

çalışmalarda farklı sonuçlar bildirilmiştir (13,28). Bu çalışmada kontrol grubunda PAI-14G/5G polimorfizmi daha yüksek oranda tespit edildi. Bu durum PAI-1 polimorfizminin SVT için etkin bir risk faktörü olmadığını düşündürmektedir.

Trombosit GP 3a polimorfizminin tromboembolik hastalık ile korele olup olmadığı halen net değildir. Bazı raporlar tromboembolik hastalık ve trombosit GP 3a polimorfizminin ilişkili olduğunu savunsa da (14), bazı çalışmalar ilişki olmadığını bildirmiştir (15). GP 3a açısından her iki grup arasında istatistiksel anlamlı bir fark olmaması, GP 3a'nın venöz tromboemboli üzerine etkinliği olmadığını düşündürmektedir.

Çalışmamızda MTHFR (C677T, A1289C), FV Leiden, FII G20210, β-fibrinojen 455 G-A, PAI-1 4G/5G polimorfizmleri SVT için risk oluşturmamaktadır. F13 V34L polimorfizminin kontrol grubunda daha yüksek oranda olup SVT'li hastalarda daha düşük olması F13 V34L polimorfizmini taşımanın SVT'ye karşı koruyucu etkisi olduğunu, venöz tromboz riskini azalttığını düşündürmektedir.

SONUÇ

SVT'nin etyolojisinde birçok faktör rol oynamaktadır. Etyolojisinde suçlanılacak edinsel bir patoloji olmayan olgularda genetik polimorfizm varlığı hala önemli görünmektedir, fakat normal popülasyonda da varlığı göz önüne alındığında polimorfizm varlığının tromboz üzerine etkisinin etnisiteden etkilenebildiğini düşündürmektedir. Yani tek başına genetik polimorfizm varlığının tromboz için etkinliği, çok merkezli daha büyük çalışmalarla araştırılmalıdır.

Bu çalışmadaki hasta popülasyonunda olgu sayısının görece az olması çalışmanın sonuçlarının güvenilirliğini kısıtlamakta olup olgu sayısının daha fazla olması sonuçları daha objektif ve güvenilir yapacaktır. Yine çalışma popülasyonu farklı etnik yapıdaki olgulardan oluşmaktaydı ve genetik polimorfizmin etnisite ile değişebileceği göz önüne alındığında bu da çalışmanın başka bir kısıtlayıcısı olabilir.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.593920

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):172-176

Evaluation of Factors Affecting Sexual Functions and Contraceptive Method Preferences of Women

Kadınların Cinsel Fonksiyonlarını Etkileyen Faktörlerin ve Kontraseptif Yöntem Tercihlerinin Değerlendirilmesi

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Geliş Tarihi / Received : 18.07.2019
Kabul Tarihi / Accepted : 05.11.2019
Çevrimiçi Yayın Tarihi / Available Online : 08.11.2019

ABSTRACT

Aim: Sexual function is a complex process that is influenced by physical, biological and emotional factors. The use of contraception is very common among women and can affect women's sexual functions in various ways. The aim of this study was to investigate of factors affecting sexual functions and contraceptive method preferences of women.

Material and Methods: The study was planned in cross-sectional descriptive pattern and women between the ages of 18-49 who were not in menopause and who used contraception were included in the study. Sociodemographic data form and Female Sexual Function Index (FSFI) were used to collect data. The independent effects of different determinants on sexual dysfunction were evaluated by logistic regression analysis model.

Results: In this study, 45.5% of women were found to have sexual dysfunction (FSFI score <26.55). Logistic regression analysis of sexual dysfunction revealed that using modern contraceptive methods (OR= 0.393, 95% CI 0.191-0.808) and considering that the income was adequate (OR= 0.405, 95% CI 0.211-0.780) were found to be protective factors, while presence of chronic disease (OR= 2.639, 95% CI 1.074-6.481), vaginal discharge (OR= 2.121, 95% CI 1.130-3.937) and self-decision on method of contraception by herself (OR= 3.331, 95% CI 1.471-7.543) were found to be risk factors.

Conclusion: The use of modern contraceptive methods can protect women from sexual dysfunction when compared to traditional contraceptive methods. If the method of contraception used by women is learned and the directions they need are made, their sexual life and quality of life can be improved.

Keywords: Contraception; female; sexuality.

ÖZ

Amaç: Cinsel fonksiyon fiziksel, biyolojik ve duygusal pek çok faktörden etkilenen karmaşık bir süreçtir. Gebelikten korunma yöntemi kullanımı kadınlar arasında oldukça yaygındır ve kadınların cinsel fonksiyonlarını çeşitli yollarla etkileyebilmektedir. Bu çalışmanın amacı kadınların cinsel fonksiyonlarını etkileyen faktörleri ve gebelikten korunma yöntemi tercihlerini araştırmaktır.

Gereç ve Yöntemler: Çalışma kesitsel tanımlayıcı desende planlandı ve 18-49 yaş arasında, menopozda olmayan ve gebelikten korunma yöntemi kullanan kadınlar çalışmaya dahil edildi. Çalışmada veri toplamak amacı ile sosyodemografik veri formu ve Kadın Cinsel Fonksiyon İndeksi (Female Sexual Function Index, FSFI) kullanıldı. Farklı belirleyicilerin cinsel işlev bozukluğu üzerindeki bağımsız etkileri lojistik regresyon analiz modeli ile değerlendirildi.

Bulgular: Bu çalışmada kadınların %45,5'inin cinsel fonksiyon bozukluğu (FSFI skoru <26,55) yaşadığı bulundu. Cinsel fonksiyon bozukluğu üzerine oluşturulan lojistik regresyon analizinde, modern korunma yöntemi kullanmanın (OR= 0,393; %95 GA 0,191-0,808) ve gelirinin yeterli olduğunu düşünmenin (OR= 0,405; %95 GA 0,211-0,780) koruyucu faktörler olduğu bulunurken; kronik hastalık varlığı (OR= 2,639; %95 GA 1,074-6,481), vajinal akıntı (OR= 2,121; %95 GA 1,130-3,937) ve korunma yöntemine kendi kendine karar vermenin (OR= 3,331; %95 GA 1,471-7,543) ise risk faktörleri olduğu bulundu.

Sonuç: Geleneksel korunma yöntemleri ile kıyaslandığında, modern korunma yöntemleri kullanılması kadınları cinsel fonksiyon bozukluğundan koruyabilir. Kadınların gebelikten korunma yöntemi tercihleri öğrenilerek ihtiyaç duydukları yönlendirmeler yapılır ise cinsel hayatları ve yaşam kaliteleri iyileştirilebilir.

Anahtar kelimeler: Kontrasepsiyon; kadın; cinsellik.

INTRODUCTION

According to the World Health Organization, sexual health is the physical, mental and social fullness of sexuality, and everyone has the right to reach out sexual information and to experience sexual intercourse for enjoyment or for breeding purposes (1). To be able to talk about complete sexual health, sexual functions must be fully functioning (2). Sexual function is a complex process which is affected by psychosocial factors such as family, social relations and religious beliefs as well as neurologic, endocrine and vascular systems (2). Sexual dysfunction is defined as the deterioration of one or more of the components of sexual desire, arousal, orgasm, and pain in the sexual response cycle, and approximately 41% of women worldwide experience sexual dysfunction (3). Factors such as lifestyle habits, urogenital and obstetric complaints and the presence of chronic diseases may cause sexual dysfunctions of female (3).

Use of contraception is necessary for the continuation of sexual activity in cases where pregnancy is not desired (4). Women can use traditional and modern contraceptive methods to prevent pregnancy (5). Contraceptive methods have many side effects such as changes in mood-state, changes in the amount of menstrual bleeding (4). These side effects can cause women to abandon the method of contraception. However, the effect of the contraceptive method on sexual function can be neglected by the patients and also by the healthcare professionals who offer both the method and the service (4).

In general, it is believed that the use of a contraceptive method has a positive effect on sexual function since it eliminates the fear of being pregnant (4). Contraception methods cause hormonal and physical changes and it is thought that this may adversely affect sexual function (4). In the literature, there are very few studies examining the difference between traditional and modern contraceptive methods in terms of their effects on female sexual function and the subject is still unclear (6). In particular, combined oral contraceptive pills (COCP) can cause vaginal dryness and cause pain in coitus, and not using contraceptive methods may adversely affect sexual function because of the concern of pregnancy (5).

Sexual function is an important factor that determines the physical, emotional and social integrity of human being since it is a sexual entity (7). Considering the widespread use of contraceptive methods, it deserves to examine the effects on sexual function in more detail (7). The aim of this study was to investigate the factors affecting sexual functions and contraceptive method preferences of women.

MATERIAL AND METHODS

This study in the cross-sectional design was conducted between 01.04.2017 and 01.06.2017 at the Reproductive Health Clinic of Izmir Katip Celebi University Atatürk Training and Research Hospital, Obstetrics and Gynecology Department. The study included women aged between 18-49 year, who were sexually active in last month and were not in the menopause period and protected from pregnancy by any means of contraception method. Patients with thyroid dysfunction, psychiatric disease, malignancy, active infection, pregnancy and hormone therapy for any reason were not included in the study. The presence of these diseases and treatments that stated by patients who were not included in the study were checked from the computer system with the verbal consent of the patients.

The number of female patients between the ages of 15-49 who were admitted to the reproductive health clinic and were sexually active and suitable for the inclusion criteria was 10 women per day. For the 2-months period during data were collected, the study population was accepted as 400 women. The study sample size to be achieved was calculated as at least 197 women with the 95% confidence level and the margin of error of 5%, incidence of sexual dysfunction taken as 48% based on a stated ratio in a previous study conducted in Turkey (7). Ethics committee approval was obtained from Izmir Katip Celebi University Non-invasive Ethics Committee on March 22, 2017, with decision number 62.

Data Collection Tools

In order to collect data, sociodemographic data form consisting of 33 questions prepared by the researchers and Female Sexual Function Index (FSFI) were used. In the sociodemographic characteristics, age was divided into three groups as 30 years and under, 30-39 years and 40 years and above because of some studies indicate that women in these age groups experience different sexual dysfunctions (3). Three groups according to the educational status (primary and lower, middle and high school, university and higher), two groups according to marital status (single and married), two groups according to income level perception (sufficient and insufficient), two groups according to the presence of chronic disease (yes and no), four groups according to the type of delivery is given to (nulliparous, normal vaginal birth, cesarean section and both normal vaginal birth and cesarean section), and the decide on the contraception method was divided into three groups (partner, with her partner, and herself). The patients were divided into two groups as those using traditional contraception methods and using modern contraception methods. The methods of hormonal contraception (COCP, injected contraceptives, subcutaneous implants, intrauterine devices (IUD), and barrier methods (condom, diaphragm, and spermicides) considered as modern contraception and the coitus interruptus (withdrawal or pull-out method) and calendar method considered as traditional methods.

Female Sexual Function Index (FSFI)

FSFI is a 19-items likert-type scale used to measure the sexual function of women. The Turkish validity and reliability study of the FSFI was conducted by Oksuz and Malhan in 2005 (8). In the Turkish version, the Cronbach Alpha coefficient of the scale was 0.95 and the test-retest reliability was 0.75-0.95. The scale consists of six items: desire, arousal, lubrication, orgasm, satisfaction, and pain. Each item is scored between 0 or 1 to 5. The lowest score is 2 and the highest is 36. The FSFI total score below 26.55 is indicative of sexual dysfunction. The presence of a score of 26.55 and above indicates normal sexual function (9).

Statistical Analysis

Data were summarized as mean±standard deviation or numbers and percentage. In univariate analyses, categorical data were evaluated using the Pearson chi-square test followed by post hoc Bonferroni method. The independent effects of different determinants on sexual

dysfunction were analyzed by multiple logistic regression analysis model with Backward method. The relationship between dependent variable sexual dysfunction and independent variables that will be included in the model was evaluated separately and the determinants of p≤0.250 were included in the regression model (10). Age and marital status were added to the regression model as they were the main factors that could affect sexual function. Statistical analyses of the data were done by using SPSS 16 package program and p values below 0.05 were considered statistically significant.

RESULTS

A total of 253 women were invited to the study. Since 32 patients did not want to answer questions related to their sexual function and 19 patients refused to participate in the study due to other reasons (lack of time or unwilling to participate in any study, etc.), the study was completed with a total of 202 women.

The mean age of the women who participated in the study was 31.96±7.05 years. Of the patients, 48.5% (n=98) had a university or higher education level. Of the patients, 95.0% (n=192) were married. While 24.3% (n=49) of the patients were using traditional contraception methods, 75.7% (n=153) were using modern contraception methods. While 45.5% (n=92) of the women participated in the study had sexual dysfunction, 54.5% (n=110) had normal sexual function.

There was no significant relationship between socio-demographic characteristics and the choice of contraceptive methods, except deciding on the method (Table 1). It was found that women who decided to contraceptive method with her partner (69.7%, n=101) or by herself (94.6%, n=35) used modern contraceptive methods more frequently than traditional contraceptive methods (p=0.004).

In univariate analysis, significant relationship was found between sexual dysfunction and income level perception, and sexual dysfunction and presence of vaginal discharge. It was found that 60.0% (n=36) of women who thought that her income was insufficient had sexual dysfunction, while 39.4% (n=56) of women who thought that her income was sufficient had sexual dysfunction (p=0.007). In terms of vaginal discharge, 52.0% (n=64) of women with vaginal discharge had sexual dysfunction and 35.4% (n=28) of women without vaginal discharge experienced sexual dysfunction (p=0.021). There was no relationship between sexual function and other socio-demographic characteristics such as age, education level, marital status, presence of chronic disease (Table 2).

Logistic regression analysis model with backward elimination method was found to be significant (p<0.001), and the number of variables remaining in the model was five at last step. According to the logistic regression analysis results, income sufficiency (OR= 0.405, 95% CI 0.211-0.780) and using modern contraception method (OR= 0.393, 95% CI 0.191-0.808) are protective factors against sexual dysfunction. Also presence of chronic disease (OR= 2.639, 95% CI 1.074-6.481), presence of vaginal discharge (OR= 2.121, 95% CI 1.130-3.937) and decide on the method of contraception by patient's herself (OR= 3.331, 95% CI 1.471-7.543) were found to be risk factors for sexual dysfunction (Table 3).

DISCUSSION

In this study, factors affecting on female sexual functions and women's contraceptive method preferences was investigated. At the end of our study, we have concluded that protection against pregnancy with modern contraceptive methods, protects women from the risk of sexual dysfunction. We found that low-income level, the presence of chronic disease, the presence of vaginal discharge, and making the decision on contraceptive method by herself, had negative effect on sexual function.

In our study, 24.3% of women were using a traditional contraception method and 75.7% of them were using a modern method. The frequency of married women using traditional methods in Turkey according to the Demographic and Health Survey conducted in Turkey in 2013 was found to be 26% and is similar with the results of our study (11). The frequency of contraception with the traditional method across the world varies between 20-40% and is most commonly used in North Africa and West Asia (12). As the accessibility to modern contraceptive methods increases, the frequency of traditional contraceptive method decreases (12,13).

Sexual dysfunction was detected in 45.5% of the women who participated in our study. According to the literature, the frequency of female sexual dysfunction in Turkey ranges from 40 to 60% (7,14). In the study of Oksuz et al. (7), the frequency of female sexual dysfunction was found to be 48.3% and in Koseoğlu et al's (14) studies, it was 57.1%. In the world, female sexual dysfunction is seen with a frequency of 30-60% (15,16). Sexual dysfunction adversely affects the quality of life and lives of individuals (3). For this reason, it will be useful for patients to investigate the causes of the prevalence of sexual dysfunction and to develop treatment options for the causes.

In this study, it was found that the prevalence of sexual dysfunction was higher in women with a perception of inadequate income, chronic disease, and vaginal discharge. In the studies of Yanıkkerem et al. (17), it was found that low-income level increased the risk of sexual dysfunction. The insufficiency of income makes the living conditions of people difficult and increases the level of stress, and this is thought to negatively affect sexual desire and sexual function in women (17). Also, Zsoldos et al. (18) showed in their studies that the presence of chronic disease negatively affects sexual function. The presence of chronic disease brings with it the symptoms and complications related to the disease and also the undesirable side effects associated with the drugs used for treatment. Considering the psychological burden of each diagnosed chronic disease, all these factors may have a negative effect on sexual function.

Vaginal discharge is one of the most common causes of referral to the gynecology outpatient clinic of women. Vaginal discharge has various causes such as vaginitis and cervicitis and women have symptoms such as itching and pain along with the discharge (19). In a review of the literature, it is stated that genitourinary problems negatively affect female sexual functions (3). Diseases associated with vaginal discharge, additional symptoms associated with these diseases, and concerns about women's urogenital health and hygiene may adversely affect sexual functions.

Table 1. Effect of sociodemographic characteristics on contraceptive method selection

Sociodemographic characteristics	Traditional (n=49)	Modern (n=153)	p
Age			
<30 years	21 (42.9)	77 (50.3)	
30-39 years	19 (38.8)	53 (34.6)	0.649
>39 years	9 (18.4)	23 (15.0)	
Educational status			
Primary and lower	10 (20.4)	22 (14.4)	
Middle and high	18 (36.7)	54 (35.3)	0.552
University and higher	21 (42.9)	77 (50.3)	
Marital status			
Single	0 (0.0)	10 (6.5)	0.122
Married	49 (100)	143 (93.5)	
Current relationship			
<5 years	29 (59.2)	66 (43.1)	
5-10 years	8 (16.3)	47 (30.7)	0.087
>10 years	12 (24.5)	40 (26.1)	
Income level perception			
Insufficient income	13 (26.5)	47 (30.7)	0.577
Sufficient income	36 (73.5)	106 (69.3)	
Presence of chronic disease			
No	42 (85.7)	133 (86.9)	0.828
Yes	7 (14.3)	20 (13.1)	
Type of delivery			
Nulliparous	17 (34.7)	33 (21.5)	
Normal vaginal birth	15 (30.6)	49 (32.0)	0.283
Cesarean section	14 (28.6)	57 (37.3)	
Both (normal + cesarean)	3 (6.1)	14 (9.2)	
Deciding the method			
Partner	3 (6.1)[a]	17 (11.1)[a]	
With her partner	44 (89.8)[a]	101 (66.0)[b]	**0.004**
Herself	2 (4.1)[a]	35 (22.9)[b]	

Table 3. Logistic regression analysis on sexual dysfunction

Determining Factors	OR	%95 CI	p
Sufficient income	0.405	0.211-0.780	**0.007**
Presence of chronic disease	2.639	1.074-6.481	**0.034**
Presence of vaginal discharge	2.121	1.130-3.937	**0.019**
Deciding the method herself	3.331	1.471-7.543	**0.004**
Modern contraceptive method	0.393	0.191-0.808	**0.011**

OR: Odds ratio, CI: Confidence Interval

Table 2. Results of univariate analysis on sexual dysfunction

Determining Factors	Sexual Dysfunction		p
	Present (n=92)	None (n=110)	
Age			
<30 years	41 (44.6)	57 (51.8)	
30-39 years	33 (35.9)	39 (35.5)	0.363
>39 years	18 (19.6)	14 (12.7)	
Educational status			
Primary and lower	18 (19.6)	14 (12.7)	
Middle and high	35 (38.0)	37 (33.6)	0.217
University and higher	39 (42.4)	59 (53.6)	
Marital status			
Single	5 (5.4)	5 (4.5)	0.772
Married	87 (94.6)	105 (95.5)	
Income level perception			
Insufficient income	36 (39.1)	24 (21.8)	**0.007**
Sufficient income	56 (60.9)	86 (78.2)	
Presence of chronic disease			
No	75 (81.5)	100 (90.9)	0.051
Yes	17 (18.5)	10 (9.1)	
Drug use			
No	83 (90.2)	105 (95.5)	0.144
Yes	9 (9.8)	5 (4.5)	
Smoke			
No	62 (65.4)	72 (65.5)	0.772
Yes	30 (32.6)	38 (34.5)	
Alcohol use			
No	83 (90.2)	95 (86.4)	0.399
Yes	9 (9.8)	15 (13.6)	
Presence of vaginal discharge			
No	28 (30.4)	51 (46.4)	**0.021**
Yes	64 (69.6)	59 (53.6)	
Type of delivery			
Nulliparous	20 (21.7)	30 (27.2)	
Normal vaginal birth	35 (38.0)	29 (26.4)	0.133
Cesarean section	27 (29.3)	44 (40.0)	
Both (normal + cesarean)	10 (11.0)	7 (6.4)	
Deciding the method			
Partner	10 (10.9)	10 (9.1)	
With her partner	59 (64.1)	86 (78.2)	0.059
Herself	23 (25.0)	14 (12.7)	
Contraceptive method			
Traditional	27 (29.3)	22 (20.0)	0.123
Modern	65 (70.7)	88 (80.0)	

In our study, there was no relationship between sexual dysfunction and age, education level, marital status, and alcohol use and smoke. In the systematic reviews of McCool-Myers et al. (3) related to the factors that may cause sexual dysfunction, the relationship between sexual dysfunction and age, educational status, marital status, and alcohol use and smoke was stated as not certain. Since the sexual function may be affected by many physical and emotional conditions, it would be more useful to evaluate the effects of the risk factors investigated on sexual function in multivariate analyses.

In our study, deciding by herself to which contraception method to use, determined as a risk factor for sexual dysfunction. In their study, Wallwiener et al. (20) concluded that emotional intimacy and long-term relationship with sexual partner positively affect sexual function. Deciding together with the partner in the method of contraception may be part of the emotional closeness between the couple. In addition, taking an important decision together with the partner, such as the decision to protecting against pregnancy, may make women feel more comfortable and this may have a positive impact on their sexual experience (20).

At the end of our study, we found that modern contraceptive methods protect women from sexual dysfunction. The number of studies investigating the effect of contraceptive methods on sexual function is quite limited in the literature. There was no significant difference in terms of sexual dysfunction in the study of Koseoğlu et al. (14) comparing the women who use IUDs and who do not use any methods. It is known that every contraceptive method may have different characteristics that affect the sexual function (pelvic pain in the use of IUD, tension, and anxiety in the use of COCP and etc.)

(14,21). Since using a traditional method of contraception means not to use a medical method (eg, COC, IUD, subcutaneous implant, etc.), it may increase the anxiety about unexpected pregnancies and this may adversely affect sexual function.

Limitations

It is a limitation that the study is conducted only on patients who apply to a tertiary care facility. Investigation of the effects of the protection methods used by the women in their daily lives on the sexual functions of the other health care providers will contribute to the elucidation of the issue. Another limitation of the study was that the data were collected only from a tertiary care hospital. For this reason, the data we achieved at the end of the study that shows the relationship between methods of protection and sexual dysfunction may not be enough in a statement for Turkey in general.

CONCLUSION

As a result of our study, the use of modern contraceptive method protects women from sexual dysfunction; low-income level, the presence of chronic disease, the presence of vaginal discharge, and making the decision on contraceptive method by herself were found to increase the risk of sexual dysfunction. In order to protect women from sexual dysfunction, it might be more beneficial to protect them from pregnancy through modern contraceptive methods. The question of whether the women who apply to the health institution for any reason, the methods of contraception, the problems with the method and especially how they affect their sexual lives and offering solutions to them will positively affect the lives of the patients.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.606028

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):177-180

The Effect of Time Elapsed from the Onset of Symptoms to Surgery on Prognosis in Patients with Foot Drop due to Lumbar Disc Hernia

Lomber Disk Hernisi Nedeniyle Düşük Ayak Gelişen Hastalarda Semptomların Başlangıcından Ameliyata Kadar Geçen Sürenin Prognoza Etkisi

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Geliş Tarihi / Received : 18.08.2019
Kabul Tarihi / Accepted : 11.11.2019
Çevrimiçi Yayın Tarihi / Available Online : 15.11.2019

ABSTRACT

Aim: The aim of this study was to evaluate the effect of the duration from foot drop development to nerve decompression on the rate and degree of recovery in foot drop clinic.
Material and Methods: We retrospectively reviewed 30 consecutive patients who had undergone microdiscectomy for foot drop clinic (ankle dorsiflexion 0/5 paresis) between April 2014 and February 2019. Patients were divided into three groups according to the time from foot drop development to surgery, as <72 hours, 72 hours to 1 week, and >1 week. Kruskal-Wallis and Bonferroni corrected Mann Whitney U test were used to evaluate the rate and degree of recovery of ankle dorsiflexion muscle strength between groups.
Results: In this study, 30 patients (18 females and 12 males) who underwent surgery for foot drop were evaluated. Mean age at the time of surgery was 46.5±13.5 (range, 18-72) years. Postoperative ankle dorsiflexion strength was 4.2±1.6 (range, 0-5) in <72 hours group, 1.7±1.6 (range, 0-5) in 72 hours - 1 week group and 1.0±1.3 (range, 0-3) in >1 week group. Postoperative muscle strength improvement level of <72 hours group was significantly different both from 72 hours - 1 week group (p=0.003) and from >1 week group (p=0.002). There was no statistically significant difference between 72 hours - 1 week group and >1 week group (p=0.427).
Conclusion: In foot drop clinic, the duration from onset of symptoms to surgical decompression was a statistically significant predictor of postoperative recovery rates.
Keywords: Foot drop; lumbar disc hernia; surgery; prognosis.

ÖZ

Amaç: Bu çalışmanın amacı, düşük ayak gelişiminden sinir dekompresyonuna kadar geçen sürenin düşük ayak kliniğinde iyileşme oranı ve derecesi üzerine olan etkilerini değerlendirmektir.
Gereç ve Yöntemler: Nisan 2014 ve Şubat 2019 arasında düşük ayak kliniği (ayak bileği dorsifleksiyonu 0/5 parazik) nedeniyle mikrodiskektomi geçirmiş olan ardışık 30 hasta retrospektif olarak incelendi. Hastalar düşük ayak gelişiminden ameliyata kadar geçen süreye göre <72 saat, 72 saat ile 1 hafta ve >1 hafta olmak üzere 3 gruba ayrıldı. Gruplar arasında ameliyat sonrası ayak bileği dorsifleksiyon kas kuvvetlerinin iyileşme oranlarını ve derecesini değerlendirmek için Kruskal-Wallis ve Bonferroni düzeltmeli Mann Whitney U testi kullanıldı.
Bulgular: Bu çalışmada, düşük ayak nedeniyle ameliyat edilen 30 hasta (18 kadın ve 12 erkek) değerlendirilmiştir. Hastaların ameliyat sırasındaki ortalama yaşı 46,5±13,5 (aralık 18-72) idi. Ameliyat sonrası ayak bileği dorsifleksiyonu kas gücü <72 saat grubunda 4,2±1,6 (aralık, 0-5), 72 saat - 1 hafta grubunda 1,7±1,6 (aralık, 0-5) ve >1 hafta grubunda 1,0±1,3 (aralık, 0-3) idi. <72 saat grubunun ameliyat sonrası kas gücü iyileşme seviyesi hem 72 saat - 1 hafta grubundan (p=0,003) hem de >1 hafta grubundan (p=0,002) anlamlı şekilde farklılık göstermekteydi. 72 saat - 1 hafta grubu ve >1 hafta grubu arasında istatistiksel olarak anlamlı bir farklılık görülmedi (p=0,427).
Sonuç: Düşük ayak kliniğinde semptomların başlangıcından cerrahi dekompresyona kadar geçen sürenin, ameliyat sonrası iyileşme oranlarında istatistiksel olarak anlamlı bir prediktör olduğu görüldü.
Anahtar kelimeler: Düşük ayak; lomber disk hernisi; cerrahi; prognoz.

INTRODUCTION

Foot drop, defined as a significant weakness of ankle dorsiflexion (ADF), can develop due to many etiologic reasons including central nervous system diseases (tumor, paralysis, amyotrophic lateral sclerosis) (1,2), peripheral nerve pathologies (peroneal or sciatic nerve compression) (3-5) and systemic diseases (multiple sclerosis, hypothyroidism) (6,7). Nevertheless, lumbar disc hernia is regarded the most frequent etiology of lumbar disc herniation causing compression of the spinal roots (8-10). Weakness of ADF may lead to falling and injuries due to a remarkable deterioration in ambulation, which, in turn, gives rise to the decrease in a person's mobility and quality of life. The development of foot drop may have a sudden onset and be progressive. It is known that it tends to show an acute onset in patients with disc herniation (11,12), which is considered as a serious symptom of an underlying lumbar pathology, and in the majority of the cases reported in the literature, surgery has been performed as the treatment option (13). A vital prognosis criterion for recovery is the degree of dorsiflexion weakness (14). However, it is indicated in the event of full loss of strength that the most important prognostic factor is the time elapsed from the onset of symptoms to the decompression of the nerve.

This study aimed to evaluate the effects of the time elapsed from the development of foot drop to nerve decompression on the recovery rate and degree in foot drop clinic.

MATERIAL AND METHODS

A total of consecutive thirty patients, who had undergone microdiscectomy due to foot drop clinic (ADF 0/5 paresis) by the same surgical team in two different state hospitals between April 2014 and February 2019, were retrospectively reviewed. Clinical records, radiological imaging reports and surgical reports were reviewed. Data on patient demographics and clinical features, the time elapsed between the development of foot drop and surgery, duration of surgery, and muscle strength of ADF in the early post-operative period were reached. The evaluation of muscle strength of the ADF was carried out by the assessment of the tibialis anterior muscle in accordance with the muscle strength scale of Medical Research Council (Table1). Comorbidities, including diabetes mellitus (DM), smokers, coronary artery disease, chronic obstructive pulmonary disease (COPD) and hypertension were ascertained from the medical records.

All procedures carried out in studies including human participants were conducted in compliance with the ethical standards of institutional and/or national research committee, the Helsinki Declaration and its amendments or comparable ethical standards. Ethical approval for the study was obtained from the institutional review board of Namık Kemal University (01.08.2019, 2019/21). Informed and written consent was obtained from all patients.

The patients were divided into three groups as regards the time elapsed from the development of foot drop to surgery, as <72 hours, 72 hours to 1 week, and >1 week.

Statistical Analysis

Normality assumption for continuous data were examined by Shapiro-Wilk test. The differences between the groups were analyzed by Kruskal-Wallis test followed by Mann Whitney U test with Bonferroni correction, since variables not showing normal distribution. Descriptive statistics given as mean±standard deviation and median (minimum-maximum). Categorical data were analyzed with Fisher-Freeman-Halton test and summarized as frequency and percentage. All statistical analyses were performed using MedCalc v.12.7.7 (MedCalc Software, Ostend, Belgium), and $p<0.05$ was considered statistically significant.

RESULTS

Thirty patients (18 females, 12 males) operated on for foot drop (ADF muscle strength 0/5 paresis) were evaluated in this study. Mean age of the patients at the time of surgery was 46.5±13.5 (range, 18-72) years. Level 2 extruded or sequestrated disc hernia was present in twenty-five patients at lumbar 4-5, and at lumbar 4-5 and lumbar 5 in sacral 1 level. Table 2 shows the subgroup demographics of the patients.

Table 1. Manual muscle test of ankle dorsiflexion based on the examination of the tibialis anterior muscle according to the modified Medical Research Council Scale of muscle strength

0	No contraction of tibialis anterior
1	Flicker of ankle dorsiflexion, but no movement of the ankle joint
2	Patient can dorsiflex ankle with the effect of gravity eliminated
3	Patient can dorsiflex ankle against gravity but no added resistance
4	Patient can dorsiflex ankle against gravity and moderate resistance
5	Patient can dorsiflex ankle against gravity and full resistance

Table 2. Demographic characteristics of participants

	<72 hours		**72 hours - 1 week**		**>1 week**		**p**
	Mean±SD	**Median (Min-Max)**	**Mean±SD**	**Median (Min-Max)**	**Mean±SD**	**Median (Min-Max)**	
Age (years)	42.0±15.8	40.5 (18-72)	48.4±15.4	48.0 (27-67)	49.5±7.8	49.5 (36-59)	0.831
Weight (kg)	72.2±4.9	71.0 (67-84)	73.7±8.8	75.5 (65-89)	73.1±10.3	72.0 (57-89)	0.905
Height (cm)	168.5±6.5	167.5 (163-179)	170.5±7.1	170.5 (160-182)	173.0±7.4	174.5 (160-181)	0.463
BMI (kg/m^2)	25.4±1.2	25.9 (23.5-27.0)	25.3±2.1	25.2 (22.2-30.1)	24.4±2.6	24.5 (21.5-28.4)	0.451
	n (%)		**n (%)**		**n (%)**		
Gender							
Female / Male	5 (50.0) / 5 (50.0)		8 (66.7) / 4 (33.3)		5 (62.5) / 3 (37.5)		0.808

BMI: Body Mass Index, SD: Standard Deviation, Min: Minimum, Max: Maximum

Medical comorbidities were included DM (five patients), smokers (16 patients), coronary artery disease (one patient), COPD (one patient) and hypertension (six patients). There was no significant difference between the subgroups in terms of comorbidity.

ADF in the early period examinations (postoperative day 1) of the patients was detected as 5/5 in 7 patients, 4/5 in one patient, 3/5 in one patient, and 0/5 in one patient out of 10 in <72 hours group; as 5/5 in one patient, 3/5 in three patients, 2/5 in two patients, 1/5 in 2 patients, and 0/5 in four patients out of 12 in 72 hours - 1 week group; and as 3/5 in two patients, 1/5 in two patients, and 0/5 in four patients out of 8 in >1 week group (Table 3).

Postoperative muscle strength was as 4.2±1.6 (range, 0-5), 1.7±1.6 (range, 0-5) and 1.0±1.3 (range, 0-3) in <72 hours, 72 hours - 1 week, and >1 week groups, respectively. Preoperative and postoperative muscle strength changes were calculated for each group. The differences between the groups were examined by Kruskal-Wallis test, and a statistically significant difference was found between the three groups (p=0.002). According to the post hoc test results, postoperative recovery level of <72 hours group showed a statistically significant difference in comparison to 72 hours - 1 week group and >1 week group (p=0.003 and p=0.002, respectively). No statistically significant difference was seen between 72 hours - 1 week group and >1 week group (p=0.427) (Table 4).

While ADF muscle strength was above 3/5 in 50.0% of our patients, 90.0%, 33.0% and 25.0% of these patients comprised those in <72 hours group, 72 hours - 1 week group, and >1 week group, respectively (Table 3).

Table 3. Distribution of postoperative ADF muscle strength improvement into groups, n (%)

Paresis	< 72 hours	72 hours - 1week	>1 week
5/5 (normal)	7 (70.0)	1 (8.3)	0 (0.0)
4/5	1 (10.0)	0 (0.0)	0 (0.0)
3/5	1 (10.0)	3 (25.0)	2 (25.0)
2/5	0 (0.0)	2 (16.7)	0 (0.0)
1/5	0 (0.0)	2 (16.7)	2 (25.0)
0/5	1 (10.0)	4 (33.3)	4 (50.0)

All patients had preoperative ADF muscle strength of 0/5 paresis, all measures of power are based upon the modified Medical Research Council Scale of muscle strength (see Table 1), ADF: ankle dorsiflexion

Table 4. Comparison of the postoperative mean ADF muscle strength values

	Mean±SD	Median (Min-Max)	p
<72 hours	4.2±1.6	5.0 (0-5)	
72 hours - 1 week	1.7±1.6	1.5 (0-5)	**0.002**
>1 week	1.0±1.3	0.5 (0-3)	

All patients had preoperative ADF muscle strength of 0/5 paresis, ADF: ankle dorsiflexion

DISCUSSION

The effect of time of surgical intervention on foot drop prognosis remains to be an issue of controversy in the literature. Therefore, numerous studies have aimed at defining predictive factors and their effect on the recovery of foot drop clinic. Nonetheless, the term 'foot drop' is defined as the apparent weakness of the ankle in clinical practice; however, the degree of weakness of the ADF may show differences in the literature. Since this condition may affect, at a great length, the prevalence and prognosis of foot drop, the severity of muscle weakness should be defined objectively. It was our aim in this study to put forth the efficiency of surgical intervention in patients with full loss of ADF (ADF 0/5 paresis).

In this study in which 30 patients with 0/5 paresis ADF muscle strength were evaluated, full recovery was seen in 8 (26.7%) patients postoperatively and partial recovery (ADF ≥ 3/5 paresis) in 15 (50.0%) patients. It was observed that our results are low when compared to those of previous studies in the literature. In the meantime, it has been reported that each 1 degree reduction in ADF muscle strength in the preoperative period results in a 10.0% decrease (Hazard ratio = 1.10) in the recovery of foot drop postoperatively (15). In a study by Matsui et al. (16) in 1995, the authors reported recovery in 80% of the patients; however, no information was given regarding the degree of recovery of the patients. Girardi et al. (17), in 2002, reported full recovery in 71.0% of the ADF loss patients after surgery, in their study included patients with mild and intermediate paresis, whose ADF muscle strength was 2/5 ≤ 4/5 paresis. In a recent study with inclusion criteria similar to ours, Aono et al. (8) have evaluated 46 patients whose ADF muscle strength was ≤ 3/5 paresis. While favorable results were reached in 41.0% of the patients, no recovery was seen in 28.0% of the patients. In a study conducted in 2009, where the patients were grouped with regard to their preoperative muscle strength values, 68.0% recovery rate was found in patients whose preoperative ADF muscle strength was as 3/5 paresis and 4/5 paresis and 27.0% recovery rate was found in those whose preoperative ADF muscle strength was ≤ 2/5 paresis (18). These differences in recovery rates reflect the differences in the range of preoperative muscle strength weakness in patient populations. One of the most important reasons of the low rates found in our study is due to the fact that all patients evaluated had a 0/5 paresis ADF muscle strength preoperatively.

While 90.0% recovery rate was ensured in <72 hours group patients undergoing early period surgical intervention, 33.0% and 25.0% recovery rates were found in 72 hours - 1 week group, and >1 week group patients, respectively. The efficiency of early period surgical intervention on foot drop prognosis has been documented many times in the literature. Postacchini et al. (19) have reported that the recovery degree of motor weakness that develop due to lumbar disc herniation is inversely proportional to the time elapsed to surgery. In a retrospective study evaluating 26 patients in whom decompression was performed due to foot drop, Bhargava et al. (20) have statistically shown that time elapsed from the development of foot drop to surgery is an important predictor in terms of recovery (Odds ratio = 0.93). In a recent study investigating the efficiency of the change in the time period elapsed from the development of foot drop to decompression on foot drop recovery, each one unit increase in the time elapsed has a negative effect on recovery at a rate of 33.0% (15). These data indicate that in order to prevent permanent damage, decompression must be performed before the inflammatory process in the

nerve tissue under compression leads to scar formation. However, nerve damages with acute development cause edema in neural transmission and a faster deterioration on methyl-glucose transport (21). While full recovery at a rate of 70.0% was established in surgeries performed during the first 72 hours of the onset of foot drop, full recovery could not be achieved in patients operated after a week.

CONCLUSION

In this retrospective study, 30 patients who developed foot drop due to lumbar disc herniation underwent microdiscectomy. Preoperative palsy duration was statistically significant predictors of foot drop improvement.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.595690

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):181-185

The Importance of Surgical Timing in Inguinoscrotal Surgical Pathologies

İnguinoskrotal Cerrahi Patolojilerde Cerrahi Zamanlamanın Önemi

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Geliş Tarihi / Received : 23.07.2019
Kabul Tarihi / Accepted : 19.11.2019
Çevrimiçi Yayın Tarihi /
Available Online : 25.11.2019

ABSTRACT

Aim: Various inguinal pathologies can occurred if the processus vaginalis cannot closed fully. The aim of this study was to evaluate all patients who underwent inguinoscrotal surgery operations between 2011 and 2018 in our clinic, in terms of age, gender and accompanying with another operation, retrospectively.
Material and Methods: In this study, records of 807 patients who were performed inguinal surgery operations including 558 inguinal hernia repair, 184 orchiopexy and 65 hydroselectomy between 2011 and 2018 at Duzce University, Faculty of Medicine, Pediatric Surgery Department were evaluated retrospectively.
Results: Mean age of the 558 patients who underwent inguinal hernia operation was 3.0±3.6 years, and 288 (51.6%) patients were older than 2 years of age. Of the patients who performed inguinal hernia operation, 411 (73.7%) were male and 147 (26.3%) were female. There was a statistically significant difference in terms of inguinal hernia repair side according to gender (p=0.038), and left inguinal hernia repair rate in females was detected higher than in males. Mean age of the 184 patients who performed orchiopexy operation was 4.0±3.4 years old, and only 46 patients (25.0%) who underwent orchiopexy were younger than 2 years of age. Mean age of the 65 patients who performed hydrocele operation was 4.6±4.1 years old.
Conclusion: According to the results of this study, it is seen that the community does not have enough information about the right operation time of inguinal hernia and undescended testis, and that the society should be informed about this issue.
Keywords: Inguinal hernia; cryptorchidism; testicular hydrocele; infertility.

ÖZ

Amaç: Processus vaginalisin tam olarak kapanmaması durumunda çeşitli inguinal patolojiler ortaya çıkabilir. Bu çalışmanın amacı kliniğimizde 2011 ve 2018 yılları arasında inguinoskrotal cerrahi operasyonu yapılmış olan tüm hastaları geriye dönük olarak yaş, cinsiyet ve başka bir operasyonla birliktelik durumu açısından değerlendirmektir.
Gereç ve Yöntemler: Bu çalışmada Düzce Üniversitesi Tıp Fakültesi Çocuk Cerrahisi kliniğinde 2011 ve 2018 yılları arasında 558 inguinal herni onarımı, 184 orşiopeksi ve 65 hidroselektomi olmak üzere inguinal cerrahi operasyonu yapılmış olan toplam 807 hastanın kayıtları geriye dönük olarak incelendi.
Bulgular: İnguinal herni operasyonu yapılmış olan 558 hastanın ortalama yaşı 3,0±3,6 yıl olup bu hastaların 288'i (%51,6) 2 yaşından daha büyük idi. İnguinal herni operasyonu yapılmış olan hastaların 411'i (%73,7) erkek ve 147'si (%26,3) ise kız idi. Cinsiyete göre inguinal herni onarım yönü bakımından istatistiksel olarak anlamlı bir farklılık vardı (p=0,038) ve kızlarda sol inguinal herni onarım oranının erkeklere göre daha yüksek olduğu tespit edildi. Orşiopeksi operasyonu yapılmış olan 184 hastanın ortalama yaşı 4,0±3,4 yıl idi ve orşiopeksi operasyonu yapılmış olan hastaların sadece 46'sı (%25,0) 2 yaşından daha küçük idi. Hidrosel operasyonu yapılmış olan 65 hastanın ortalama yaşı ise 4,6±4,1 yıl idi.
Sonuç: Bu çalışmanın sonuçlarına göre, toplumun inguinal herni ve inmemiş testisin doğru operasyon zamanı hakkında yeterli düzeyde bilgi sahibi olmadığı ve toplumun bu konuda bilgilendirilmesi gerektiği görülmektedir.
Anahtar kelimeler: İnguinal herni; kriptorşidizm; testiküler hidrosel; infertilite.

INTRODUCTION

A peritoneal extension which begins to occur in the male fetus at the third month of pregnancy goes down the scrotum through the inguinal ring. This peritoneal extension, called the processus vaginalis; normally disappears as the obliteration of in the last trimester of pregnancy after the testes to fall to scrotum. In girls, the same structure enters the inguinal canal following the ligamentum teres uteri and named as Nuck diverticulum. If the processus vaginalis remains fully or partially open, it therefore forms the basis of various inguinal pathologies (1,2).

Clinical diagnosis of inguinal hernia is usually easy. It is possible to identify with anamnesis only. Occurrence of an inguinal or scrotal swelling from time to time, and suppression of it or loss of it by lying on its back is sufficient for the diagnosis of hernia. Treatment of inguinal hernia in children, morbidity and mortality is very low and technically quick and easy surgical procedure. However, delaying the treatment for various reasons may cause hernia suffocation, the most important and dangerous complication of hernia. Therefore; if the child does not have a condition that prevents him from taking anesthesia, such as an upper respiratory tract infection, the procedure should be performed as soon as possible; not urgent but without waiting (3). The most feared complication of pediatric inguinal hernia is incarceration. The smaller the child's age and the size of the hernia, the greater the risk of incarceration (2,3).

In hydrocele, instead of the organ the only liquid enter inside the processus vaginalis. Since there are no intra-abdominal organs, there is no risk of incarceration. If the hydrocele sac is related to peritoneum, it is called communicating hydrocele, but not related with the peritoneum, it is called non-communicating hydrocele. In the anamnesis there is scrotal mass since birth and on physical examination, a cystic mass is palpated in the scrotum. In the pediatric age group, large parts of the hydrosels are the communicating hydrocele type. A special type of hydrocele; of the proximal and distal parts of the processus vaginalis to be obliterated. On physical examination, 1-2 cm cystic mass is palpated in the inguinal canal. When the ipsilateral testis is pulled down, this mass moves downward together with testis and this conditon is called cord hydrocele (cord cyst).

Cryptorchidism may be due to one of four reasons; anorchidia, ectopic testis, retractile testis and undescended testis. Cremasteric reflex is more active in children than in adults. This reflex causes the testis to be pulled up by the stimulation or cold effect of the perineum. In the case of retractile testis, the testis cannot be found in the scrotum. However, testis can be easily lowered to its normal position from high scrotal position in the superficial inguinal pouch or in inguinal canal. There is no indication for surgical treatment even after retractile testis that escaped again after a while. It improves spontaneously until adolescence (4).

Normally, the testes descend to the scrotum and are present in the scrotum for life. Intraabdominal testes in the fetus enter the inguinal canal in the intrauterine 7th month and settle into the scrotum near the birth. This migration of the testis at one end of the testis at the other end adhering to the scrotum of the gubernaculum contracted shrink is thought to be effective. In 30% of premature babies and in about 3% of babies born at term, the testes have not yet reached the scrotum. However, when the same children were re-examined at the end of the first year, it was seen that 5% of premature infants and only 0.5% of those who were born at term of one or two sided testis were still not fall (5). Diagnosis of undescended testis can be made at the earliest 3 months of age. Embryologically, the undescended testis is more common on the right because the left testis has already been falled to the scrotum. Up to 10% of all undescended testes are bilateral.

The following points are considered in the differential diagnosis of retractile testis with undescended testis. The testes can be lowered to the bottom of the scrotum without difficulty. After the examination, the testis does not immediately retract and remains in the scrotum for a while. The testis was sometimes seen in the scrotum by the family. The testis is of normal size and the hemiscrotum on the same side is fully developed. Care should be taken in the ambient and hand temperature during the examination. Follow-up is recommended in cases that cannot be clear diagnosed. In cases where one or both of the testes cannot be palpated in the scrotum; the retractile testis and ectopic testis must be distinction from the undescended testis using the above-mentioned features (3). Anorchidia is not possible to distinguish by physical examination. Because of the need for surgical exploration for definitive diagnosis of anorchidia, there is no condition for differential diagnosis with undescended testis before surgery.

The aim of this study was to retrospectively evaluate age, gender and accompanying operation data of patients with surgical pathologies of inguinoscrotal region (inguinal hernia, undescended testis and hydrocele) who operated in Duzce University Faculty of Medicine, Department of Pediatric Surgery between 2011 and 2018, and to show the severity of the undescended testis operation timing with the possibility of causing infertility.

MATERIAL AND METHODS

In this study, 807 patients who performed inguinal hernia (n=558), undescended testis (n=184) or hydrocele (n=65) operations between 2011 and 2018 in Duzce University, Faculty of Medicine, Department of Pediatric Surgery were included. Patients with incomplete file information and operated for other reasons were excluded. Ethical approval was obtained from the local ethics committee of Duzce University Medical Faculty (15.05.2019, 2019/101). Operations was performed by three surgeons. The age of the patient, the gender of the inguinal hernia patient and presence of accompanying surgical pathology (circumcision, etc.) were investigated retrospectively. Informed consent was obtained from all patients. Patients were generally examined by anesthesia specialist with hemogram and coagulation (Protrombin Time; PT, International Normalized Ratio; INR, Parsiyel Tromboplastin Time; aPTT) results one day before the operation and American Society of Anesthesiologists (ASA) score and anesthesia risks were determined. Patients who received anesthesia approval were brought by families with a minimum of 4 hours fasting period on the day of operation. After the vascular access was opened in the service, his mother and father were brought to the

operating room to ensure that the child is not afraid. In the operating room door after premedication with (iv) midazolam, the child was taken to the operating room while he was in a quiet state. After a period of anesthesia by the child followed in the wake-up department followed and then he was taken to the service with his father and his mother. Oral feeding was started at 2-3 hours postoperatively and he was discharged on the same day when oral tolerance was good.

Statistical Analysis

Statistical analyses were performed using IBM SPSS® Statistics for Windows®, version 23.0 (IBM Corp., Armonk, NY, USA). Pearson chi-square test with post hoc Bonferroni method was used to analyze categorical data. Continuous data were expressed as mean±standard deviation (minimum, maximum), and categorical data were summarized as frequency and percentage. Statistical significance level was considered as 0.05.

RESULTS

Of the 558 patients who performed inguinal hernia operation, 411 (73.7%) were male and 147 (26.3%) were female. The mean age of the patients who performed inguinal hernia operation was 3.0±3.6 (range, 0-17) years. Of the patients who performed inguinal hernia operation, 270 (48.4%) were <2 years of age (Table 1). Three hundred and thirty-nine patients (60.8%) had no additional surgical pathology. The most common surgical additional operation was circumcision (n=212, 38.0%). Appendectomy was performed in 7 patients (1.3%) during the inguinal hernia operation because of they had Amyand's hernia. Of the 558 patients undergone inguinal hernia operation, 325 (58.2%) had right inguinal hernia repair, 167 (29.9%) had left, and 66 (11.8%) had bilateral (Table 2). Of the 411 male patients, 248 (60.3%) were performed right inguinal hernia repair, 111 (27.0%) were left and 52 (12.7%) were bilateral. And of the 147 female patients, 77 (52.4%) were performed right inguinal hernia repair, 56 (38.1%) were left and 14 (9.5%) were bilateral. There was a statistically significant difference between males and females according to the operation side (p=0.038). It was found that the left inguinal hernia rate was higher in females, and there was no statistically significant difference between males and females both in right and bilateral inguinal hernia (Table 3).

The mean age of the 184 patients who performed orchiopexy operation was 4.0±3.4 years old (range, 0-16). This age was much higher than the 2-year-old age at which the orchiopexy operation was performed at the latest to avoid the development of infertility. Only 46 patients (25.0%) who performed orchiopexy operation were <2 years of age (Table 1). There was no additional surgical pathology in 80 patients (43.5%) who performed orchiopexy operation. The most common surgical additional operation was circumcision (n=100, 54.3%). Hypospadias repair was performed in 4 (2.2%) patients who performed orchiopexy operation. Twelve (6.5%) of the orchiopexy operations were performed laparoscopically with the diagnosis of nonpalpable testis. Of the patients, 88 (47.8%) had right orchiopexy, while 50 (27.2%) had left and 46 (25.0%) had bilateral (Table 2).

The mean age of the 65 patients who performed hydrocele operation was 4.6±4.1 years (range, 0-17). Thirty three (50.8%) patients performed hydrocele surgery had no additional surgical pathology. The circumcision as most common surgical additional operation was performed in 32 (49.2%) patients. Right hydrocele repair was performed in 39 (60.0%) patients and left hydrocele repair was performed in 26 (40.0%) patients (Table 2).

Table 1. Inguinoscrotal surgical pathologies by age

Age	İnguinal Hernia (n=558)	Undescended Testis (n=184)	Hydrocele (n=65)
≤2	270 (%48.4)	46 (%25.0)	9 (%13.8)
3-4	106 (%19.0)	63 (%34.2)	29 (%44.6)
5-6	73 (%13.1)	31 (%16.8)	12 (%18.5)
7-8	41 (%7.3)	14 (%7.7)	4 (%6.2)
>8	68 (%12.2)	30 (%16.3)	11 (%16.9)

Table 2. Inguinoscrotal surgical pathologies by side

Side	İnguinal Hernia (n=558)	Undescended Testis (n=184)	Hydrocele (n=65)
Right	325 (%58.2)	88 (%47.8)	39 (%60.0)
Left	167 (%29.9)	50 (%27.2)	26 (%40.0)
Bilateral	66 (%11.8)	46 (%25.0)	0 (%0.0)

Table 3. Comparison of operation side by gender

	İnguinal Hernia		
Side	**Male (n=411)**	**Female (n=147)**	**p**
Right	248 (%60.3)[a]	77 (%52.4)[a]	
Left	111 (%27.0)[a]	56 (%38.1)[b]	**0.038**
Bilateral	52 (%12.7)[a]	14 (%9.5)[a]	

DISCUSSION

The inguinal hernia occurs when the distal portion of the processus vaginalis closes and the proximal portion of the inguinal canal remains open; the small intestines in both boys and girls, and ovaries in girls can entered into the sac and it is characterized by a swelling in the inguinal region. When the processus vaginalis remains completely open, the organs underlie to the scrotum and named as scrotal hernias. In the pediatric age group, hernias are almost always of the indirect type unlike adults. Of inguinal hernias, 60% are seen in the right, 30% in the left and 10% in the bilateral. The incidence of normal children is 2% and gradually decreases with age. It is 10 times more common in boys than girls (2).

