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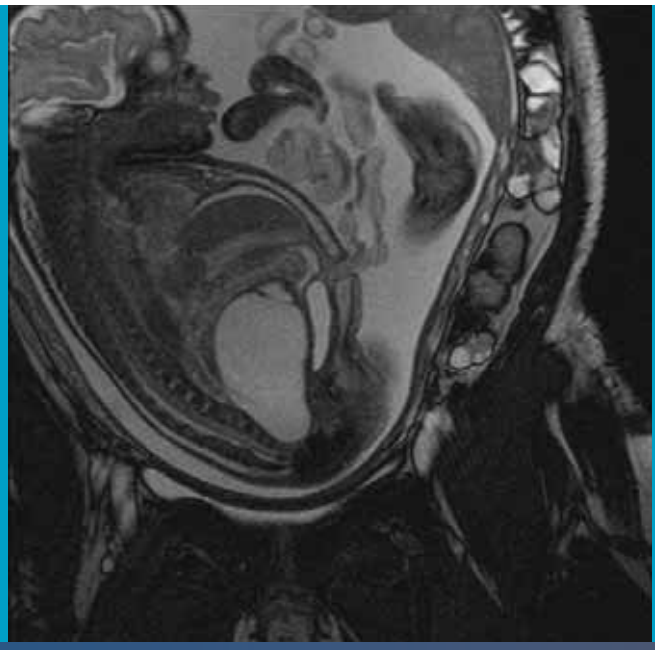

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ARVELES®

DEKSKETOPROFEN TROMETAMOL

ARVELES® TABLET

Hafif ve orta şiddetteki ağrıların
semptomatik tedavisinde,

ARVELES® AMPUL IM/IV

Postoperatif ağrı
Renal Kolik
Bel ağrısı

gibi orta ve ağır şiddetteki akut ağrıların
semptomatik tedavisinde kullanılan

bir ağrı kesicidir...[1]

REFERANSLAR 1- ARVELES® Tablet / **ARVELES®** Ampul Ürün Bilgisi

ARVELES®

FORMÜL: Her bir tablet 25 mg deksketoprofene (INN) tekabül eden 36,9 mg deksketoprofen trometamol ve titanyum dioksit (E 171) içerir. Her bir 2 ml'lik ampul 50 mg deksketoprofen'e eşdeğer 73,8 mg deksketoprofen trometamol, 200 mg etanol (%96), 8 mg sodyum klorür, sodyum hidroksit q.s., enjeksiyonluk su q.s. 2 ml içerir. **FARMAKOLOJİK ÖZELLİKLER:** Deksketoprofen trometamol, steroid olmayan antiinflamatuar ilaç grubuna dahil analjezik, antiinflamatuar ve antipiretik bir ilaçtır. **ENDİKASYONLAR: ARVELES®** *25 mg Tablet:* Muskülo-skeletal ağrı, dismenore, diş ağrısı, postoperatif ağrı gibi hafif ve orta şiddetteki ağrıların semptomatik tedavisinde kullanılır. **ARVELES®** *50 mg Ampul:* Oral kullanımın uygun olmadığı postoperatif ağrı, renal kolik ve bel ağrısı gibi orta ve ağır şiddetteki akut ağrıların semptomatik tedavisinde kullanılır. **KONTRENDİKASYONLAR: ARVELES®** Tablet ve Ampul aşağıdaki olgularda uygulanmamalıdır: •Deksketoprofene, diğer NSAİİ'lere veya üründeki herhangi bir yardımcı maddeye karşı daha önce duyarlılığı olan hastalar •Benzer etkili (Örn. Aspirin veya diğer NSAİİ'ler) bileşiklerin astım, bronkospazm, akut rinit krizlerine yol açtığı veya nazal polipler, ürtiker veya anjiyonörotik ödeme neden olduğu hastalar •Aktif veya şüpheli gastrointestinal ülseri olan veya gastrointestinal ülser veya kronik dispepsi hikayesi olan hastalar •Gastrointestinal kanama veya diğer aktif kanamaları veya kanama bozukluğu olan hastalar •Crohn hastalığı veya ülseratif koliti olan hastalar • Şiddetli kalp yetmezliği olan hastalar •Orta veya şiddetli böbrek fonksiyon bozukluğu olan hastalar • Şiddetli karaciğer fonksiyon bozukluğu olan hastalar •Hemorajik diatezi veya diğer pıhtılaşma bozukluğu olan veya antikoagülan tedavisi gören hastalar • Bronşiyal astım geçmişi olan hastalar • Gebelik ve laktasyon dönemlerinde •**ARVELES®** *Ampul*'ün, etanol içermesinden dolayı nöraksial (intratekal veya epidural) yolla alımı kontrendikedir. **ÖZEL UYARILAR ve ÖZEL KULLANIM TEDBİRLERİ:** Çocuklarda kullanım güvenilirliği tespit edilmemiştir. Alerji hikayesi olan hastalarda kullanırken dikkatli olunmalıdır. Deksketoprofen trometamol alan hastalarda ender oluşabilecek gastrointestinal kanama veya ülserasyon durumlarında, tedaviye hemen son verilmelidir. NSAİİ'ler, trombosit agregasyonunu baskılayabilir, kanama süresini uzatabilirler. Kumarin tedavisi alan hastalar dikkatle izlenmelidir. Tüm NSAİİ'ler plazma üre azotunu ve kreatinini artırabilir. Tüm NSAİİ'ler bazı karaciğer parametrelerinde geçici küçük artışlara ve SGOT ve SGPT'de anlamlı artışlara neden olabilir. Bu durumda tedavi sona erdirilmelidir. Karaciğer, böbrek veya kardiyak fonksiyon bozukluğu olan hastalarla, sıvı retansiyonuna neden olan diğer hastalıkları olan hastalarda dikkatli olunmalıdır. Bu hastalarda renal fonksiyonlar kötüleşebilir ve sıvı retansiyonu ile sonuçlanabilir. Nefrotoksisite riskinde artma olması nedeniyle diüretik tedavisi gören hastalar ile hipovolemik olabilecek hastalarda da dikkat gereklidir. Kalp yetmezliğini tetikleme riski artabileceğinden, kalp hastalığı hikayesi bulunan hastalara özel dikkat gösterilmelidir. Tüm NSAİİ'ler infeksiyöz hastalıkların semptomlarını maskeleyebilir. Yaşlı hastalar, istenmeyen etkilere daha fazla duyarlıdır ve sonuçlar daha ciddi olabilir. Yaşlı hastalarda hepatik ve renal fonksiyonlar izlenmelidir. Hemopoietik bozukluklar, sistemik lupus eritematozus veya karışık bağ dokusu hastalığı olan hastalarda dikkatli kullanılmalıdır. **Gebelik ve Laktasyonda Kullanım:** *Gebelik Kategorisi:* **C. ARVELES®** Tablet ve Ampul hamilelik ve laktasyonda kullanılmamalıdır. **ARAÇ ve MAKİNE KULLANMAYA ETKİSİ:** Baş dönmesi ve uyuklama olasılığı nedeniyle makine veya araç kullanma yeteneği üzerinde hafif veya orta şiddette etkiler oluşturabilir. **YAN ETKİLER/ADVERS ETKİLER: ARVELES®** Tablet ile %1-10 sıklıkta görülen istenmeyen etkiler, bulantı ve/veya kusma, abdominal ağrı, diyare, dispepsi ve Ampul için bulantı, kusma, enjeksiyon yeri ağrısıdır. Sık olmayan (%0,1-1) yan etkiler uyku bozuklukları, anksiyete, baş ağrısı, baş dönmesi, vertigo, palpitasyonlar, gastrit, konstipasyon, ağız kuruluğu, gaz çıkarma, cilt döküntüleri, yorgunluk, sıcak basması, ağrı, asteni, rigorlar, hasta hissetmedir. Ayrıca ender olarak (%0,01-0,1) parestezi, hipertansiyon, periferik ödem, bradipne, peptik ülserasyon, hemoraji veya perforasyon, anoreksi, hepatik enzimlerde artma, ürtiker, akne, terlemede artma, poliüri, dişide menstrüel bozukluklar; erkekte prostatik bozukluklar, sırt ağrısı, senkop ve çok ender-izole olarak da (<%0,01) nötropeni, trombositopeni, görme bulanıklığı, tinnitus, taşikardi, hipotansiyon, bronkospazm, dispne, pankreas hasarı, karaciğer hasarı, şiddetli mukokütanöz cilt reaksiyonları (Stevens Johnson, Lyell sendromları), anjiyoödem, dermatolojik reaksiyonlar, fotosensitivite reaksiyonları, prurit, böbrek hasarı (nefrit veya nefrotik sendrom), anaflaksi, fasiyel ödem bildirimleri bulunmaktadır. Belirgin olarak sistemik lupus eritematozus veya karışık bağ dokusu hastalığı olan hastalarda oluşabilen aseptik menenjit ve hematolojik reaksiyonlar (purpura, aplastik ve hemolitik anemi, ve ender olarak agranülositoz ve medullar hiperplazi). BEKLENMEYEN BİR ETKİ GÖRDÜĞÜNÜZDE DOKTORUNUZA BAŞVURUNUZ. **İLAÇ ETKİLEŞMELERİ ve DİĞER ETKİLEŞMELER:** Aşağıdaki etkileşmeler genelde tüm steroid olmayan antiinflamatuar ilaçlar (NSAİİ) için geçerlidir: Önerilmeyen kombinasyonlar: •Salisilatlar, diğer NSAİİ'ler •Oral antikoagülanlar, parenteral heparin ve tiklopidin •Lityum •Metotreksat •Hidantoinler ve sulfonamidler. **KULLANIM ŞEKLİ ve DOZU: ARVELES®** *Tablet:* Genel Popülasyon: Ağrının cinsine ve şiddetine göre önerilen doz genellikle her 4-6 saatte bir 12,5 mg veya 8 saatte bir 25 mg'dır. Postoperatif ağrı tedavisinde önerilen doz her 8 saatte bir 25 mg'dir. Günlük toplam doz 75 mg'yi geçmemelidir. **ARVELES®** *Ampul:* Yetişkinlerde: Tavsiye edilen doz her 8-12 saatte bir 50 mg'dır. Günlük maksimum doz olan 150 mg'yi aşmamak şartıyla, 6 saat arayla uygulanabilir. **ARVELES®** Tablet ve 50 mg/2 ml Enjektabl Çözelti İçeren Ampul, kısa süreli kullanım içindir ve tedavi akut semptomatik dönem ile sınırlandırılmalıdır (Ampul için maksimum 2 gün). **Uygulama Yöntemi:** *IM uygulama:* 1 adet ampul içeriği kas içine derin ve yavaş bir enjeksiyon ile verilmelidir. *IV uygulama: IV infüzyon:* Bir ampul (2 ml) içeriği normal NaCl, glikoz veya ringer laktat solüsyonu ile 30 lia 100 ml'lik hacim oluşturacak şekilde seyreltilmelidir, 10 ile 30 dakika arası bir sürede yavaş bir şekilde damar içine infüzyon ile verilmelidir. Solüsyon daima direkt güneş ışığından korunmalıdır. *IV bolus:* Gerekli ise, bir **ARVELES®** 50 mg/2 ml Enjektabl Çözelti İçeren Ampul içeriği 15 saniyeden uzun bir sürede yavaş İV bolus ile verilebilir. **DOZ AŞIMI:** Kazara veya fazla alınımda, acilen semptomatik tedavi uygulanmalı ve gerekiyorsa mide yıkanmalıdır. Deksketoprofen trometamol diyalizle uzaklaştırılabilir. **SAKLAMA KOŞULLARI:** 30°C'nin altında ve oda sıcaklığında, ışıktan korunacak şekilde saklayınız. Çocukların ulaşamayacakları yerlerde ve ambalajında saklayınız. **TİCARİ TAKDİM ŞEKLİ ve AMBALAJ İÇERİĞİ:** 20 film kaplı çentikli tablet. 2 ml Enjektabl çözelti içeren cam ampuller (6 ampul). **RUHSAT SAHİBİNİN İSİM ve ADRESİ:** İFSA İlaç Sanayi Tic. A.Ş., Davutpaşa Cad., No: 12, 34473 Topkapı-İSTANBUL Tel: (0212) 467 11 11, Faks: (0212) 467 12 12. **RUHSAT TARİHİ ve NUMARASI: ARVELES®** *Tablet:* 30.12.2003-115/18, **ARVELES®** *Ampul:* 29.12.2006-121/67, **KDV DAHİL PERAKENDE SATIŞ FİYATI** (Nisan 2009 itibarıyla): **ARVELES®** *Tablet:* 12,56 TL.- **ARVELES®** 6 Ampul: 17,17 TL.- **ÜRETİM YERİ ve ADRESİ: ARVELES®** *Tablet:* A. Menarini Industrie Sud S.r.l. Via Campo di Pile – 67100 L'Aquila-İTALYA, / Laboratorios Menarini SA Alfons XII, 587 08918 Barselona – İspanya, **ARVELES®** *Ampul:* A. Menarini Manufacturing Logistics And Services S.r.l. Via Sette Santi, 3, Floransa-İTALYA. Reçete ile satılır, Ayrıntılı bilgi için prospektüse bakınız. Daha geniş bilgi için firmamıza başvurunuz. **PROSPEKTÜS ONAY TARİHİ: ARVELES®** *Tablet:* 05.07.2005, **ARVELES®** *Ampul:* 14.08.2007

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Hayata Kesintisiz Devam...

Günde 2 Tablet

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Aims and Scope

Journal of the Turkish-German Gynecological Association is an official journal of the Turkish-German Gynecological Education and Research Foundation, Turkish-German Gynecological Association and the Turkish Society of Reproductive Medicine and is published quarterly on March, June, September and November.

The target audience of Journal of the Turkish-German Gynecological Association includes gynaecologists and primary care physicians interested in gynecology practice. It publishes original work on all aspects of gynecology. The aim of Journal of the Turkish-German Gynecological Association is to publish high quality original research articles. In addition to research articles, reviews, editorials, letters to the editor and case presentations are also published.

It is an independent peer-reviewed international journal printed in English language. Manuscripts are refereed in accordance with "double-blind peer reviewed" process for both referees and authors.

Papers written in English language are particularly supported and encouraged.

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FERLOS®

Demir (III) Hidroksit Polimaltoz Kompleksi

Anemi tedavisini keyfe dönüştürür!

Santa Farma

İlacın ticari adı: Ferlos® Oral Solüsyon

Etken maddenin onaylanmış jenerik adı: 100 mg elementer demire eşdeğer demir (III) hidroksit polimaltoz kompleksi. Bileşimindeki etken maddelerin birim dozdaki miktarları: Her bir oral flakon (5 ml); etkin madde olarak 100 mg elementer demire eşdeğer demir (III) hidroksit polimaltoz kompleksi, tatlandırıcı olarak şeker ve sorbitol, koruyucu olarak sodyum metil hidroksibenzoat, sodyum propil hidroksibenzoat ve ayrıca krema esansı ile karamel esansı içerir. Güncelleştirilmiş KÜB'e uygun ruhsatlandırılmış endikasyonu: Özellikle demir eksikliği anemisi başta olmak üzere tüm latent ve belirgin demir eksikliklerinin tedavisinde kullanılır. Kullanış şekli ve dozajı: Ferlos® Oral Solüsyon, yemekler sırasında veya hemen yemekten sonra alınmalıdır. Çocuklar (> 12 yaş), erişkin ve yaşlılar: Latent demir eksikliği: Günde 1/2-1 flakon (50-100 mg) Ciddi demir eksikliği: Günde 2-3 defa 1 flakon (200-300 mg) Tedavi süresi; demir metabolizmasının durumuna (azalmış alım, artan ihtiyaç, patolojik kayıp) ve eritrosit sayısının normalleşmesine bağlıdır. Belirgin demir eksikliğinde normal kan değerlerine ulaşmak ortalama 3-5 aylık tedavi ile olur. Latent demir eksikliğinde tedavi süresi 1-2 aydır. Hb konsantrasyonunun normale dönmesinden sonra depoların dolması için 2-3 aylık süre boyunca her gün 1 flakon içilmesi gereklidir. Uygulaması: Oral yolla uygulanır. Başlıca yan etkiler ve alınması gereken önlemler: Demir (III) hidroksit polimaltoz kompleksindeki demir (III) esasen non-iyonik olduğundan Ferlos® Oral Solüsyon ile iyonize demir tuz preparatlarında gözlenen gastrointestinal irritasyon, epigastrik dolgunluk, bulantı, diare, kabızlık gibi istenmeyen etkiler nadirdir. Başlıca etkileşimleri: Demir (III) hidroksit polimaltoz kompleksindeki demir (III), kompleks yapmış olduğundan yiyeceklerdeki bileşenlerle (fitin, oksalat, tannin) ve birlikte uygulanan ilaçlarla (tetrasiklin, antiasidler) iyonik etkileşme görülmez. Buna karşın demir iyonları (ferröz tuzları); yukarıda sayılan maddelerle çözünmeyen ketatlar oluşturarak demir emilimini azaltırlar. Dışkıda gizli kan aranması sırasında yanlışya neden olmaz. Bu nedenle, bu inceleme sırasında tedavinin kesilmesine gerek yoktur. Kontrendikasyonları, uyarılar ve ürün kullanılırken dikkat edilmesi gereken durumlar. Kontrendikasyonları: Demir yüklenmesi bulunanlarda veya demirin kullanımında bir bozukluğun söz konusu olduğu durumlarda (örneğin; hemokromatoz, hemosideroz, kurşun anemisi, sidero akrestik anemi, talasemi). Demir eksikliğinin neden olmadığı anemiler (örneğin; hemolitik anemi). Uyarılar/Önlemler: İnfeksiyöz veya kansere bağlı oluşan anemilerde demir, retiküloendoteliyal sistemde depolanmakta ve ancak primer hastalığın tedavisiyle mobilize olmakta ve kullanılmaktadır. Oral demir preparatlarının kullanımı sırasında dışkının rengi koyulaşabilir; bu durum, normal olup herhangi bir önlem gerektirmez. İmalatçının ismi ve adresi: SANTA FARMA İLAÇ SANAYİİ A.Ş. 34382 Şişli - İSTANBUL. Ruhsat tarihi ve numarası: 31.01.2006 - 207/15. "Daha geniş bilgi için firmamıza başvurunuz." Reçete ile satılır. Prospektüsün son güncellenme tarihi: 04.12.2007. Perakende satış fiyatı (K.D.V. dahil) ve onay tarihi: 16.93 TL. (20 Nisan 2009).

İlacın ticari adı: Ferlos® Çiğneme Tableti

Etken maddenin onaylanmış jenerik adı: 100 mg elementer demire eşdeğer demir (III) hidroksit polimaltoz kompleksi ve 0,35 mg folik asit Bileşimindeki etken maddelerin birim dozdaki miktarları: Her bir çiğneme tableti, etkin madde olarak 100 mg elementer demire eşdeğer demir (III) hidroksit polimaltoz kompleksi ve 0,35 mg folik asit; tatlandırıcı olarak aspartam ve dekstrat ile çikolata aroması ve karamel aroması içerir. Güncelleştirilmiş KÜB'e uygun ruhsatlandırılmış endikasyonu: Latent ve manifest demir eksikliğinin tedavisinde, ayrıca gebelik boyunca, gebelik öncesinde ve sonrasında (laktasyon döneminde) görülen demir ve folik asit eksikliğini engellemede endikedir. Kullanış şekli ve dozajı: Manifest demir eksikliği: Hemoglobin değerleri normal değerlere ulaşana kadar günde 2-3 kez birer tablet, daha sonra demir depolarının doldurulması amacı ile gebelik boyunca günde 1 tablet. Latent demir eksikliği ve demir/folik asit eksikliğinin engellenmesi: Günde 1 tablet. Ferlos® Çiğneme Tableti'nin yemek sırasında veya yemekten sonra çiğnenmesi ve üzerine bir yudum sıvı alınması önerilir. Komprimeleri bütünüyle biraz sıvı ile yutmak mümkündür. Demir depolarını doldurmak için, kan parametrelerinin (Hb, Hct, eritrosit) normale dönüşünden yaklaşık bir ay sonrasına kadar tedavi sürdürülmelidir. Uygulaması: Oral yolla uygulanır. Başlıca yan etkiler ve alınması gereken önlemler: Çok ender olarak tokluk hissi, epigastrik ağırlık hissi; bulantı; kabızlık ve ishal gibi yan etkiler görülebilir, ilacın kesilmesiyle bu şikayetler kaybolur. Dışkıda görülebilecek koyu renkin klinik olarak hiçbir önemi yoktur. Başlıca etkileşimleri: Demir (III) hidroksit polimaltoz kompleksi, kompleks şeklinde ve iyonik olmayan demir içerdiğinden besinlerde bulunan unsurlarla (fitatlar, oksalatlar, taninler gibi) veya aynı zamanda verilen ilaçlarla (tetrasiklinler, antiasitler gibi) etkileşimleri yoktur. Ferlos® Çiğneme Tableti, dişlerde boyanmaya sebep olmaz. Dışkıda gizli kan aranması sırasında yanlışya neden olmaz. Bu nedenle bu inceleme sırasında tedavinin kesilmesine gerek yoktur. Kontrendikasyonları, uyarılar ve ürün kullanılırken dikkat edilmesi gereken durumlar: Kontrendikasyonları: Organizmaya aşırı dozda demir yüklenmesi (hemokromatoz, hemosideroz), demir kullanımı bozuklukları (kurşun anemisi, sidero akrestik anemi, talasemi), B12 vitamini eksikliğine bağlı megaloblastik anemi ve hemolitik anemilerde kullanılmamalıdır. Uyarılar/Önlemler: Çocuklar tarafından yanlışlıkla fazla miktarda ilacın alınması akut demir zehirlenmesine neden olabileceğinden, ilaç, çocukların erişemeyeceği yerlerde saklanmalıdır. Enfeksiyona ya da kansere bağlı anemilerde yerine konulan demir retikuloendoteliyal sistemde depolanır ve ancak primer hastalık tedavi edildikten sonra kullanılabilir. Her bir tabletin 0,04 dilim ekmeğe eşdeğer olduğu diyabetiklerde dikkate alınmalıdır. İmalatçının ismi ve adresi: SANTA FARMA İLAÇ SANAYİİ A.Ş. 34382 Şişli - İSTANBUL. Ruhsat tarihi ve numarası: 14.08.2006 - 208/65. "Daha geniş bilgi için firmamıza başvurunuz." Reçete ile satılır. Prospektüsün son güncellenme tarihi: 16.08.2006. Perakende satış fiyatı (K.D.V. dahil) ve onay tarihi: 12.59 TL (20 Nisan 2009).

