VAN SAĞLIK BİLİMLERİ DERGİSİ

VAN HEALTH SCIENCES JOURNAL

Yıl: 2019 Cilt/Volum: 12 Sayı/Number: 2

Yıl: 2019

ISSN: 2667-5072

VAN SAĞLIK BİLİMLERİ DERGİSİ
VAN HEALTH SCIENCES JOURNAL

Yayın Kurulu

İçindekiler

Orjinal Araştırma Makalesi/OriginalPaper

Van Sag Bil Derg 2019;12(2):1-7

Sigara Kullanan Bireylerde Farklı Periodontal Teşhise Sahip Dişlerin AdenozinDeaminaz ve Katalaz Aktivitelerinin Karşılaştırılması

Comparison of AdenosineDeaminase and Catalase Activity of Periodontally Different DiagnosedTeeth in Smokers

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Geliş Tarihi: 18.09.2019, Kabul Tarihi: 11.11.2019

ÖZET

Amaç: Periodontitis, periodontal dokularda ve dişeti oluğu sıvısında (DOS) oksidatif hasar belirteçlerinde artış ile karakterize bir hastalıktır. Katalaz (KAT) antioksidan, adenozindeaminaz (ADA) ise lenfosit çoğalması/farklılaşması ile ilişkili bir enzimdir. Bu çalışmanın amacı periodontal açıdan umutsuz dişleri bulunan ve çekim kararı verilen dişler ile aynı bireyde bulunan tedavi edilebilecek periodontitisli ve gingivitisli dişlerin periodontal klinik parametreleri ve dişeti oluğu sıvısındaki ADA ve KAT aktivite seviyelerinin karşılaştırılmasıdır. Bu çalışma literatürdeADA'nın DOS'ta değerlendirildiği ilk çalışmadır.

Gereç-Yöntem: Periodontoloji kliniğine periodontal hastalık şikâyeti ile başvuran ve günde en az bir paket sigara içtiğini belirten 14 hasta bu çalışmaya dahil edilmiştir. Hastaların tüm ağız ve her bir grup için ayrı ayrı periodontal klinik parametreleri kaydedilmiştir. Her hastadan faz 1 tedavi öncesi periodontal olarak umutsuz olan diş (grup-1), periodontitis (grup-2) ve gingivitis teşhisi konulan dişlerinden (grup-3) DOS örneği alınmıştır. Alınan DOS örneklerinde ADA ve KAT aktivite seviyeleri spektrofotometrik yöntem kullanılarak ölçülmüştür.

Bulgular: Bu çalışmada periodontal hastalık şiddeti arttıkça KAT seviyesinde azalma, ADA seviyesinde ise artış olduğu gözlenmiştir. Üç grup arasında ADA ve KAT seviyesinin istatistiksel olarak anlamlı derecede farklı olduğu belirlenmiştir ($p<0.05$). Sondlanan cep derinliği açısından grup-1 ile grup-3 ve grup-2 ile grup 3 arasındaki fark istatistiksel olarak anlamlı bulunmuştur ($p<0.05$).

Sonuç: ADA'nın sigara içen bireylerde, hücre aracılı immün yanıttaki rolünden dolayı önemli bir aktivite belirteci olarak kullanılabileceği öngörülmektedir. ADA'nınperiodontal hastalık etiyopatogenezindeki öneminin tamamıyla anlaşılması için, daha fazla sayıda klinik araştırmaya gerek olduğu düşünülmektedir.

Anahtar kelimeler: Dişeti oluğu sıvısı, Adenozindeaminaz, Katalaz, Periodontitis

ABSTRACT

Aim: Periodontitis is a disease characterized by an increase in oxidative damage markers in periodontal tissues and gingival crevicular fluid (GCF). The aim of this study was to compare periodontal clinical parameters, ADA and CAT levels in GCF of periodontally hopeless teeth, teeth with periodontitis and teeth with gingivitis in the same patients. This preliminary study is the first study in the literature where ADA is assessed in GCF.

Materials and Methods: Fourteen patients (at least 1 package cigarette smokers daily) were admitted to this study. Full-mouth and separately 3 groups' periodontal parameters were recorded before the phase I theraphy. GCF samples were collected from periodontally hopeless tooth (group-1), tooth with periodontitis (group-2) and tooth with gingivitis (group-3). Collected GCF samples were evaluated in terms of ADA and CAT levels using spectrophotometry.

Results: In this study, it was determined that a decrease of CAT and increase of ADA levels as the severity of periodontal disease increases. In addition ADA and CAT levels in GCF were reported statistically significantly different between all groups (group-3 >2>1) ($p<0.05$). There were statistically significant differences between group-1 and group-3, also group-2 and group-3 in terms of probing depth ($p<0.05$).

Conclusion: It is anticipated that ADA may be used as an indicator of significant activity due to its role in cell-mediated immune response in smokers. It is thought that more clinical investigations are needed to fully understand the role of ADA in the ethiopathogenesis of periodontal disease.

Keywords: Gingival crevicular fluid, adenosine deaminase, catalase, periodontitis

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GİRİŞ

Periodontitis mikrobiyal ilişkili ve konak aracılı inflamasyon ile karakterize disbiyotik inflamatuar bir hastalıktır. Periodontitisin patofizyolojisinde marjinal periodonta lligament liflerin kaybı ve bağlantı epitelinin apikale doğru göç ettiği gözlenir, bunun sonucunda biyofilmapikal yöne doğru kök yüzey boyunca yayılır (Hajishengallis, 2015; Tonetti ve ark., 2018).

Literatürde bulunan epidemiyolojik çalışmalar gözden geçirildiğinde, periodontal hastalıkların diş kaybına sebep olma oranını %16-30 aralığında tespit eden çalışmalara (İskoçya, Bangladeş, Hırvatistan, Ürdün, Almanya, Gu¨ney Afrika, Nijerya) rastlandığı gibi, bu oranın %30-45'lere kadar arttığını belirten çalışmalara da (Libya, Yunanistan, Nijerya, Hindistan, Japonya, Singapur, Kuveyt, Afganistan) rastlanmaktadır (Morita ve ark., 1994; Ong, 1996; McCaul ve ark., 2001; Taani, 2003; Spalj ve ark., 2004; Al-Shammari, 2005; Al-Shammari ve ark., 2006; Akhter ve ark., 2008; Lesolang ve ark., 2009; Anand ve ark., 2010; Esan ve ark., 2010; Byahatti, 2011; Chrysanthakopoulos, 2011; Danielson, 2011; Glockman ve ark., 2011).

Türkiye'de yapılan bir tez çalışmasında, periodontal hastalığın tu¨mdünyada olduğu gibi ülkemizde de diş kayıplarındaki önemini korumakta olduğu ve çekilen her dört dişten birinin periodontal nedenle çekildiği tespit edilmiştir (Ayrancı, 2012).

Yapılan araştırmalar, sigaranın periodontitis gelişimi için bir risk faktörü olduğunu göstermiştir. Amerikan Periodontoloji Akademisi tarafından 2018 yılında tanıtılan yeni sınıflamada da sigaranın tanımlanmış bir risk faktörü olduğu ve periodontitisin ilerlemesine etki ettiği belirtilmektedir (Tonetti ve ark., 2018). Sigara; immün sistemi baskılamakta, damarlanmayı azaltmakta ve özellikle nötrofil fonksiyonlarında değişiklikler meydana getirmektedir. Sigara içenler, içmeyenlere göre daha fazla alveoler kemik kaybı, derin periodontal cepler ve şiddetli periodontalhastalık sergileme eğilimindedir. Bu sebeplere bağlı olarak sigara içen bireyler, içmeyenlere göre periodontitise 2-8 kat daha yatkındırlar. Ayrıca, sigara dumanı ve içeriği, reflektif olarak tükürük akış hızının artırması nedeniyle diş taşı oluşumunda artma, oksidatif redüksiyon potansiyelini değiştirerek anaerobik floranın artmasına olanak tanıma gibi etkileriyle periodontal hastalık oluşma riskini arttırır. İnatçı kronik periodontitis hastalarının %90'ının sigara kullanıcısı olduğu ve mekanik tedavi sonrası iyileşmenin sigara içenlerde daha yavaş ilerlediği belirtilmektedir (Doğan, 1999;Burt, 2005; Johnson, 2007; Luzzi, 2007; Ojima ve ark., 2007).

Periodontitis, ayrıca periodontal dokularda ve dişeti oluğu sıvısında (DOS) oksidatif hasar belirteçlerinde artış ile karakterizedir. Son yıllarda oksidatif stresin periodontitis patogenezinde rolü ile ilgili güçlü kanıtlar elde edilmiştir (Dahiya ve ark., 2013).

Birçok normal biyolojik süreç için serbest radikaller ve reaktif oksijen türleri gereklidir. Bu serbest radikaller yüksek konsantrasyonlarda doku yaralanmasına neden olabilir. Serbest radikallerin uzaklaştırılması ve hasarın onarılması için enzimatik ve nonenzimatik antioksidan mekanizmalar vardır. Redükte glutatyon, katalaz (KAT), süperoksitdismutaz gibi bazı enzimatik antioksidanlar, serbest oksijen radikallerinin neden olduğu oksidatif hasara karşı dokuları korurlar (Mates ve Sánchez-Jiménez, 1999; Day, 2009).

Adenozindeaminaz (ADA) ise pürin bazların yıkımıyla ilgili olan ve adenozinin /deoksiadenozinin, inozine/deoksiinozine dönüşmesini sağlayan bir enzimdir. Adenozin ve deoksiadenozin yaşayan hücreler için oldukça toksik olduğundan, ADA detoksifikasyonda kritik öneme sahiptir. ADA hücre proliferasyonu/diferansiyasyonunda önemli rol oynar ve serbest radikallerin oluşumuna direkt veya indirekt etki gösterir (Kameoka, 1993; Xia, 1996; Aldrich ve ark. 2003; Okur ve ark., 2006). Özellikle monositlerin makrofajlara differansiyasyonunda gerekli olduğu belirtilmektedir. ADA'nın biyokimyasal ve immünomorfolojik çalışmalarda önemli bir immünoenzim belirteci olduğu rapor edilmiştir. Literatürde çeşitli inflamatuar ve infeksiyöz hastalıklarda üzerinde çalışılan ADA'nın, yine infeksiyöz ve inflamatuar bir hastalık olan periodontitiste, DOS'taki aktivite seviyesinin değerlendirildiği bir çalışmaya rastlanmamıştır

(Dikensoy ve ark., 2002; Liao ve ark., 2012; Saghiri ve ark., 2012).

Bu çalışmanın amacı; periodontal açıdan umutsuz dişleri bulunan ve çekim kararı verilen dişler ile aynı bireyde bulunan periodontitisli ve gingivitisli dişlerin periodontal klinik parametreleri ve DOS'taki ADA ve KAT aktiviteseviyeleri açısından karşılaştırılmasıdır. Bu çalışma literatürde ADA' nın DOS'ta değerlendirildiği ilk çalışmadır

MATERYAL ve METOT

Bu çalışmaya Van Yüzüncü Yıl Üniversitesi Diş Hekimliği Fakültesi Periodontoloji AD başvuran, 31-55 yaş arasında, günde en az 1 paket sigara içen, 14 periodontitis hastası dahil edilmiştir. Çalışmaya dahil edilen hastaların en az bir dişine periodontal hastalık sebebiyle çekim kararı verilmesi; en az bir dişinde 5 mm ve üzeri patolojik cep bulunması ve en az bir dişinde patolojik cep bulunmaması koşulu aranmıştır.