According to our current study, of the 558 patients with inguinal hernia operation, 411 (73.7%) were male and 147 (26.3%) were female. This was inconsistent with the classical knowledge that indirect inguinal hernias were 10 times more common in boys than in girls. The mean age of patients performed inguinal hernia operation was 3.0±3.6

years. Two hundred and eighty-eighth (51.6%) patients who performed inguinal hernia were >2 years of age. In order to avoid incarceration, the incidence of inguinal hernia is the most feared and smaller as the age decreases but this contradicted with "inguinal hernia operations should be done as soon as possible'' knowledge (3). Appendectomy was performed in 7 (1.3%) patients during the inguinal hernia operation because of they had Amyand's hernia (6). Of the 147 female patients, 77 (52.4%) were performed right inguinal hernia repair, while 56 (38.1%) were left and 14 (9.5%) were bilateral.

It is unethical to perform hydrocele surgery within the first year because of the possibility that the hydrocele may recover spontaneously (1). In surgery, the drainage of fluid in the pouch and the interruption of the peritoneum with high ligation, as in the inguinal hernia repair are sufficient. According to our current study, the mean age of the 65 patients who performed hydrocele operation was 4.6±4.1 years.

Cryptorchidism is that one or both of the testis are not present in the scrotum (non-palpable testis). Why do testes need to be lowered to the scrotum?

Fertility protection; normally, intrascrotal heat is about 2°C below the body temperature. Continuous body temperature remaining undescended testis; it has been shown experimentally that serious disorders occur in the seminiferous tubules. Due to the fact that these disorders occurred after 5 years of age in light microscopy studies; until the 1980s, it was believed that the surgery should be done at the age of 5 years. However, in the ultrastructural investigations possible by the use of electron microscopy; in fact, it shows that spermatogenesis disorders began to appear much earlier, around 2 years of age (7-9). According to our current study; only 46 (25.0%) patients who performed orchiopexy operation were <2 years of age. This showed that these patients were at risk for infertility in the future and that families were still unaware of the fact that the undescended testis operation had to be operated by no later than 2 years of age. It is very clear that the society should be informed more about the undescended testis operations should be done without delay and on time.

Prevention of malignancy; studies in men with testicular tumors have shown that 10% of them develop in undescended testes. In patients with undescended testis, the risk of developing testicular tumors is 40 times higher than in the normal population (10). The tumors that develop in undescended testes are of germ cell origin, most of them being seminomas (11).

Trauma and torsion protection; torsion is easier in intraabdominal undescended testes. Testicular torsion should also be included in possible diagnoses in children who have abdominal pain and who are found to have undescended testis. A testis in the inguinal canal can be more easily traumatized from the outside (12).

Surgical treatment is essential in undescended testis. The surgery should be performed after the end of the first age, before the second age, around 1.5 years old (13). The aim of surgical treatment is to down the testis to normal scrotal position in one or sometimes two sessions. When faced with dysgenetic and atrophic testicular tissue, it is more appropriate to perform orchiectomy instead of orchiopexy (14).

According to our current study; the mean age of the 184 patients who performed orchiopexy operation was 4.0±3.4 years. This age was much higher than the 2-year-old age at which the orchiopexy operation was performed at the latest to avoid the development of infertility. Of the patients, 88 (47.8%) had right orchiopexy, 50 (27.2%) had left, and 46 (25.0%) had bilateral.

According to our current study; in inguinal hernia, undescended testis and hydrocele operations in the inguinoscrotal surgical pathologies group, the most common additional operation was circumcision performed in 344 (42.6%) patients. When inguinal hernia, undescended testis and hydrocele in inguinoscrotal surgical pathologies group were compared in terms of repair side of pathology, there was a statistically significant difference because of the left inguinal hernia was more common in girls and the hydrocele operation was not performed bilaterally in any patient.

CONCLUSION

This study shows that the community is not well informed about the treatment of inguinal hernia and undescended testis is not possible without the choice of surgical treatment and the correct time of operation and that the community should be informed about these issues.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.536936

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):186-191

Travmatik Yaşantıların Benlik Saygısı Üzerine Etkisi

The Effect of Traumatic Experiences on Self-Esteem

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Geliş Tarihi / Received : 12.03.2019
Kabul Tarihi / Accepted : 29.11.2019
Çevrimiçi Yayın Tarihi / Available Online : 09.12.2019

ÖZ

Amaç: Bu çalışmanın amacı psikiyatrik hasta grubu ile psikiyatrik hastalığı olmayan sağlıklı kontrol grubunun yaşadıkları travma şiddetini karşılaştırarak, travmanın benlik saygısı üzerine olan etkisini ve benlik saygısının psikiyatrik semptomlarla ilişkisini araştırmaktır.
Gereç ve Yöntemler: Çalışmaya Düzce Üniversitesi Tıp Fakültesi Psikiyatri Anabilim Dalı'na başvuran psikotik hastalığı olmayan, depresyon, anksiyete bozuklukları, somatoform bozuklukları, obsesif kompulsif bozuklukları, travma sonrası stres bozukluğu olan 100 hasta ile 100 sağlıklı kontrol grubu alındı. Hasta ve kontrol gruplarının sosyodemografik özellikleri kaydedildi. Travma algısının şiddeti Görsel Anolog Skala (VAS) ile değerlendirildi. Yaşanılan travmayı tespit etmek için Travmatik Yaşantılar Ölçeği (TYÖ), bilişsel durumu belirlemek için Travma Sonrası Bilişler Envanteri (TSBE), benlik saygısı için Rosenberg Benlik Saygısı Ölçeği (RBSÖ) ve psikolojik semptomları belirlemek için Belirti Tarama Listesi (SCL-90R) kullanıldı.
Bulgular: Hasta grubunun hem kendilerinin hem de ebeveynlerinin eğitim seviyesi kontrol grubundan düşükken, VAS ise yüksek bulundu. RBSÖ açısından benlik saygısı, anne-baba ilgisi ve babayla ilişki hasta grubunda kontrol grubuna göre daha düşük iken, eleştiriye duyarlılık, depresif duygulanım, hayalperestlik, psikosomatik belirtiler, kişilerarası ilişkilerde tehdit hissetme ve psikolojik izolasyon yüksek saptandı. Hasta grubunda TYÖ ve TSBE değerleri ve SCL-90R'deki tüm semptomlar hasta grubunda daha fazla idi.
Sonuç: Hasta grubunda kontrol grubuna göre travma puanları yüksek benlik saygısı ise düşük bulunmuştur. Hem travmanın kendisi hem de benlik saygısının düşüklüğü psikiyatrik belirtilerin hasta grubunda daha fazla olmasına sebep olmuştur.
Anahtar kelimeler: Travma; benlik saygısı; psikiyatrik semptomlar.

ABSTRACT

Aim: The aim of this study was to investigate effect of trauma on self-esteem and relationship between self-esteem and psychiatric symptoms, by comparing severity of trauma experienced by psychiatric patient group and healthy control group without psychiatric disease.
Material and Methods: The study included 100 patients with depression, anxiety disorders, somatoform disorders, obsessive-compulsive disorders, posttraumatic stress disorder and no psychotic disorder, and 100 healthy control groups, applying to Duzce University Faculty of Medicine Department of Psychiatry. Socio-demographic characteristics of the patient and control groups were recorded. The severity of trauma perception was evaluated with Visual Analogue Scale (VAS). Traumatic Experiences Checklist (TEC) for determining experienced trauma, Post-Traumatic Cognitive Inventory (PTCI) for determining cognitive status, Rosenberg Self-Esteem Scale (RSES) for self-esteem, and Symptom Checklist-90 Revised (SCL-90R) for determining psychological symptoms were used.
Results: Both the self and parental education levels of patient group was lower than control group, while VAS was found higher. In terms of RSES, self-esteem, parental interest and relationship with father were found lower in the patient group than the control group, while sensitivity to criticism, depressive mood, dreaminess, psychosomatic symptoms, feeling threat in interpersonal relationships and psychological isolation were found high. Both TEC and PTCI scores and all symptoms in SCL-90R were higher in the patient group.
Conclusion: In the patient group trauma scores were higher and self-esteem were lower than the control group. Trauma and low self-esteem caused to be higher psychiatric symptoms in the patient group.
Keywords: Trauma; self-esteem; psychiatric symptoms.

GİRİŞ

Travma, kişinin fiziksel veya psikolojik olarak yaşamsal bütünlüğünü tehdit eden veya bozan her türlü olaydır. Psikolojik travma, kişinin yaşamında değişiklik yapan, yeniden uyum gerektiren, psikolojisini tehdit eden, duygusal ve düşünsel olarak baş etmekte zorlandığı olaylar, deneyimler veya durumlardır. Travmatik olaylar yaygın yaşanır ve önemli bir halk sağlığı sorunudur (1).

Psikolojik travmaya verilen cevaplar çok farklı olabilir. Bunu da belirleyen travmanın tipi, şiddeti, yaşama biçimi, kişi için ne anlam ifade ettiği, daha önce benzer veya farklı travmalarla karşılaşıp karşılaşmadığı gibi toplumsal, biyolojik ve kişilik özellikleri gibi birçok etkene bağlıdır.

Travma kişinin kendisini, başkalarını ve dış dünyayı algılamasını, yargılamasını etkileyerek kişinin bilişsel sürecini değiştirebilir (2). Biliş, kişinin başkalarını ve olayları algılama, değerlendirme, yargılama biçimidir. Her insan kendi algılama, değerlendirme ve yargılama alışkanlıklarına göre olaylardan sonuç çıkarır. Kişi olaylardan olumsuz sonuç çıkarırsa bu durum benlik saygısında yıkıcı etki yapabilir ve çeşitli psikolojik sorunlara yol açabilir (3,4).

Benlik kişinin kendini algılama biçimidir. Kişinin kendini algılaması yaşadıklarıyla şekillenir. Normal, artmış veya azalmış benlik saygısı kişinin geçmiş deneyimleriyle ve yaşantılarıyla ilişkilidir. Olumsuz bilişsel süreç yaşayan insanlar genellikle düşük benlik saygısına, olumlu bilişsel süreç yaşayanlar ise yeterli veya yüksek benlik saygısına sahiptir (5).

Bu çalışmada, psikiyatrik hasta grubu ile sağlıklı kontrol grubunun yaşamış olduğu travma şiddetlerini karşılaştırarak, travmanın benlik saygısı üzerine etkisini, travmanın ve benlik saygısının psikiyatrik belirtilerle olan ilişkisinin araştırılması amaçlanmıştır.

GEREÇ VE YÖNTEMLER

Çalışmaya Ekim 2017 - Ekim 2018 tarihleri arasında kullanılan ölçekleri uygun bir şekilde anlayıp cevaplayabilecek, gönüllülük esasına uygun olarak seçilen, yaşları 19-65 yaş arasında olan 200 kişi alınmıştır. Düzce Üniversitesi Tıp Fakültesi Etik Kurulundan (11.09.2017 tarih ve 2017/120 sayılı karar) çalışma için onay alınmıştır. Düzce Üniversitesi Tıp Fakültesi Psikiyatri Anabilim Dalı'na başvuran hastalardan klinik görüşme ile DSM-V tanı kriterlerine göre depresyon, anksiyete bozuklukları, somatoform bozuklukları, obsesif kompulsif bozuklukları, travma sonrası stres bozukluğu tanısı alan ve travmatik geçmişi olan 100 hasta ile sağlıklı 100 kişilik kontrol grubu çalışmaya alınmıştır.

Her iki gruptaki katılımcılara araştırmacı tarafından görüşme sırasında doldurulan sosyo-demografik form ve katılımcıların kendi dolduracağı Travmatik Yaşantılar Ölçeği (TYÖ), Rosenberg Benlik Saygısı Ölçeği (RBSÖ), Travma Sonrası Bilişler Envanteri (TSBE) ve psikolojik Belirti Tarama Listesi (SCL-90R) uygulanmıştır.

Sosyo-demografik formun içeriğinde katılımcıların yaş, cinsiyet, meslek, kardeş sayısı, eğitim yılı, medeni hali, anne ve babanın eğitim yılı, yaşadığı yer, bireyin aylık gelir algısı, sigara-alkol-madde kullanımı, travma sonrası ruh sağlığı ve hastalıkları uzmanına gidip gitmediği sorgulanmıştır. Ayrıca aynı formda bireyin travma algı şiddeti 1-10 arasında numaralandırılmış olan görsel analog skala (VAS) ile değerlendirilmiştir. Travmatik olayın veya olayların şiddet seviyesini belirlemek için 1-10 arasında puanlama ile belirlenecek bir VAS hazırlanmıştır. Katılımcılara yaşadıkları travmatik olay veya olayların kendilerini ne derece etkilediklerini ve hissettikleri seviyeyi seçmeleri istenmiştir. Bir en düşük hissedilen şiddet, 10 ise en yüksek hissedilen şiddet olarak işaretlenmiştir.

TYÖ, katılımcıların yaşadıkları travmaları saptayıp ne kadar etkilendiklerini öğrenmek için uygulanmaktadır. Kişilerin başından geçmiş olabilecek bazı travmatik olaylar sıralanmaktadır. Yirmi dokuz çeşit travma yaşantısı sorulmaktadır. Sorularda üç esas vardır. Birincisi olayın yaşanıp yaşanmadığı, ikincisi olay sırasında kaç yaşında olunduğu, üçüncü olarak da olayın psikolojik açıdan kişiyi ne kadar etkilediği üzerinde durulmaktadır (6).

RBSÖ katılımcıların kendilerine verdikleri değeri ve saygıyı ölçmek için uygulanmaktadır. Ölçek 63 madde içeren 12 alt ölçekten oluşmaktadır. Bu alt ölçekler benlik saygısını, kendilik kavramının sürekliliğini, insanlara güven duymayı, eleştiriye duyarlılığı, depresif duygulanımı, hayalperestliği, psikosomatik belirtileri, kişilerarası ilişkilerde tehdit hissetmeyi, tartışmalara katılabilme derecesini, anne-baba ilgisini, babayla ilişkiyi ve psişik izolasyonu ölçmektedir. (7).

TSBE travma sonrası stres bozukluğunun ortaya çıkmasında ve sürmesinde etken olduğu düşünülen, travmayla ilişkili bilişleri değerlendirmek amacıyla geliştirilmiştir. Kişi, ölçekteki 36 madde ile kendini değerlendirmektedir. Yedili likert ölçek üzerinde katılımcının her bir maddeye ne oranda katıldığını belirtmesi istenmektedir. Ölçekten alınabilecek puan 36 ile 252 arasında değişmektedir. Ölçekten alınan yüksek puanlar travmatik yaşantıya ilişkin hatalı bilişlerin yoğunluğunu göstermektedir (8).

SCL90-R psikiyatrik belirti tarama aracıdır. Ölçek psikiyatrik belirti ve yakınmalarını içeren 90 maddesi ile 9 ayrı belirti boyutunda değerlendirme yapmak üzere yapılandırılmıştır (9).

İstatistiksel Analiz

Çalışmada elde edilen verilere ait tanımlayıcı istatistikler ortalama±standart sapma, ortanca (minimum-maksimum), sayı ve yüzde olarak hesaplanmıştır. Kategorik yapıdaki değişkenlerin analizi Pearson ki-kare veya Fisher's Exact test ile incelenmiş, sayısal tipteki değişkenler bakımından grupların karşılaştırılmasında ise Independent samples t-test ve Mann-Whitney U test kullanılmıştır. İstatistiksel anlamlılık düzeyi 0,05 olarak alınmış ve hesaplamalarda SPSS v.18 programı kullanılmıştır.

BULGULAR

Hasta grubunda travma sonrası psikiyatrik destek oranı, sigara kullanım oranı ve travma algısının şiddeti kontrol grubuna göre anlamlı düzeyde yüksek iken, kontrol grubunda eğitim yılı ile anne ve babalarının eğitim yıllarının ise hasta grubuna göre daha yüksek olduğu görülmüştür. Diğer özellikler bakımından hasta ve kontrol grubunun benzer olduğu görülmüştür. Hasta ve kontrol grubunun sosyo-demografik özelliklerinin dağılımı ve karşılaştırma sonuçları Tablo 1'de verilmiştir.

RBSÖ açısından benlik saygısı, anne-baba ilgisi ve babayla ilişki hasta grubunda kontrol grubuna göre daha düşük iken, eleştiriye duyarlılık, depresif duygulanım,

hayalperestlik, psikosomatik belirtiler, kişilerarası ilişkilerde tehdit hissetme ve psikolojik izolasyon ise daha yüksek saptanmıştır. Kendilik kavramının sürekliliği, insanlara güven duyma ve tartışmalara katılabilme derecesi de yine hasta grubunda düşük olmakla birlikte istatistiksel anlamlılık saptanmamıştır. Benlik saygısı yüksek düzeyde olanların oranı kontrol grubunda daha fazla iken orta düzeyde olanların oranı ise hasta grubunda daha fazla görülmüştür. Eleştiriye çok duyarlı olanlar hasta grubunda daha yüksek oranda bulunmuştur. Orta ve yüksek düzeyde depresif duygulanım hasta grubunda anlamlı düzeyde daha yüksek oranda saptanmıştır. Orta ve yüksek düzeyde hayalperestlik hasta grubunda anlamlı düzeyde daha yüksek oranda görülmüştür. Kontrol grubunda psikosomatik belirtiler az ve orta olanların oranı daha fazlayken, hasta grubunda ise psikosomatik belirtiler yüksek olanların oranı daha fazla bulunmuştur. Kontrol grubunda kişilerarası ilişkilerde tehdit hissedilmediği, hasta grubunda ise yüksek düzeyde tehdit hissedildiği saptanmıştır. Kontrol grubunda anne-baba ilgisi çok, hasta grubunda ise anne-baba ilgisi az olanların oranının daha fazla olduğu görülmüştür. Hasta grubunda babayla ilişki az ve orta düzeyde bulunmuştur. Kontrol grubunda psişik izolasyon olmayanların oranı yüksekken hasta grubunda ise psişik izolasyon çok olanların daha fazla oranda olduğu görülmüştür (Tablo 2).

Tablo 1. Hasta ve kontrol gruplarının sosyo-demografik özellikleri

	Hasta	Kontrol	p
Yaş	36,55±10,89	34,79±10,09	0,237
Cinsiyet			
Kadın	54 (54,0)	60 (60,0)	0,391
Erkek	46 (46,0)	40 (40,0)	
Medeni Durum			
Bekar	27 (27,0)	35 (35,0)	
Dul	10 (10,0)	4 (4,0)	0,162
Evli	63 (63,0)	61 (61,0)	
Yaşadığı Yer			
Kentsel	72 (72,0)	82 (82,0)	0,093
Kırsal	28 (28,0)	18 (18,0)	
Aylık Gelir			
İyi	18 (18,0)	23 (23,0)	
Orta	68 (68,0)	69 (69,0)	0,324
Kötü	14 (14,0)	8 (8,0)	
Kardeş Sayısı	3,81±1,82 3 (1-10)	3,34±1,99 3 (0-9)	0,080
Eğitim Yılı	10,16±4,18 11 (0-18)	12,64±4,37 15 (4-25)	**<0,001**
Anne Eğitim Yılı	3,66±3,44 5 (0-17)	5,12±4,20 5 (0-15)	**0,009**
Baba Eğitim Yılı	5,51±4,35 5 (0-17)	6,78±4,65 5 (0-16)	**0,041**
Travma Algısının Şiddeti	8,20±1,85 8 (3-10)	3,56±2,04 3 (1-8)	**<0,001**
Travma Sonrası Psikiyatrik Destek	76 (76,0)	4 (4,0)	**<0,001**
Madde	4 (4,0)	1 (1,0)	0,369
Sigara	50 (50,0)	35 (35,0)	**0,032**
Alkol	21 (21,0)	11 (11,0)	0,054

TSBE'nin alt boyutları ve ortalama puanı hasta grubunda kontrol grubuna göre istatistiksel olarak anlamlı şekilde yüksek saptanmıştır (Tablo 3).

SCL90-R ölçeğinden elde edilen puanlar ruhsal belirtileri normal, yüksek ve çok yüksek olarak kategorize edildiğinde, kontrol grubunda ruhsal belirtileri normal olanların oranı fazlayken, hasta grubunda ise bu belirtiler yüksek ve çok yüksek oranda olanların daha fazla olduğu saptanmıştır (Tablo 4).

TYÖ puanları hasta grubunda kontrol grubuna göre istatistiksel anlamlı şekilde yüksek saptanmıştır (Tablo 5).

Tablo 2. Rosenberg benlik saygısı ölçeğine ait alt boyutların gruplara göre dağılımı, n (%)

	Hasta	Kontrol	p
Benlik Saygısı			
Yüksek	27 (27,0)[a]	56 (56,0)[b]	
Orta	70 (70,0)[a]	44 (44,0)[b]	**<0,001**
Düşük	3 (3,0)[a]	0 (0,0)[a]	
Kendilik Kavramının Sürekliliği			
Fazla	15 (15,0)	23 (23,7)	0,121
Az	85 (85,0)	74 (76,3)	
İnsanlara Güven Duyma			
Çok	72 (72,0)	82 (82,0)	
Orta	28 (28,0)	18 (18,0)	0,093
Az	0 (0,0)	0 (0,0)	
Eleştiriye Duyarlılık			
Az	26 (26,3)[a]	52 (54,2)[b]	**<0,001**
Çok	73 (73,7)[a]	44 (45,8)[b]	
Depresif Duygulanım			
Yok	2 (2,1)[a]	15 (15,8)[b]	
Az	18 (18,6)[a]	51 (53,7)[b]	**<0,001**
Orta	49 (50,5)[a]	28 (29,5)[b]	
Yüksek	28 (28,9)[a]	1 (1,1)[b]	
Hayalperestlik			
Az	40 (44,9)[a]	65 (70,7)[b]	
Orta	25 (28,1)[a]	14 (15,2)[b]	**0,002**
Yüksek	24 (27,0)[a]	13 (14,1)[b]	
Psikosomatik Belirtiler			
Az	10 (31,3)[a]	55 (69,6)[b]	
Orta	11 (34,4)[a]	19 (24,1)[a]	**<0,001**
Yüksek	11 (34,4)[a]	5 (6,3)[b]	
Kişilerarası İlişkilerde Tehdit Hissetme			
Yok	17 (17,0)[a]	41 (42,7)[b]	
Az	14 (14,0)[a]	17 (17,7)[a]	**<0,001**
Orta	32 (32,0)[a]	25 (26,0)[a]	
Yüksek	37 (37,0)[a]	13 (13,5)[b]	
Tartışmalara Katılabilme Derecesi			
Az	49 (49,0)	44 (45,4)	
Orta	32 (32,0)	32 (33,0)	0,851
Yüksek	19 (19,0)	21 (21,6)	
Ana-Baba İlgisi			
Çok	43 (44,3)[a]	69 (71,9)[b]	
Orta	30 (30,9)[a]	18 (18,8)[a]	**<0,001**
Az	24 (24,7)[a]	9 (9,4)[b]	
Babayla İlişki			
Az	78 (80,4)[a]	89 (92,7)[b]	
Orta	15 (15,5)[a]	3 (3,1)[b]	**0,012**
Fazla	4 (4,1)[a]	4 (4,2)[a]	
Psişik İzolasyon			
Yok	28 (28,0)[a]	53 (54,6)[b]	
Az	37 (37,0)[a]	30 (30,9)[a]	**<0,001**
Çok	35 (35,0)[a]	14 (14,4)[b]	

Tablo 3. Travma sonrası bilişler ölçeğinin karşılaştırılması

	Hasta	Kontrol	p
Kişinin Kendisiyle İlgili Olumsuz Bilişler	3,86±1,49 4 (1-7)	1,95±0,81 2 (1-5)	**<0.001**
Dünyayla İlgili Olumsuz Bilişler	4,13±1,81 4 (1-7)	2,56±1,43 2 (1-6)	**<0.001**
Kendini Suçlama	3,63±1,45 4 (1-7)	1,87±0,77 2 (1-5)	**<0.001**
Genel	3,89±1,48 4 (1-7)	2,05±0,82 2 (1-5)	**<0.001**

Tablo 4. SCL90-R ölçeğine ait alt kategorilerin dağılımı

	Hasta	Kontrol	p
SCL-90R			
Normal	35 (35,4)[a]	94 (94,9)[b]	
Yüksek	37 (37,4)[a]	4 (4,0)[b]	**<0,001**
Çok Yüksek	27 (27,3)[a]	1 (1,0)[b]	

Tablo 5. Travmatik yaşantılar ölçeğinin karşılaştırılması

	Hasta	Kontrol	p
Travmatik yaşantılar ölçeği	6,51±4,46 6 (0-19)	1,78±1,96 1 (0-8)	**<0,001**

TARTIŞMA

Travmayı olağan dışı yapan en önemli özelliği, kişinin gündelik yaşamını, işlevselliğini ve uyumunu ciddi anlamda etkilemesidir. Bu nedenle travma genellikle subjektif ve kişisel bir deneyimdir.

Sigara kullanımının hasta grubundaki bireylerde kontrol grubuna göre daha fazla görülmesi, sigaranın stresle baş etme yolu olarak öğrenilmesi olabilir. Ayrıca sigara beyinde mono amino oksidaz enzimini baskılayarak nörepinefrin gibi nörotransmitterlerin salınımının artmasına neden olmakta bu da strese karşı savunma mekanizması olarak kullanılabilmektedir (10,11).

Hasta grubunda bulunan kişilerin ve anne-babalarının eğitim seviyelerinin düşük bulunması anne ve babaların stresle başa çıkma yollarını öğrenme ve bilmede yetersiz olabilmelerine, çocuklarına stresle baş etmenin yollarını aktarmada ve model olmada yetersizlik yaşamalarına bağlanabilir. Eğitim düzeyi, travma sonrası oluşan stres tepkilerini ve benlik saygısını etkileyebilmektedir. Eğitim seviyesi düşük olanların daha fazla travmatik stres tepkisi gösterdikleri bulunmuştur (12). Öte yandan eğitim ve deneyimin tekrarlayan travmatik olayların etkisini de azalttığı gösterilmiştir (13). Kaya ve ark. (14) ilköğretim 8. sınıf öğrencilerinin benlik saygısı düzeylerine benlik saygısı geliştirme programının etkilerini inceledikleri çalışmalarında, programın düşük benlik saygısına sahip öğrencilerin benlik saygısını artırmada etkili olduğunu bulmuşlardır.

Travmanın oluşturduğu stres, depresyon, anksiyete, uyku bozukluğu gibi çeşitli psikiyatrik belirtilere yol açabilmektedir (15). Bu nedenle bu hastalar daha fazla psikiyatrik destek almaktadır. Bu da bireylere koruyucu sağlık hizmeti olarak psikiyatrik belirtiler göstermeden önce, travma ile baş etme yöntemleri eğitiminin aldırılması gerekliliğini ortaya koymaktadır.

Travma algısı şiddeti, kişilik özelliklerine, travma ile baş etme yöntemlerine, daha önceki travmatik yaşantılara ve deneyimlere, travmayı yorumlama biçiminin farklı olmasına, yaşanmış olan travmalar sebebiyle daha sonra yaşanan her türlü stres verici olaya çok daha duyarlı olabilmeye, yaşanılan olayı diğerlerine göre daha şiddetli hissedebilmeye, yaşına, cinsiyetine, medeni haline, sosyal desteğe, kişinin ve ailenin eğitim düzeyine bağlı olabilir (16-19). Bu çalışmada hasta grubundaki bireylerde travma algısı şiddetinin yüksek bulunması ve bunun travmatik yaşantılar ölçeği ile paralellik göstermesi, bu kişilerin daha önceki yaşadıkları travmalara bağlı olarak sonraki travmalara karşı daha duyarlı olduklarını göstermektedir. Yaşanan travmaların bir sonraki travmalara karşı kişiyi daha duyarlı yapması, öğrenilmiş korkunun oluşturduğu biyolojik değişikliklere bağlı olmasıyla ve ayrıca bu korkunun kişiyi korumak amacıyla beyinde bulunan anı merkezlerinde sürekli canlı tutulmasıyla ilişkili olabilir.

Güçray (20), çocuk yuvasında ve ailelerinin yanında kalan çocukları karşılaştırdığı çalışmasında, yuvada kalan çocukların benlik saygısının olumsuz etkilendiğini bulmuştur. Benlik saygısı düşük olan kişilerde çeşitli psikolojik sorunlar ve psikiyatrik hastalıklar sıklıkla görülmektedir (19). Bu çalışmada da benlik saygısının travmatik hasta grubunda kontrol grubuna göre düşük olduğu bulunmuştur. Travmatik kişiler kendilerini değersiz görebilir, stresle baş edemez, olaylardan çok çabuk etkilenebilirler. Anksiyete düzeyleri yüksek, her şeye karşı isteksiz, saldırgan davranışlara yatkın, diğer insanlara bağımlı, sıkılgan, pasif ve içe kapanık olabilirler (21). Bu çalışmada elde edilen bulgular da travmanın kişinin kendisine olan güvenini ve kendini algılama biçimini olumsuz bir şekilde etkilediğini göstermektedir.

Benlik saygısı düşük olanlarda, kendilik kavramının sürekliliği de düşük bulunmuştur. Travma kişide süreklilik gösteren benlik oluşumunu bozabilir. Kişi benlik bütünlüğü oluşturmada birbiri ile ilişkili bütüncül bir benlik süreci yaşayamaz. Yaşanan travmatik geçmişler kişide sürekliliği olan bir kendilik algısı ve farkındalık oluşmasını bozabildiğinden bu insanların duyguları düşünce ve davranışları değişken, tutarsız ve dengesiz olabilir. Travmatik olaylar yaşamdaki öncelikleri sorgulatmakta, bu durum benliğin yeniden tanımlanması konusunda kişiyi yönlendirebilmektedir (22,23). Böylece benlik anlamında bireylerin geçmişleri, bugünleri ve gelecekleri arasında bir kopukluk yaşanmaktadır (24).

Travmatik grubun eleştiriye duyarlı olması, benlik saygısının düşüklüğüne bağlıdır. Travma benlik saygısını düşürmekte, benlik saygısının düşüklüğü de eleştiriye duyarlılığı artırmaktadır. Benlik algılamaları yetersiz olan kişiler, kendileri hakkında dışarıdan gelen değerlendirmelere karşı çok daha duyarlı olabilmekte ve olumsuz değerlendirmelerden çok fazla etkilenebilmektedir (25).

Yapılan bir çalışmada yüksek benlik saygısının psikopatolojik semptomlarda azalmaya neden olduğu bulunmuştur (26). Travma geçiren hasta grubunda hem travmanın doğrudan etkisi hem de travmanın benlik saygısını düşürmesi, bu kişilerde olumsuz bilişsel düşünce kalıpları oluşturabilmekte ve buna bağlı depresif duygulanımlar daha fazla görülebilmektedir.

Hayalperestlik ve psişik izolasyonun yüksek olması, bu kişilerin çekingen, içe dönük olmalarına, güvensizlik ve yetersizlik düşünceleri nedeni ile gerçekleştirmek

istedikleri birçok sosyal olaylardan geri kalmalarına, kendilerini gösterme, ortaya koyma güçlerini azaltmaya neden olabilmektedir. Bu durum fantezilerle yetersizlik duygularını doyurmaya çalışmalarına sebep olur. Benlik saygısının düşük olması nedeniyle de kurdukları hayaller kendilerinin önemlilik ve değerlilikleri ile ilgili düşünceler içermektedir. Bu durum aynı zamanda bir savunma mekanizmasıdır.

Travmanın benlik saygısı üzerindeki yıkıcı etkisi, kişinin sosyal ve psikolojik baş etme gücünü olumsuz etkilediğinden zorluklar karşısında bir savunma mekanizması olarak psikosomatik yakınmalar ve belirtiler kullanmalarına yol açabilmektedir.

Kişilerarası ilişkilerde yüksek tehdit algısı, hasta grubunda yüksek bulunmuştur. Yaşanılan travma, öğrenilmiş korku koşullanmasını ortaya çıkarabilmektedir. Ayrıca travmanın neden olduğu düşük benlik saygısı kişide yetersizlik, güçsüzlük, çaresizlik düşünceleri uyandırabilmekte bu da her uyaranın bir tehdit olarak algılamasına neden olabilmektedir.

Anne-baba ilgisizliği ve ilişkilerin yetersizliği, kişilerde çocukluklarından itibaren başlayan korunmama, değer verilmeme, sevilmeme gibi düşünceleri yaşattığından, kendilerini değersiz görmelerine yol açarak benlik saygılarını bozabilmektedir. Anne-baba tarafından kabul görme, onay, sevgi, birinin varlığında olmanın gurunun yaşanması çocuğun benlik saygısını arttırmaktadır (27).

Kişilerin, kendileri ile ilgili olumlu düşüncelere sahip olması çevrelerine ve kendilerine daha güvenli olmalarını sağlar. Olumlu benlik algısı bireylerin yaşamlarından doyum alması ve yüksek benlik saygısı oluşabilmesi demektir. Benlik ve benlik saygısındaki artışın kişinin psikolojik sağlığının artmasını sağladığı gösterilmiştir (28,29). Böylece kişilerin psikolojik sorunlar yaşama olasılığı azalmaktadır.

Travmanın bilişsel süreci bozmasına bağlı olarak hasta grubunda bilişsel süreç düşük bulunmuştur. Travma bilişsel süreci etkileyerek olumsuz düşünce kalıpları oluşturabilmektedir. Olumsuz düşünceler, kendini algılama, olayları algılama ve başkalarını algılamayla ilişkilidir. Bu olumsuz düşünceler, olayların üstesinden gelebilme, sorunları çözebilme, kendini ortaya koyabilme, insanlarla sağlıklı ilişki kurabilmeyi etkilemekte bu da benlik saygısını bozabilmektedir. Bu durum kişinin karamsar, her olaya olumsuz bakan ve her olaydan da olumsuz beklenti içerisinde olan düşünceler yaratmasına neden olarak bir kısır döngü oluşturabilmektedir. Böylece yaşanılan travma, bilişsel süreci bozarak benlik saygısını etkileyebilmekte bu da çeşitli psikiyatrik semptomlara yol açabilmektedir (30).

Travmanın bilişsel süreci etkilemesiyle kişinin kendini değerlendirme süreci değişebilmektedir. Düşünce yapısındaki farklılıklar ve oluşan bozulmalar sonucu kişinin kendilik algısı etkilenerek, kendini değerlendirmesi bozulabilir. Kişi kendisini değersiz, yetersiz, faydasız, işe yaramaz, yaşadıklarını hak ettiği gibi bir düşünce süreci yaşamaya başladıkça, benlik saygısını yitirmeye başlar bunun sonucu olarak da çeşitli davranış, uyum bozuklukları ve psikiyatrik bozukluklar ortaya çıkabilir. Bu çalışmada da psikiyatrik semptomlar travmatik hasta grubunda yüksek bulunmuştur.

Kişinin çevre ile ilgili olumsuz ve karamsar düşünceleri, aynı zamanda kişinin kendini algılamasını da olumsuz olarak etkileyebilmektedir. Kişide yetersiz kendilik algısı, benlik saygısında azalma ve diğer sorunları ortaya çıkarabilmektedir. Tüm psikiyatrik semptomların, travmatik grupta yüksek olması aynı zamanda bu hastalarda benlik saygısının düşük olması ile ilişkili olarak başta depresyon olmak üzere psikosomatik, anksiyete gibi semptomları ortaya çıkardığını düşündürmektedir.

Sonuç olarak hasta grubunda kontrol grubuna göre daha fazla travma yaşanması ve bu grupta benlik saygısının düşüklüğü, travmanın benlik saygısını azalttığını desteklemektedir. Kişinin yaşadığı travma sonucu bilişsel süreç etkilenmekte ve benlik saygısı bozulabilmektedir. Travmanın kendisi ve bozulan benlik saygısı ise çeşitli psikiyatrik semptomlara yol açabilmektedir.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.608616

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):192-196

The Effect of 900-Megahertz Electromagnetic Field Exposure in the First and Middle Adolescent Period on the Spleen in Male Rats: A Biochemical and Histopathological Study

İlk ve Orta Adolesan Dönemdeki Erkek Sıçanlara Uygulanan 900-Megahertz Elektromanyetik Alanın Dalak Üzerine Etkileri: Biyokimyasal ve Histopatolojik Çalışma

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Geliş Tarihi / Received : 21.08.2019
Kabul Tarihi / Accepted : 29.11.2019
Çevrimiçi Yayın Tarihi / Available Online : 09.12.2019

ABSTRACT

Aim: Adolescents are at risk due to the intensive use of mobile phones. The aim of this study was to investigate the histopathological and biochemical effects of 900-Megahertz electromagnetic field on spleen in late adolescent period, exposed during periods of early and mid-adolescence.

Material and Methods: In this study, 24 Sprague Dawley 21-day-old male rats were divided into control (n=8), sham (n=8) and electromagnetic field groups (n=8). Control group rats were not subjected to any application. Electromagnetic field group rats were taken into the electromagnetic field cage and were exposed to 900-Megahertz electromagnetic field (1 hour per day for 25 days). Sham group rats were taken into the electromagnetic field cages but were not exposed to electromagnetic field. At the end of the treatment, all animals were sacrificed by cervical dislocation method and the spleens were removed. After histological procedures, tissue sections were taken and stained with hematoxylin-eosin and periodic acid Schiff. Histopathological evaluation was performed on the spleen tissues. Oxidative stress parameters including lipid peroxidation, superoxide dismutase, glutathione and catalase levels were investigated via biochemical analysis.

Results: Histopathological evaluation revealed megakaryocyte cells, enlarged white pulps and dilated sinusoids in spleen tissues of adolescent rats in electromagnetic field group. According to biochemical analysis results, it was determined that glutathione and lipid peroxidation values were increased, but superoxide dismutase and catalase values were decreased.

Conclusion: It can be said that the 900-Megahertz electromagnetic field applied in adolescent period caused morphological changes on spleen tissue and caused oxidative stress in male rats.

Keywords: Adolescent; spleen; electromagnetic field; oxidative stress.

ÖZ

Amaç: Adolesanlar cep telefonlarının yoğun kullanımından dolayı risk altındadır. Bu çalışmanın amacı ilk ve orta adolesan dönemlerde maruz kalınan 900-Megahertz elektromanyetik alanın, geç adolesan dönemde dalak üzerindeki histopatolojik ve biyokimyasal etkilerini araştırmaktır.

Gereç ve Yöntemler: Bu çalışmada 24 adet 21-günlük Sprague Dawley tipi adolesan erkek sıçan, kontrol (n=8), sham (n=8) ve elektromanyetik alan (n=8) gruplarına ayrıldı. Kontrol grubu sıçanlara herhangi bir uygulama yapılmadı. Elektromanyetik alan grubuna ayrılan sıçanlar, elektromanyetik alan kafesi içerisine alındı ve 900-Megahertz elektromanyetik alana (25 gün boyunca her gün 1 saat) maruz bırakıldı. Sham grubu sıçanlar ise elektromanyetik alan kafesine alındı fakat elektromanyetik alana maruz bırakılmadı. Uygulamaların bitiminde tüm hayvanlar servikal dislokasyon yöntemiyle sakrifiye edilerek dalakları çıkarıldı. Histolojik işlemlerden sonra, dokulardan kesitler alındı ve hematoksilen-eozin ve periyodik asit Schiff tekniğiyle ile boyandı. Dalak dokularında histopatolojik değerlendirme yapıldı. Biyokimyasal analizler ile oksidatif stres parametrelerinden lipit peroksidasyonu, süperoksit dismutaz, glutatyon ve katalaz düzeyleri incelendi.

Bulgular: Histopatolojik değerlendirmede elektromanyetik alan grubu adolesan sıçanların dalak dokularında megakaryosit hücreler, genişlemiş beyaz pulpalar ve dilate sinüzoidaller izlendi. Biyokimyasal analiz sonuçlarına göre glutatyon ve lipit peroksidasyonu değerlerinin arttığı, ancak süperoksit dismutaz ve katalaz değerlerinin azaldığı tespit edildi.

Sonuç: Adolesan dönemde uygulanan 900-Megahertz elektromanyetik alanın erkek sıçanların dalak dokusu üzerinde morfolojik yapıda değişiklikler meydana getirdiği ve oksidatif strese neden olduğu söylenebilir.

Anahtar kelimeler: Adolesan; dalak; elektromanyetik alan; oksidatif stres.

INTRODUCTION

As the use of apparatus emitting electromagnetic field (EMF) increases (cellular phones, base stations, broadcast antennas, Wireless Fidelity (WiFi), etc.), environmental exposure to the EMF increases. Mobile phones have been the focus of researchers because of their widespread use as well as their close proximity during their use to the human body. The overuse of mobile phones by the adolescents is predicted to result in an increased EMF influence on their tissues, which are still developing. The spleen is a lymphoid organ that acts as a biological sieve where macrophages mature and interact with T and B cells (1). Any exposure that would disturb the development of the spleen will affect the development of the whole immune system. This risk will increase further, especially considering that the development of tissues continues during adolescence. There are many factors that cause oxidative stress in the spleen, one of which is EMF (2,3). Cells have different mechanisms to overcome oxidative stress and repair damaged macromolecules. The primary defense mechanism is mediated by the antioxidants that have been shown to remove free radicals and reactive oxygen species (ROS), enzymatically or non-enzymatically. It has been previously shown that antioxidant enzymes like catalase (CAT) and superoxide dismutase (SOD), as well as non-enzymatic antioxidants such as glutathione (GSH) are significantly affected under oxidative stress (1).

A comprehensive analysis of the previous studies suggest that exposure to EMF could cause significant physiological, pathological changes and behavioral disorders in children. It is highly likely that adolescent children, whose tissues and organs are yet to be completely developed, will be impacted by EMF and exposed to its pathological effects more than adults. These notions make us wonder the effects of EMF exposure in adolescence. Tirelli et al. (4) describes adolescence as the period of 21-59 days in rodents. They have categorized the adolescent period into three age-intervals as early (21-34 days), mid (34-46 days), and late (46-59 days) adolescence.

There is no consensus within the scientific community over the effects of exposure to EMF. Some researchers propose negative effects of EMF (5-10), while some others claim that EMF has no effect (11,12) or even is beneficial (14-16). In light of all these studies, here in this paper we investigated the histological and biochemical effects of 900 Megahertz (MHz) EMF exposure to male rats during early and middle adolescence, on the spleen tissue in late adolescence.

MATERIAL AND METHODS

Laboratory Settings, Groups and Ethics Statement

All animal procedures were approved by the Karadeniz Technical University Animal Experiments Local Ethical Committee (Date: 19.06.2014, Protocol Number: 2014/30) and were carried out according to the principles of the Guide for the Care and Use of Laboratory Animals. The animals were housed in Karadeniz Technical University experimental animals laboratory. The animals were kept in an automatically adjusted 12 hour light and 12 hour dark cycle, with an average temperature of 22±2 ºC and 50±5% humidity. Tap water and standard rat chow (Bayramoglu Feed Industry and Trade CO., Erzurum, Turkey) were used. In this study, a total of 24 Sprague Dawley 21-day-old male rats of were divided into three groups equally with 8 rats in each group as control group (C-G), sham group (S-G) and electromagnetic field group (EMF-G). No treatment was applied to the C-G rats. EMF-G rats were taken into the EMF cage every day at the same time (between 10.00-11.00 am) and were exposed to EMF of 900 MHz (1 hour per day for 25 days). S-G rats were taken into the EMF cages in the same schedule throughout the experiment but not exposed to EMF.

Electromagnetic Field Application System

This system has previously been used in many studies (2,6,8,12,13,17-19). Cage used for EMF application was made of plexiglas material. The cage dimension was 30x42x50 cm. Also, the cage had a 126 cm base area. A high-speed oscillator with an output power of approximately 300 mW and a frequency set to 900 MHz was inserted into the cage for the generation of 900 MHz EMF (1218-BV, Lockable Oscillator, 900-2000 MHz, General Radio Company, Concord, Massachusetts, USA, Serial No. 1483). A stationary uninterrupted power supply was used for both the operation of the oscillator and the continuous supply of energy (1267-B Regulated Power Supply, General Radio Company, Concord Massachusetts, USA, Serial No. 903). The output of the oscillator was connected by a coaxial cable to a half-wave 15 cm-long and 1 mm-wide copper dipole antenna. The antenna was placed in the middle, approximately 11 cm inside from the top open surface. During the EMF application, the electric field intensity was measured at different points of the cage using a broadband field intensity-meter with a measuring range of 100 Kilohertz (kHz)-2.5 GHz (C.A 43 Isotropic Electrical Field Intensity Meter, Chauvin Arnoux Group, Paris, France). Intermediate values outside the measurement points were determined by interpolation (SAR: specific absorption ratio, Rad Haz SAR Equivalency Calculator Version 1.0, Richard Tell Associates, Inc., Mesquite, NV). The mean electric field intensity, the power intensity and the SAR value were calculated as 8.8 V/m, 0.21 W/m^2 and 0.0395 W/Kg, respectively.

Histological Analyses

Spleen tissues were formalin-fixed and paraffin embedded through histological procedures. 5-micrometer sections in thickness were cut using microtome (Thermo Scientific Shandon Finesse 325 microtome, UK). Spleen tissues were stained with hematoxylin-eosin (H&E) and periodic acid Schiff (PAS), then evaluated at x60 magnification under the light microscope. BX53 light microscope was used for histopathological examinations and a DP 72 camera was used for microscopy (Olympus Optical Co., Tokyo, Japan).

Biochemical Analyses

Tissue samples (0.5 g) were taken from each animal and homogenized in 4.5 ml of suitable buffer. SOD, CAT, GSH and lipid peroxidation (LPO) levels were assessed in the spleen tissues. LPO determination was performed using thiobarbituric acid test and the results were reported as nmol MDA/mg tissue (20). The presence of CAT was measured via H_2O_2 dissociation at 240 nm and the results were reported as µmol/min/mg tissue (21). SOD was measured in accordance with the method developed by Sun et al. (22) and the results were given in mmol/min/mg

tissue. The GSH amount in the tissues was determined via the method of Sedlak and Lindsay (23) with modifications and the results were given in nmol/mg tissue units.

Statistical Analysis

Distribution of variables were checked by Shapiro-Wilk test and histogram graph. One way ANOVA test was used for group comparisons since the normality and variance homogeneity assumptions were met. Then, Tukey post hoc test was applied for pairwise comparisons. Descriptives were calculated as mean±standard deviation. SPSS v.22 statistical package was utilized for statistical analysis and $p<0.05$ was considered statistically significant.

RESULTS

Histopathological Evaluation of the Spleen Tissue

Sections taken from spleen tissues of all groups were stained with H&E and PAS, and were evaluated histologically under the light microscope. Sections taken from the EMF-G were compared with the sections from the C-G and S-G. H&E staining of the spleen sections showed megakaryocytes, enlarged and fused white pulp and enlarged sinusoid in the EMF-G rats. No pathology was observed in the spleen sections of C-G and S-G (Figure 1 and 2). Megakaryocytes, erythrocytes and myeloid series cells were observed in the PAS-stained sections of the EMF-G. No pathology was found in the spleen sections of C-G and S-G (Figure 3).

Findings on the Biochemical Parameters

There were significant differences between groups for all biochemical parameters, LPO ($p=0.001$), GSH ($p<0.001$), CAT ($p=0.027$) and SOD ($p<0.001$). According to post hoc test results, significant increases were found in terms of LPO ($p=0.001$) and GSH ($p=0.022$) activities while CAT ($p<0.001$) and SOD ($p<0.001$) activities were found significantly lower in the EMF-G when compared to C-G. In addition, SOD ($p<0.001$) activity was found statistically lower in the S-G compared to C-G, while there were no significant differences between S-G and C-G in terms of LPO ($p=0.827$), GSH ($p=0.461$) and CAT ($p=0.192$) activities. When EMF-G compared with S-G, a significant increases was found in LPO ($p=0.004$) activity, but the increase in GSH activity was not found statistically significant ($p=0.199$). And both the decreases in CAT ($p<0.001$) and SOD ($p=0.027$) activities were found significant in EMF-G compared to S-G (Table 1).

DISCUSSION

Devices that emit EMF have become an integral part of our life, which has brought about the desire to investigate the health-related effects of EMF as well. There are several studies in the literature that are associated with negative effects of EMF exposure on health (5-9,16-18,24-28). However, there are only a limited number of studies that delve into the effect of EMF on the spleen.

Tissues are protected themselves against oxidative stress-inducing damages via enzymatic antioxidant defense mechanisms such as CAT and SOD as well as antioxidant defense mechanisms, which are non-enzymatic like GSH. Any circumstance that will disrupt this harmony will result in oxidative stress in the tissues. One such reason that disrupts this harmony and causes oxidative stress in tissues is exposure to EMF. In line with this, previous studies have shown that EMF application for different durations and with

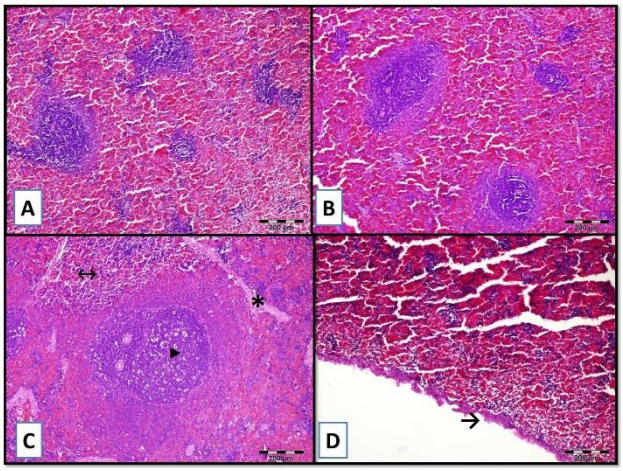

Figure 1. Microscopic view of the spleen in control (A), sham (B) and electromagnetic field (C,D) group rats (x20). (→) Capsule, (*) Trabeculae, (↔) White pulp and (►) Red pulp. Spleen sections were stained with hematoxylin-eosin. The spleen appears normal in A and B sections. C section shows enlarged and fused white pulp. D section displays normal spleen membrane structure.

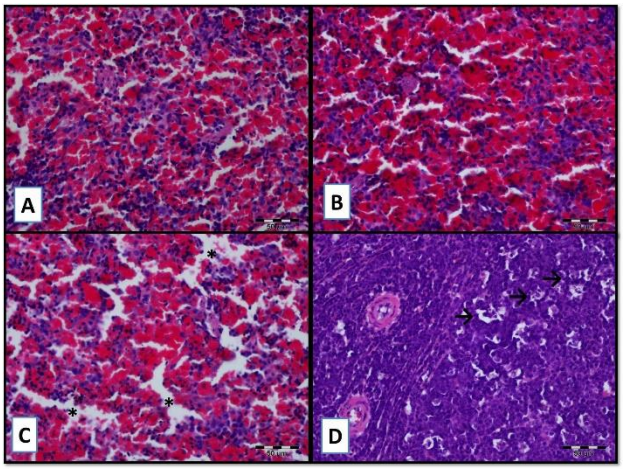

Figure 2. Microscopic view of the spleen in control (A), sham (B) and electromagnetic field (C,D) group rats (x60). Spleen sections were stained with hematoxylin-eosin. C section indicates (*) dilated sinusoids and D section shows (→) megakaryocyte cells.

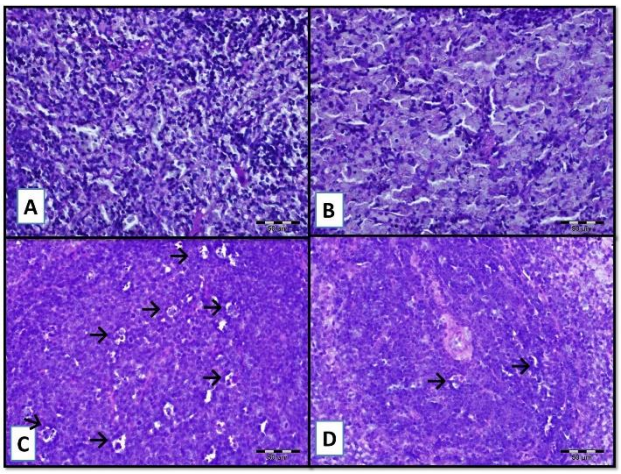

Figure 3. Microscopic view of the spleen in control (A), sham (B) and electromagnetic field (C,D) group rats (x60). Spleen sections were stained with periodic acid Schiff. The spleen appears normal in A and B sections. C and D sections show (→) megakaryocytes, erythrocytes and myeloid series cells.