Journal of the
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- The Journal name should be abbreviated as "J Turkish German Gynecol Assoc"

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FORMÜLÜ: Triptorelin asetat ENDİKASYONLARI: IVF, Endometriozis, uterus miyomu KONTRENDİKASYONLARI: Klinik olarak belirgin osteoproz ya da osteoproz riski (örn. Azalmış kemik yoğunluğu), Hamilelik , Laktasyon Yardımlı üreme tekniklerinde kullanımında; özellikle polikistik overli hastalarda, ultrasonografi ile tespit edilen foliküller 10' dan fazla olduğunda Decapeptyl kullanımında önlemlerin sayısı artırılmalıdır.Triptorelin, poli (DL-laktid-ko-glikolid), dekstran veya diğer herhangi bir bileşene duyarlılık gösteren kişilerde kontrendikedir. UYARILAR/ ÖNLEMLER: Tedavi seks steroidlerinin serum düzeylerine göre ayarlanmalıdır. Özellikle polikistik overleri olanlarda aşırı uyarılmayı önlemek için foliküler büyüme ve luteal faz dikkatle izlenmelidir. Tedaviden önce gebelik durumu kontrol edilmelidir. Tedavinin ilk ayında kadınlar hormonal olmayan kontraseptifler kullanmamalıdırlar. Decapeptyl® tedavisi sırasında kadınlar östrojen pereparatı kullanmamalıdırlar. Uterus miyomu tedavisi sırasında uterusun ve miyomun boyutları, örneğin ultrasonografi ile düzenli olarak ölçülerek takip edilmelidir. Az sayıdaki vakada, miyom dokusuna göre orantısız olarak uterus hacminin hızla küçülmesi, kanamaya ve sepsise neden olmuştur. Gebelik ve laktasyon: Gebelikte kullanım kategorisi X. Gebelik ve laktasyon döneminde kesinlikle kullanılmaz. ARAÇ VE MAKİNA KULLANIMINA ETKİSİ: Araç ve makina kullanıma hiçbir etkisi yoktur. YAN ETKİLER/ ADVERS ETKİLER: Hormon üretiminin baskılanması sonucu en çok sıcak basması olmak üzere %75-100 hastada yan etkiler görülebilir. Kanama veya deride lekelenme, terleme, vajinal kuruma ve /veya disparoni, libido azalması ve ruh hali değişiklikleri kadınların %10'unda görülür. Depresif ruh hali, bulantı, miyalji, artralji, yorgunluk; uyku bozuklukları; aşırı duyarlık reaksiyonları (kaşıntı; cilt döküntüsü; ateş), uygulama noktasında geçici ağrı ve nadir olarak serum kolesterol düzeyinde hafif artış görme bozuklukları; parestezi , sırt ağrısı, yükselmiş enzim seviyeleri (LDH, _GT, SGOT, SGPT), anafilaksi, uygulama noktasında yabancı vücut reaksiyonu gözlenmitir. Hafif trabekül kemik kaybı görülebilir. Bu durum, tedavinin kesilmesini takiben 6-9 ay içinde genellikle geçer. Triptorelin kullanımında iki epifizyoliziz capitis femoris vakası bildirilmiştir. Nedensel ilişki saptanamamıştır. BEKLENMEYEN BİR ETKİ GÖRÜLDÜĞÜNDE DOKTORUNUZA BAŞVURUNUZ. İLAÇ ETKİLEŞİMLERİ ve DİĞER ETKİLEŞMELER: Östrojen içeren hiçbir ilaçla birlikte kullanılmamalıdır. KULLANIM ŞEKLİ ve DOZU: Mutad doz, 7 gün süreyle 0.5 mg'dır ve deri altına zerkedilir. Daha sonra idame dozu, 0,1 mg uygulanır. IVF'te dozaj uygulanan protokole göre değişir. Genellikle, siklus/ilk foliküler fazı ilk gününden itibaren hCG uygulamasına kadar günde 0.1mg (kısa protokol) siklus/ilk foliküler fazı ilk gününden itibaren hCG uygulamasına kadar üç gün 0.1mg'dır (çok kısa protokol), SAKLAMA KOŞULLARI: Decapeptyl® 0.1mg buzdolabında (2-8°C) saklanmalıdır. Tek kullanımlık enjektörler ambalajı içinde ve ışıktan korunarak saklanmalıdır. TİCARİ TAKDİM ŞEKLİ ve AMBALAJ MUHTEVASI: Decapeptyl® 0,1 mg; 1 ml solüsyon içeren, kullanıma hazır 7 şırıngalık kutularda RUHSAT SAHİBİ: FERRING İlaç San. Tic. Ltd. Şti. Büyükdere Cad. Nurol Plaza, No: 71 A Blok Kat 13, Maslak / İstanbul RUHSAT TARİHİ ve NO: 02.11.2006 ve 121/7 KDV DAHİL PERAKENDE SATIŞ FİYATI: 127,27 TL (Nisan 2009 itibariyle). ÜRETİM YERİ: Ferring GmbH Kiel, Almanya REÇETE İLE SATILIR. Ayrıntılı bilgi için lütfen firmamıza başvurunuz.

DECAPEPTYL® Depot Ürün Kısa Prospektüs Bilgisi
FORMÜLÜ: Triptorelin asetat (3.75 mg triptorelin'e eşdeğer) ENDİKASYONLARI: Uterus myomları ve endometriyoziste, overyen hormon yapımının baskılanması gereken durumlarda.Yardımlı üreme teknikleri: Luteal fazda prematüre LH piklerinin önlenmesi; foliküler fazda ise flare-up etkisinden yararlanmak amacıyla. KONTRENDİKASYONLARI: Klinik olarak belirgin osteoproz ya da osteoproz riski (örn. Azalmış kemik yoğunluğu)., Hamilelik, Laktasyon Yardımlı üreme teknikleri: Özellikle polikistik overli hastalarda, ultrasonografi ile tespit edilen foliküller 10' dan fazla olduğunda Decapeptyl® Depot kullanımında önlemlerin sayısı artırılmalıdır. Triptorelin, poli (DL-laktid-ko-glikolid), dekstran veya diğer herhangi bir bileşene duyarlılık gösteren kişilerde kontrendikedir. UYARILAR/ ÖNLEMLER: Seks steroidlerinin serum düzeyleri belirlenerek tedavinin izlenmesi gerekmektedir. Tedaviye başlamadan önce potansiyel olarak fertil kadınların gebe olmadıkları kesin olarak saptanmalıdır. Hasta tedavi sırasında hormonal olmayan kontraseptifleri kullanmalıdır, endometriyozis veya miyom vakalarında hormonal olmayan kontraseptiflere, adet kanamaları düzene girinceye kadar devam edilmelidir. Decapeptyl® Depot tedavisi boyunca kadınlar, östrojen içeren preparatlar kullanmamalıdır. Uterus miyomu tedavisi sırasında uterus ve miyom boyutları ultrasonografi yardımıyla düzenli olarak ölçülmelidir. Rahim hacminin miyom dokusuna kıyasla orantısız olarak hızla küçülmesi bazı vakalarda kanama ve sepsise neden olmuştur. Decapeptyl® Depot tedavisi sırasında adet kanamaları duracağından, hasta regüler menstürasyonun sürmesi halinde doktoruna bilgi vermesi hususunda uyarılmalıdır. Yetişkinlerde ve çocuklarda allerjik ve anafilaktik reaksiyonların görüldüğü bildirilmiştir. Bu reaksiyonlara, lokal yan reaksiyonların ve sistemik semptomların her ikisi de dahildir, Patogenez açıklanamamıştır, Çocuklarda görülen reaksiyonların daha sık bildirilmesi nedeniyle DECAPEPTYL® DEPOT'un çocuklarda kullanılmaması önerilir, Gebelik ve laktasyon: Gebelikte kullanım kategorisi X, İnsanlarda yeterli çalışma olmadığından tedaviye başlamadan önce hastanın gebe olup olmadığı mutlaka tespit edilmelidir. Decapeptyl® Depot'nun laktasyon sırasında kullanımı ile ilgili veriler yeterli değildir. ARAÇ VE MAKİNA KULLANIMINA ETKİSİ: Decapeptyl® Depot'nun araç ve makina kullanıma hiçbir etkisi yoktur veya ihmal edilebilir düzeydedir. YAN ETKİLER/ ADVERS ETKİLER: Hormon üretiminin baskılanması sonucu en çok sıcak basması olmak üzere (erkeklerde %30 ve kadınlarda %75-100) hastalarda yan etkiler görülebilir. Kanama veya deride lekelenme, terleme, vajinal kuruma ve /veya disparoni, libido azalması ve ruh hali değişiklikleri kadınların %10'unda görülür. Depresif ruh hali, bulantı, miyalji, artralji, yorgunluk; uyku bozuklukları; aşırı duyarlık reaksiyonları (kaşıntı; cilt döküntüsü; ateş), uygulama noktasında geçici ağrı ve nadir olarak serum kolesterol düzeyinde hafif artış görme bozuklukları; parestezi , sırt ağrısı, yükselmiş enzim seviyeleri (LDH, _GT, SGOT, SGPT), anafilaksi, uygulama noktasında yabancı vücut reaksiyonu gözlenmitir, Hafif trabekül kemik kaybı görülebilir. Bu durum, tedavinin kesilmesini takiben 6-9 ay içinde genellikle geçer. Triptorelin kullanımında iki epifizyoliziz capitis femoris vakası bildirilmiştir. Nedensel ilişki saptanamamıştır. BEKLENMEYEN BİR ETKİ GÖRÜLDÜĞÜNDE DOKTORUNUZA BAŞVURUNUZ. İLAÇ ETKİLEŞİMLERİ ve DİĞER ETKİLEŞMELER: Östrojen içeren hiçbir ilaçla birlikte kullanılmamalıdır. KULLANIM ŞEKLİ ve DOZU: Decapeptyl® Depot, her 28 günde bir kez ya subkutan ya da intramüsküler olarak injekte edilir. İnjeksiyon her seferinde farklı bir yere uygulanmalıdır. Uterus myomu ve endometriyozis: Genellikle 6 aylık bir tedavi dönemi yeterlidir. Yardımlı üreme teknikleri: Siklusun 2. ya da 3. günü (foliküler faz), veya 21. gününde (luteal faz) tek injeksiyon uygulaması. DOZ AŞIMI: Zehirlenme belirtileri: Etken madde triptorelinin geniş tedavi alanı nedeniyle dozaşımı veya zehirlenme belirtisi beklenmemektedir, Böyle bir durumun olması halinde semptomatik tedavi uygulanmalıdır. SAKLAMA KOŞULLARI: Decapeptyl® Depot buzdolabında (2-8°C) saklanmalıdır. TİCARİ TAKDİM ŞEKLİ ve AMBALAJ MUHTEVASI: Bir kutuda; 3.75 mg triptorelin eşdeğeri triptorelin asetat içeren bir şırınga, süspansiyon sıvısını içeren tek kullanımlık injektör, injeksiyon iğnesi ve şırınga adaptörü bulunur. RUHSAT SAHİBİ: FERRING İlaç San. Tic. Ltd. Şti. Büyükdere Cad. Nurol Plaza, No: 255 A Blok Kat 13, Maslak / İstanbul RUHSAT TARİHİ ve NO: 02.10.2006 ve 120/93 KDV DAHİL PERAKENDE SATIŞ FİYATI: 255,95 TL (Nisan 2009 itibariyle). ÜRETİM YERİ: Ferring GmbH Kiel, Almanya REÇETE İLE SATILIR. Ayrıntılı bilgi için lütfen firmamıza başvurunuz.

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FORMÜLÜ: Liyofilize toz içeren bir flakonda: 75 I.U. FSH (follikül stimüle eden hormon) ve 75 I.U. LH'a (luteinizan hormon) tekabül eden yüksek derecede saflaştırılmış (HP) menotropin (insan menopozal gonadotropini, HMG) vardır. 1 ml çözücü içeren bir ampulde: 1 ml izotonik sodyum klorür solüsyonu bulunur. **ENDİKASYONLARI:** Hipo veya normogonadotropik over yetersizlikleri olan kadınlarda kısırlık tedavisinde (follikül büyümesinin uyarılması), hipo veya normogonadotropik hipogonadizm olan erkeklerde kısırlık tedavisinde (HCG ile birlikte, spermatojenezin uyarılması) kullanılır. **KONTRENDİKASYONLARI:** Menopur®, gonadotropinlere ve laktoza hassasiyeti olan kişilerde kullanılmamalıdır. Kadınlarda; gebelik, over büyümesi veya polikistik over sendromunun neden olmadığı kistler, nedeni bilinmeyen jinekolojik kanamalar, uterusta, overde ve memede tümör. Erkeklerde; prostat kanseri, testislerde tümör. **UYARILAR/ÖNLEMLER:** Menopur®, gebe hastalara verilmemelidir. Anormal genital kanaması olan hastalarda, meme, uterus, prostat, yumurtalık veya testislerin hormon duyarlı tümörler, over kistler, polikistik over sendromunun neden olmadığı over kistler veya bunların büyümesinde kullanılmamalıdır. Menopur® ile tedaviye başlamadan önce, infertilite nedenleri olarak hipofiz veya hipotalamik lezyonlar, adrenal veya tiroid bozuklukları ve hiperprolaktineminin ortadan kaldırılması için uygun şekilde tedavi edilmelidir. Over büyümesi yaşayan hastalar, ruptüre olma riski taşırlar. Pelvik muayeneden kaçınılmalı veya muayene dikkatle yapılmalıdır. Böyle bir risk mevcut iken cinsel ilişkiden kaçınılmalıdır. Tedavi sırasında hastanın yakın takibi şarttır. İstemeden aşırı uyarılma olursa tedavi derhal durdurulmalıdır. Gebelik ve Laktasyonda Kullanım: Gebelik kategorisi: X. Menopur®, gebelerde kullanılmamalıdır. Anne sütüne geçip geçmediği bilinmediğinden, emziren annelerde dikkatle kullanılmalıdır. **YAN ETKİLER/ADVERS ETKİLER:** Kadınlarda: Pulmoner ve vasküler komplikasyonlar, over hiperstimülasyon sendromu, hemoperiton, adnexal torsion, hafiften ortaya değişen over büyümesi, over kistleri, abdominal ağrı, Menopur®'a duyarlılık, gastrointestinal semptomlar (bulantı, kusma, diyare, abdominal kramplar, şişkinlik), ağrı, döküntü, şişkinlik ve/veya enjeksiyon bölgesinde irritasyon, deri döküntüleri, baş dönmesi, taşikardi, dispne, takipne görülebilir (Uyarılar/Önlemler'e bakınız). Aşağıdaki olaylar, Menopur® tedavisinden sonra oluşan gebeliklerde rapor edilmiştir: Ektopik gebelik, konjenital anomali. Erkeklerde: Menopur® tedavisi sırasında bazen jinekomasti, göğüste ağrı, mastit, bulantı, anormal lipoprotein fraksiyonu, anormal SGOT ve SGPT oluşabilir. HMG ile tedavide sık sık aşırı duyarlılık reaksiyonu oluşabilir. Bununla beraber, bu durum, daha çok HCG'nin ovülasyonu indüklemesi için uygulanmasından sonra klinik olarak ortaya çıkar. Bu durumda büyük over kistleri oluşur ve rüptüre olarak karın içi kanamalara neden olur. Buna ek olarak, karın boşluğunda sıvı birikimi (asit), göğüs boşluğunda sıvı birikimi (hidrotoraks), idrarda azalma (oligüri), kan basıncında düşme (hipotansiyon) ve kan pıhtısıyla kan damarlarının tıkanması (tromboembolik olay) olabilir. Aşırı uyarılmanın ilk belirtileri ortaya çıktığında tedavi hemen durdurulmalıdır. Gebelikle beraber bu yan etkiler şiddetlenebilir ve uzun süre devam eder; hayatı tehdit edecek nitelikte olabilir. HMG ile tedavi sırasında istenmediği halde birden çok gebelik olabilir. Çok ender olarak uzun süreli tedavi, antikor oluşumuna neden olarak tedaviyi etkisiz kılabilmektedir. BEKLENMEYEN BİR ETKİ GÖRÜLDÜĞÜNDE DOKTORUNUZA BAŞVURUNUZ. **İLAÇ ETKİLEŞİMLERİ:** Başka ilaçlarla etkileşimi bilinmemektedir. Kısır erkeklerde HMG, HCG ile bir arada enjekte edilebilir. **KULLANIM ŞEKLİ VE DOZU:** Ambalajın içindeki çözücü ile çözüldükten sonra I.M. ya da S.C. olarak uygulanır. Hekim tarafından başka türlü tavsiye edilmedikçe, aşağıdaki dozlarda uygulanır: Kadınlarda Kısırlık: Normo veya hipogonadotropik kadınlarda folliküllerin büyümesini başlatmak için verilen HMG dozu, hastaya göre değişir. HMG, intramüsküler veya subkutan olarak uygulanır ve genellikle tedaviye günlük doz, 75-150 I.U. FSH'a tekabül edecek şekilde başlanır. Eğer, overler cevap vermezse, dozaj, östradiol salgısında yükselme ve folliküllerde büyüme olana kadar yavaş yavaş yükseltilir. Aynı dozda HMG ile tedavi, ovülasyon öncesi östradiol serum düzeyleri sağlanana kadar devam ettirilir. Eğer bu düzey çok çabuk yükselirse, doz azaltılmalıdır. Not: Eğer uygulanan HMG dozu hastaya yüksek gelirse, daha sonra verilen HCG overleri aşırı uyarabilir. Erkeklerde Sterilite: Başlangıçta, haftada, 3x1000-3000 I.U. HCG/hafta uygulanır. Normal testesteron serum düzeyleri sağlandığında, birkaç ay ek olarak, haftada bir HMG intramüsküler olarak uygulanır; verilecek olan doz: 3x75-150 I.U. FSH + 75-150 I.U. LH'dır. **SAKLAMA KOŞULLARI:** Menopur®, ışıktan korunarak, 25°C'nin altında saklanmalıdır. **TİCARİ TAKDİM ŞEKLİ VE AMBALAJ MUHTEVASI:** Enjeksiyon için toz içeren, 5 adet flakon ve 5 ampul çözücü. **RUHSAT SAHİBİ:** FERRING İlaç San. ve Tic. Ltd. Şti. Ayazağa Mah. Meydan Sok. Beybi Giz Plaza, Kat 26, Daire 2626, Maslak-Şişli/İstanbul. **RUHSAT TARİHİ VE NO:** 27.07.2006 tarih ve 120/63 sayılı. **KDV DAHİL PERAKENDE SATIŞ FİYATI:** 229,12 TL (Nisan 2009 itibariyle). Reçete ile satılır. Ayrıntılı bilgi için lütfen firmamıza başvurunuz.

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Journal of the
Turkish-German
Gynecological Association

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Artık Yalnız Değilsiniz.