Hastalardan klinik periodontal indeksler alınmıştır. Klinik parametreler plak indeksi (Pİ), gingival indeks (Gİ), sondlamada kanama (SK), sondlanan cep derinliği (SCD), klinik ataşman seviyesi (KAS) ve dişeti çekilmesi derinliği (DÇD) olarak belirlenmiştir. Periodontal hastalık sebebiyle çekilecek dişlerden en derin cebin bulunduğu bölge (Grup-1), periodontitis teşhisi konulan ancak çekim kararı verilmeyen dişten en derin cebin bulunduğu bölge (Grup-2) ve patolojik cebin bulunmadığı bölge (Grup-3) (gingivitis (G)) tespit edilerek gruplara atanmıştır.

Klinik parametrelerin kaydedilmesinden 24 saat sonra hastaların dişeti oluğu sıvısı toplanması için kliniğe tekrar gelmeleri istenmiştir. Dişeti oluğu sıvısının kontaminasyonunu engellemek için ilgili bölge pamuk peletler ile izole edilmiştir. Örnek alınacak dişlerden kağıt şerit kullanılarak (30 sn) dişeti oluğu sıvıları toplanmıştır. Kağıt şeritler laboratuar analizleri yapılana kadar -40^{0}C de fosfat tamponlu solüsyon içerisinde bekletilmiştir. Dişeti oluğu sıvısı örneklerinde; ADA aktivitesi Giusti metodu kullanılarak (Giusti, 1974), KAT enziminin aktivitesi, substrat olarak H_2O_2 kullanılarak ölçülmüştür (Aebi ve Bergmayer, 1974) H_2O_2'nin bozunması, 5 dakika boyunca 240 nm'de spektrofotometre ile izlenmiştir Sonuçlar, litre başına birim (U/L) olarak kaydedilmiştir

İstatistiksel Analiz

Bu çalışmada veriler normal dağılım göstermediği için non-parametrik testler kullanılmıştır. İstatistiksel verilerin değerlendirilmesinde SAS programı (version 9.4) kullanılmıştır. Grupların karşılaştırılmasında Kruskal-Wallis testi uygulanmıştır. Anlamlı çıkan karşılaştırmalarda farkın hangi gruptan kaynaklandığını belirlemek için ise Bonferroni düzeltmeli Wilcoxon işaret testinden yararlanılmıştır. Tüm istatistiksel analizlerde $p<0.05$ istatistiksel olarak anlamlı kabul edilmiştir.

BULGULAR

Bu çalışmaya 10 erkek, 4 kadın toplam 14 hasta dahil edilmiştir. Çalışmaya katılan bireylerin yaş ortalaması 41.60±7.82 (31-55 yaş) yıl olarak hesaplanmıştır. Çalışmaya katılan bireylerde periodontal sebeplerle çekim endikasyonu konulan diş sayısı ortalama ve standart sapması 3.20±1.94 olarak tespit edilmiştir. Çalışmaya katılan hastaların ağzında bulunan mevcut diş sayısı ise 20.5±5.75 olarak hesaplanmıştır.

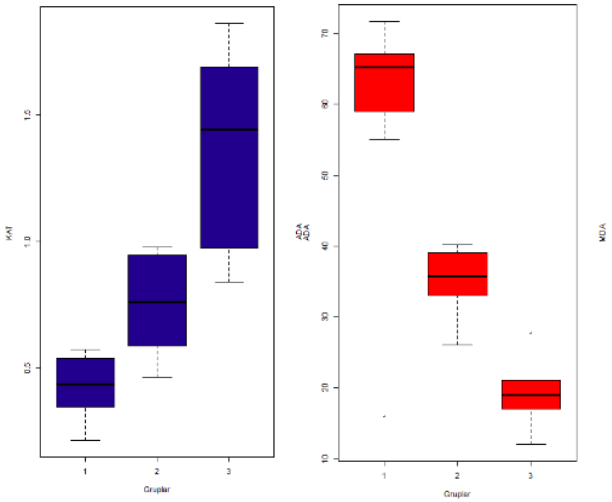
Periodontal klinik parametreler tüm ağız ve diş bazında ayrı ayrı hesaplanmıştır. Tüm ağız skorları Gİ için 2.20±0.59, Pİ için 2.20±0.36, SK için % 62.50 ±18.50, SCD için 3.39±0.86 mm, KAS için 3.50±1.01 mm ve DÇD için 0.81 ±0.52 mm olarak hesaplanmıştır. DÇD değerleri açısından gruplar arasındaki fark istatistiksel olarak anlamlı bulunmamıştır ($p>0.05$). Gİ, Pİ, SK, SCD ve KAS değerleri gruplar arasında istatistiksel olarak anlamlı fark göstermiştir ($p<0.05$) (Tablo 1).

DOS'taki KAT seviyesi açısından bakıldığında Grup-1'de 0.42 ±0.12 U/L, Grup-2'de 0.75±0.20 U/L ve Grup-3'de 1.34±0.38 U/L olarak hesaplanmıştır. Gruplar arasında KAT seviyeleri açısından tespit edilen fark istatistiksel olarak anlamlı bulunmuştur ($p<0.001$) (Şekil 1a, Şekil 2) (Tablo 1).

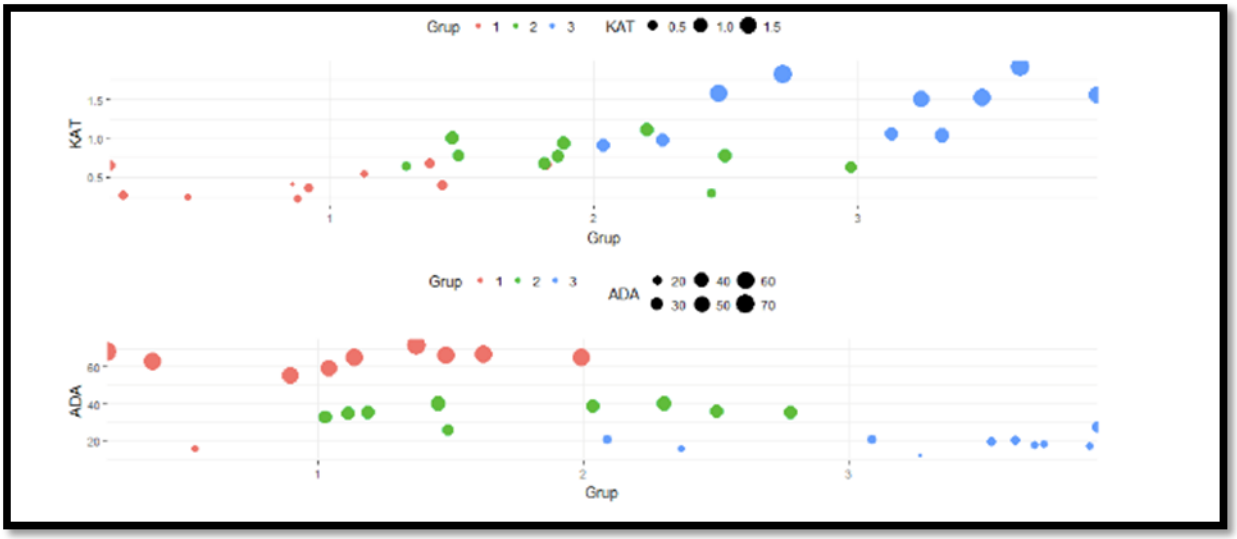
DOS'ta ADA seviyesi, Grup-1'de en yüksek, Grup-3'te en düşük olarak tespit edilmiştir ($p<0.001$). Periodontal hastalığın şiddeti arttıkça DOS'ta ADA seviyesinin istatistiksel olarak anlamlı derecede arttığı gözlenmiştir ($p<0.001$). Grup-1 için ADA 59.65±16.01 U/L, Grup-2 için 35.41±4.17 U/L ve Grup-3 için 19.08±4.09 U/L olarak tespit edilmiştir (Şekil 1b, Şekil 2 (Tablo 1).

Tablo 1: Klinik ve biyokimyasal parametreler.

	Grup 1	Grup 2	Grup 3	p
GI	2.30 ±0.78	1.90 ±0.58	1.40 ± 0.46	0.031*
PI	2.30 ± 0.69	1.80 ± 0.61	1.30 ± 0.32	0.023*
SK	72.21 ± 25.12	47.54 ± 12.52	30.08 ± 10.24	0.009*
SCD	4.28 ± 1.21	4.05 ± 1.12	2.31 ± 0.46	0.009*
KAS	4.82± 1.58	4.08 ± 1.75	2.24 ± 0.86	0.008*
DÇD	0.95 ±0.62	0.54±0.35	0.22±0.15	0.08
KAT(U/L)	0.42 ±0.12	0.75±0.20	1.34±0.38	< 0.001
ADA(U/L)	59.65±16.01	35.41±4.17	19.08±4.09	< 0.001



Şekil 1. a. Gruplara göre DOS'taki KAT seviyesi **b.** Gruplara göre DOS'taki ADA seviyesi



Şekil 2. Gruplara göre KAT ve ADA seviyeleri

TARTIŞMA

Periodontitis patogenezinde oksidatif stresin rolü ile ilgili literatürde güçlü kanıtlar bulunmaktadır. Yüksek konsantrasyonda doku hasarına neden olan serbest radikallerin ortadan kaldırılmasında görev alan antioksidan mekanizmalar aynı zamanda hasarıniyileşmesine de katkıda bulunmaktadır. Katalaz da antioksidan bir enzimdir (Mates ve Sánchez-Jiménez, 1999; Day, 2009). Periodontitis hastalarında KAT seviyesinin dişeti oluğu sıvısında sağlıklı bireylere göre daha az olduğu, tedavi sonrasında katalaz seviyesinin arttığı belirtilmektedir. Bu bağlamda bu çalışmada gözlemlenen periodontal hastalığın şiddeti arttıkça KAT seviyesinde azalma olması, literatürdeki çalışmalar ile uyumlu bir sonuç olarak değerlendirilmektedir (Dahiya ve ark., 2016; Trivedi ve Lal, 2017).

ADA, adenosini inosine hidrolize eden bir enzimdir ve hücre aracılı immünite için iyi bir belirteç olduğu belirtilmiştir. İnozin ise inflamatuar sitokinlerin üretimini inhibe etmektedir (TNF-α, IL-1, IL-12, macrophage-inflammatory protein-1α and IFN-γ) (Haskove ark 2000). ADA insanlarda inflamasyon biyobelirteci olarak kabul edilmektedir (Mishra ve ark 1994). KVS ilaçların ADA üzerine etkisinin değerlendirildiği bir çalışmada, ADA'nın stress cevabını düzenlemede ve doku hipoksisi yoluyla hücresel hasarı düzenlemede çok önemli bir rol oynadığını ve inflamasyonda arttığı belirtilmiştir (Kowalczyk ve ark., 2009).

ADA'nın skuamoz hücreli karsinomu için bir biyobelirteç olabileceği, sjögren sendromunda tükrükte ADA seviyesinin arttığını belirten çalışmaların yanı sıra romatoid artritli hastaların serumunda ADA düzeyinin anlamlı derecede arttığını belirten çalışmalar literatürde mevcuttur (Rai ve ark., 2011; Hameed ve ark., 2018). Literatürde periodontitis hastalarında tükrükte ADA seviyesinin değerlendirildiği ilk çalışma 2018 yılında yayınlanmıştır. Bu çalışmanın sonucunda diabetli periodontitis hastalarında, diabetli ancak sağlıklı periodonsiyuma sahip bireylere göre ADA seviyesinin daha yüksek olduğu belirtilmiştir (Sarhat ve ark., 2018).