Table 1. Biochemical parameters of spleen tissues

Biochemical Parameters	C-G (n=8)	S-G (n=8)	EMF-G (n=8)	p
Lipid peroxidation (nmol/mg tissue)	35.26±1.57[a]	38.55±7.33[a]	59.89±14.92[b]	**0.001**
Catalase (µmol/min/mg tissue)	0.34±0.04[a]	0.37±0.03[a]	0.11±0.01[b]	**<0.001**
Superoxide dismutase (mmol/min/mg tissue)	8.84±0.32[a]	6.40±0.26[b]	5.70±0.59[c]	**0.027**
Glutathione (nmol/mg tissue)	4.40±0.29[a]	4.64±0.23[ab]	4.99±0.45[b]	**<0.001**

C-G: Control group, S-G: Sham group, EMF-G: Electromagnetic field group, a,b,c: Different superscript letters denote significant differences between the groups.

different intensities cause oxidative stress in the spleen tissue (2,3,27). EMF causes depletion in the amount of antioxidants in the spleen, which consequently results in oxidative stress and suppression of hepatic and immune function in the spleen (3). In this study, we observed that the levels of LPO in the spleen tissues of EMF-G rats were increased. This increased level indicates that EMF exposure causes oxidative stress in the spleen. In addition, CAT and SOD enzyme activities were significantly reduced but there was an increase in the GSH levels of the EMF-G rats. GSH levels are normally expected decreased; however, there are studies suggesting increased GSH levels in tissues after prolonged exposure to EMF (29,30). Similar to our findings, Li et al. (3) showed oxidative stress induction due to EMF application with different intensities, accompanied by decreased SOD and CAT values. Furthermore, GSH level was increased in the long-term pulsed EMF while it was decreased in control group. The microscopic evaluations in this study show that the 900 MHz EMF applied to male rats in adolescent period caused alterations in the spleen tissue. Images obtained from the EMF-G spleen tissue sections indicated enlarged sinusoids, enlarged and fused white pulp, megakaryocytes, erythrocytes and myeloid series cells. Similar studies such as Kamel et al. (31) reported the multi-nucleated giant cell types in the spleen tissue as megakaryocytes (polykaryocytes). In another study, it was shown that EMF applied at different intensities caused degeneration of the spleen tissue and loss of megakaryocytes and monocytes (28). Moreover, another study evaluating 21 day postpartum spleen tissue after EMF application during the prenatal period revealed the presence of cells with large eosinophilic, granular cytoplasm and cells that are similar to oncocytic cells with round and oval nuclei, as well as megakaryocytes, erythrocytes and myeloid series cells (2). A study evaluating the effects of EMF with different intensities on spleen tissue under the light microscope detected dilatation in the sinusoid cavities and the white pulp, together with disruptions in the white pulp appearance; which were explained by hyperplasia of the lymphoid tissue (32). On the other hand, in a study conducted by a group of researchers, it was stated that EMF had no negative biochemical and histological effects on the body (11).

In conclusion, we determined that 900MHz EMF applied to adolescent male rats caused pathological changes in their spleen tissue, accompanied by increased levels of LPO, which affected the antioxidant defense systems and caused oxidative stress.

Acknowledgements: The authors would like to thank Assoc. Prof. Serdar ÇOLAKOĞLU for his support.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.629638

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):197-203

Comparison of Transtibial and Anteromedial Portal Techniques Used in Anterior Cruciate Ligament Repair Using Autogenous Hamstring Tendon Graft

Ön Çapraz Bağ Tamirinde Otojen Hamstring Tendon Grefti Kullanılarak Uygulanan Transtibial ve Anteromedial Portal Tekniklerin Karşılaştırılması

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Geliş Tarihi / Received : 05.10.2019
Kabul Tarihi / Accepted : 06.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 11.12.2019

ABSTRACT

Aim: The aim of this study was to investigate the effects of transtibial (TT) and anteromedial portal (AMP) techniques used in anterior cruciate ligament repair on knee joint function after anterior cruciate ligament reconstruction.
Material and Methods: Sixty patients who were surgically treated in our clinic for anterior cruciate ligament tear were included in the study. Thirty patients underwent TT technique and 30 patients underwent AMP. Functional evaluations were performed according to Lysholm, International Knee Documentation Committee (IKDC) and Tegner scoring preop and postop. The angle between the femoral tunnel and the distal joint face was measured in postoperative Anteroposterior and Lateral knee graphs and its effect on the knee joint functional outcome was examined.
Results: Eighty percent of the patients included in the study were male (n=47) and 20% were female (n=13). The gender distribution according to the groups was homogeneous (p=0.476). The mean age of the subjects was 32.75±8.81 (16-53) years. The postoperative Lysholm score was significantly higher in the AMP group than in the TT group (p<0.001). The postoperative Tegner score was significantly higher in the AMP group than in the TT group (p<0.001). Mean femoral tunnel obliquity was 59.3° in the TT group and 41.4° in the AMP group.
Conclusion: It is thought that oblique femoral tunnel placement is more beneficial for the rotational stability of anterior cruciate ligament. In our study, we think that AMP technique is more beneficial than femoral obliquity in terms of functional outcome.
Keywords: Anatomic anterior cross ligament reconstruction; autogenous hamstring; anteromedial portal; trans tibial technique.

ÖZ

Amaç: Bu çalışmada, ön çapraz bağ tamirinde kullanılan transtibial (TT) ile anteromedial portal (AMP) teknik arasındaki farklılıkların, ön çapraz bağ rekonstrüksiyonu sonrası hastaların diz eklemi fonksiyonları üzerine etkilerinin araştırılması amaçlanmıştır.
Gereç ve Yöntemler: Çalışmamıza kliniğimizde ön çapraz bağ yırtığı nedeniyle cerrahi olarak tedavi edilen 60 hasta dahil edildi. Otuz hastaya TT teknik, 30 hastaya AMP teknik uygulandı. Fonksiyonel değerlendirmelerde Lysholm, Uluslararası Diz Belgelendirme Komitesi (International Knee Documentation Committee, IKDC) ve Tegner skoru preop ve postop olarak bakıldı. Postoperatif anteroposterior ve lateral diz grafilerinde femur tüneli ile distal eklem yüzü arasındaki açı ölçüldü ve diz eklemi fonksiyonel sonucu üzerine etkisi incelendi.
Bulgular: Çalışmaya dahil edilen hastaların %80'i erkek (n=47) ve %20'si kadındır (n=13). Gruplara göre cinsiyet dağılımı homojendir (p=0.476). Bireylerin ortalama yaşı 32.75±8.81 (16-53) olarak tespit edildi. AMP uygulanan grupta ölçülen operasyon sonrası Lysholm skor değeri, TT teknik uygulanan grupta ölçülen değerinden anlamlı düzeyde daha yüksek bulunmuştur (p<0.001). AMP tekniği uygulanan grupta ölçülen operasyon sonrası Tegner skoru değer, TT teknik uygulanan grupta ölçülen değerinden anlamlı düzeyde daha yüksek bulunmuştur (p<0.001). Ortalama femur tüneli oblikitesi TT grubunda 59,3°, AMP grubunda ise 41,4° bulunmuştur.
Sonuç: Oblik femoral tünel yerleşiminin, ön çapraz bağın rotasyonel stabilitesine daha fazla yarar sağladığı düşünülmektedir. Çalışmamızda AMP teknik uygulanmasının TT tekniğe göre femoral oblisite artışının fonksiyonel sonuca katkısının daha yararlı olduğu kanaatindeyiz.
Anahtar kelimeler: Anatomik ön çapraz bağ rekonstrüksiyonu; otojen hamstring; anteromedial portal; trans tibial teknik.

Presented as a poster at 27th National Turkish Orthopedics and Traumatology Congress (October 24-29, 2017, Antalya, Turkey).

INTRODUCTION

Anterior cruciate ligament (ACL) injuries often occur as a result of non-contact pivot injuries. The inadequacy of ACL providing proprioception, stabilization against valgus and varus stresses, tibial rotation, anterior translation of the tibia will prevent the knee from performing its normal function (1,2). ACL injury is the instability injuries that may cause knee symptoms such as meniscal tears or chondral injuries and osteoarthritis (3,4). It is estimated that around 3,000 ACL injuries occur in our country with the increasing interest of the society in sports. Therefore, the diagnosis and treatment of ACL is one of the most important issues in today's sports surgery. ACL is one of the most injured structures in the knee (Figure 1).

Discussions on ACL injuries focus on the timing of surgery, graft selection and the most appropriate surgical technique. The main purposes of the reconstruction of this ligament are to increase the range of motion and stability of the knee joint for individuals interested in sports and to make their stability be able to sport; to prevent complaints from instability for individuals who are not interested in sports actively; to regain the range of motion and stability of knee joint. Studies on ACL reconstruction have reported that femoral tunnel placement applied by using the transtibial (TT) technique is more difficult than the anteromedial portal (AMP) technique (5). A better approach to the natural femoral origin of the ACL has been adopted with femoral tunnel placement, which has been shown to play a vital role in biomechanical, stability and clinical outcomes after ACL reconstruction. The AMP approach technique is thought to locate the femoral tunnel better within the footprint of the natural ACL and drill the graft hole more posteroinferior to the lateral femoral condyle wall than the traditional TT approach (6). In this study, we concluded that the reconstruction of the ACL applied by using AMP technique is clinically and functionally more successful than TT technique.

MATERIAL AND METHODS

This study was approved by Duzce University Clinical Research Ethics Committee (05.05.2016 and 2016/03). It was decided to recruit a total of sixty patients to obtain clinically and statistically significant difference in accordance with the study with a 5% significance level,

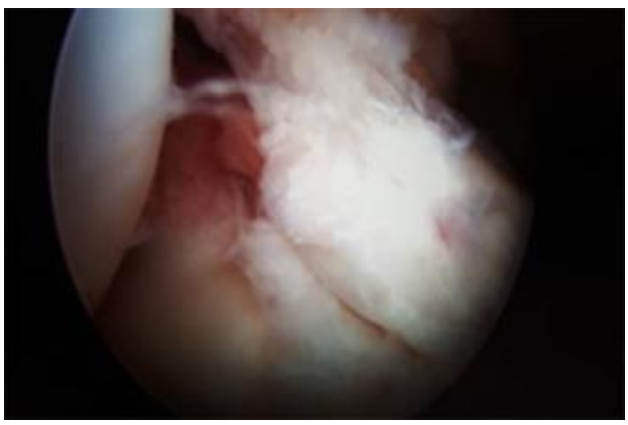

Figure 1. Intraoperative arthroscopic view of anterior cruciate ligament rupture

80% power and an effect size of 0.32. Totally 60 patients with autogenous hamstring tendon graft half of whom (n=30) were operated with AMP Technique, and half of whom (n=30) operated with TT technique were evaluated retrospectively due to the total ACL tear between January 2003 and June 2016. Eighty percent of the patients (n=47) included in the study were male and 20% were female (n=13). The average age at surgery was 30.03±7.83 (18-45) in the AMP technique and 35.37±9.03 (16-53) in the TT technique group. In the AMP technique group, 17 patients had right-sided lesions and 13 patients had left-sided lesions. There were 15 right and 15 left side lesions in the TT technique group. The attention was paid on that all patients had primary ACL rupture and autogenous hamstring tendon graft was used. In addition, endobutton was used for femoral fixation and biodegradable screws and U-Screws was used for tibial fixation in all the patients.

Drawing forth, the measurement of the knee flexions, Lachman and Pivot-Shift tests were performed during the examination, under anesthesia and postoperatively. In addition to the examination findings of our patients, the results were confirmed by performing magnetic resonance imaging (MRI). Lysholm score, Tegner activity score and International Knee Documentation Committee (IKDC) evaluation form were filled in all patients' preoperative and control examinations.

A standard arthroscopy protocol was performed and ACL rupture was confirmed before the removal of the graft. Hamstring autograft was used in all patients. Standard technique was applied in both TT and AMP groups for tibial tunnel. The tibial tunnel was prepared at a 45° angle to the tibial shaft at the footprint of the ACL (7). In the TT group, the standard targeting guide with a 7 mm offset was placed through the tibial tunnel at the right knee 11 and the left knee at the 1 o'clock position (8). Three-portal techniques (anterolateral, central anteromedial and low anteromedial) were used in the AMP group. The low AMP formed under arthroscopic imaging; A spinal needle just above the anterior horn of the medial meniscus and 1.5 cm medial to the medial border of the patellar tendon was carried forward and the femoral tunnel was created independently from the tibial tunnel (9). The midpoints of the remnants of the anteromedial and posterolateral bundles of ACL were marked with a microfracture instrument. Lateral intercondylar and lateral bifurcated protrusion were determined as femoral anatomical bone point (10). The lateral bifurcated protrusion is an osseous sign extending from the anterior to posterior and separating the femoral attachment region of the anteromedial and posterolateral bundles (11). The surgical position was designed to allow knee flexion of 120-130 degrees and the guide wire was placed in the middle of the two insertion areas and low AMP (11). A femoral drill was selected according to the graft diameter and the tunnel was drilled with a cannulated reamer. An endobutton device was used for femoral fixation of the graft. The anterior stretch of the graft was performed by flexing and extending the knee across the range of motion. It was confirmed with an arthroscopic examination whether the graft was stuck or not. The tibial fixation was performed by using a biodegradable screw and U-screw over the remnant graft at 20° flexion of the knee.

In the TT group, the accessory AMP was not required. The tibial guide angle was adjusted to 45 degrees in the way that the bottom part of the guiding system remained in the incision. The other side of the tibial guide was placed in 5-7 mm front of the posterior cruciate ligament and on the lateral edge of the medial eminence by inserting into the portal drilled from the anteromedial (7). The attention was paid on keeping the angle of the guide on the frontal plane and on the tibia approximately 30 degrees. After that, the guide wire was sent from the bottom of the guide inside to the knee while the guide was being held in the appropriate position. The exit point of the guide wire was checked and the reachable enterance point for the femoral tunnel, which will be drilled through the tibial tunnel, by directing towards the medial wall of the femoral lateral condyle and whether there will be any associated compression or not were checked. The tibial tunnel was drilled with a reamer suitable to graft's diameter. In the next stage, the intraarticular exit point of the tunnel was adjusted by cleaning with a shaver to prevent the graft damage while passing through the tunnel. Later, the femoral guide off-set (Bull's Eye), whose thickness was calculated to be two mm greater than the semidiameter thickness of the hamstring autograft was placed in the way of its notch standing up to the posterior cortex by passing inside of the tibial tunnel. Thus, it was aimed to prevent posterior penetration of femoral tunnel. The femoral tunnel was engraved directly via endobutton drill on the guidewire and the tunnel distance was calculated. Next, the femoral tunnel was drilled directly over the guidewire with a reamer suitable for the previously determined graft diameter. A 4-layer autogenous hamstring graft was suspended from the middle with a carrier rope pulled towards the tibial tunnel. The carrier rope's endpieces standing outside were pulled towards the proximal of the graft (Figure 2).

Arthroscopically, the tension of the graft and the presence of compression were evaluated, and the procedure was ended when no problem was detected. After the anatomic closure of the layers, the tourniquet was ended by placing the hemovac drain. The postoperative two-sided knee radiography was performed in all the postop patients. It is identified that the femoral tunnel obliquity was lower in AMP-treated patients (Figure 3-4).

The preoperative infection prophylaxis was applied with cefazolin sodium 2x1 g/iv for 72 hours. The low-molecular-weight heparin (LMWH) prophylaxis was completed to 3 weeks. Our patients used angle-adjustable locked knee braces for 4 weeks by increasing the graded flexion enabling the knee to reach its full range of motion at 3th week. After the knee brace removed, rapid walking was allowed. The flat racing at the 5th month; the training after the 6th month; and competition sports were allowed after 9 months.

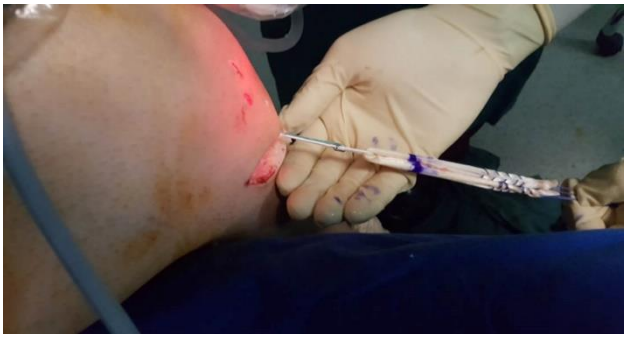

Figure 2. Placement of the graft in tunnels

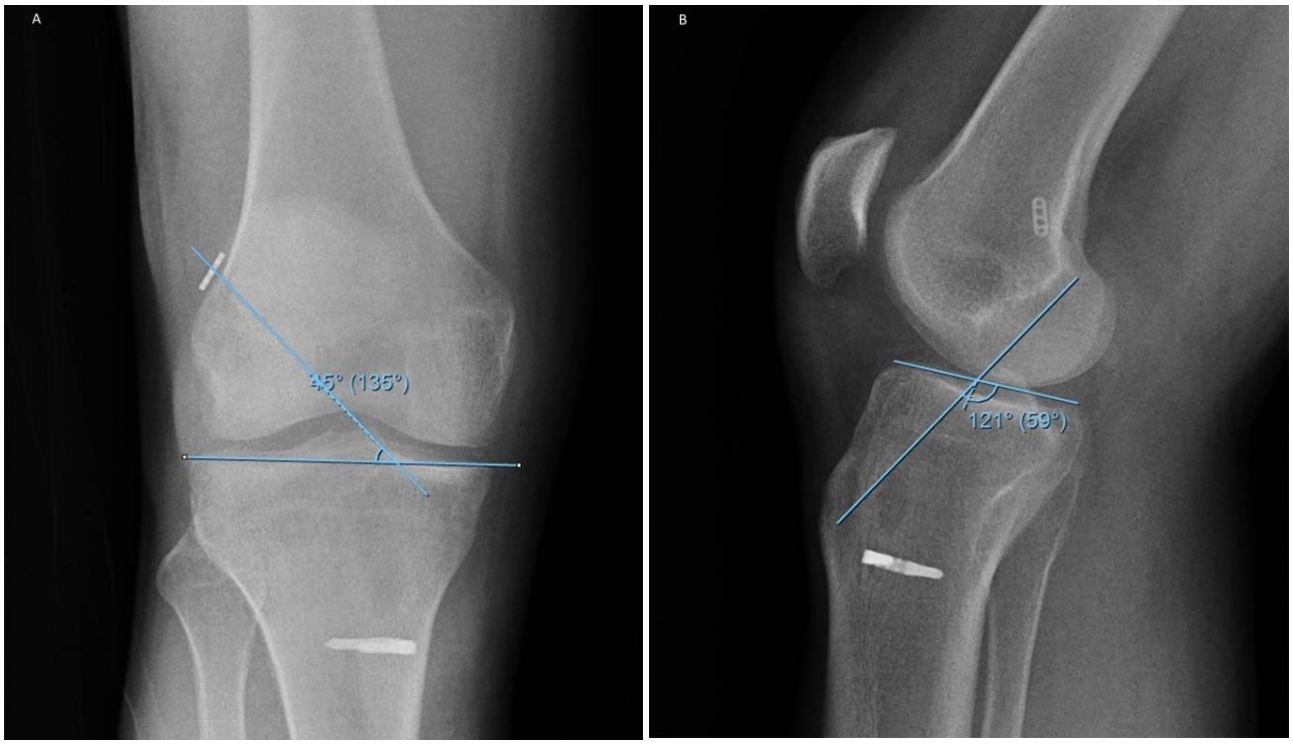

Figure 3. A) Anteromedial portal anterior cruciate ligament radiological image anteroposterior, B) Anteromedial portal anterior cruciate ligament radiological image lateral

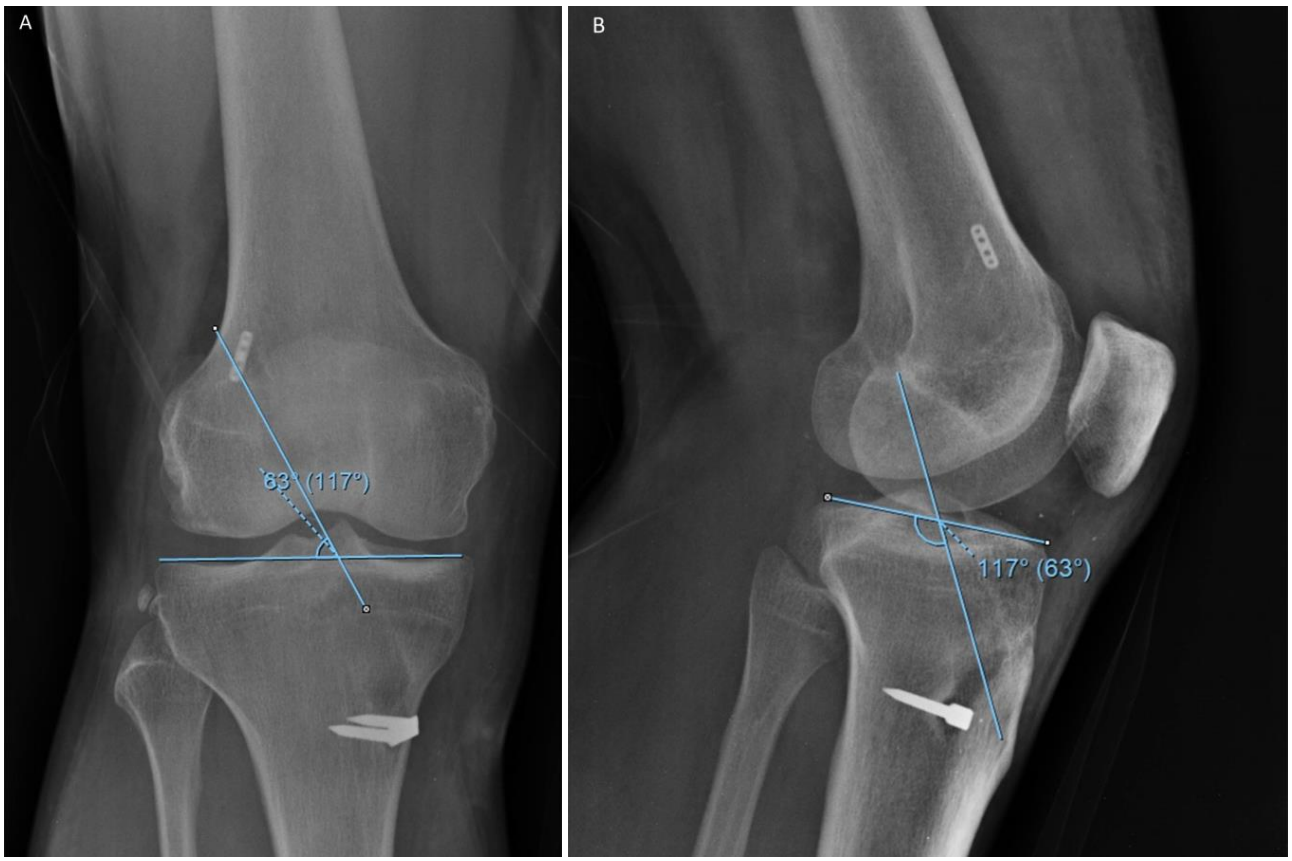

Figure 4. A) Transtibial anterior cruciate ligament radiological image anteroposterior, B) Transtibial anterior cruciate ligament radiological image lateral

Statistical Analysis

Patients were evaluated functionally using IKDC knee evaluation form, Lysholm knee score and Tegner activity scores and compared with preoperative functional scores. Descriptive statistics (average, standard deviation, median, minimum, maximum, Interquartile range-IQR) of all data in the study were calculated. The normality assumption of quantitative variables was examined with Shapiro-Wilk test. Independent samples t test was used for comparisons between groups. Parameter estimations were obtained with the help of the most appropriate model using the Generalized Estimating Equations method (Gamma with log link, ordinal probit and logistic models; post hoc: LSD) in the comparison of score variables' measurement values, which did not provide the normality assumption in different periods between groups. The Pearson Chi-Square and Fisher-Freeman-Halton tests were used for the relationships between categorical variables. Statistical evaluations were performed in SPSS v.22 program. $p<0.05$ was considered significant statistically.

RESULTS

Eighty percent of the individuals included in the study are male and 20% are female. The gender distribution according to the groups is homogeneous (p=0.476). The average age of the individuals is 32.75±8.81 (16-53). There is no significant difference between groups in terms of average age (p=0.052). The sociodemographic and clinical characteristics of the patients are given in detail (Table 1).

Descriptive values of knee flexion and Lysholm scale score and comparison results are given in Table 2. It is found that the difference between preoperative and postoperative knee flexion measurements is significantly different both in two groups or the difference between the groups changes in each period ($p<0.001$). According to the post hoc test results, the preoperative knee flexion measurement value in AMP group was significantly higher than TT group ($p<0.001$). Whereas there is no significant difference between preoperative and postoperative knee flexion measurements in AMP group (p=0.098), the preoperative knee flexion measurement is found to be significantly lower than the postoperative measurement in TT group ($p<0.001$). In addition, the change in knee flexion measurement value measured in TT group is approximately 112% higher than in AMP group ($p<0.001$). It is found that the difference between Lysholm score values measured preoperative and postoperative was different significantly in both groups; or the difference between the groups changed in each period ($p<0.001$). According to the advanced test results, preoperative Lysholm score values were similar in both groups (p=0.389). The postoperative Lysholm score was significantly higher in AMP group than in TT group ($p<0.001$). In addition, the change in Lysholm score value measured in TT group is approximately 37% less than in AMP group ($p<0.001$). In both groups, preoperative and postoperative knee extension values were zero.

Descriptive values and comparison results of IKDC and Tegner score values are given in Table 3. There is a

significant difference between the groups in terms of the change between preoperative and postoperative IKDC scores (p<0.001). While there is no significant difference between preoperative and postoperative IKDC scores in TT group (p=0.480), preoperative IKDC values were significantly lower than postoperative values (p<0.001) in AMP group. In addition, the positive change in IKDC score value measured in AMP group is approximately 518% higher than the change in TT group (p<0.001). The difference between preoperative and postoperative Tegner score values is found to be significantly different in both groups, or the difference between the groups is changed in each period (p=0.049). According to the advanced test results, the preoperative Tegner score values were similar in both groups (p=0.345). The postoperative Tegner score is significantly higher in AMP group than in TT group (p<0.001). While the preoperative Tegner score measured in AMP group was significantly lower than the postoperative measured value (p<0.001 for each), no such change was observed in TT group.

Table 1. Sociodemographic and clinical characteristics of patients

	Anteromedial Portal			Transtibial			Total			p
	n	Row%	Column%	n	Row%	Column%	n	Row%	Column%	
Sex										
Male	22	46.8	75.9	25	53.2	83.3	47	100	79.7	0.476
Female	7	58.3	24.1	5	41.7	16.7	12	100	20.3	
Side										
Right	17	53.1	58.6	15	46.9	50.0	32	100	54.2	0.506
Left	12	44.4	41.4	15	55.6	50.0	27	100	45.8	
Etiology										
Sport İnjuries	20	51.3	69.0	19	48.7	63.3	39	100	66.1	
Traffic Accident	0	0.0	0.0	2	100	6.7	2	100	3.4	
Work Accident	2	100	6.9	0	0.0	0.0	2	100	3.4	0.504
Fall	1	33.3	3.4	2	66.7	6.7	3	100	5.1	
Other	6	46.2	20.7	7	53.8	23.3	13	100	22.0	
Tracking Time*	16,31±7,68 (7-36)			18.37±8.23 (4-39)			17.36±7.96 (4-39)			0.325
Age*	30.03±7.83 (18-45)			35.37±9.03 (16-53)			32.75±8.81 (16-53)			0.052

*mean±standard deviation (minimum-maximum)

Table 2. Descriptive values of knee flexion measurement value and Lysholm scale score and comparison results

	Group	Period	Mean±SD	Median	Min-Max	IQR	OR for Group*Period (95% Wald CI)
Knee Flexion	**Anteromedial Portal**	Preop	127.8±9.9	130	90-135	10	1.127 (1.049-0.210)
		Postop	132.8±2.9	135	125-135	5	
	Transtibial	Preop	109.3±21.5	115	50-130	40	
		Postop	128.0±5.4	130	110-135	0	
Lysholm	**Anteromedial Portal**	Preop	42.2±5.8	40	34-58	8	0.634 (0.561-0.717)
		Postop	90.7±8.5	95	55-98	10	
	Transtibial	Preop	44.9±16.8	47	10-76	20.25	
		Postop	61.3±7.6	60	45-78	11	

SD: Standard Deviation, Min: Minimum, Max: Maximum, IQR: Interquartile Range, OR: Odds Ratio, CI: Confidence Interval

Table 3. Descriptive values and comparison results of IKDC and Tegner score values

	Group	Period	Median	Min-Max	IQR	OR for Group*Period (95% Wald CI)
IKDC[#]	**Anteromedial Portal**	Preop	1	1-2	1	6.186 (2.673-14.317)
		Postop	4	1-4	2	
	Transtibial	Preop	2	1-3	1	
		Postop	2	2-4	1,25	
Tegner	**Anteromedial Portal**	Preop	5	3-7	2	3.081 (1.006-9.435)
		Postop	7	3-7	1,5	
	Transtibial	Preop	5	4-7	1	
		Postop	5	4-8	0,5	

Min: Minimum, Max: Maximum, IQR: Interquartile Range, OR: Odds Ratio, CI: Confidence Interval, IKDC: International Knee Documentation Committee, [#]Scoring A:4, B:3, C:2, D:1

DISCUSSION

Anterior cruciate reconstruction with AMP technique was superior to TT technique. ACL injuries are the most common sports injury of the knee joint (12). Conservative treatment in patients with ACL tear can be selected according to the age, lifestyle and physical activity of the patient (13,14). Patients who are followed up with conservative treatment may have instability attacks even if they change their lifestyle and maintain their lives in that way. In untreated knees with ACL lesions, meniscus lesions and chondral damage are likely to take place due to instability attacks (3).

Sports injuries are the leading cause of ACL injuries (12). According to Howell et al. (15), it is stated that the rate of ACL tears due to sports injuries is 93%. In this study, it was found that this rate is 63.3% (19 of 30 patients) of the patients operated with TT technique and 69% (20 of 29 patients) of patients operated with AMP portal technique.

There are also undesirable side effects of allografts depending on the immunogenic properties such as rejection, long remodeling time and being expensive (16). Since 4-layer semitendinosus-gracilis tendons had 138% more durability than patellar tendon, we preferred to use autogenous hamstring tendon graft for all our patients. In the studies performed by Eriksson K et al. (17) and Tuncay et al. (18), no significant difference was found between hamstring tendon grafts and patellar tendon bone graft in terms of knee stability and functional results after the surgery.

While there was an age limit for patients over 45 years and having unclosed epiphysis children in the past, these criteria also changed nowadays. Thus, in cases of that the reconstruction is socially necessary, the surgery is applied before epiphysis closing (19). In our study, while the average age was 30.03±7.83 (18-45) in the group performed with AMP technique, it was 35.37±9.03 (16-53) in TT technique without taking a definite limit on age, which is appropriate for the literature.

In a retrospective study of 47 patients, Alentorn-Geli et al. (20) compared clinical and functional outcomes of 26 patients operated with AMP technique and 21 patients operated with TT technique. In the group of patients operated with AMP technique, they reported a higher IKDC knee Evaluation Form Score and a shorter return time to athletic activity. In our study, it is observed that the preoperative IKDC value was significantly higher in the AMP group than the postoperative values ($p<0.001$). In addition, it is found that the positive change in IKDC score in the group applied anatomic technique was approximately 518% higher than the change in TT.

Kim et al. (5) found that the Lysholm score in 33 cases performed with AMP technique was preop 45.3, postop 86.2. Also, in 33 cases performed with TT technique, preop Lysholm score was 45.8 and postop score was 86.4. In our study, we found the Lysholm score 42.2 postoperatively and 90.7 preoperatively in the AMP group. We found that the Lysholm score was 44.9 preop and 61.3 post op in TT technique. The postop Lysholm score value measured in AMP technique was found to be significantly higher than TT technique group. ($p<0.001$).

The TT femoral tunnel drilling technique may not be effective to reduce the inclination of the femoral tunnel because the curvature of the femoral tunnel is determined by the tibial tunnel. Loh et al. (21) and O'Neill DB (22) reported that the femoral tunnel obliquity is very important for achieving rotational stability. Moreover, Kim et al. (5) found that the average femoral tunnel obliquity is 59° in the TT group and 31° in the AMP group. We found femoral tunnel obliquity 59.3° in the TT group and 41.4° in the AMP group.

In a recent cadaver study by Tompkins et al. (23) compared the TT technique to the AMP technique, it showed that the tunnel was placed more accurately in the opening of the femoral tunnel in the AMP approach. It is showed that the AMP technique placed 97.7% of the tunnel in the natural femoral footprint and 61.2% was seen with TT perforation. The AMP method also stabilizes the graft in a more horizontal direction, providing a better rotation control and inhibiting translation stability. In our study, we demonstrated that ACL reconstruction allows the anatomic reconstruction of ACL using AMP technique and it is effective in improving an anterior stability and a rotational stability.

Eysturoy et al. (24) showed a significantly different postoperative Tegner score when AMP and TT technique were compared, thus it is proved that it provides a higher level of return to sports activities. In our study, we found that the postoperative Tegner score value applied with the AMP technique is significantly higher than the value measured by TT technique.

The traditional TT approach for femoral tunnel placement is limited to the opening of the tibial tunnel, which restricts the placement of the femoral tunnel and places the femoral tunnel higher into the intercondylar notch, typically resulting in a nonantomic proximal femoral and posterior tibial tunnel placement (8). In our study, we found that the femoral tunnel placement of AMP technique is easier than TT.

CONCLUSION

We concluded that the anteromedial approach is a better surgical technique than TT technique, with its good visual field, low obliquity, closer anatomical reconstruction, the better rotation function and the knee stability during ACL reconstruction.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.621788

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):204-209

A Comparison of Personality Characteristics between Patients with Cancer and the Control Group

Kanser Hastalarının Kişilik Özelliklerinin Kontrol Grubu ile Karşılaştırılması

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Geliş Tarihi / Received : 18.09.2019
Kabul Tarihi / Accepted : 06.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 11.12.2019

ABSTRACT

Aim: It is known that personality can affect most of the issues related to physical and mental health. It is thought that some personality features carry importance as a factor in cancer development, and therefore, the theory of a cancer-prone personality continues to attract researchers' attention. The aim of this study is to investigate and compare the differences in personality characteristics between patients with different types of cancer and healthy control group.
Material and Methods: A total of 193 participants, patients with different types of cancer (n=100) and healthy individuals as the control group (n=93), were included in this study. Hacettepe Personality Inventory (HPI) was used to obtain the data related with personality traits.
Results: The mean score of self-realization (SR) and emotional stability (ES), which are personal adaptation subscales of the HPI, was found to be significantly lower in cancer group compared to control group (p=0.016 and p=0.009). As a result of further analyses performed according to cancer types, it was found that both SR and ES scores in head-neck cancer group were lower than both control group and other subgroups of cancer types (p=0.004 and p=0.001).
Conclusion: The results of this study revealed that there are differences between cancer and control groups in terms of personality characteristics. Overall, it was thought that the personality characteristics that are unique to patients with head-neck cancers may be the reactions that appear as a result of the development of head-neck cancer rather than a significant factor in cancer development.
Keywords: Cancer; personality; personality characteristics; Hacettepe Personality Inventory.

ÖZ

Amaç: Kişiliğin hem fiziksel hem de ruhsal sağlıkla ilişkili pek çok faktör üzerinde etkili olabildiği bilinmektedir. Bazı kişilik özelliklerinin kanser gelişiminde de bir faktör olarak önem taşıdığı düşünülmekte ve bu nedenle de kansere yatkın kişilik kavramı araştırmacıların ilgisini çekmeye devam etmektedir. Bu çalışmanın amacı, farklı türden kanser hastaları ile sağlıklı kontrol grubu arasındaki kişilik özelliklerindeki farklılıkları incelemek ve karşılaştırmaktır.
Gereç ve Yöntemler: Bu çalışmaya farklı türden kanser tanısı olan hastalar (n=100) ve kontrol grubu olarak da sağlıklı bireylerden (n=93) oluşan toplam 193 kişi dahil edilmiştir. Kişilik özellikleri ile ilgili verilerin elde edilmesi için Hacettepe Kişilik Envanteri (HKE) kullanılmıştır.
Bulgular: HKE'nin kişisel uyum alt ölçeklerinden olan Kendini Gerçekleştirme (KG) ve Duygusal Kararlılık (DK) puan ortalamalarının kontrol grubu ile karşılaştırıldığında, kanser grubunda anlamlı şekilde daha düşük olduğu bulunmuştur (p=0,016 ve p=0,009). Kanser türlerine göre yapılan ileri analizler sonucunda ise, baş boyun kanseri alt grubunda hem KG hem de DK puanlarının, hem kontrol grubundan hem de diğer kanser türlerine sahip alt gruplardan daha düşük olduğu görülmüştür (p=0.004 ve p=0.001).
Sonuç: Bu çalışmanın sonuçları, kanser grubu ve kontrol grubu arasında kişilik özellikleri açısından farklılıklar olduğunu ortaya koymaktadır. Genel olarak, baş boyun kanserli hastalara özgü kişilik özelliklerinin kanser gelişiminde önemli bir faktör olmaktan ziyade, baş boyun kanseri gelişimi sonucu ortaya çıkmış olan tepkiler olabileceği düşünülmüştür.
Anahtar kelimeler: Kanser; kişilik; kişilik özellikleri; Hacettepe Kişilik Envanteri.

INTRODUCTION

Cancer, one of the foremost health problems of the age, has taken on greater significance in preventive health services due to the increase in the incidence of this disease (1,2). While cancer was ranked as 7th and 8th among the diseases causing death by the early part of this century, it is today ranked 2nd, following cardiac diseases, in many countries including Turkey (1,3). Cancer is a chronic disease, which symbolizes death and limited control over life. In other words, cancer is the symbol of an unknown danger, suffering, pain, guilt, shame, isolation, chaos, and anxiety (1,4). Because life expectancy has increased, cancer has become one of the chronic health problems nowadays. In response to this threat, there have been innovations in diagnosis and treatment methods, increased use of healthcare organizations, and developments in the diagnosis and treatment of many acute and chronic disease (2,4). Ateşçi et al. (5) define cancer as a persistent and terminal disease as well as an important problem causing emotional, mental, and behavioral reactions.

The concept of personality involves the adaptive traits that are particular to an individual and that distinguish him or her from others. These traits include perception, mentality, and behavior patterns that are developed for the adaptation to the inner and external world based on cognitive evaluations. Individuals with these behavior patterns have the ability to display particular emotional reactions in particular situations and are equipped with coping and defense mechanisms to deal with inhibition and conflict. In other words, personality is the dynamic organization of psychophysical systems determining an individual's behavior and thoughts. Personality has two main components, temperament and character. While the character is defined as individuals' view and perception of life and their survival skills, temperament is defined as individuals' inborn behavioral tendencies, which are more inherently biological (6).

It is thought that some personality features carry importance as a factor in cancer development. The theory of a cancer-prone personality continues to attract researchers' attention, and many studies have been conducted in this field. While some of these studies supported this theory, others revealed contradictory results (7-16). For instance, Dattore et al. (10) compared premorbid personality traits between cancer patients and healthy controls by using the Minnesota Multiphasic Personality Inventory (MMPI). They found that cancer patients premorbid displayed lesser repression and much more self-reported depression than healthy individuals in the control group. Moreover, You et al. (16) investigated personality, coping strategies, and survives of Chinese cancer patients. They proposed that personality traits have an effect on survives of cancer patients by the linkage with the relationship between coping strategies and personality traits.

There are several studies in the literature, which compare personality characteristics between different types of cancer by using different personality inventories (7-16). We could not find any study, which compares several cancer types by using a current personality inventory in a single study. The aim of this study is to investigate and compare the differences in personality characteristics between patients with different types of cancer and the control group consisting of healthy individuals.

MATERIAL AND METHODS

Participants

The participants in the cancer group were selected from individuals with a diagnosis of cancer who received treatment in the Oncology Department of four different university hospitals between the years 2010 and 2011. To determine the sample size of this study, we looked at similar studies in the literature that suggested the number of participants for determining the difference between groups as at least 70 participants for each group with 5% significance level and 80% power. In terms of sampling type, we used purposive sampling with the following criteria for selecting the participants: the capability to understand and answer the scale accurately and a minimum of a primary education. The participants took part in the study on a volunteer basis. Researchers followed principals of Declaration of Helsinki for the ethical rules about participants in this study. Moreover, an informed consent was taken from each participants after informing them to participate in this research. The ethical permission for this study was obtained from the Ethical Committee of Düzce University Medical Faculty with the number of 2011/238 at 27.01.2012 before data collection.

The participants were asked about eight socio-demographic parameters including age, gender, educational level, marital status, income status, place of residence, and family type. After completing the exclusion process based on the aforementioned criteria, a total of 100 patients (50 females, 50 males) constituted the cancer group. A total of 93 healthy volunteers (47 females, 46 males) with similar sociodemographic characteristics constituted the control group.

Instruments

Hacettepe Personality Inventory (HPI): The HPI, an inventory developed by Özgüven İE (17) in 1992 in order to determine individuals' personal and social adaptation level, was used in the study. As a result of reliability studies conducted on various groups by applying the inventory, reliability coefficients were calculated ranging from 0.58 to 0.92 with an average of 0.82. The HPI consists of 8 subscales; four of them constitute the personal adaptation section, and the other four constitute the social adaptation section. Each subscale consists of 20 questions, and the validity scale consists of 8 questions, therefore, the HPI, in total, consists of 168 questions. The following four subscales were used to measure personal adaptation: the subscale of Self-Realization (SR), which investigates self-confidence, self-awareness of the skills, self-determination, self-expression, and the feeling of acceptance and usefulness; the subscale of Emotional Stability (ES), which determines the level of emotional determination; the subscale of Neurotic Tendencies (NT), which indicates the disposition to neurotic tendencies; and the subscale of Psychotic Symptoms (PS), which indicates the disposition to psychotic symptoms. In order to measure social adaptation, the following four subscales were used: the subscale of Family Affairs (FA), which measures individuals' skills of communication within their families; the subscale of Social Relations (SRe), which indicates the quality of their relationship with people other than family members; the subscale of Social Norms (SN), which measures the characteristic of being respectful to social principles, the values of the society, and others' rights as

well as legal obligations; and the subscale of Antisocial Tendencies (AT), which indicates whether an individual has antisocial tendencies. The lower scores taken from any sub-scale of HPI show a lower level of adaptation than expected. In other words, lower scores indicate higher defined characteristics and lower level of adaptation according to the norms of the society (17).

Statistical Analysis

PASW (SPSS 18.0.) software was used for the statistical analyses. The normality hypothesis of continuous quantitative variables was examined by Shapiro Wilk test and homogeneity control of variances was examined by Levene test. The descriptive statistics such as mean, standard deviation, and number and percentage frequencies regarding the data obtained are presented in tables. Either One Way Variance Analysis or a Chi-Square test was used based on its appropriateness in order to compare the demographic characteristics of the groups. Covariance analysis was used to examine the differences between the HPI scores of both groups. Since the demographic characteristics are thought to have an influence on the scores, demographic characteristics were taken as the covariant, thus, their effect on the scores was eliminated. Statistical significance level was considered as 0.05, and post hoc Tukey test was used to indicate the significance.

RESULTS

Regarding socio-demographic characteristics of groups, no significant difference was found between the groups according to the variables of age, gender, educational level, marital status, place of residence, and family type. The results revealed a significant difference just for income status between the groups (p=0.005). Half of the cancer patients were male in the cancer group, 59% was over 50 years old and 87% was married. Three-fourths had a primary education degree; half lived in a city, and approximately two-thirds had a middle-income status. In addition, two-thirds of the patients defined their families as a nuclear family (Table 1).

The distribution of cancer types among the cancer group was as follows: lung cancer (n=14), breast cancer (n=22), head-neck cancer (n=40), and other types of cancer (n=24). All of the patients with the diagnosis of lung cancer were males, and all of the patients with the diagnosis of breast cancer were females (Table 2).

The mean score of the SR subscale, a personal adjustment subscale of the HPI, was found to be significantly lower in the cancer group compared to the control group (p=0.016). Similarly, the mean score of the ES subscale was found to be significantly lower in the cancer group compared to the control group (p=0.009). The results revealed no significant difference in the other two personal adaptation subscales, NT and PS. No significant difference was found between the groups regarding the social adaptation sub-scales, which were FA, SRe, SN, and AT (Table 3).

When the sub-scale scores of HPI were compared according to cancer types, the results revealed no significant difference between the groups in terms of their scores on the NT subscale. On the other hand, when the HPI subscales were investigated between control group and the different groups of cancer types, it was found that there were significant differences among groups in terms

Table 1. The Socio-demographic characteristics, n (%)

	Cancer	Control	p
Gender			
Female	50 (50.0)	47 (50.5)	0.940
Male	50 (50.0)	46 (49.5)	
Age			
<40	14 (14.0)	14 (15.1)	
40-49	27 (27.0)	31 (33.3)	0.529
50-59	31 (31.0)	30 (32.3)	
≥60	28 (28.0)	18 (19.4)	
Marital Status			
Married	87 (87.0)	81 (87.1)	
Single	5 (5.0)	6 (6.5)	0.845
Other	8 (8.0)	6 (6.5)	
Educational Level			
Primary	74 (74.0)	65 (69.9)	
Secondary	21 (21.0)	22 (23.7)	0.801
College	5 (5.0)	6 (6.5)	
Occupation			
Housewife	38 (38.0)	35 (37.6)	
Officer	1 (1.0)	5 (5.4)	
Employee	16 (16.0)	11 (11.8)	0.456
Retired	27 (27.0)	24 (25.8)	
Self-employed	18 (18.0)	18 (19.4)	
Place of Residence			
Village	11 (11.0)	13 (14.0)	
District	37 (37.0)	38 (40.9)	0.609
City	52 (52.0)	42 (45.2)	
Income			
Low	29 (29.0)	11 (11.8)	
Middle	67 (67.0)	72 (77.4)	**0.005**
High	4 (4.0)	10 (10.8)	
Family Type			
Nuclear	65 (65.0)	68 (73.1)	0.223
Extended	35 (35.0)	25 (26.9)	

Table 2. Distribution of the groups according to gender, n (%)

	Female	Male	Total
Lung Cancer	0 (0.0)	14 (100)	14 (100)
Breast Cancer	22 (100)	0 (0.0)	22 (100)
Head-neck Cancer	20 (50.0)	20 (50.0)	40 (100)
Other Types of Cancer*	8 (33.3)	16 (66.7)	24 (100)
Control Group	47 (50.5)	46 (49.4)	93 (100)
Total	97 (50.2)	96 (49.7)	193 (100)

*: Cancers related to gastrointestinal, skin, musculoskeletal and hematological systems

Table 3. Scores of the cancer and control groups regarding the sub-scales of HPI

HPI Sub-Scales	Cancer	Control	p
Personal Adaptation (PA)			
Self-realization	12.03±0.63	13.15±0.61	**0.016**
Emotional Stability	9.24±0.65	10.50±0.63	**0.009**
Neurotic Tendencies	10.10±0.77	10.48±0.76	0.506
Psychotic Symptoms	9.33±0.67	10.03±0.66	0.158
Total PA	40.62±2.26	43.99±2.21	**0.045**
Social Adaptation (SA)			
Family Affairs	13.31±0.75	13.18±0.74	0.811
Social Relations	11.60±0.68	12.48±0.67	0.081
Social Norms	14.16±0.45	14.48±0.44	0.334
Antisocial Tendencies	12.59±0.61	12.17±0.60	0.359
Total SA	51.61±1.78	52.20±1.74	0.655
General Adaptation (PA+SA)	92.22±3.72	96.30±3.65	0.140

HPI: Hacettepe Personality Inventory, Descriptive statistics given as mean±standart deviation

of SR, ES, and PS scores (respectively; p=0.004, p=0.001, and p=0.038). Further analysis of these results by the post hoc Tukey test showed that, the mean SR score of the group with head-neck cancer was significantly lower than the mean score of the control group (p=0.018). However, no significant difference was found between control group and the groups with lung cancer, breast cancer, and other types of cancer in terms of their mean SR scores. When the ES scores were compared, a significant difference was found between control group and the group with head-neck cancer using further statistical methods to test significance (p=0.015). No significant difference was found between control group and the groups with lung cancer, breast cancer, and other types of cancer again in terms of their mean ES scores. A significant difference was also found between the head-neck cancer group and control group in terms of PS scores by using further statistical methods. These statistics revealed that the mean PS score of the group with head-neck cancer was significantly lower than the mean PS score of control group (p=0.005). There was no significant difference between control group and the other cancer groups in terms of their mean PS scores. Lastly, comparing the scores of the groups with cancer and control group on the subscales FA, SRe, SN, and AT, the social adaptation subscales of the HPI, the mean scores of all groups were also found to be similar (Table 4).

DISCUSSION

The studies on the theory of a cancer-prone personality maintain its popularity in the literature due to the increasing incidence of cancer (7-16). While some studies asserted that there exists a set of personality traits that are prone to cancer exists, some revealed contradictory results (7-16,18-23). Epidemiological studies during the late 19th century and the early 20th century seemed to support a premorbid personality hypothesis (7-9). These studies have supported the previous clinical observations that cancer patients experience the loss of a meaningful love object, which can be more frequently explained compared to the situation of significant emotional stress (9-10). LeShan et al. (11), in their study on the mental aspects of cancer, conducted personality investigations with 455 cancer patients and also applied therapy in 71 end-stage cancer cases. He observed that 68 of the 71 patients receiving the therapy already had a mood of hopelessness prior to developing cancer. From this point of view, he concluded that cancer mostly occurred in patients who are prone to feelings of desperation, hopelessness, and depression. On the other hand, Hansen et al. (18) conducted o prospective study to investigate the relationship between personality and cancer by using the Eysenck Personality Inventory (EPI). They found no significant relationship between different dimensions of EPI and risk for any cancer type and researchers proposed that certain personality characteristics are not associated with any cancer risk. Considering the literature, in spite of the many studies investigating cancer and cancer disposition through the lens of personality traits, we did not come across a study using the HPI for cancer patients (7-16,18-26). So, the present study aimed to investigate and compare personality traits between the patients with different cancer types and the control group consisting of healthy individuals by examining personality characteristics with HPI as a different well-structured personality inventory. As far as we know, this study is the first study in terms of using the HPI for examining personality characteristics of cancer patients.

In the present study, the socio-demographic characteristics of the cancer group and control group were found to be similar, however, a difference regarding the income status was observed. The analysis regarding the socio-demographic data revealed that the income of the cancer patients was lower than controls. However, using the appropriate statistical method inactivated this difference, and its effect on further analyses was prevented. The gender distribution of the cancer group was different, even though the female/male ratio was equal in the entire group of participants. Similar to the incidence of cancer types according to gender, all those with lung cancer were males and all those with breast cancer were females (9,18).

According to the results of the present study, the scores of the group with head neck cancer on the SR and ES subscales that are used to measure personal adaptation in the HPI were lower than the scores of control group. The low scores on the SR and ES indicate that these individuals display the personality type that is characterized by introversion and tend to be unable to express their feelings, indecisive, insecure, and less self-sufficient. The difference

Table 4. Scores on the sub-scales of HPI according to cancer types

HPI Sub-Scales	Head-neck (n=40)	Lung (n=14)	Breast (n=22)	Other Types* (n=24)	Control (n=93)	p
Personal Adaptation (PA)						
Self-realization	11.28±0.55	12.00±0.70	12.73±0.67	12.54±0.56	13.57±0.31	**0.004**
Emotional Stability	8.03±0.50	10.36±0.82	8.68±0.74	10.33±0.68	10.70±0.37	**0.001**
Neurotic Tendencies	9.10±0.68	11.50±1.06	10.95±0.80	10.71±0.92	11.12±0.38	0.089
Psychotic Symptoms	8.90±0.55	11.36±0.67	10.36±0.66	10.17±0.70	10.78±0.36	**0.038**
Total PA	37.30±1.93	45.21±2.59	42.73±2.52	43.71±2.54	46.10±1.20	**0.004**
Social Adaptation (SA)						
Family Affairs	13.28±0.60	14.14±0.93	15.09±0.71	14.71±0.82	14.23±0.37	0.360
Social Relations	11.90±0.52	12.71±0.71	13.14±0.72	12.46±0.96	13.55±0.32	0.120
Social Norms	13.75±0.0	13.36±0.60	14.00±0.50	13.92±0.53	14.22±0.21	0.620
Antisocial Tendencies	11.80±0.50	12.79±0.73	13.55±0.64	13.58±0.61	12.61±0.29	0.099
Total SA	50.80±1.46	53.00±1.71	55.77±1.45	54.42±2.27	54.52±0.87	0.154
General Adaptation (PA+SA)	87.68±3.24	98.21±3.94	98.55±3.63	98.13±4.61	100.60±1.85	**0.011**

HPI: Hacettepe Personality Inventory, *: Cancers related to gastrointestinal, skin, musculoskeletal and hematological systems, Descriptive statistics given as mean±standart deviation

between the group with cancer and control groups in terms of the SR and ES scores supports the hypothesis that the individuals who are insufficient in terms of SR and ES are more prone to cancer. Some previous studies and evaluations also argued that cancer can be related to emotional inhibition and emotional trauma (11,19,20). Additionally, it was observed in many studies that the suppression of emotion as an entity involving the features of the ES subscale and the sense of anger as a consequence of this suppression can increase cancer risk (19,20). Shaffer et al. (21), in their studies on medical students with a 30-year follow-up, found that those who suppressed their feelings and were observed as "loners" were 16 times more likely to get cancer than those who were extroverts and stressed their feelings. Moreover, You et al. (16) proposed that personality traits have an effect on survives of breast cancer patients by the linkage with the relationship between coping strategies and personality traits. They claimed that personality traits and coping strategies have an effect on emotion adjustment of patients with breast cancer.