Extra Yaşam Kalitesi
Extra His

ExTT Terapi
Extra Mutluluk

1.İnkontinas (İdrar Kaçırma)
Raslantı Oranı: 40lı yaşlar (% 45) 50li yaşlar (48%) 60lı yaşlar (56%)
. Türkiyede yaklaşık 5 milyon hastanın, dünyada ise 200 milyondan fazla hastanın idrar tutamama sorunu vardır.
. Idrar tutamama nedeni her zaman yaşlanma nedeniyle değildir.
Kadın hastaların üçte biri 35 yaşından önce idrar tutamama sorununu yasar
2.Vajinal gevşeme Sendromu
. Vajinal gevşeme Sendromu çocuk doğumunda, sık ilişki, yaşlanma ve obeziteden kaynaklanır.
. Bu durum cinsel isteği azaltır ve böylece cinsel ilişkide orgazma ulaşmak için başarısız olunur
. Kadınlar, güven ve cinsel ilişki isteğini kaybettiği ve partnerinin başka bir kadın tercih edebilir olmasından endişe edebilir
. Daha güçlü vajinal sıkılaştırılması ile partnerinizle daha iyi bir cinsel ilişki olur
3.SexualDysfunction
. Tipleri: ilgisizlik , hissizlik , orgazm sorunu , Ağrı ve rahatsızlık
kadınların yaklaşık% 43ünde cinsel işlev bozukluğu sorunlarından bir tür vardır
4.Stress
. Fonksiyonel müzik (bilinçaltı müzik / bilinçaltı etkisi)

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Editorial

Prof. Dr. Cihat Ünlü
Editor in Chief of the JTGGA
President of TAJEV

Prof. Dr. Klaus Vetter
Editor in Chief of the JTGGA
President of DTGG

Assoc. Prof. Dr. Kubilay Ertan
General Secretary of DTGG
CO-Editor of JTGGA

Dear Colleagues,

We all were delighted to hear the positive feedbacks after a successful congress. Being encouraged both from participants and esteemed lecturers who have been approved by the scientific community, as well as from the positive criticisms and compliments in the press, we have already begun the planning and preparation of the upcoming 9th congress of our society which is planned to be held in 2011.

On behalf of the Turkish-German Gynecological Association (TGGA), we owe a great depth of gratitude to all our colleagues who have contributed their efforts in the preparation of the congress, particularly to Congress Secretary (notably to Assoc. Prof. Dr. Cem Demirel) and to the representatives of the Serenas Company who have excellently undertaken the organization.

As such in other disciplines, it is essential for gynecology to keep pace with the developing technologies. Especially in surgical gynecology, "robotic surgery", which has quickly become widespread worldwide, creates a new cult. This current development in gynecology has been integrated into Turkey for the first time and was introduced in our congress as an innovative technology. In the same way, technological innovations and current techniques (3D/4D, power doppler, tissue harmonic imaging, tissue doppler, tui, etc.) in perinatology have been successfully used for prenatal diagnosis and performed on patients by our colleagues. Our society is also planning to carry out courses in this issue in our countries in the future.

In the last two years, after TAJEV has been established and has become an official association, its' consistency was assured for the first time by this highly productive congress which TAJEV has taken all the responsibility. Besides, TAJEV has also carried out educational and informative courses and provided screening tests for individuals in all regions of the country by the contributions of our esteemed educators. Moreover, TAJEV has provided scholarship opportunities for young scientists, who fulfill certain criteria to carry out scientific researches, both in Europe and in US for six months. By this time, the scholar number has reached to 30 and it has been decided that this grant will be provided to successful doctors working in Turkey and Germany in the future.

Our fundamental purpose, within the frame of regulations and conditions in Turkey, is formalizing our mutual collaboration with German-Turkish Gynecological Association (DTGG, Deutsch-Türkische Gynaekologengesellschaft), which was founded in 1993 in Cologne, Germany, that aims to build up bilateral medical and sociocultural relationships between Turkey and Germany. The most important example of the cooperation is the representative election of a DTGG board member as an administrative board member for TAJEV, with a decision taken during the annual meeting of TAJEV in Istanbul, in September. Owing to this attempt, as is also understood from the names of our association, foundation and journal published regularly, the continuity of the cooperation between Turkey and Germany will be provided formally with a more intensive tempo.

Moreover, various courses will be planned by the collaboration of TAJEV and DTGG, both in Turkey and in Germany.

The participation with a large number of representatives and the arrangement of associated symposiums in the traditional congress which will be held in Germany in 2010 is also planned. By this way, it is our aim to gain the members of DTGG, which has already been conducted its' activities, for further projects.

Our baby, born in 2000 is doing very well, its already has left its childhood behind by becoming professional and reached puberty under the name of Journal of the Turkish-German Gynecological Association (JTGGA). On this opportunity, on behalf of TGGA, I owe a great depth of gratitude to our national and international editorial board members for maintaining the continuity of our journal successfully and notably to Assist. Prof. Eray Caliskan, Assist. Prof. Gazi Yildirim and Assoc. Prof. Alper Tanrıverdi.

The long-term success of our journal can be achieved by publications with high scientific quality. To reach this purpose, we need support from all our members and our scientists.

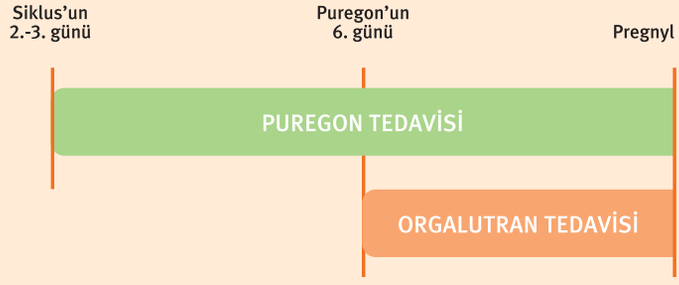
In this context, we intent to deliver the current issue of our journal to all the Chairs of the Departments of Gynecology and Obstetrics in University Hospitals and in the affiliated teaching hospitals, in Turkey and Germany as well. The maintenance of our success will be possible by your support.

On behalf of TAJEV and DTGG, we wish you a sunny autumn.

ART'de hızlı, pratik, etkili seçenek![2,3,6]

- Kısa süreli tedavi[5]
- Kullanıma hazır enjektör[4]
- Hastaların tercihi[2]

ORGALUTRAN REJİMİ



Hayalleri tamamlayan çözümler[1,2,3]

1'Lİ VE 5'Lİ KUTULARDA

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1. Borm G et al. Human Reproduction. 2000;15 :1490-1498 **2.** Fluker et al. Fertil Steril. 2001; 75 :38-45 **3.** The European and Middle East Orgalutran® Study Group. Human Reproduction 2001.16:644-51 **4.** Orgalutran® SmPC
5. Al-Inany HG, et al. Cochrane Database Syst Rev. 2006; 3: CD 001750 **6.** Shapiro D, et al. Fertil and Steril Vol. 80 Suppl 1, 2003.

Orgalutran® 0.25 mg / 0.5 ml Enjeksiyonluk Çözelti

Formülü: Önceden dolum yapılmış bir şırınga 0.5 ml solüsyonda etkin madde olarak 0.25 mg ganirelix yardımcı maddeler olarak da 23.5 mg mannitol, 0.1 mg asetik asit, pH ayarı için sodyum hidroksit ve/veya asetik asit ve yeteri miktarda enjeksiyonluk su içerir. Orgalutran® , hipotalamik-hipofizer-gonadal ekseni hipofiz bezindeki GnRH reseptörlerine kompetitif olarak bağlanmak suretiyle etkileyen bir GnRH antagonistidir. Orgalutran®'ın subkütan uygulamayı takiben biyoyararlanımı yaklaşık %91'dir.0.25 mg/gün dozunda mükerrer uygulamayı takiben 0.6 ng/ml'lik durağan durum düzeyine 2-3 gün içerisinde ulaşılmaktadır. **Endikasyonları:** Kontrollü over hiperstimülasyonu (COH) uygulanan kadınlarda prematür LH salgılanmasının önlenmesi. **Kontrendikasyonları:** Etken maddeye veya yardımcı maddelerden herhangi birine karşı aşırı duyarlılık,GnRH veya diğer GnRH analoglarına karşı aşırı duyarlılık, Gebelik ve laktasyon. **Uyarılar ve önlemler:** Alerjisi olmakla birlikte o anda semptom sergilemeyen hastalara Orgalutran® güvenli bir şekilde uygulanabilir. Mevcut ciddi alerji semptomları olan hastalara Orgalutran® uygulanması tavsiye edilmemektedir. Alerjik reaksiyon oluşması halinde hastaların doktorla temasa geçmeleri önerilmektedir. **Gebelik ve laktasyonda kullanım:** Orgalutran® gebelik veya laktasyon sırasında kulanılmamalıdır. **Araç ve makina kullanmaya etkisi:** Araç ve makina kullanma üzerinde herhangi bir etki gözlenmemiştir. **Yan etkiler / Advers etkiler:** Orgalutran® enjeksiyon yerinde cilt reaksiyonuna yol açabilmekte fakat normal koşullarda bu reaksiyon uygulamadan 4 saat sonra kaybolmaktadır. Nadiren baş ağrısı (<%4) ve bulantı (<%2) rapor edilmiştir. Rapor edilen diğer advers olaylar, Orgalutran®'dan ziyade destekli üreme tekniklerine (ART) yönelik kontrollü over hiperstimülasyonu ile bağlantılıdır (örneğin karın ağrısı, over hiperstimülasyon sendromu (OHSS), ektopik gebelik ve düşük). **BEKLENMEYEN BİR ETKİ GÖRÜLDÜĞÜNDE DOKTORUNUZA BAŞVURUNUZ. Kullanım şekli ve dozu:** FSH ile kontrollü over hiperstimülasyonuna adet döneminin 2 veya 3'üncü gününde başlanılabilmektedir. Orgalutran® (0.25 mg), tercihen FSH uygulamasının 6. gününden itibaren başlanılarak günde tek sefer subkütan yoldan enjekte edilmelidir. Orgalutran® FSH ile karıştırılmamalı, fakat her iki preparat yaklaşık olarak aynı saatlerde uygulanmalıdır. Günlük Orgalutran® uygulamasına, yeterli büyüklükte ve yeterli sayıda follikül oluşana kadar devam edilmelidir. İlk Orgalutran® enjeksiyonu ile son Orgalutran® enjeksiyonu ile hCG enjeksiyonu arasındaki süre, 30 saati geçmemelidir. Orgalutran® subkütan yoldan uygulanmalıdır. Lipoatrofi oluşmaması için enjeksiyon yeri değiştirilmelidir. Hasta veya partneri, yeterli eğitim almaları ve bilgi için uzmanlara ulaşabilmeleri koşuluyla Orgalutran® enjeksiyonunu kendileri yapabilir. **Uygulama Şekli:** Orgalutran® enjektör ile yavaşça, ciltaltına enjekte edilir (örneğin üst bacak). Uygulama şekli için prospektüsü inceleyiniz. **Enjeksiyonun unutulması:** Orgalutran®'ı enjekte etmeyi unuttuğunuzu fark ettiğiniz anda enjeksiyonu yapınız, doktorunuza danışınız. Çift enjeksiyon yapmayınız. **Saklama koşulları:** 25ºC' nin altındaki oda sıcaklığında saklayınız. Işıktan koruyunuz. Dondurmayınız. **Ticari takdim şekli:** Orgalutran® 0.25 mg/0.5ml, 5 adet önceden doldurulmuş, tek kullanımlık şırınga içinde 0.5 ml solüsyon, karton kutuda veya 1 adet önceden doldurulmuş tek kullanımlık şırınga içinde 0.5 ml solüsyon karton kutuda. **Genel uyarılar:** Çocukların ulaşamayacakları yerlerde ve ambalajında saklayınız. Hekime danışmadan kullanılmamalıdır. Başvurularda ambalaj seri numarasını belirtiniz. **Ruhsat Sahibi:** Schering-Plough Tıbbi Ürünler Ticaret A.Ş., Yıldırım Oğuz Göker Cad., Maya Plaza, 34335, Akatlar-İstanbul **Ruhsat tarihi:** 23.09.2003 Ruhsat no. 114/76 **Fiyat:** 5'lik Paket: PSF (KDV Dahil) 336,09 TL; 1'lik Paket: PSF (KDV Dahil) 77,27 TL (Ocak 2009)

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Orgalutran®
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WHORG09Q1-03

Kontrollü Ovaryen Hiperstimulasyonda[1,2]

Puregon® Pen
recombinant FSH follitropin beta

- Kolay uygulama
- Rahat kullanım
- Pratik tedavi

Hayalleri tamamlayan çözümler[3]

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1. Platteau P. et al. Human Reproduction Vol.18, No.6 1200-1204:2003 **2.** Pang SC et al. RBM Online Vol. 7 No.3 319-326:2003 **3.** Al Inany H. et al. Human Reproduction Vol.18 No.2 305-313: 2003

Puregon® 300 IU/0,36 ml. kartuş, Puregon® 600 IU/0,72 ml. kartuş ve Puregon® 900 IU/1,08 ml. kartuş - Enjeksiyon için Solusyon

Formül: Puregon® kartuş, 0,36 ml.lik enjeksiyonluk solusyonda net toplam 300 IU, 0,72 ml.lik enjeksiyonluk solusyonda net toplam 600 IU ve 1,08 ml.lik enjeksiyonluk solusyonda net toplam 900 IU insan rekombinant folikül uyarıcı hormon (rec.FSH) (follitropin beta) içerir. Puregon® Kalemi (Puregon® Pen) ile beraber kullanılmak üzere geliştirilmiştir. **Endikasyonlar: Kadında:** Klomifen sitrat'a cevap vermeyen anovulasyon (PCOD dahil). İVF/ET, GIFT ve ICSI gibi yardımlı üreme programlarında kontrollü over hiperstimülasyonu için. **Erkekte:** Hipogonadotropik hipogonadizm nedenli spermatogenez eksikliğinde. **Kontrendikasyonlar**: Over, meme, uterus, hipofizer veya hipotalamik tümörler, gebelik veya laktasyon, tanı konmamış vaginal kanama, Puregon® Enjeksiyon için Solusyon'daki maddelerden her hangi birine karşı aşırı duyarlılık, primer over yetmezliği, over kistleri veya büyümüş overler (Polikistik over hastalığına bağlı olmayan), genital organ malformasyonları, gebelikle bağdaşmayan fibroid tümörler, primer testiküler yetmezlik. Uyarılar/Önlemler: Tedavi edilmemiş gonad dışı endokrinopatiler (tiroid, adrenal, hipofizer bozukluklar) ekarte edilmelidir. Gonadotropik ilaçlarla yapılan ovulasyon indüksiyonunu takiben oluşan gebeliklerde çoğul gebelik, ektopik gebelik, gebelik kaybı, konjenital malformasyon oranları artmaktadır. Bu ebeveyne ait karakteristiklere (anne, baba yaşı, sperm özelliği, tubaların yapısı) ve çoğul gebeliğe bağlı olabilir. Yardımla üreme tekniklerindeki hiperstimülasyon dışında oluşabilecek over hiperstimülasyon (OHS) riski ultrason ve estradiol değerleri ile takip edilmelidir. Hiperstimülasyon durumlarında Puregon® uygulamasına son verilmelidir, hCG uygulaması yapılmamalıdır. Hafif over hiperstimülasyon (OHS) klinik bulguları arasında karın ağrısı, bulantı, diyare ve overlerde ve kistlerde hafif büyüme görülür. Nadir oluşan şiddetli vakalarda ise hayati tehlike söz konusu olabilir. Bu durumlarda rüptüre meyilli büyük over kistleri, hidrotoraks ve kilo artışı görülebilir. Arter veya venlerde tromboembolizm görülebilir. Tromboemboliye meyilli risk taşıyanlarda (trombofili, obezite, geçmişte kendisinde veya ailede tromboembolik şikayet olanlarda) IVF tedavisi ile riskler kıyaslanmalıdır. Erkeklerde artmış FSH düzeyleri primer testiküler yetmezliğin belirtisidir ve bu hastalar Puregon® tedavisine cevap vermezler. Erkeklerde tedavinin yanıtını değerlendirmek için 4-6 ay süre ile sperm analizi önerilir. Jinekomasti ve akne nadiren görülebilir.**Gebelik ve Emzirme Döneminde Kullanım:** Gebelik ve emzirme sırasında kullanılmamalıdır. **Yan etkiler/Advers Etkiler:** İntramüsküler veya subkütan uygulama sonrasında çoğu kez hafif olarak ağrı, morarma, kızarıklık, kaşıntı görülebilir. Nadiren sistemik reaksiyon gözlenmiştir. Beklenmeyen bir etki görüldüğünde doktorunuza başvurunuz. **İlaç etkileşimleri ve diğer etkileşimler:** Klomifen sitrat ile Puregon®'un birlikte kullanımı folikül cevabını artırabilir. GnRH agonisti kullanılan vakalarda ise Puregon® dozunu artırmak gerekebilir. **Kullanım şekli ve dozu:** Puregon® tedavisi fertilite problemlerinde tecrübeli hekim kontrolünde olmalıdır. Kullanılan doz kişiden kişiye ve kişinin kendi içinde büyük değişiklikler gösterebilir. Doz hastanın over yanıtına göre ultrason ve estradiol ölçümleri ışığında düzenlenir. Enjeksiyon kalemi kullanımı ile hastaya ortalama %18 oranında daha çok FSH verilebileceği unutulmamalıdır. Puregon® ve üriner FSH karşılaştırmalı çalışmalarda, Puregon®'un üriner FSH'dan daha etkili olduğu gösterilmiştir. Üriner FSH'dan Puregon®'a geçişlerde daha az doz tercih edilerek OHSS'dan sakınılmalıdır. Uygulamaya genellikle 50 IU ile başlanıp 7 gün devam edilmeli, yanıt alınmazsa her 7 günde bir doz %40-60 oranında artırılmalıdır. Ultrasonda 18 mm folikül, 300-900 pg/ml (1000-3000 pmol/l) estradiol tesbiti preovulatuvar şartların geliştiğinin göstergesidir. Genellikle 7-14 günlük tedavi buna yetmektedir. Günlük E2 değerinin 2 kattan fazla artması veya 14 mm'den büyük birden fazla folikül oluşumu çoğul gebelik riskini artırır. Bu durumda hCG verilmemelidir. Yardımla üreme programlarında kontrollü over hiperstimülasyon protokolleri uygulanır. Bu tedavilerde başlangıç dozu olarak dört gün 100-225 IU, idame olarak 6-12 gün boyuncu 75 – 375 IU kullanılabilir. Ultrasonda 16-20 mm foliküller (ortalama 18 mm) ve kan E2 değerlerinin 300-400 pg/mol (1000-1300 pg/mol/L) gözlenmesi ile hCG yapılıp 34-35 saat sonra oositler elde edilir. **Erkekte doz**: Haftalık Puregon® dozu 450 IU olmalıdır. Tercihen bu doz 150 IU' lik 3 doza bölünebilir ve hCG ile birlikte kullanılabilir. Tedavi en az 3-4 ay devam etmelidir, bu süreden önce spermatogenezde gelişme beklenemez. Eğer hasta bu tedavi süresinden sonra yanıt vermezse kombinasyon tedavisi sürdürülebilir. Son klinik tecrübeler spermatonogezin gerçekleşmesi için tedaviye 18 ay ya da daha uzun süre devam etmenin gerekli olabileceğini göstermektedir. **Uygulama şekli:** Kartuşlardaki enjeksiyonluk Puregon® solüsyonu, Puregon® Kalemi ile kullanılmak üzere geliştirilmiştir ve subkütan yoldan uygulanmalıdır. Kalemi kullanmak için hazırlanmış özel açıklamalar dikkatlice takip edilmelidir. Lipoatrofinin önlenmesi için enjeksiyon yeri değiştirilmelidir. Doktor tarafından gerekli açıklamalar yapılmışsa, Puregon®'un enjeksiyonu hasta tarafından yapılabilir. **Doz aşımı:** İnsanlarda Puregon®'un akut toksisitesi ile ilgili bir veri yoktur. Çok yüksek dozda FSH overlerin hiperstimülasyonuna neden olabilir (bkz. Uyarılar/Önlemler bölümü). **Eczacı tarafından saklama koşulu:** 2 ˚C-8 ˚C de saklayınız, dondurmayınız, ışıktan koruyunuz. **Hasta tarafından saklama koşulu: 1)** 2 ˚C-8 ˚C saklayınız, dondurmayınız, ışıktan koruyunuz. **2)** 25 ˚C altında, oda sıcaklığında, maksimum 3 ay saklanabilir. Berrak olmayan veya partikül içerdiği görülen solüsyonlar kullanılmamalıdır. Puregon® kaleminin uygulamasında, kullanma talimatı dikkatle takip edilmelidir. Puregon® kartuşlar, kartuş içinde başka ilaçla karıştırılmak üzere hazırlanmamışlardır. Enjeksiyonun hemen ardından kullanılan iğneler atılmalıdır. Tedavi sonunda, kullanılmamış ilaç ve artık malzeme yerel gereklilikler çerçevesinde imha edilmelidir. Çocukların ulaşamayacağı yerlerde ve ambalajında saklayınız. **Ticari takdim şekli:** Puregon® 300 IU/0.36 ml ve 600 IU/ 0,72 ml Enjeksiyon için solusyon, karton kutuda follitropin beta taşıyan bir kartuş ve Puregon® Kalemi ile beraber kullanılmak üzere 7 iğneden oluşur. **KDV dahil PSF:** 300 IU kartuş 240.63 TL, 600 IU kartuş 457.64 TL ve 900 IU kartuş 671.62 TL (Ocak 2009). **Piyasada mevcut diğer farmasotik dozaj şekilleri:** Puregon® 50 IU/ ml ve 100 IU/ml Enjeksiyon için liyofilize toz. **Ruhsat Sahibi:** Schering-Plough Tıbbi Ürünler Ticaret A.Ş., Yıldırım Oğuz Göker Cad., Maya Plaza, 34335, Akatlar-İstanbul **Ruhsat Tarihi ve No:** 06.08.2003-114 / 40 **Üretim Yeri:** N.V. Organon, Oss, Hollanda adına Velter Pharma-Fertigung GmbH&Co.KG, Almanya. Reçete ile satılır.