Bu çalışma DOS'ta ADA seviyesinin değerlendirildiği ilk çalışma olduğu için, literature verileri ile direct olarak kıyaslanamamıştır. Ancak periodontal hastalığın inflamatuar tabiatı göz önünde bulundurulduğunda, periodontal hastalığın şiddeti arttıkça ADA seviyesinin artmasının desteklenebilir bir hipotez olabileceği düşünülmektedir. 2018 yılında yapılan ve periodontitis hastalarını kapsayan yegane çalışmada (Sarhat ve ark., 2018) tükrükte artan ADA seviyesi, bu çalışmadaki DOS'taki artış ile parelel sayılabilir.

Sigara dumanına maruz bırakılan ratlarda serum ADA seviyesinin, sigara dumanına maruz bırakılmayanlara gore istatistiksel olarak anlamlı derecede düşük olduğunu belirten çalışmalar literatürde mevcuttur (Thome ve ark., 2009). Bu çalışmaya dahil edilen bireylerin hepsinin "ağır sigara içicisi" olduğu göz önünde bulundurulduğunda, DOS'taki ADA seviyelerinin, sigara içmeyen bireylerde daha yüksek U/L değerlerinde olabileceği düşünülebilir.

Bu çalışmanın limitasyonları; tükrüğünde derlendirilmemiş olması, sigara içen ve içmeyen bireylerin karşılaştırılmaması, tedavi öncesi ve tedavi sonrası ADA seviyesindeki değişimlerin değerlendirilmemesi olarak sıralanabilir.

Bu çalışmadan elde edilen veriler, DOS'ta KAT seviyesinin periodontal sağlık bozuldukça anlamlı derecede azaldığını ve ADA seviyesinin anlamlı derecede arttığını göstermektedir. ADA'nın hücre aracılı immün yanıttaki rolünden dolayı periodontitiste de önemli bir aktivite belirteci olarak kullanılabileceği öngörülmektedir. ADA'nın periodontal hastalık etiyopatogenezindeki öneminin tamamıyla anlaşılması için daha fazla sayıda klinik araştırmaya gerek olduğu düşünülmektedir.

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Orjinal Araştırma Makalesi/OriginalPaper

Van Sag Bil Derg 2019;12(2):8-14

Effect of Urinary Incontinence on the Quality of Life of Patients in Postmenopausal Age Group who Applied to The Urogynecology Polyclinic

Ürojinekoloji Polikliniğine Başvuran Postmenopozal Yaş Grubundaki Üriner İnkontinansın Hasta Yaşam Kalitesine Etkisi

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Geliş Tarihi: 18.10.2019, Kabul Tarihi: 16.12.2019

ÖZET

Amaç: İdrar kaçırma, kadın popülasyonunda sık görülen bir sağlık sorunudur. Bu çalışmada üriner inkontinans risk faktörlerini ve Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Ürojinekoloji ve üriner inkontinanslı poliklinik kliniğine başvuran postmenopozal kadınların yaşam kalitesi üzerine etkilerini değerlendirdik.
Gereç-Yöntem: Çalışmamız, Ocak 2003-Nisan 2013 tarihleri arasında polikliniğimize başvuran ve idrar kaçırma şikayetleri ile başvuran 139 postmenopozal hastayı içeren kesitsel ve retrospektif bir çalışmadır. Biz çalışmaya dahil edilen hastalara UDI-6 ve 7'yi sorgulayan IIQ-7 yaşam kalite anket formunu uyguladık.
Bulgular: Üriner inkontinansı olan 139 postmenopozal kadının yaş ortalaması 57,19 ± 9 idi. Vücut kitle indeksi artışı (p> 0.05), menopoz süresi (p> 0.05), noktüri sayısı (p> 0.05) ve gece ıslatma (p <0.005), doğum yapma (p> 0.05), kürtaj (p>0.05), hipertansiyon (p <0.05) ve bazı kronik hastalıklar, ilaç kullanımı (p <0.05), üriner inkontinanslı postmenopozal kadınlarda yaşam kalitesinde değişikliğe neden olmamıştır. Aciliyet şikayeti olmayan hasta grubuna göre ani aciliyeti olan grupta yaşam kalitesinin anlamlı şekilde etkilendiği bulundu (p <0,005).

Sonuç: Üriner inkontinansı olan hastalarda yaşam kalitesi özellikle psikososyal sağlığı bozar. Nesnel olarak gösterilen idrar kaçırma şiddetine bakılmaksızın, yaşam kalitesi olumsuz etkilenir.

Anahtar kelimeler: Üriner inkontinans, ürojinekoloji, postmenopozal kadınlar, yaşam kalitesi

ABSTRACT

Aim: Urinary incontinence is a common health problem in women population. In this study, it was evaluated the urinary incontinence risk factors and its effect on the quality of life of the postmenopausal women applying to Bakırköy Dr. SadiKonuk Education and Training Hospital Urogynecology outpatient clinic with urinary incontinence.
Materials and Method: This study is cross-sectional and retrospective investigation which included 139 postmenopausal patients who applied to the outpatient urogynecology clinic with the complaints of urinary incontinence between January 2003-April 2013. It was performed UDI-6 and 7 questioned IIQ-7 life quality quessionaire form to the patients who were included in the study.
Results: The mean age of 139 postmenopausal women with urinary incontinence was 57.19±9. Body mass index increase (p> 0.05), duration of menopause (p> 0.05), the number of nocturia (p> 0.05) and night-time wetting (p <0.005), making birth (p> 0.05), abortion (p> 0.05), hypertension (p <0.05) as well as some chronic diseases, medication use (p <0.05) did not cause a change in the quality of life in postmenopausal women with urinary incontinence. It was found that the quality of life was significantly affected in the group with sudden urgency when compared with the group of patients who did not have urgency complaint (p<0,005).
Conclusion: Quality of life deteriorates, especially psychosocial health, in patients with urinary incontinence. Regardless of the severity of the urinary incontinence that is shown objectively, the quality of life is negatively affected.

Keywords: Urinary incontinence, urogynecology, postmenopausal women, quality of life

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INTRODUCTION

Urinary incontinence (UI) is involuntary urinary leakage affecting the social lives of patients and creating hygiene-related problems (Abrams et al., 1998). UI is not only a symptom but also a disorder that can affect the entire social life of an individual. It is well-known that urinary leakage causes psychological disorders as serious as depression due to the disturbance caused by continuous wetness and irritation (Fantl et al., 1996).

In this study, it was aimed to determine the effects of risk factors for urinary leakage on the quality of life in postmenopausal women who presented to the Urogynecology Outpatient Clinic.

MATERIAL AND METHODS

A total of 139 postmenopausal women who had presented to the Urogynecology Outpatient Clinic of SBÜ Bakırköy Dr. Sadi Konuk Training and Research Hospital with the complaint of urinary leakage between January 2013 and April 2013 were included in this study, and the charts of these patients were retrospectively reviewed. The patients registered in ourunitareperiodically examined and treated according to their clinical status. The risk factors that might lead to urinary incontinence were investigated together with the effects of these risk factors on thequality of life in postmenopausal patients involved in the study.

The medical and family history, the obstetric-gynecological history, the pattern, frequency, and duration of urinary leakage, diaperuse, systemic disorders, drug use, and surgical history of the patients admitted to the Urogynecology Outpatient Clinic were questioned. The results of fasting blood sugar, complete urinalysis, and urine culture were investigated, and on physical examination, pelvic organ prolapsus (POP-Q) staging was performed in all patients.

IIQ-7, which is a scale of incontinenc equality of life, is an index validated by Cam et al. (2006) like UDI-6. In this study, it was used the short form of IIQ-7, having seven items.

Statisticallyanalysis

In this study, descriptive statistics for the categorical variables (characteristics) were presented as count and percent. For determination relations among the categorical variables, Spearman correlation coefficients were calculated. Statistical significance levels were considered as 5% and NCSS statistical program was used for all statistical computations.

RESULTS

Of this patients included in the study, 66 (47.5%) had hypertension, 32 (23%) diabetes mellitus (DM), 5 (3.6%) chronic heart failure, 11 (7.9%) thyroid disorder, and 11 (7.9%) asthma. The presence of a gynecological operation in the medical history was found in 42 (30.2%) patients.

Constipation was present in 55 (39.9%) patients, and the incidence of drug use was 51.8% (72 patients). Frequent urination was present as a symptom in 47 (33.8%) patients and absent in 93 (66.2%) patients. Nocturia was present in 89 (64.5%) patients, whereasurgency in 108 (77.7%). Nocturnal wetness was present in 42 (30.2%), dysuria in 33 (23.7%), stress incontinence in 95 (68.3%), and urgeincontinence in 100 (71.9%) patients. 62 (44.6%) patients were using diapers. Urinary retention was present in 38 (27.3%), and the urinary stress test was positive in 63 (45.3%) patients (Table 1).

The average duration of symptoms in patients was 3.80±5.58, the mean of nocturia was 2.53±1.09 m (1-6), the mean of IIQ-7 was 9.11±4.77 (0-21), the mean UDI-6 was 10.39±4.01 (0-18), and the mean duration of menopause was 8.82±8.37 (1-40).

No significant relationship was determined between IIQ-7 scoreand age, gravida, parity, NSD, C/S, BMI, duration of symptoms, duration of menopause, and the number of nocturia episodes ($p>0.05$). No significant relationship was determined between UDI-6 score and age, NSD, C/S, BMI, duration of symptoms, duration of menopause, and the number of nocturia episodes ($p>0.05$). A positive relationship was determined between UDI-6 score and gravida and parity values ($r=0.168$ $p=0.049$, $r=0.186$ $p=0.03$) (Table 2).

Table 1. The distribution of the complaints and drug usage of patients

		n	%
Constipation	Present	55	39.9
Drug Usage	Present	72	51.8
Frequency	Present	46	33.1
Nocturia	Present	89	64.5
Urgency	Present	108	77.7
Nocturnal Wetness	Present	42	30.2
Dysuria	Present	33	23.7
Stress Incontinence	Present	95	68.3
Urge Incontinence	Present	100	71.9
Diaper Usage	Present	62	44.6
Urinary Retention	Present	38	27.3
Urinary Stress Test	Present	63	45.3

Table 2. The effect of the sociodemographic characteristics of patients on Quality of Life Indexes

		IIQ7	UDI6
Age	**r**	0.016	-0.043
	p	0.853	0.614
Gravida	**r**	-0.032	**0.168**
	p	0.709	**0.049**
Parity	**r**	0.058	**0.186**
	p	0.501	**0.03**
NSD	**r**	0.036	0.168
	p	0.682	0.053
C/S	**r**	0.025	0.088
	p	0.771	0.307
BMI	**r**	-0.05	0.13
	p	0.556	0.128
Duration of Symptoms	**r**	0.083	0.161
	p	0.332	0.058
Duration of Menopause	**r**	0.05	-0.037
	p	0.558	0.664

An anterior defect was not present in 99 (71.2%) of patients. A stage 1 anterior defect was present in 15 (10.8%), a stage 2 anterior defect in 18 (12.9%), a stage 3 anterior defect in 6 (4.3%) patients, and a stage 4 anterior defect was present in 1 (0.7%) patient.