When the cancer group and control group were compared in terms of their scores on the NT subscale, both groups displayed characteristics such as expressing emotional conflicts in a physical way and the frequency of somatic symptoms. In other words, the results indicated that NT was not a significant factor in cancer development. On the other hand, Kissen and Eysenck (24) claimed that a high extroversion and low neuroticism score obtained using the EPI characterize individuals who are prone to lung cancer. Another prospective study with the larger sample size, by Schapiro et al. (27), did not found any relationship between extroversion and neuroticism as personality dimensions and the risk of cancer similar to our study. They claimed that differences in the results related to NT between studies could be associated with using different inventories in different types of cancer patients in these studies. This claim can be appropriate with the abovementioned and the present studies' results. Additionally, Kissen and Eysenck (24) examined only patients with lung cancer by using EPI. In the present study, we compared much more types of cancer patients but we used a different inventory than EPI. Both using different personality inventory and examining different types of cancer patients can cause differences in the findings related to the relationship between cancer and personality. It seems that in this field, there is a need to conduct much more study, which examines different types of cancer with similar personality inventories.

In the present study, there was also a significant difference between the head neck cancer group and control group in terms of PS. The characteristics of PS moving away from people, being alone, unable to focus attention, and continuous dreaming was observed especially in head neck cancer group. Regarding social adaptation subscales of HPI, the present study indicated no difference between the cancer group and control group in terms of their scores on the FA, SRe, and SN subscales. It can be said that some of the social adaptation subscales of the HPI (FA, SRe, and SN) are defined similarly to the extroversion dimension of the EPI. The present study's findings related to these dimensions consistent with previous studies (22-25). Schapiro et al. (27) in their study investigating the relationship between the development of hormone-based cancer types and personality traits reported that extroversion and neuroticism are not related with the risk of hormone-based cancers including the organs such as breast, uterus, prostate etc. Nakaya et al. (22) investigated the relationship between cancer and personality in the groups with the cancers of stomach, lung, colorectal, and breast using the EPI and found no difference in terms of personality traits in the groups with cancer types and in the entire group. In a prospective study conducted by Hansen et al. (18) also proposed that there is not a relationship between neuroticism or extraversion and the risk for any kind of cancer.

Since there is found a significant difference between cancer patients and control group in terms of the SR subscale a further analysis conducted among the subtypes of cancer patients. According to this analysis, it was found that these differences stem from the subgroup of the head-neck cancer type. Moreover, ES and PS scores only in the head-neck cancer group were found to be lower than other cancer types and the control group.

The low scores of SR in the HPI indicate that an individual is insecure, indecisive, and hesitant and has the feeling that he\she is not accepted in the society and is useless. The low SR scores of the group with head-neck cancer compared to other groups probably infer that these patients are more indecisive, unconfident, and withdrawn as well as these individuals are not accepted in the society and are in a feeling that they are useless.

Head-neck cancers have some unique problems among all other cancer types. Patients with head-neck cancer experience face deformity, xerostomia, subnutrition, aphonia, and communication difficulties more often than most of other cancer types (26). All these difficulties might explain the tendency of the people to be alone, their attempt to move away from people and to be alone, and their imagination in their inner world at an extreme level (their low scores on the SR sub-scale). In other words, the personality traits of the group with head-neck cancer that are different from the other groups might be the reactions emerged as a result of the head-neck cancer development rather than being a noteworthy factor in the cancer development. There are limited studies measured psychotic features in patients with cancer and none of them is conducted with the patients with head-neck cancer (12-21). Garcia-Torres et al. (12) compared the patients with breast cancer with controls based on their psychotic features. They found that patients with breast cancer have higher psychotic features than other those in the control group. They also observed that psychotic features predict depressive symptoms in the patients with breast cancer. It can be helpful to examine psychotic features and its relationships with other clinical issues in head neck cancer patients with larger sample sized and new studies.

Considering the results of the present study from a broader point of view independently of the cancer types, a difference was found between the group with cancer and control group regarding their scores on the SR and ES subscales. When the cancer types were considered, a difference was found in the group with head-neck cancer regarding the subscales PS as well as SR and ES. The fact that a significant difference regarding PS was found only in the group with head and neck cancer suggests that question that "is this difference an outcome of the cancer type?" Consequently, the personality characteristics of the group with head-neck cancer that is different from the

other groups seem to be the reactions emerged as a result of the head-neck cancer development rather than being a noteworthy factor in the cancer development. Future studies need to be done in the large clinical head neck cancer samples and with the different personality inventory to clarify this relationship.

In terms of limitations of the present study, having a relatively small sample size and the using only one personality inventory as data collection tool are the main limitations of this study. Assessing the personality characteristics of patients at the only one-time point is another limitation of this study. It would be helpful for future studies to examine personality characteristics at least one of the time points consist of premorbid assessments of participants.

CONCLUSION

The present study revealed that there are differences between cancer and control groups according to personality characteristics. The personality characteristics that are unique to the patients with head-neck cancers may be the reactions that appear as a result of the development of head-neck cancer rather than a significant factor in cancer development. Despite the limitations of the present study, the findings of this study are promising for further studies, which will compare the effects of different personality characteristics of different cancer patients with several personality inventories.

Conflict of Interest: No conflict of interest is declared by the authors.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.630806

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):210-213

Hand Grip Strength in Elderly Rheumatoid Arthritis Patients

Yaşlı Romatoid Artrit Hastalarında El Kavrama Gücü

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Geliş Tarihi / Received : 08.10.2019
Kabul Tarihi / Accepted : 08.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 16.12.2019

ABSTRACT

Aim: Previous studies have shown that rheumatoid arthritis and aging are independent risk factors for decreased hand grip strength. However, little is known about how coexisting rheumatoid arthritis would affect the reduced hand grip strength in the elderly population. Therefore, the aims of this study were to compare the hand grip strength of elderly female rheumatoid arthritis patients with controls and to investigate the factors associated with hand grip strength in the patients with rheumatoid arthritis.

Material and Methods: This cross-sectional study included 45 elderly women with rheumatoid arthritis and 43 age-matched controls. All subjects were provided with self-reported questionnaires measuring physical disability, anxiety and depression, sleep quality, cognitive impairment, and fatigue severity. Hand grip strength was measured with hand dynamometer. The disease activity was assessed by the Disease Activity Score.

Results: There were no significant differences in values of age, body mass index, physical disability, anxiety and depression, sleep quality, cognitive impairment, fatigue severity, and grip strength between the groups. Disease period, physical disability, and disease activity were variables which showed statistically significant negative correlation with grip strength in rheumatoid arthritis patients. In further linear regression analysis, it is found that only long disease duration was associated with decreased grip strength.

Conclusion: Rheumatoid arthritis does not seem to significantly affect aging-related muscle strength loss. Disease duration was found to be the only independent factor associated with hand grip strength in elderly rheumatoid arthritis patients.

Keywords: Hand strength; rheumatoid arthritis; sarcopenia.

ÖZ

Amaç: Önceki çalışmalar romatoid artritin ve yaşlanmanın, azalmış el kavrama gücü için bağımsız risk faktörleri olduğunu göstermiştir. Bununla birlikte, bir arada var olan romatoid artritin yaşlı popülasyondaki azalmış el kavrama gücünü nasıl etkileyeceği konusunda çok az şey bilinmektedir. Bu nedenle, bu çalışmanın amaçları, yaşlı kadın romatoid artritli hastaların el kavrama gücünü kontrollerle karşılaştırmak ve romatoid artrit hastalarında el kavrama gücü ile ilişkili faktörleri araştırmaktır.

Gereç ve Yöntemler: Bu kesitsel çalışmaya 45 romatoid artritli yaşlı kadın ve 43 yaşa göre eşleştirilmiş kontrol dahil edildi. Tüm deneklere fiziksel özürlülük, anksiyete ve depresyon, uyku kalitesi, bilişsel bozulma ve yorgunluk şiddetini ölçen kendi kendine bildirilen anketler verildi. El kavrama gücü, el dinamometresi ile ölçüldü. Hastalık aktivitesi, Hastalık Aktivite Skoru ile değerlendirildi.

Bulgular: Gruplar arasında yaş, vücut kitle indeksi, fiziksel özürlülük, anksiyete ve depresyon, uyku kalitesi, bilişsel bozulma, yorgunluk şiddeti ve kavrama gücü değerleri açısından anlamlı fark yoktu. Hastalık süresi, fiziksel özürlülük ve hastalık aktivitesi romatoid artrit hastalarında kavrama kuvveti ile istatistiksel olarak anlamlı düzeyde negatif korelasyon gösteren değişkenlerdi. Sonraki doğrusal regresyon analizinde, sadece uzun hastalık süresinin kavrama kuvvetinin azalması ile ilişkili olduğu bulundu.

Sonuç: Romatoid artrit, yaşlanmaya bağlı kas kuvveti kaybını önemli ölçüde etkilemiyor gibi görünmektedir. Hastalık süresi, yaşlı romatoid artrit hastalarında el kavrama gücü ile ilişkili tek bağımsız faktör olarak bulunmuştur.

Anahtar kelimeler: El gücü; romatoid artrit; sarkopeni.

INTRODUCTION

Hand grip strength (HGS) defines the strength of the hand muscles used to grip (1). HGS, measured by manual dynamometry, has been recommended in the clinical practice as an easy measure in the definition of musculoskeletal function, as well as of disability (2). Especially in diseases that affect hands such as rheumatoid arthritis (RA), measuring HGS is of paramount importance. HGS in RA patients was demonstrated to be lower than controls (3). Another important condition that is known to be independently associated with reduced HGS is sarcopenia, which is described as age-related loss of muscle function and mass (4). However, it has not yet been fully discussed how coexisting RA would affect the reduced HGS in the elderly population.

It has been shown that decreased HGS in RA was associated with a variety of factors, including disease severity, pain, deformity, loss of joint range, functionality, joint damage, fatigue, sleep quality (3,5,6). However, studies regarding factors associated with decreased HGS in the elderly RA population are lacking (7).

Therefore, the purposes of the current study were to measure the HGS of elderly participants with RA, compared with controls, and to exam the factors associated with HGS in elderly RA patients.

MATERIAL AND METHODS

Participants

This cross-sectional case-control study was conducted with elderly female patients with RA followed up at least 1 year at the Physical Medicine and Rehabilitation outpatient clinic, Ankara Numune Training and Research Hospital, Turkey. Female controls matched by age were selected from patients' friends or family members. This study was approved by the Clinical Researches Ethics Committee of Ankara Numune Training and Research Hospital (dated 04.10.2018 and numbered 2246) and all individuals provided written informed.

Participants 65 years old or older were included. RA patients had to fulfill the criteria formulated by the American College of Rheumatology and the European League against Rheumatism in 2010 (8). The exclusion criteria were as follows: a history of a neuromuscular disorder, including carpal tunnel syndrome and polyneuropathy, or orthopedic disorder or a history of hand surgery that may impair hand function. Participants with unstable myocardial ischemia, significant anemia (hemoglobin <11 g/dl), severe renal failure, diabetes mellitus, malignancy, and smokers were also excluded.

Data on demographics, age (year), disease period (year), body mass index (BMI) (kg/m2), swollen and tender joint counts, visual analogue scale (VAS), and C-reactive protein (CRP) values were recorded.

Assessment of Functional Ability

Disability was evaluated by the Health Assessment Questionnaire (HAQ) (9,10). It is performed using a four-point scale (0=no problems, 3=unable to do) to score participants performing 8 categories of daily living activities.

Assessment of Disease Activity

It was measured by using the Disease Activity Score 28-CRP (DAS28-CRP) (11).

Assessment of Anxiety and Depression

We used the validated Turkish version of Hospital Anxiety and Depression Scale (HADS) to detect the level of anxiety and depression. It is a fourteen item scale (seven questions for anxiety and seven questions for depression) (12,13).

Assessment of Sleep Quality

The Turkish version of the Pittsburgh Sleep Quality Index (PSQI) was performed to assess sleep quality. The PSQI is an 18-item self-reported instrument to evaluate sleep quality, sleep onset latency, sleep efficiency, sleep length, sleep deprivation, daytime dysfunction, and use of pills for sleeping. Higher scores than 5 indicate poorer sleep quality (14).

Assessment of Cognitive Impairment

We used the Mini-Mental State Examination (MMSE) questionnaire (range 0-30) to assess cognitive function. Lower scores than 25 indicate cognitive impairment (15,16).

Assessment of Fatigue Severity

The Turkish version of the Fatigue Severity Scale (FSS) was used to assess fatigue symptoms. It was a self-reported 9-item scale with scores ranging between 1 and 7 per item (1=completely disagree, 7=completely agree). Pathological fatigue was defined as "FSS≥4/9" (17,18).

Measurement of Hand Grip Strength

HGS was measured using a manual hand dynamometer (Sammons Preston, Inc., Bolingbrook, IL, USA) by the same examiner to prevent the inter-observer error. It was evaluated with the patients sitting on a chair, with 90° elbow flexion, forearms and wrists in a neutral position. The participants were instructed to squeeze the handle as hard as possible during the measurements. Three evaluations were made for each hand, and the mean value was recorded in kilograms (kg) (19).

Statistical Analysis

Shapiro-Wilk test was used to test normality assumption. Mann-Whitney U test was applied for comparison of groups in terms of variables not meet the normality assumption, while Student's t test was used for variables showing normal distribution. Descriptive statistics were given as mean±standard deviation and median (minimum-maximum) values. Spearman's correlation analysis was utilized to analyze correlation between the HGS and age, BMI, disease duration, PSQI, MMSE, FSS, HADS-depression, HADS-anxiety, HAQ, and DAS28-CRP values. Multiple linear regression analysis was used for significantly correlated variables in the univariate analysis to assign independent factors of HGS in RA patients. According to the univariate analysis, three variables including disease duration, HAQ, and DAS28-CRP were entered into the regression model. Data were analyzed using the SPSS v.17 statistical package and p values <0.05 were considered statistically significant.

RESULTS

Among 88 participants, 45 were in RA group with a mean age of 73.1±3.2 years; 43 in control group with a mean age of 72.5±3.2 years. The participants in RA and control groups had similar age, BMI, and scores of PSQI, MMSE, FSS, HADS-depression, HADS-anxiety, and HAQ. The mean HGS for dominant hand in RA and control groups were 18.8±7.0 kg and 21.2±5.4 kg, respectively, and there was not a statistically significant difference between groups (p=0.082, Table 1).

In RA group, the mean period of RA disease was 12.4±7.8 years and DAS28-CRP score was 2.8±1.2. When we compare the dominant HGS with all parameters, a significant negative correlation was found between HGS and disease duration (r=-0.336, p=0.028), HAQ (r=-0.209, p=0.023) and DAS28-CRP (r=-0.324, p=0.035). There was no correlation between HGS with the age, BMI, and scores of PSQI, MMSE, FSS, HADS-depression, and HADS-anxiety (Table 2). Further evaluation by using multiple linear regression analysis with enter procedure was applied with the variables that were significant in univariate analyses. Even though there was significant association among HGS and disease duration, HAQ, DAS28-CRP in univariate analysis, regression analysis revealed that only disease duration had an independent effect on HGS values (p=0.009, R^2=0.250, Table 3).

DISCUSSION

It has been shown that, independently of each other, RA and aging have impacted on HGS negatively. However, the effect of RA on HGS in the elderly population has not been fully addressed. To clarify this, we compared the HGS between aging individuals with RA and age-matched healthy controls, and we found similar values in both groups. In addition, using a multiple linear regression analysis, we demonstrated that only disease duration was associated with HGS in the elderly population with RA.

Our finding of no significant difference in HGS for both groups is clearly inconsistent with other studies which reported that the participants with RA had significantly lower HGS than healthy controls (5,20). Firstly, it has been shown that HGS can be affected by functional ability, sleep quality, anxiety and depression, cognitive impairment, fatigue; therefore, we also evaluated the groups in terms of these factors to prevent bias and found no significant difference (3,21). Perhaps, we cannot fully explain this discrepancy; however, this may be due to some factors. One reason for this may be explained by selection as elderly RA patients with severe muscle weakness had less willingness to participate in the study. As a matter of fact, RA participants in our study generally tended to have low disease activity. As a second reason, advances in management with improvement of patient outcomes might influence HGS positively, therefore, it may not be rational to compare the results with those of previous studies that was done in the pre-biologics era. The etiopathogenesis of sarcopenia is complex and includes numerous factors, including hormonal, inflammatory, metabolic factors (22). Similar to the RA pathogenesis, inflammatory cytokines have been demonstrated to have a substantial role in the pathogenesis of sarcopenia. We can speculate that drugs used for RA to suppress inflammatory cytokines may also suppress these cytokines in the process of sarcopenia and so causes less muscle strength loss than expected in elderly RA patients. The inverse association between inflammation and HGS requires further exploration. For example, the question of whether using inflammation-suppressing drugs in healthy aging population to prevent sarcopenia should be investigated.

In our study, we found the correlation between HGS and DAS28, HAQ, and disease duration in RA group. However, after linear regression analysis, we found that duration of RA disease was the only independent factor

Table 1. Socio-demographic data of participants

	RA n=45	Control n=43	p
Age, years	73.1±3.2 74 (65-77)	72.5±3.2 73 (65-77)	0.348
Body mass index, kg/m²	29.4±5.5 28 (22-48)	29.6±5.7 28 (18-47)	0.841
HGS, kg (dominant hand)	18.8±7.0 19 (6-35)	21.2±5.4 22 (10-32)	0.082
HGS, kg (nondominant hand)	18.8±7.1 18 (8-35)	20.9±5.9 20 (10-32)	0.113
PSQI	7.2±3.6 6 (0-17)	8.2±4.3 9 (0-18)	0.220
MMSE	20.1±3.8 21 (10-27)	21.3±4.1 21 (10-29)	0.164
FSS	4.0±2.2 3 (1-8)	4.3±1.9 5 (1-8)	0.568
HADS-Depression	7.2±5.1 7 (0-17)	8.5±4.7 8 (1-21)	0.650
HADS-Anxiety	7.6±4.1 8 (1-18)	8.0±4.1 8 (1-17)	0.201
HAQ	1.0±0.9 0.7 (0-3)	0.9±0.6 0.6 (0-3)	0.967

RA: Rheumatoid Arthritis, PSQI: Pittsburgh Sleep Quality Index, MMSE: Mini-Mental State Examination, FSS: Fatigue Severity Scale, HADS: Hospital Anxiety and Depression Scale, HAQ: Health Assessment Questionnaire, Descriptive statistics given as mean±standard deviation, median (minimum-maximum)

Table 2. Correlations between handgrip strength and socio-demographic and clinical variables in RA patients

	Correlation Coefficient	p
Age	-0.063	0.681
Body mass index	0.092	0.546
Disease duration	-0.336	**0.028**
PSQI	-0.221	0.145
MMSE	0.125	0.412
FSS	-0.159	0.297
HADS-Depression	-0.188	0.217
HADS-Anxiety	-0.100	0.514
HAQ	-0.209	**0.023**
DAS28-CRP	-0.324	**0.035**

RA: Rheumatoid Arthritis, PSQI: Pittsburgh Sleep Quality Index, MMSE: Mini-Mental State Examination, FSS: Fatigue Severity Scale, HADS: Hospital Anxiety and Depression Scale, HAQ: Health Assessment Questionnaire, DAS28-CRP: Disease Activity Score 28-CRP

Table 3. Relationship between hand grip strength and clinical variables in RA patients

		B	SE	p	95% CI	
Grip Strength	**Disease duration**	-0.263	0.122	**0.037**	-0.509	-0.016
	HAQ	-1.931	1.126	0.094	-4.207	0.344
	DAS28-CRP	-1.359	0.786	0.092	-2.948	0.230

B: Regression coefficient, SE: Standard Error, CI: Confidence Interval, HAQ: Health Assessment Questionnaire, DAS28-CRP: Disease Activity Score 28-CRP

associated with HGS. The present study confirms previously reported inverse relationship between HGS and disease duration (6,22-24). In these previous studies, HGS was also associated with several other factors such as disease activity, functional status, or radiological damage (6,23,24). However, the subsequent regression analysis was not performed in these studies. Duration of the disease might better reflect joint damage, inflammatory burden, which may accumulate over time, and so that may led to decreased HGS.

There are some limitations of this study. First, we cannot eliminate the impact of individual motivation in HGS tests. Second, our sample is composed of female; therefore, the results may not be generalized to the general population.

In conclusion, we found that no significant difference in HGS between elderly individuals with RA and controls and the duration of RA disease was only independent factor associated with HGS in RA patients.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.653549

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):214-217

Elevated Levels of Fecal Calprotectin in Cirrhotic Patients and Spontaneous Bacterial Peritonitis

Sirotik Hastalarda ve Spontan Bakteriyel Peritonitte Fekal Calprotectin Düzeylerinde Artış

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Geliş Tarihi / Received : 01.12.2019
Kabul Tarihi / Accepted : 09.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 20.12.2019

ABSTRACT

Aim: The aim of this study is to investigate the relationship between fecal calprotectin (FC) which is a marker for intestinal inflammation and complications of cirrhosis which are due to increased bacterial translocation and intestinal inflammation.

Material and Methods: Out of 156 cirrhotic patients aged between 18-80 years who are admitted to our hospital, 64 were excluded according to exclusion criteria and a total of 92 patients, and 20 volunteers with similar age and sex as a control group were included in this study. Serum samples were taken at admission to measure erythrocyte sedimentation rate (ESR), c-reactive protein (CRP) and white blood cell count (WBC). All patients and the control group provided a single stool sample within 24 hours after admission. The study group divided into five subgroups (Child-Pugh Grade A, Grade-B, Grade-C, spontaneous bacterial peritonitis and hepatic encephalopathy) to investigate whether FC levels change as the disease progress or complications occur.

Results: Median FC levels were 168.8 mg/kg for cirrhotic patients and 9.8 mg/kg for control group, and the difference between the groups was statistically significant (p=0.039). In the subgroup analysis, the differences between spontaneous bacterial peritonitis and all other subgroups were statistically significant (p=0.002). In cirrhotic patients, FC levels were not correlated either with ESR (r=0.439, p=0.545) or CRP (r=0.403, p=0.321) or WBC count (r=0.061, p=0.645).

Conclusion: FC levels are increased in cirrhotic patients and early increase in FC levels before the rise of systemic inflammation markers can be used as a diagnostic marker for spontaneous bacterial peritonitis.

Keywords: Calprotectin; cirrhosis; secondary peritonitis.

ÖZ

Amaç: Bu çalışmanın amacı, intestinal inflamasyonun göstergesi olan fekal calprotectin (FC) ile artmış intestinal inflamasyon ve buna bağlı artan bakteriyel translokasyon sonucu meydana gelen sirozun komplikasyonları arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Hastanemize başvuran 18 ve 80 yaş arası 156 sirotik hastadan, dışlama kriterlerine göre 64'ü çıkartıldı ve toplam 92 hasta ve benzer yaş ve cinsiyette 20 gönüllü kontrol grubu olarak çalışmaya dahil edildi. Başvuru sırasında alınan kan örneklerinden eritrosit sedimantasyon değeri (ESR), c-reaktif protein (CRP) ve beyaz küre sayımı (WBC) çalışıldı. Her hastadan ve kontrol grubundan başvurudan sonraki 24 saat içinde bir adet spot gaita örneği alındı. Çalışma grubu, sirozun evresi ilerledikçe veya komplikasyonlar meydana geldiğinde FC değerlerinin değişip değişmediğini incelemek için beş alt gruba (Child-Pugh Evre-A, Evre-B, Evre-C, hepatiks ensefalopati ve spontan bakteriyel peritonit) ayrıldı.

Bulgular: Ortanca FC değerleri sirotik hastalarda 168,8 mg/kg ve kontrol grubunda 9,8 mg/kg idi ve gruplar arasındaki farklılık istatistiksel olarak anlamlıydı (p=0,039). Alt grup incelemesinde, spontan bakteriyel peritonit grubu ile diğer tüm alt gruplar arasındaki farklılıklar istatistiksel olarak anlamlıydı (p=0,002). Sirotik hastalarda FC ile ESR (r=0.439, p=0.545) veya CRP (r=0.403, p=0.321) ya da WBC sayımı (r=0.061, p=0.645) arasında korelasyon saptanmadı.

Sonuç: Sirotik hastalarda FC değerleri yükselmektedir ve sistemik inflamasyon belirteçlerinden önce FC değerlerinin erken yükselmesi sayesinde, spontan bakteriyel peritonitte tanısal bir test olarak kullanılabilir.

Anahtar kelimeler: Calprotectin; siroz; sekonder peritonit.

INTRODUCTION

Calprotectin was first described as an anti-microbial protein, which resides in the cytoplasm of granulocytes (1). It works as a pleiotropic molecule by activating endothelial cells and levels of calprotectin increase during active inflammatory processes. The soluble form of calprotectin can be found in blood, urine, and feces during inflammatory reactions because it is secreted from stimulated neutrophils and monocytes (2).

Fecal calprotectin (FC) levels increase in patients with inflammatory bowel diseases (IBD) and FC levels correlates with disease activity because inflammatory cytokines upregulate neutrophil migration to intestinal mucosa which causes high neutrophil turnover (3). FC levels also correlate with intestinal permeability (4).

Structural changes happen in the intestinal mucosa of the cirrhotic patients, such as vascular congestion, edema, fibromuscular proliferation, reduced villi to crypt ratio and thickening of muscularis mucosa. These changes increase intestinal permeability and facilitate bacterial translocation which is the driving factor for spontaneous bacterial peritonitis (SBP) and hepatic encephalopathy (HE). Increased bacterial activity causes the release of chemokines and triggers the inflammatory response. This defense mechanism paradoxically increases bacterial translocation because of the changes in tight junctions. Cirrhotic patients also have reduced chemotactic, opsonic and phagocytic activity that would cause systemic response and the degree of bacterial translocation increase as the disease progress (5).

In this study, we investigated the relationship between FC which is a marker for intestinal inflammation and complications of cirrhosis which are due to increased bacterial translocation and intestinal inflammation.

MATERIALS AND METHODS

Patients

One hundred fifty-six consecutive patients with cirrhosis, aged between 18 and 80 who were admitted to our hospital enrolled in this study after obtaining written consent. Demographic data, drug history and the cause of cirrhosis were recorded. Patients which had known causes for abnormal FC levels such as IBD, gastroenteritis, malignancies, drugs (proton pump inhibitors, non-steroidal anti-inflammatory drugs), gastro-esophageal reflux disease and Celiac disease (6) were excluded. Twenty volunteers with a similar age and sex distribution participated as a control group.

This study was performed in accordance with the principles of Good Clinical Practice, the principles of the Declaration of Helsinki and national laws. The study protocol was approved by the local ethics committee. (Eskişehir Osmangazi University, Non-drug Clinical Research Ethics Committee, dated 14.05.2013 and numbered 06).

Study Design

Diagnosis of cirrhosis was made by histopathologic assessment directly or indirectly with findings related to cirrhosis that indicate portal hypertension and impaired hepatic function. Child-Pugh classification (CP) was used to establish the severity of the disease. West-Haven criteria were used to determine HE and SBP were established as polymorphonuclear (PMN) leukocyte count was >250 cell/mm3.

We divided the study group into five groups to investigate whether FC levels change as the disease progress or complications occur:

i. 20 patients with CP Grade-A
ii. 21 patients with CP Grade-B
iii. 18 patients with CP Grade-C
iv. 17 patients with HE
v. 16 patients with SBP

Serum samples were taken at admission to measure erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell count (WBC). All patients and the control group provided a single stool sample within 24 hours after admission. Stool samples stored properly at -80°C. Fecal calprotectin was assayed by an enzyme-linked assay (Phi-Cal Calprotectin ELISA Kit; Immundiagnostik AG, Bensheim, Germany) and FC values above 50 mg/kg were regarded as positive according to the manufacturer's instructions.

Statistical Analysis

The statistical analysis was performed with IBM SPSS Statistics for Windows, version 21.0 (SPSS Inc., Chicago, IL, USA). Shapiro-Wilk's test was used to determine the normality of the data. Descriptive statistics are given by median and interquartile range (IQR) or mean and standard deviation, depending on the distribution of data. Student's t-test was used as a parametric test, Mann-Whitney U test was used to compare two groups and Kruskal-Wallis test was used to compare more than two groups as nonparametric tests. Spearman's correlation coefficient was used to examine the relationship between levels of FC, ESR, CRP, and WBC.

RESULTS

Baseline characteristics of the study and control groups are presented in Table 1. Sixteen patients were lost to follow-up and forty-eight patients had known factors that cause abnormal FC levels, therefore 92 patients (57 male, 35 female, mean age 60.5±11.9 years) and 20 healthy volunteers (12 male, 8 female, mean age 61.6±11.0 years) enrolled in this study. There was no statistically significant differences between patient and control groups in terms of sex (p=0.870) and age (p=0.430).

Median FC levels were 168.8 mg/kg (IQR 73.1-315.6 mg/kg) for cirrhotic patients vs. 9.8 mg/kg (IQR 6.8-13.8 mg/kg) for control group and the difference were statistically significant (p=0.039).

The etiology of cirrhosis was hepatitis C in 25,0% (n=23), hepatitis B in 19,6% (n=18), non-alcoholic steatohepatitis (NASH) in 21,7% (n=20), cryptogenic in 18,5% (n=17), alcohol in 8,7% (n=8), autoimmune hepatitis (AIH) in 4,3% (n=4) and primary biliary cholangitis (PBC) in 2,2% (n=2) of the patients.

FC levels in subgroups, as CP-A, CP-B, CP-C, HE and SBP are presented in Table 2. There was a significant difference in terms of FC levels between the subgroups (p=0.002). In the subgroup analysis, the difference between SPB and other groups was statistically significant (p=0.016, 0.011, 0.039 and 0.043, respectively). FC levels were higher in the CP Grade-C group but the difference was not statistically significant (Table 2).

In cirrhotic patients, FC levels were not correlated either with ESR (r=0.439, p=0.545) or CRP (r=0.403, p=0.321) or WBC count (r=0.061, p=0.645).

Table 1. Characteristics of the study group

	Cirrhotic Patients (n=92)	Control Group (n=20)	p
Sex, n (%)			
Male	57 (62.0)	12 (60.0)	0.870
Female	35 (38.0)	8 (40.0)	
Age, years, mean±SD	60.5±11.9	61.6±11.0	0.430
FC, mg/kg, median (IQR)	168.8 (73.1-315.6)	9.8 (6.8-13.8)	**0.039**
Etiology, n (%)			
Hepatitis-B	18 (19.6)		
Hepatitis-C	23 (25.0)		
NASH	20 (21.7)	-	-
AIH	4 (4.3)		
PBC	2 (2.2)		
Alcohol	8 (8.7)		
Cryptogenic	17 (18.5)		

SD: Standard Deviation, IQR: Interquartile Range, FC: Fecal Calprotectin, NASH: Non-alcoholic Steatohepatitis, AIH: Autoimmune Hepatitis, PBC: Primary Biliary Cholangitis

Table 2. Subgroup analysis

	FC, mg/kg, median (IQR)	p
CP Grade-A	135.0[a] (32.5-215.6)	
CP Grade-B	130.0[a] (59.4-365.0)	
CP Grade-C	152.5[a] (54.4-395.0)	**0.002**
HE	145.0[a] (78.8-292.5)	
SBP	363.8[b] (296.9-550.0)	

FC: Fecal Calprotectin, IQR: Interquartile Range, CP: Child-Pugh classification, HE: Hepatic Encephalopathy, SBP: Spontaneous Bacterial Peritonitis, a,b: According to the pairwise comparison results, FC levels in SPB subgroup was significantly higher than all other subgroups while the other four subgroups were similar each other

DISCUSSION

In this study, we found that FC levels in cirrhotic patients are significantly increased compared to healthy subjects and based on this data, FC can be considered as a valid marker for intestinal inflammation in cirrhotic patients. We also found that systemic markers of inflammation such as ESR, CRP and WBC count did not elevate despite a significant increase in FC levels. This finding also supports that FC is a sensitive and specific marker for intestinal inflammation in cirrhotic patients. Therefore FC can be a marker to diagnose the onset and severity of complications in cirrhotic patients.

The first study to investigate the prognostic value of calprotectin in cirrhotic patients was performed by Homann et al. (7). They showed that high levels of plasma calprotectin was related to poor survival in alcohol-related cirrhosis. They also described a subgroup of patients with recurrent bacterial infections which had higher levels of plasma calprotectin (8).

FC levels in IBD patients were investigated thoroughly in the literature (9-11) but we found only three studies investigating the relationship between FC and complications of cirrhosis. The first study by Yagmur et al. (12) found that FC levels in cirrhotic patients were significantly higher in cirrhotic patients. Other studies by Gundling et al. (13) and by Ibrahim et al. (14) had similar results. We also found that FC levels were significantly higher in cirrhotic patients 168.8 mg/kg (IQR 73.1-315.6 mg/kg) for cirrhotic patients vs. 9.8 mg/kg (IQR 6.8-13.8 mg/kg) for control group).

Contrary to our findings, both studies showed that FC levels also increase as the disease progress assessed by CP score and FC levels in HE patients were significantly higher. One explanation for this difference may be the routine use of prophylactic treatments in our clinic such as lactulose and rifaximin. Lactulose is degraded by colonic bacteria and the resultant acidic environment reduces the bacteria that produce ammonia and the risk of HE decrease in cirrhotic patients (15). Rifaximin also modulates gut microbiota and significantly decrease HE episodes and hospitalizations (16). Another explanation may be the timing of stool sampling. Especially in HE patients, most of the stool samples were obtained after the start of treatment that may have caused a reduction in FC levels. It should also be noted that FC has a biologic variability as day-to-day and even in spot one time only sampling (17).

Yagmur et al. (12) and Gundling et al. (13) also investigated the relationship between FC and markers of systemic inflammation such as CRP, WBC, interleukin-6, interleukin-8 and interleukin-10 and they did not find any significant influence of those laboratory parameters to FC levels. We also did not find any correlation between FC levels with either CRP, ESR or WBC count. The increase in FC levels before the rise of systemic inflammation markers also strengthen the rationale for the use of FC to diagnose the onset and severity of complications in cirrhotic patients.

FC levels in SBP patients were increased in all three studies mentioned above and Yagmur et al. (12) reported that the highest FC levels were determined in SBP group. We also found that FC levels were significantly higher in the SBP group (363.8 mg/kg) and the highest FC level (2108 mg/kg) was determined in this group.

CONCLUSION

The main conclusions of this study are the following: (i) FC levels are increased in cirrhotic patients and (ii) early increase in FC levels before the rise of systemic inflammation markers can be used as a diagnostic marker for SBP. Further comprehensive studies involving a larger number of patients are needed to confirm these suggestions and to determine whether FC can be used as a screening test to predict the complications of cirrhosis.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.531909

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):218-222

Types, Courses and Outcomes of Renal Failure in Hospitalized Patients: A Single Center Experience

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Geliş Tarihi / Received : 25.02.2019
Kabul Tarihi / Accepted : 10.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 20.12.2019

ABSTRACT

Aim: The aim of this study was to determine how to eliminate the treatment uncertainties, and correct and prevent inappropriate treatment in patients with renal failure.
Material and Methods: We retrospectively evaluated the biochemistry department's records of 438 patients with creatinine values >1.5 mg/dL that were followed-up at our hospital for the last five years. Demographics, type of renal dysfunction, related risk factors (use of nephrotoxic agents, surgical procedures, comorbidity, etc.), dialysis treatment, complications, and clinical outcome of these patients were recorded and analyzed.
Results: The most important result of the study is that the quality of the medical data recorded was very poor. The most common type of acute renal injury was prerenal acute renal injury. Among the cases, the most common etiological factors were dehydration and use of nephrotoxic agents. Surgical procedures and comorbid conditions facilitated the development of renal dysfunction, and all complications observed were more common and serious in the elderly patients. Among the patients with chronic renal injury, more of those with diabetic nephropathy required hospitalization. Interestingly, nosocomial infections were the most common cause of mortality in the patients hospitalized due to renal dysfunction.
Conclusion: Only a few medical records were suitable for retrospective evaluation. We think that if the quality of hospital data collection/storage systems could be improved, the quality of research data obtained in such studies would likewise improve and these data will bring preventive and corrective approach to mortality and morbidity.
Keywords: Renal injury; morbidity; mortality.

ÖZ

Amaç: Bu çalışmanın amacı, böbrek hasarı olan hastalarda tedavi belirsizliklerinin nasıl giderileceğinin belirlenmesi ve tedavideki uygunsuzlukların düzeltilmesi ve önlenebilmesidir.
Gereç ve Yöntemler: Kreatinin değeri >1,5 mg/dL olan ve hastanemizde son beş yılda takip edilen 438 hastanın biyokimya anabilim dalı kayıtları geriye dönük olarak değerlendirilmiştir. Hastaların demografik özellikleri, böbrek fonksiyon bozukluğu tipleri, ilişkili risk faktörleri (nefrotoksik ajanların kullanımı, cerrahi prosedürler, komorbidite, vb.), diyaliz tedavisi, komplikasyonlar ve klinik sonuçları kayıt altına alındı ve analiz edildi.
Bulgular: Çalışmanın en önemli bulgusu, kaydedilmiş olan tıbbi verilerin kalitesinin çok düşük olmasıdır. En sık görülen akut böbrek hasarı tipi prerenal akut böbrek hasarı idi. Olgular arasında en yaygın etiyolojik faktörler dehidratasyon ve nefrotoksik ajanların kullanımı idi. Cerrahi işlemlerin ve eşlik eden hastalıkların böbrek fonksiyon bozukluğu gelişimini kolaylaştırdığı, gözlenen tüm komplikasyonların yaşlı hastalarda daha sık ve ciddi seyirli olduğu belirlendi. Kronik böbrek hasarı olan hastalar arasında, diyabetik nefropatisi olanların çoğunun hastaneye yatması gerekiyordu. İlginç olarak, böbrek fonksiyon bozukluğu ile izlenen yatan hastalarda en önemli mortalite nedeninin nozokomiyal infeksiyonlar olduğu belirlendi.
Sonuç: Retrospektif değerlendirme için sadece birkaç tıbbi kayıt uygundu. Hastane veri toplama/depolama sistemlerinin kalitesinin iyileştirilebilmesi durumunda, bu tür çalışmalarda elde edilen araştırma verilerinin kalitesinin de aynı şekilde gelişeceğini ve bu verilerin mortalite ve morbidite konusunda önleyici ve düzeltici bir yaklaşım getirmeyi kolaylaştıracağını düşünmekteyiz.
Anahtar kelimeler: Böbrek hasarı; morbidite; mortalite.

INTRODUCTION

Worldwide, renal injury (RI) is a serious health problem whose treatment is challenging; follow-up of patients is difficult both for patients and physicians, and is an economic burden to everyone involved. Collection of data regarding the causes, complications, treatment, and consequences of RI is an ongoing process. Collection of such data is necessary in order to identify and prevent this problem. Data collected in every country and hospital are important, even though they may differ. In Turkey, national data collection activity has been increasing, however, inadequacies remain. In England, acute renal injury (ARI) data were collected and published in 2007 (1).

With early recognition of RI and adequate measures, partial or complete recovery is possible, and the disease progression rate can be lowered. Currently, due to the fact that there is an ever-increasing number of medical specialties and healthcare problems, many renal complications that could be diagnosed early, and reversed or at least minimized are misdiagnosed by physicians; this is according to our observations made in Turkey and in the hospital in which the present study was conducted. We think that appropriate investigation of this issue will increase the knowledge of physicians treating such patients. The present retrospective study aimed to evaluate the types, causes, follow-up, and outcome of renal impairment in patients hospitalized due to renal function diseases.

MATERIALS AND METHODS

The study included all patients with serum creatinine levels >1.5 mg/dL who were treated as inpatients at Mersin University Medical Faculty Hospital for five years. This study was approved by the local Ethics Committee of Mersin University Medical Faculty (30/11/11/06). Serum creatinine levels were obtained from the biochemistry department's electronic data files. Among the patients, those with complete personal data, clinical follow-up notes, a definitive diagnosis, records of all laboratory and investigative work leading to diagnosis, and final state at discharge were included. Adult patients that did not meet these criteria, children, and those with ≥2 charts were excluded from the study.

The following data were recorded for all the participants: chart number, age, gender, social security number, reason for referral, type of renal function failure, type of primary renal disease if any, comorbid diseases, surgical history (hospitalized patients), treatment history, follow-up blood pressure measurements, need for dialysis, type of dialysis performed (hemodialysis or peritoneal dialysis) and complications, access points for hemodialysis and complications, systemic complications during hospitalization, history of renal transplantation and related complications, most recent clinical conditions, and cause of death.

Statistical Analysis

SPSS v.22 was used for data analysis. The frequency and percentage of characteristics that could be related to renal function failure or considered a risk factor, such as cause for referral, comorbid diseases, surgical history, history of drug treatment, need for hemodialysis, blood pressure, type of dialysis performed and complications, history of blood transfusion, history of diabetes, renal transplantation and complications, and outcome, as well as patient age, gender, and social security status were calculated.

RESULTS

In total, 30619 registered patients with serum creatinine levels >1.5 mg/dL were ascertained at our hospital during the study period. Among these patients, 438 that had complete personal data, clinical follow-up notes, a definitive diagnosis, all laboratory and investigative work leading to diagnosis, and final state at discharge included in their charts were included in the study.

In all, 156 (35.6%) of the patients were female and 282 (64.4%) were male. Mean age was 58.4±16.9 years. The types of renal function failure in the patients are shown in Table 1. Most of the patients with ARI had prerenal etiology (84.8%, n=206), whereas 7.0% (n=17) had renal and 8.2% (n=20) had postrenal etiology.

Among the patients, 33.3% (n=146) underwent surgical intervention. The majority of ARI patients that were diagnosed via surgery had prerenal etiology (83.9%; n=78).

Most of the patients (52.3%, n=229) had a history of nephrotoxic drug use. The most commonly used drugs were non-steroidal anti-inflammatory drugs (NSAIDs) and radiocontrast agents. Of the 243 patients followed-up for ARI, 60.5% (n=147) had a history of nephrotoxic drug use. Among the patients treated with drugs, 20.4% (n=30) used only NSAIDs, 7.5% (n=11) used only nephrotoxic antibiotics (aminoglycoside, amphotericin B, vancomycin), 32.7% (n=48) used only contrast agents, and 0.7% (n=1) used only antineoplastics (cisplatin, oxaliplatin), whereas 8.8% (n=13) used NSAIDs and nephrotoxic antibiotics, 11.6% (n=17) used NSAIDs and contrast agents, 4.8% (n=7) used NSAIDs and antineoplastics, 6.1% (n=9) used nephrotoxic antibiotics and contrast agents, 3.4% (n=5) used nephrotoxic antibiotics and antineoplastics, and 4.1% (n=6) used contrast agents and antineoplastic agents (Table 2). In total, 60.7% (n=125) of the 206 patients with ARI of prerenal etiology used nephrotoxic drugs.

Among the patients, 13.9% (n=61) required dialysis; 96.7% (n=59) of the patients that underwent dialysis had chronic renal injury (CRI), whereas 3.3% (n=2) had ARI. In all, 88.5% (n=54) of the patients that underwent dialysis received hemodialysis, 8.2% (n=5) received peritoneal dialysis, and 3.3% (n=2) that received hemodialysis previously had peritoneal dialysis during follow-up. The primary renal disease in most of the 54 patients that had hemodialysis was unknown (Table 3). Etiology in the 21 patients that had hemodialysis for the first time is shown in Table 3.

Among the 56 patients that underwent hemodialysis, the primary method of access to blood was an arteriovenous fistula (41.1%, n=23), a permanent jugular catheter (19.6%, n=11), a transient jugular catheter (28.6%, n=16), a transient femoral catheter (8.9%, n=5), and a permanent subclavian catheter (1.8%, n=1).

The patients' blood pressure was followed-up and recorded; 40.8% (n=179) of the patients had normal blood pressure, 40.0% (n=175) had elevated blood pressure, and 19.2% (n=84) had low blood pressure.

The clinical follow-up results in the ARI patients are summarized in Table 4 and the cause of mortality in all the patients that died is shown in Table 5.

Among the 184 CRI patients, 32.1% (n=59) required dialysis and 64.4% (n=38) of these patients were chronic

dialysis cases; 78.9% (n=30) of these 38 patients and 85.7% (n=18) of the 21 patients that received dialysis for the first time received dialysis due to end stage renal disease (ESRD). In all, 59.8% (n=110) of the 184 CRI patients in the study had chronic renal disease and 13.0% (n=24) of these 184 patients were died. In 1.1% (n=2) of these 184 patients, outcome could not be ascertained due to such reasons as self-initiated discharge or lack of file data, etc. The cause of death in 24 of the 184 CRI patients in total was as follows; 29.2% (n=7) were cardiovascular disease, 29.2% (n=7) were infectious disease, 16.7% (n=4) were cerebrovascular disease, and 25.0% (n=6) were unknown.

DISCUSSION

Currently, RI is a clinical problem with an increasing prevalence rate. As it affects all organ systems, it has a wide complication spectrum, therefore, it concerns not only nephrology departments, but all other departments and its management should be approached in a multidisciplinary manner. The present retrospective study aimed to determine how to eliminate treatment uncertainties, and correct and prevent inappropriate treatment in RI patients at our hospital. We collected data regarding RI types, etiology, and consequences, and patient file quality, as compared to national and international data quality and reliability.

The prevalence of both ARI and CRI is increasing worldwide, which has led to expanding epidemiological research on RI in many countries (2-4). It has been reported in the archives of Turkish Nephrology Association that the numbers of new dialysis patients and dialysis centers have increased in 2006 substantially, as compared to the year before. The number of ARI cases reported in Turkey in 2006 was approximately 4000. Prevention of this disease will in turn decrease its associated healthcare expenditures significantly. ARI is a disease that could lead to ESRD and even mortality if not diagnosed early and treated accordingly. ARI and CRI share high mortality and morbidity rates due to comorbid disorders, and are expensive to treat (5-7). Unfortunately, in Turkey the prevalence, etiology, relationship to gender and age, accompanying clinical and social consequences, treatment modalities, preventive measures, and treatment outcomes of ARI and CRI, and the total work force loss they cause are poorly known.

The majority (84.8%) of the ARI patients in the present study had prerenal etiology. The most common cause of prerenal ARI was dehydration and use of nephrotoxic agents. Most (60.5%) of the patients that were followed-up due to ARI and the majority of the 206 prerenal ARI patients used nephrotoxic drugs. The most common nephrotoxic agents used were contrast agents and NSAIDs. Radiocontrast nephropathy is one of the most common causes of nephrotoxic ARI (8). NSAIDs are relatively cheap and accessible in Turkey, and the fact that even one dose can affect renal functions is neglected by physicians. Moreover, although there were hints of renal function disorder in some patients' routine test results, these drugs were routinely prescribed. The most common cause of ARI in hospitalized patients is acute tubular necrosis (ATN) due to ischemia and nephrotoxic agents (5,8). ATN is a consequence not only of ischemia and

Table 1. Types of renal function failure in the patients (n=438)

	n (%)
Acute Renal Failure	243 (55.5%)
Prerenal	206 (84.8%)
Renal	17 (7.0%)
Postrenal	20 (8.2%)
Chronic Renal Failure	170 (38.8%)
Acute exacerbation of Chronic Renal Failure	14 (3.2%)
Unknown	11 (2.5%)

Table 2. Distribution of nephrotoxic drugs used by acute renal injury patients (n=147)

	n (%)
NSAIDs	30 (20.4)
Antibiotics	11 (7.5)
Contrast agents	48 (32.7)
Antineoplastics	1 (0.7)
NSAIDs + Antibiotics	13 (8.8)
NSAIDs + Contrast agent	17 (11.6)
NSAIDs + Antineoplastic	7 (4.8)
Antibiotics + Contrast agent	9 (6.1)
Antibiotics + Antineoplastic	5 (3.4)
Contrast agent + Antineoplastic	6 (4.1)

NSAIDs: non-steroidal anti-inflammatory drugs

Table 3. Etiology in the hemodialysis patients

	All (n=54)	Already (n=33)	New (n=21)
Diabetic nephropathy	11 (20.4)	4 (12.1)	7 (3.3)
Glomerulonephritis	3 (5.6)	3 (9.1)	-
Hypertension nephropathy	2 (3.7)	-	2 (9.5)
Nephrotic syndrome	2 (3.7)	1 (3.0)	1 (4.8)
Nephrolithiasis	1 (1.9)	1 (3.0)	-
Polycystic kidney	2 (3.7)	-	2 (9.5)
Amyloidosis	2 (3.7)	-	2 (9.5)
Obstructive nephropathy	2 (3.7)	1 (3.0)	1 (4.8)
Lupus nephritis	2 (3.7)	1 (3.0)	1 (4.8)
Vesicoureteral reflux	1 (1.9)	1 (3.0)	-
Myeloma kidney	1 (1.9)	1 (3.0)	-
Unknown	25 (46.3)	20 (6.6)	5 (23.8)

Table 4. Outcomes in acute renal failure patients (n=243)

	n (%)
Functional full recovery	137 (56.4)
Death	93 (38.3)
Chronic renal failure	7 (2.9)
Unknown	6 (2.5)

Table 5. Causes of death in acute renal failure patients (n=93)

	n (%)
Infection	34 (36.6)
Cardiovascular disease	20 (21.5)
Cerebrovascular disease	7 (7.5)
Respiratory failure	2 (2.2)
Gastrointestinal bleeding	1 (1.1)
Unknown	29 (31.2)

nephrotoxic agents individually, but also in combination (9). In the 2006 report of the Turkish Nephrology Association, dehydration was the most common etiology, but surprisingly nephrotoxic agent use was not listed. Nonetheless, the use of nephrotoxic agents is regarded as one of the most common causes of ARI in some European countries (10). This example is an important sign that data collection in Turkey is not yet efficient or reliable.

In the present study 56.4% of the patients with ARI had complete recovery, 2.9% progressed to CRI, and 38.3% died. When compared with international data, the percentage of patients with complete recovery is similar (58%), whereas the mortality rate is higher and the rate of progression to CRI is lower.

Renal failure is a common problem in surgical patients that increases morbidity and mortality rates (11). Of the 438 patients in the present study, 146 had undergone surgical interventions, 93 of these patients had ARI, of which 78 had prerenal etiology. In these patients, dehydration and nephrotoxic drug use were common, which indicates that high-risk surgical patients should be carefully monitored before, during, and after surgery for hemodynamic instability, electrolyte-fluid balance, and use of drugs that adversely affect renal functions. Moreover, necessary consultations should be offered, even when the slightest abnormality is noted, in order to prevent more serious complications. Clinical trials have shown that early nephrology consultation is important in both ARI and CRI (12-14).

In 50.7% (n=222) of the patients in the present study primary renal disease progressed to renal failure. Diabetic nephropathy and hypertension nephropathy were the two most common renal diseases. In most of the patients the cause of nephropathy was unclear, as the primary disease was unknown or not recorded, which is another indication of inadequate record keeping. According to the literature, diabetic nephropathy and hypertension nephropathy are the most common causes of CRI, and in some countries diabetic nephropathy constitutes the primary cause of >40% of renal replacement therapy, and its incidence is growing (15-17). Both diabetes mellitus and hypertension are diseases that can be controlled with appropriate therapies. It was determined that nephropathy related with both of these diseases does not occur at early ages, but it does occur in both sexes and its incidence increases with age (most commonly in those >68 years of age).

In the present study, it was found that comorbid infectious, neurologic, and/or cardiovascular system diseases were associated with impaired renal functioning. The fact that these diseases were noted in most of the patients illustrates that careful and well-planned management of renal failure patients is critical.

Worldwide, hemodialysis is the most common renal replacement therapy in RI patients. In the present study 88.5% of the patients underwent dialysis and the treatment of choice was hemodialysis. Most (53.3%) of the dialysis patients received dialysis for a long time and the etiology of ESRD was unclear. That such data were not recorded is a significant patient management failure.

Diabetic nephropathy was the most common cause of ESRD in the present study, which is similar to previous reports. Only 1 patient in the present study was accessed via the subclavian vein, which is a positive sign of our treatment protocol, as it is associated with a nearly 50% chance of thrombosis or stenosis in the subclavian vein, rendering that side of the body useless for a fistula in the arm and use of a previous fistula (18).

In all, 175 of all the patients in the present study and 38 of the 54 patients that received hemodialysis were hypertensive, this is an indication that hypertension frequently accompanies renal function impairment and that it is frequently maltreated. Hypertension is also an essential risk factor for cardiovascular and cerebrovascular incidents. It is most probable that uncontrolled hypertension plays a role in the fact that patients with renal function impairment frequently encounter these complications.

An interesting finding of the present study is that complications occurred more frequently and with greater severity in the elderly patients. It is well-known that anatomic and functional loss occurs in all tissue and organs as age increases. Some studies reported that after the age of 30 years there is an annual 1 mL/min decrease in the glomerular filtration rate (19). Renal capacity decreases with age and the kidneys become more sensitive to any stress. A recent study suggested that ARI in the elderly is solely a risk factor for mortality (1). In Turkey the mean age of patients diagnosed as ARI was 51 and 25% of these patients were aged, >65 years. All these data indicate that the management of elderly patients should receive more scrutiny and that complications in this patient group can have rapid onset and be of a critical nature.