WHPUR09Q1-05

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Cytokine and nitric oxide concentrations in follicular fluid and blood serum of patients undergoing assisted reproductive treatment: relationship to outcome

IVF tedavisi alan hastaların serum ve foliküler sıvı sitokin ve nitrik oksit konsantrasyonları: başarı ile ilişkisi

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Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Yeditepe University Hospital, Istanbul, Turkey

Abstract

Objective: The role of cytokines and nitric oxide (NO) in ovarian folliculogenesis and the development of mature and fertilizable oocytes is controversial. The aim of this study is to determine the concentrations of interleukin (IL)-1β, IL-6, IL-8, IL-12, tumor necrosis factor (TNF)-α and NO in the follicular fluid (FF) and blood serum (S) of patients undergoing assisted reproductive treatment (ART) and to investigate whether these cytokines could be used as a predictive parameter for ART outcome.

Material and Methods: A retrospective clinical study was performed at a university hospital including a total of 85 women who underwent ART. FF and serum samples were collected at the time of oocyte retrieval and measured for interleukin (IL)-1β, IL-6, IL-8, IL-12, tumor necrosis factor (TNF)-α by the enzyme-linked immunosorbant assay (ELISA) technique, using commercially available kits and NO by the nitrate/nitrite colorimetric assay. The results were compared between the women who became pregnant and those who did not following ART.

Results: No significant difference was found in the FF and blood serum concentrations of the cytokines and NO between pregnant and non-pregnant women.

Conclusion: Follicular fluid and blood serum concentrations of IL-1β, IL-6, IL-8, IL-12, TNF-α and NO do not predict pregnancy achievement following ART. (J Turkish-German Gynecol Assoc 2009; 10: 132-6)

Key words: Assisted reproductive treatment; cytokines; follicular fluid; nitric oxide; pregnancy

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Özet

Amaç: Folikül sıvısı içindeki sitokinlerin ve nitrik oksitin matur oosit gelişimi üzerindeki etkisi tartışmalıdır. Bu çalışmanın amacı, tüp bebek tadavisi alan hastaların folikül sıvısı (FF) ve serumunda (S) interlökinleri IL-1β, IL-6, IL-8, IL-12, tümor nekrozis faktör (TNF)-α ve NO düzeylerini saptamak ve bunların başarı ile ilişkisini araştırmaktır.

Gereç ve Yöntemler: Bir üniversite hastanesinin tüp bebek merkezinde retrospektif çalışma planlandı. 85 kadın çalışmaya dahil edildi. IL-1β, IL-6, IL-8, IL-12, tümor nekrozis faktör (TNF)-α düzeyleri ELISA ile, NO düzeyleri ise nitrat/nitrit kolorometrik assay ile saptandı.

Bulgular: Gebe kalan ve kalamayan kadınların S ve FF sitokin ve NO konsantrasyonları arasında fark bulunamadı.

Sonuç: Serum ve folüküler sıvı IL-1β, IL-6, IL-8, IL-12, tümör nekrozis faktör (TNF)-α ve NO düzeyleri tüp bebek tedavilerinde başarıyı predikte etmez.

(J Turkish-German Gynecol Assoc 2009; 10: 132-6)

Anahtar kelimeler: Yardımla üreme teknikleri tedavisi, sitokinler, foliküler sıvı, nitrik oksit, gebelik

Geliş Tarihi: 28 Nisan 2009 **Kabul Tarihi:** 10 Ağustos 2009

Introduction

A connection is suggested to be present between the endocrine and cytokine systems. Cytokines have been shown to play an important role in the regulation of follicular development and also follicular atresia (1). FF provides a microenvironment for the developing oocyte and contains immunological factors for the regulation of its development. Changes in the expression and the concentrations of certain cytokines can influence oocyte and embryo quality, resulting in a reduced ability to implant. Several FF markers were suggested to affect oocyte developmental potential in IVF (2, 3).

Different cytokines have been investigated for their effects on various steps in assisted reproductive treatment (ART) cycles, namely follicular development, fertilization, embryo development and implantation. The correlations between various cytokines and ART outcome have been sought extensively and controversial results have been reported.

Gonadotropins used in assisted reproduction were reported to induce local and systemic production of interleukin-1beta (IL-1β, 4). Some authors suggested increased (4), some suggested decreased (5) and some suggested no different (6) FF IL-1β concentrations in pregnant women compared to non-pregnant ones. FF IL-6, IL-8 and IL-12 levels were also investigated in IVF cycles (6-8). FF IL-6 concentrations were noted

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to be significantly higher in pregnant women (6). No correlation was found between FF IL-8 concentrations and fertilization or implantation rates (8). FF IL-12 concentrations were reported to be associated with a negative outcome in IVF treatment (6, 8). On the contrary, some researchers found no significant difference in FF IL-12 concentrations between pregnant and non-pregnant patients (5, 7). Another cytokine investigated in the follicular fluid with regard to IVF parameters is tumor necrosis factor-alpha (TNF-α). Some researchers revealed no significant difference in FF TNF-α levels of pregnant and non-pregnant patients (6,9). However, it was suggested that FF TNF-α levels influenced oocyte quality, and significantly higher FF TNF-α concentrations were found in follicles containing poor quality oocytes (9). High levels of nitric oxide (NO) in follicular fluid was also proposed to be detrimental, as embryo quality was observed to decrease in patients with high FF NO levels (10). Similarly in another study, follicles that contained oocytes that fertilized and went on to divide beyond the 6 cell stage were found to have significantly lower FF NO levels as compared to follicles that contained oocytes that did not fertilize or failed to develop beyond the 5 cell stage (11). However, no significant difference was found in FF NO levels of pregnant and non-pregnant patients (9).

As seen from the literature, a number of factors found in the follicular fluid can influence assisted reproduction outcome. This study was undertaken to investigate whether FF and serum concentrations of cytokines IL-1β, IL-6, IL-8, IL-12, TNF-α and NO differ according to the pregnancy achievement following ART. The results might lead to the use of these factors as the determinants of pregnancy after IVF. To the best of our knowledge, our patient cohort is one of the largest series reported so far.

Materials and Methods

Patients and protocols

This retrospective clinical study was performed at the Center for Reproductive Medicine of Yeditepe University Hospital, Istanbul, Turkey between July 2006 and October 2008. FF and serum samples obtained during oocyte retrieval from 85 women who underwent ART were analyzed for this study. FF samples contaminated with blood were not included. Patients with endometriosis, PCOS, recurrent abortions and immunological disorders were excluded from the study. Informed consent was obtained from all patients, allowing future scientific investigations on the collected FF and serum samples. The ethics committee of the hospital approved this study.

Patients were stimulated with either GnRH agonist long or antagonist protocol. Patients given GnRH agonist long protocol were administered leuprolide acetate (Lucrin®, Abbott, France), starting on the 21st day of the preceding cycle. On the third day of menses gonadotropins recombinant FSH (Puregon®, Organon, Netherlands or Gonal-F®, Serono, Switzerland) were initiated at a dose of 225-450 IU/day according to age, ovarian reserve and previous cycles. Patients given GnRH antagonist protocol were administered the same gonadotropins mentioned above at the same doses on the second day of menses after the ultrasound evaluation. When the leading follicle reached 14 mm, GnRH antagonist (Orgalutran®, Organon, Netherlands or Cetrotide®, Serono, Switzerland) was added at a dose of 0.25 mg daily until the day of HCG injection. In both stimulation protocols, ovarian response was monitored by serial ultrasound scans and serum estradiol measurements and daily gonadotropin doses were adjusted accordingly. When the leading follicle reached 20 mm, HCG (Pregnyl®, Organon, Netherlands) 10000 IU was administered and oocyte pick-up was performed 35 hours later. ICSI was the usual method of fertilization. Two to five days after oocyte retrieval, the embryos were transferred into the uterus under ultrasound guidance. Luteal support was given starting on the day of oocyte pick-up with i.m. progesterone (Progynex®, Kocak, Turkey) 50 mg daily plus vaginal progesterone gel (Crinone®, Serono, Switzerland) once daily and continued up to the pregnancy test; in women who were pregnant only the vaginal gel was continued until the 12th gestational week. About 12 days after the transfer procedure, serum beta HCG measurement >10 IU/l determined the pregnancy.

Biochemical assays

FF and blood serum samples were obtained simultaneously from 85 women during the oocyte pick-up procedure. FF samples were collected in each woman from the leading follicles and pooled. Only the visually blood-free samples of follicular fluid were included in the analysis. FF and serum samples obtained were immediately centrifuged at 350 g for 10 min and supernatants were then collected and stored in tubes at -70˚C until assay. In FF and serum samples, the concentrations of IL-1β, IL-6, IL-8, IL-12, TNF-α and NO were measured with commercially available kits. IL- 1β was measured with The AssayMax Human IL-1beta ELISA kit (Assaypro, USA), intra-assay CV 5.1%, inter-assay CV 7.5% and minimum detectable level <3 pg/ml. *IL-6* with The AssayMax Human IL-6 ELISA kit (Assaypro, USA), intra-assay CV 5.1%, inter-assay CV 7.0% and minimum detectable dose <10 pg/ml. IL-*8* with The AssayMax Human IL-8 ELISA kit (Assaypro, USA), intra-assay CV 5.0%, inter-assay CV 7.2% and minimum detectable dose <1 pg/ml. IL-*12* with The BioSource Human IL-12 +p40 ELISA kit (BioSource International Inc., USA), intra-assay CV 3.9%, inter-assay CV 4.0% and minimum detectable level <2 pg/ml. TNF-α with The AssayMax Human TNF-alpha ELISA kit (Assaypro, USA), intra-assay CV 5.5%, inter-assay CV 7.0% and minimum detectable level <10 pg/ml. NO with Nitrate/Nitrite Colorimetric Assay Kit Cat. No. 780001 (Cayman Chemical Company, USA), intra-assay CV 2.7%, inter-assay CV 3.4% and the detection limit is 2.5 μM.

Statistical analysis

To determine whether serum and FF markers could distinguish the patients who became pregnant from those who did not, FF and blood serum cytokine and NO measurements were compared between pregnant and non-pregnant patients following ART. Statistical calculations were made using the Statistical Package for the Social Sciences (version 12.0, SPSS Inc., Chicago, IL, USA). For continuous variables Student's t-test and for categorical variables Chi-squared test and Fisher's exact test were used, where applicable. Results are expressed as

means±SD or percentages (counts) as appropriate. Statistical significance was defined as a value of P <0.05.

Results

Demographic features and cycle characteristics evaluated in 85 women constituting the studied groups are shown in Table 1. The patients who became pregnant were significantly younger than patients who did not (29.7±4.7 years vs. 32.2±4.8 years, respectively; p=0.02). In the 85 women recruited for the study, the indication for ART was unexplained infertility in 26% (n=22), tubal disease in 8% (n=7), and male factor in 66% (n=56). No significant difference was found between pregnant and non-pregnant patients regarding infertility etiology (Table 1). When cycle characteristics are concerned, significantly lower amounts of gonadotropins were required in patients who became pregnant compared with the patients who did not (2500±967 IU vs. 3278±1265 IU, respectively; p=0.002) and the number of total oocytes retrieved was significantly higher in patients who achieved pregnancy compared to non-pregnant ones (13.0±6.2 vs. 10.0±6.2, respectively; p=0.03). No significant difference was observed between the two groups regarding other cycle parameters (Table 1).

FF cytokine and NO concentrations in both groups are presented in Table 2. No significant difference was found in values between the women who became pregnant and those who did not (Table 2).

Blood serum concentrations of cytokines and NO in the two groups of patients are shown in Table 3. There was no significant difference between pregnant and non-pregnant women (P>0.05).

Discussion

Numerous studies have attempted to find differences between the serum and/or FF cytokine concentrations of pregnant and non-pregnant women following IVF treatment. Given the ambiguous findings regarding the association of FF/serum cytokine levels and IVF outcome, we evaluated whether the concentrations of various cytokines and NO were altered in pregnant cycles following IVF. To the best of our knowledge, our study is one of the largest series to assess multiple relevant cytokines in serum and follicular fluid simultaneously in relation to the pregnancy achievement following IVF. In the present study, we observed no significant differences in the FF and blood serum cytokine and NO concentrations investigated between pregnant and non-pregnant cycles.

Table 2. Follicular fluid cytokine and nitric oxide concentrations of pregnant versus non-pregnant women following ART

Variable	Pregnant	Non-pregnant	P
FF IL-1β (pg/ml)	3.9±1.6	4.3±1.6	NS
FF IL-6 (pg/ml)	27.3±15.7	23.5±12.7	NS
FF IL-8 (pg/ml)	21.1±9.4	20.1±8.7	NS
FF IL-12 (pg/ml)	61.6±28.8	60.0±24.8	NS
FF TNF-α (pg/ml)	31.1±8.2	29.3±2.9	NS
FF NO (μM)	0.5±0.2	0.5±0.2	NS

(FF, follicular fluid; IL-1β, interleukin 1 beta; IL-6, interleukin 6; IL-8, interleukin 8; IL-12, interleukin 12; TNF-α, tumor necrosis factor alpha; NO, nitric oxide; NS, not significant, p>0.05).
Student's t-test

Table 3. Blood serum cytokine and nitric oxide concentrations of pregnant versus non-pregnant women following ART

Variable	Pregnant	Non-pregnant	P
S IL-1β (pg/ml)	3.4±2.5	3.6±2.9	NS
S IL-6 (pg/ml)	17.1±10.3	15.6±5.9	NS
S IL-8 (pg/ml)	29.8±18.6	23.3±19.5	NS
S IL-12 (pg/ml)	54.4±22.9	50.9±23.6	NS
S TNF-α (pg/ml)	36.6±13.7	32.4±7.5	NS
S NO (μM)	1.7±1.6	1.7±1.1	NS

The values are given as mean±SD.
(S, serum; IL-1β, interleukin 1 beta; IL-6, interleukin 6; IL-8, interleukin 8; IL-12, interleukin 12; TNF-α, tumor necrosis factor alpha; NO, nitric oxide; NS, not significant, p>0.05).
Student's t-test

Table 1. Demographic features and cycle characteristics of pregnant versus non pregnant women following ART

Variable	Pregnant (n=51)	Non-pregnant (n=34)	P
Age (years)	29.7±4.7	32.2±4.8	0.02
Infertility duration (years)	6.8±4.1	8.0±5.2	NS
Cause of infertility %, (n)			
Tubal	6 (3)	12 (4)	NS
Male	69 (35)	62 (21)	NS
Unexplained	25 (13)	26 (9)	NS
Gonadotropins used (IU)	2500±967	3278±1265	0.002

The values are given as mean±SD or percent (numbers).
(HCG, human chorionic gonadotropin; E2, estradiole; MII, metaphase II; ET, embryo transfer; NS, not significant, p>0.05).
Student's t-test, Chi-squared test and Fisher's exact test

Interleukins are known to be involved in the immune system and play a role during inflammation. The ovarian follicle is suggested to be a site of inflammatory reactions. Thus various studies were performed to investigate the concentrations of proinflammatory cytokines in the follicular fluid of patients undergoing IVF treatment. The increased follicular fluid levels of some interleukins were noted to probably influence oocyte quality and fecundability by deteriorating the follicular microenvironment.

It has been reported that follicular fluid exerts chemotactic effects on neutrophilic granulocytes and the concentration of this activity is related to the outcome of IVF (12). About 5-15% of the cellular pool of the FF consists of macrophages, and intraovarian macrophages are involved in the production of IL-1β (13,14). IL-1 has been suggested to be one of the regulators of ovarian steroidogenesis (15). Previous studies suggested that serum and FF IL-1β concentrations were correlated with the pregnancy achievement (4,5). However, the results are controversial. Barrionuevo et al. (11) investigated FF IL-1β concentrations in relation to fertilization and embryo cleavage rates and revealed no correlation. Karagouni et al. (4) showed significantly higher amounts of FF IL-1β in the implantation versus non-implantation cycles. In contrast, Leal et al. (5) found FF IL-1β levels to be significantly higher in non-pregnant women. In the study by Bedaiwy et al. (6), FF IL-1β concentrations were found to be similar in pregnant and non-pregnant cycles. Similarly, we found no significant difference in FF and serum IL-1β concentrations between pregnant and non-pregnant patients.

IL-6 is one of the cytokines that can influence granulosa cell steroidogenesis (16). Changes in E2 levels seen during gonadotropin stimulation were found to induce changes in serum IL-6 and TNF-α levels (17). Studies regarding FF IL-6 levels between pregnant and non-pregnant patients following ART are scarce. In a recent study, FF IL-6 concentrations were shown to be significantly higher in pregnant cycles compared to those in non-pregnant ones (6). However, we found similar FF and serum IL-6 concentrations between pregnant and non-pregnant women after IVF. In one study, serum IL-6 levels were found to be significantly higher in PCOS women undergoing IVF compared to those in normally ovulating women undergoing IVF for male factor infertility (18). In some studies, elevated levels of serum IL-6 levels were reported in OHSS cases (19). Conversely, in another study, serum IL-6 levels were found to be correlated negatively with E2 levels (17). FF IL-6 concentrations were also compared between low and high responder patients undergoing ART, and no difference was found (20). In our study, the peak serum E2 levels were similar between the two groups and we did not include the PCOS cases in the study.

IL-8 is one of the potent leukocyte chemotactic cytokines found in the preovulatory follicle. IL-8 was suggested to be an essential part of folliculogenesis. In a previous study, FF IL-8 concentrations were compared between pregnant (n=11) and non-pregnant (n=33) women following IVF and were found to be no different (8). Our results are in accordance with them.

IL-12 is a potent immunomodulatory cytokine involved in inflammatory processes with antiangiogenic effects (21). Gazvani et al. (8) investigated IL-12 levels in FF and reported that its presence in FF was associated with a negative outcome in IVF treatment. Similarly, in another study FF IL-12 concentrations were found to be significantly lower in pregnant compared with non-pregnant cycles (6). In another study, serum and FF IL-12 levels were studied in relation to the outcome in women undergoing IVF and no association of either serum or FF IL-12 levels with the outcome was demonstrated (5). Another study also reported no significant difference in FF IL-12 concentrations between pregnant and non-pregnant patients (7). Similarly, we observed no significant difference in FF and serum IL-12 concentrations between patients who became pregnant and those who did not following ART.

Regarding FF and serum TNF-α concentrations, very few studies exist in the literature. Bedaiwy et al. (6) in their study compared FF TNF-α concentrations between pregnant and non-pregnant cycles and found no difference. Similarly, Lee et al. (9) revealed no significant difference in FF TNF-α levels of pregnant and non-pregnant patients. However, significantly higher TNF-α concentrations were found in follicles containing poor quality oocytes. In accordance with the above-mentioned studies, similar FF and serum TNF-α concentrations were found in the present study between patients who became pregnant and those who did not following ART.

Nitric oxide (NO), a potent vasodilator, is also produced in the ovary and is involved in folliculogenesis (22). However, the association of FF NO concentrations with pregnancy potential in IVF remains controversial. In a study about FF NO concentrations in IVF cycles, the relationship to embryo grading was sought and it was reported that high NO levels in human follicles may be detrimental (10, 23). Similarly, lower FF NO levels at the time of oocyte retrieval were suggested to be associated with adequate fertilization and embryo cleavage rates (11). However, FF NO concentration was proposed to be of no use as a prognostic marker for the prediction of the pregnancy outcome (24, 25). Concerning the plasma NO levels, its concentration was found to be inversely correlated with uterine artery PI (26). The measurement of impedance to uterine blood flow in IVF cycles has been suggested to contribute to the evaluation of endometrial receptivity (27, 28). The decrease in peripheral impedance in the uterine vascular bed, reflected by a low PI, is a consequence of increased blood flow and tissue perfusion, which may improve uterine receptivity (29). Further studies incorporating Doppler measurements are needed to clarify this point.

Relevant studies in the literature reported various mean values for the serum or FF cytokines. A possible explanation for inconsistency may be related to patients' characteristics and also the timing of sample collection. Furthermore, the discrepancies may be due to technical variations in cytokine measurements, for example, to the different sensitivity of the ELISA system used.

One limitation of our study might be considered as the inclusion of unexplained infertility cases in the study. However, a previous study evaluated FF IL-6 and IL-8 levels according to the etiology of infertility and reported no significant difference (30).