A posterior defect was not present in 111 (79.9%) of patients. A stage 1 posterior defect was present in 11 (7.9%), a stage 2 posterior defect in 11 (7.9%), a stage 3 posterior defect in 5 (3.6%) patients, and a stage 4 posterior defect was present in 1 (0.7%) patient.

An apical defect was not present in 121 (87.1%) of patients. A stage 1 apical defect was present in 5 (3.6%), a stage 2 apical defect in 6 (4.3%), a stage 3 apical defect in 5 (3.6%), and a stage 4 apical defect in 2 (1.4%) patients. No significant relationship was determined between the IIQ-7

score and the values of the anterior, posterior, and apical defects (p>0.05). No significant associationwas found between the UDI-6 score and the values of posterior defects (p>0.05). A significant negative correlation was determined between UDI-6 value and the values of anterior and apical defects (r=-0.194 p=0.022, r=-0.194 p=0.022) (Table 3).

Table 3. The effect of POP-Q Staging of patients on Quality of Life Indexes

		IIQ7	UDI6
Anterior Defect	**r**	-0.162	**-0.194**
	p	0.057	**0.022**
Posterior Defect	**r**	-0.091	0.001
	p	0.286	0.998
Apical Defect	**r**	-0.06	**-0.194**
	p	0.480	**0.022**

No significant difference was determined regarding the mean value of UDI-6 between the patient group with a positive gynecological operation history and the patient group in which such a history was absent (p=0.121). The patient group with nocturia was found to have a significantly higher mean value of UDI-6 than the group that nocturia was absent (p=0.001). The mean UDI-6 value of the group that urgency was present was considerably higher than that of the group with no urgency (p=0.0001). No significant difference was found regarding the mean UDI-6 value between the groups with and without nocturnal wetness (p=0.110). The group using diapers had a significantly higher mean value of UDI-6 when compared to the group not using diapers (p=0.02). No significant difference was present between the groups having and not having dysuria regarding the mean UDI-6 value (Figure 1). No significant difference was determined regarding the mean IIQ-7 value between the patient group with a positive gynecological operation history and the patient group in which such a history was absent (p=0.055). No significant difference was found between the patient groups with and without nocturia regarding the mean IIQ-7 value (p=0.284). The mean IIQ-7 value of the group that urgency was present was significantly higher than that of the group with no urgency (p=0.004). No significant difference was found regarding the mean IIQ-7 value between the groups with and without nocturnal wetness (p=0.955). No significant difference was present between the groups having and not having dysuria regarding the mean IIQ-7 value (p=0.817). The groups using and not using diapers did not have a significant difference in the mean IIQ-7 value (p=0.140). (Figure 2).

DISCUSSION

Urinary incontinence is a common problem in the community. The prevalence of urinary incontinence varies between 10-60% (Bump et al., 1992, Koçak et al., 2009). The studies conducted in our country revealed that this rate was over 50% (Cam et al., 2006). As many authors have pointed out, the main reasons for such discrepancies in reported prevalence rates are the differences between the communities that the studies were conducted, clinical studies being more in number, and the differences regarding the definition of urinary incontinence (Lasserre et al., 2009, Çetinel et al., 2005). When it was look at the studies investigating the urinary incontinence and its treatment status in the literature, Ertem et al. stated that 66.6% of women had encountered urinary incontinence symptoms for 2 years or more (Ertem et al., 2002). In this study, the mean duration of urinary incontinence complaints was determined as 3.80±5.80. This situation suggests that the knowledge level of the community on urinary incontinence in women is insufficient. Additionally, anterior defects were identified in various stages according to the POP-Q Staging in 28.8%, posterior defects in 20.1%, and apical defects in 12.9%on gynecological examination of postmenopausal women with urinary incontinence. It was found that the quality of life of postmenopausal women with urinary incontinence and having an anterior or apical defect were negatively affected, whereas the quality of life of women with posterior defects were not significantly affected.

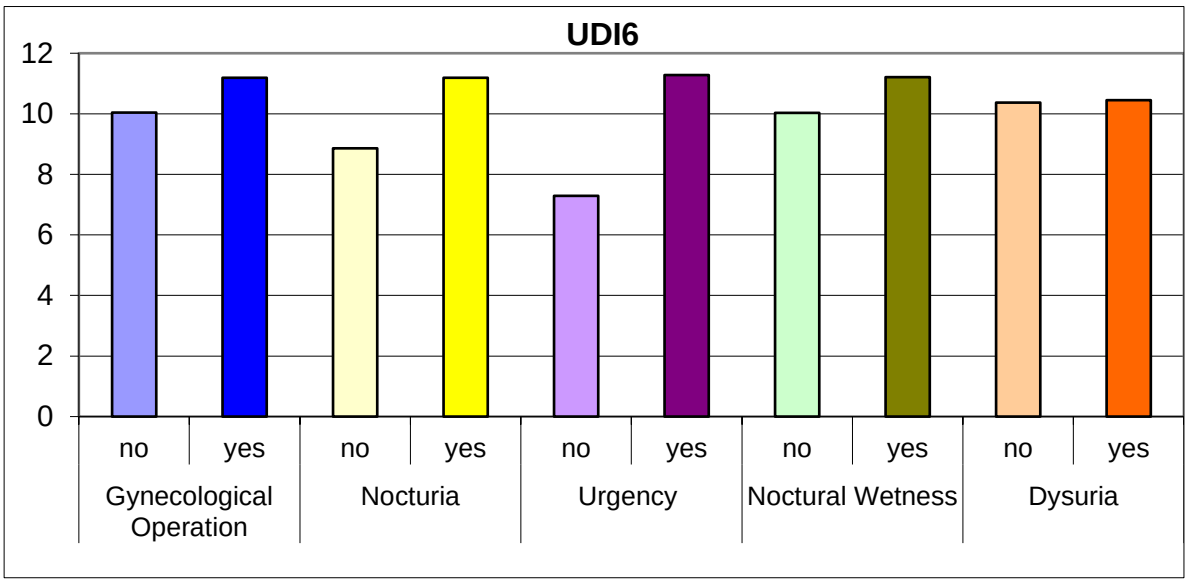

Figure 1. The distribution of the effects of patients' complaintson UDI6 Quality of Life Index

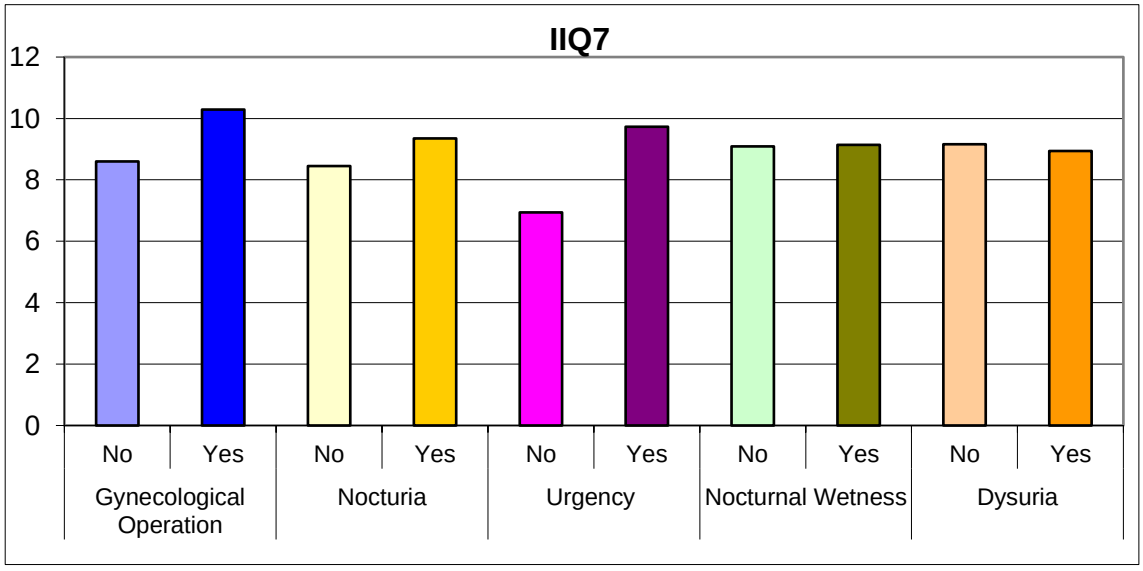

Figure 2. The distribution of the effects of patients' complaints and urinary test results on IIQ7 Quality of Life Index

Several conducted studies have reported a relationship between gynecological operations and urinary incontinence (Parazzini et al., 2000, Hsieh et al., 2008). In this study, we determined that there was no difference between the group of postmenopausal women who had undergone a gynecological operation and those who had not, regarding the mean IIQ-7 quality of life score; thus, it were unable to determine any significant relationship between undergoing gynecologic surgery and the quality of life of patients. Milsom et al (1993) reported that a relationship was present between the high parity value and urinary incontinence; a significant rise in the incidence of urinary incontinence was particularly present following the first childbirth (Milson et al., 1993). In the study conducted by Parazzini et al.(2000), it was found that while the urinary incontinence rate was 20% in nulliparous women, this rate increased to 53% after first pregnancy, 34% after two pregnancies, 39% after three pregnancies, 54% after 4 pregnancies, and 62% after 5 or more pregnancies (Parazzini et al., 2000). In this study, the mean gravida value was

found as 5.72±2.94, and the mean parity value as 4.04±2.31. We did not determine any significant relationship between the IIQ-7 score, the gravida value, and the parity value; however, it was determined signification relationships of UDI-6 score with the gravida and parity values.

Additionally, we determined a significant relationship between hypertension and urinary incontinence. In present study, we determined the presence of drug use in 72% of the patients with urinary incontinence. 47.5% of these patients were using hypertension-related drugs. Especially diuretics used in the treatment of hypertension, by leading to polyuria, frequent urination, and urgency, and alpha-blockers, by leading to urethral relaxation, may cause urinary incontinence. Moreover, in this study, it was found that diapers were being used by 44.6% of the patients with urinary incontinence, and the mean value of UDI-6 in the group using diapers was significantly higher when compared to the group of patients not using any diapers. However, no significant difference was determined between these groups regarding the mean IIQ-7 value. Frequent diaper use due to the fear of urinary incontinence may cause chronic irritation and infection. Koçak et al. (2005), in their study conducted on 1012 women aged 18 years or older, reported 242 cases of urinary incontinence. In the same study, when the frequency of urinary incontinence was investigated, it was found as less than once a week in 45.9%, twice or thrice a week in 17.4%, once a day in 9.9%, a few times a day in 13.2%, and all the time in 13.6% (11). In this study, we found that the mean UDI-6 and IIQ-7 values were high in the group urinating more than 8 times a day. Therefore, the complaint of frequent urination adversely affects the quality of life of patients. Nocturia at least once was present in 64.5% of the patients with urinary incontinence. The UDI-6 score of the patient group with nocturia was significantly higher when compared to the group with no nocturia. It was reported that patients having urinary incontinence had been uncomfortable and embarrassed due to their complaints, and for this reason, had restricted their social activities. In the study conducted by Choo et al., it was reported that urinary incontinence had affected the social life and the quality of life negatively (Choo et al., 2007). Van Brummen et al. (2006), in their study conducted on 474 women using the UDI-6 and IIQ-7 questionnaires, determined that the physical, social, and emotional scores of women were low, and urinary incontinence restricted their lifestyle (Van Brummen et al., 2006). When we look at the related data in our country, in the study, conducted by Kök following development of the survey questionnaires himself, investigating the effect of urinary incontinence on social life, a moderate-level influence was determined (Kök et al., 2006). In present study also, the quality of life of women having urinary incontinence were found to be affected at a moderate level according to the IIQ-7 index.