In the present study infections were the most common cause of death (36.6%), versus cardiovascular diseases according to national data. In RI patients, infections do not always follow a typical course (there may not be fever, there could be rapid progression to severe sepsis or septic shock), acute phase reaction markers are not always helpful, inadequate host response can be lethal, and drug treatment must be monitored closely (20). The infections or microorganisms that were associated with mortality in the present study could not be obtained from the patients' records, suggesting that infection was not managed well in patients with ARI and that the mortality rate was too high for a group of patients with a health problem that can be prevented or effectively treated.

The present study has some limitations, including the low quality of the data obtained due to a poorly designed data collection/storage system, the lack of some target data that is included in national and international data pools (duration of hospitalization, first 90-day mortality rate for ESRD patients), incomplete follow-up data, and the inability to determine the origin of some essential problems.

In conclusion, our hospital's data collection/storage system was of poor quality. The causes of renal failure observed in the present study are similar to those according to national and international data pools, advanced age and nephrotoxic drug use were important factors in renal function impairment, and the rate of mortality due to preventable causes (infection) was higher than that according to international data. We think that if the quality of hospital data collection/storage systems could be improved the quality of research data would likewise improve, which may help lower morbidity and mortality rates (21).

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.596227

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):223-232

Sleeve Gastrektomi Sonrası İlk Altı Ayda Besin Ögeleri Alımının Bazı Biyokimyasal Parametrelere Etkisi

Effect of Nutrient Intake on Some Biochemical Parameters in the First Six Months After Sleeve Gastrectomy

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Geliş Tarihi / Received : 24.07.2019
Kabul Tarihi / Accepted : 11.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 20.12.2019

ÖZ

Amaç: Bu çalışmanın amacı sleeve gastrektomi sonrası ilk altı ayda olası besin ögesi ve protein yetersizliğini belirlemek ve bazı biyokimyasal parametrelere etkisini saptamaktır.
Gereç ve Yöntemler: Bu çalışma, 13.07.2017 ve 06.01.2018 tarihleri arasında, Şişli Florence Nightingale Hastanesi Genel Cerrahi kliniğinde sleeve gastrektomi ameliyatı olan ve ameliyat sonrası en az altı ay uzman diyetisyen takibini sürdüren, 18-65 yaş arasında 102 hasta (75 kadın ve 27 erkek) ile yapılmış bir müdahale çalışmasıdır. Hastaların ameliyat öncesi ve ilk altı ay boyunca antropometrik ölçümleri, üç günlük besin tüketimleri ve biyokimyasal parametreleri takip edilmiştir.
Bulgular: Ameliyat sonrası ilk altı ayda hastaların vücut ağırlıklarında %27,4 oranında azalma görülmüştür. Hem vücut ağırlığındaki azalma hem de vücut yağ oranındaki ve beden kütle indeksindeki düşüş istatistiksel olarak anlamlı bulunmuştur ($p<0,001$). Hastaların ameliyat öncesi ve post-op 6.ayda biyokimyasal parametreleri; serum HbA1c, insülin, ürik asit, total protein, total kolesterol, HDL-kolesterol, LDL-kolesterol, trigliserit, demir, demir bağlama kapasitesi, ferritin, çinko, D vitamini, kalsiyum, parathormon, folat ve B12 vitamini arasında istatistiksel olarak anlamlı fark bulunmuştur ($p<0,001$). Sleeve gastrektomi sonrası ilk ay protein tozu desteği kullanan ve kullanmayan hastaların 6. aydaki serum total protein seviyeleri arasındaki farklılık istatistiksel olarak anlamlı bulunmuştur ($p=0,002$).
Sonuç: Obezite tedavisinin sürdürülebilir olması için ameliyat sonrası multidisipliner ekip ve düzenli takip ile hastaların yaşam tarzının düzenlenmesi ve aktif yaşamla desteklenmesinin gerekli olduğu unutulmamalıdır.
Anahtar kelimeler: Bariatrik cerrahi; beslenme, sleeve gastrektomi.

ABSTRACT

Aim: The aim of this study is to determine the possible nutrient and protein deficiency in the first six months after sleeve gastrectomy and to determine its effect on some biochemical parameters.
Material and Methods: This study is an intervention study including 102 patients (75 female and 27 male) aged between 18-65 years, who had undergone sleeve gastrectomy operation at the General Surgery Clinic of Şişli Florence Nightingale Hospital between 13.07.2017 and 06.01.2018 and been followed up by a dietician for at least six months postoperatively. Anthropometric measurements, three-day food intake, and biochemical parameters were followed pre-operatively and during the first six months.
Results: There was a 27.4% decrease in body weight of the patients in first six months after surgery. Both decrease in body weight, and decrease in body fat ratio and body mass index were found statistically significant ($p<0.001$). A statistically significant difference was found between preoperative and postoperative 6th month biochemical parameters; serum HbA1c, insulin, uric acid, total protein, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, iron, iron binding capacity, ferritin, zinc, vitamin D, calcium, parathormone, folate and vitamin B12 levels of the patients ($p<0.001$). The difference between 6th month serum total protein levels of patients using and not using whey protein powder in the first month after sleeve gastrectomy was found statistically significant ($p=0.002$).
Conclusion: It should be kept in mind that regulating patients' lifestyle with post-operative multidisciplinary team and regular follow-up, and supporting with active life are necessary for obesity treatment to be sustainable.
Keywords: Bariatric surgery; nutrition; sleeve gastrectomy.

GİRİŞ

Obezite, Dünya Sağlık Örgütü (DSÖ) tarafından insanlarda sağlığı bozacak ölçüde vücutta anormal veya aşırı yağ birikimi olarak tanımlanmakta ve beden kütle indeksi (BKİ) ile (BKİ ≥30 kg/m^2) belirlenmektedir (1,2). Dünya genelinde her geçen gün obez ve fazla kilolu birey prevalansı artmakta olup, bu artış ülkelerin ekonomik durumundan bağımsız olarak gerçekleşmektedir. Ağırlık artışı, etnik yapıya, cinsiyete, yaş grubuna göre farklılık göstermektedir. Dünyada fazla kilolu olarak nitelenen 1,9 milyar yetişkinin yaklaşık 600 milyonu obezdir (1,3).

Obezite, genetik, çevresel ve psikolojik etkileşimleri olan, irade yetersizliği ile açıklanamayacak kadar ciddi, birçok tıbbi problemi beraberinde getiren, erken ölümlere neden olan, tedavi edilmesi gereken, karmaşık ve kronik bir hastalıktır (4,5). Obezitenin giderek artan ciddi bir halk sağlığı sorunu olması, hem fazla kilolu ve obez bireyleri hem de uzmanları tedavi arayışına yönlendirmektedir (6).

Obezite tedavisinde, tıbbi beslenme tedavisi, egzersiz, farmokolojik tedavi ve davranış değişikliği tedavisi gibi geleneksel yöntemlerin yanı sıra yeni tekniklerin kullanıldığı cerrahi yöntemler de ülkemizde ve dünyada giderek yaygınlaşmaktadır (7). Cerrahi yöntemlerin tercihi belirli endikasyonlara bağlanmıştır. Bu endikasyonlardan biri BKİ ≥40 kg/m^2 olması, diğeri obez bireylerin obezitede konservatif tedavi yöntemlerini denemiş ve etkili olmadığının görülmüş olmasıdır. Bu koşullarda bariatrik cerrahinin gerekli olduğu düşünülmektedir (6,8).

Obeziteyi tedavi etmeyi amaçlayan cerrahi prosedürlerin keşfi, geliştirilmesi ve her geçen yıl çeşitliliğinin artması, ağırlık kaybı için çabalayan birçok bireye umut kaynağı olmuştur. Bariatrik cerrahi prosedürleri yaşamı olumlu yönde değiştirebilecek çözümler sunmaktadır (9).

Bariatrik cerrahi uygulamaları, obez bireyin genel sağlığını iyileştirse de bireyi ciddi beslenme yetersizliklerine karşı daha duyarlı hale getirebilmektedir. Ameliyattan sonra kısıtlanmış mide hacmi, yetersiz enerji alımına, hızlı ve aşırı ağırlık kaybına, gıda intoleransına, besin takviyelerinin düzensiz kullanılmasına ya da uzun süren kusma şikayetlerine ve ciddi beslenme yetersizliklerine sebep olabilir. Bariatrik cerrahiden kaynaklanan beslenme yetersizliklerinin patofizyolojisi çok yönlüdür. Bu yetersizliklerin şiddeti tercih edilen cerrahi yönteme bağlıdır (10).

Yapılan çalışmalarda az miktarda besin tüketimi, ameliyat sonrası besinlerin sindirim ve emilimlerinde olan değişiklikler ve beslenme kalitesinin yetersizliğine bağlı olarak demir, B12 vitamini, folat, kalsiyum ve D vitamini eksikliklerinin görülebileceği vurgulanmaktadır. Bariatrik cerrahiyi takiben beslenme yetersizliği çok yönlü olduğu için erken müdahale ve ameliyat sonrası besin alımının takibi zorunlu olmalıdır. Olası cerrahi komplikasyon sonucu olarak ortaya çıkabilecek sorunların yanı sıra cerrahiyi takiben beslenme sorunlarını da göz önünde bulundurmak gerektiği unutulmamalıdır. Bariatrik cerrahi sonrası yandaş hastalıklarda iyileşmenin ise uzun vadede kalıcı ağırlık kaybına bağlı olarak gerçekleştiği öngörülmektedir (10,11).

Tüm bu bilgiler doğrultusunda, bu çalışmada bariatrik cerrahi endikasyonu olan ve cerrahi teknik olarak laporoskopik sleeve gastrektomi (SG) uygulanan obez bireyler, ameliyat sonrası ilk altı aylık dönemde izlenmiştir. Bu çalışmanın amacı SG sonrası ilk altı ayda olası besin ögesi ve protein yetersizliğini belirlemek ve bazı biyokimyasal parametrelere etkisini saptamaktır.

GEREÇ VE YÖNTEMLER

Bu çalışma, 13.07.2017 ve 06.01.2018 tarihleri arasında, Şişli Florence Nightingale Hastanesi Genel Cerrahi kliniğinde SG ameliyatı olan ve ameliyat sonrası en az altı ay uzman diyetisyen takibini sürdüren 18-65 yaş arasında, 75'i (%73,5) kadın ve 27'si (%26,5) erkek 102 hasta ile yapılmış bir müdahale çalışmasıdır.

Obezite ve metabolizma cerrahisi için hekime başvuran hastalardan, ilk hekim muayenesi sonrasında gastroenteroloji, anestezi, göğüs hastalıkları, psikoloji ve endokrinoloji konsültasyonları istenmiştir. Bu konsültasyonlar neticesinde hastalar, Amerikan Metabolik ve Bariatrik Cerrahi Derneği'nin (American Society for Metabolic and Bariatric Surgery, ASMBS) bariatrik cerrahi ilkelerince hekim tarafından değerlendirilerek operasyona alınmışlardır.

<18 yaş, >65 yaş bireyler, gebe ve emzikli kadınlar, hekim tarafından ameliyata uygun görülmeyenler veya farklı bir cerrahi tekniğin uygulandığı hastalar, ameliyat sonrası altı ay boyunca diyetisyen takibinde olmayan ve BKİ <35kg/m^2 olan bireyler çalışmaya dahil edilmemiştir.

Bu çalışma İstanbul Bilim Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından 04.07.2017 tarih ve 60/01 sayılı karar ile uygun bulunmuştur. Her katılımcıya onam formu okutulup imzalattırılmıştır.

Bireylere ilişkin bilgilerin (yaş, eğitim durumu, sağlık durumu, genel beslenme alışkanlıkları, ana ve ara öğün tercihleri, su tüketimi, ameliyat öncesinde ağırlık kaybı için denediği yöntemler, fiziksel aktivite durumu vb.) elde edilebilmesi için açık uçlu sorulardan oluşan veri toplama formu uygulanmıştır. Veri toplama formu uygulanmadan önce hastalar araştırmacı tarafından bilgilendirilmiş ve gönüllü onam formu okutulup imzalattırılmıştır.

Veri toplama formunu takiben ameliyat öncesi ve ameliyat sonrası 1., 3. ve 6. ayda bireylerin biyoelektrik impedans analizi ile vücut bileşimi (vücut yağ kütlesi, yağsız vücut kütlesi) alınmış, TANİTA-SC-330 cihazı kullanılarak değerlendirilmiştir.

Tüm bireylerin ameliyat öncesi ve sonrası 8 saatlik açlık sonrası kan örneklerinde, açlık kan şekeri, ürik asit, kreatinin, Alanin aminotransferaz (ALT), Aspartat aminotransferaz (AST), toplam kolesterol, yüksek yoğunluklu lipoprotein (HDL) kolesterol, düşük yoğunluklu lipoprotein (LDL) kolesterol, trigliserit, toplam protein, çinko, 25-OH-vitamin D, insülin, tiroid uyarıcı hormon (TSH), serbest T3, serbest T4, kalsiyum, sodyum, potasyum, vitamin B12, demir, demir bağlama kapasitesi, ferritin ve hemogram düzeyleri değerlendirilmiştir.

Ameliyat sonrası bireylerin beslenme durumlarının değerlendirilmesi için iki gün hafta içi, bir gün hafta sonu olmak üzere üç günlük besin tüketim kaydı alınmıştır. Hastaların günlük ortalama aldıkları makro ve mikro besin ögelerinin analizi Ulusal Gıda Kompozisyon Veri Tabanı (Türkomp) kullanılarak hesaplanmıştır.

Ameliyat endikasyonu olup, hekim tarafından SG ameliyatı uygun görülmüş hastalara, ameliyat öncesi antropometrik ölçümlerin ve beslenme durumunun değerlendirilmesi yapıldıktan sonra, ameliyat sonrası döneme yönelik beslenme eğitimleri uzman diyetisyen

tarafından verilmiştir. Hastalara ameliyat öncesinde ASMBS'nin beslenme ilkelerinde belirtilen 1. aşama diyeti, 2. aşama diyeti ve 3. aşama diyetinin beslenme ilkeleri bireysel olarak anlatılmıştır. Tablo 1'de ameliyat sonrası önerilen beslenme programları gösterilmiştir.

Her hastaya post-op 1. ay, 3. ay ve 6. ayda kan bulgularına göre hekim tarafından vitamin-mineral desteği, mide koruyucu (şurup/tablet) medikal ilaç, 3. aşama diyetine kadar 400 ml suda çözdürülmüş 1 ölçek/gün protein tozu desteği (27g whey izolatı) önerilmiş ve hastaların düzenli olarak kullanımı sorgulanmıştır.

İstatistiksel Analiz

Analizler IBM SPSS v.20 paket programı kullanılarak yapılmıştır. Verilerin normal dağılıp dağılmadığı Kolmorogov-Smirnov testi ile incelenmiştir. Gruplar arası karşılaştırmalar için Independent samples t test veya Mann Whitney U testi, pre-op ile post-op 6. ay karşılaştırmaları için Paired Samples t test veya Wilcoxon testi, değişkenler arası ilişkiler için Pearson korelasyon analizi ve Spearman korelasyon analizi, pre-op ve post-op 1. ay, 3. ay ve 6. ay takip edilen ölçümler arasında farklılaşma olup olmadığını test etmek için tekrarlı ölçümler için ANOVA testi, anlamlı fark bulunması durumunda da Bonferroni testi kullanılmıştır. Kategorik veriler yüzde ve frekans, sürekli veriler dağılım şekline bağlı olarak aritmetik ortalama ve standart sapma veya ortanca değer (minimum-maksimum) olarak özetlenmiştir. İstatistiksel anlamlılık düzeyi 0,05 olarak dikkate alınmıştır.

BULGULAR

Hastaların yaş ortalaması 40,36±10,02 yıl olup 75'i (%73,5) kadın, 27'si (%26,5) erkektir. Kadınların pre-op BKİ'si 45,32±6,90 kg/m^2, erkeklerin pre-op BKİ'si ise 43,47±4,92 kg/m^2'dir.

Tablo 2'de hastaların ameliyat öncesi hastalık, ilaç kullanımı ve diyet yapma durumları gösterilmiştir. Kadın hastaların 18'inin (%24,0) herhangi bir hastalığı yokken, 40'ı (%53,3) ameliyat öncesinde diyabet ve/veya insülin direnci, 12'si (%16,0) hormonal hastalık, 5'i (%6,7) ise hipertansiyon veya kalp hastalığı tanısını almıştır. Erkek hastaların 12'sinin (%44,4) herhangi bir hastalığı yokken, 9'u (%33,3) ameliyat öncesinde diyabet ve/veya insülin direnci, 2'si (%7,4) hormonal hastalık, 4'ü (%14,8) ise hipertansiyon veya kalp hastalığı tanısını almıştır.

Tablo 1. Ameliyat sonrası önerilen beslenme programları

Diyet Aşamaları	Başlangıç	Sıvılar/Yiyecek
Aşama-1	Post-op 1/2.gün	Şeffaf sıvılar; karbonhidratsız, kalorisiz, şekersiz, kafeinsiz içecekler
Aşama-1 (*Vitamin-mineral destekleri hekim kontrolünde başlanmıştır.)* • Çiğnenebilir multivitamin[a] • IV 350-500 µg/gün B12 vitamini • D vitamini 3000 IU/gün[b] • Likid anti-asit preparatları	Post-op 3.gün (*taburcu*)	Şeffaf sıvılar: • Şekersiz sıvılar (tatlandırıcı kullanılabilir) • Tam sıvı diyet: • Tuz ilaveli sıvılar (ayran) • Protein tozu 1 ölçek/gün • (27g whey protein izolatı)
Aşama-2 (*Vitamin-mineral desteklerine hekim kontrolünde devam edilmiştir.)* • Çiğnenebilir multivitamin[a] • IV 350-500 µg/gün B12 vitamini • D vitamini 3000 IU/gün[b] • Likid anti-asit preparatları	Post-op 10-14.gün	Şeffaf sıvı tüketimi arttırılmalıdır (>1200-1800 ml). Sıvı diyet yerini; yumuşak, püre edilmiş proteinden zengin yiyeceklere bırakmalıdır. Protein tozu 1 ölçek/gün (27g whey protein izolatı) Protein kaynakları: yumurta, kıyma, püre yapılmış tavuk veya hindi eti, haşlanmış veya fırınlanmış balık, kıvamlı çorbalar, süzme peynir, az yağlı peynir, yoğurt
Aşama-2 (*Vitamin-mineral desteklerine hekim kontrolünde devam edilmiştir.)* • Çiğnenebilir multivitamin[a] • IV 350-500 µg/gün B12 vitamini • D vitamini 3000 IU/gün[b] • Likid anti-asit preparatları	Post-op 2-4. hafta	Tolerasyon göz önünde bulundurulmalıdır. • Protein tozu 1 ölçek/gün (27g whey protein izolatı) • Proteinden zengin besinler • İyi pişmiş sebzeler • Yumuşak veya püre edilmiş meyveler
Aşama-2 (*Vitamin-mineral destekleri hekim kontrolünde tablet şeklinde önerilmiştir.)* • Tablet/çiğnenebilir multivitamin[a] • IV 350-500 µg/gün B12 vitamini • D vitamini 3000 IU/gün[b] • Kapsül proton pompa inhibitörü	Post-op 5.hafta	Protein tüketimi sebze ve meyve eşliğinde devam ettirilmelidir. • Protein tozu 1 ölçek/gün (27g whey protein izolatı) Tolerasyona göre salata tüketimi 1. ay sonrası önerilebilir.
Aşama-3 (*Günlük vitamin-mineral desteği hekim kontrolünde sürdürülmüştür.)* • Tablet/çiğnenebilir multivitamin[a] • IV 350-500 µg/gün B12 vitamini • D vitamini 3000 IU/gün[b]	Post-op 5.hafta - 6.ay Açlık hissinin artması ve daha fazla miktarda besinin tolere edilebilmesi	Tolerasyon göz önünde bulundurularak sağlıklı katı yiyeceklerin tercih edilmesi Proteinden zengin besinler, iyi pişmiş et ürünleri, çiğ salata, kuru baklagiller

[a]: Multivitamin: 60 mg Magnezyum, 90 mg C vit, 30 mg B3 vit, 30 mg E vit, 15 mg Çinko, 2 mg Bakır, 2 mg Manganez, 70 µg Selenyum, 10 mg B5 vit, 1,5 mg B1 vit, 1,7 mg B2 vit, 4 mg B6 vit, 160 µg K vit, 1000 µg A vit, 120 µg Krom, 20 µg D vit, 600 µg Folik asit, 600 µg Biotin, 500 µg B12 vit, 150 µg İyot içermektedir. [b]: D vitamini hastanın biyokimyasal bulguları göz önünde bulundurularak gerekli ise önerilmiştir.

Ağırlık kaybetmek için başvurulan yöntemler sorgulandığında, kadın hastaların 6'sının (%8,0) diyetisyen, 8'inin (%10,7) egzersiz ve 61'inin (%81,3) ise tüm yöntemlere (doktor, diyetisyen, egzersiz, akupunktur, zayıflama ilaçları) başvurduğu ve bu hastaların 71'inin (%94,7) verdiği ağırlıktan fazlasını geri kazandığı, 4'ünün (%5,3) ise kaybettiği kadar ağırlığı geri kazandığı saptanmıştır. Erkek hastaların 8'inin (%29,6) diyetisyen, 5'inin (%18,5) egzersiz, 14'ünün (%51,9) ise tüm yöntemlere (doktor, diyetisyen, egzersiz, akupunktur, zayıflama ilaçları) başvurduğu ve bu hastaların da 23'ünün (%85,2) verdiği ağırlıktan fazlasını geri kazandığı, 3'ünün (%11,1) kaybettiği kadar ağırlığı geri kazandığı, 1'inin (%3,7) ise kaybettiği ağırlıktan az geri ağırlık kazandığı saptanmıştır.

Tablo 3'te hastaların cinsiyete göre post-op op 1. ay, 3. ay ve 6. ayda aldıkları enerji ve tükettikleri makro besin ögeleri arasında farklılaşma olup olmadığı gösterilmiştir. Kadınların post-op enerji (p=0,001) ve yağ alımlarında (p=0,022) anlamlı fark olduğu, çoklu karşılaştırma sonucuna göre bu farkın post op 1. ay ile post op 3. ay ve post op 1. ay ile post op 6. ay arasında ortaya çıktığı görülmüştür. Erkekler de ise enerji ve protein alımlarında farklılık olduğu (sırasıyla p=0,029 ve p=0,030), bu farkın da post op 3. ay ile post op 6. ay arasında olduğu saptanmıştır.

Tablo 4'te cinsiyete göre pre-op ve post-op dönemdeki ortalama BKİ, vücut ağırlığı ve vücut kompozisyonu analizi ile belirlenmiş olan yağ ve kas kütlesi ağırlıkları gösterilmiştir. Kadın hastaların pre-op dönemde ortalama BKİ 45,3±6,9 kg/m^2'den post-op 6. ayda 33,13±5,6 kg/m^2'ye gerilemiş (p<0,001), pre-op vücut ağırlığı ortalaması 121,9±18,6 kg'den 89,1±15,6 kg'ye (p<0,001), yağ kütlesi 47,8±3,8 kg'den 38,30±5,91 kg'ye (p<0,001), yağsız vücut kütlesi 62,9±8,6 kg'den 53,8±6,8 kg'ye (p<0,001) azalmış olup post-op takiplerin her biri arasında istatistiksel olarak anlamlı fark saptanmıştır. Erkek hastaların pre-op dönemde ortalama BKİ 43,5±4,9 kg/m^2'den post-op 6. ayda 30,9±3,8 kg/m^2'ye gerilemiş (p<0,001), vücut ağırlığı ortalaması ise 136,7±16,8 kg'den 97,2±11,6 kg'ye (p<0,001), yağ kütlesi 41,9±7,3 kg'den 29,8±8,1 kg'ye (p<0,001), yağsız vücut kütlesi 75,0±11,1 kg'den 66,9±8,8 kg'ye (p<0,001) azalmış olup sadece yağsız kütle açısından post-op 1. ay ve 3. ay takipleri benzerken diğer tüm post-op takiplerin her biri arasında istatistiksel olarak anlamlı fark saptanmıştır.

Tablo 2. Hastaların ameliyat öncesindeki hastalık, ilaç kullanımı ve diyet yapma durumu

	Kadın (n=75)	Erkek (n=27)
Tanı Konulan Hastalıklar		
Yok	18 (24,0)	12 (44,4)
Diyabet ve/veya İnsülin Direnci	40 (53,3)	9 (33,3)
Hormonal Hastalıklar	12 (16,0)	2 (7,4)
Diğer (kalp hastalığı/hipertansiyon)	5 (6,7)	4 (14,8)
İlaç Kullanımı		
Yok	40 (53,3)	15 (55,6)
Diyabet ve/veya İnsülin Direnci	16 (21,3)	6 (22,2)
Hormonal Hastalıklar	12 (16,0)	2 (7,4)
Diğer (kalp hastalığı/hipertansiyon)	7 (9,3)	4 (14,8)
Ailesinde Obez Olma Durumu		
Evet	62 (82,7)	24 (88,9)
Hayır	13 (17,3)	3 (11,1)
Obez Aile Üyesi (n=86)		
Anne	15 (24,2)	7 (29,2)
Baba	10 (16,1)	5 (20,1)
Hem Anne Hem Baba	37 (59,7)	12 (50,0)
Ağırlık Kaybı Yöntemi		
Diyetisyen	6 (8,0)	8 (29,6)
Egzersiz	8 (10,7)	5 (18,5)
Hepsi (diyet/egzersiz/akupunktur/ilaç)	61 (81,3)	14 (51,9)
Tekrar Ağırlık Kazanımı		
Verdiği ağırlık kadar	4 (5,3)	3 (11,1)
Verdiği ağrılıktan daha az	0 (0,0)	1 (3,7)
Verdiği ağırlıktan daha fazla	71 (94,7)	23 (85,2)

Tablo 3. Hastaların post-op 1. ay, 3. ay ve 6. ayda aldıkları enerji ve makro besin öğeleri karşılaştırılması

	Post-op 1. ay	Post-op 3. ay	Post-op 6. ay	p
Kadın (n=75)				
Enerji	616,8±164,6^a	687,9±194,6^b	702,7±162,1^b	**0,001**
Protein	43,8±18,5	43,5±15,9	48,2±13,4	0,150
Karbonhidrat	42,7±27,9	36,0±16,9	38,7±15,4	0,128
Yağ	30,4±9,4^a	34,4±12,1^b	33,4±7,4^b	**0,022**
Erkek (n=27)				
Enerji	720,3±188,2^{ab}	663,4±155,0^a	792,6±199,0^b	**0,029**
Protein	56,5±18,6^{ab}	47,0±16,8^a	57,7±11,5^b	**0,030**
Karbonhidrat	47,6±31,2	35,5±15,6	39,91±24,1	0,139
Yağ	32,4±9,8	35,9±8,9	39,7±11,0	0,070

Tablo 4. Hastaların ameliyat öncesi ve sonrası beden kütle indeksi ve vücut analizi değişimi

	Pre-op	Post-op 1. ay	Post-op 3. ay	Post-op 6. ay	p
Kadın (n=75)					
BKİ	45,3±6,9^a	41,0±6,4^b	37,1±6,0^c	33,1±5,6^d	**<0,001**
Ağırlık	121,8±18,6^a	110,2±17,5^b	99,8±16,6^c	89,1±15,6^d	**<0,001**
Yağ	47,8±3,8^a	45,7±4,1^b	42,3±5,3^c	38,3±5,9^d	**<0,001**
Yağsız Kütle	62,9±8,6^a	58,5±7,4^b	56,3±6,9^c	53,8±6,8^d	**<0,001**
Erkek (n=27)					
BKİ	43,5±4,9^a	39,1±4,5^b	34,9±4,4^c	30,9±3,8^d	**<0,001**
Ağırlık	136,7±16,7^a	122,8±15,2^b	109,8±14,0^c	97,2±11,6^d	**<0,001**
Yağ	41,9±7,3^a	39,1±7,9^b	33,8±7,7^c	29,8±8,1^d	**<0,001**
Yağsız Kütle	75,0±11,1^a	71,1±10,2^b	70,1±8,5^b	66,9±8,8^c	**<0,001**

Tablo 5'te ameliyat öncesi ve sonrası biyokimyasal parametrelerdeki değişim gösterilmiştir. Çalışmaya katılan hastaların ameliyat öncesi ve post-op 6. ayda değerlendirilen biyokimyasal parametreleri, serum HbA1c, insülin, ürik asit, total protein, total kolesterol, HDL-kolesterol, LDL-kolesterol, trigliserit, demir (Fe), demir bağlama kapasitesi, ferritin, çinko (Zn), D vitamini, kalsiyum (Ca), parathormon (PTH), folat ve B12 vitamini düzeyleri ortalamaları arasında istatistiksel olarak anlamlı fark bulunmuştur (p<0,001). Serum Hemoglobin (Hb) seviyesinin pre-op ve post-op 6.ay ortalaması arasında anlamlı bir fark bulunmamıştır (p=0,104).

Tablo 6'da SG sonrası BKİ değişimi ile bazı biyokimyasal parametreler arasındaki korelasyon gösterilmiştir. Ameliyat sonrası 6 aylık süreçte BKİ'deki azalma ile hastaların post-op 6. aydaki serum D vitamini değişimi, AKŞ, insülin ve HbA1c değerleri arasında anlamlı bir korelasyon bulunmazken (sırasıyla p=0,605; p=0,297; p=0,141 ve p=0,785), HDL-kolesterol değerleri ile pozitif yönlü zayıf korelasyon saptanmıştır (r=0,208; p=0,036).

Hastaların 68'i (%66,7) önerilen protein tozunu kullanmış, 34'ü (%33,3) tüm önerilere rağmen protein tozunu kullanmamıştır. SG sonrası ilk ay protein tozu desteği kullanan ve kullanmayan hastaların 6. aydaki vücut kompozisyonları ve bazı biyokimyasal parametrelerindeki değişim Tablo 7'de verilmiştir. SG sonrası ilk ay protein tozu desteği kullanan ve kullanmayan hastaların ameliyat sonrası ilk 6 aylık süreçte serum total protein seviyelerindeki değişim istatistiksel olarak anlamlı bulunmuştur (p=0,002).

Çalışmaya katılan 102 kişiden hiçbirinin ameliyat öncesi düzenli egzersiz yapmadıkları belirlenmiştir. Çalışmaya katılanların %45,1'i (n=46) ameliyat sonrası düzenli egzersiz yapmaya başlamıştır. Ameliyat sonrasında düzenli egzersiz yapmaya başlayanların %97,8'i (n=45) yapmış oldukları egzersizi 6 ay boyunca sürdürmüş, %2,2'si (n=1) post-op 6. ayda egzersiz yapmayı bırakmıştır. Düzenli egzersiz yapmaya başlayanların %8,7'si (n=4) ise yapmış olduğu egzersizin sıklığını azaltmıştır.

Tablo 5. Ameliyat öncesi ve ameliyat sonrası 6. aydaki biyokimyasal parametrelerin karşılaştırılması

	Pre-op		Post-op		p
	Ortalama±SS	**Ortanca (Min-Maks)**	**Ortalama±SS**	**Ortanca (Min-Maks)**	
HbA1c (%)	5,8±1,0	5,7 (4,6-11,8)	5,1±0,6	5,1 (1,6-6,8)	**<0,001**
İnsulin (µU/ml)	22,6±16,5	18,3 (2,9-83,6)	11,4±10,1	8,8 (2,2-51,2)	**<0,001**
Ürik Asit (mg/dl)	5,9±1,5	59,6 (14,3-179,3)	5,2±1,2	5,1 (2,4-8,8)	**<0,001**
Total Protein (g/dl)	7,4±0,6	7,4 (5,9-10,6)	7,0±0,5	7,0 (5,9-9,3)	**<0,001**
Kolesterol (mg/dl)	201,8±38,5	198,0 (124,0-300,0)	186,6±41,8	180,5 (98,0-348,0)	**<0,001**
HDL-Kolesterol (mg/dl)	47,6±10,2	46,0 (29,0-79,0)	50,8±10,4	49,0 (27,0-79,0)	**0,003**
LDL-Kolesterol (mg/dl)	131,3±35,4	123,0 (65,0-240,1)	119,7±34,5	117,5 (48,0-236,0)	**<0,001**
Trigliserit (mg/dl)	137,5±83,8	123,5 (50,0-688,0)	103,8±46,6	96,5 (48,0-420,0)	**<0,001**
Hb (g/dl)	13,4±1,6	13,4 (8,6-16,3)	13,7±1,4	14,0 (9,4-17,3)	0,104
Fe (µg/dl)	70,3±41,4	64,5 (22,5-367,0)	89,1±35,0	87,0 (22,0-236,0)	**<0,001**
Demir Bağlama Kapasitesi (µg/dl)	358,2±67,5	345,5 (193,0-518,1)	297,4±67,8	292,5 (114,0-542,0)	**<0,001**
Ferritin (ng/dl)	67,7±84,8	34,7 (3,2-387,0)	88,8±81,0	66,3 (4,2-399,0)	**<0,001**
Zn (µg/dl)	101,0±14,2	101,0 (52,0-128,0)	94,8±12,4	95,0 (59,0-147,0)	**<0,001**
D Vitamini (µg/dl)	15,8±6,8	15,0 (3,3-38,0)	20,1±10,7	16,1 (9,8-66,0)	**<0,001**
Ca (mg/dl)	9,5±0,5	9,5 (8,5-10,8)	9,6±1,0	9,8 (0,0-9,7)	**<0,001**
PTH (pg/ml)	67,1±35,9	59,6 (14,3-179,3)	53,7±22,0	52,5 (18,0-159,9)	**<0,001**
Folat (ng/ml)	6,5±3,1	5,7 (1,8-14,6)	9,3±5,3	7,9 (1,0-26,7)	**<0,001**
B12 Vitamini (pg/ml)	337,5±152,6	305,0 (154,0-897,0)	446,9±176,1	430,0 (141,3-1298,0)	**<0,001**

SS: Standart Sapma, Min: Minimum, Maks: Maksimum, Hb: Hemoglobin, Fe: Demir, Zn: Çinko, Ca: Kalsiyum, PTH: Parathormon

Tablo 6. Ameliyat sonrası beden kütle indeksi değişimi ile bazı biyokimyasal parametreler arasındaki korelasyon

	Korelasyon Katsayısı	p
HDL-Kolesterol	0,208	**0,036**
D Vitamini	0,052	0,605
Açlık Kan Şekeri	0,104	0,297
İnsülin	0,147	0,141
HbA1C	0,027	0,785

Tablo 7. Ameliyat sonrası whey protein tozu kullanan ve kullanmayan hastaların 6. ay vücut analizi kompozisyonu ve bazı biyokimyasal parametrelerinin karşılaştırılması

	Kullanan (n=68)	Kullanmayan (n=34)	p
Vücut Ağırlığı (kg)	34,3±8,7	35,0±10,8	0,771
Vücut Yağ Kütlesi (kg)	10,8±5,8	9,1±3,1	0,056
Yağsız Vücut Kütlesi (kg)	8,3±5,7	10,0±5,6	0,131
Serum Total Protein (g/dl)	0,29±0,50	0,61±0,44	**0,002**

TARTIŞMA

Morbid obezite neden olduğu yandaş hastalıklarla birlikte ciddi bir halk sağlığı sorunudur. Yapılan çalışmalar obez hastalarda mortalite riskinin %50-100 oranında arttığını ve bu durumun bireyin BKİ ile orantılı olduğu göstermiştir (12-14). Pérez ve ark. (15) tarafından yapılan çalışmada obez bireylerin yaşam beklentisinde 2-5 yıl, morbid obez bireylerin yaşam beklentisinde 13 yıl azalma olabileceği vurgulanmıştır. İstenmeyen ağırlık artışı, günlük enerji alımı ve tüketimi arasındaki dengesizliğe bağlı oluşan anormal yağ dokusu birikimine bağlıdır, fakat obeziteye eşlik eden çeşitli sistemik yandaş hastalıklar da hastaların yaşam süresini kısaltarak mortaliteyi artırmaktadır (16). Obeziteye eşlik eden yandaş hastalıkların başında diabetes mellitus (DM), hiperlipidemi, kardiyovasküler hastalıklar, solunum sistemi hastalıkları, kas iskelet sistemi hastalıkları gelmektedir (17). Bu çalışmada da ameliyat öncesinde kadın hastaların %53,3'ü, erkek hastaların %33,3'ü diyabet veya insülin direnci, kadın hastaların %6,7'si erkek hastaların %14,8'i hipertansiyon veya kalp hastalığı tanısını almıştır.

Obezitenin tedavisinde etkili çözüm yollarından biri olan bariatrik cerrahide günümüzde sıklıkla tercih edilen SG ve gastrik bypass (GB) ameliyatlarıdır. SG'de mide hacminin azaltılması kısa zamanda tokluk hissi sağlamaktadır. GB'de ise midenin bypass edilmesi ile de oreksijenik hormonların salgılanması önlenmekte ve terminal ileumda sindirilmemiş besin varlığı, inkretin hormonunu tetiklemektedir. Metabolik sendromdaki bu kısa dönemdeki iyileşme, ağırlık kaybından bağımsız olarak açıklanmaktadır (18).

Bu çalışmada da ameliyat öncesinde ağırlık kaybı için bireylerin başvurduğu yöntemler değerlendirildiğinde, kadın hastaların %8,0'i ve erkek hastaların %29,6'sının diyetisyen desteği ile ağırlık kaybetmeye çalıştığı, kadınların %94,7'sinin, erkeklerin ise %85,2'sinin verdiği ağırlıktan daha fazlasını geri kazandığı saptanmıştır. Hastalar, geleneksel yöntemleri defalarca denemiş, başarısız olmuşlar ve obezitenin tedavisinde bariatrik cerrahiyi en son seçenek olarak düşünmüşlerdir. Sjöström ve ark. (19) yaptığı bir çalışmada, bariatrik cerrahi sonrası hastalar 10 yıl süre ile takip edilmiştir. Çalışmanın sonucunda bariatrik cerrahinin obezitenin tedavisinde uygun bir seçenek olabileceği, bu durumun yalnızca ağırlık kaybı ile ilişkili olmadığı, beraberinde hastalarda obeziteye bağlı gelişen kronik hastalıkların seyrinde azalma ve uzun dönemde genel mortalite, miyokard enfarktüsü, felç, kanser gibi hastalıkların görülme olasılığının da azaldığı ve hastaların yaşam süresinin artabileceği vurgulanmıştır.

Bariatrik cerrahinin obezite tedavisi üzerine olumlu etkilerinin bilinmesine rağmen, sınırlı sayıdaki çalışmada sistematik olarak bariatrik cerrahi sonrası hastaların besin tüketimleri değerlendirilmiştir. Bazı çalışmalarda et, sebze, meyve, tatlı gibi besinlerin belirli türlerinin alımları üzerine, bazı araştırmalarda kalsiyum gibi belirli mikro besin ögeleri veya makro besin ögelerine, bazı çalışmalarda ise günlük enerji alımı veya günlük protein miktarı üzerine odaklanılmıştır (20-23).

Obez hastalarda BKİ ile birlikte antropometrik ölçümlerin, metabolik riskin en iyi belirleyicilerinden olduğu bilinmektedir. Bu ölçümler referans değerlerin üzerinde olduğunda metabolik sendrom riski artmaktadır (21). Bu çalışmada hastaların BKİ değerlerinin istatistiksel olarak anlamlı şekilde azaldığı görülmüştür. Muir ve Rice (24) tarafından yapılan çalışmada da SG sonrası ilk 6 ay BKİ ve vücut ağırlığındaki düşüşün en hızlı dönem olduğu vurgulanmış ve istatistiksel olarak anlamlı bulunmuştur. Bu çalışmadaki ağırlık kaybı ve BKİ'deki değişimin de literatür ile benzer olduğu bulunmuştur.

Bettini ve ark. (25) tarafından yapılan çalışmada 154 laparoskopik SG hastası 1 yıl süre ile takip edilmiş, düzenli aralıklarla indirekt kalorimetre ile dinlenme metabolik hızları ölçülmüş ve vücut analizleri yapılmıştır. Yapılan çalışmada dinlenme metabolik hızları, beklentilerin aksine daha az düşüş göstermiştir. Bunun sebebi, SG sonrası hastaların metabolik adaptasyonlarının yüksek olmasına bağlanmıştır. Browning ve ark. (26) tarafından yapılan derleme çalışmasında, çoğu çalışmada gastrik kısıtlamayı takiben hastaların 12 ayda dinlenme metabolik hızları ve yağsız vücut kütlesindeki düşüşün anlamlı bulunduğu ve bazı çalışmalarda da dinlenme metabolik hızının 12 ay boyunca 740 kkal azaldığı belirtilmiştir (27).

Kadınlarda, SG sonrası enerji ve yağ alımlarında post op 1. ay ile post op 3. ay ve post op 1. ay ile post op 6. ay arasında fark bulunmuştur. Erkeklerde ise enerji ve protein alımlarında post op 3. ay ile post op 6. ay arasında fark saptanmıştır.

Bu çalışmada kadın hastalar, alınan enerjinin %21'ini karbonhidratlardan, %27'sini proteinlerden, %43'ünü yağlardan sağlamıştır. Erkek hastalar ise alınan enerjinin %20'sini karbonhidratlardan, %29'unu proteinlerden, %45'ini yağlardan sağlamıştır. Türkiye'ye Özgü Beslenme Rehberine (TÜBER-2015) göre günlük enerji gereksiniminin %45-60'ı karbonhidratlardan, %10-20'si proteinlerden, enerjinin en fazla %35'i yağlardan sağlanmalıdır (28). Hastaların ilk 6 aylık diyetlerindeki karbonhidrat, protein ve yağ yüzdelerinin TÜBER-2015'in sağlıklı yetişkin bireyler için önerdiği oranlardan farklı olduğu görülmektedir. Karbonhidrat düşük, protein ve yağ önerilerin üzerindedir. Bu çalışmada hastalara ameliyat sonrası ASMBS önerileri ve diğer literatür bilgileri göz önünde bulundurularak beslenme eğitimleri verilmiştir. Günlük enerji dağılımının ilk 6 ayda TÜBER önerilerinden farklı olmasının, gastrik hacmin azalmasından ve önerilen beslenme programlarından kaynaklandığı düşünülmektedir. Gastrik hacmin ve besine olan toleransın da arttığı ve obezitenin büyük ölçüde tedavi edildiği post-op 1. yıl ve sonrasında TÜBER önerileri doğrultusunda beslenme eğitimlerinin sürdürülmesi gerekir. Ayrıca, erken dönemde yapılan beslenme eğitimlerinde sağlıklı yiyecek saklama, hazırlama ve pişirme yöntemleri hakkında mutlaka bireylere bilgi verilmelidir.

Hastaların biyokimyasal bulguları değerlendirildiğinde ise önerilenin üzerinde B12 vitaminin alınması ve hekim tarafından önerilen rutin multivitamin desteğine rağmen serum B12 vitamini seviyesi normal sınırlar arasında fakat alt sınıra yakın bulunmuştur. Bu durum SG sonrası değişen gastrik emilim ve intrinksik faktör kaybı ile açıklanabilir. Bu bilgiler ışığında SG ve GB ameliyatları sonrası ilk yıl düzenli vitamin ve mineral desteğinin alınması önerilmektedir (29).

Hızlı ağırlık kaybı, sadece yağ dokusundan değil yağsız vücut dokusundan da kayıplara neden olmaktadır. Bu çalışmada da kadın ve erkek hastaların pre-op ve post-op

1. ay, 3. ay, 6. aydaki ağırlık, BKİ, vücut yağ kütlesi ve yağsız vücut kütlesindeki düşüş istatistiksel olarak anlamlı bulunmuştur. Ameliyat sonrası yağsız vücut kütlesindeki düşüş nedeniyle protein desteğinin bu hastalar üzerinde olumlu etkilerinin olacağı düşünülmektedir (30). Bu çalışmada hastalara günlük protein miktarı 60 gramın altında olmaması için ameliyat sonrası ilk ay whey protein tozu (1 ölçek/gün) desteği önerilmiştir. Hastaların %66,7'sı önerilen protein tozunu kullanmış; %33,3'ü tüm önerilere rağmen protein tozunu kullanmamıştır. Whey protein tozu kullanan ve kullanmayan hastaların ağırlık, vücut yağ kütlesi ve yağsız vücut kütlesi arasında anlamlı fark bulunmamış, fakat protein tozu kullanan grup ile kullanmayan grubun serum total protein seviyesi kıyaslandığında, protein tozu kullanan hastaların post-op 6. ayında total protein seviyesi kullanmayan hastalara göre daha yüksek saptanmış ve bu fark istatistiksel olarak anlamlı bulunmuştur. Aksoy ve ark. (31) tarafından yapılan çalışmada SG sonrası 12 ay boyunca hastalar takip edilmiş ve biyokimyasal parametreler değerlendirilmiştir. Hastaların takip edildiği sürede total protein seviyesinin düştüğü görülmüş, fakat bu düşüş istatistiksel olarak anlamlı bulunmamıştır. Gomes ve ark. (32) bariatrik cerrahi sonrası protein tozu kullanan ve kullanmayan hastaları 2 yıl boyunca takip etmişlerdir. Çalışma sonucunda protein tozu kullanan hastaların uzun dönemde daha fazla ağırlık kaybettiği ve yağ kütlesinin daha fazla azaldığı saptanmıştır.

Ameliyat sonrası oral protein alımı, proteinden zengin besinlerin intoleransı, önerilen protein takviyesinin kullanılmaması, azalan mide HCI ve pepsinojen enzimi hipoalbuminemiye sebep olabilmektedir. Ameliyat sonrası protein alımında belirgin bir düşüş olduğu için günlük en az 60gr/gün protein alımı önerilmektedir (33).

Ito ve ark. (34) yaptığı bir çalışmada RYGB ve SG sonrası hastaların protein alımının 60 gr/gün'ün altında olduğu ve anlamlı ölçüde yağsız kütle kaybı olduğu saptanmıştır. İncelenen pek çok çalışmada günlük protein alımı ile serum protein seviyeleri arasında ilişki bulunamamıştır (35-36). Bu çalışmada da protein tozu desteğinin vücut kompozisyonu üzerine anlamlı bir etki yapmadığı saptanmıştır.

Hady ve ark. (37) SG'nin hastalardaki metabolik etkilerini incelemek amacıyla yaptığı çalışmada post-op 6. ayda HDL-kolesterol değerleri her grupta anlamlı olarak artmıştır. Çalışmada takip süresince HDL-kolesterol anlamlı olarak artmış, ancak post-op 3. aydaki sonuçlar anlamlı bulunmamıştır. Bu çalışmada da post-op 6. ayda HDL-kolesterolün anlamlı olarak arttığı ve ameliyat sonrası 6 aylık süreçteki BKİ değişimi ile HDL-kolesterol seviyesi arasında pozitif yönlü korelasyon saptanmıştır. Carr ve Brunzell (38) tarafından yapılan çalışmada, Tip 2 diyabetli bireylerde BKİ ile HDL-kolesterol arasında negatif bir korelasyon saptanmış ve BKİ'deki her bir birimlik değişiklik HDL-kolesterol seviyesinde kadınlarda 0,69 mg/dl değişime neden olmuştur. Wing ve ark. (39) tarafından yapılan çalışmada, Tip 2 diyabetli bireylerin vücut ağırlıklarındaki %5-10'luk kaybın glisemiyi, kan basıncını, trigliserid düzeyini ve HDL-kolesterol düzeylerini pozitif yönde etkilediği belirtilmiştir.

Schauer ve ark. (40) tarafından yapılan çalışmada ise, GB ve SG sonrası hastalar 1 yıl boyunca takip edilmiş olup, GB'li hastaların pre-op tetkiklerinde HbA1c düzeyi ortalaması %7,5 ve ilaçla tedavi edilirken, 1 yıl kadar sonrasında %6,4'e; SG'li hastaların HbA1c düzeyleri de %6,6'ya gerilemiş ve ilaç tedavisine gerek duyulmamıştır. Aynı hastaların 3 yıl sonraki kan değerleri incelendiğinde glisemik kontrolün GB'li hastalarda daha iyi ve farkın istatistiksel olarak anlamlı olduğu bulunmuştur. Bu çalışmada da hastaların pre-op HbA1c ortalaması %5,8 iken, post-op 6.ayda %5,1'e gerilemiştir. Jiang ve ark. (41) yaptıkları çalışmada Tip 2 diyabetli hastaların ağırlık kaybı ile kan glukoz regülasyonu arasında olumlu yönde ilişkinin olduğunu saptamışlardır. Ağırlık kaybı, insülin sensitivitesinde artışa, insülin seviyesinde düşüşe sebep olmaktadır. Buna bağlı olarak açlık ve tokluk kan glukozu düşmekte, glukotoksik etki önlenmekte, beta hücresi insülin sekresyonunun düzelmesi sağlanmaktadır (42). Bu çalışmadaki HbA1c düzeyindeki düşüşün ağırlık kaybı ile ilişkili olabileceği düşünülmektedir.

Woelnerhanssen ve ark. (43) GB'li ve SG'li hastaların erken dönemdeki adiponektin ve lipid metabolizmasındaki değişikleri saptamak amacıyla bir çalışma yapmışlardır. Her iki grupta da erken dönemde adiponektin seviyeleri ve adiponektin/kg seviyesi anlamlı düzeyde azalmıştır. Azalmış olan adiponektin seviyeleri her iki grup için değerlendirildiğinde GB'li ve SG'li hastalar arasında anlamlı bir fark bulunmamıştır. Hastaların lipid profilindeki değişiklikler de anlamlı bulunmuş, her iki grup arasındaki değişiklik anlamlı bulunmamıştır. Adiponektin, total kolesterol, LDL-kolesterol ve trigliserit seviyeleri her iki grupta da anlamlı olarak azalmış, fakat bu azalmanın erken dönem yerine ameliyat sonrası post-op 3. ayda daha anlamlı olduğu saptanmıştır. Bu çalışmada hastaların pre-op kolesterol ve TG seviyesi post-op 6. aya göre anlamlı olarak azalmış, fakat LDL-kolesterol seviyesi literatürün aksine post-op 6. ayda anlamlı olarak artmıştır. Obezite çeşitli lipid bozukluklarına neden olmaktadır. Trigliserid düzeyindeki yükselme, HDL-kolesterol düzeyinde düşme ve LDL-kolesterol düzeyinde artış tipik belirtilerdir. Bu durum lipid anormallikleriyle birlikte koroner kalp hastalığı gelişme riskini de artırmaktadır (44).

Birçok bilimsel çalışmada, bariatrik cerrahiden sonra kemik yoğunluğunda azalmanın gerçekleştiği bildirilmektedir. Bariatrik cerrahiden sonra hastalarda görülen kemik yoğunluğu değişikliklerinin tek sebebinin ağırlık kaybı olmadığı vurgulanmaktadır. Bu durum, bilimsel çalışmalarda, ameliyat sonrası hastalarda osteoporoz riskinin gelişebileceği konusunun da değerlendirilmesi gerektiğini ortaya koymaktadır. Özellikle kemik mineral oranı düşük olan hastalarda kemik kaybının önlenmesi esastır. Önleme, fiziksel aktiviteyi, kalsiyum ve D vitamini alımını ve güneşe maruziyeti de kapsamaktadır. Son yıllarda vitamin eksikliğinin araştırıldığı çalışmalar, bariatrik cerrahi hastalarında genel popülasyondaki insanlara kıyasla D vitamini eksikliğinin daha sık görüldüğüne işaret etmektedir. Çalışma sonuçları, SG sonrası kemik yoğunluğu kaybının, D vitamini düzeyi veya takviyesi ile ilgili olmayan faktörler tarafından da belirlendiğini düşündürmektedir (31,45-49). Bu çalışmada ameliyat sonrası 6 aylık sürede D vitamini seviyesi anlamlı olarak yükselmiş fakat D vitamini seviyesi ile BKİ arasında bir korelasyon saptanmamıştır. Düşük vitamin D düzeyi obezite ile ilişkilendirilmektedir. Fakat yapılan

çalışmaların çoğu kesitsel çalışmalar olduğu için verilerin standardizasyonu zor ve çelişkilidir (49). Yapılan bazı çalışmalarda D vitamin düzeyi düşük yetişkinlerde obezitenin daha sık görüldüğü gösterilmiştir (50).

Çalışmaya katılan 102 kişiden hiçbirinin ameliyat öncesi düzenli egzersiz yapmadıkları belirlenmiştir. Ameliyat sonrasında ise çalışmaya katılanların %45,1'i düzenli egzersiz yapmaya başlamışlardır. Ameliyat sonrasında düzenli egzersiz yapmaya başlayanların %97,8'i yapmış oldukları egzersizi 6 ay boyunca sürdürmüş, %2,2'si post-op 6. ayda egzersiz yapmayı bırakmış, düzenli egzersiz yapmaya başlayanların %8,7'si yapmış olduğu egzersizin sıklığını azaltmıştır. Obezitenin tedavisinde önerilen fiziksel aktivite programları aerobik-anaerobik egzersizler, dirençli egzersizler, aralık eğitimi ve fleksibilite egzersizlerini içerir. 150-250 dakika/hafta orta yoğunluklu fiziksel aktivite, vücut ağırlığında %3'ün üzerinde ağırlık kaybı sağlayabilir, ancak klinik olarak anlamlı ağırlık kaybı için 225-420 dakika/hafta egzersiz yapılması önerilmektedir. Bariatrik cerrahi sonrasında dirençli egzersizler kardiyorespiratuvar fitnes programlarının ağırlık kaybı ve vücut kompozisyonu değişikliği, kas gücü ve fleksibiliteyi arttırdığı vurgulanmaktadır (51,52). Villa-González ve ark. (53) bariatrik cerrahi sonrası uzun dönemde hastaların geri ağırlık kazanımlarından yola çıkarak, uzun dönemde hastaların takibi ve fiziksel aktivite fonksiyonlarının iyileştirilmesini amaçlayarak egzersiz çalışma protokolü geliştirmiştir. Bu çalışmada hastalar ameliyat sonrası 7-14 gün içinde haftada 3 gün 60 dakika egzersize başlatılmış ve uzman kontrolünde 16 hafta takip edilmiştir. Ouellette ve ark. (54) bariatrik cerrahi sonrası erken ve uzun dönemde hastaların fiziksel aktivitelerini incelemişlerdir. Hastalar ameliyat sonrası fiziksel olarak daha aktif olurken, ameliyat sonrası erken dönemin fiziksel aktivite alışkanlığı kazandırılmasında daha etkili olabileceğini vurgulamışlardır.