In conclusion, the concentrations of follicular fluid and blood serum IL-1β, IL-6, IL-8, IL-12, TNF-α and NO do not appear to be determinants of the outcome of IVF treatment. Accordingly,

these cytokines and NO cannot be used in the prediction of pregnancy following IVF. Future studies with larger patient numbers are required to understand the regulatory mechanisms in in vitro fertilization treatments, which might show the importance of some cytokines as biomarkers for the success of IVF.

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Family planning attitudes of women and affecting factors

Kadınların aile planlamasına ilişkin tutumları ve etkileyen faktörler

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Abstract

Objective: This descriptive research was conducted to determine the attitudes of women towards family planning and the factors affecting these attitudes.

Material and Methods: Universe of the study has been composed of women who are married and older than 15 years and living in Ankara Kale district. 300 women were included. Kale district is a low socioeconomical slum area of the capital city of Turkey. Questionnaire and Family Planning Attitude Scale were used to collect data.

Results: 38% of the women were in the 30-39 years age group and 66.7% of them were graduates of primary school. 73.3% of the women had information about some contraceptive method and 53% of them had used an effective method. Mean score taken from the Family Planning Attitude Scale was 120.11±13.8. The scores obtained from the scale were significantly higher in the women who were graduates of elementary school, whose husbands were graduates from high school and higher, who had heard about any contraceptive method and had been using some method and who had had 1-3 pregnancies ($p<0.05$). Economical status, family type, presence of a chronic disease, using regular medicine and smoking have not affected family planning attitude ($p>0.05$).

Conclusion: It was found that the attitudes of the women towards family planning were at a good level, nearly half of the women were using an effective method, and the level of education, number of pregnancies, unwillingness to have another child in the future, having information about contraceptive methods and using some contraceptive method had influenced family planning attitudes. In order to turn this attitude into practice with high rate, family planning education programs and consultancy services must be planned and implemented.

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Key words: Family planning, woman, family planning attitude

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Özet

Amaç: Bu araştırma, evli kadınların aile planlamasına ilişkin tutumlarını ve etkileyen etkenleri belirlemek amacıyla tanımlayıcı nitelikte yapılmıştır.

Gereç ve Yöntemler: Araştırmanın evrenini, Ankara kalesi bölgesinde yaşayan 15 yaşından büyük ve evli kadınlar oluşturmuştur. Örnekleme 300 kadın alınmıştır. Kale bölgesi, Türkiye'nin başkentinde yer alan düşük sosyoekonomik statüye sahip bir gecekondu bölgesidir. Verilerin toplanmasında anket formu ve Aile Planlaması Tutum Ölçeği kullanılmıştır.

Bulgular: Kadınların %38'i 30-39 yaş grubunda, %66.7'si ilkokul mezunudur. Kadınların %73.3'ünün daha önce herhangi bir aile planlaması yöntemi duyduğu, %53'ünün etkili bir yöntem kullandığı belirlenmiştir. Kadınların aile planlaması tutum ölçeğinden aldıkları ortalama puan 120.11±13.8 'dir. Ortaokul ve üzeri mezunu olan, eşi lise ve üzeri mezunu olan, herhangi bir aile planlaması yöntemi duyan ve kullanan, 1-3 gebelik geçiren, gelecekte çocuk istemeyen kadınların aile planlaması tutum ölçeğinden aldıkları puanların anlamlı şekilde daha yüksek olduğu belirlenmiştir ($p<0.05$). Kadınların ekonomik durumu, aile tipi, kronik hastalığının olması, sürekli ilaç kullanması, sigara içmesi gibi özellikleri aile planlaması tutumunu etkilememiştir ($p>0.05$).

Sonuç: Kadınların aile planlamasına yönelik tutumlarının iyi düzeyde olduğu; yaklaşık yarısının etkili bir aile planlaması yöntemi kullandığı ve öğrenim düzeyi, gebelik sayısı, gelecekte çocuk isteme, herhangi bir aile planlaması yöntemi duyma ve kullanma gibi özelliklerinin aile planlamasına yönelik tutumlarını etkilediği sonucuna varılmıştır. Kadınların aile planlamasına ilişkin tutumlarının yüksek oranda davranışa dönüşebilmesi için aile planlaması eğitim programları ve danışmanlık hizmetleri planlanması ve uygulanması önerilmektedir.

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Anahtar kelimeler: Aile planlaması, kadın, aile planlaması tutumu

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Introduction

In recent years, although there have been significant developments in our country, the effects of these developments on the indicators of population and health are not yet sufficient. According to the results of the Turkey, Population and Health Research; both the birth and abortion statistics are still at high levels. It is indicated that 15% of the pregnancies are terminated because they are unwanted and the undesired, and unplanned pregnancies lead to 20 million unsafe abortions besides 80.000 deaths (1).

Each year, use of contraceptive methods increase, but the necessity for family planning services still continues. The unmet rate of contraceptive necessity is 7.9% (1). Women are influenced by several factors while preferring contraceptive methods. These can be summarized as the reliability of the method, false beliefs and incorrect applications of the methods, expectations of the society, attitudes of the individual

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and the family (2). Spouse's demand for using a contraceptive method and avoidance of the method by the woman because of religious beliefs can be given as examples of these factors (3, 4). Though the negative effects of undesired/unplanned pregnancies on woman/child health are known, there are still high rates of undesired/unplanned pregnancies. In order to prevent the undesired/unplanned pregnancies, effective contraceptive methods are preferred as the first choice. For planning the training and consultancy services to be given to the women and for effective presentation of those services, it is necessary to determine the attitudes and behaviors of women which are playing the key role in family planning activities.

Material and Method

This research was conducted on women above 15 years and married who live in the Ankara Kale district to determine their attitudes, behaviors related to family planning and the factors affecting these attitudes.

Sample

The sample group comprised of women who are older than 15 years, married and living in the Ankara Kale district. In this district the population of women is estimated as approximately 2000 (5). 300 women were included in the research. This survey has been conducted in accordance with the principles of the Helsinki Declaration. Before filling the questionnaire form, the women were informed about the purpose of the research. Participation in this study was voluntary.

The Kale district, where we performed our research, is a low socioeconomic slum area of the capital city of Turkey. In this area, half of the population (49.3%) is female (3257 women). The majority of those women are illiterate/literate/primary school graduates (83%) (5). The Kale district is a slum area that keeps the traditional structure and receives migration from all over Turkey.

The significance of this study is limited by the fact that it pertains to only one area of Turkey and only married women were taken into consideration. Therefore the findings cannot be generalized to all Turkish women.

Data Collection

A questionnaire form prepared by researchers was used for data collection. The questionnaire form consisted of two parts. The first part included questions about the socio-demographic characteristics of women such as age, education level, working status, economical status; the fertility characteristics and family planning applications. The second part consisted of Family Planning Attitude Scale.

Family Planning Attitude Scale

Family Planning Attitude Scale was developed by Örsal and Kubilay and validity and reliability was performed by them. The Cronbach alpha value was found as 0.87 (2).

The scale was evaluated in three subgroups. These are; attitudes toward methods (12 items), attitudes toward pregnancy (8 items) and attitudes of the society toward family planning (14 items). The scale was graded as, "Completely Agree: 1", "Agree: 2", "Neither agree nor disagree: 3", "Disagree: 4", and "Completely Disagree: 5". By adding all the item scores in every subgroup, the subgroup total and by adding the subgroup totals, the total score of the scale was obtained. The lowest score in the scale was 34 and the highest score was 170. The higher score indicated the positive attitude toward s family planning.

Data Analysis

The Statistical Package for the Social Sciences (SPSS, version 11.5 for Windows) was used to analyze the data. The percentage, mean, student t-test, and one-way variance analysis (ANOVA) were used to evaluate the data. The p value 0.05 (95% confidence interval) was accepted as significant.

Results

38% of the women were in the 30-39 years age group, 66.7% of them were primary school graduates, 79% lived in a nuclear family and 57.3% of them evaluated their socio-economic status as a moderate level (Table 1).

It was determined that 73.3% of the women had heard about a method of contraceptive, 68.7% of them had already used one of the methods and 53% of them used an effective method of contraceptive. It was also determined that 60% of the women had had 3 or more pregnancies, 36% of them had one male child, and 74.3% of them did not want any children in the future. 24.2% of the women who did not use any contraceptive method expressed that they wished children in the future and 14.2% of them were pregnant during the study so they neither wanted nor needed to apply contraceptive methods (Table 2).

The mean score of the Family Planning Attitude Scale was 120.1 ± 13.8. In regard to the mean scores taken from subgroups of the scale, the mean score of attitude of society towards family planning was 54.80 ± 8.1, the mean score of attitude towards methods was 36.81 ± 5.2 and the mean score of attitude towards pregnancy was 28.50 ± 4.2.

It was determined that the number of women who were elementary school and higher graduates, whose husbands were graduates of high school or higher, who had ever heard about contraceptive method and used any contraceptive method, who had had 1-3 pregnancies, who did not wish any more children in the future had higher scores and the difference between the groups was statistically significant ($p < 0.05$) (Table 3).

The characteristics of the women such as economical status, family type, having a chronic illness, using regular medicine and smoking did not affect the family planning attitudes ($p > 0.05$).

Discussion

Family planning services in our country are still developing and parallel to this, there are some advances in the health indicators, but the need for family planning which cannot be met still stands out as an important health problem. In this study as well, the fact that about half of the women (47%) were not using an effective contraceptive method points out the significance of the subject. Supporting this finding, in Kaya et al's study (6) 39.9 %; Aydın and Aytekin's study (7) 47.1%; Özdemir et al's

Table 1. Sociodemographic characteristics of the women

Sociodemographic characteristics	n	%
Age groups		
<20 years	16	5.3
20-29 years	88	29.3
30-39 years	114	38.0
≥40 years	82	27.3
Education level		
Not illiterate	45	15.0
Primary school graduate	200	66.7
Elementary school graduate and higher	55	18.3
Education level of husband		
Not illiterate	17	5.6
Primary school graduate	194	64.7
Elementary school graduate	47	15.7
High school graduate and higher	42	14.0
Having social insurance		
Yes	248	82.7
No	52	17.3
Family type		
Nuclear family	237	79.0
Broad family	63	21.0
Socioeconomic status		
Good	38	12.7
Moderate	172	57.3
Poor	90	30.0
Any chronic illness		
Yes	66	22.0
No	234	78.0
Using regular medicine		
Using	57	19.0
Not using	243	81.0
Cigarette smoking		
Smoking	63	21.0
Not smoking	247	79.0

Table 2. Characteristics of Attitude to Fertility and Family Planning Implementations

Characteristics About Fertility and Family Planning Implementations	N	%
Spontaneous abortus		
Yes	71	23.7
No	229	76.3
Medical abortus		
Yes	61	20.3
No	240	79.7
Gravity		
Null gravity	47	15.7
1-2	73	24.3
≥3	180	60.0
Ever hearing about a contraceptive method		
Yes	219	73.3
No	81	26.7
Using any contraceptive method		
Using	206	68.7
Not using	94	31.3
Using effective contraceptive method		
Yes	159	53.0

study (8) 46.1%; Özgür et al's study (9) 45.3%; and Tanrıverdi et al's study, 39.2% of the women do not use an effective contraceptive method. In other studies conducted in Turkey, it was also seen that the rate of family planning use was not at the desired level. According to the results of the Turkey, Population and Health Research, it was determined that only 42.5% of the women use an effective method (1). When the rates in our country are compared with the others, it is seen that rates of using an effective contraceptive method in developed countries are higher (10-12) and in underdeveloped countries are lower (13-15) than our country.

Family planning applications can be affected by many factors such as traditional beliefs, religion, family type, knowledge about contraceptive and problems in provision of health services. These affecting factors lead the formation of family planning behaviors. Norms, habits, learning processes, environmental conditions, and attitudes influence the behavior. Attitude is a notional concept and although it cannot be observed directly, the effects on behavior are well known (2). In this study, women's attitudes towards family planning were evaluated and the level of attitude is quite high. However, approximately half of the women's avoidance of using any effective method for contraceptive indicates that the attitudes do not turn into behaviors sufficiently. Similar to this, Agyei and Migadde (16) determined that women's use of contraceptive methods is much lower than their attitudes. Chopra and Dhaliwal (14) also determined that, although their attitudes were positive, women's use of effective contraceptive methods for long term were low.

Environmental conditions, habits, and expectations have effects on turning the attitudes into behaviors (17). Even when women have developed positive attitudes towards family planning, it is thought that the beliefs on this subject, the level of information and environmental factors have effects on turning the attitudes into behaviors. In our country, although many studies considering the knowledge and behaviors on family planning have been conducted, the studies considering the attitudes are not sufficient. Attitude is a concept that develops and transforms in time.

Table 3. Mean Scores Obtained From Family Planning Attitude Scale According to Some Characteristics

Characteristics	N	X ± SS	p
Education level			
Not illiterate	45	111.09±11.8	F:
Primary school graduate	200	119.81±13.1	22.859
Elementary school graduate and higher	55	128.58±12.9	<0.05
Husband's education level			
Not illiterate	17	114.24±11.7	F:
Primary school graduate	194	117.32±13.5	13.218
Elementary school graduate	47	126.57±12.9	<0.05
High school graduate and higher	42	128.12±11.7	
Ever hearing about a contraceptive method			
Yes	219	121.21 ± 14.3	F:
No	81	117.12 ± 12.2	5.237
			<0.05
Using any contraceptive method			
Yes	206	122.56±13.6	F:
No	94	114.72±12.9	22.215
			<0.05
Parity			
Nulliparous	8	109.13 ± 11.5	F:
1-3	189	122.37 ± 13.7	8.383
4 and more	103	116.81 ± 13.2	<0.05
Wishing a child in the future			
Yes	61	116.46± 11.3	F:
No	223	121.31 ± 14.5	3.381
Hesitant	16	117.19 ± 11.2	<0.05

Attitudes are not gained by birth, they are learned and adopted by experiences and culturally gained during socialization (17). Attitudes of women towards family planning are influenced by education and experiences such as pregnancy. It was determined that women who are graduates of elementary school or higher, who had experienced 1-3 pregnancies and who did not want any more children in the future got higher scores from the family planning attitude scale. As the education level increases, the number of children desired decreases (1). The higher score of higher level educated women can be explained by more possibilities of obtaining knowledge on family planning and having more awareness about the subject. Similar to this, Tuladhae & Marahatta (18) determined that women's awareness increases as their education level increases. Higher scores from family planning attitude in women who have had 1-3 pregnancies and who did not want any more children in the future, is an expected result. Many and frequent pregnancies may affect the mother-child health negatively and increase the risk of maternal mortality (19). It is thought that the attitude level is higher because women do not want to have more children than they desire and also they demand for more effective contraception.

It was determined that, besides the education level and pregnancy situation, the level of awareness about contraceptive also affects the attitudes of women. In this study, the higher attitude towards family planning of the women who have heard about family planning and/or apply any method of contraceptive is notable. This finding can be explained by easy access to the contraceptive methods by women and having more information about the subject.

Family planning attitude scale is evaluated in three subgroups, attitudes towards methods, attitudes towards pregnancy and attitudes of the society towards family planning. In this study, it was determined that, for all the subgroups, the scores of women were at a moderate level.

The moderate level of attitude of the women towards the methods can be evaluated as a positive finding. This finding can show that women want to use contraceptive methods. The rate of 24% wish to have a baby in the study group and the rate of pregnancy of 14% during the study supports this finding.

The attitudes related to pregnancy exist on the basis of attitudes related to family planning (2). Pregnancy brings social status to woman in traditional societies. Also in this study, the moderate level of attitude towards pregnancy can originate from the feelings of desire to feel worthy and wish to earn status by the women. It is thought that the traditional structure and the lower status of women in this district affect the results of the attitudes of the women. Three or more pregnancy rate of 60 % in the district also supports this result.

On the development of family planning attitudes of the society, socio-cultural characteristics play important role. Since the number of children indicates the power of the male, giving importance and precedence to male child can be examples of this situation (2). Society's moderate level of family planning attitude can be explained by the families' desire to have more male children. The rate of 25.3% not having a male child and the rate of 36% having one male child may affect the attitude of the society. It is thought that probably this can be caused by the district's traditional structure, namely the husband or mother-in-law is closely involved with the decision about contraceptives.

In conclusion, women's attitudes towards family planning were at a proper level; approximately half of them use an effective contraceptive method and the characteristics of the level of education, the number of pregnancies, desire to have a baby in the future, having heard about contraceptive methods and using any contraceptive method all affect the family planning attitudes. According to these results, it is suggested that, in order to transform the women's attitudes towards family planning into behavior, family planning training programs and consultancy services should be planned and applied. The implications for research include the need for replication of this study in other geographic areas that also represent a diverse sample of women with a wide range of education, income and other socio-demographic characteristics.

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The characteristics of sexual behavior and extent of condom usage among sexually active Croatians from Eastern Croatia

Doğu Hırvatistandaki cinsel aktif kadınların kondom kullanımı hakkındaki görüşleri ve cinsel davranış biçimleri

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Abstract

Objective: To determine the extent of condom usage as a method of protection from sexually transmitted infections (STIs) among sexually active individuals obliged to present for periodical health examination at the Institute of Public Health for the Osijek-Baranya County, in Osijek, eastern Croatia.

Material and Methods: During February 2004, a cross-sectional questionnaire survey was conducted. The research tool was an unidentified 20-item questionnaire addressing the sexual behavior of study subjects and their partners and methods of protection from STIs. Descriptive statistics and χ^2 – test were used for data analysis.

Results: The response rate was 84.2% (278/330). A total of 278 subjects, 96 (34.5%) males and 182 (65.5%) females, 167 (60.1%) married and 111 (39.9%) single, mean age 31.3±8.4, age range 18-52 years were enrolled in the study. Study results revealed 22.3% (62/278) subjects to have had two or more sexual partners over the one-year period and the use of condom was reported by 40.3% (25/62) of those subjects.

Conclusions: The obtained results point to the need for additional education on protection from sexually transmitted infections and on risky sexual behavior, with special reference to the role of condom usage in the prevention of these diseases and their detrimental effects on the reproductive health of sexually active individuals.

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Key words: Sexual behavior, sexually transmitted infection, condom, Osijek, Croatia

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Özet

Amaç: Doğu Hırvatistan bölgesindeki Osijek-Baranya ilçesi Halk Sağlığı Enstitüsüne başvuran cinsel aktif kadınların cinsel temasla bulaşan hastalıkların (CTBH) önlenmesinde kondom kullanım durumlarını saptamak,

Gereç ve Yöntemler: Şubat 2004 de kesitsel bir çalışma yürütüldü. 20 soruluk bir anket hazırlandı. Veri analizi için ki kare ve betimleyici analizler uygulandı.

Bulgular: Yanıt oranı %84.2 (278/330) idi. Evli 167 (%60.1) ve bekar 111 (%39.9) yaşları 31.3±8.4, dağılımı 18-52 olan kadınlar çalışmaya dahil edildi. Çalışma, %22.3 kadının son bir yıl içinde bir veya daha fazla cinsel partnerinin olduğunu ortaya çıkardı. Kondom kullanımı %40.3 (25/62) idi.

Sonuç: CTBH kontrolünde eğitim gereklidir ve kondom kullanımının bu hastalıkların önlenmesindeki önemi öğretilmelidir.

(J Turkish-German Gynecol Assoc 2009; 10: 142-7)

Anahtar kelimeler: Cinsel davranış, cinsel temasla bulaşan hastalıklar, kondom, Osijek, Hırvatistan

Geliş Tarihi: 12 Mart 2009 **Kabul Tarihi:** 16 Temmuz 2009

Introduction

Sexually transmitted infections (STIs) still pose a considerable health problem in both industrialized and developing countries. According to World Health Organization data, about 340 million people are infected with an STI, AIDS excluded, in the world *per* year (1). The epidemiological pattern of STIs differs considerably in different parts of the world. During the 1990s, the north and west European countries witnessed a dramatic decrease in the incidence of STIs, especially of gonorrhea and syphilis. This trend is believed to most likely result from a combination of factors, primarily early school education on sexuality, behavioral modifications to reduce sexually risky behaviors, promoting condom usage, and accessibility of appropriate STI treatments (2, 3). In developing countries, both the prevalence and incidence of STIs is still quite high, thus these diseases present a considerable public health

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problem (2). In the last few decades, the pattern of STI-s has been reported to change with a lower incidence of the "classic" STI-s and increasing rates of Chlamydia, genital herpes, human papilloma virus and, of course, HIV (4-7). This trend was noted in Croatia in the early 90-s when significant increase of HPV infection among men and women in Croatia was discovered (8). Other studies conducted in Croatia have dealt mainly with the problem of STI among vulnerable population subgroups, such as urban adolescent sexually active females, high school students, Croatian young people in general, Croatian migrant workers such as seafarers, construction workers and truck drivers and finally, clients tested for HIV infection at the Voluntary Counseling and Testing Center (VCT) (9-16).