In postmenopausal female patients with urinary incontinence, the quality of life of patients, mainly the emotional status and social life, are impaired. This situation, which is commonly met in the community, may cause many psychological disorders. It should be considered important that patients feel well in social life, and both psychological and medical support should be provided to the patient. For this reason, more importance should be given by the medical personnel to the diagnosis and treatment of urinary incontinence, patients should be informed that urinary incontinence is not a part of the aging process, and by this way, the quality of life of postmenopausal women should be increased.

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Orjinal Araştırma Makalesi/Original Paper

Van Sag Bil Derg 2019;12(2):15-21

Determination of Median Values of First Trimester Screening Tests: A Tokat Scale Retrospective Study

Birinci Trimester Tarama Testlerinin Medyan Değerlerinin Belirlenmesi: Tokat Ölçekli Retrospektif Bir Çalışma

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Geliş Tarihi: 03.09.2019, Kabul Tarihi: 10.12.2019

ÖZET

Amaç: Birinci trimester tarama testinde bakılan maternal serum gebelikle ilişkili plazma protein A (PAPP-A) ve serbest beta-human koryonik gonadotropin (free ß-hCG) değerlerinin daha sonraki gebelik haftalarında gelişebilen komplikasyonları tahmin edebilme kapasitesini ve ikili tarama testlerimizin performansını artırabilmek için hastanemize ait medyan değerlerini hesaplamayı amaçladık.
Gereç ve yöntem: Çalışmaya Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi Eğitim ve Araştırma Hastanesi Biyokimya Laboratuvarına başvuran 16-46 yaş arası, gebelik yaşları 10 hafta 6 gün ile 13 hafta 6 gün arasında tekil canlı gebeliği olan, kötü obstetrik öyküsü ve sistemik bir hastalığı bulunmayan ve sigara kullanmayan 3166 gebenin sonuçları retrospektif olarak değerlendirildi. Hastane laboratuvarına özel medyan değerleribelirlenerek, kullanılan yazılım programının değerleriyle karşılaştırıldı.
Bulgular: Hastaların yaşlarının ortalaması 27,43±5,46 ve ağırlıkları 65,66±13,13 kilogramdı. Baş popo mesafeleri (CRL) 60,71±8,56 mm olarak belirlendi. Serbest ß-hCG değerleri, 55,1±132,07ng/mL, PAPP-A değerleri ise 3683,53±2486 mIU/l olarak ölçüldü. Ense kalınlığı ölçümü (NT) ise 1,38±0,37mm olarak saptandı. PAPP-A ve Serbest ß-hCG MoM değerleri sırasıyla 1,23±0,68 ve 1,23±0,88 idi. β-hCG'nin yeni medyan değerlerinin, programdaki medyan değerlerinden anlamlı olarak düşük olduğu tespit edilirken ($p<0.05$), PAPP-A değerlerinin ise anlamlı şekilde yüksek olduğu görüldü ($p<0.05$).
Sonuç: Sonuç olarak, nöral tüp defekti ve kromozomal anomalilerin tanısında kullanılan ve ileri girişimsel işlemler için yol gösterici olan, birinci Trimester tarama testlerinin doğruluğunun ve performansının artırılmasının önemliolduğu, bölgeye ve hatta laboratuvara özel medyan değerlerinin belirlenmesinin de artık kaçınılmaz bir hale geldiği kanısına varılmıştır.

Anahtar kelimeler: Free ß-hCG, PAPP-A, İkili tarama testi, Birinci Trimester

ABSTRACT

Objectives: The aim of this study was to determine the ability of maternal serum plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (free ß-hCG) values measured in the first trimester screening test to predict the complications that may develop in later gestational weeks, calculate the median values of these parameters and compare them with those of software we use.
Materials and methods: The study included 16-46 years old women who applied to biochemistry laboratory of Tokat Gaziosmanpasa University School of Medicine with gestational ages of 10 weeks and 6 days to 13 weeks and 6 days. The results of 3166 pregnant women were evaluated retrospectively.
Results: The mean age of the patients was 27.43 ± 5.46 and their weight was 65.66 ± 13.13 kilograms. Crown rump lengthes (CRL) were determined as 60.71 ± 8.56 mm. Free ß-hCG levels were 55.1 ± 132.07 ng / mL and PAPP-A values were 3683.53 ± 2486 mIU / l. Nuchal translucency measurements (NT) were determined as 1.38 ± 0.37mm. PAPP-A and Free ß-hCG MoM values were 1.23 ± 0.68 and 1.23 ± 0.88, respectively. New median values of β-hCG were found to be significantly lower than those of the program ($p <0.05$), while PAPP-A values were significantly higher ($p <0.05$).
Conclusion: The accuracy and performance of first trimester screening tests should be improved. Determination of median values specific to the region and even to the laboratory is now inevitable

Key words: Free ß-hCG, PAPP-A, Binary screening test, First Trimester

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Orjinal Araştırma Makalesi/Original Paper

Van Sag Bil Derg 2019;12(2):15-21

INTRODUCTION

Screening tests are performed to identify a specific group that carries a certain level of risk for specific diagnostic evaluation in a healthy population (Şanlı and Kartkaya, 2011). Hereditary diseases such as Down (Trisomy 21), Edward (Trisomy 18), Patau (Trisomy 13) syndromes and Neural Tube Defect cause physical and mental disorders that lead to both social and economic problems. The most common chromosomal anomaly in the newborn is Down Syndrome and its prevalence is 1/800. In the 1970s, only maternal age was used for prenatal screening of hereditary diseases. Therefore, all mothers over the age of 35 were considered to be at risk and were referred for amniocentesis. However, only one third of the cases could be detected (James et al., 2008). Maternal age was found to be an inadequate screening method and in the 1980s. In the screening method developed by N. J. Wald, in the first trimester, various analytes detected of maternal serum were combined with maternal age. It has been increasingly used in the last 30 years as the average gestational age increases.

In the 1990s, when the population of women aged thirty-five years and over is examined, It was determined that increase in nuchal translucency (NT) thickness determined by ultrasonography between 10-15 weeks of gestation was related to increase in maternal serum free beta-human chorionic gonadotropin (freeβ-hCG) and decrease in pregnancy related plasma protein-A (PAPP-A) (Nicolaides et al., 1992; Brizot, Snijders et al., 1994). As a result, dual-marker screening captures 75% or more of pregnancies affected by trisomy 21 and other aneuploidies (Kappel et al., 1987), while the rate of detecting false positives decreases to 5% (Cuckle 2001; Kagan et al,. 2017).

Depending on the result of the selected screening test, it is then decided whether interventional tests are necessary for diagnosis. Combining screening tests and diagnostic tests ensures that the maximum number of patients can obtain accurate information about their personal risk status (James et al. 2008). With the development of prenatal screening tests, the need for interventional procedures such as chorionic villus sampling and amniocentesis has decreased. Interventional diagnostic procedures can cause serious complications; such as bleeding, preterm labor and fetal loss (Marteau et al., 1992; Ananth et al., 2017). The psychological dimension of all tests and interventional procedures that can affect both pregnant and fetus is also important (Marteau et al., 1992). Interventional diagnostic tests are known to have fetal loss rates of 1.5% in chorionic villus biopsy, 2% in amniocentesis performed in first trimester and 1% in amniocentesis performed in the second trimester. According to the results of the second trimester screening test, the risk of Down Syndrome must be 1/250 and higher in order to recommend interventional tests (Creasy et al., 2004). Laboratories unitize the values of the measured biochemical parameters in multiples of median (MoM) calculated according to the gestational week to be standard, more understandable and easier to evaluate. Mom value is calculated by dividing the analysis result by the median value of that analyte for the week of gestation (Assessment, 2000).

In calculating these values, each geographic region, even each clinical laboratory in the region, should estimate its own median values and evaluate the screening tests according to this median average (Alp et al., 2018).

Furthermore, when calculating MoM values, adjustments can be made by taking into account other maternal factors such as maternal age, weight and race that affect analyte levels. Today, MoM values; Down Syndrome, Trisomy 18 and neural tube defect risk are commonly used to standardize biochemical analyte values and convert them into a more interpretable unit.

In this study, we aimed to evaluate retrospectively the data of binary screening tests that we have worked in our hospital laboratory within two years and to calculate the median values of our screening tests, especially to improve the performance of our double screening tests.

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MATERIAL AND METHODS

In this study, the results of pregnants (n=3166) who are living in or around Tokat city and applied to the Tokat Gaziosmanpaşa University Medical Faculty Hospital Central Laboratory for the double screening test, between January 2017 and December 2018 were evaluated retrospectively.

They were between 16-46 years of age, their gestational ages were between 10 weeks and 6 days to 13 weeks and 6 days. They had a live single pregnancy, no poor obstetric history and no systemic disease and who did not smoke were evaluated. Diabetic pregnants, smoking pregnant women, twin pregnancies and those who became pregnant by in vitro fertilization (IVF) method were excluded from the study.

Fetal NT values, serum PAPP-A and free β-hCG values of pregnant women between the 11 and 14th weeks of gestation were used for statistical analysis.

All of the biochemical parameters in blood samples taken for paired screening tests were measured on the IMMULITE 2000 device (Diagnostic Product Corporation, USA), which was operated by chemiluminescence immunoassay.

The SsdwLab 5 program is used in the laboratory to determine the risk in a double-screening test. The risk of Down Syndrome must be 1/250 and higher in order to define as high risk.

Descriptive analyzes were conducted to give information about the general characteristics of the study groups. Data of continuous variables were expressed as mean ± standard deviation; categorical variables are given as n (%).

When comparing the averages of the quantitative variables between the groups, the significance test of the difference between the two means and the one-way analysis of variance are used. Pearson correlation coefficient is used for correlation between quantitative variables. p values less than 0.05 were considered statistically significant.

In the calculations, ready-made statistical software was used (IBM SPSS Statistics 19, SPSS inc., An IBM Co., Somers, NY).

RESULTS

Demographic data of the pregnant women participating in the study, the values of biochemical tests and MoM values of these tests are summarized in Table 1.

Comparison of quantitative variables according to gestational week was given in Table 2. In Table 3, qualitative variables are evaluated. In Table 4, the risk status of trisomy 21 is compared with qualitative variables.

The reports given to all pregnant women included in the study were evaluated and the rates of pregnant women reported at high risk were evaluated. 1.9% (59 pregnant) of 3166 pregnant women included in the dual screening test was reported to be at high risk for Down Syndrome using the median values available in the program. 0.1% (2 pregnant) of the pregnant women was found to be at high risk for trisomy 18.

In the correlation studies between the quantitative variables, a negative correlation was found between the weight of the pregnant women and the PAPP-A values, a positive correlation between CRL and PAPP-A, and a negative correlation between CRL and NT MoM.

There was a weak positive correlation between β-hCG and β-hCG MoM. There was a very strong positive correlation between NT and NT MoM and a weak positive correlation between NT and the risk of trisomy 21. There was a weak positive correlation between NT MoM and the risk of trisomy 21.