Ameliyat sonrası düzenli hasta takibi, beslenme eğitimleri, davranış değişikliği terapileri, fiziksel aktivitenin yaşam tarzı haline getirilebilmesi, yeterli protein ve besin ögesi alımı bu hastaların obezite tedavisi için son derece önemlidir (52).

SONUÇ

SG sonrası yeterli ağırlık kaybı ve obezite ve ilişkili komorbiditelerde iyileşmenin sağlanabilmesi için cerrahi yöntemin yanında multidisipliner ekip çalışmasının olması gerekmektedir. Kaybedilen vücut ağırlığının uzun süre kalıcı olması ve diyet, davranış değişikliklerinin gerçekleşmesi için multidisipliner ekibin içinde mutlaka bu konuda deneyimli olan bir diyetisyene de yer verilmelidir.

Besin ögesi destekleri klinik sonuçlara göre hekim gözetiminde önerilmeli, hastalar diyetisyen tarafından bariatrik cerrahi sonrası aşama diyetlerine göre bireye özgü beslenme programları ile takip edilmelidir. Hastalar fiziksel aktivite için teşvik edilmeli, sağlık profesyonellerine yönlendirilmeli ve fiziksel aktivitenin alışkanlık haline getirilmesi sağlanmalıdır.

TEŞEKKÜR

Çalışmaya katkılarından dolayı Prof. Dr. Halil COŞKUN ve Uzm. Dyt. Nida YILDIZ'a teşekkür ederiz.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.638625

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):233-237

Is the Sleep Perception of Obstructive Sleep Apnea Patients Reliable?

Obstrüktif Uyku Apnesi Hastalarının Uyku Algıları Güvenilir mi?

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ABSTRACT

Aim: The aim of this study, is to evaluate the consistency with the polysomnography (PSG) data of the patients and the data reported by the patients themselves after PSG examination in the morning.
Material and Methods: One hundred and thirty-four consecutive individuals who were admitted to the Chest Disease Polyclinic for Sleep Disorders of Duzce University Medical Faculty were included in the study. PSG and the questions related to sleep perception was applied by the same physician with face to face interview to all participants.
Results: Of the patients included in the study 90 (67.2%) were male and 44 (32.8%) were female, and the mean age was 47.3±12.6 years. While there was a significant correlation (p=0.042, r=0.301) between the sleep time reported by the patients themselves after waking up in the morning and the sleep time measured by the PSG in patients without obstructive sleep apnea (OSA), there was no correlation in OSA (+) patients (p=0.269, r=0.125). Similarly, while there was a significant correlation (p=0.026, r=0.352) between the sleep latency reported by the patients themselves after waking up in the morning and the sleep latency measured by the PSG in OSA (-) patients, there was no correlation in OSA (+) patients (p=0.060, r=0.223).
Conclusion: While evaluating OSA patients and explaining their treatment before and after PSG, it should be kept in mind that they might have impaired perception. Therefore, we thought that we should spend more time to patients, and to make our explanations more clearly and understandably.
Keywords: Perception; sleep apnea.

ÖZ

Amaç: Bu çalışmanın amacı, hastaların polisomnografi (PSG) verileri ile PSG incelemesi sonrası sabah hastaların kendileri tarafından bildirilen verilerin birbiri ile uyumunu değerlendirmektir.
Gereç ve Yöntemler: Çalışmaya Düzce Üniversitesi Tıp Fakültesi Göğüs Hastalıkları Uyku Polikliniği'ne başvurmuş ardışık 134 kişi dahil edildi. PSG ve uyku algısı ile ilgili sorular tüm katılımcılara aynı hekim tarafından yüz yüze görüşme ile uygulandı.
Bulgular: Çalışmaya dahil edilen hastaların 90'ı (%67,2) erkek ve 44'ü (%32,8) kadın olup yaş ortalaması 47,3±12,6 yıl idi. Obstrüktif uyku apnesi (OUA) negatif olan hastalarda, hastaların sabah uyandıktan sonra kendileri tarafından bildirilen uyku süresi ile PSG cihazı ile ölçülen uyku süresi arasında anlamlı bir korelasyon varken (p=0,042; r=0,301), OUA (+) olan hastalarda hastaların sabah uyandıktan sonra kendileri tarafından bildirilen uyku süresi ile PSG cihazı ile ölçülen uyku süresi arasında korelasyon yoktu (p=0.269, r=0.125). Benzer şekilde, OUA (-) olan hastalarda hastaların sabah uyandıktan sonra kendileri tarafından bildirilen uyku latansı ile PSG cihazı ile ölçülen uyku latansı arasında anlamlı bir korelasyon varken (p=0.026, r=0.352), OUA (+) olan hastalarda hastaların sabah uyandıktan sonra kendileri tarafından bildirilen uyku latansı ile PSG cihazı ile ölçülen uyku latansı arasında korelasyon yoktu (p=0.060, r=0.223).
Sonuç: OUA hastalarını değerlendirirken ve hastaların PSG sonrası ve öncesi tedavilerini açıklarken, hastaların algılarının bozulmuş olabileceği akılda tutulmalıdır. Bu nedenle, hasta ile görüşmelerde daha çok zaman ayırmak ve açıklamalarımızı daha açık ve anlaşılır bir şekilde yapmak gerektiğini düşünmekteyiz.
Anahtar kelimeler: Algı; uyku apnesi.

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Geliş Tarihi / Received : 26.10.2019
Kabul Tarihi / Accepted : 16.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 22.12.2019

INTRODUCTION

The most common type of sleep disordered breathing (SDB) is obstructive sleep apnea (OSA) (1). OSA characterized by repetitive collapse of the upper airway during sleep and this condition leading to oxygen desaturation, sympathetic activation, and recurrent arousals. Previous studies point out that OSA is associated with high morbidity and mortality and indicate a causal relationship between OSA and many diseases including cardiovascular disease, diabetes mellitus, and neurocognitive dysfunction (2,3).

Cognitive processing, sustained attention, executive functioning, and memory have all been reported to be impaired in OSA. However, the causal mechanisms of these deficits have not been entirely clarified, and the relative contribution of intermittent hypoxia and sleep disruption in OSA is particularly controversial (4).

In this study, it is aimed to evaluate the consistency with the polysomnography (PSG) data of the patients and the data reported by the patients themselves after PSG examination in the morning. In this way, we planned to compare the sleep perceptions of OSA patients with objective measurements.

MATERIAL AND METHODS

Study Group

One hundred and thirty-four consecutive individuals who were admitted to the Chest Disease Polyclinic for Sleep Disorders of Duzce University Medical Faculty were included in the study. Ethics committee approval was received for this study from the ethics committee of Duzce University Medical Faculty (dated 21.10.2019 and numbered 227). PSG and the questions related to sleep perception was applied by the same physician with face to face interview to all participants. Informed consent was obtained from all study participants. Individuals under 18 years of age, and pregnant women were excluded.

Polysomnography (PSG)

PSG was performed on all patients for a minimum of 6 hours. A PSG digital system was used (Alice 5 Sleep System, Philips, Respironics, Pennsylvania, United States). At the same time electroencephalography, electrooculography, chin electromyography, oral and nasal airflow (nasal-oral 'thermistor' and nasal cannula), thorax movements, abdominal movements, arterial oxygen saturation (pulse oximetry instrument), electrocardiography and snoring recordings (>6 hours) were obtained from all patients. The same device was used for all of these parameters. All records were scored manually in computer environment. Apnea Hypopnea Index (AHI) is represented by the number of apnea and hypopnea events per hour of sleep. Patients with AHI ≥5 were diagnosed with OSA. The severity of OSA was considered as follows (5): normal (AHI <5); mild sleep apnea (AHI 5-15); moderate sleep apnea (AHI 16-30); and severe sleep apnea (AHI >30).

Questions

The questions asked to patients about the duration of night sleep are as follows:

1. How long does it take you to fall asleep? (Answer as minutes)
2. How many hours did you sleep during the night?
3. Do you remember how long you were awake during the night?
4. How long did you stay awake during the night?

Statistical Analysis

Data were analyzed using the SPSS v.20 statistical package. Descriptive statistics (mean±standard deviation, median, minimum, maximum) of all variables were calculated. Firstly, whether the normality of distribution of variables was examined by Kolmogorov-Smirnov test. Nonparametric tests were used because the data was not appropriate normal distribution. According to the severity of OSA, Kruskal-Wallis Test was used in the comparison of groups in terms of numerical data. Mann-Whitney U test was used in binary subgroup comparisons and Bonferroni correction was performed. Chi-Square test was used to examine the relationships between categorical variables and Spearman's non-parametric correlation test was used in all correlation analyzes. A p value <0.05 was considered statistically significant.

RESULTS

Ninety (67.2%) male and 44(32.8%) female patients were included in the study. The mean age of the patients included in the study was 47.3±12.6 years. OSA was negative in 48 (35.8%) cases while 86 (64.2%) were positive. Based on AHI values, OSA severity was reported as mild among 34 (25.4%), moderate among 22 (16.4%), and severe among 30 (22.4%) patients. General characteristics of the patients are given in Table 1.

Sleep efficacy was statistically increased with increasing severity of OSA (p=0.001), and this increase was significant for all subgroups of OSA patients (p<0.0083, according to Bonferroni correction). In the subgroup analysis, only in severe OSA patients, arousal index and body mass index (BMI) were significantly higher than OSA (-) patients (p=0.006, p<0.0083, according to Bonferroni correction). The general characteristics of patients according to the severity of OSA and their PSG findings are shown in Table 2.

When the patients were evaluated according to whether they remember the awake time during the night or not, 23.1% (n=31) patients did not remember the awake time during the night, in total. Of these 31 patients, 8.3% (n=4) of OSA (-) patients and 31.4% (n=27) of OSA (+) patients reported that they did not remember the awake time during the night (p=0.002, Table 3).

Table 1. General characteristics of patients

Characteristics	n (%) or mean±SD (min-max)
Gender	
Male	90 (67.2)
Female	44 (32.8)
Age (years)	47.3±12.6 (18-85)
BMI (kg/m^2)	33.4±7.8 (18-73)
OSA (+)	86 (64.2)
Mild OSA	34 (25.4)
Moderate OSA	22 (16.4)
Severe OSA	30 (22.4)
Comorbidities	
None	102 (76.1)
Lung diseases	19 (14.2)
Heart diseases	16 (14.2)
Thyroid diseases	3 (2.2)

SD: Standard Deviation, Min: Minimum, Max: Maximum, BMI: Body Mass Index; OSA: Obstructive Sleep Apnea

Table 2. The comparison of clinical and polysomnographic features of patients with and without obstructive sleep apnea

Clinical and polysomnographic features	OSA (-) (n=48)	Mild OSA (n=34)	Moderate OSA (n=22)	Severe OSA (n=30)	p
Age (years)	40.0 (22-70)	47.5 (23-69)	47.5 (28-73)	44.0 (27-74)	0.288
BMI (kg/m2)	28.9 (23.3-49.1)	31.5 (22.5-73.5)	33.3 (24.7-62.8)	35.9 (22.3-62.4)	**0.001**
AHI (event/h of sleep)	1.75 (0.0-4.5)	8.25 (5.1-13.4)	21.5 (14.1-29.0)	54.25 (30.5-99.3)	**<0.001**
TST (min)	337.0 (168.0-473.8)	339.7 (144.1-451.0)	361.0 (204.0-458.0)	340.25 (98.5-470.0)	0.298
Sleep efficacy (%)	77.6 (41.3-94.2)	75.3 (8.0-96.4)	85.7 (45.6-98.1)	83.9 (68.4-99.0)	**0.001**
Arousal index (event/h of sleep)	7.65 (1.4-53.5)	11.45 (0.9-71.0)	21.7 (0.7-47.6)	27.45 (2.1-70.7)	**0.001**

OSA: Obstructive Sleep Apnea, AHI: Apnea Hipopnea Index, TST: Total Sleep Time, BMI: Body Mass Index, Descriptive statistics given as median (minimum-maksimum)

Table 3. Comparison of patients remembering or not how long they remain awake at night in terms of obstructive sleep apnea severity and gender

	Remember (n=103)	Not Remember (n=31)	p
Gender			
Male	69 (76.7)	21 (23.3)	0.938
Female	34 (77.3)	10 (22.7)	
OSA			
OSA (+)	59 (68.6)	27 (31.4)	**0.002**
OSA (-)	44 (91.7)	4 (8.3)	
OSA			
None	44 (91.7)	4 (8.3)	**0.005**
Mild	27 (79.4)	7 (20.6)	
Moderate	14 (63.6)	8 (36.4)	
Severe	18 (60.0)	12 (40.0)	

OSA: Obstructive Sleep Apnea, Remember: Patients remember the awake time they remain during the night, Not Remember: Patients not remember the awake time they remain during the night

While there was a significant correlation between the sleep time reported by the patients themselves after waking up in the morning and the sleep time measured by the PSG (p=0.042, r=0.301) in OSA (-) patients, there was no correlation between the sleep time reported by the patients themselves after waking up in the morning and the sleep time measured by the PSG (p=0.269, r=0.125) in OSA (+) patients (Figure 1).

While there was a significant correlation between the sleep latency reported by the patients themselves after waking up in the morning and the sleep latency measured by the PSG (p=0.026, r=0.352) in OSA (-) patients, there was no correlation between the sleep latency reported by the patients themselves after waking up in the morning and the sleep latency measured by the PSG (p=0.060, r=0.223) in OSA (+) patients (Figure 2).

DISCUSSION

In this study, while there was no significant correlation between PSG measurements and patient's reports regarding to sleep time and latency in patients with OSA, there was a significant correlation in those of patients without OSA. When the rate of remembering the time to stay awake at night was evaluated, we found that the rate of not remembering the awake time was significantly higher in patients with OSA. We found that OSA patients did not correctly perceive the duration of sleep, sleep latency and also did not remember how long they were awake during the night.

Previous studies investigating the effects of OSA on alertness and cognitive functions have demonstrated that apnea recurrence, sleep fragmentation, and nocturnal hypoxemia may affect diurnal behavior, cognitive function, and well-being in these patients. A wide range of cognitive impairment has been identified in OSA patients, from attention and vigilance to memory and executive functions (6).

Castronovo et al. (7) compared 17 OSA patients and 15 healthy controls in terms of functional magnetic resonance imaging (fMRI) scanning and neurocognitive tests in their study. Patients who diagnosed OSA and had no positive airway pressure (PAP) treatment before, treated 3 months with PAP, then compared with the control group. They found that effective PAP treatment is associated with a reduction of activation in prefrontal and hippocampal areas, which parallels an improvement of neuropsychological test performance.

The hippocampus and frontal cortex are closely associated with memory processes and executive functions (8). The intermittent upper airway obstruction during sleep leads to episodic hypoxia, which may be severe with hemoglobin oxygen saturations frequently reaching 50-60%. In addition, periodic alveolar hypoventilation and repeated arousal either behavioral or electroencephalographic occur leading to sleep fragmentation and deprivation (9,10). Using an experimental model of OSA in rats exposed for 2 weeks to intermittent hypoxia, the authors found a neuronal loss or apoptosis indicating a greater vulnerability of the frontal lobe to hypoxemia (9).

As a result of sleep fragmentation due to respiratory events and respiratory effort, OSA patients are unable to sleep deeply and effectively and their perception of sleep is impaired (11).

A study by Ulukavak Çiftçi et al. (12) evaluated 73 patients divided into two groups according to AHI <5 and AHI ≥5. In the group with AHI <5, sleep history and PSG data were correlated, whereas in the group with AHI ≥5, no correlation was found. As a result of the study, it was found that OSA patients mistakenly perceive their sleep periods. Again, when compared to whether they sleep adequately or not; the group consisting of healthy individuals perceived 2.09 times more accurately.

In our study, patients were similarly divided into two groups as AHI <5 and AHI ≥5, and when compared in terms of sleep latency and night sleep duration, patient's reports and PSG values were not correlated in the AHI ≥5 group and contrarily, those were correlated in AHI <5 group.

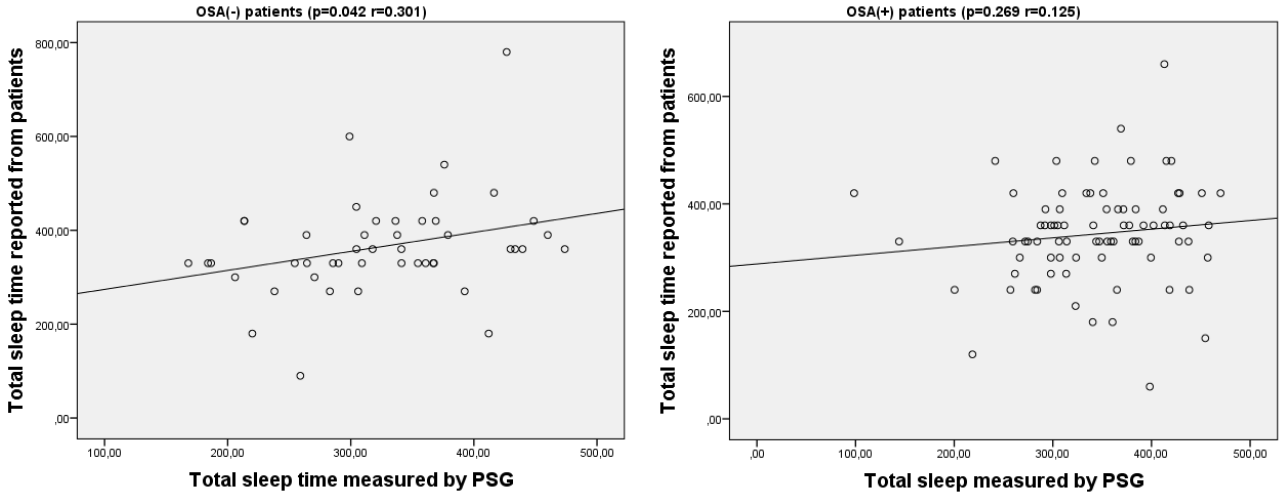

Figure 1. Correlation between sleep duration reported by patients and sleep duration measured by polysomnography

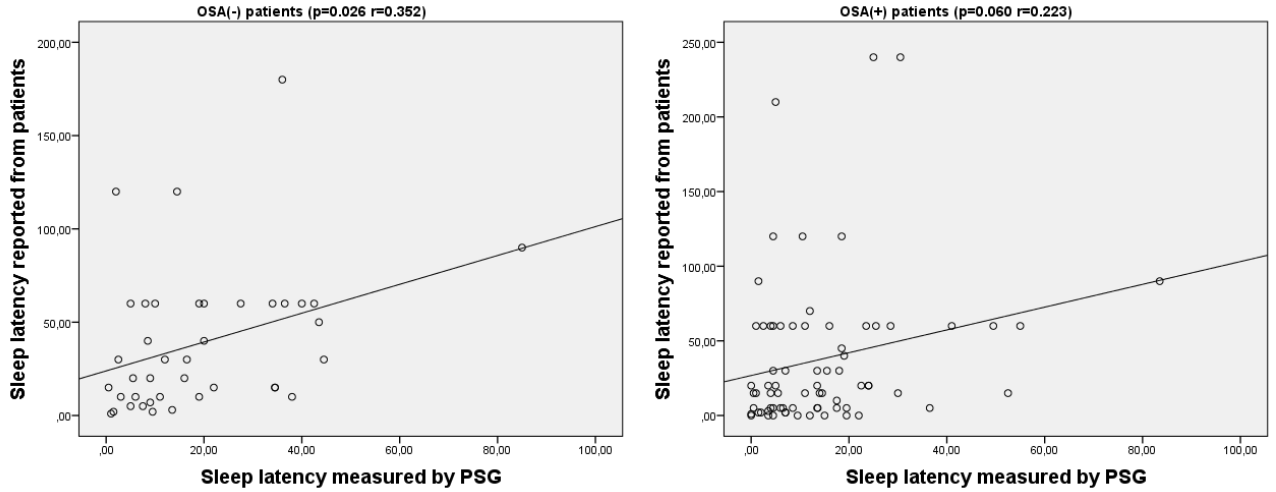

Figure 2. Correlation between sleep latency reported by patients and sleep latency measured by polysomnography

In the study by Savaş Bozbaş et al. (11), although patients stated that they fell asleep after a long time and had difficulty in falling asleep, they found that, the sleep latency evaluated by PSG was shorter than the time declared by the patient. They found that the sleep latency declared by patients and determined by PSG was correlated in the non-OSA group, similar to our study. In our study, we also found that OSA patients did not remember the time to stay awake compared to patients without OSA.

In conclusion, we found that sleep perception of OSA patients was impaired. While evaluating OSA patients and explaining their treatment, it should be kept in mind that they might have impaired perception. We thought that we should spend more time to patients and make our explanations more clearly.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.641962

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):238-242

The Relationship between Pain Beliefs and Psychiatric Symptoms of Patients with Fibromyalgia Syndrome

Fibromyalji Sendromu Hastalarının Ağrı İnançları ile Psikiyatrik Belirtileri Arasındaki İlişki

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Geliş Tarihi / Received : 03.11.2019
Kabul Tarihi / Accepted : 21.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 26.12.2019

ABSTRACT

Aim: This study was conducted to examine the relationship between the pain beliefs and psychiatric symptoms of the patients with fibromyalgia syndrome (FMS).
Material and Methods: This cross-sectional study was conducted with 145 patients diagnosed with FMS between August 2018 and January 2019 in the Physical Therapy and Rehabilitation polyclinic of Aksaray University Training and Research Hospital. The sociodemographic data form prepared by authors, Pain Beliefs Scale (PBS), Depression Anxiety Stress Scale (DASS) and Visual Analogue Scale (VAS) were applied to the patients.
Results: Mean age of FMS patients is 35.42±9.10 years, 57.9% (n=84) are female, 70.3% (n=102) are married and 95.9% (n=139) live in nuclear families. Of the patients, 46.9% (n=68) were reported that they perceived the pain at the severity of 9-10 (mean: 8.12±1.29) according to VAS. Mean score of organic beliefs was 4.87±0.77, and mean score of psychological beliefs was 5.17±0.52. It was found that depression (62.8%) and anxiety (33.1%) levels were very advanced, and stress (45.5%) levels were advanced. A statistically significant positive correlation was detected between the DASS total and the subscales of depression, anxiety and stress and both organic beliefs and psychological beliefs (all p values <0.001).
Conclusion: The patients' pain beliefs and pain perception levels were found high and the rate of accompanying psychiatric symptoms was also high. While the patients' pain beliefs increase, their depression, anxiety and stress levels also increase. It is important to use holistic approaches to strengthen the response given to treatment in patients with FMS.
Keywords: Fibromyalgia syndrome; pain beliefs; psychiatric symptoms.

ÖZ

Amaç: Bu çalışma fibromiyalji sendromlu (FMS) hastaların ağrı inançları ile psikiyatrik belirtileri arasındaki ilişkiyi incelemek amacıyla yapılmıştır.
Gereç ve Yöntemler: Kesitsel türdeki bu çalışma, Aksaray Üniversitesi Eğitim ve Araştırma Hastanesinin Fizik Tedavi ve Rehabilitasyon polikliniğinde Ağustos 2018 ve Ocak 2019 tarihleri arasında FMS tanısı almış olan 145 hasta ile yapılmıştır. Hastalara yazarlar tarafından hazırlanmış olan sosyodemografik veri formu, Ağrı İnançları Ölçeği (AİÖ), Depresyon Anksiyete Stres Ölçeği (DASÖ) ve Vizüel Analog Skala (VAS) uygulanmıştır.
Bulgular: FMS hastalarının yaş ortalamaları 35,42±9,10 yıl olup %57,9'u (n=84) kadın, %70,3'ü (n=102) evli ve %95,9'u (n=139) çekirdek ailede yaşamaktadır. Hastaların %46,9'u (n=68) VAS'a göre ağrıyı 9-10 (ortalama: 8,12±1,29) şiddetinde algıladığını bildirmiştir. Organik inançlar puan ortalaması 4,87±0,77 ve psikolojik inançlar puan ortalaması ise 5,17±0,52'dir. Depresyon (%62,8) ve anksiyete (%33,1) düzeylerinin çok ileri düzeyde olduğu, stres (%45,5) düzeylerinin ise ileri düzeyde olduğu bulunmuştur. DASÖ toplam ve alt ölçeklerden, depresyon, anksiyete ve stres ile hem organik inançlar hem de psikolojik inançlar arasında istatistiksel olarak anlamlı pozitif korelasyon saptanmıştır (tüm p değerleri <0,001).
Sonuç: Hastalarının ağrı inançları ve ağrı algılama düzeylerinin yüksek olduğu, aynı zamanda eşlik eden psikiyatrik belirti oranının da yüksek olduğu tespit edilmiştir. Hastaların ağrı inançları artarken depresyon, anksiyete ve stres düzeyleri de artmaktadır. FMS hastalarında tedaviye verilen yanıtı güçlendirebilmek için bütüncül yaklaşımların kullanılması önemlidir.
Anahtar kelimeler: Fibromiyalji sendromu; ağrı inançları; psikiyatrik belirtiler.

INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic and complexed syndrome with non-musculoskeletal clinical symptoms such as sleep disorder, tiredness, weakness, headache and depression together with prevalent musculoskeletal pains in the body, its etiology is still not known exactly (1,2). While FMS can be observed in all the ethnic groups, in every age and gender, it is seen more frequently between the ages of 40 and 60 and in female patients (3). Its prevalence is between 2-8%. In a research conducted in Turkey, the FMS prevalence was found 3-6% (4). It is reported that FMS decreases the functionality of the individuals in the physical, psychological and social terms, and it has a negative effect on cognitive performance, personal relations (including sexuality and parenting), activities of work and daily living (5). In patients with FMS, pain is one of the most important symptoms influencing the quality of life in a negative way (6).

Pain experience and severity is a phenomenon which shows individual differences and is difficult to diagnose (7,8). Pain perception is influenced by many emotional, behavioral and cognitive factors such as gender, education and culture. Moreover, the severity and frequency of the pain and coping ability are affected by personal traits and beliefs of the individual (9,10). According to the cognitive view, pain beliefs are considered as the keystone of the individual's thought system.

Pain beliefs also affect the severity of the pain perception and coping abilities (11,12). Pain has organic and psychological dimensions. Organic pain belief means to believe in having physical injuries or threatened well-being, that is, pain will be as high as the severity of the damage and injury. In the psychological pain belief, psychological factors such as depression and anxiety are believed to be the cause of pain (13,14).

Even though pain is the major symptom of FMS, conditions like depression, anxiety, stress and sleep disorders affect the quality of life in patients. Depressive disorders are the most frequently observed psychiatric comorbidity in FMS, and its prevalence varies between 20-80% (15). Besides, it is also stated that the chronic pain observed in FMS may lead to depression or anxiety by affecting especially the social life in a negative way (6).

In a study conducted abroad, lifelong affective disorder rate of FMS patients was discovered as 71% (16). In a study conducted with FMS patients in Turkey, depression symptoms were found by 54.8%, and in another study in Turkey, 37.3% of the patients were diagnosed with major depression. In the study, depression in FMS was demonstrated to be linked with pain and disease severity (17). However, no relationship was detected between pain severity and depression, and between depression severity and FMS severity in FMS patients, but there are studies indicating a relationship with anxiety (18). In this study, it was aimed to contribute to the etiology of the disease by investigating the relationship between pain beliefs and psychiatric symptoms of FMS patients.

MATERIALS AND METHODS

This cross-sectional study was conducted with 145 patients diagnosed with FMS between August 2018 and January 2019 in the Physical Therapy and Rehabilitation polyclinic of Aksaray University Training and Research Hospital. Patients who were under 18 years of age, had mental problems or communication difficulties, and disagreed to participate in the study, were excluded.

Before the study, written permission was obtained from the Head Physician of Aksaray University Training and Research Hospital and Aksaray Provincial Directorate of Health. Ethics committee approval of the study was received from Aksaray University Human Researches Ethics Committee (dated 29.06.2018 and numbered 144). The patients who participated were informed about the study, and the data were collected after explaining that personal information would remain confidential.

Data Collection Tools

For the collection of the data, the Sociodemographic Data Form prepared by authors, Visual Analogue Scale (VAS), Pain Beliefs Scale (PBS) and Depression Anxiety Stress Scale (DASS) were used.

Sociodemographic Data Form: It consists of questions prepared by researchers in line with the literature (1,3,6,10,14-18), and the questions include the ages, educational statuses, professions, economic conditions, family structures and pain perceptions of the patients.

Pain Beliefs Scale (PBS): It was developed by Edwards et al. (19) in 1992 in order to evaluate the beliefs related to the cause and treatment of pain. It was adapted to Turkish following the validity and reliability study conducted by Berk HÖS (20) in 2006. Consisting of 12 items in total, the scale has two test areas as organic beliefs (8 items) and psychological beliefs (4 items). The organic belief test shows that pain is mostly of organic origin and the psychological belief test shows that pain experience is under the influence of psychological factors (21). Scores are in the 6-point Likert type varying between 1 (never) and 6 (always) for each item. For each subtest, the total score is calculated by summing the scores obtained from the items in that subtest and dividing it into the number of the items of that subtest. There is no cut point for the scale scores, the increase in the score obtained from the subscore of the scale points out that the pain beliefs of that test are high, and the decrease in the score indicates that the pain beliefs of that test are low. The highest score that can be obtained from the subdimensions of organic and psychological beliefs is 6, and the lowest score is 1 (19,21). In the reliability study of the scale, the Cronbach alpha coefficient for internal consistency scores were found as 0.71 for the organic beliefs subtest and 0.73 for the psychological beliefs subtest (20). In this study, it was obtained as 0.85 for the organic beliefs subtest and 0.35 for the psychological beliefs subtest.

Depression Anxiety Stress Scale (DASS): The scale developed by Lovibond and Lovibond (22) in 1995 consists of 42 items in total as depression (14 items), anxiety (14 items) and stress (14 items). The depression items measure the individuals' discontentment, desperation, insignificance, loss of interest and low energy levels. The anxiety items assess the individual's autonomic arousal, situational anxiety, subjective anxiety, and muscle response levels. The stress items measure the levels of the symptoms of relaxation difficulty, nerve stimulation, easy distress and boredom, discomfort, overreaction and intolerance. High scores obtained from each of the depression, anxiety and stress dimensions show that the individual has that problem. The total scores of the scale

vary between 0 and 42 for each subdimension. The DASS is a 4-point Likert type scale, and the items are scored between 0 and 3 (22). The DASS was adapted to Turkish by Akın and Çetin (23) in 2007. The internal consistency coefficients Cronbach alpha were found as follows 0.89 for the whole scale, 0.90 for depression, 0.92 for anxiety and 0.92 for stress. In this study, they were found as follows, 0.98 for the whole scale, 0.97 for depression, 0.92 for anxiety and 0.95 for stress.

Statistical Analysis

SPSS v.24 package program was used for evaluation of the data. Descriptive statistics such as frequency, percentage, mean±standard deviation, median and minimum-maximum were used. Whether the data had a normal distribution was assessed with Kolmogorov-Smirnov test. Because the data did not have a normal distribution, Spearman correlation analysis was used for determination of the relationship between the variables. The level of $p<0.05$ was considered statistically significant.

RESULTS

Of the 145 FMS patients included in the study 57.9% (n=84) were female, 37.9% (n=55) were aged between 31 and 40 (mean age 35.42±9.10 years), 70.3% (n=102) were married and 95.9% (n=139) were living in nuclear families. Of the patients 37.9% (n=55) were high school graduates, 53.8% (n=78) did not work, 89.7% (n=130) had a moderate economic status and 62.8% (n=91) were retired (Table 1).

Table 1. Sociodemographic characteristics of patients

Characteristics	n (%)
Age, mean±SD	35.42±9.10
Age	
19-30 years	52 (35.9)
31-40 years	55 (37.9)
41-68 years	38 (26.2)
Gender	
Female	84 (57.9)
Male	61 (42.1)
Marital Status	
Married	102 (70.3)
Single	43 (29.7)
Education	
Primary school	48 (33.1)
Secondary school	14 (9.7)
High school	55 (37.9)
University and above	28 (19.3)
Employment	
Working	67 (46.2)
Not working	78 (53.8)
Economic Status	
Good	10 (6.9)
Moderate	130 (89.7)
Bad	5 (3.4)
Family Structure	
Nuclear	139 (95.9)
Large	6 (4.1)
Social Security	
Retirement fund	31 (21.4)
Artisans and self-employed	17 (11.7)
Retired	91 (62.8)
Green Card	6 (4.1)

SD: Standard Deviation

When pain characteristics are reviewed, most of the FMS patients (56.6%, n=82) reported that they had pain for a while between 1 and 6 months, 31.0% (n=141) stated that their pain was in their back-waist area, and 46.9% (n=68) perceived pain at the severity of 9-10 according to the VAS. Plus, 87.6% (n=127) do not use any psychiatric drugs (Table 2).

The patients' PBS mean score of organic beliefs subdimension is 4.87±0.77, and their mean score of psychological beliefs subdimension is 5.17±0.52. The mean DASS total score was 66.24±29.04, and in the sub-dimensions, the mean score of depression was found as 28.51±12.40, anxiety as 14.01±8.14 and stress as 23.72±9.53 (Table 3).

When the anxiety and stress levels of the patients were reviewed, it was discovered that depression (62.8%) and anxiety (33.1%) levels were very advanced and stress (45.5%) levels were advanced (Table 4).

A positively strong correlation was detected between the DASS total score (r=0.800) and the subdimensions of depression (r=0.821), anxiety (r =0.752), stress (r=0.773) and organic beliefs, and a positively moderate and significant relationship was found between the DASS total score (r=0.496) and the subdimensions of depression (r=0.518), anxiety (r=0.498), stress (r=0.473) and psychological beliefs (All p values <0.001, Table 5).

Table 2. Characteristics related to patients' pain

Characteristics	n (%)
VAS, mean±SD	8.12±1.29
VAS	
Perception at the severity of 5-6	20 (13.8)
Perception at the severity of 7-8	57 (39.3)
Perception at the severity of 9-10	68 (46.9)
Pain Duration	
1-6 months	82 (56.6)
7-12 months	32 (22.0)
≥13 months	31 (21.4)
Psychiatric Medicine	
Using	18 (12.4)
Not using	127 (87.6)
Pain Location, (n=455)*	
Head-neck	135 (29.7)
Back-waist	141 (31.0)
Arm-shoulder	88 (19.3)
Leg-knee	78 (17.1)
Other	13 (2.9)

SD: Standard Deviation, VAS: Visual Analogue Scale, *: More than one option were allowed and percentages were calculated over 455 response.

Table 3. PBS and DASS scores

Scale	Mean±SD	Median (Min-Max)
PBS		
Organic Beliefs	4.87±0.77	5.00 (3-6)
Psychological Beliefs	5.17±0.52	5.25 (3-6)
DASS		
Depression	28.51±12.40	34.00 (1-42)
Anxiety	14.01±8.14	15.00 (0-31)
Stress	23.72±9.53	27.00 (4-36)
Total DASS	66.24±29.04	76.00 (6-103)

SD: Standard Deviation, Min: Minimum, Max: Maximum, PBS: Pain Beliefs Scale, DASS: Depression Anxiety Stress Scale

Table 4. Depression, anxiety and stress levels of patients

	Depression	Anxiety	Stress
Normal	14 (9.7)	36 (24.9)	32 (22.1)
Slight	11 (7.5)	7 (4.7)	11 (7.6)
Moderate	16 (11.0)	25 (17.2)	21 (14.5)
Advanced	13 (9.0)	29 (20.1)	66 (45.5)
Very advanced	91 (62.8)	48 (33.1)	15 (10.3)

Table 5. Correlation between patients' pain beliefs and depression anxiety stress scale scores

	Organic Beliefs		Psychological Beliefs	
	r	p	r	p
Depression	0.821	<0.001	0.518	<0.001
Anxiety	0.752	<0.001	0.498	<0.001
Stress	0.773	<0.001	0.473	<0.001
Total DASS	0.800	<0.001	0.496	<0.001

DASS: Depression Anxiety Stress Scale

DISCUSSION

Pain severity of the patients who participated in the study was evaluated by VAS and the mean value was obtained as 8.12. In a study conducted by Türkyılmaz et al. (24) in 2011, the VAS mean value in fibromyalgia patients was reported as 7.9. In various studies, VAS values were detected similarly (25-27). It is seen that this value in our study complies with the results of other studies.

When the pain beliefs of the patients in our study were assessed, the mean score of the organic beliefs subdimension was found as 4.87±0.77, and the mean score of the psychological beliefs subdimension was obtained as 5.17±0.52. Considering that the score to be received from the scale is at least one and maximum six, both organic and psychological pain beliefs of the patients are high. In a study conducted with patients with chronic pain, the mean score of organic beliefs of 86 patients was discovered as 2.83±0.99 and the mean score of psychological beliefs was found as 2.39±1.47 (28). In a study conducted with the elderly people living in a nursing home, the quality of life, pain levels and pain beliefs of the elderly people were examined, and the mean score of organic beliefs was detected as 3.02±0.74, the mean score of psychological beliefs was discovered as 1.80±0.73 (29). In our study, we can say that both organic and psychological belief levels of the patients with FMS are quite high.

In our study, the depression, anxiety and stress levels of the patients were found at an advanced level. It is known that a significant part of the FMS patients has depression, and in some studies, it has been reported that there is a relationship between depressive symptoms and pain severity (30,31). As a result of the study conducted by Vespa et al. (32) in 2015, through the comparison of 57 FMS patients and 203 healthy individuals, the depression levels of the healthy individuals were found to be low and moderate, however, the depression levels of FMS patients were at a high level. In various studies, FMS patients were reported to have depressive symptoms (6,15). In a study examining the quality of life and psychiatric symptoms of fibromyalgia patients, anxiety was observed in 67.4% of the patients and depressive symptoms in 87.2% (33). In a study researching psychiatric symptoms, 50% of 191 FMS patients reported high anxiety and depression. Tiredness and sleep disorder were found to be correlated with high depression (34). We can say that psychiatric symptoms such as depression and anxiety are more common in FMS patients than healthy individuals, and the presence of depression and anxiety increases pain severity, affecting the quality of life in a negative way.

In our study, a relationship was detected between the DASS total score and the subdimensions of depression, anxiety, stress and organic (positively strong) and psychological (positively moderate) beliefs. While the pain beliefs of the patients increase, their depression, anxiety and stress levels also increase. When the results of the studies on different populations were reviewed in the literature, it was reported in a study that the risk of FMS patients increased in terms of depressive symptoms, and they tended to be more unhappy and feel discontent (34). In another study, a statistically significant relationship was discovered between pain and psychological well-being and organic pain belief and psychological well-being (28). We can say that this finding in our study is parallel with the results of the studies in the literature.

CONCLUSION

In our study, the FMS patients' pain beliefs and pain perception levels were found high, and the rate of accompanying psychiatric symptoms was also high. While the pain beliefs of the patients increase, their depression, anxiety and stress levels also increase. Considering that FMS is not a physiological disease or mental disorder alone and it is a cluster of symptoms consisting of the combination of the symptoms in this area, it is believed that treatment interventions with a holistic approach is important before the disease becomes chronic.

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Araştırma Makalesi / Research Article
doi: 10.18678/dtfd.638343

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):243-247

The Evaluation of SCUBE-1 and sCD40L Levels in Diabetic Nephropathy

Diyabetik Nefropatide SCUBE-1 ve sCD40L Seviyelerinin İncelenmesi

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Geliş Tarihi / Received : 25.10.2019
Kabul Tarihi / Accepted : 21.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 26.12.2019

ABSTRACT

Aim: There is a close link between diabetic nephropathy and atherosclerotic heart disease. We aimed to evaluate the changes of SCUBE-1 and sCD40L, which play role in the course of atherosclerosis, with the progression of nephropathy in patients with type 2 diabetes.
Material and Methods: Thirty healthy subjects (group 1) and 74 patients with type 2 diabetes (divided into 3 groups as normal albuminuria group (group 2, n=33), moderately increased albuminuria group (group 3, n=22) and severely increased albuminuria group (group 4, n=19)) were enrolled in the study. Plasma SCUBE-1 and sCD40L levels were measured using the enzyme-linked immunosorbent assay technique.
Results: Mean SCUBE-1 levels were significantly higher in group 4 compared to group 1 and group 2 (p=0.005 and p=0.014, respectively) and in group 3 compared to group 1 and group 2 (p=0.011 and p=0.028, respectively). Mean sCD40L levels were significantly higher in group 4 than in other three groups (all p<0.001), and in group 3 than in group 1 and group 2 (p=0.001 and p=0.016, respectively). Furthermore, SCUBE-1 level was positively correlated with total cholesterol level (r=0.212, p=0.031) and triglyceride (r=0.194, p=0.049). Likewise, sCD40L level was positively correlated with only creatinine level (r=0.297, p=0.002).
Conclusion: SCUBE-1 and sCD40L levels increased with the progression of nephropathy in type 2 diabetes. This increment suggested that SCUBE-1 and sCD40L may play key role in the course of atherosclerosis due to diabetic nephropathy and, diabetic nephropathy may affect the levels of these parameters.
Keywords: SCUBE-1; sCD40L; atherosclerosis; diabetic nephropathy.

ÖZ

Amaç: Diyabetik nefropati ve aterosklerorik kalp hastalıkları arasında yakın bir ilişki mevcuttur. Biz de, ateroskleroz sürecinde rol oynadığı bilinen SCUBE-1 ve sCD40L'ın tip 2 diyabeti olan hastalarda, nefropatinin ilerlemesi ile birlikte nasıl değiştiğini araştırmayı amaçladık.
Gereç ve Yöntemler: Otuz sağlıklı kişi (grup 1) ve 74 tip 2 diyabeti olan hasta (normal albuminüri grubu (grup 2, n=33), orta derece artmış albuminüri grubu (grup 3, n=22) ve şiddetli derecede artmış albuminüri grubu (grup 4, n=19) olarak üç gruba ayrıldı) çalışmaya dahil edildi. Plazma SCUBE-1 ve sCD40L seviyeleri, enzim-bağlı immunosorbent analiz tekniği kullanılarak ölçüldü.
Bulgular: Ortalama SCUBE-1 seviyeleri grup 1 ve grup 2 ile karşılaştırıldığında, grup 4'te (sırasıyla p=0,005 ve p=0,014) ve grup 1 ve grup 2 ile karşılaştırıldığında grup 3'te (sırasıyla p=0,011 ve p=0,028) anlamlı olarak yüksekti. Ortalama sCD40L seviyeleri grup 4'te diğer üç gruptan (tüm p<0,001) ve grup 3'te ise grup 1 ve grup 2'den (sırasıyla p=0,001 ve p=0,016) anlamlı olarak yüksekti. Ayrıca SCUBE-1 seviyeleri total kolesterol seviyesi (r=0,220; p=0,025) ve trigliserit (r=0,194; p=0,049) ile pozitif yönlü koreleydi. Yanı sıra, sCD40L seviyesi ise sadece kreatinin seviyesi (r=0,297; p=0,002) ile pozitif yönlü koreleydi.
Sonuç: SCUBE-1 ve sCD40L seviyeleri tip 2 diyabette nefropatinin progresyonu ile artmaktadır. Bu artış SCUBE-1 ve sCD40L'ın diyabetik nefropatiye bağlı ateroskleroz sürecinde anahtar rol oynuyor olabileceğini ve diyabetik nefropatinin bu parametrelerin seviyelerini etkiliyor olabileceğini düşündürmektedir.
Anahtar kelimeler: SCUBE-1; sCD40L;ateroskleroz; diyabetik nefropati.

INTRODUCTION

Diabetic nephropathy (DN) is a leading complication of diabetes mellitus progressing to end-stage renal disease (ESRD) (1). Patients with DN have exceptionally high risk of cardiovascular morbidity and mortality (2). It has been considered a close link between atherosclerotic heart disease and DN and they shared common predisposing factors such as hyperglycemia, dyslipidemia, hypertension, obesity and genetic background (3). Furthermore, atherosclerosis was more frequent in ESRD of DN (4).

Signal peptide-CUB (complement C1r/C1s, Uegf and Bmp1) epidermal growth factor-alanine-containing protein-1 (SCUBE-1) is a member of the SCUBE gene family and a cell surface protein (5). SCUBE-1 is secreted in the vascular endothelium and platelets (5-7). It has been shown that SCUBE-1 level was elevated in atherosclerosis related diseases such as coronary artery disease, hypertension and stroke (8-10).

CD40 Ligand (CD40L) produced by variety of cells as a proinflammatory mediator. Soluble form of CD40L (sCD40L) may be secreted by activated platelets (11). It has been shown that sCD40L has a role in the course of atherosclerosis and it was an independent prognostic marker for cardiovascular diseases among healthy individuals (12-16).

Both SCUBE-1 and sCD40L levels has been shown to be increased in ESRD (17-20). To the best of our knowledge, there are no studies evaluating SCUBE-1 or sCD40L levels with diabetes mellitus of type DN 2 at an early stage (T2DM). Herein, we aimed to the evaluate changes of SCUBE-1 and sCD40L with the progression of nephropathy in patients with T2DM.

MATERIAL AND METHODS

Participants

Randomly selected 74 outpatients diagnosed as T2DM who admitted to Harran University Education and Research Hospital Endocrinology Department were enrolled. The study protocol was approved by the Harran University School of Medicine Ethics Committee with number 17/02/06 in 09.02.2017. All subjects approved the written consent. The study was performed in accordance to the Declaration of Helsinki. Patients with severe organ failure, systemic inflammatory disease, malignancy, pregnancy and any renal disease other than DN were not included. Microalbumin to creatinine ratio was measured in early morning spot urine samples. The mean of two measurements was evaluated. Age and gender matched 30 healthy subjects were accepted as control group (group 1). T2DM patients were divided into three groups considering the level of proteinuria; the groups of normal albuminuria (albumin/creatinine <30 mg/g, group 2, n=33), moderately increased albuminuria (albumin/creatinine =30-300 mg/g, group 3, n=22) and severely increased albuminuria (albumin/creatinine >300 mg/g, group 4, n=19).

Biochemical Measurement

Blood samples were drawn from antecubital vein after an overnight fasting, centrifuged at 2000× g for 15 min, and stored at -80°C until analysis. A commercial kit following the manufacturer's instructions (Elabscience Biotechnology Co., Ltd., China, Catalog no: E-EL-H5405, Lot: AK0015NOV30024) using the enzyme-linked immunosorbent assay technique were performed to measure plasma SCUBE-1 and sCD40L levels.

Statistical Analysis

The data were analyzed using SPSS v.20. Chi-square test was performed to compare categorical data. Distribution of variable was controlled with Kolmogorov-Smirnov test. For continuous variables with normal distribution, One-way ANOVA was used to compare data between groups. LSD, as a post-hoc test, was performed to evaluate significance of the groups. Kruskal-Wallis test was used for non-normal data, and Mann-Whitney U test for separately each two groups in case of need. Spearman correlation analysis was used to determine correlations. A value of $p<0.05$ was considered to be statistically significant. All data were expressed as mean±standard deviation and median (minimum-maximum).

RESULTS

The groups were similar in terms of age and gender ($p=0.402$ and $p=0.397$, respectively, Table 1). There was a significant difference between groups in terms of mean plasma glucose levels ($p<0.001$) and it were significantly higher in diabetic groups according to the control group (all $p<0.001$). There was a significant difference between groups in terms of A1c levels ($p=0.031$). According to the post hoc test results, mean A1c levels of groups 3 and 4 were significantly higher than those of group 2 ($p=0.041$ and $p=0.020$, respectively). Mean blood urea and creatinine levels were significantly different between groups (all $p<0.001$). Mean blood urea and creatinine levels were significantly higher in group 4 than in the other groups in post hoc tests (all $p<0.001$). Moreover, there was a significant difference between groups in terms of mean total cholesterol level ($p=0.039$) and it was significantly higher in group 4 compared to group 1 ($p=0.011$).

Furthermore, SCUBE-1 and sCD40L levels were found to be significantly different between groups ($p=0.006$ for SCUBE-1 and $p<0.001$ for sCD40L). According to the post hoc test results, mean SCUBE-1 levels were significantly higher in group 4 than in group 1 and group 2 ($p=0.005$ and $p=0.014$, respectively), and in group 3 compared to group 1 and group 2 ($p=0.011$ and $p=0.028$, respectively). Moreover, mean sCD40L levels were significantly higher in group 4 than in other 3 groups (all $p<0.001$), and in group 3 than in group 1 and group 2 ($p=0.001$ and $p=0.016$, respectively).

In correlation analyze, SCUBE-1 level was positively correlated with total cholesterol ($r=0.220$, $p=0.025$) and triglyceride ($r=0.194$, $p=0.049$) levels. sCD40L level was positively correlated with only creatinine ($r=0.297$, $p=0.002$) level (Table 2).

DISCUSSION

In our study, we found following issues: i) SCUBE-1 and sCD40L levels were increased depending on the degree of DN, ii) SCUBE-1 was correlated with total cholesterol and triglyceride, and iii) sCD40L was correlated with creatinine.

SCUBE-1 is a platelet-endothelial adhesion molecule that plays pathological roles in atherothrombosis (9). It has been showed that SCUBE-1 level increased in acute thrombotic and ischemic events; e.g., acute coronary syndrome, ischemic stroke and mesenteric ischemia (8,10,21,22). Furthermore, as a chronic atherosclerotic process, Ozkan et al. (23) found that SCUBE-1 level increased in

Table 1. Comparison of clinical and laboratory parameters between groups

	Group 1 (n=30)	Group 2 (n=33)	Group 3 (n=22)	Group 4 (n=19)	p
Gender					
Male	16 (53.3%)	17 (51.5%)	14 (63.6%)	7 (36.8%)	0.397
Female	14 (46.7)	16 (48.5%)	8 (36.5%)	12 (63.2%)	
Age (year)	48.9±10.1	49.7±10.0	52.3±10.4	52.9±8.1	0.402
	49.0 (34.0-65.0)	51.0 (33.0-65.0)	54.5 (32.0-65.0)	55.0 (35.0-64.0)	
Glucose (mg/dL)	88.4±7.4[a]	180.3±78.3[b]	209.5±99.5[b]	220.9±96.8[b]	**<0.001**
	89.0 (67.0-99.0)	160.0 (94.0-398.0)	179.5 (109.0-480.0)	207.0 (106.0-425.0)	
A1c (%)	-	7.9±1.9[a]	9.2±2.0[b]	9.4±2.6[b]	**0.031**
		7.4 (5.2-11.8)	9.2 (5.9-12.7)	9.0 (6.7-14.6)	
Urea (mg/dL)	30.6±9.8[a]	31.2±7.0[a]	29.6±7.6[a]	50.9±31.3[b]	**<0.001**
	30.3 (12.5-49.0)	30.0 (18.4-46.1)	29.5 (15.3-43.8)	42.0 (19.8-138.0)	
Creatinine (mg/dL)	0.8±0.1[a]	0.8±0.1[a]	0.9±0.2[a]	1.2±0.5[b]	**<0.001**
	0.7 (0.4-1.2)	0.8 (0.6-1.2)	0.9 (0.6-1.2)	1.1 (0.6-2.0)	
Total-C (mg/dL)	170.6±39.3[a]	174.3±38.2[ab]	194.9±45.3[ab]	202.5±47.7[b]	**0.039**
	163.0 (105.0-258.0)	178.0 (113.0-273.0)	200.0 (124.0-301.0)	202.0 (122.0-323.0)	
Triglyceride (mg/dL)	153.2±68.1.2	184.8±92.0	236.0±192.0	210.4±82.7	0.069
	155.0 (60.0-348.0)	150.0 (65.0-408.0)	164.5 (63.0-821.0)	213.0 (88.0-345.0)	
HDL-C (mg/dL)	45.3±9.7	40.5±8.9	40.8±10.7	43.2±8.4	0.187
	44.8 (29.2-68.8)	40.2 (23.7-59.7)	42.1 (23.4-66.7)	45.0 (30.4-58.7)	
LDL-C (mg/dL)	96.8±36.8	97.9±32.5	108.9±29.7	117.2±39.6	0.147
	87.2 (34.7-178.8)	92.9 (36.8-176.0)	103.1 (64.7-169.0)	108.4 (71.2-227-7)	
SCUBE-1 (ng/ml)	1.6±0.6[a]	1.8±0.9[a]	2.8±2.2[b]	2.9±2.8[b]	**0.006**
	1.5 (0.8-2.9)	1.6 (0.8-4.2)	2.5 (0.8-10.8)	1.6 (0.8-11.6)	
sCD40L (pg/ml)	108.9±68.5[a]	385.4±237.9[a]	950.8±918.1[b]	2053.2±1669.5[c]	**<0.001**
	100.2 (37.9-302.3)	388.5 (48.1-973.4)	540.8 (176.4-3652.4)	1419.8 (294.4-5069.1)	

A1c: Glycosylated Hemoglobin, Total-C: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, SCUBE-1: Signal peptide-CUB (complement C1r/C1s, Uegf and Bmp1) Epidermal growth factor-alanine-containing protein-1, sCD40L: Soluble form of CD40 Ligand, [a,b,c]: Different superscript letters denote significant differences between the groups, Descriptive statistics given as mean±standart deviation and median (minimum-maximum)

Table 2. Correlation analyses of sCD40L and SCUBE-1 with other parameters

	SCUBE-1		sCD40L	
	r	**p**	**r**	**p**
Age	-0.087	0.379	0.092	0.354
Glucose	0.189	0.055	0.576	**<0.001**
A1c	0.222	0.057	0.005	0.968
Urea	0.190	0.051	0.130	0.189
Creatinine	0.120	0.223	0.297	**0.002**
Total-C	0.220	**0.025**	0.128	0.197
Tri-glyceride	0.194	**0.049**	0.130	0.189
HDL-C	-0.186	0.058	-0.129	0.192
LDL-C	0.152	0.124	0.120	0.225

A1c: Glycosylated Hemoglobin, Total-C: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, SCUBE-1: Signal peptide-CUB (complement C1r/C1s, Uegf and Bmp1) Epidermal growth factor-alanine-containing protein-1, sCD40L: Soluble form of CD40 Ligand

hypertensive patients. Moreover, Ulusoy et al. (17) found that hemodialysis patients had high level than healthy subjects. More recently, Icel et al. (24) showed that SCUBE-1 was increased with the presence and progression of diabetic retinopathy. However, SCUBE-1 has not been studied in DN until now. We showed that SCUBE-1 level increased with the progression of nephropathy in T2DM at first time.