Considering the findings of all the above mentioned studies, it is obvious that in the Croatian context one of the most important factors contributing to the spread of STIs is low and irregular condom use with casual partners combined with a low level of knowledge about sexuality and prevention of STIs (9-16). The fact that there has been no study about the extent of condom usage as a method of protection from STIs among sexually active individuals from the general population in Croatia (17) and the fact that, in the eastern part of Croatia, there has been only one study dealing with various risk behaviors in high school students from Osijek-Baranya County (including risky sexual behavior), which confirmed a strong influence of parental health-risk behaviors on their children's health-risk behaviors (18), motivated us to embark on the present study. The aims of our study were to investigate the characteristics of sexual behavior and condom usage as a method of protection from STIs in a group of sexually active individuals obliged to present for periodical examinations at the Outpatient Clinic of the Institute of Public Health for the Osijek-Baranya County in the capital of eastern Croatia, Osijek. The frequency of condom usage was especially assessed in individuals having two or more partners during the one-year study period

Material and Methods

All individuals presenting for obligatory periodical health examinations at the Institute of Public Health for the Osijek-Baranya County in Osijek according to the By-law on population protection from infectious diseases (19), during February 2004 were invited to participate in a questionnaire study. These individuals (mainly workers from food industries, restaurants, schools, cosmetic salons as well as health professionals working in various health institutions) were obliged to undergo periodical health examinations at the Epidemiological Department of the Institute of Public Health for the Osijek-Baranya County in Osijek according to the By-law on population protection from infectious diseases. Each year, around 3 300 clients (60% females and 40% males) are examined at the Epidemiological Department. Upon examination during February 2004, the potential study subjects received a cover letter telling them about the study and a responsible epidemiologist explained them in detail the aim of the study and asked them to participate in it on a voluntary basis, by filling-out an unidentified questionnaire. The Ethical Committee of the Institute of Public Health approved the study and each participant filled out an informed consent before he/she filled-out an unidentified questionnaire. All together, 330 potential study subjects were asked to participate in the study, and 52 (15.8%) of them refused. Among non-respondents there were 30 males (57.7%) and 22 females (42.3%). A total of 278 men and women participated in the study and the overall response rate was 84.2% (278/330).

The study was performed using an unidentified questionnaire containing 20 questions: 5 questions on demographics (age, sex, marital status, age at first intercourse, sexual orientation); 9 questions on sexual behavior of the study subjects and their partners (number of sexual partners during last year, history of any diagnosed STIs in study subject or his/her sexual partner/s, type of sexual intercourse, gender of sexual partners, risky sexual activities such as unprotected sexual intercourse with casual partner and sexual activities combined with drug or alcohol abuse without proper protection, sexual activities with partners of risky sexual behavior meaning promiscuous partners or sex workers); and 6 questions on methods of protection from STIs (primarily use of condoms during each type of sexual intercourse with casual partners, hepatitis B vaccination, testing for HIV). The questionnaire was constructed in collaboration between the Department of Public Health School of Medicine University of J. J. Strossmayer in Osijek, Department of Computer Science, Faculty of Electrical Engineering University of Josip Juraj Strossmayer in Osijek, Institute of Public Health for the Osijek-Baranya County in Osijek and Andrija Stampar School of Public Health in Zagreb, and several pilot studies were performed before the final version. It took about 15 minutes to fill out the entire questionnaire and then subjects were instructed to put these filled out forms in a specially designed box that was positioned in the waiting room area and could not be opened or seen through.

Comparison of particular answer frequencies was made by the χ^2-test. The level of statistical significance of difference was set at $p < 0.05$. Statistical analysis was done by using Microsoft Excel 2000 (Microsoft Corporation, Redmond, WA, USA).

Results

Results are presented in Figures 1-3. A total of 278 participants, 96 (34.5%) males and 182 (65.5%) females, mean age 31.31±8.42 (range 18-52) years, all declaring themselves as being sexually active (in the sense that they had at least one sexual intercourse during past year), consented to take part in the study. Out of 278 study subjects, 78 (28.1%) were in 18-24, 95 (34.2%) in 25-34, 89 (32.0%) in 35-44 and 16 (5.7%) in 45-52 age groups and 167 (60.1%) were married while 111 (39.9%) were single. Of 96 men, 52 (54.2%) were married and 44 (45.8%) were single. Of 182 women, 115 (63.2%) were married and 67 (36.8%) were single (Figure 1).

The mean age at starting sexual activity was 17.72±1.94 (range 13-27) years. According to sexual orientation, there were 4 (1.4%) subjects of homosexual (1 male and 3 females) and 274 (98.6%) subjects of heterosexual orientation.

Analysis of questionnaire answers revealed that 62 (22.3%) study subjects had had two or more sexual partners during the

one-year study period. According to marital status, two or more sexual partners during the study period were reported by 43 (38.7%) of single and 19 (11.4%) of married subjects. According to sex, 38 (39.6%) male and 24 (13.2%) female subjects had two or more sexual partners during the one-year period, the difference being statistically significant ($p=0.0000$, $\chi^2=24.366$). Analysis of questionnaire answers revealed 25 (22.5%) single men and 18 (16.2%) single women to have had two or more partners during the study period, the difference being statistically significant ($p=0.0015$, $\chi^2=10.040$). In the group of married subjects, 13 (7.8%) men and 6 (3.6%) women reported two or more partners during the study period, also yielding a statistically significant difference ($p=0.0002$, $\chi^2=13.899$). According to sex and marital status, two or more sexual partners during the one-year period were reported by 25 (56.8%) single men, 13 (25.0%) married men, 18 (26.9%) single women and 6 (5.2%) married women (Figure 2).

The use of the condom as a measure of protection against STIs was reported by 25 out of 62 (40.3%) subjects with two or more sexual partners during the one-year study period, i.e. 15/38 (39.5%) men and 10/24 (41.7%) women. The sex difference was not statistically significant ($p=0.8639$, $\chi^2=0.029$) (Figure 3). Further analysis of the group of subjects with two or more partners who reported use of the condom as a measure of protection revealed it to be most frequently used by single subjects aged 18-24 of both sexes (14/25; 56%).

Discussion

The present study is a first attempt to describe the characteristics of sexual behavior and to determine the extent of condom usage as a method of protection from sexually transmitted infections (STIs) among sexually active individuals from the Croatian general population. Numbers and types of sexual partnerships, especially concurrent partnerships, defined as a sexual partnership in which one or more of the partnership members have other sexual partners while continuing sexual activity with the original partner, remain the dominant individual and population risk factors for STI acquisition (20, 21). In that sense it was valuable to discover that 62 (22.3%) of all study subjects in the present study have had more than one sexual partner during the one-year period. Among all single subjects (111) there were 43 (38.7%) with more than one sexual partner during the one-year period and among married ones (167) there were 19 (11.4%) of them. According to sex, 62 study subjects, 38 men and 24 women, yielding a statistically significant sex difference and indicating male subjects from the Osijek area to be significantly more frequently involved in promiscuous sexual relations than female subjects, reported sexual relations with two or more partners during the one-year period. In these findings probably also lies part of the explanation why so few males answered the questionnaire because it is well known that subjects involved in risky behavior are much less motivated to disclose their sexual habits and consequently to even participate in such a survey (22, 23). The other part of the explanation lies in the fact that around 60% of all subjects obliged to undergo the periodical health examination at the

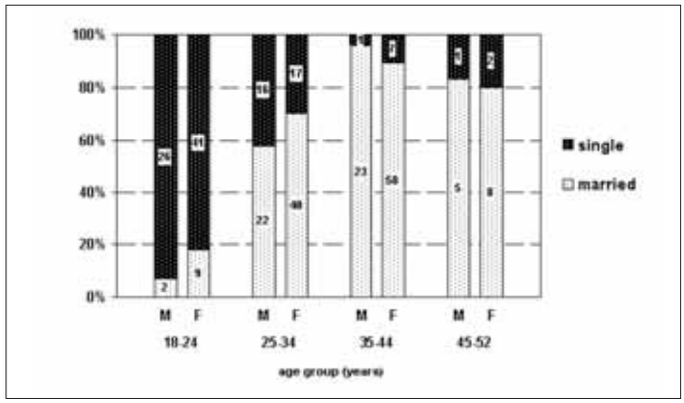

Figure 1. Study subjects (obliged to present for periodical examinations at the Institute of Public Health for the Osijek-Baranya County) according to age group, sex and marital status

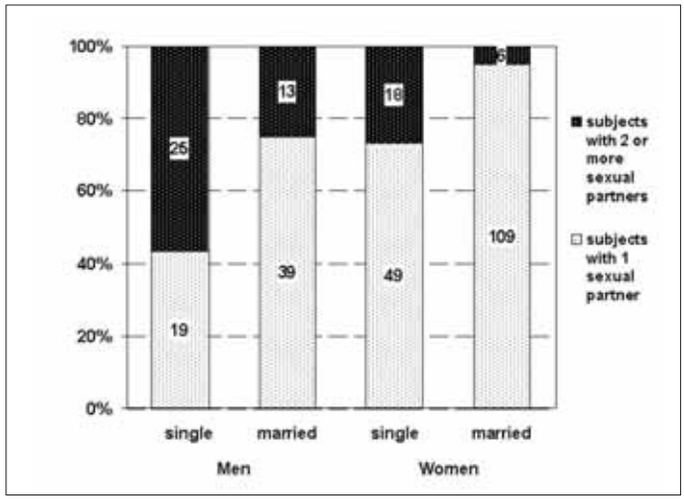

Figure 2. Study subjects (obliged to present for periodical examinations at the Institute of Public Health for the Osijek-Baranya County) according to sex, marital status and number of sexual partners during 2003

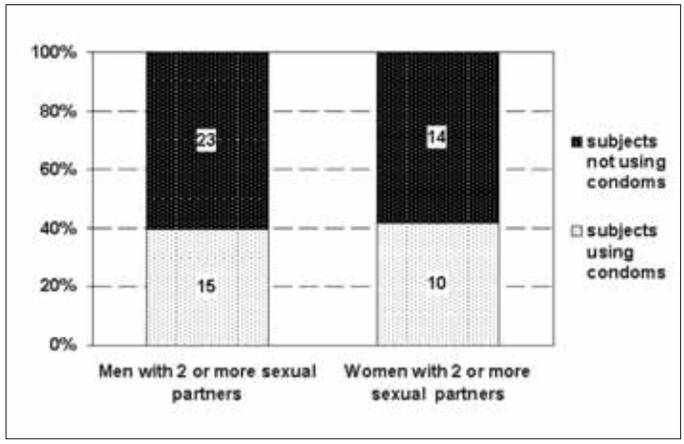

Figure 3. Study subjects (obliged to present for periodical examinations at the Institute of Public Health for the Osijek-Baranya County) with 2 or more sexual partners during 2003 according to sex and use of condom

APPENDIX

QUESTIONNAIRE

Please write or circle Your answer!

1. Birth year: _____ 2. Gender: Male Female 3. Age at first intercourse: _____

4. Marital status: a) married b) single (never married) c) divorced or widowed

5. Sexual orientation: a) heterosexual b) homosexual c) bisexual

6. Number of sexual partners during last year: a) 0 b) 1 c) 2 or more

7. Have you ever been diagnosed with any type of sexually transmitted disease?
   a) yes b) no
   If yes, please write what type_____

8. To your knowledge, has your current sexual partner ever been diagnosed with any type of sexually transmitted disease? a) yes b) no
   If yes, please write what type_____

9. Type of sexual intercourse that you practice:
   a) solely vaginal type of sexual intercourse
   b) mostly vaginal and beside them sometimes anal and/or oral type of sexual intercourse
   c) solely anal type of sexual intercourse
   d) solely oral type of sexual intercourse

10. Gender of your sexual partners: a) male b) female c) male and female

11. During sexual intercourse with casual partners in lifetime I have ALWAYS used condoms: a) yes b) no

12. I have NEVER in my lifetime involved myself in sexual activities combined with drug or alcohol abuse without condom: a) yes b) no

13. Have you EVER in lifetime involved yourself in sexual intercourse with promiscuous partners or sex workers? a) yes b) no

14. To your knowledge, has your current sexual partner EVER in lifetime involved himself/herself in sexual intercourse with promiscuous partners or sex workers?
    a) yes b) no

15. How often during VAGINAL sexual intercourse do you use condoms?
    a) always b) mostly c) sometimes d) never e) I don't practice them at all

16. How often during ANAL sexual intercourse do you use condoms?
    a) always b) mostly c) sometimes d) never e) I don't practice them at all

17. How often during ORAL sexual intercourse do you use condoms?
    a) always b) mostly c) sometimes d) never e) I don't practice them at all

18. To your knowledge, how often does your current sexual partner use condoms during various types of sexual intercourses?
    a) always b) mostly c) sometimes d) never

19. Have you EVER in lifetime received hepatitis B virus (HBV) vaccination?
    a) no b) I don't know c) yes (three doses) d) yes (less than three doses)

20. Have you EVER in lifetime been tested for HIV? a) yes b) no

Thank You very much for Your cooperation!

Epidemiological Department of the Institute of Public Health for the Osijek-Baranya County in Osijek, according to the By-law on population protection from infectious diseases, are females because they represent the vast majority of employees in food industries, restaurants, schools, cosmetic salons as well as in the Croatian health sector. Furthermore, questionnaire answers indicated that 25 (40.3%) subjects with two or more sexual partners during the study period used condoms as a measure of protection against STIs with non-detectable sex difference among these subjects. This result is consistent with the results reported from studies conducted in other parts of the world, ranging from 31% to 58% of subjects confirming the use of the condom (24-27). In our study, 81 (29.1%) of all subjects reported sexual relations without the use of appropriate protection, 34 (42.0%) of them were married and 47 (58.0%) single. The difference in practicing risky sexual relations according to marital status was statistically significant, suggesting that this type of risky sexual behavior was characteristic of unmarried subjects, which is also consistent with other study reports (28-30). Furthermore, among 24 (8.6%) study subjects reporting sexual contacts with partners of risky sexual behavior, 15 (62.5%) of them were single. As expected, unmarried subjects were found to be at an increased risk of STIs considering sexual relations without appropriate protection and with partners characterized by risky sexual behavior as risk factors for STIs. According to age, the use of condoms in the group of subjects with two or more sexual partners during the one-year study period showed the highest rate in the subgroup of unmarried subjects aged 18-24, whereas 14 (56%) of them had reported the use of condoms. This age group (including single and married subjects) also accounted for 26 (41.9%) of those having sexual relations with two or more partners during the one-year period. These data are consistent with the results reported from other studies conducted elsewhere and among Croatian youth, which show the rate of condom usage to be higher among younger individuals who generally have a greater number of sexual partners (11,12, 31-35). In this way, by frequent use of condoms as a method of protection, young persons tend to neutralize the effect and prevent the occurrence of detrimental consequences (primarily HIV infection) of their more liberal attitude towards promiscuous relations (36-38). The sample included in the present study could not be considered representative for the sexually active population of the Osijek area, because it was a convenience sample comprising only individuals presenting during February 2004 for obligatory examination at the Institute of Public Health for the Osijek-Baranya County. However, the results obtained in this study gave some valuable information about sexual behavior in the Croatian general population. The significance of these findings is even larger knowing that sexual behavior is a major determinant of sexual and reproductive health and taking into account all problems connected with investigating sensitive topics such as sexual behavior (first of all discomfort and lack of privacy in the study) and dealing with the STIs care and prevention that are often accompanied by stigma and shame (39-43).

Sexual educational programs as the major tool for improving sexual health, especially for improving the prevention of sexually transmitted diseases is accepted differently among different age groups of the population in various European countries. Also, a political context within each country still exerts a strong influence. In countries such as Denmark and the Netherlands, sexual education is widely accepted and supported, while objections are forcefully made in countries such as the Czech Republic, Germany, Ireland and Poland (44). The results obtained in the present study definitely point to the need for additional education on the protection from and on the risk factors favoring the occurrence of STIs, which should address sexually active individuals of all age groups. Each contact by individuals with health professionals, from the teenage years throughout the following years should be used as an opportunity for adjusting prevention activities and counseling. Mass media should play an important role in delivering the information about the possibilities of protection from STIs and about risk factors favoring their occurrence to the whole population. Nongovernmental organizations should increase the awareness about the problem in specific subgroups of the population and the school-based and university-based programs should reach the young generations. In all educational messages, the role of condoms in reducing the risk of almost all STIs, including HIV, should be emphasized, as in this way the harmful sequels of these diseases affecting the reproductive health of sexually active individuals are prevented, and this is of paramount and nationwide importance.

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The relationship of gestational smoking with pregnancy complications and sociodemographic characteristics of mothers

Gebelikte sigara içen anne adaylarının sosyodemografik özellikleri ve bu durumun gebelik komplikasyonları ile ilişkisi

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Abstract

Objective: In this study, we aimed to assess the relationship of gestational smoking and passive smoking with pregnancy complications like preterm delivery, low birthweight, early membrane rupture, abruptio placentae, fetal distress and preeclampsia. We also analyzed the sociodemographic features of mothers who smoked during their pregnancy.

Material and Methods: Pregnant women have been questionned for their habits of smoking and household members' usage of tobacco products during their antenatal visits. Perinatal outcome of gestational smoking was assessed by the type of the delivery, birthweight, occurrence of preeclampsia, early membrane rupture and fetal distress during pregnancy. Differences in group means were analyzed with the Fisher's exact test, Chi-square test and ANOVA.

Results: There wasn't any significant statistical difference between the smokers' (n=86), passive smokers' (n=118) and nonsmokers' (n=77) groups in terms of maternal age, socioeconomic status of the family, gestational age, Apgar scoring and the rate of delivery by cesearian section. However, gestational smoking was found to be more common in mothers with poor or none education ($p=0.001$).There wasn't any significant statistical change in the rates of fetal distress, early membrane rupture, abruptio placentae and preeclampsia by gestational smoking ($p>0.05$). But, infants of mothers who smoked more than 10 cigarettes per day showed statistically significant birthweight deficits ($p<0.05$).

Conclusions: Data from this study indicate that gestational smoking is more common among women with low education and results in low birthweight. Therefore, it is essantial to educate the women before pregnancy and implement new smoking cessation programs for pregnancy. (J Turkish-German Gynecol Assoc 2009; 10: 148-51)

Key words: Gestational cigarette smoking, passive smoking, perinatal complications, sociodemographic features

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Özet

Amaç: Bu çalışmada gebelikte aktif ve pasif sigara içiminin preterm doğum, düşük doğum ağırlığı, erken membran rüptürü, dekolman ve preeklampsi gibi kötü gebelik sonuçları ile ilişkisi araştırıldı. Ayrıca gebeliğinde sigara içen kadınların sosyodemografik analizi yapıldı.

Gereç ve Yöntemler: Antenatal vizitlerde gebelere sigara içimleri ve erkek arkadaşalrının sigara kullanımları soruldu. Preterm doğum, düşük doğum ağırlığı, erken membran rüptürü, dekolman ve preeklampsi gibi kötü gebelik sonuçları kaydedildi. Verilerin analizi için Fisher kikare, kikare ve ANOVA testleri kullanıldı. .

Bulgular: Sigara içen (86) ve pasif içiciler (118) ve içmeyen (77) gebeler arasında anne yaşı, sosyoekonomik durumu, gebelik yaşı, apgar skoru ve sezaryen oranı açısından anlamlı bir fark saptanmadı. Sigara içen anne adayları genellikle düşük eğitim grubundan idi ($p=0.001$). Fetal distres, erken membran rüpütrü, dekolman ve preeklampsi ile sigara içimi arasında bir ilişki saptanmadı. Ancak günde 10 dan fazla sigara içen kadınların bebeklerinin doğum kilosu istatistiksel olarak daha düşük olarak saptandı ($p<0.05$).

Sonuç: Bu verilerle gebelikte sigara içiminin düşük eğitimli kişlerde ve düşük doğum ağırlıklı doğum yapan kadınlarda daha sık olduğu söylenebilir. Bu nedenle gebelik öncesi kadınların bu konuda eğitilmesinin önemi büyüktür.

(J Turkish-German Gynecol Assoc 2009; 10: 148-51)

Anahtar kelimeler: Gebelikte sigara içimi, pasif içicilik, perinatal komplikasyonlar, sosyodemografik veriler

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Introduction

Maternal smoking during pregnancy has long been considered an important risk factor for intrauterine growth retardation (1, 2). A remarkably constant 100-300 g difference in birthweight between cigarette smokers' and nonsmokers' newborns has been determined in many studies since 1957 (3-6). Previous studies also have shown that cigarette smok-

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ing during pregnancy increases the risk of fetal mortality and morbidity (3, 5). The perinatal mortality rate among smokers is 150% greater than is seen in nonsmokers (1, 2). It has been suggested that smoking is responsible for 15% of all preterm births and 20–30% of all low birthweight (LBW) infants (1). There is good epidemiological evidence to support an association between smoking during pregnancy and increased risk of premature rupture of membranes, abruptio placentae, placenta praevia and a modest increase in the risk for preterm delivery (1-3, 7-9). On the other hand, maternal cigarette smoking during pregnancy was associated with decreased risk for preeclampsia by many studies (10, 11).