In Table 5, the median values obtained from the double screening results were compared with the median values of SsdwLab5 software in pregnant women admitted to our hospital, and it was estimated that the new median values of β-hCG were significantly lower than those of the program ($p < 0.05$) and PAPP-A values were significantly found to be high ($p < 0.05$).

Table 1: Quantitative variable distribution

	n	Mean	Standard Deviation	Minimum	Maximum
Age (Years)	3166	27,43	5,46	16,00	46,00
Weight (Kilograms)	3166	65,66	13,13	,00	144,00
CRL (mm)	3166	60,71	8,56	41,00	84,00
β-HCG(ng/mL)	3166	55,10	132,07	3,43	3514,42
PAPPA(mIU/l)	3166	3683,53	2486,00	363,00	25501,00
NT (mm)	3166	1,38	,37	,50	3,70
β-HCG MoM	3166	1,23	,88	,16	8,81
PAPPA MoM	3166	1,23	,68	,09	6,13
NT MoM	3166	,89	,25	,26	2,74
Age Risk (%)	3166	,0016	,0026	,0006	,0609
Trisomy 21 Risk (%)	3166	,0006	,0052	,0000	,1780
Trisomy 18 Risk (%)	3166	,0001	,0040	,0000	,2265

Table 2: Distribution of quantitative variables according to gestational week

	Gestational Week				p
	11	12	13	14	
Age (Years)	27,86±5,69 (ab)	27,15±5,37 (a)	27,71±5,47 (b)	27,85±5,68 (ab)	0,017
Weight (Kilograms)	65,88±12,7	65,15±13,27	66,18±12,98	67,63±13,26	0,063
CRL (mm)	47,55±1,9 (a)	57,27±3,56 (b)	68,9±3,51 (c)	79,29±2,16 (d)	<0,001
β-HCG(ng/mL)	55,2±95,8 (ab)	60,6±136,5 (a)	48,9±141,1 (ab)	30,46±77,17 (b)	0,018
PAPPA(mIU/l)	2271,4±1555,5 (a)	3269,1±2124,6 (b)	4599,2±2666,9 (c)	5956,7±3378,1 (d)	<0,001
NT (mm)	1,31±0,41 (a)	1,36±0,36 (a)	1,44±0,35 (b)	1,48±0,39 (b)	<0,001
β-HCG MoM	1,17±0,83 (a)	1,27±0,91 (b)	1,23±0,9 (b)	0,96±0,57 (a)	<0,001
PAPPA MoM	1,31±0,77 (a)	1,26±0,71 (a)	1,17±0,59 (b)	1,09±0,56 (b)	<0,001
NT MoM	1,01±0,31 (a)	0,91±0,25 (a)	0,83±0,21 (b)	0,77±0,2 (b)	<0,001
Age Risk (%)	0,0019±0,0042	0,0015±0,0026	0,0015±0,0019	0,0017±0,0021	0,158
Trisomy 21 Risk(%)	0,0016±0,012 (a)	0,0005±0,0035 (b)	0,0005±0,0036 (b)	0,0002±0,0011 (b)	0,002
Trisomy 18 Risk(%)	0±0,0002	0±0,0003	0,0002±0,0073	0±0,0001	0,561

One way analysis of variance was used. (abcd): The common letter as a line indicates statistical insignificance.

Table 3: Distribution of qualitative variables

		n	%
Gestational Week	11	362	11,4
	12	1689	53,3
	13	975	30,8
	14	140	4,4
Age Risk Category	Low Risk	3166	100,0
	High Risk	0	0,0
Trisomy 21 Category	Low Risk	3107	98,1
	High Risk	59	1,9
Trisomy 18 Category	Low Risk	3164	99,9
	High Risk	2	0,1

Table 4: Distribution of Trisomi21 Risk by qualitative variables

	Trisomy21 Risk		p
	Low Risk (n=3107) Mean	**High Risk (n=59) Mean**	
Age(Years)	27,32±5,34	33,27±7,83	<0,001
Weight(Kilograms)	65,66±13,16	65,78±11,15	0,944
CRL(mm)	60,75±8,53	58,5±9,52	0,045
β-HCG(ng/mL)	53,22±129,04	154,46±223,38	<0,001
PAPPA(mIU/l)	3708,9±2489,01	2347,26±1906,91	<0,001
NT(mm)	1,37±0,35	1,89±0,87	<0,001
β-HCG MoM	1,2±0,84	2,78±1,59	<0,001
PAPPA MoM	1,24±0,68	0,9±0,77	<0,001
NT MoM	0,88±0,23	1,28±0,66	<0,001
Age Risk(%)	0,0015±0,0019	0,0077±0,0116	<0,001
Trisomy 21 Risk(%)	0,0002±0,0004	0,023±0,0307	<0,001
Trisomy 18 Risk(%)	0,0001±0,0041	0,0002±0,0005	0,796

Significance test of difference between two means was used.

Table 5: Comparison of newly estimated median values with the software program

Gest. Week	**Free β-hCG(ng/mL)**				**PAPP-A (mIU/l)**		
	CaseNumber	**New Estimated Median**	**Software Median**	**p value***	**New Estimated Median**	**Software Median**	**p value***
11	362(11,4)	36,76	51,79	<0,001	1836	1337	<0,001
12	1689(53,3)	33,64	41,75	<0,001	2719	1919	<0,001
13	975(30,8)	28,51	35,70	<0,001	4052	2926	<0,001
14	140(4,4)	20,89			5370	4358	<0,001

Wilcoxon test used.

DISCUSSION

Dual screening tests are now in routine use with increasing gestational age and they lead to interventional application when high risk is reported. So those, accuracy of their results are very important. False positive and false negative results can negatively affect the life of the pregnant and the baby (Assessment, 2000).

Due to the advanced procedures performed in pregnant women due to false positivity in the double screening test; the risk of obstetric complications such as preterm labor, pre-eclampsia, low birth weight, intrauterine growth retardation, perinatal fetus death increases. While analytical performance is within acceptable limits, variations in measurements are not effective in predicting risk in low-risk groups, but are highly effective in predicting risk in high-risk groups and high maternal age groups. The analytical accuracy of the measured biochemical parameters for the combined test is important and can lead to high variations in risk calculation. These variations result in repetition of the test or carry the patient to amniocentesis, which is an invasive procedure and causes anxiety in the patient.

Many studies have shown a relationship between Down Syndrome and low levels of maternal serum PAPP-A and high levels of free β-HCG levels in the first trimester (Spencer, Macri et al., 1992). In the first trimester, a combined test is obtained by evaluating two biochemical parameters measured in maternal serum and NT measurement, an ultrasound data (Wald and Hackshaw, 1997). The combined test has a risk detection rate of 82-87%, with a false positivity of 5%. The performance was evaluated

as better than the triple test performed in the second trimester (Ananth et al., 2017). According to the 2007 clinical guidelines for ACOGs (American Congress of Obstetricians and Gynecologists), the combined test is an effective screening test for Down Syndrome in the general population (Goetzl, 2002). In terms of the effect of analytical variations on risk calculation, there are many studies related to the second trimester tests, but there are no studies related to the first trimester tests (Holding, 1991).

The use of devices of different brands and models and the analysis kits of different manufacturers may cause the laboratories where prenatal screening tests are performed to contain different analytical processes (Alp et al., 2018). The important factorsthat increase the variability of the risk analysis are the use of different biochemical markers in different screening protocols and the calculation of different components with various software in risk calculation. The result of the analysis are affected by the algorithms used by the software program used in the laboratory and the factors used in the steps of the calculation (such as accuracy of biochemical analysis, demographic data [gestational age and gestational age and BPD measurement] and / or USG date).

Atak et al. (2014) performed a retrospective study of 5820 singleton pregnant women in the Adıyaman region using dual screening data obtained with the Beckman-Coulter Unicel DxI 800 device and compared the median values of the Benetech PRA package program with the median values. Both β-hCG and PAPP-A were significantly lower than those of the program at all weeks ($p < 0.05$). Sucu et al. (2018) conducted a retrospective study of triple screening data of 1572 singleton pregnant women using the Immulite One device in Istanbul and compared the median values of the Prisca4.0 Typolog software with those of the firm software program. Values were significantly different in all weeks except 11th gestational week. In addition, Alp et al. (2018) in their retrospective study using the double screening data obtained by the Immulite 2000 device in 1413 single pregnant women for Van region, compared with those of the Prisca 5.0 Typolog software. New median values of β-hCG was found to be significantly lower than those of the program ($p < 0.05$), but no difference was found for PAPP-A ($p > 0.05$).

In our study; the data obtained from Immulite 2000 device in 3166 single pregnant women admitted to our hospital with the median values of SsdwLab5 software. Estimated median values of β-hCG were found to be significantly lower than those of the program ($p < 0.05$), while PAPP-A values were significantly higher ($p < 0.05$).

Estimation of different median values is due to the influence of different kits, devices, software programs, laboratories and regions. This makes it necessary for each laboratory to estimate its own median values. In all of the aforementioned studies, this is a common opinion. Our study has also supported this view. Since first trimester screening test is performed in other hospitals in our province, our results reflect only the results of patients admitted to our hospital.

These results once again showed that the analytical performance of the 1st Trimester screening tests should be kept at optimum levels. It is important to have experienced laboratory personnel, high quality and the highest level of laboratory equipment. This also requires a strict internal and external quality control programs. Additionally, it is inevitable to estimate the region-specific and even laboratory-specific median values.

Acknowledgement

We would like to thank our all of the staff, especially our data processing staff, for their valuable contributions in the collection and processing of data for this study.

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Olgu Sunumu/Case Report

Van Sag Bil Derg 2019;12(2):22-24

A Rare Complication of Left Atrial Dilatation in Childhood: Vocal Cord Paralysis and Ortner Syndrome

Çocukluk Çağı Sol Atriyal Dilatasyonun Nadir Bir Komplikasyonu: Vokal Kord Paralizi ve Ortner Sendromu

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Geliş Tarihi: 04.11.2019, Kabul Tarihi: 17.12.2019

ÖZET

Bu yazıda, çocukluk çağında literatürde sıklıkla bildirilmeyen, rekürren romatizmal kardit ve buna ikincil sol atriyal dilatasyona bağlı Ortner sendromu gelişen hasta sunuldu. Sydenham koresi tanısı olan ve penisilin profilaksisini kullanmayan 15 yaşındaki kız çocuğu tekrarlayan romatizmal kardit atağı ile başvurdu. Hasta yatırıldı ve oral steroid tedavisi ile intramüsküler benzatin profilaksisi başladı. Ayrıca hastanın yatışı sonrası başlayan ses kısıklığı, sıvı gıda alımı sonrası öksürük ve hematez yakınmaları vardı. Yapılan laringoskopik muayenede sol vokal kord paralizisi saptandı. Hastaya vokal kord enjeksiyonu yapıldı ve sıvı alımı sonrası öksürüğü geriledi, ancak ses kısıklığı devam etti. Sol atriyal basıncı azaltmak ve kalıcı laringeal sinir hasarı gelişimini önlemek için mitral ve aort kapak replasmanı yapıldı. Ortner sendromu nadir görülebilmesine rağmen, ses kısıklığı nedeniyle başvuran çocuklarda da akılda tutulmalıdır.

Anahtar Kelimeler: Sol atriyal genişleme, Ortner sendromu, romatizmal kardit, Sydenham koresi.