It is believed that, CD40L has a key role in the course of progressive atherosclerosis in healthy and diabetic subjects (25). Varo et al. (26) showed that sCD40L plasma levels were higher in T2DM patients according to healthy subjects. Lajer et al. (27) found that plasma sCD40L levels were elevated nephropathy of type 1 diabetes. Furthermore, Chiarelli et al. (25) showed that type 1 diabetic patients with persistently increased sCD40L levels had increased risk of nephropathy. On the other hand, Desideri et al. (19) indicated prognostic value of sCD40L for cardiovascular prognosis in patients with ESRD. To the best of our knowledge, the level of sCD40L in DN of T2DM is not known. We firstly showed that sCD40L level increased with the degree of nephropathy in T2DM.

Increased albuminuria has been accepted to be a principle risk factor of cardiovascular and renal diseases in T2DM (28). Barrios et al. (29) found that, patient with any stages of DN had higher risk of atherosclerosis compared to non-diabetic chronic kidney disease. Momeni et al. (30) showed that proteinuria was associated with atherosclerosis in T2DM. Platelets contribute to the onset and continuity of atherosclerosis as well as acute atherosclerotic events (31). Tarnow et al. (32) showed that DN due to T1DM was associated with increased circulating activated platelets and platelet hyper reactivity. SCUBE-1 mediates platelet-platelet or platelet-matrix interactions and is considered a biologically important molecule in the vascular system (6). The important role of sCD40L has been found in the bridge between inflammation, atherosclerosis, and thrombosis (33). Our

results suggested that increased SCUBE-1 and sCD40L might be the result of DN or might contribute to the progression of DN. Our study design could not distinguish this dilemma. So that, further studies with follow-up design are need to detect exact role of SCUBE-1 and sCD40L in DN and atherosclerosis. This situation is the most important limitation of our study.

Interestingly, we found that sCD40L level was correlated with renal function (i.e. creatinine level), but SCUBE-1 level with the lipid parameters (i.e. total cholesterol and triglyceride). Thus, we thought that increased atherosclerosis in DN may be related with different mechanisms. As discussed previously, risk of nephropathy is increased in type 1 diabetic patients with persistently increased sCD40L (24). The same predictor role of sCD40L in T2DM to estimate nephropathy risk should be explored in further studies.

CONCLUSION

We showed that SCUBE-1 and sCD40L levels increased with the progression of nephropathy in T2DM. This increment may be one of the pathological pathways causing to atherosclerosis or subclinical atherosclerosis may be the reason of this increment. Extensive studies are needed to confirm the results of the present study.

Acknowledgement: This study was supported by Harran University Scientific Research Coordination Board with number 17020.

Conflict of Interests: All authors declare that they have no conflict of interests.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.596713

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):248-250

Mesanenin Nadir Benign Neoplazmı: Mesane Leiomyomu

Rare Benign Neoplasm of the Bladder: Leiomyoma of the Bladder

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ÖZ

Mesanenin benign mezenşimal lezyonları oldukça nadirdir ve tüm mesane tümörlerinin %1-5'inin oluştururlar. Bunların içinde de en sık leiomyoma saptanmaktadır. Benign lezyonlar radyolojik olarak maling kitleleri taklit etmesi nedeniyle klinik öneme sahiptir. Tanı radyolojik tetkiklerle kitlenin saptanması ve sonrasında yapılan cerrahi eksizyon ya da biyopsi ile histopatolojik olarak konulmaktadır. Ekstravezikal ve intramural form sistoskopik olarak saptanamayabilirken intravezikal leiomyomlar sistoskopi ile saptanabilir. Sistoskopi sırasında mesane içinde protrüde, kısmen düzgün sınırlı ve yüzeyi mesane mukozası ile kaplı lezyonlar görüldüğünde mesane leiomyomu ayırıcı tanıda düşünülmelidir. 44 yaşında kliniğimize irritatif semptomlarla tarafımıza başvuran ve mikroskopik hematüri saptanan erkek hastada mesanede 2x2 cm kitle saptandı. Minimal invaziv tedavi (TUR-mesane) sonrasında leiomyoma tanısı konulan vaka sunulmaktadır.
Anahtar kelimeler: Leiomyom; mesane.

ABSTRACT

Benign mesenchymal lesions of the bladder are very rare and constitute 1-5% of all bladder tumors. Among these, leiomyoma is the most common. Benign lesions are clinically important because they mimic radiologically malign masses. The diagnosis is made histopathologically by detecting the mass by radiological examinations and subsequent surgical excision or biopsy. Extravesical and intramural forms may not be detected cystoscopically, while intravesical leiomyomas can be detected by cystoscopy. Bladder leiomyoma should be considered in the differential diagnosis when protruding, partially smoothly bound and covered bladder mucosa lesions are observed during cystoscopy. A 44-year-old male patient who presented to our clinic with irridative symptoms and was found to have microscopic hematuria and 2x2 cm mass in the bladder. A case of leiomyoma diagnosed after minimally invasive treatment (TUR-bladder) is presented.
Keywords: Leiomyoma; bladder.

GİRİŞ

Mesanenin benign mezenşimal lezyonları oldukça nadirdir ve tüm mesane tümörlerinin %1-5'ini oluşturmakla birlikte en sık leiomyoma saptanmaktadır (1-3). Klinik semptomlar tümörün bulunduğu yer ve büyüklüğüne bağlı olarak obstriktif ya da irritatif semptomlar, hematüri ile farklı şekillerde karşımıza çıkabildiği gibi aynı zamanda lezyonlar insidental olarak da saptanabilir (1-4). Mesane leiomyomları yerleşimine göre ekstravazikal, intramural ve intravezikal olarak sınıflandırılabilir ve çoğunlukla da intravezikal saptanır (3,5,6,8). Tanıda ultrason, bilgisayarlı tomografi (BT), manyetik rezonans görüntüleme (MR) ve intravenöz pyelografi (İVP) kullanılabilir.

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Geliş Tarihi / Received : 25.07.2019
Kabul Tarihi / Accepted : 17.09.2019
Çevrimiçi Yayın Tarihi / Available Online : 07.11.2019

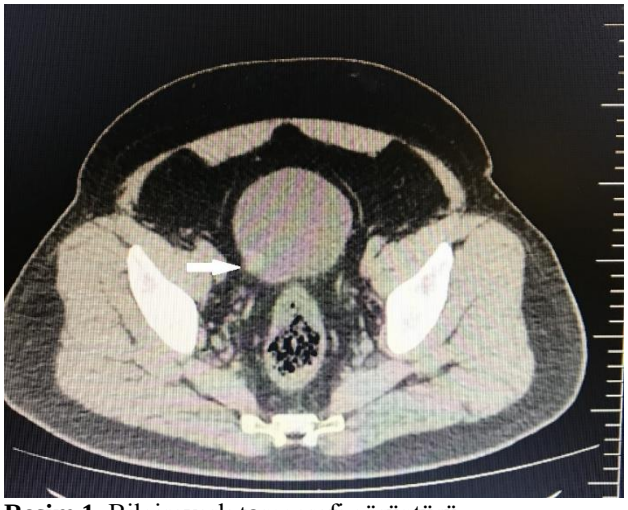
4. Ulusal Ürolojik Cerrahi Kongresinde (31 Ekim-04 Kasım 2018, Antalya) poster olarak sunulmuştur.

Tanı kitlenin görüntüleme yöntemleri ya da sistoskopik olarak saptanmasından sonra dokunun histopatolojik incelenmesi sonrasında konulmaktadır. Tedavi cerrahi olmakla birlikte kitlenin yeri ve büyüklüğüne göre açık ya da endoskopik olarak uygulanabilir (1-7). Biz de bu çalışmada ultrasonografi ve BT'de belirlenen kitleye transüretral rezeksiyon uyguladığımız ve sonrasında patoloji raporu ile mesane leiomyomu saptanan vakayı sunmayı amaçladık.

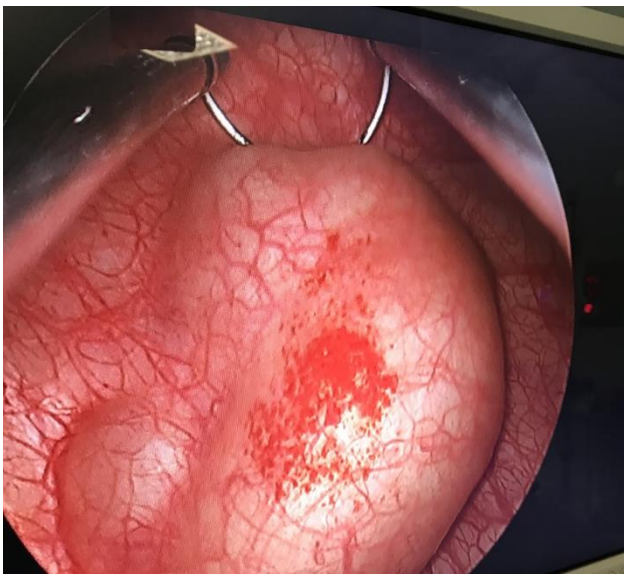
OLGU SUNUMU

Kırk dört yaşında erkek hasta yan ağrısı ve urgency şikayetleri ile kliniğimize başvurdu. Yapılan tetkiklerde mikroskobik hematüri saptandı. Bunun üzerine hastaya abdomino-pelvik ultrasonografi yapıldı ve bu incelemede mesane sağ posterolateralinde sağ üreter alt uca uyan alanda lümene protrüde kistik 2x2 cm görünüm izlendi (üreterosel?). Bunun üzerine hastaya kontrastlı abdomen BT görüntülemesi istendi ve mesane sağ yan duvarda 10x14 mm boyutunda kontrastlanan polipoid hiperdens lezyon tespit edildi (Resim 1).

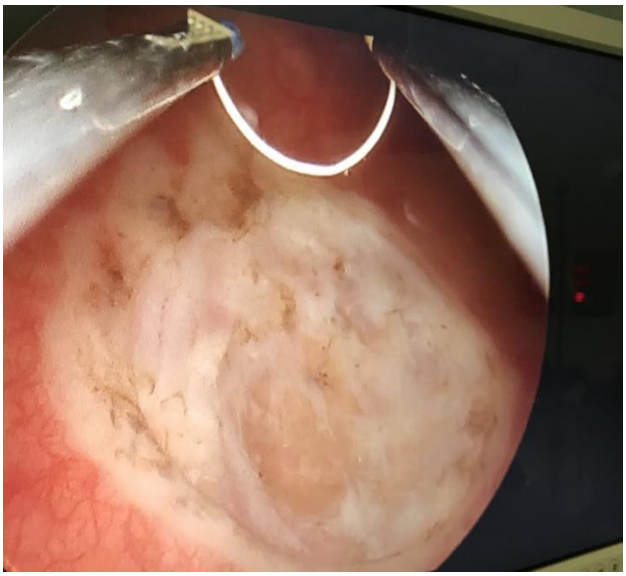
Bu gelişmeler sonrasında hastaya endoskopik işlem yapılmasına karar verildi ve sistoskopide; üretra doğal, sağ orifisin posteriorunda mesane sağ yan duvar arka duvar bileşkesinde 2 cm'lik düzgün yüzeyli lümene protrüde solid lezyon gözlendi (Resim 2). Sağ orifis ve geri kalan mesane mukozası normaldi. Hastanın mesanesindeki lezyona 2017 yılı Ekim ayında transüretral rezeksiyon uygulandı (Resim 3) ve intraoperatif, postoperatif komplikasyon gözlenmedi. Operasyon sonrasında 2. gün üretral kateter çekilerek hasta taburcu edildi. Hematoksilen-Eozin (H&E) ile yapılan histopatolojik incelemede düzgün sınırlı nodüler yapılanmalar oluşturan, birbirini çaprazlayan kalın demetler halinde düz kas fasikülleri dikkati çekti (Resim 4). Ayrıca yapılan immünohistokimyasal incelemede de fusiform, künt uçlu ve birbirini çaprazlayan demetler teşkil eden düz kas hücrelerinin epitelyal membran antijeni negatif, desmin ve düz kas aktini pozitif boyandı. Histomorfolojik bulgular leiomyom lehine değerlendirildi. Postoperatif sistoskopik ve radyolojik kontrollerde mesane normal olarak değerlendirildi. Hastadan vaka sunumu amaçlı bilgilendirilmiş olur için onam alındı.



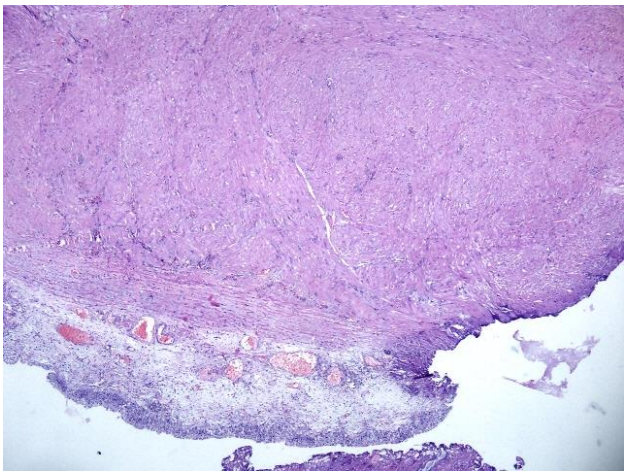
Resim 1. Bilgisayarlı tomografi görüntüsü



Resim 2. Sistoskopik görüntü



Resim 3. Rezeksiyon sonrası görüntü



Resim 4. Histopatolojik incelemede düzgün sınırlı nodüler yapılanmalar oluşturan, birbirini çaprazlayan kalın demetler halinde düz kas fasikülleri dikkati çekti (H&E, x40)

TARTIŞMA

Leiomyom mesanenin benign mezenşimal tümörüdür (1-7). Benign lezyonlar kitle görüntüsü nedeniyle histopatolojik tanı konularak malign lezyonlardan ayrılmalıdır. Mesanenin benign mezenşimal kitleleri; myomlar, fibromlar, angiomlar, miksomlar ve leiomyomlar olarak sayılabilir (2). Literatürde 250 civarında mesane leiomyomu olgusu saptanmıştır (8).

Campbell ve Gislason (3) tarafından leiomyom; benign mesane lezyonları arasında en sık görülen tip olarak belirtilmiştir. Jiang ve ark. (9) tarafından leiomyomun en fazla depolama semptomları ile prezente olurken neredeyse üçte birlik kısmı asemptomatik olarak rapor edilmiştir.

Goluboff ve ark. (10) 37 vakayı inceledikleri literatür taramasında leiomyomun kadınlarda ve 4. dekatta daha sık saptandığını belirtmişlerdir. Yine aynı çalışmada %63 intravezikal ve en sık semptom obtstriktif semptomlar olarak bildirilmiştir. Park ve ark. (7) tarafından sunulan 9 hastalık seride tüm hastalar kadın olarak saptanmıştır. Fakat Knoll ve ark. (11) 5 vakalık çalışmalarında irritatif semptomların daha sık görüldüğünü bildirmişlerdir.

Bizim sunduğumuz vakada hastanın yan ağrısı ve irridatif semptomları mevcut ve hasta cinsiyeti erkekti. Tanı radyolojik tetkiklerle kitlenin saptanması ve sonrasında yapılan cerrahi eksizyon ya da biyopsi ile histopatolojik olarak konulmaktadır. İVP, ultrason, BT, MR yöntemleri tanı koymada önemli yardımcı tetkiklerdir. İntravezikal form sistoskopik olarak tek, normal mesane mukozasıyla kaplı olarak görülebilirken ekstravezikal ve intramural form sistoskopik olarak saptanamayabilir (11). Bizim vakamızda da sistoskopi de benzer görüntü görüldü.

Bizim vakamızda şikayetleri takiben ilk olarak ultrasonografi yapılmıştır ve ön tanı olarak üreterosel düşünülmüştür. Ardından yapılan kontrastlı abdominopelvik BT'de mesane arka duvarda kontrastlanan solid kitlenin görülmesiyle birlikte kesin tanı spinal anestezi altında gerçekleştirilen sistoskopi ve devamında transüretral rezeksiyon ile konulmuştur. En fazla vaka sayısına sahip Goluboff ve ark. (10) tarafından yapılan çalışmada hastaların %87'sinde tanının sistoskopik olarak konulduğu belirtilmiştir. Tedavi cerrahi olmakla birlikte cerrahinin şekli, tümörün boyutu ve yeri, üreter orifisleri ve sfinkter ile olan ilişkisine bağlı olarak değişkenlikler gösterebilir. Boyut olarak göreceli küçük intravezikal leiomyom transüretral rezeksiyon ile eksize edilebilirken, büyük kitleler, üreter orifisi ile ilişkili ya da intramural, ekstravezikal kitleler için en iyi seçenek açık parsiyel rezeksiyon ya da enükleasyondur (11,12).

Cerrahi tedavi seçenekleri ile ilgili olarak Silva-Ramos ve ark. (13) tarafından yapılan çalışma iyi bir örnektir. Bu çalışmada 90 olgu değerlendirilmiş olup vakaların %62,2'sine açık cerrahi, %30'una TUR, %5,6'sına ise transvajinal rezeksiyon yapılarak tedavi edildiği bildirilmiştir.

Sonuç olarak literatürde henüz mesane leiomyomunun malign dönüşümü saptanmadığı için semptomatik hastalarda tedavinin amacı; semptomları hafifletmek ve malign kitleleri ekarte etmektir. Sistoskopi sırasında mesane içinde protrüde, kısmen düzgün sınırlı ve yüzeyi mesane mukozası ile kaplı lezyonlar görüldüğünde mesane leiomyomu ayırıcı tanıda düşünülmelidir. Malign kitlenin dışlanması amacıyla kitleden biyopsi ya da cerrahi eksizyon ile alınan dokunun histopatolojik incelemesi yapılmalıdır. Böylelikle hem hastanın lezyondan kaynaklanan şikayetlerine yönelik tedavi yapılırken ayrıca malign lezyon tanısı da ekarte edilmiş olacaktır.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.587448

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):251-253

Cardiopulmonary Resuscitation with Extracorporeal Membrane Oxygenation for Cardiotomy Cardiogenic Shock: Case Report

Post Kardiotomi Kardiyojenik Şok Nedeniyle Ekstrakorporeal Membran Oksijenasyon ile Kardiopulmoner Resüsitasyon: Olgu Sunumu

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ABSTRACT

Extracorporeal membrane oxygenation is a life-saving method when it is used with appropriate indications in cases of combined failure where cardiovascular system failure, respiratory system failure or each two system has failed with different proportions. Extracorporeal membrane oxygenation was successfully used in 1972 in a group of patients with lung failure. Today, it is widely used in patients with postoperative resistant low-flow rates. Extracorporeal membrane oxygenation may be used in cases of post-cardiotomy, resistant cardiogenic shock, or with some limited indications, in cardiopulmonary resuscitation. Extracorporeal membrane oxygenation implantation is rare with indications of both conditions. In this case report, we aimed to present a 47-year-old female patient who underwent successful extracorporeal cardiopulmonary resuscitation rather than entering cardiopulmonary bypass for the third time after sudden cardiac arrest resistant to medical therapy.
Keywords: Extracorporeal membrane oxygenation; cardiopulmonary resuscitation; cardiopulmonary bypass.

ÖZ

Ekstrakorporeal membran oksijenasyonu, kardiyovasküler sistem yetmezliği, solunum sistemi yetmezliği veya her iki sistemin farklı oranlarda başarısız olduğu durumlarda uygun endikasyonlarla kullanıldığında hayat kurtarıcı bir yöntemdir. Ekstrakorporeal membran oksijenasyon, ilk olarak 1972 yılında bazı akciğer yetmezliği olan hastalarda başarılı şekilde kullanılmıştır. Günümüzde postoperatif dirençli düşük debi gelişen hastalarda yaygın olarak kullanılmaktadır. Ekstrakorporeal membran oksijenasyon uygulaması genelde postkardiotomi dirençli kardiyojenik şok olgularında ya da bazı sınırlı endikasyonlar ile kardiopulmoner resüsitasyonda kullanılabilir. Her iki durumun birlikte olduğu endikasyon ile ekstrakorporeal membran oksijenizasyon uygulaması nadirdir. Bu olgu sunumunda, medikal tedavisi sürerken ani kardiak arrest sonrası üçüncü defa kardiyopulmoner bypassa girmek yerine başarılı şekilde ekstrakorporeal kardiyopulmoner resüsitasyon uyguladığımız 47 yaşında kadın hastayı sunmayı amaçladık.
Anahtar kelimeler: Ekstrakorporeal membran oksijenasyon; kardiyopulmoner resüsitasyon; kardiyopulmoner bypass.

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a life-saving method when it is used with appropriate indications in cases of combined failure where cardiovascular system failure, respiratory system failure or each two system has failed with different proportions. ECMO was successfully used in 1972 in a group of patients with lung failure (1). Today, it is widely used in patients with postoperative resistant low-flow rates (2). Recently, ECMO has been used for limited indications in cardiopulmonary resuscitation (3). The indications of the use of ECMO as both postcardiotomy low-flow syndrome and ECMO cardiopulmonary resuscitation (e-CPR) are rare. In this report, we aimed to present a 47-year-old female patient who had low flow cardiac arrest after postcardiotomy, and had a sudden cardiac arrest for the third time while

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Geliş Tarihi / Received : 05.07.2019
Kabul Tarihi / Accepted : 09.10.2019
Çevrimiçi Yayın Tarihi / Available Online : 07.11.2019

medical treatment was in progress, we performed successful e-CPR instead of going on cardiopulmonary bypass again.

CASE REPORT

A 47-year-old female patient was admitted to the cardiology clinic with chest pain. According to coronary angiography, elective coronary artery bypass graft surgery (CABG) operation was decided in cardiology and cardiovascular surgery council. Preoperative transthoracic echocardiography (TTE) revealed no pathology and the ejection fraction (EF) was 50%. The patient underwent elective CABGx5. The patient developed hypotension which was resistant to medical treatment. The patient was immediately cannulated and went on the cardiopulmonary bypass (CPB). All grafts were found to be patent. Ao-LAD bypass was performed on the beating heart as a vasospasm in the LIMA graft detected.

An intra-aortic balloon pump (IABP) was inserted through the left femoral artery. CPB with IABP and the medical treatment was started. The patient was decannulated. Hypotension followed by the cardiac arrest occurred during bleeding control. Internal cardiac massage was started immediately. Cardiac massage was continued 100 times per minute and mean arterial pressure was 80-90 mmHg (under invasive arterial monitoring). Instead of restarting the CPB, it was decided to administer ECMO. For this purpose, percutaneous right femoral artery-left femoral vein veno-arterial (VA) e-CPR procedure was performed. At the 10th minute of internal cardiac massage, non-pulsatile arterial pressure was achieved with ECMO support.

Distal perfusion in the femoral artery was achieved with percutaneous 9F introducer sheath. Then the heart started to beat in sinus rhythm. When the heart started, pulsatile arterial blood pressure was obtained at an average of 70 mmHg in ECMO support. Following the bleeding control, the patient was taken to the intensive care unit with ECMO and IABP support by closing only the skin (open sternum). Heparin infusion was started targeting an average activated coagulation time (ACT) of 160-180 seconds. The patient was conscious and there was no major neurological complication on postoperative day 1. The patient was stable with ECMO support. ECMO's rounds per minute (rpm) support could not be reduced at the end of the first 2 days postoperatively. As the patient tolerated, ECMO rpm was gradually reduced after the second postoperative day. The patient was separated from ECMO support on the postoperative 4th day after the hemodynamic parameters were stable on clinical follow-up and on TTE, EF was found to be 30%. Since ECMO cannulae were inserted percutaneously, decannulation was performed in the intensive care unit. Bleeding control was achieved with approximately 1 hour of compression. Following IABP and inotropic support ceased. The patient was taken to the normal ward. There were no complications related to ECMO's vascular application in the clinical follow-up. During the follow-up period, EF was 40% and the patient was discharged on the 25th postoperative day. The patient had no complaints at the postoperative 2nd month out-patient clinic control and the EF on TTE was 50% (the same as the preoperative EF value). Informed consent form was obtained.

DISCUSSION

Extracorporeal membrane oxygenator is an important vital support system used in refractory post-cardiotomy low flow syndrome. In postcardiotomy low flow syndrome, the first step in treatment is medical treatment. In cases resistant to medical treatment, the second stage is IABP. ECMO may be used with appropriate indications as the third stage in low-flow conditions that do not improve with medical treatment and IABP. ECMO is used to bridge the patient to complete recovery or to implantation of left ventricular assist device. In our case, ECMO was used as a bridge to complete recovery from low flow postcardiotomy syndrome. Normally, in postcardiotomy low flow syndromes, if the patient is decannulated and resistant to medical treatment (including IABP), they can be recannulated and put onto CPB. In recent years, the use of ECMO during CPR has been raised (e-CPR). It has been reported that e-CPRs have superior results compared to classical CPRs with correct indications (3). The most important indication of e-CPR is that cardiac arrest has a reversible cause and that the CPR is started in the first 10 minutes after cardiac arrest. In our case, it was decided to start an ECMO support (instead of entering CPB for the 3rd time) since we administered effective internal cardiac massage and made sure that there was a reversible cause of the cardiac arrest. In this regard, e-CPR was applied in our case. There is no specific definition of e-CPR. When the literature is reviewed, it is seen that e-CPR has been cited as a CPR performed by ECMO in patients with cardiac arrest within the hospital perimeters following certain rules. In this respect, we think that our case meets the e-CPR approach. Due to the effective internal cardiac massage under real-time arterial blood pressure monitoring, we took the e-CPR decision relatively easily. We think that the fast decision-making process and the fast organization are also effective. In the literature, we could not find any cases of VA ECMO implantation with both postcardiotomy low flow and e-CPR indications.

In general, we think that percutaneous VA ECMO may be implanted in patients who are suitable after post-cardiotomy cardiac arrest instead of going on CPB for several times. In elective cases, cannulation sites are generally determined by the choice of the surgeon and following the indications. In peripheral VA ECMO applications, femoral artery or subclavian artery may be preferred for arterial cannulation. Arterial cannulation can be achieved by direct cannulation or grafting. Although direct cannulation is an advantage in speed, it has a significant disadvantage in terms of distal extremity ischemia. In these cases, distal perfusion can be provided with introducer sheath (4). In emergency cases, time is important and percutaneous techniques are preferred. In our case, percutaneous techniques were preferred because time limitation was important. The right femoral artery was preferred for arterial cannulation and the left femoral vein was preferred for venous cannulation. Because of direct cannulation, distal perfusion was achieved with 9F sheath to avoid distal ischemia. Peripheral ECMO may develop vascular complications related to cannulation site. Acute extremity ischemia and bleeding are the most common complications (5). There was no complication related to cannulation site in our

case. The other route used for peripheral arterial cannulation in peripheral ECMO applications is the subclavian artery. In patients with VA ECMO who underwent subclavian artery cannulation due to flow direction, renal perfusion and upper body parts were shown to be better perfused. In peripheral VA ECMO, femoral artery cannulation for arterial cannulation is not a highly desirable method for brain and myocardial perfusion. In the subclavian artery cannulation, nerve damage can also be seen as a vascular complication. We prefer the subclavian artery for arterial cannulation in elective VA ECMO implantations (with graft). However, the subclavian artery could not be used due to time constraint in our case.

In our case, no systemic complications (renal failure, central nervous system complications, etc.) were observed with femoral artery cannulation.

ECMO provides non-pulsatile continuous flow. If peripheral arterial cannulation is performed on the femoral artery, ECMO will provide continuous retrograde flow in both systole and diastole. Therefore, cerebral, coronary and renal perfusion will vary depending on whether the heart generates pulsatile flow or not. The perfusion pressures will become quite complex if the event is joined by the IABP. If the heart does not generate adequate flow rate, IABP (femoral artery-mediated) will decrease cerebral and coronary perfusion, since cerebral and coronary perfusion will be completely ECMO dependent (due to descending aortic occlusion in diastole by the IABP). IABP will increase cerebral blood flow when the heart is ejecting properly (7). For this reason, it is very important that the heart is adequately operated in patients with peripheral ECMO with IABP. In our case, we achieved cardiac sinus rhythm within 10 minutes after implantation of peripheral ECMO and no neurological complications were detected.

As a result, direct VA ECMO implantation (e-CPR) is an important alternative treatment method in patients with postcardiotomy sudden cardiac arrest.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.587591

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):254-256

Perforated Jejunal Diverticulitis, An Unusual Cause of Intraabdominal Abscess

Nadir Bir Batın içi Abse Nedeni, Jejunal Divertikülit Perforasyonu

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ABSTRACT

Jejunal diverticulosis is a sporadic seen disease which was generally asymptomatic. Severe diverticulitis complications such as obstruction, hemorrhage, or perforation with a delayed diagnosis can be life-threatening. An 82 year old male patient applied to the emergency service with abdominal pain, and his physical examination was compatible with acute abdomen and peritonitis. He was diagnosed with perforation due to extraluminal air and abscess on computerized abdominal tomography. The patient underwent exploratory laparotomy and was diagnosed with perforation of jejunal diverticulitis, perioperatively. Segmental small intestine resection and end-to-end anastomosis were performed. He was discharged with no complications on the postoperative 25th day. In this case report, it is aimed to report a rare cause of acute abdomen in an elderly patient with perforation of jejunal diverticulitis due to delayed diagnosis.
Keywords: Diverticulitis; jejunal diverticulosis; acute abdomen; intraabdominal abscess.

ÖZ

Jejunal divertikulozis genellikle asemptomatik seyreden çok nadir görülen bir hastalıktır. Obstruksiyon, kanama ve perforasyon gibi divertikülite sekonder oluşan ciddi komplikasyonlar geç tanı konulduğunda yaşamı tehdit edici olabilir. Seksen iki yaşında erkek hasta acil servise karın ağrısı şikayetiyle başvurmuş olup, fizik muayenesi akut batın ve peritonit ile uyumlu idi. Bilgisayarlı abdomen tomografide serbest hava ve apse nedeniyle hastaya perforasyon tanısı konuldu. Eksploratif laparatomi yapılan hastaya ameliyat sırasında peroperatif jejunal divertikülit perforasyonu tanısı konuldu. Segmental ince bağırsak rezeksiyonu ve uçtan uca anastomoz uygulandı. Ameliyat sonrası 25. günde komplikasyonsuz olarak taburcu edildi. Bu olgu sunumunda, gecikmiş tanı nedeniyle jejunal divertikülit perforasyonu olan yaşlı bir hastada nadir bir akut karın nedeninin sunulması amaçlanmıştır.
Anahtar kelimeler: Divertikülit; jejunal divertikülozis; akut karın; batın içi abse.

INTRODUCTION

Diverticula is predominantly localized in the colon but might be seen in any part of the digestive tract beginning from the esophagus (1). In the small intestine, diverticulosis is mostly located in the duodenum, followed by the jejunum and the ileum (2). Generally, jejunal diverticulosis (JD) is asymptomatic, but due to complications of diverticulitis like hemorrhage, intestinal obstruction, jejunal perforation, mesenteric abscess, generalized peritonitis, it can be symptomatic.

CASE REPORT

An 82 year old male patient applied to the emergency department with abdominal pain, vomiting, nausea persisting for five days with fever. Anamnesis revealed no history of chronic illness except Alzheimer's disease. On physical examination, there were signs of peritoneal irritation on the left upper quadrants of the abdomen with rebound and tenderness. Except for increased total leukocyte count, the laboratory tests were in normal limits. Fever was 38.9 °C. Abdomen computed tomography (CT)

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Geliş Tarihi / Received : 05.07.2019
Kabul Tarihi / Accepted : 22.10.2019
Çevrimiçi Yayın Tarihi / Available Online : 07.11.2019

revealed air-fluid, especially around the loop of the jejunal intestine with localized abscess (Figure 1). Perforation was the presumptive diagnosis; therefore, explorative laparotomy was performed. Multiple diverticulosis was seen between the 40 cm segment of the jejunum and the thirty cm distance of Treitz ligament, and a perforation was detected in one of the diverticula with abscess (Figure 2). The abscess was drained, segmental small intestine resection and end-to-end jejuno-jejunal anastomosis were performed. The patient began to intake fluid on the fifth postoperative day, and the drain was extracted on the sixth postoperative day. During the postoperative period, the patient was followed in the intensive care unit due to respiratory complications. He was recovered and discharged home on the postoperative 25th day. Histopathological examination of the specimen confirmed multiple diverticulosis, one of which was a perforated jejunal diverticulum, with acute inflammation consisting mucosa and submucosa without the muscularis propria layer (Figure 3,4,5). Written informed consent which was necessary was obtained from the patient for treatment, surgery, and publication.

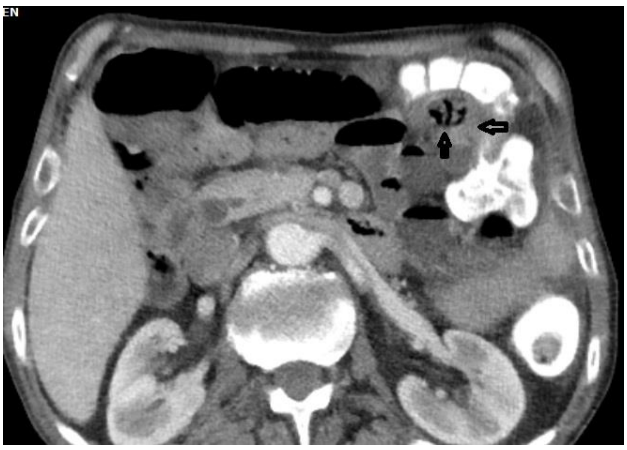

Figure 1. Abdomen Computed Tomography (CT) was showed air-fluid especially around the loop of jejunal intestine with localized abscess

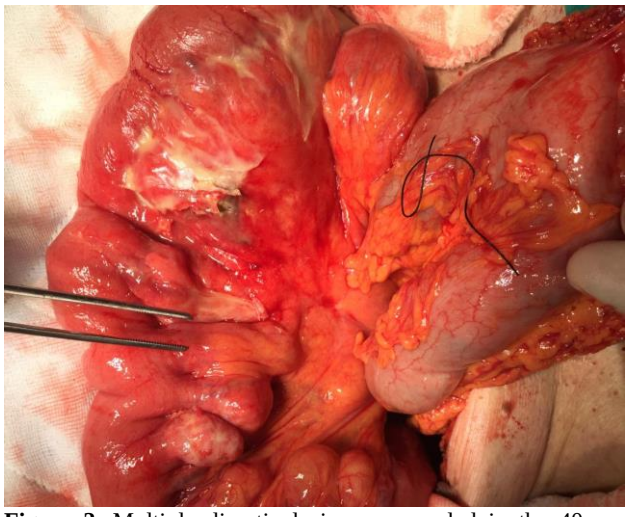

Figure 2. Multiple diverticulosis was revealed in the 40 cm segment of jejunum from the thirty cm distance Treitz ligament, and a perforation was detected in one of them due to diverticulitis

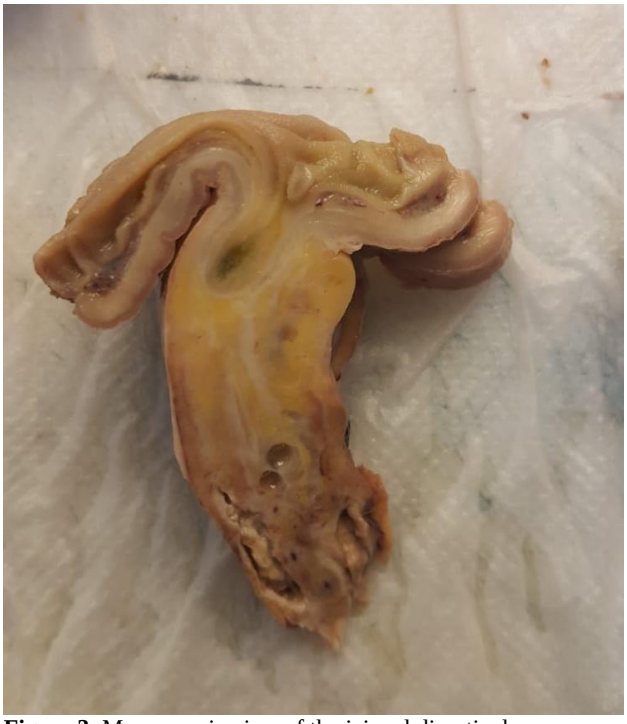

Figure 3. Macroscopic view of the jejunal diverticulum

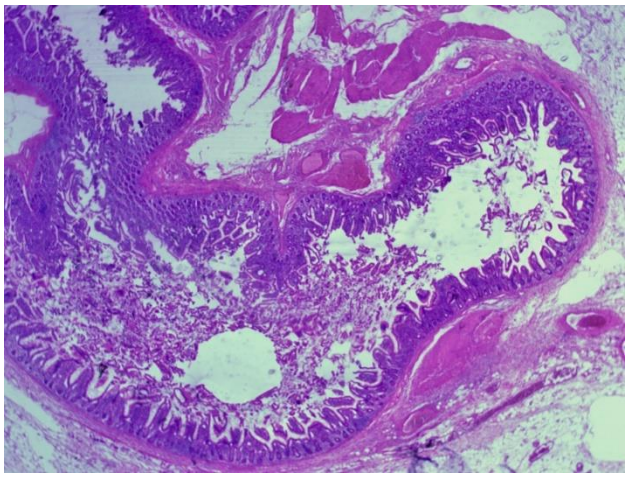

Figure 4. Jejunal diverticulum: A wall of mesenteric fat that does not contain muscularis propria in the wall, the jejunal tissue extending into the tissue, H&E x40

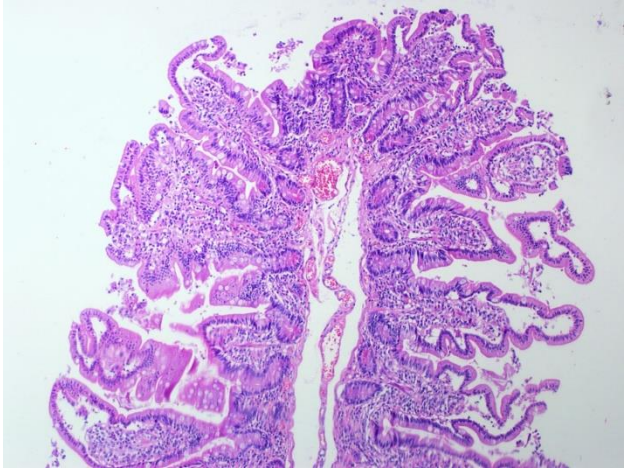

Figure 5. Jejunal diverticulitis: Mixed polymorphonuclear leukocytes and lymphoplasmacytic inflammation in the diverticula mucosa, H & E x100

DISCUSSION

Jejunal diverticulosis (JD) is a type of pseudo-diverticula which occurs mainly in the vasa recta regions of the mesenteric side of the intestine due to the herniation of the mucosa and submucosa (1,2). It is reported that the incidence of JD was 0.2-1.3% in autopsy series (3,4). JD most commonly occurs during the sixth and seventh decades of life and mainly seen in male patients. Compared to the female population, JD is 1.5 times higher in males (2). The symptoms and signs of JD are nonspecific, such as chronic abdominal pain, nausea, constipation, diarrhea, dyspepsia. The disease generally presents with acute abdomen and peritonitis signs since the complications of perforated diverticulitis are perforation, peritonitis, mesenteric abscess, hemorrhage, and intestinal obstruction. The etiopathogenesis of JD is predicted to be due to intestinal dyskinesia, dysfunction of intestinal motility, and increased intraluminal pressure, which causes diverticula on the mesenteric side of the small intestine (1,2). Although imaging studies can be helpful, complicated JD is mostly diagnosed perioperatively with surgery. Sub-diaphragmatic free air can be seen in chest X-Ray of complicated JD during radiological examination (2,5). Multi-detector row computed tomography (MDCT) with oral and intravenous contrast is the highly sensitive imaging method that can be a guide for presumptive diagnosis (6,7). MDCT can evaluate various complications, such as perforation with extraluminal air, inflammation and thickened intestinal wall, mesenteric abscess, heterogeneity of mesenteric fatty tissue around the jejunal intestinal loop (1,2). As in our case, CT revealed the dilatation in the jejunal ans, localized perforation with abscess and showed the heterogeneity due to the mesenteric inflammation.

Most of studies and case reports indicate that surgery is still the first choice in the treatment of complicated JD (1,2). As in our case, surgical treatment, resection, and anastomosis should be performed quickly, if the patient's general condition is suitable. Other surgical techniques such as diverticulectomy and capitonnage of the perforated diverticulum are recommended due to the high leak, sepsis, and death rate (1,5). For peridiverticular abscess, a non-surgical way with intravenous antibiotics and CT-guided drainage can be used in selected and the compatible patients with no symptoms of peritonitis and acute abdomen or sepsis (8). In our case, antibiotherapy and drainage were the first treatment choice. However, with the CT evaluation, which revealed inflammation in jejunal intestinal loops with abscess and occlusion in the mesenteric vascular vessel leading to the presumptive diagnosis of mesenteric ischemia; therefore, explorative laparotomy was performed.

Short bowel syndrome due to extensive resection should be kept in mind in multiple JD with extensive segment involvement, so the resection must be limited with the short segments that include perforated diverticulitis loops (1,5). Resection is not recommended in asymptomatic diverticula discovered during surgery or incidentally diagnosed by imaging methods (1,5).

In conclusion, jejunal diverticulitis which can be life-threatening with delayed diagnosis due to complications must be kept in mind as a cause of acute abdomen, especially in elderly patients. The surgeon should remember that extensive resection can cause short bowel syndrome; therefore, resection must be limited with the short segments, including perforated diverticulitis loops.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.554740

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):257-259

A Very Rare and Serious Complication of Pediatric Supracondylar Humerus Fracture Reduction: Pulseless Upper Extremity and Surgical Treatment

Pediatrik Suprakondiler Humerus Fraktür Redüksiyonun Çok Nadir ve Ciddi Bir Komplikasyonu: Nabızsız Üst Ekstremite ve Cerrahi Tedavisi

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ABSTRACT

In pediatric cases with supracondylar humerus fractures, one of the serious complications that may occur after closed reduction is vascular injuries. Since it can cause serious complications like extremity loss, is an important issue to be considered. There are different opinions in terms of conservative and surgical approach in the event of a pulse failure after reduction. It should be kept in mind that if there are conditions requiring surgical intervention such as coldness, paleness and pulse failure in the extremity, the repair of the damaged vessel segment may be insufficient and it may be necessary to change the entire damaged vessel segment to eliminate endothelial damage caused by traction. In this case report, a surgical approach to iatrogenic brachial artery injury is presented in a 5 years old child who has no radial and ulnar pulse after supracondylar humerus fracture.
Keywords: Humeral fractures; brachial artery; upper extremity; vascular system injuries.

ÖZ

Suprakondiler humerus fraktürü gelişen pediatrik olgularda oluşabilecek ciddi komplikasyonlardan biri kapalı redüksiyon sonrası oluşabilecek vasküler yaralanmalardır. Ekstremite kaybı gibi ciddi komplikasyonlara neden olabilecek olduğundan, bu durum üzerinde durulması gereken önemli bir konudur. Redüksiyon sonrası nabız yetersizliği durumunda konservatif ve cerrahi yaklaşım açısından farklı görüşler vardır. Ekstremitede soğukluk, solukluk ve nabız yetmezliği gibi cerrahi müdahale gerektiren durumlar varsa, hasarlı damar segmentinin onarımının yetersiz olabileceği, traksiyon nedeniyle oluşabilecek olan endotel hasarını ortadan kaldırmak için tüm hasarlı damar segmentinin değiştirilmesi gerekebileceği akılda tutulmalıdır. Bu olgu sunumunda, suprakondiler humerus kırığı sonrası radial ve ulnar nabzı olmayan 5 yaşındaki bir çocukta iyatrojenik brakiyal arter hasarına cerrahi yaklaşım sunulmaktadır.
Anahtar kelimeler: Humerus kırığı; brakial arter; üst ekstremite; vasküler sistem yaralanmaları.

INTRODUCTION

Supracondylar humerus fractures are the most common fractures in children under 7 years of age and require the most frequent surgery among pediatric traumas (1). The frequency of vascular injury after supracondylar fracture in children is 12% (2). To determine the approach in cases of vascular injury; The color of the limb, heat and the condition of the pulse are important. A conservative approach is preferred in some cases of vascular injury, and in some cases early aggressive surgical interventions may prevent loss of limb or prevent long-term volkmann ischemic contracture as a complication (3). In this case report, we discussed the importance of intervention to vascular injury after supracondylar fracture reduction.

CASE REPORT

A five-year-old male patient was admitted to our emergency room with complaints of pain and swelling of the left arm. At radiogram, supracondylar fractures were

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Geliş Tarihi / Received : 17.04.2019
Kabul Tarihi / Accepted : 04.11.2019
Çevrimiçi Yayın Tarihi / Available Online : 11.11.2019

diagnosed by orthopedics (Figure 1). And closed reduction and fixation was performed. There were no radial and ulnar pulses after closed reduction. The hand was slightly cold and pale compared to the other hand. Monophasic flow was detected in arterial doppler ultrasonography. Vascular surgical intervention was decided. Brachial artery exploration was performed in the patient who does not have radial and ulnar pulses. The 1.5 cm segment was resected and embolectomy and end-to-end anastomosis was performed. Patient who could not receive postoperative radial and ulnar pulses had a monophasic flow seen as a result of Doppler USG and the patient was operated again. The patient underwent re-embolectomy. It was seen that there were transverse multiple lacerations involving fibrin on the endothelial tissue due to traction. Approximately 4 cm of the brachial artery was resected (Figure 2). And the saphenous vein graft interposition was performed until the undamaged segment was reached. Radial and ulnar pulses were available after the operation. The patient was admitted to the intensive care unit without any complications. Heparin infusion continued for the first 24 hours. Radial and ulnar pulses are palpable in the postoperative period. The patient was discharged on the 4th postoperative day.

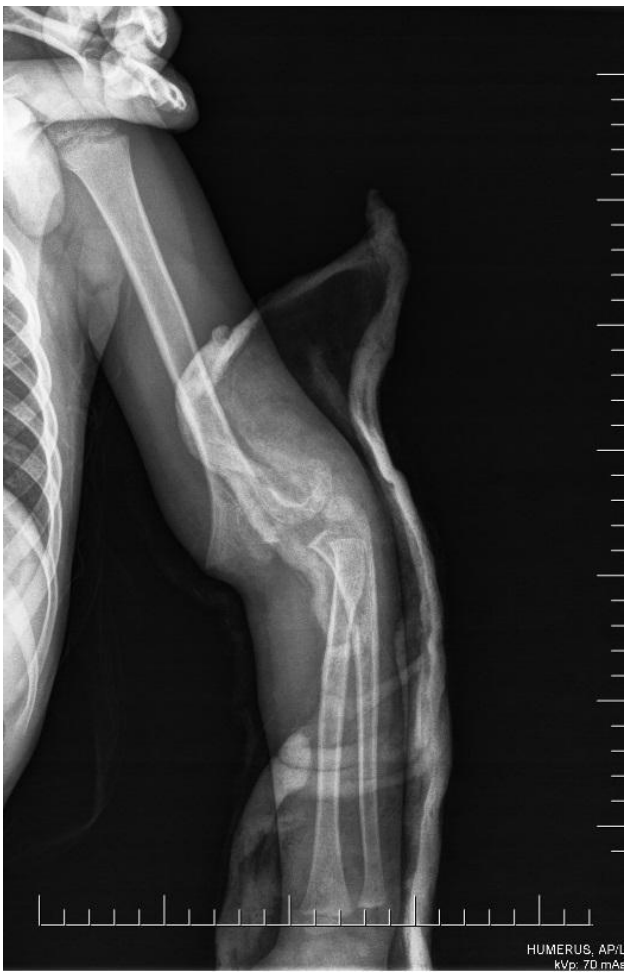

Figure 1. X-ray image of the supracondular humerus fracture

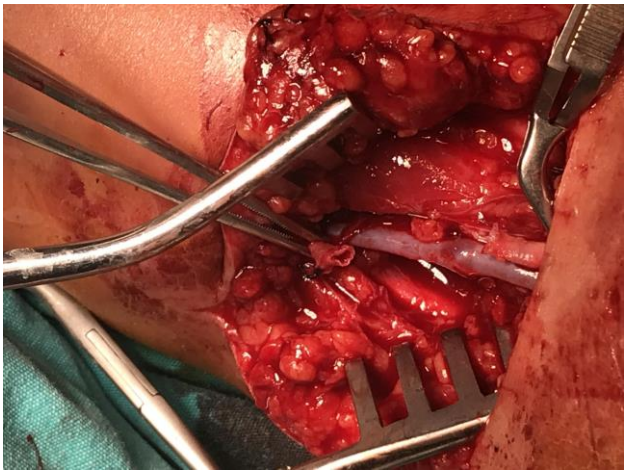

Figure 2. Intraoperative view of the brachial artery lumen after resection of the damaged brachial artery segment

DISCUSSION

Supracondylar humerus fractures are common traumas in children. Of these children, 2.6% don't have pulses on radial and ulnar artery (4). Surgical exploration is usually recommended in the presence of cold and pale hands in the absence of radial pulse (5). There is also an indication for emergency surgical intervention in cases of poor perfusion and severe circulatory disorders (6). Treatment planning should be performed in patients with circulatory failure after reduction, considering thrombosis, vascular spasm, partial tear, as well as the degree of traction applied to the vessel endothelial wall.

It is reported that brachial artery injury is mostly seen in fractures with posterolateral separation. In supracondylar humerus fractures, arterial injury may be spasm, embolism, thrombosis, intimal tear, laceration and pseudoaneurysm. If the circulation cannot be restored after fracture reduction, open reduction internal fixation and brachial artery exploration are performed. If the patient has cyanotic and cold hands, emergency surgical intervention should be planned. Firstly, reduction should be done in the emergency department. Elbow hyperflexion that compresses the brachial artery more in the emergency department should be avoided. If there is no improvement in vascular status despite reduction, preparation for open surgery and revascularization is required. Often perfusion is restored following the necessary reduction and nailing. Although the hand is warm, pink and capillary filling, radial pulse may not be obtained. In this case, there are different opinions about the approach to the patient. However, close follow-up is generally recommended in such patients without immediate vascular surgery. There is a significant relationship between the degree of separation and vascular injury.

One of the issues discussed in the treatment is that the fracture should be reduced and stabilized as soon as possible (7). There is also agreement that surgery for vascular injury should be performed for patients with impaired circulatory limbs after reduction. The real discussion continues on patients with no pulse after reduction but good circulation in the distal extremity. There are several different trends. In order to eliminate the possibility of vascular injury after reduction, despite the urgency of urgent surgery for vascular injury; immediate reduction and then close follow-up should be applied.

There is no consensus reached for the methods that should be used to diagnose vascular injuries. Interventional (angiography) and non-invasive (MR angiography, Doppler USG, color Doppler USG) imaging methods are used in this regard (8). There are some authors who recommend that interventional methods such as angiography should be performed against those who say that non-invasive methods are sufficient for diagnosis. Pre-operative routine use of angiography is not recommended by many specialists because of the allergic reaction to the contrast agent, its reduction and delay in vascular repair. However, it can be used to determine the site of injury and to plan the surgery in patients who will undergo vascular repair.