Tobacco smoke contains thousands of compounds that may have adverse effects on the human body. The major compounds of significance are nicotine and carbon monoxide. Nicotine crosses the placenta and can be detected in the fetal circulation at levels that exceed maternal concentrations by 15%, while amniotic fluid concentrations of nicotine are 88% higher than in maternal plasma (1). The antenatal effects of nicotine are mainly a predictable decrease in uterine artery blood flow, variable changes in umbilical artery flow, and variable changes in fetal oxygenation and acid-base balance. Nicotine can also cause a decrease in fetal heart rate and an increase in mean arterial pressure (1, 2).

Carbon monoxide (CO) crosses the placenta rapidly and is detectable in the fetal circulation, equilibrating at levels that are 15% higher than in maternal blood (1). Carboxyhemoglobin is formed by the binding of CO and hemoglobin, shifting the oxygen dissociation curve to the left and resulting in a decrease in the availability of oxygen to fetal tissues (1, 2).

While medical researchers and health care providers studied the health risks of cigarette smoking in pregnant women and their offspring, social science researchers have produced studies concerning factors determining smoking choices during pregnancy (12). These social science researches indicated that factors influencing the choice to smoke during pregnancy include age, employment status, economic status, race, education, birth parity and the provision of prenatal care (8, 12).

In this study, we aimed to analyse the sociodemographic features of mothers who smoked during their pregnancy. We also wanted to show the relationship of maternal smoking and passive smoking during pregnancy with perinatal complications such as preterm delivery, premature rupture of membranes, abruptio placentae, fetal distress and preeclampsia.

Material and Methods

Two hundred and eighty-one pregnant women who applied for antenatal examinations within a month at Sisli Etfal Education and Research Hospital, Istanbul, Turkey were recruited for this study. The participants filled out a detailed written questionnaire while attending antenatal services and their consent was obtained along with the questionnaire. Data on their smoking habits, age, pre-pregnancy weight, household members' smoking habits, education periods by years (no education, 1-5 years of primary school education, secondary school or higher education) and their economic status determined by the monthly income (low class: min. wage or lower, upper class: 2000.-TL or more, middle class: from min. wage up to 2000.-TL) were obtained from this questionnaire. The mother`s weight gain was noted at each antenatal visit. The delivery room interview ascertained the information about her smoking habits. Mothers were asked how many cigarettes they smoked per day. If they had stopped smoking, they were asked when and how many cigarettes they smoked per day before they stopped. The household members' smoking habits were also ascertained in the delivery room interview. Passive smokers were defined only from those who had a household member who smoked more than 10 cigarettes per day inside the house. The perinatal outcome of gestational smoking was assessed by the type of delivery, birth weight, gestational age, occurrence of preeclampsia, early membrane rupture and fetal distress during pregnancy. The initial examination of the newborns conducted within the first 24 hours after birth included birth weight, complete physical examination and 1 and 5 minutes Apgar scorings. Infants were weighed naked on a beam balance to the nearest 10 g using standard techniques. Gestational age

Table 1. General characteristics of the mothers and the neonates

	Nonsmokers (n=77)	Passive smokers (n=118)	Smokers <5 cigarettes/day (n=34)	Smokers 5-10 cigarettes/day (n=30)	Smokers >10 cigarettes/day (n=22)	p
Maternal Age (year)	25.7±5.7	26.3±6.1	24.3±4.5	23.7±3.7	28.0±5.9	0.30
Prepregnancy weight (kg)	59.4±9.6	59.8±11.0	59.4±9.8	54.7±7.2	54.6±8.7	0.08
Weight gain during pregnancy (kg)	13.7±4.0	12.8±2.8	12.4±4.4	13.6±4.0	12.9±3.4	0.59
Gestational Age by Naegela Formula (wk)	38.1±2.9	38.2±3.3	39.3±1.4	38.9±1.4	38.7±3.0	0.43
Gestational Age by USG (wk)	38.1±2.4	37.7±2.0	38.5±1.7	37.4±2.9	36.7±1.9	0.23
Birthweight of the neonate (gr)	3293±649	3161±672	3260±493	3048±482	2884±524	0.04*
Apgar 1'	8±1	8±1	8±1	8±1	8±1	0.30
Apgar 5'	9±1	9±1	9±1	9±1	9±1	0.37

Significance of difference (in bold): *p < 0.05

was calculated by the Naegele formula and by gestational ultrasonography prior to delivery. A fetal tococardiography was performed prior to delivery to assess fetal distress. Ethical approval for this study was obtained from the ethics committee of Sisli Etfal Education and Research Hospital.

For statistical analysis, the ANOVA test was used for the parametric variables in Table 1. Nonparametric categorical data such as mother's education level and the economic status of the family were compared using the Fisher's exact test and Chi-square test (Table 2 and 3). To compare the type of delivery and perinatal complications ,the Chi-square test was used (Table 4 and 5). P-values less than 0.05 were considered statistically significant. The statistical analyses were performed using the SPSS software, version 16.0 for Windows.

Results

Out of 281 pregnant women who participated in our study, 77 were nonsmokers, 118 were passive smokers and 86 were smokers; 34 smoked less than 5 cigarettes per day, 30smoked 5-10 cigarettes per day and 22 smoked more than 10 cigarettes per day.

There were no significant statistical difference between the smokers' passive smokers and nonsmokers groups in terms of maternal age, maternal prepregnancy weight and weight gain during pregnancy (Table 1). The gestational age calculated by the Naegele formula and fetal ultrasonography did notreveal any difference between the groups (Table 1). The 1 and 5 minutes Apgar scorings were within normal ranges in all 3 groups (8 and 9 respectively). However, birthweight of neonates showed significant differences between the groups. Infants of mothers who smoked more than 10 cigarettes showed statistically significant birthweight deficits ($p<0.05$) (Table 1).

In Table 2, the mothers' education showed differences between groups ($p = 0.001$). Gestational smoking was found to be more common in mothers who had either no education or who had an education of less than 5 years ($p=0.001$). The mother group with higher education was found to be less prone to gestational smoking.

In Table 3, there were no significant differences in terms of the mother's economic status between the groups. Table 4 revealed that there were no statistically significant difference in the rate of delivery by caesarian section between smokers, nonsmokers, and passive smokers groups.

Table 5 shows the rates of some perinatal complications that could be caused by gestational smoking. Compared to nonsmokers, passive smokers and smokers showed no statistically significant increase in the rates of fetal distress, early membrane rupture, abruptio placentae or preeclampsia during their pregnancies ($p>0.05$).

Discussion

The results obtained in the present study revealed that gestational smoking rate does not change with the mother's age or socioeconomic status. Only, the mother's education shows changes between the smokers, passive smokers and

Table 2. Mother's Education

	Nonsmokers (n=77)	Passive smokers (n=118)	Smokers <5 cigarettes/day (n=34)	Smokers 5-10 cigarettes/day (n=30)	Smokers >10 cigarettes/day (n=22)	p
No Education	7	18	3	4	8	0.001*
1-5 years	57	90	20	17	8	
5-10 years	11	10	10	9	5	
Higher education	2	0	1	0	1	

Table 3. Economic Status of the Family

	Nonsmokers (n=77)	Passive smokers (n=118)	Smokers <5 cigarettes/day (n=34)	Smokers 5-10 cigarettes/day (n=30)	Smokers >10 cigarettes/day (n=22)	p
Low Class	31	69	17	20	13	0.34
Middle Class	42	45	16	9	8	
Upper Class	3	4	1	1	1	

Table 4. Type of Delivery

	Nonsmokers (n=77)	Passive smokers (n=118)	Smokers <5 cigarettes/day (n=34)	Smokers 5-10 cigarettes/day (n=30)	Smokers >10 cigarettes/day (n=22)	p
Spontaneous	53	80	24	24	17	0,68
C- section	24	38	10	6	5	

Table 5. Perinatal Complications

	Nonsmokers (n=77)	Passive smokers (n=118)	Smokers <5 cigarettes/day (n=34)	Smokers 5-10 cigarettes/day (n=30)	Smokers >10 cigarettes/day (n=22)	p
No Complications	67	93	28	25	17	0.86
Fetal distress	6	15	3	2	3	
EMR	3	5	2	3	2	
Abruptio Placentae	1	1	0	0	0	
Preeclampsia	0	4	1	0	0	

nonsmokers groups. We also demonstrated that the neonates born to mothers who smoked more than 10 cigarettes per day showed significant birthweight deficits compared to neonates of the nonsmokers.

Studies carried out either by medical scientists (8) or by social scientists (12) show that many sociodemographic features play a part in smoking behavior of mothers during pregnancy. These studies found that high parity numbers, passive smoking at home, age, socioeconomic status of the family and maternal education were associated with a significantly increased risk for continued smoking during pregnancy. High levels of education and high age at onset of smoking decreased the risk of gestational smoking (12). In our study, gestational smoking was found to be more common in mothers with poor or none education ($p=0.001$).

Smoking during pregnancy is considered an antepartum cause of fetal hypoxia, which occurs as a result of fetoplacental respiratory and nutritional insufficiency (2). Carboxyhemoglobinemia and chronic hypoxemia, impairment of chorionic histoarchitecture and placentation, vasoconstriction of uteroplacental circulation and intermediary metabolic disturbance are the ethiopathogenetic basis of growth retardation in neonates of smoker mothers (2). For years, smoking during pregnancy has been strongly associated with an increase in pregnancies complicated by intrauterine growth restriction and LBW, as well as an overall 150-250 g decrement in mean birthweight (1, 3-7). In the present study, a birthweight deficit of 400-450 g in neonates of mothers who had smoked more than 10 cigarettes per day was found to be significant compared to neonates of nonsmokers ($p=0.04$) (Table 1).This is an important finding because in many studies the growth deficit of neonates of smokers was found to persist in their postpartum life, affecting their intellectual and physical development until 1 year of age (4-7).

Preterm delivery (1, 7), abruptio placentae (9, 1), early membrane rupture (1) and fetal distress (1, 2) are all found to be increased in rate related to the effect of nicotine and CO in pregnancies complicated by maternal smoking. Paradoxically, the risk of preeclampsia is found to be decreased by an estimated 30% among smokers (10, 11).

In our study, we could not reveal any relationship of gestational smoking with these pregnancy complications. We suggest multicenter studies with higher numbers of subjects for this purpose.

In conclusion, data from this study indicate that gestational smoking is more common among women with low education and results in low birthweight. Therefore, it is essential to educate women before pregnancy and implement new smoking cessation programs for pregnancy.

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A comparative study of folate and vitamin B_{12} serum levels in preeclamptic versus normotensive pregnant women in correlation with uterine and umbilical artery Doppler findings and pregnancy outcome

Normotansif ve preeklamptik gebelerde serum folat ve vitamin B12 düzeylerinin uterin ve Umbilikal arter Doppler sonuçları ve gebelik sonuçlarıyla karşılaştırılması

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Abstract

Objective: To detect the serum levels of folate and B12 in both preclamptic and normotensive pregnant women and to determine whether there is any relation between these levels with the uterine and umbilical artery Doppler indices as well as the pregnancy outcome.

Material and Methods: This case controlled study comprised 79 pregnant patients with preeclampsia and 113 healthy, normotensive pregnant women with singleton pregnancies at gestational ages ranging from 34- 40 weeks. Patients were not obese (BMI<30) and did not suffer from chronic hypertension, chronic renal or liver disease nor diabetes mellitus. Serum folate and B12 were detected in all cases. They were also subjected to a Doppler study of both the uterine and umbilical arteries. Serum folate and B12 blood levels as well as the Doppler study indices (RI and PI) were compared in both groups.

Results: The serum folate level was significantly lower in preeclamptic patients than normal pregnant women ($p<0.001$). It was significantly correlated to uterine artery Doppler indices (RI and PI) and negatively correlated to umbilical artery Doppler indices (RI and PI). Low serum folate was significantly correlated to poor maternal outcome. Low serum folate was also significantly correlated to poor perinatal outcome. Serum B12 level was not significantly different in preeclamptic patients from the control group (P value=0.14).

Conclusion: Serum folate was significantly lower in preeclamptic pregnant women with a significant correlation to increased uterine and umbilical RI, PI and poor maternal and neonatal outcome.

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Key words: Preeclampsia, serum folate, serum vitamin B12, umbilical artery Doppler, uterine artery Doppler

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Özet

Amaç: Normotansif ve preeklamptik gebelerde serum folat ve vitamin B12 düzeylerini uterin ve umbilikal arter doppler sonuçları ve gebelik sonuçlarıyla karşılaştırmak.

Gereç ve Yöntemler: Bu vaka kontrol çalışması 34-40 haftalara arasındaki 79 preeklamptik ve 113 normotansif gebe ile yapıldı. Hastalar obez değillerdi (BMI<30) ve kronik hipertansiyon, böbrek veya karaciğer rahatsızlığı olanlar ile, diabetli hastalar çalışmaya alınmadı. Serum folat ve vitamin B12 düzeyleri tüm vakalarda bakıldı. Ayrıca uterin ve umbilikal arter Doppler çalışması yapıldı.

Bulgular: Preeklamptik hastalarda serum folat düzeyleri anlamlı olarak dah düşük idi ($p<0.001$). Bu uterin arter Doppler indeksleri ile pozitif, umbilikal arter Doppler indeksleri ile negatif yönde korele idi. Düşük serum folat seviyeleri kötü obstetrik sonuç ile de ilişkili idi. Serum B12 vitamin seviyeleri farklı değildi.

Sonuç: Serum folat seviyeleri preeklamptik gebelerde anlamlı olarak daha düşüktür ve uterin arter Doppler indeksleri ve kötü obstetrik sonuç ile koreledir.

(J Turkish-German Gynecol Assoc 2009; 10: 152-7)

Anahtar kelimeler: Preeklampsi, serum folat, serum vitamin B12, umbilikal arter Doppleri, uterin arter Doppleri

Geliş Tarihi:10 Şubat 2009 **Kabul Tarihi:** 09 Haziran 2009

Introduction

Pre-eclampsia is a disease with worldwide significance. In developing countries, it accounts for 20–80% of the maternal mortality. Folate and vitamin B_{12} play an important role in the metabolism of homocysteine. Many studies prove hyperhomocysteinemia to be a factor that causes endothelial injury in pre-eclampsia. Perinatal mortality of infants of pre-eclamptic

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mothers is five-fold greater than for non pre-eclamptic women, and indicated preterm deliveries for pre-eclampsia account for 15% of preterm births (1).

Current concepts of the genesis of pre-eclampsia that include endothelial dysfunction, inflammatory activation, oxidative stress and predisposing maternal factors provide targets for well-designed nutritional investigation (2).

The amount of homocysteine in the blood is regulated by three vitamins: folic acid, vitamin B_{12}, and vitamin B_6. Reduced folate intake or genetic abnormalities of folate metabolism are associated with increased serum homocysteine concentration (3). Many studies prove hyperhomocysteinemia ,to be a factor that causes endothelial injury in pre-eclampsia (4-6).

Recent interest has emerged addressing folate deficiency and various pregnancy complications e.g. pre-eclampsia (7,8), abruptio placentae (9), neural tube defects (10), preterm deliveries (11), intra-uterine growth restriction (12) in addition to other non pregnancy related complications e.g. cardiovascular diseases (13), cognitive impairment (14) and cancer (15). Some investigators show decreased serum B_{12} in pre-eclamptic patients while others demonstrate no change (5, 16-20).

Material and Methods

Study design: case-control study

Participants: This study was conducted at Kasr El-Aini hospital, Cairo, Egypt from March 2006 until February 2008. Two groups of patients were included in the study, 79 pregnant patients who were diagnosed as having pre-eclampsia and a control group included 113 normotensive pregnant women who were both age and gestational age matched. Preclampsia was defined by having a blood pressure above 140/90 measured at least twice, 6 hours apart and proteinuria > 300mg/24hours or $\geq = +1$ proteinuria in the absence of another cause of proteinuria suggested by urine analysis (1). All patient ages ranged from 20-35 years. They were all non obese (BMI < 30) and had a singleton pregnancy at 34-40 weeks gestation. The preclamptic patients included in the study did not suffer from chronic hypertension, chronic renal or liver disease or diabetes mellitus.

A full history was taken including age, gestational age, parity, symptoms of severity (in pre-eclamptic cases), state of vitamin supplementation (considered positive in case of regular intake of B complex containing vitamins throughout pregnancy), and blood pressure measurement.

Laboratory investigations

Routine investigations: blood samples were collected on EDTA tubes for CBC analysis as well as on plain tubes for alanine aminotransferase (ALT), and aspartate aminotransferase (AST) and creatinine which were analyzed using commercial kits on the Synchron CX5 analyzer (Beckman Instruments Inc., USA) (21). Fresh morning urine samples were also collected for complete urine analysis.

Special investigations: Serum folate and B_{12}: Venous samples were withdrawn from all patients after an overnight fast, centrifuged and serum was stored at -20°c until the time of analysis. Serum folate and B_{12} were measured by a radioimmunoassay kit (simulTRAC B12/folate -SNB 57Co/125I radioimmunoassay kit) (MP Biomedicals, USA). The procedure of analysis is as described by the manufacturer pamphlet. The sensitivity of the kit for folate is 1.38nmol/l, and for B_{12} is 75pg/ml (Gutcho and Mansbach, 1977).

Ultrasound examination

Ultrasound assessment of uterine artery Doppler velocimetry by transabdominal technique with investigation of the main uterine artery at its crossing with the iliac vessels using the Accuvix (Medison,Korea) was made. Doppler indices were taken (RI and PI). The velocimetries of both uterine arteries were taken and the average indices were calculated. Assessment of umbilical artery velocimetry: using the same machine, a random site for the umbilical artery was determined and the Doppler indices were taken (PI, RI). Neonatal APGAR score, birth weight as well as admission to neonatal ICU were recorded.

Statistical analysis:

Data were statistically described in terms of mean ± standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables between the study groups was done using Student t test for independent samples in comparing 2 groups when normally distributed, and Mann Whitney U test for independent samples when not normally distributed. For comparing categorical data, Chi square (χ^2) test was performed. Correlations between various variables were done using Pearson moment correlation equation. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs *Microsoft Excel version 7* (Microsoft Corporation, NY, USA) and *SPSS* (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) statistical programs for Microsoft Windows.

Results

This study showed that serum folate was significantly lower in pre-eclamptic patients versus normal pregnant women (9.4 ± 8.8 nmol/L versus 20.2 ± 13.9 nmol/L $p < 0.001$). On the other hand serum B_{12} level was not significantly different in pre-eclamptic patients from the control group (350.7 ± 283 pg/ml versus 424 ± 364 pg/ml, p-value = 0.14) (Table 1). Folate supplementation was significantly lower in pre-eclamptic patients (5.1% in pre-eclamptic versus 34.5% in control group, $p < 0.001$).

Table 1. Difference in serum folate and B12 in pre-eclamptic versus control pregnant women

Group		Folate (nmol/L)	B_{12} (pg/ml)
PE cases (n = 79)	Mean	9.4	350.7
	SD	8.8	283.1
Controls (n = 113)	Mean	20.2	424.8
	SD	13.9	364.7
P-value		< 0.001	0.14

The serum folate is significantly higher in supplemented group (21.5±13.8 nmol/L in supplemented versus 8.7±8 nmol/L in non supplemented group, p=0.037).

Uterine and umbilical artery Doppler velocimetry showed a statistical difference between pre-eclamptic patients and the control pregnant women: Uterine RI and PI were significantly higher in pre-eclamptic group (RI: 0.58±0.1 versus 0.44±0.07, p<0.001; PI: 1.05 ± 0.29 versus 0.67 ± 0.18, p<0.001). Umbilical RI, PI were significantly higher in pre-eclamptic patients (RI: 0.63±0.09 versus 0.56±0.07, p=0.008; PI: 1.027±0.27 versus 0.82±0.16, p<0.001).

Serum folate was significantly correlated to uterine artery RI (Pearson correlation=-0.43, p<0.001) and PI (Pearson correlation=-0.46, p<0.001) (Figure 1) as well as umbilical artery RI (Pearson correlation=-0.22, p=0.002), PI (Pearson correlation=-0.22, p=0.002) (Figure 2).

Our study demonstrates no significant difference in hemoglobin levels between pre-eclamptic and control groups, but a significant difference exists in systolic blood pressure (SBP), diastolic blood pressure (DBP), platelet count, ALT, AST, creatinine level, neonatal birth weight (NBW) (Table 2), neonatal APGAR score and neonatal ICU admission .

Our results showed that 12 newborns of the preeclampsia group (15.1 %) had an APGAR score at 5minutes of less than7 whereas 67 newborns of the preeclampsia group (84.4%) had an APGAR score at 5minutes equal to or more than 7.All the newborns of the control group 113(100%) had an APGAR score at 5minutes equal to or higher than 7.

59 newborns of preclamptic group (74.7%) had a history of admission to the neonatal intensive care unit, whereas the 20 other newborns (25.3%) had not been admitted there, also none of the newborns of the control group 113(100%) had not been admitted to the neonatal intensive care unit.