ABSTRACT

In this report, a patient was presented with the diagnosis of Ortner syndrome secondary to recurrent rheumatic carditis and left atrial dilatation, which was not commonly reported in the literature in childhood. A 15-year-old girl with Sydenham's chorea who did not use penicillin prophylaxis was presented with recurrent rheumatic carditis attack. She was hospitalized and oral steroid therapy and intramuscular benzathine prophylaxis was initiated immediately. She also had the complaints of hoarseness, cough after liquid intake, and hematemesis after her hospitalization. In the laryngoscopic examination left vocal cord paralysis was detected. Vocal cord injection was performed and her cough after liquid intake regressed, but hoarseness did not. Mitral and aortic valve replacement was performed in order to decrease left atrial pressure and to prevent the development of permanent laryngeal nerve damage. Ortner syndrome although seen rarely should be kept in mind also in children who have been admitted because of hoarseness.

Key words: Left atrial enlargement, Ortner syndrome, rheumatic carditis, Sydenham's chorea.

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Olgu Sunumu/Case Report

Van Sag Bil Derg 2019;12(2):22-24

INTRODUCTION

Left-sided vocal cord paralysis and hoarseness developing as a result of compression of the recurrent laryngeal nerve secondary to cardiac pathologies, such as left atrial dilatation, aortic aneurysm or pulmonary hypertension, between the pulmonary artery and the aorta is called Ortner syndrome. In this report, a 15-year-old girl who developed Ortner syndrome secondary to recurrent rheumatic carditis and left atrial dilatation was presented since it was rarely reported in the literature in childhood.

CASE

The patient who was diagnosed as Sydenam's chorea because of weakness and involuntary movements in the extremities three years before the last admission, was presented with recurrent rheumatic carditis attack and she did not use the prophylaxis. The patient had aortic (3rd degree) and mitral (4th degree) valvular regurgitation, the left atrium and ventricle were markedly dilated in echocardiography (figure 1 and figure 2). Cardiac contraction and valvular movements of her heart were decreased, ejection fraction was calculated as 45% in M-mode echocardiography. Steroid and congestive heart failure treatment was started to the patient, but she had the complaints of hoarseness, cough after liquid, and hematemesis. The endoscopic examination was performed by the gastroenterology department and the upper gastrointestinal system was evaluated as normal. Laryngoscopic examination was performed due to hoarseness and all laryngeal structures were found normal other than left vocal cord paralysis (figure 3). Vocal cord injection was performed by using calcium hydroxyapatite (radiesse) material, the only long-acting injectable laryngeal material approved by the FDA, as the temporary treatment and aspiration attacks were improved despite hoarseness. Because of the severe regurgitations of mitral and aortic valves, two valve replacement was performed to reduce left atrial pressure and to prevent the development of permanent laryngeal nerve damage. In the surgery the recurrent laryngeal nerve on the left side was seen close to the left atrium and ventricle there was evidence of stretch injury on pericardium on the left side. Hoarseness and the other complaints of the patient regressed consecutively within a month after surgery.

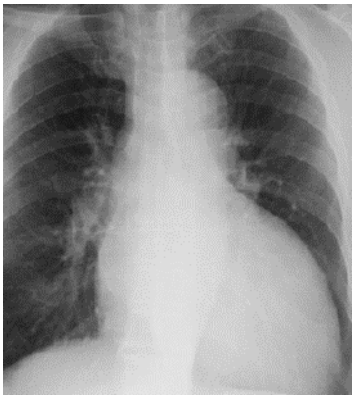

Figure 1: Chest x ray of the patient showing marked left heart dilatation

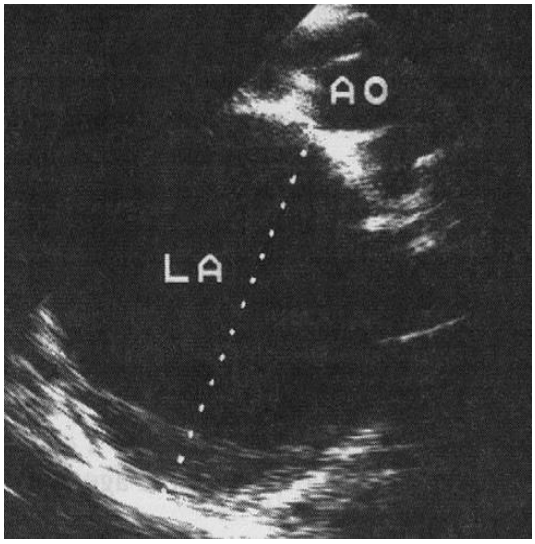

Figure 2: Echocardiographic imaging of the patient showing marked left heart dilatation

Figure 3: Laryngoscopic examination imaging of the patient showing left vocal cord paralysis.

DISCUSSION

Vocal cord paralysis may occur due to intralaryngeal or more frequently extralaryngeal pathologies. The most common two causes of unilateral vocal cord paralysis are intra-thoracic malignancies causing mediastinal lymphadenopathies, and surgical interventions (Karataş et al., 2006). Ortner syndrome was first described by Ortner in 1987 as a compression of the recurrent laryngeal nerve between the enlarged left atrium and the aortic arch in a patient with mitral stenosis (Ortner, 1987). However, it was accepted as a hoarseness due to compression of the recurrent laryngeal nerve that innervates the vocal cords between the pulmonary artery and the aorta or aortic ligaments (Thirlwall, 1997). Ortner syndrome, also known as cardio-vocal syndrome, is not as common in childhood as in adults. Congenital heart diseases such as atrial septal defect, ventricular septal defect, patent ductus arteriosus, total abnormal pulmonary venous return, idiopathic pulmonary hypertension have been reported as the most common causes of Ortner syndrome in the pediatric population.

Rheumatic mitral stenosis has been shown to be the most common cause in older children (Karataş et al., 2006). In this case, the etiology of the disease was recurrent rheumatic carditis leading to left atrial dilatation.

Although it is mainly hoarseness but dyspnea, hemoptysis, chest pain, cough are the other common symptoms of the disease. In our case, hoarseness, cough and hematemesis were the symptoms developed during the course of the treatment of rheumatic carditis.

Imaging methods have an important role in the diagnostic algorithms of causes of vocal cord paralysis (Yuan, 2014). Contrasted thorax tomography showed no pathology other than left atrial dilatation in accordance with the echocardiographic examination in our patient.

The main aim of the treatment is the elimination of the pressure on the nerve. In our patient, contractility of the heart returned to the normal with the treatment of heart failure, but patient's symptoms did not regress. In the laryngoscopic examination left vocal cord paralysis was detected and prevention of permanent nerve injury was planned the patient had aortic and mitral valve replacement. There was a marked reduction in the left atrium diameter after the surgery and the hoarseness of the patient regressed.

The hoarseness caused by isolated left atrial dilatation as a result of recurrent rheumatic carditis in children has not been previously described in the literature. However, few cases with similar complaints in different cardiac diseases have been reported in the adult age group (Özyurtlu et al., 2013). Ortner syndrome should be kept in mind also in children who have been admitted because of hoarseness but who have left atrial dilatation on echocardiography and who do not have any pathological findings on laryngoscopic examination other than vocal cord paralysis.

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Derleme/Review

Van Sag Bil Derg 2019;12(2):25-31

The Effects of Coffee Consumption on Cardiovascular Heart Diseases and Other Diseases

Kahve Tüketiminin Kardiyovasküler Kalp Hastalıkları ve Diğer Hastalıklar Üzerine Etkileri

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Geliş Tarihi: 24.10.2019, Kabul Tarihi: 11.12.2019

ABSTRACT

Coffee is the most consumed drink in daily life after tea and water. Coffee has become an indispensable part of our sociocultural life. Most people start their day with coffee and finish with this. Coffee can be called superfood because it has many bioactive components, minerals and vitamins that affect human health. Therefore, coffee has attracted the attention of many researchers with its rich bioactive components and then studies about the effects of coffee on animal and human health have been realized. In this review, we aimed to investigate the effects of coffee on health, especially cardiovascular disease (CVD) and cardiovascular risk factors.

Keywords: Antioxidant, Bioactive Components, Cardiovascular Diseases, Coffee, Health

ÖZET

Kahve, çay ve sudan sonra günlük yaşamda en çok tüketilen içeceklerdir. Kahve, sosyokültürel yaşamımızın vazgeçilmez bir parçası haline gelmiştir.Çoğu insan güne kahve ile başlar ve kahveyle bitirir. Kahve süper besin olarak isimlendirilebilir çünkü insan sağlığını etkileyen birçok biyoaktif bileşeni, mineralleri ve vitaminleri vardır.Böylece kahve, zengin biyoaktif bileşenleri ile birçok araştırmacının dikkatini çekmiş ve ardından kahvenin hayvan ve insan sağlığı üzerindeki etkileri ile ilgili çalışmalar yapılmıştır.Bu derlemede kahvenin sağlığa, özellikle kardiyovasküler hastalıklar (CVD) ve kardiyovasküler risk faktörleri üzerine etkilerini irdelemeyi planladık.

Anahtar Kelimeler: Antioksidan, Biyoaktif Bileşenler, Kardiyovasküler Hastalıklar, Kahve, Sağlık

INTRODUCTION

Coffee is one of the most consumed drink on worldwide and it has taken important place in populations since at least 1200 years (Bonita et al., 2007). Countries where coffee is consumed mostly are Finland, Norway and Danmarkrespectively (ICO, 2016). Itis estimated that coffee consumption will increase as nontraditionally in Africa, Asia, and Oceania in many years and it is predicted that the request for coffee marketing will expand by 2.5% in North America and by 1% in Europe (ICO, 2018).

Coffee belongs to Rubiaceae family and it has two main type forms (*Coffea arabica L.* and *Coffea canephora*) that have originated from Ethiopia and in tropical Africa (ICO, 2016). The coffee is generally prepared by hot water and ground coffee but it can be consumed in different forms. It is drinked as espresso in Italy that is prepared by extracting finely ground powder with high-pressure hot water. In today, the coffe can be cooked by the coffee machine that hot water is forced up through the coffee to the top of the machine (Martini et al., 2016).

The coffee and bioactive components

Coffee is a complex mixture of chemical structures and it is the main source of caffeine (Figure 1). Also, it contains many different chemicals such as carbohydrates, lipids, nitrogenous compounds, vitamins, minerals, alkaloids and phenolic components (Spiller, 1984).

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The polyphenols are represented by chlorogenic acid and its components such as caffeine, caffeic acid, trigonelline, chlorogenic acid and diterpenes that have effects on human health (Frost-Meyer et al.,2012).

Caffeine: Caffeine (1,3,7-trimethylxanthine)is a purine alkaloid(Louarn et al., 2001).There is between 84 mg and 112 mg caffeine in a cup of coffee (Gilbert et al., 1976).Caffeine is an antagonist of phosphodiesterases and adenosine receptors(Boswell-Smith et al., 2009; Holtzman et al., 1991). It affects the central nervous system by increasing dopamine, nor adrenaline and glutamate (Ferré et al., 1997). It may incease heartbeat, systolic and diastolic blood pressure and it may reduce cerabral and coronary blood flow (Namdar et al., 1990; Namdar et al., 2009). Mitani et al. have observed that caffeine might suppress lipid accumulation in adipocytes by inhibiting the secretion of inflammatory cytokines (Mitani et al., 2017).