Both invasive and non-invasive methods are available in vascular lesion research. Angiography is the diagnostic test that gives us the strongest benefit. In addition to angiography, which is an invasive procedure, Doppler and magnetic resonance imaging is also a noninvasive test. Doppler ultrasonography is recommended as the first test for any vascular injury suspicion and is considered to be sufficiently useful for the assessment of arterial patency. If necessary, or in cases where ultrasonography is inadequate, angiography can be used to make a definitive diagnosis and decide on the intervention. However, since it is an invasive procedure and requires a specialist team, computed tomographic angiography is a more common and safe method.

In the light of the present findings, we believe that it is sufficient to perform fracture reduction and stabilization immediately after tight fracture monitoring in patients who do not have a circulatory disorder despite the absence of pulse at the distal extremity after fracture. We suggest surgery for vascular injury in cases of circulatory disorders in the extremities, persistent pain or impaired neurological examination. In such a case, the embolectomy performed on the thrombotic segment is insufficient for circulation and the damaged segment must be replaced.

Informed Consent: Informed consent was obtained from patient about case presentation.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.639211

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):260-262

Fatal Neutropenic Enterocolitis Following Methotrexate Overdose: A Case Report

Yüksek Doz Metotreksat Alımı Sonrası Gelişen Fatal Nötropenik Enterokolit: Olgu Sunumu

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ABSTRACT

Methotrexate, a folic acid antagonist, is widely used in the treatment of neoplasms in addition to diseases such as psoriasis and rheumatoid arthritis. Although well tolerated under normal conditions, the use of more than the recommended doses may cause life-threatening toxicities. Toxicity due to high doses of methotrexate is manifested by bone marrow inhibition, gastrointestinal mucosal damage and pancytopenia. Most cases result from overdose. However, serious adverse events that result in mortality, in particular those of mixing medication in elderly patients, are rare. Herein, we present the case of a 72-year-old man who admitted to the emergency department with painful oral ulcers, inability to swallow and a general impaired condition, and died of sepsis after developing neutropenic enterocolitis following a fever and neutropenia.
Keywords: Methotrexate; overdose; pancytopenia; neutropenic enterocolitis.

ÖZ

Bir folik asit antagonisti olan metotreksat, psoriazis ve romatoid artrit gibi hastalıklara ek olarak, neoplazmaların tedavisinde yaygın olarak kullanılır. Normal koşullarda iyi tolere edilse de önerilen dozlardan fazla kullanılması hayatı tehdit eden toksikasyonlara neden olabilir. Yüksek doz metotreksat'a bağlı toksisite, kemik iliği inhibisyonu, gastrointestinal mukozal hasar ve pansitopeni ortaya çıkabilir. Çoğu durumda doz aşımı sonucu ortaya çıkar. Bununla birlikte, özellikle yaşlı hastalardaki ilaçları karıştırmak gibi, ölümcül sonuçlanan ciddi yan etkiler daha nadirdir. Burada, acil servise ağrılı oral ülser, yutkunma bozukluğu ve genel durum bozukluğu ile başvuran, ateş ve nötropeninin ardından nötropenik enterokolit geliştikten sonra sepsisten ölen 72 yaşında bir erkek olguyu sunuyoruz.
Anahtar kelimeler: Metotreksat; aşırı doz; pansitopeni; nötropenik enterokolit.

INTRODUCTION

Methotrexate (MTX) is a folic acid antagonist with antiproliferative effect used in high doses in the treatment of malignancies and in low doses in the treatment of chronic inflammatory diseases such as psoriasis and rheumatoid arthritis (RA) (1). Methotrexate particularly affects rapidly proliferating cells, such as bone marrow and mucosa. As a result, its side effects include myelosuppression, mucositis and hepatic and tubular necrosis (2,3). One of the most common causes of MTX intoxication stems from incorrect application in the amount and range of doses (4). Some errors may occur in the use of MTX, especially in the elderly and in patients with multiple drug intake. One of the dreaded complications following neutropenia is neutropenic enterocolitis with its high mortality. Here, we present a case of neutropenia and neutropenic enterocolitis admitted with a generally impaired condition, difficulty in swallowing, widespread oral mucositis and a maculopapular rash on the trunk which, according to a detailed drug interrogation, had developed as a result of mistakenly using a high dose of methotrexate.

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Geliş Tarihi / Received : 28.10.2019
Kabul Tarihi / Accepted : 06.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 11.12.2019

CASE REPORT

A 72-year-old male patient was admitted to the emergency department having complaints of fatigue, malaise, burning in the mouth and sore throat for approximately five days. Upon physical examination, his general condition was moderate and he was conscious and alert, orientated and cooperative. His temperature was 36.9 °C, pulse 130/min, blood pressure 130/100 mmHg, respiratory rate 20/min, and oxygen saturation 94%. The patient had signs of dehydration due to lack of oral intake and white plaques compatible with candida infection were seen on the tongue and hard palate mucosa. The oropharynx was hyperemic and he was unable to swallow because of oral mucosal pain. The patient had a diffuse maculopapular rash on his back, neck and extremities, with no other findings upon pathological examination. His history showed no chronic disease other than RA. Laboratory tests revealed white cell count 800/uL, neutrophil 360/uL, hemoglobin 12.5 g/dL, hematocrit 35.9%, platelet 108000/uL, C-reactive protein 44.8 mg/dL, urea 71 mg/dL, creatinine 0.93 mg/dL and albumin 3.21 g/dL. He was admitted to the Infectious Diseases Department with preliminary diagnosis of neutropenic rash etiology and candida mucositis. The patient had a fever of 38.5 °C on the first day of hospitalization and after cultures were taken, fluconazole 400 mg / day was started intravenously. On the second day of hospitalization, the patient complained of severe abdominal pain and black stools; air-fluid levels were seen in the patient's erect radiography of the abdomen. Abdominal ultrasonography was performed and no pathology was detected except for a hydropic sac and intestinal wall thickness. Upon calculating the glomerular filtration rate, meropenem, teicoplanin and metronidazole were added to the treatment plan for neutropenic enterocolitis with a preliminary diagnosis of neutropenia. Stool microscopy showed multiple leukocytes and erythrocytes, no signs of parasites, and was negative for clostridium toxin A-B. Hematological consultation was made concerning the white cell count of 300/uL, neutrophil count of 80/uL and platelet count of 19000/uL. When the patient and his medications were examined in detail to discover the cause of the neutropenia, it was learned that the MTX report was prepared seven months previously and that the patient had been taking this medication intermittently. Finally, when the joint pain did not pass, he was mistakenly administered MTX at 15 mg/day IM for 7-10 days. When it was understood that the cause of neutropenia was MTX, irradiated-platelet replacement and granulocyte-colony stimulating factor were started. On the fourth day of treatment, the patient's general condition deteriorated and consciousness was impaired. The patient was taken to intensive care and colistin (2 × 150 mg IV) was added to his current treatment because a multi-drug resistant *Acinetobacter* spp was detected in his blood cultures. On the seventh day of hospitalization, he died due to sepsis-associated DIC. Consent was obtained from the patient's relatives for the case report.

DISCUSSION

Methotrexate is one of the first drugs of choice for the treatment of rheumatoid arthritis, an autoimmune systemic disease. Even in low dose therapy, hematologic toxicity, gastrointestinal mucositis, pulmonary symptoms, hepatotoxicity, acute renal failure and skin erythema can be seen (3). Skin ulcers are considered as early signs of systemic toxicity. Mucositis is usually occurs within 3-7 days, and a few days later there is a decrease in the number of granulocytes and platelets. More severe toxicity findings such as deep neutropenia, neutropenic enterocolitis and sepsis similar to the example of our patient carry high morbidity and mortality. In a review by Gutierrez-Urena et al. (5), 1-2% of RA patients receiving MTX therapy had clinically significant pancytopenia.

Neutropenic enterocolitis is a complication of immunosuppressive drugs. This clinical syndrome is characterized by transmural inflammation of the small and large intestines, mainly the cecum (6). Ultrasonography reveals intestinal wall thickness, a dilated cecum, an inflammatory mass in the right lower quadrant and pericaecal fluid. Although computed tomography (CT) is the most commonly used method, in our patient, CT could not be performed because of his high creatinine level and generally deteriorated condition, and thus, neutropenic enterocolitis was diagnosed clinically. On the fourth day of hospitalization the patient was admitted to the intensive care unit due to development of impaired consciousness and renal failure and he died on the seventh day.

In the literature, there are numerous case studies and publications on MTX toxicity. In some publications, gastrointestinal toxicity has been found to develop from low doses of MTX. Tsukada et al. (7) reported pancytopenia and gastrointestinal mucosal necrosis in a patient receiving 8 mg / week of MTX. Misuse of the dosage range was reported by Peker et al. (8) with a case of GI bleeding and pancytopenia in a patient using MTX daily instead of weekly. The use of the wrong drug is one of the rarer causes of overdose side effects. Bidaki et al. (9) published a report of two geriatric patients mistakenly given MTX instead of digoxin at the pharmacy, in which one patient died due to development of toxicity. Publications on MTX toxicity are often case reports of oral overdose or mistaken use in place of another drug (10). Cases like ours, where daily parenteral administration of MTX as a presumed analgesic and development of severe neutropenia and neutropenic enterocolitis ending in patient death, are less frequently reported.

In conclusion, although it is well tolerated under normal conditions, the use of more than the recommended doses may cause life-threatening toxicities. In patients with RA, MTX toxicity should be kept in mind when symptoms such as pancytopenia, oral ulcers and GI problems occur. When considering starting MTX treatment in the geriatric patient group in particular, it is important that all healthcare workers be extremely careful about drug compliance and follow-up.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.653558

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):263-264

Hepatocellular Carcinoma with Increased AFP Levels and Extrahepatic Manifestation after Liver Transplantation: A Case of Late-Onset Recurrence

Karaciğer Nakli Sonrası AFP Yüksekliği ve Extrahepatik Tutulum Saptanan Hepatoselüler Karsinoma: Gecikmiş Rekürensli bir Olgu Sunumu

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ABSTRACT

Liver transplantation is the best treatment modality in patients with hepatocellular carcinoma. The major concern after liver transplantation for hepatocellular carcinoma treatment is recurrence, because it's the most important factor for the long term survival. There are two forms of recurrence; early-onset (within 2 years of liver transplantation) and late-onset (after 2 years of liver transplantation). A lot of factors have been reported in the literature to foresee recurrence after liver transplantation and one of them is alpha-fetoprotein. Many studies have shown that high levels of pre-transplant alpha-fetoprotein is related to early-onset recurrence and worse outcomes in the long term. In this case report, we report a case of late-onset recurrence, despite having high levels of pre-transplant alpha-fetoprotein in contrary to the literature, and still survive with a high quality of life 6 years after transplantation.
Keywords: Hepatocellular carcinoma; alpha-fetoprotein; recurrence.

ÖZ

Hepatoselüler karsinoma tedavisinde en iyi tedavi metodu karaciğer transplantasyonudur. Hepatoselüler karsinoma tedavisi için uygulanan karaciğer transplantasyonu sonrası en büyük endişe rekürenstir, çünkü uzun dönem sağkalım için en önemli faktördür. Rekürens erken (karaciğer transplantasyonu sonrası 2 yıl içinde) ve geç (karaciğer transplantasyonundan 2 yıl sonra) olmak üzere iki çeşittir. Literatürde karaciğer transplantasyonu sonrası rekürensi öngörmek için pek çok faktör öne sürülmüştür ve bunlardan biri de alfa-feto proteindir. Pek çok çalışma, transplantasyon öncesi yüksek alfa-feto protein düzeylerinin erken rekürens ve uzun dönemde kötü sonuçlar ile ilişkili olduğunu göstermiştir. Bu olgu sunumunda, literatürde bildirilenin aksine transplantasyon öncesi yüksek alfa-fetoprotein düzeylerine sahip olmasına rağmen geç rekürens gösteren ve transplantasyondan 6 yıl sonra hala yüksek bir yaşam kalitesi ile sağkalım gösteren bir vaka bildiriyoruz.
Anahtar kelimeler: Hepatoselüler karsinoma; alfa-fetoprotein; rekürens.

INTRODUCTION

Liver transplantation (LT) is the best treatment option for hepatocellular carcinoma (HCC) in select cases. LT is usually performed according to Milan Criteria, but the recurrence can be seen up to 15% of cases. Recurrence is the biggest concern after LT because it's the most important prognostic factor. There are two forms of recurrence; (1) early-onset (<2 years after LT) and late-onset (>2 years after LT). Serum markers are useful to determine and to foresee recurrence after LT (1).

Alfa-fetoprotein (AFP) is the most used serum marker for HCC and it can also be used to determine recurrence after LT. There is a correlation between pre-transplant high AFP levels and post-transplant recurrence (2).

CASE REPORT

A 64-year-old male patient with the diagnosis of chronic viral hepatitis-B in 2007 and on routine follow-up under entecavir treatment. During routine follow-up in 2011, abdominal ultrasound showed two focal lesions in the right lobe of the liver and

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Geliş Tarihi / Received : 01.12.2019
Kabul Tarihi / Accepted : 09.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 20.12.2019

dynamic liver magnetic resonance imaging (MRI) confirmed the diagnosis of HCC in segment-7 (2 cm) and segment-8 (1.5 cm). Radiofrequency ablation (RFA) has been performed separately. Three months after the procedure both lesions were progressed up to 5 cm and new lesions were found in the right lobe of the liver. Trans-arterial chemoembolization (TACE) was performed and the patient had LT in 2012 despite being out of the Milan Criteria and with an AFP level of 3295 IU/ml. Three months after LT, AFP levels were 5 IU/ml.

On routine follow-up in 2015, a sudden increase in AFP levels (145 IU/ml) was encountered but no lesions were detected on the MRI. AFP levels kept increasing and no lesions were detected on routine trimonthly MRI scans. AFP levels reached up to 2049 IU/ml in 2017, therefore the patient diagnosed as recurrence and started on Sorafenib treatment. 6 months after initiation of the therapy, AFP levels kept rising up to 7724 IU/ml and MRI showed pre-caval 20x13mm and pre-aortic 20x18mm HCC lesions (Figure 1). Positron emission tomography (PET-CT) showed a pre-caval lymph node (SUVmax:4) and a pre-aortic lymph node (SUVmax:6.7) consistent with HCC (Figure 2). The patient started on regorafenib treatment. A signed informed consent form was obtained from the patient for this case presentation.

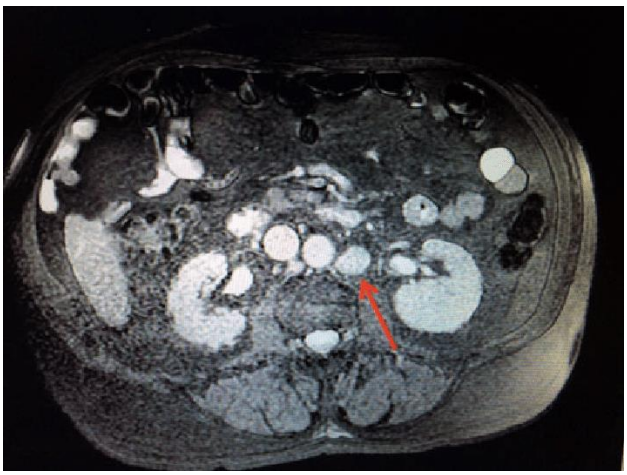

Figure 1. Para-aortic lymph node in magnetic resonance imaging

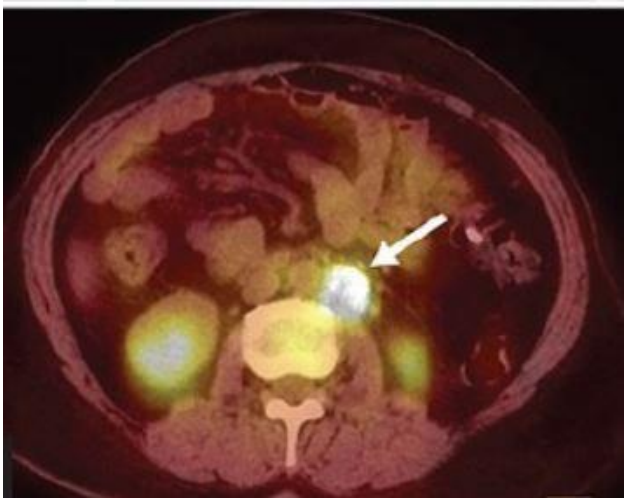

Figure 2. Para-aortic lymph node in positron emission tomography

DISCUSSION

We presented a case of late-onset recurrence after LT, despite having pre-transplant high levels of AFP and detected in a rare localization. Pre-transplant high levels of AFP (>400 IU/ml) were identified as a high-risk factor for recurrence after LT (3). In our case, pre-transplant AFP was 3295 IU/ml but we did not encounter early-onset recurrence. Microvascular invasion, large tumor diameter, high AFP levels, and poor histological differentiation are defined as high risk factors for recurrence after LT (4). Despite having a large tumor diameter and high AFP levels, the patient had a long-term survival with a late-onset recurrence. This can be explained with tumor biology and heterogenicity. The clinical course of HCC may vary significantly. Multifocal mutations can be seen even in a single tumor and tumor doubling time may vary between tumor nodules (5). It should also be noted that the tumor microenvironment has high inflammatory properties and may cause changes in tumor behavior (6).

The liver, lungs, and bones are the most common sites of recurrence after LT respectively (7). In our case, we found metastatic lymph nodes in a very rare localization. We suggest that in suspected cases of late-onset recurrence, rare localizations for the tumor should be suspected and PET-CT can be used to strengthen the diagnosis.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.645577

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):265-267

Pyoderma Gangrenosum Triggered by Acute Ischemia of Lower Extremity: A Case Report

Alt Ekstremitenin Akut İskemisi ile Tetiklenen Pyoderma Gangrenosum: Olgu Sunumu

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ABSTRACT

Pyoderma gangrenosum is a very rare condition of unclear etiology with an estimated incidence of 3 to 10 cases per million people per year. We report a case of pyoderma gangrenosum triggered by acute ischemia of lower extremity without a prior history. Seventy-seven years old female patient was admitted to the emergency department with necrosis on the anterior side of her left limb. Digital subtraction arteriography revealed total occlusion of the left common femoral artery for which thrombectomy under local anesthesia was performed successfully. The necrotic area was debrided and biopsies were obtained. Pathological examination revealed pyoderma gangrenosum and steroid treatment was began. The patient was discharged on the 10th postoperative day with prednisone 48 mg per day for the following 30 days. During the management of ischemic peripheral artery disease patients with persistent skin findings, pyoderma gangrenosum should be in the list of differential diagnoses.
Keywords: Pyoderma gangrenosum; risk factors; wound healing.

ÖZ

Piyoderma gangrenozum, tahmini insidansı yılda milyon kişi başına 3 ila 10 vaka olan, etiyolojisi açıklanamamış çok nadir görülen bir durumdur. Alt ekstremitenin akut iskemisi ile tetiklenen, daha önce öyküsü olmayan bir pyoderma gangrenozum vakası bildiriyoruz. Yetmiş yedi yaşında kadın hasta acil servise sol alt ekstremite anteriyor yüzde nekrotik yara ile başvurdu. Digital subtraction arteriography ile total tıkalı olduğu saptanan sol ana femoral artere lokal anestezi altında başarılı bir şekilde thrombektomi uygulandı. Nekrotik alan debride edildi ve biyopsiler alındı. Patolojik incelemede pyoderma gangrenozum saptandı ve steroid tedavisi başlandı. Hasta postoperative 10. günde 30 gün boyunca günlük 48 mg prednisone tedavisi ile taburcu edildi. Sebat eden cilt lezyonlu iskemik perifer arter hastalığı olan hastaların tedavisi sırasında, piyoderma gangrenozum ayırıcı tanılar listesinde bulunmalıdır.
Anahtar kelimeler: Piyoderma gangrenozum; risk faktörleri; yara iyileşmesi.

INTRODUCTION

Pyoderma gangrenosum (PG) is a very rare condition with an unclear etiology with an estimated incidence of 3 to 10 cases per million people per year and characterized by aseptic dense infiltration of neutrophils into the epidermis, dermis or both (1). It may be associated with systemic diseases (2). The diagnosis is made by excluding other causes of cutaneous ulcerations with similar appearance including infection, malignancy, vasculitis, collagen vascular diseases, diabetes, and trauma. Pathergy based new ulcerations may be seen after trauma or injury to the skin. We report a case with PG triggered by acute ischemia of lower extremity without a prior history.

CASE REPORT

Seventy-seven years old female patient was admitted to emergency department with necrosis on the anterior side of her left limb. Medical history revealed prominent pain for the last 20 days and necrosis was first seen 2 weeks ago. Initial physical examination revealed absence of femoral, popliteal and distal pulses with motor deficit

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Geliş Tarihi / Received : 11.11.2019
Kabul Tarihi / Accepted : 23.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 27.12.2019

on the left limb. Right limb arterial pulses were palpable. Digital subtraction arteriography revealed total occlusion of the left common femoral artery. Laboratory findings were normal. The patient had sinusal cardiac rhythm on electrocardiography. Transthoracic echocardiography findings were normal. After taking patient's informed consent for both operation and publishing, left common femoral artery thrombectomy under local anesthesia was performed sucessfully. Massive hemorrhage occurred from the necrotic site on the first postoperative day; surgical haemostasis was done emergently, necrotic area was debrided and tissue biopsies were obtained. The patient was consulted with plastic and reconstructive surgery department. Postoperative medical treatment included antithrombotic and anticoagulant therapies. The wound was dressed postoperatively with Chlorhexidine Acetate BP 0.5% in white soft paraffin BP. The debridement material was macroscopically brown in color with partial necrotic appearance. On microscopic examination, the epidermis was ulcerated; dense inflammatory infiltration and coagulation necrosis were observed in the dermis and subcutaneous tissue. Inflammatory infiltration consisted of neutrophils, lymphocytes, and histiocytes. The biopsy specimen was evaluated in accordance with PG (Figure 1). Prednisone 48 mg/daily was added to the treatment. The patient was discharged on the 10th postoperative day and was treated with prednisone 48 mg per day for the following 30 days (Figure 2).

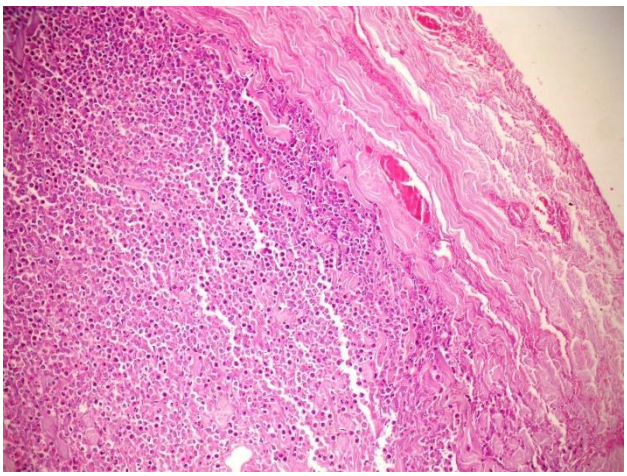

Figure 1. Ulcerated epidermis, diffuse infiltrate of neutrophils, lymphocytes, and histiocytes in the dermis. HEx200

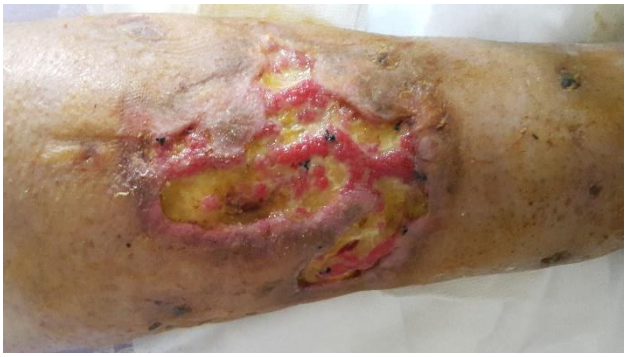

Figure 2. Postoperative first-month control

DISCUSSION

PG is an uncommon, ulcerative skin condition of unclear etiology. The disease was first described in 1930 with unusual skin eruption (3). There are several subtypes of PG according to lesions such as bullous (atypical) PG, pustular PG, vegetative PG and ulcerative (classic) PG which represents the majority of cases like our patient (1). PG is a diagnosis of exclusion. Simsek et al. (4) well described differential diagnosis of the disease and stressed he need to follow a thorough diagnostic evaluation including careful data collection of medical history, awareness of characteristic features on physical examination, obtaining a skin biopsy for not only histopathological purposes but also for tissue culture, and performing laboratory investigations aiming to rule out the diagnosis that mimic PG. Paralel to Simsek et al. (4), Neill et al. (5) reported to challenges to diagnosis and described "5p" for aiding to reach conclusion. Misdiagnosis of skin ulcers as PG can occur up to 10% according to the literature (6,7). In our case, we thought that arterial occlusion triggered the process and the wound was due to ischemia; but the biopsy results revealed the definitive diagnosis. Although varying degree (17%-74%) of associated diseases have been described in the literature (8) and the most commonly associated disorders were inflammatory bowel disease arthropathies and hematologic disorders such as paraproteinemia (9-11), our case did not have any associated diseases.

There is a lack of any definitive guidelines for the treatment of PG. Usually, a combination of topical and systemic suppression of inflammatory process and wound care were suggested for optimizing healing. Treatment options can be summarized in 3 topics; 1) Wounds should be cared gently to promote a moist environment and a non-adherent dressing should be preferred. Due to pathergy risk, surgery for wound management in PG is in the grey zone. In our case, we preferred Chlorhexidine Acetate BP 0.5% in white soft paraffin BP. 2) Medical treatment options are local steroids, local calcineurin inhibitors, systemic steroids, intravenous immunoglobulin, systemic cyclosporine. Basically, lesion severity and resistance to recovery force clinician to choose a treatment option. Lack of efficient data and guideline for treatment is challenging the clinicians. We preferred systemic prednisone 48 mg/daily tapered and stopped at the30th day and complete healing achieved. 3) Pain management is required for most of the patients. Usually, pain may improve with treatment and some patients may require narcotic analgesics.

Bennett et al. (12) reported complete remission at 11.5±11.1 months in patients with classic PG and 9±13.7 months in patients with bullous PG. Saracino et. al. (13) reported complete ulcer healing within 6 months. But this study had a limitation with follow-up. Only 46% of the patients were available to follow up for 6 months and 6 of 12 patients had complete ulcer healing in this study.

CONCLUSION

PG represents a diagnostic challenge which requires many specialists to be involved. During the management of ischemic peripheral artery disease patients with persistent skin findings, PG should be in the list of differential diagnosis.

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Olgu Sunumu / Case Report
doi: 10.18678/dtfd.656125

Düzce Tıp Fakültesi Dergisi / Duzce Medical Journal
2019;21(3):268-270

Gastric Squamous Cell Carcinoma: A Case Report

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ABSTRACT

Gastric squamous cell carcinoma is rarely seen and affects mostly elder patients. A 78-year-old woman presented with nausea, vomiting, weight loss, and epigastric pain. There was an ulcero-vegetative mass in the posterior area from the large curvature to the antrum in the endoscopic examination. The gastroesophageal junction and cardia were also normal. We performed a diagnostic endoscopic biopsy. Histopathologically, it was composed of atypical squamous cells displaying infiltrating solid nests in a desmoplastic stroma. Immunohistochemically, the neoplastic cells also showed positivity for p40 and p63 and negativity for CEA. Besides, there was no radiological evidence of metastasis from other organs. We herein presented a case of gastric squamous cell carcinoma and discussed its clinical and morphological features with the literature.
Keywords: Stomach; squamous cell; carcinoma.

ÖZ

Gastrik skuamöz hücreli karsinom nadir görülür ve çoğunlukla yaşlı bireyleri etkiler. Yetmiş sekiz yaşında kadın hasta bulantı, kusma, kilo kaybı ve epigastrik ağrı şikayeti ile başvurmuştur. Endoskopik incelemede posterior bölgede büyük kurvaturdan antrum'a kadar ülsero vejetatif bir kitle saptanmıştır. Özofagogastrik bileşke ve kardiya ayrıca normal olarak izlenmiştir. Hastaya tanı amaçlı endoskopik biyopsi yapılmıştır. Histopatolojik olarak, tümörün desmoplastik bir stromada infiltre yuvalar oluşturan atipik skuamöz hücrelerden meydana geldiği görülmüştür. İmmünohistokimyasal olarak neoplastik hücrelerde p40 ve p63 ile pozitiflik saptanmış olup CEA ile immünekspresyon izlenmemiştir. Başka bir organ kaynaklı buraya metastazı düşündürecek radyolojik bulgu da saptanmamıştır. Burada bir gastrik skuamöz hücreli karsinom vakası sunulmuş olup klinik ve morfolojik özellikleri literatür eşliğinde tartışılmıştır.
Anahtar kelimeler: Mide; skuamöz hücre; karsinom.

INTRODUCTION

Malignant epithelial tumors of stomach are categorized as adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma, undifferentiated carcinoma, gastroblastoma, neuroendocrine tumor, neuroendocrine carcinoma, and mixed neuroendocrine/non-neuroendocrine carcinoma according to WHO 2019 classification (1). Gastric squamous cell carcinoma that is a rare cancer accounts for 0.04-0.07% of all gastric malignant epithelial tumors (2). It was described for the first time in 1895 by Rörig et al (3). We herein report a case of gastric squamous cell carcinoma and discussed its clinical and morphological features with regard to the literature.

CASE REPORT

A 78-year-old woman presented with nausea, vomiting, weight loss, and epigastric pain. She had gone to a special hospital for treatment of weakness in 3 months ago.

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Geliş Tarihi / Received : 06.12.2019
Kabul Tarihi / Accepted : 23.12.2019
Çevrimiçi Yayın Tarihi / Available Online : 27.12.2019

There was no family history. She was taking indapamide for hypertension. The patient's complete blood count was consistent with anemia (Hb: 6 g/dl). Other routine abnormal biochemical values were direct-bilirubin: 0.26 mg/dl, indirect-bilirubin: 1.54 mg/dl, urea: 44.47 mg/dl, BUN: 21.18 mg/dl, albumin: 3.22 g/dl and LDH: 310 U/L. Ultrasonographically, there was thickening in the large curvature wall of the stomach and lymphadenopathy (16x11 mm) in adjacent adipose tissue. Contrast computed tomography of the stomach showed infiltrative wall thickening that was localized from the large curvature to the antrum, in addition to lymphadenopathies that were consistent with metastasis. Other organs and anatomical structures were within normal limits. In the endoscopic examination, there was a ulcero-vegetative mass in previously described localization (Figure 1). The gastroesophageal junction and cardia were also normal. We performed a diagnostic endoscopic biopsy. Histopathologically, it was composed of atypical squamous cells displaying infiltrating nests in a desmoplastic stroma. Histochemically, mucin production was absent. The neoplastic cells also immunohistochemically showed positivity for p40 and p63 and negativity for CEA (Figure 2-4). The lesion was diagnosed as squamous cell carcinoma. Three units of erythrocyte suspension were given for anemia. The patient was informed about his pathology and advised to undergo gastrectomy. Unfortunately, she went to another institution and we, therefore, lost to clinical follow-up.

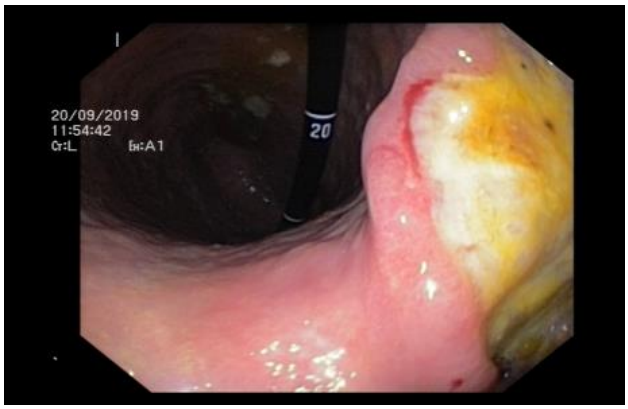

Figure 1. Endoscopic view of the tumor

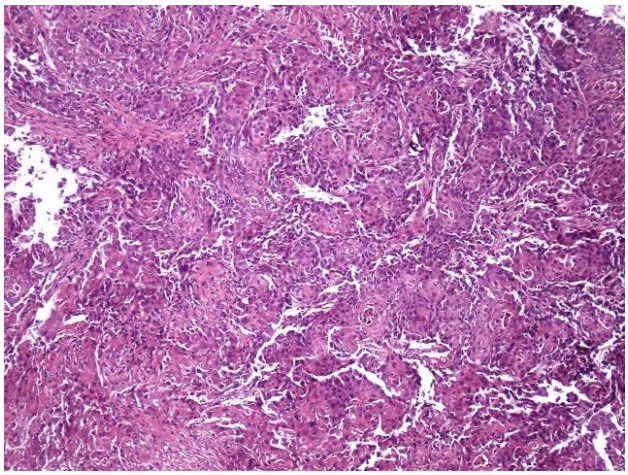

Figure 2. The tumor was consisted of squamoid nests in a desmoplastic stroma. There was no any glandular component (H&E, x100).

DISCUSSION

Gastric malignant tumors which constitute about 5.7% of all malignant tumors are the fifth common neoplasm after those of lung, breast, prostate, and thyroid in Turkey. Although gastric adenocarcinomas are common subtypes, gastric squamous cell carcinomas constitute less than 1%. It is most commonly seen in descending order in the upper, lower and middle gastric regions (1). It occurs predominantly in men (4). The clinical symptoms are similar to other carcinomas of the stomach (1). Diagnostic criteria that were first reported by Parks RE (5) as follows: (i) not originated from the cardia, (ii) not extend from the esophagus, and (iii) no evidence of metastatic squamous cell carcinoma from other organs or tissue. And then, the Japanese Gastric Cancer Association (6) stated that all tumor cells must be atypical squamous cells without any glandular differentiation and these cells must originate in the gastric mucosa.

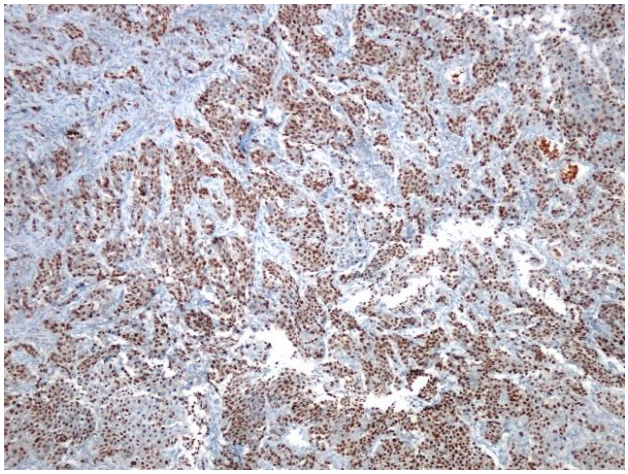

Figure 3. p63 immunopositivity in neoplastic cells (x100)

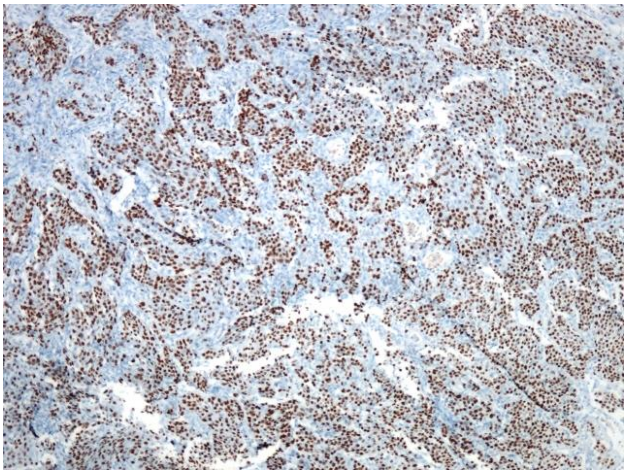

Figure 4. p40 immunopositivity in neoplastic cells (x100)

Molecular data are not available due to the rarity of this tumor. The etiology is completely unknown; however, positive smoking history is related to some cases (4). Viral carcinogenesis is controversial and any proven data has not been available in the literature (4). Zhou et al. (7) reported a patient with concurrent *H. pylori* gastritis and primary gastric squamous cell carcinoma. We could not comment on the presence of *H. pylori* since all of our samples consisted of tumoral tissues. Some authors stated that pluripotent stem cells displaying squamous metaplasia or ectopic squamous nests can be related to carcinogenesis (4). Macroscopic features are similar to other gastric cancers. Microscopic features are also the same as those of other organs such as the esophagus. Sufficient sampling and exclusion of metastasis history are important for the correct diagnosis. Although gastrectomy could not be performed, endoscopic and radiological findings suggest that the tumor may be primarily of gastric origin in the present case. CEA negativity also revealed that there was no other component in the samples of our case.

This tumor commonly presents at an advanced stage that is related to a poor outcome. Distant metastases occur primarily in the liver (1). Due to the lower frequency of this tumor, specific prognostic factors have not been reported so far. However, gastric squamous cell carcinoma is more aggressive compared with the same stage of gastric adenocarcinomas (8-10). Similar to gastric adenocarcinoma, the main treatment is surgery involving gastrectomy and lymph node resection. Adjuvant chemotherapy consisting of 5-fluorouracil, platin and taxane-based regimens can be given (11).

As a result, gastric squamous cell carcinoma is rarely seen. Esophageal tumoral infiltration and metastasis originated from other organs or tissue should be considered in the differential diagnosis.

Informed Consent: Written informed consent was obtained from the case.

Conflict of Interest: All the authors declare that there is no conflict of interest.

Financial Disclosure: The authors declared that there is no financial support.

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YAZARLARA BİLGİLENDİRME

BİLİMSEL SORUMLULUK

Bilimsel yayıncılık standartları açısından, gönderilecek makaleler, Uluslararası Tıbbi Dergi Editörler Kurulu (ICMJE), Dünya Tıbbi Editörler Birliği (WAME) ve Yayın Etik Kurulu (COPE) kriterlerine uygun olarak hazırlanmalıdır.

- Gönderilecek makalelerde araştırma ve yayın etiğine uyulması zorunludur. Makalelerin sorumluluğu yazarlarına aittir.
- Makalelerin daha önce hiç bir yerde yayınlanmamış ve/veya yayınlanmak üzere değerlendirme sürecinde olmaması gerekir.
- Değerlendirme sürecinin başlaması için makaleler, tüm yazarlar tarafından imzalanmış Telif Hakkı Devir Formu ile birlikte gönderilmelidir. Yazar sıralaması için Telif Hakkı Devir Formu'ndaki imza sırası dikkate alınır.
- Sorumlu yazar, tüm yazarlar adına makalenin son halinin sorumluluğunu taşır.

ETİK SORUMLULUK

- "İnsan" öğesini içeren tüm çalışmalarda Helsinki Deklerasyonu Prensipleri'ne (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/) uygunluk aranır. Bu tip çalışmalarda yazarların, GEREÇ VE YÖNTEMLER bölümünde çalışmayı bu prensiplere uygun olarak yaptıklarını, kurumlarının etik kurullarından onay ve çalışmaya katılmış insanlardan "bilgilendirilmiş olur" (informed consent) aldıklarını belirtmeleri gerekmektedir.
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- Olgu sunumlarında hastalardan "bilgilendirilmiş olur" (informed consent) alınmalıdır.
- Etik kurul onay bilgisi GEREÇ ve YÖNTEMLER bölümünde kurul adı, onay tarihi ve sayısı ile birlikte belirtilmelidir.
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- Yazarlar çalışma ile ilgili kişisel ve finansal tüm ilişkilerin bildirilmesinden sorumludur. Makalenin başvurusu ve/veya değerlendirmesi ile ilişkili herhangi bir çıkar çatışması olup olmadığının açıkça beyan edilmesi gerekmektedir.
- Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğundadır.

BAŞVURU DOSYALARI

Makaleler aşağıda belirtilen şekilde ayrı dosyalar halinde sisteme yüklenmelidir.

Telif Hakkı Devir Formu: Başvuru sırasında sistemden alınacak Telif Hakkı Devir Formu tüm yazarlar tarafından makaledeki yazar sıralamasına uygun şekilde imzalanmış olmalıdır.

Başvuru Mektubu: Makalenin türü, daha önce hiç bir yerde yayınlanmamış ve/veya yayınlanmak üzere değerlendirme sürecinde olmadığı, varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve bu kuruluşların yazarlarla olan ilişkileri (yoksa olmadığı) belirtilmelidir. Makalenin konusuyla ilgili olarak önerilen, yazarlarla ve kurumlarıyla ilgisi olmayan en az iki hakemin adları, akademik unvanları, kurumları, iletişim bilgileri ve e-posta adresleri yazılmalıdır. Editörlerin hakemleri seçme hakkı saklıdır.

Başlık Sayfası: Makalenin başlığını (Türkçe ve İngilizce), 40 karakteri geçmeyen kısa başlık, tüm yazarların adlarını, akademik unvanlarını, ORCID® numaralarını, kurumlarını, e-posta adreslerini ve ayrıca sorumlu yazarın adını, yazışma adresini, telefon numarasını, e-posta adresini içermelidir. Makale daha önce bilimsel bir toplantıda sunulmuş ise toplantı adı, tarihi ve yeri (yoksa sunulmadığı) belirtilmelidir.

Ana Metin: Makalenin başlığı (Türkçe ve İngilizce), 40 karakteri geçmeyen kısa başlık, Öz (Türkçe ve İngilizce), Anahtar kelimeler (Türkçe ve İngilizce), Ana Metin (gönderilen makalenin türüne uygun olarak bölümlere ayrılmış), Kaynaklar, Tablolar ve Şekil açıklamaları yer almalıdır.

Etik Kurul Onay Belgesi: Tüm araştırma makaleleri için Etik Kurul Onay Belgesi ayrı bir dosya olarak yüklenmelidir.

Not: Makalede şekil, resim veya fotoğraf varsa bunların da her biri ayrı birer dosya olarak yüklenmelidir.

MAKALE TÜRÜNE GÖRE METİNDE KULLANILMASI GEREKEN BÖLÜMLER

Araştırma Makalesi
ÖZ (Türkçe ve İngilizce), GİRİŞ, GEREÇ VE YÖNTEMLER, BULGULAR, TARTIŞMA, SONUÇ, KAYNAKLAR
ÖZ/ABSTRACT 200-250 kelime arasında olmalıdır.
ÖZ, "Amaç, Gereç ve Yöntemler, Bulgular, Sonuç" şeklinde yapılandırılmalıdır.
ABSTRACT, "Aim, Material and Methods, Results, Conclusion" şeklinde yapılandırılmalıdır.

Derleme (Sadece Davetli)
ÖZ (Türkçe ve İngilizce), GİRİŞ, Konu ile İlgili Alt Başlıklar, SONUÇ, KAYNAKLAR
ÖZ/ABSTRACT 150-200 kelime arasında olmalıdır.

Olgu Sunumu
ÖZ (Türkçe ve İngilizce), GİRİŞ, OLGU SUNUMU, TARTIŞMA, KAYNAKLAR
ÖZ/ABSTRACT 100-150 kelime arasında olmalıdır.

Diğer
Bu üç temel makale türü dışındaki (editöre mektup, editöryel yorum/tartışma vb.) yazıların hazırlanmasında da genel yazım kuralları geçerlidir. Bu tür yazılarda başlık ve öz bölümleri yoktur. Kaynak sayısı 5 ile sınırlıdır. İthaf olunan makale sayı ve tarih verilerek belirtilmelidir. Yazının sonunda yazarın ismi, kurumu ve adresi yer almalıdır. Mektuba cevap, editör veya makalenin yazarları tarafından, yine dergide yayınlanarak verilir.

YAZARLARA BİLGİLENDİRME

YAZIM KURALLARI
- Makaleler Microsoft Word® belgesi olarak hazırlanmalıdır.
- Sayfa kenarlarında 2,5 cm boşluk bırakılmalıdır.
- Sayfa numaraları sayfanın sağ alt köşesine yerleştirilmelidir.
- Tüm metinler 12 punto Times New Roman karakteri kullanılarak çift satır aralığı ile sola hizalanmış olarak yazılmalıdır.
- Türkçe makalelerde Türk Dil Kurumu'nun Türkçe sözlüğü (http://www.tdk.org.tr), ayrıca Türk Tıbbi Derneklerinin kendi alanlarına ait terimler sözlüğü esas alınmalıdır.

ANAHTAR KELİMELER
- Anahtar kelime sayısı en az 2 olmalı, kelimeler birbirlerinden noktalı virgül (;) ile ayrılmalıdır.
- Türkçe anahtar kelimeler Türkiye Bilim Terimleri (TBT)'ne (http://www.bilimterimleri.com), İngilizce anahtar kelimeler Medical Subject Headings (MESH)'e (http://www.nlm.nih.gov/mesh/MBrowser.html) uygun olarak verilmelidir.

İSTATİSTİKSEL YÖNTEMLER
- Tüm araştırma makaleleri biyoistatistik açıdan değerlendirilmeli ve uygun plan, analiz ve raporlama ile belirtilmelidir. Bu makalelerde, GEREÇ VE YÖNTEMLER bölümünün son alt başlığı "İstatistiksel Analiz" olmalıdır.
- Bu bölümde çalışmada kullanılan istatistiksel yöntemler ne amaçla kullanıldığı belirtilerek yazılmalı, istatistiksel analiz için kullanılan paket programlar ve sürümleri belirtilmelidir.
- p değerleri ondalık üç basamaklı (p=0,038; p=0,810 vb.) olarak verilmelidir.
- Makalelerin biyoistatistik açıdan uygunluğunun kontrolü için ek bilgi www.icmje.org adresinden temin edilebilir.

KISALTMALAR
- Terim ilk kullanıldığında parantez içinde kısaltmayla birlikte açık olarak yazılmalı ve tüm metin boyunca aynı kısaltma kullanılmalıdır.
- Uluslararası kullanılan kısaltmalar Bilimsel Yazım Kurallarına uygun şekilde kullanılmalıdır.

TABLOLAR VE ŞEKİLLER
- Metinde ilgili cümlenin sonunda (Tablo 1) ve/veya (Şekil 1) şeklinde belirtilmelidir.
- Tablolar (başlıklarıyla birlikte) ve şekiller (açıklamalarıyla birlikte) kaynaklardan sonra ve her biri ayrı bir sayfada olacak şekilde metnin sonuna eklenmelidir.
- Tablo başlıkları tablo üstünde (Tablo 1. Tablo başlığı), şekil açıklamaları ise şeklin altında (Şekil 1. Şekil açıklaması), ilk harfleri büyük olacak şekilde yazılmalıdır.
- Tablolarda ve şekillerde kısaltma veya sembol kullanılmış ise altında dipnot olarak açıklanmalıdır.
- Şekiller ve fotoğraflar, .png, .jpg vb. formatta ve en az 300 dpi çözünürlükte ayrı dosyalar halinde yüklenmelidir.
- Şekil ve fotoğraf alt yazıları, son tablonun olduğu sayfadan sonra, ayrı bir sayfada sırasıyla verilmelidir.
- Daha önce basılmış şekil, resim, tablo, grafik vb. kullanılmış ise yazılı izin alınmalı ve açıklama olarak belirtilmelidir. Bu konudaki hukuki sorumluluk yazarlara aittir.

TEŞEKKÜR
- Eğer çıkar çatışması/çakışması, finansal destek, bağış ve diğer bütün editöryel (İngilizce/Türkçe değerlendirme) ve/veya teknik yardım varsa, bu bölümde, KAYNAKLAR bölümünden önce belirtilmelidir.

KAYNAKLAR
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Main Text: The title of the article (English and Turkish), short title which is not exceed 40 characters, Abstract (English and Turkish), key words (English and Turkish), Main Text (sectioned according to the type of article submitted), References, Tables and Figures should be included.

Ethics Committee Approval Document: Ethics Committee Approval Document should be uploaded as a separate file for all research articles.

Note: If there are figures, pictures or photographs in the article, each of them must be uploaded as separate files.

SECTIONS THAT SHOULD BE USED ACCORDING TO THE TYPE OF ARTICLE

Research Article

ABSTRACT (English and Turkish), INTRODUCTION, MATERIAL AND METHODS, RESULTS, DISCUSSION, CONCLUSION, REFERENCES

ÖZ/ABSTRACT should be between 200-250 words.

ÖZ, should be structured as "Amaç, Gereç ve Yöntemler, Bulgular, Sonuç".

ABSTRACT should be structured as "Aim, Material and Methods, Results, Conclusion".

Review (Invited Only)

ABSTRACT (English and Turkish), INTRODUCTION, Subtitles Related to the Subject, CONCLUSION, REFERENCES

ÖZ/ABSTRACT should be between 150-200 words.

Case Report

ABSTRACT (English and Turkish), INTRODUCTION, CASE REPORT, DISCUSSION, REFERENCES

ÖZ/ABSTRACT should be between 100-150 words.

Other

The general writing rules are applied for the preparation of the writings (letter to the editor, editorial comment/discussion, etc.) except these three basic types of article. There is no title and abstract sections in these writings. The number of references is limited to 5. The dedicated article should be specified by giving the number and date. The name, institution and address of the author should be included at the end of writing. Answer to the letter is given by the editor, or authors of the dedicated article, by publishing again in the journal.

AUTHOR GUIDELINES

WRITING RULES

- Articles should be prepared as Microsoft Word® document.
- The required margins are 2.5 cm on all sides.
- Page numbers should be placed to bottom right corner of pages.
- All texts must be typed with double-space as left-aligned using 12 point Times New Roman font.
- In Turkish articles, the Turkish dictionary of the Turkish Language Association (http://www.tdk.org.tr) and also term glossary of Turkish Medical Associations' belonging their own field should be taken as basis.

KEYWORDS

- Number of the keywords must be at least 2, words should be separated from each other by a semicolon (;).
- Keywords in Turkish must be given in accordance with Türkiye Bilim Terimleri (TBT) (http://www.bilimterimleri.com), and keywords in English must be given in accordance with Medical Subject Headings (MESH) (http://www.nlm.nih.gov/mesh/MBrowser.html).

STATISTICAL METHODS

- All research articles should be assessed in terms of biostatistics and indicated with appropriate plan, analysis and report. In these articles last subtitle of the MATERIAL and METHODS section should be the “Statistical Analysis”.
- In this section, the statistical methods used in the study should be written by indicating the purpose of use, package programs and versions used for statistical analysis should be specified.
- p values should be given in three decimal digits (p=0.038; p=0.810 etc.).
- Further information to control the convenience of articles in terms of biostatistics, can obtained from www.icmje.org.

ABBREVIATIONS

- The term should be written in full words with the abbreviation in parenthesis where first mentioned, and the same abbreviation should be used throughout the entire text.
- Abbreviations used internationally should be used in accordance with the Scientific Writing Rules.

TABLES AND FIGURES

- Should be indicated at the end of the relevant sentence in the text as (Table 1) and/or (Figure 1).
- Tables (with headings) and figures (with captions) must be added after references at the end of the text as each to be on a separate page.
- The table headings should be written at top of the table (Table 1. Table heading) and the figure captions should be written below the figure (Figure 1. Figure caption) as their first letters being upper case.
- If any abbreviation or symbol is used in tables and figures, it should be explained as a footnote below.
- The figures and photographs should be upload as separate files in .png, .jpg, etc. format and at least 300 dpi resolution.
- Captions of figure and photograph should be given on a separate page respectively, after the page including last table.
- If figure, picture, table, graphic etc. which have been published before is used, written permission must have and it should be stated in the explanation of figures, pictures, tables, graphics. The legal responsibility in this regard belongs the authors.

ACKNOWLEDGEMENT

- If any conflict of interest, financial support, donation and other editorial (English/Turkish evaluation) and/or technical support, it must be stated in this section before the REFERENCES section.

REFERENCES

- References should be numbered according to the order of use and stated with numbers in parentheses as (1) or (1,2) or (3-5) at the end of the relevant sentence in the text.
- Reference list should be formed according to the reference order used in the text.
- If the number of authors are 6 or less, all authors should be specified, if there are 7 or more "et al.” ("ve ark." for Turkish articles) should be added after the first 6 authors are specified.
- The conference papers, personal experiences, unpublished papers, theses and internet addresses should not be used as references.
- DOI is the only acceptable online reference.

Article:

Al-Habian A, Harikumar PE, Stocker CJ, Langlands K, Selway JL. Histochemical and immunohistochemical evaluation of mouse skin histology: comparison of fixation with neutral buffered formalin and alcoholic formalin. J Histotechnol. 2014;37(4):115-24.

Aho M, Irshad B, Ackerman SJ, Lewis M, Leddy R, Pope T, et al. Correlation of sonographic features of invasive ductal mammary carcinoma with age, tumor grade, and hormone-receptor status. J Clin Ultrasound. 2013;41(1):10-7.

Book:

Buckingham L. Molecular diagnostics: fundamentals, methods and clinical applications. 2nd ed. Philadelphia: F.A. Davis; 2012.

Book Chapter:

Altobelli N. Airway management. In: Kacmarek R, Stoller JK, Heuer AJ, editors. Egan’s fundamentals of respiratory care. 10th ed. St. Louis: Saunders Mosby; 2013. p.732-86.


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