Caffeic acid: Caffeic acid is one of the metabolities of chlogenic acid (Sato et al., 2011). Caffeic acid has anti-inflammatory, anticancerogenic, and enzyme-inhibiting properties (Chung et al., 2004). It has been shown that there is a negative linear relationship between the serum caffeic acid levels and colon cancer risk. Also, it has been observed that caffeic acid might inhibit IL-8 production in colon cells (Shin et al.,2015).

Chlorogenicacid: Chlorogenic acids have quinic acid and trans-cinnamic acids components (Upadhyay and Mohan Rao, 2013). The major source of chlorogenic acid is coffee that is intaken by diet and the amount of chlorogenic acid depends on daily coffee consumption (Mohan Rao et al., 2012). It is uncertain that it prevents or induces DNA damage. Some researchersclaim that it has protective effects against free radical induced DNA oxidation in human colon HT29 and liver HepG2 cancer cell lines. On the other hand, some other researchers observed that the increased concentration of chlorogenic acid triggered DNA damage (Glei et al., 2006).

Kahweol: Kahweol is a coffee-specific diterpene that is found in Arabic coffee beans oil and its concentration in coffeechangesinbetween the ranges 0.1 to 7 mg/mL (Gross et al.,1997; Arab, 2010). Itmay increase serum cholesterol levels on

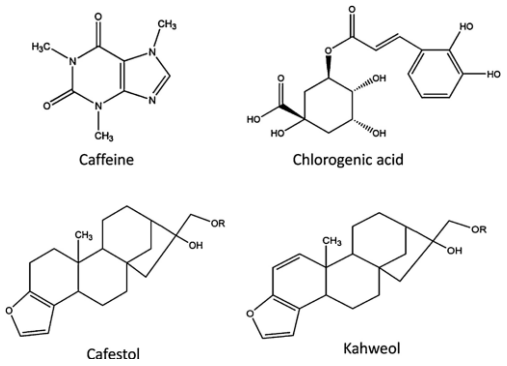

Figure 1. The chemical structures of bioactive components of coffee (Bae et al., 2014)

animals and human (DeRoos et al., 1999). However, it may haveprotective properties against carcinogens (Huber et al.,1997).

Hiypertension: The effects of consumption coffee consumption is transient on hypertensionis transient. It has been observed that the coffee increases acute blood pressure rarely andthe coffee's blood pressure effects are not important on chronic coffee consumers (Mesas et al., 2011).When coffee is consumed regularly, the tolerance develops against its hemodynamic and humoral effects (Robertson et al., 1981). In a study, it has been demonstrated that 6 cups of coffee consumption daily were not associated with increased risk of hypertension (Robertson et al., 2005).

Type 2 Diatebes Mellitus (T2DM): The coffee consumption may reduce the risk of T2DM according to results of cohort studies (Carlsson et al., 2004). There are two hypotheses that for reductionof the risk of diabetesdue to coffee consumptionmay reduce the risk of diabetes. One of them is that the chlorogenic acid component of coffee may inhibit glucose-6-phosphatase system and it may be competitive inhibitor of glucose- 6-phosphate translocase (Arion et al., 1997). Other hypothesis is inhibition of intestinal glucose absorption by chlorogenic acid and other phenolic components of coffee (Welschet al., 1989). In a prospective study, the risk of T2DM was %50% lower in adults consuming at least 7 cup of coffee daily compared to less coffee consumers (<2 cups of coffee) (VanDam et al., 2002).

Insulin Sensitivity: In a recenty study, the researchers have observed that 5 cups of coffee

consumption reduced insulin resistance and it increased tissue adiponectin tissue levels (Wedick et al., 2011).

Hyperlipidemia: Coffee contains cholesterol increasing components such as diterpenes, cafestol and kahweol but the concentrations of these compounds depend on method of how coffee is preparationed (Urgert et al., 1997). In a study, the volunteers were dividedersed into three groups. The first 2 groups consumed 4 to 6 cups of boiled or filtered coffee daily and the other group was placebo. After 9 weeks, there was significant rise in total serum cholesterol levels in volunteers consuming boiled coffee and there was no significant rise serum LDL levels in this group.There was no significant difference in serum lipid levels between other groups (Grobbee et al., 1989). In another study, there was no evidence about the filter coffee increasing serum lipid levelsincrease dur to filter coffee consumption (Lopez-Garcia et al., 2006).

Homocysteine: It has been demonstrated that coffee consumption may increase plazsma total homocysteine levels in man as dose-dependentlytedin researchs (Husemoen et al., 2004). In a study, the homocysteine levels were found higher in participants consuming one liter of unfiltered coffee daily compared to those consuming one liter of filtered coffee (Urgert et al., 2010).

Stroke: Coffee consumption may reduce the risk of stroke. The meta-analysis of seven prospective studies demonstrated that 1 to 3 cups coffee consumption was associated with reduced stroke risk. Other hand, it has been observed that more than 6 cups of coffee consumptioning did not reduce the stroke risk in another study. According to researchers, the coffee is not associated with high stroke risk but habitual moderate coffee may provide protective effects (D'Elia et al., 2012).

Cardiovascular heartdiseases: The studies that have investigated the association between coffee consumption and coronary heart diseases are contradictory. In a meta-analysis with case-control and cohort studies, the coffee consumption was significant associated with cardiovascular heart diseases in short-term but same relationship could not been observed in long-term (Greenberg et al., 2007). The researchers detected that coffee consumption reduced CVD risks and inflammatory diseases in only post menopousal women because of its antioxidant and antiinflamatory properties (Andersen et al., 2006). Butin 21 cohort prospectivestudies, it has been observed that moderate coffee consumption reduced CVD risks in long- term. Also the adults consuming moderate coffee had lower CVD risk compared to those who less consumed (Wu et al., 2009). In another study including patients with STEMI history, there was no cardiacarrhythmia increase in patients due to vagal tonus activation. The researchers agree that the coffee consumption may be confident the patients with STEMI history (Richardson et al., 2009). In conclusion, there are contradictions between studies and the prospective cohort studies have not found significant associations between coffee consumption and CVD risk (Higdonand Frei, 2006).

Heart Failure (HF): There was interesting association between HF risk and coffee consumption. In a recenly study, more or less coffee consumption increased HF risk but 4 cups of coffee consumption daily reducedHF risk. But the patientswere not categorized according to their sex, age, MI or DM history in this study (Mostofsky et al., 2012).

Table 1. The cardiovascular effects of coffee on human health

The acute effects of coffee are transient on blood pressure and it may not increase the risk of hipertension on chronic coffee consumers.
Coffee may reduce the development of T2DM risk.
The effect of coffee on serum lipid levels varies according to types of cooking.
Although there is no strong evidence that coffee reduced high stroke risk, moderate coffee consumption may be protective against stroke.
There are contradictory claims about association between coffee and CVD risk. But coffee may reduce CVD risk in post menopousal womenbecause of reduced inflammation.
Coffee consumption is confident for patients with STEMI history.
The effects of coffee on HF changes as dose dependent
Coffee can reduce all-cause deaths by reducing cardiovascular risk.
Coffeine does not cause serious ventricular and supraventricular cardiac arrhythmias. Also, there is no association between AF and coffee consumption.

Cardiovascular mortality: The coffee was found to be protective on cardiovascular mortality in elderly patients in a study (Greenberg et al., 2007). In another study, the participants with no cancer and no CVD history were included and they were followed during long-term. The results of the study, it has been observed showed that coffee consumption reduced all-cause mortality due to moderately reduced risk of CV disease mortality. Also decaffeinated coffee slightly reduced in all-cause and CV disease mortality (Lopez-Garcia et al., 2008).

Cardiac Arrhythmia: The recent studies demonstrated that coffee consumption did not increase arrhythmia risk. In a study, habitual coffee consumption was inversely associated with hospitalization due to cardiac arrhythmia during long-term follow-up (Klatsky et al., 2011). According to recent studies, high doses coffee consumption did not eaffect heartbeat rate, available rhythmand did not cause serious ventricular and supraventricular arrhythmias (Newcombe et al., 1988). More recently, two prospective studies could find no association between coffee and the risk of atrial fibrillation development atrial fibrillation (Wilhelmsen et al., 2001).

The other effects of coffee on human health

Cancers: Many studies have shown that the coffee consumption was associated with reduced cancer risks but these studies were mostly case-control studies (Nawrot et al., 2003). In the result of the metaanalysis of 17 trials, four or more cups daily coffee consumption causedby 24% reduction of colorekctal cancer risk (Giovannucci et al., 1998). A prospective cohort study indicated that increased coffee consumption was negatively correlatedion with hepatocellular carcinoma risk (Inoue et al., 2005).

Cirrhosis: Coffee consumption was inversely associated with risk of cirrhosis in several case-control studies. A study in Norway, the death from cirrhosis was found by 40% lower in patients consuming two cups of coffee daily compared to those who never consumed (Tverdal et al., 2003).

Parkinson disease: Studies in animal models submitted suggestedthat caffeine consumption decreased the risk of Parkinson's disease by protecting against dopaminergic neurotoxicity (Schwarzschild et al., 2002). In a cohort study, the coffee consumption prevented the death from Parkinson diseases in men but not woman. Perhaps eustrogen replacement theraphy may decrease the benefit of coaffeinein women (Ascherio and Chen, 2003).

Bone fracture: It is claimed that highmuch coffee consumption provoked by 14% more bone fracture because of negative effects on calcium absorption and bone mineral density (Lee et al., 2014; Heaney, 2002; Hallström 2013). However, the researchers explored that 400mgcoffee consumption daily might not damage the calcium absorption and bone mineral density (Wikoff et al., 2017).

Antiinflammatory and antioxidant effects: Several studies have reported that coffee has antinflammatory and antioxidant effects due to bioactive components such as especially caffeine and chlorogenic acid. The researchers agree that coffee may prevent lipid peroxidation, DNA damage and it may reduce the expression of pro-inflammatory cytokines (Sukyoung et al., 2018).

Table 2. The other effects of coffee on human health

It has anti-inflammatory and antioxidant effects.
It decreases the risk of suicide and the symptoms of depression.
It reduces the death from cirrhosis
It is associated with lower colorectal cancer risks.
It has benefict effects on Parkinson disease.
It may have negative effects on bone mineral density and may reduce calcium absorption to bone.

Suicide, anxiety and depression: Each cup of coffee can reduce the risk of suicide by 24% (Kawachi et al., 1996). Also, the coffee consumption may relieve the depreesion symptoms and it is associated with lower risk of anxiety (Tse et al., 2009; Wang et al., 2016).

Adverse effect of coffee and caffeine:

The coffee may cause tachycardia, palpitations, insomnia, restlessness, nervousness, tremor,

headache, abdominal pain, nausea, vomiting, diarrhea and dieresis depending on caffeine component of coffee (Engebretsen et al., 2001). Caffeine may cause withdrawals symptoms including headaches, fatigue, drowsiness, and irritability, difficulty concentrating and depressed mood in consuminglong-termconsumption (Dews et al., 1999). Caffeine may increase the adverse effects of sympathetic agents and acetaminophen. It may inhibit antipsychotic agents' elimination and metabolism (Mendelsohn, 2001).

CONCLUSION

Although coffee is one of the mostconsumed drinks and it has rich bioactive components, the studies on human health are still controversial. Therefore, health professionals should be aware of the effects and side effects of coffee consumption and should be careful. Alsorandomized controlled prospective and high-evidence studies that will clearly demonstrate the effects of coffee consumption on heart and human health are needed.

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