Low serum folate was significantly correlated to poor maternal outcome (higher maternal serum creatinine, Pearson correlation=-0.354 P<0.001, higher serum ALT (Pearson correlation=-0.213, p=0.004), higher serum AST (Pearson correlation=-0.244, p=0.001) and lower platelet count (Pearson correlation=-0.235, p=0.047) and poor perinatal outcome (preterm labour, low birth weight, low APGAR score-less than 7 at 5minutes- and neonatal ICU admission); the serum level in poor outcome cases was 8.53±9.37 nmol/L versus 18.9±13.4 nmol/L in good perinatal outcome cases, p<0.001 (Figure 3).

Discussion

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection, which contribute greatly to maternal morbidity and mortality. How pregnancy incites or aggravates hypertension remains unsolved despite decades of intensive research. Indeed, hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics.

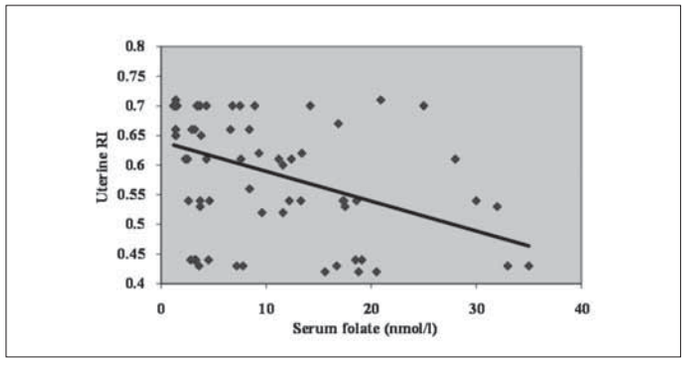

Figure 1. Correlation between serum folate (nmol/l) and uterine artery RI in Preeclamptic cases

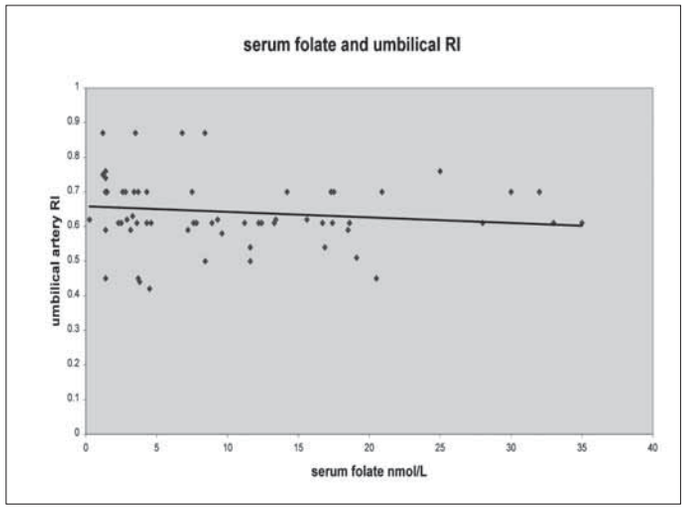

Figure 2. Correlation between serum folate (nmol/l) and umbilical artery RI in PE cases

Table 2. Mean and standard deviation of serum creatinine, ALT, AST, platelets and neonatal birth weight (NBW) in pre-eclamptic versus control pregnant women

Group		PLT (x103/μL)	ALT (U/L)	AST (U/L)	Creatinine (mg/dl)	NBW (g)
PE cases (n=79)	Mean	145.9	33.2	35.6	0.77	2359
	SD	55.2	44.8	44.2	0.16	4273
Controls (n=113)	Mean	192.9	11.4	11.9	0.48	3216
	SD	41.9	4.23	5.36	0.12	5035
P value		0.009	0.000	0.000	0.028	0.000

PLT: platelets

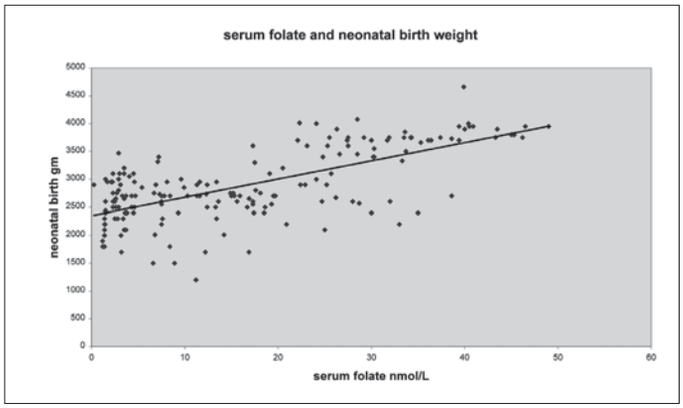

Figure 3. correlation between serum folate and neonatal birth weight

The neonatal birth weight in our study was significantly lower in the pre-eclamptic patients. This was similar to other previous studies (22-25). Neonatal intensive care unit admissions were significantly higher in pre-eclamptic patients. This result was also obtained by Ray, 2001(24).

Uterine RI and PI were significantly higher in the pre-eclamptic group. These results are supported by previous studies (26-28) and were explained by lack of normal trophoblastic invasion in pre-eclamptic patients. We found in our results that the umbilical RI, PI were significantly higher in pre-eclamptic patients.These results were in agreement with other studies (29-31).

Serum folate was significantly lower in pre-eclamptic patients versus normal pregnant women.This was the same evaluation as that reached by previous studies (7, 8, 32). The scientific plausibility of this result may be related to the important role of folate in the metabolism of amino acid homocysteine which has a protective role in the prevention of hyperhomocysteinemia,the same result as that by Holmes et al., 2005 (33). Hyperhomocysteinemia in turn is regarded a risk factor of pre-eclampsia (5, 34, 35) leading to endothelial injury and to hyper-coagulable states, as stated by El-Khairy, 2003(36). Folate is also important in DNA synthesis, so it may have an important role in trophoblastic proliferation and invasion of maternal spiral arteries, the derangement of which is a key feature in pre-eclampsia. This result of folate level disagreed with other previous studies (4, 6, 19) . However, most of these studies were carried out on a small sample size and no adequate exclusion criteria were considered in the pre-eclamptic group. The view that there is a need for further research with adequate sample size was mentioned in a meta-analysis done by Ray et al. 2001(24). The possible protective role of folate in the prevention of pre-eclampsia is supported by our results regarding folate supplementation, which is significantly lower in pre-eclamptic patients (5.1% in pre-eclamptic versus 34.5% in control group, $p < 0.001$). The serum folate is significantly higher in the supplemented group (21.5 ± 13.8 nmol/L in supplemented versus 8.7 ± 8 nmol/L non supplemented group, $p = 0.037$). This is similar to the result of a study done by Hermann et al. 2005 study (8).

As regards the correlation of serum folate to uterine and umbilical artery Doppler velocimetry in our study,serum folate was significantly correlated to uterine artery RI and PI. This result supported the hypothesis that folate may be involved in the pathogenesis of pre-eclampsia. No similar study reported this relation. Serum folate was also significantly correlated to umbilical artery RI and PI. This also supported the hypothesis that folate may be important in adequate trophoblastic proliferation including the tertiary stem villi. Also no similar study reported this relation to our knowledge.

In our study, there was a significant correlation between serum folate and both maternal and neonatal outcome: Low serum folate was significantly correlated to poor perinatal outcome parameters which involve preterm labour, low birth weight, low APGAR score –less than 7 at 5minutes- and neonatal ICU admission. This was similar to results presented by Mitchell et al. 2004(37). Low serum folate was significantly correlated to poor maternal outcome. As far as we know no similar studies showed these relations.

Our results showed that serum B_{12} level did not show any significant difference between both pre-eclamptic patients and the control group,and this was similar to other previous studies (7, 8) but was contradictory to the results reached by Laivouri et al. 1999(16) who found decreased serum B_{12} in pre-eclamptic patients, but this study's sample was small compared to ours (20 pre-eclamptic patients and 20 pregnant control). Their results may be explained by the fact that, in spite of the role of B_{12} in the metabolism of homocysteine, folate may be more important in this metabolism in protecting against pre-eclampsia.

The strength of our study was based on adequate sample size (79 pre-eclamptic patients and 113 controls), exclusion of known risk factors of pre-eclampsia to allow proper assessment and measuring serum folate and B_{12} much more accurately by blood sampling in the fasting state. However, there were some limitations in our study which deserve consideration .The serum level of folate in this cross-sectional study was significantly lower in pre-eclamptic patients versus control pregnant women, which proved the presence of association between low serum folate and the occurrence of pre-eclampsia.This association might be either a cause of pre-eclampsia or a result of some metabolic derangement in the course of the disease. it supported the idea that this association was most probably a cause, and was the role of folate in decreasing the homocysteine level and that vitamin supplementation was less likely to be present in pre-eclamptic patients. Some studies such as VanPampus et al. 1999. (38) demonstrated the presence of hyperhomocysteinemia long after delivery, supporting the view that hyperhomocysteinemia may be a cause of pre-eclampsia rather than an effect.

Since our pregnant women took either multivitamins containing folate (the majority) or B-complex vitamins throughout pregnancy, other confounding variables (the presence of other protective elements against pre-eclampsia in the multivitamin-minerals such as vitamin C, E) may affect our conclusion regarding the protective effect of folate against pre-eclampsia. but supported our conclusion that a significant correlation existed between low serum folate and poor maternal and neonatal outcome in pre-eclamptic patients and abnormal uterine and umbilical artery Doppler velocimetry findings. Also Hernandez-Diaz et al. 2002(39) demonstrated in their study that there

was a lower risk of pre-eclampsia in pregnancies with folate supplementation. However, due to the relatively small number of these studies, this area will need further research work.

In Conclusion, Serum folate was significantly lower in pregnancies complicated by pre-eclampsia. It was significantly correlated to abnormal uterine and umbilical artery Doppler velocimetry and poor maternal and neonatal outcome, So folate deficiency might have a role in the aetiology of pre-eclampsia and also folate supplementation throughout pregnancy might decrease the incidence of pre-eclampsia. Folate supplementation throughout pregnancy, and folic acid fortification of food could help to decrease the risk of pre-eclampsia especially in poor socioeconomic pregnant women who had an inadequate folate intake. There was no significant difference in serum B_{12} level in pre-eclamptic versus control pregnant women but further studies would be needed to support our results.

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Investigation of the correlation between 100 gram oral glucose tolerance test results and maternal leptin levels during pregnancy

Gebelikte oral 100 gr glukoz tolerans testi sonucu ile maternal serum leptin düzeyi korelasyonunun araştırılması

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Abstract

Objective: To investigate the correlation between maternal leptin levels and 100 gram oral glucose test (OGTT) results as well as the correlation between leptin levels and the development of gestational diabetes mellitus (GDM) and glucose intolerance during pregnancy.

Material and Method: 104 subjects with gestational weeks ranging from 24 to 32 weeks who had increased 50 gr OGTT values (>140) were included in this study. After the screening test, 100 gr OGTT was administered to the subjects. Sixty cases were selected from these subjects; twenty patients with one abnormal test result were identified as "glucose intolerant" group (Group 1), 20 patients with two abnormal test values were diagnosed with GDM (Group 2) and 20 patients with normal test results constituted the control group. The serum leptin levels of the groups were measured with enzyme linked immunosorbent assay (ELISA).

Results: The serum leptin level was 8.4±5.1 ng/ml for group 1, 9.1±5.3 ng/ml for group 2 and 6.3±4.6 ng/ml for the control group. Although serum leptin levels for group 1 and 2 was observed to be higher than the control group, the result was not statistically significant (p>0.05). This result did not change after adjusting for body mass index (BMI).

Conclusion: There is no statistically significant difference between leptin levels among three groups.

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Key words: Gestational Diabetes Mellitus, Oral Glucose Tolerance Test, Leptin

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Özet

Amaç: Gebelikte maternal leptin seviyelerinin 100 gr oral glukoz tolerans testi sonuçları ve gestasyonel diyabet veya glukoz intoleransı gelişimi ile korelasyonunun araştırılması.

Gereç ve Yöntemler: Gebelik haftası 24-32 haftalar arasında olup 50 gr yükleme testi >140 mg/dl olan 104 vaka çalışmaya dahil edildi. tarama sonrası 100 gr testi uygulandı. Altmış vaka seçildi ve tek değeri bozuk olan 20 hasta "glukoz intolerans" grubu (Grup 1) olarak adlandırıldı. İki değeri yüksek olan hasta GDM tanısı aldı (Grup 2). Sonucu normal olan 20 hasta ise kontrol grubu olarak sınıflandırıldı. serum leptin düzeyleri ELISA ile ölçüldü.

Bulgular: Serum leptin seviyeleri grup 1 için 8.4±5.1 ng/ml, grup 2 için 9.1±5.3 ng/m ve kontrol grubu için 6.3±4.6 ng/ml idi. Grup 1 ve 2 deki serum leptin düzeyleri kontrol grubuna göre yüksek olsa da bu istatistiksel olarak anlamlı değildi (p>0.05). Sonuçlar vücut kitle indeksi ayarlaması yapıldıktan sonra da değişmedi.

Sonuç: Her üç grup arasında serum leptin seviyeleri açısından anlamlı fark saptanmadı. (J Turkish-German Gynecol Assoc 2009; 10: 158-61)

Anahtar kelimeler: Gebelik diyabeti, oral glukoz tolerans testi, leptin

Geliş Tarihi: 04 Mayıs 2009 **Kabul Tarihi:** 14 Ağustos 2009

Introduction

Leptin is a polypeptide hormone that is secreted by adipose tissue cells, a product of the obesity (ob) gene, and is related to energy regulation (1). Research results indicate that the serum leptin level increases during pregnancy, independent of the body mass index (BMI). It is claimed that there is a link between the development of gestational diabetes mellitus (GDM) and leptin concentration. It is suggested that the measurement of leptin along with the assessment of other risk factors could help in identifying women at risk of developing GDM (2). The measurement of leptin level is interesting since GDM is a common metabolic complication of pregnancy and is related to type 2 diabetes and obesity (2).

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It is estimated that the incidence of perinatal morbidity such as macrosomia increases in patients who have a single value abnormality in 100 gram OGTT (3). Researchers suggest that these patients may be treated like GDM patients (4). It is found that insulin resistance is related to increased plasma leptin levels independent of the BMI (5). Plasma leptin concentration is also expected to be high in patients with glucose intolerance.
The aim of this study is to investigate the correlation between maternal leptin levels and 100 gr OGTT results as well as the correlation between leptin levels and development of GDM and glucose intolerance during pregnancy.

Material and Method

One hundred and four subjects at gestational weeks ranging from 24 to 32 with 50 gr OGTT values above 140 mg/dl were included in this study. The study was approved by the Ethics Committee of the hospital and informed consent was obtained from all patients. The histories of the patients were obtained, maternal age, gravidity and parity were recorded. Heights and weights of the patients at the time of glucose tolerance testing were measured and used to calculate the BMI as body weight (kg) /(body height (m))². All the patients were administered the 100 gr OGTT. In this test, serum fasting glucose levels and glucose values in the first, second and third hour which were above 95, 180, 155, 140 mg/dl respectively were treated as abnormal values. Out of these104 subjects; 20 patients were randomly selected from women with one abnormal test value and were designated as the “glucose intolerant” group (Group 1), 20 patients with two abnormal test results were diagnosed as GDM and designated as group 2 and 20 patients were randomly selected from women with normal test results as the control group. The serum leptin levels of these patients were measured with enzyme linked immunosorbent assay (ELISA). The blood samples for measurement of 100 gr OGTT and leptin were taken between 8-11 am after 10-12 hours of fasting. The blood samples were centrifuged at 5000 turns/ minute for 5 minutes and serum samples were stored at -70 °C. The serum leptin levels were analyzed by enzyme linked immunosorbent assay (ELISA) (Biosource Company , catalog number KAP 2281).
The resultant data was expressed as mean ± SD. Kruskal–Wallis Test and Mann-Whitney Test were used as statistical tests. Data from cross-tables were analyzed using Chi-square test. Spearman correlation test and linear regression analysis were used for the evaluation of the effects of different factors on leptin levels. SPSS for Windows version 13.0 was used for statistical analysis and $p<0.05$ was accepted as statistically significant.

Results

The clinical characteristics of the groups are shown in Table 1. There was no statistically significant difference in maternal ages, gestational weeks and parity between the groups.
A history of diabetes mellitus (DM) in their previous pregnancies was reported in 2 patients (10%) in group 1 and 4 patients (20%) in group 2. The patients in the control group had no history of DM. The BMI in the control group was statistically lower than group 1 ($p=0.032$) and 2 ($p=0.036$) (Table 1).
The serum leptin level was 8.4±5.1 ng/ml for group 1, 9.1±5.3 ng/ml for group 2, and 6.3±4.6 ng/ml for the control group. Although serum leptin levels for group 1 and 2 were higher than the control group, this was not statistically significant ($p>0.05$). The result did not change after adjusting for BMI. There was also no statistically significant correlation between BMI and maternal leptin levels ($p=0.644$). There was a positive but weak correlation between blood glucose and leptin levels ($r=0.276$, $p=0.032$) (Figure 1).

Discussion

In the present study, although serum leptin levels of subjects who were glucose intolerant or diagnosed with GDM were observed to be higher than subjects with normal blood glucose levels, the difference was not statistically significant. This result did not change after adjusting for BMI. Although the data is limited by the small sample size, it is suggested that this is

Table 1. Demographic characteristics of patients included in study

	Group 1	Group 2	Group 3
BMI (kg/m²)	29.1 ± 3.6	29.0 ± 3.2	26.2 ± 3.6
Maternal age (years)	29.4 ± 4.3	29.6 ± 5.8	27.5 ± 4.2
Gestational age at diagnosis(weeks)	28.2 ± 2.5	27.8 ± 2.5	26.9 ± 1.8
Number of pregnancies	2.8 ± 1.5	2.8 ± 1.4	2.4 ± 1.4
Number of deliveries	1.3 ± 0.1	1.3 ± 1.0	0.8 ± 0.8
Values are mean ±S.D. or n			

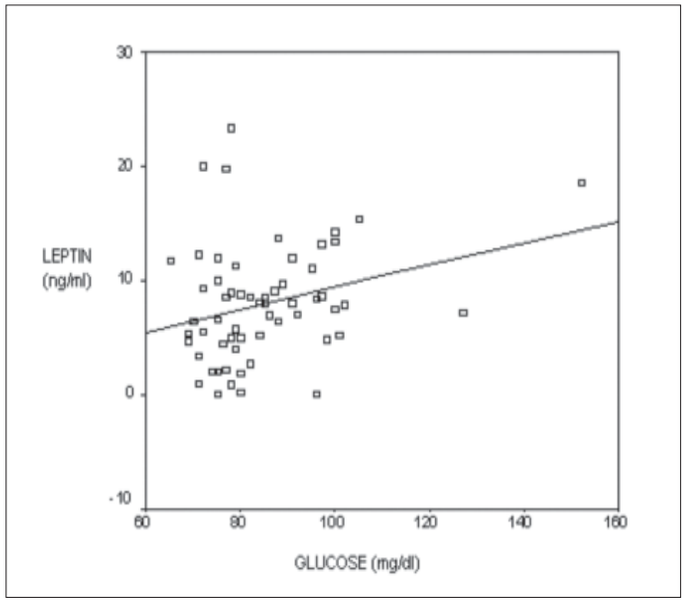

Figure 1. Relationship of blood glucose levels and leptin levels. There is a positive but weak correlation between maternal blood glucose level and leptin level ($r=0.276$, $p=0.032$)

likely a result of effects of other confounding factors in addition to insulin resistance on leptin levels. It is estimated that insulin resistance is related to increased plasma leptin levels independent of the BMI, but leptin production is not only dependent on the plasma insulin (5). Besides insulin; maternal weight gain, excessive energy, cytokines, estrogen, retinoic acid, corticosteroids and IL-1 regulate leptin have an effect (6). Lee et al. suggested that adiponectin but not leptin was associated with impaired glucose tolerance after adjusting for potential confounding factors. Low levels of adiponectin may increase the risk of glucose intolerance and type 2 diabetes (7).

In the literature it is claimed that glucose homeostasis is provided by increased insulin secretion and this is accompanied by decreased sensitivity to insulin (8). Yılmaz et al. showed that women with GDM had significantly higher levels of serum insulin and leptin concentrations compared to women with normal blood glucose levels. They did not find any correlation between serum leptin levels and insulin resistance but they found a negative correlation between leptin levels and insulin sensitivity. They suggested that leptin may contribute to the development of GDM by decreasing insulin sensitivity but not increasing insulin resistance (9). German et al. suggested that hormones such as insulin and leptin act in the hypothalamus to regulate energy balance and glucose metabolism. They showed that hypothalamic leptin action increased peripheral insulin sensitivity which primarily affects the liver by enhancing suppression of hepatic glucose production, with no change of insulin stimulated glucose utilization (10).

Wiznitzer et. al reported that there is a statistically significant positive correlation between plasma leptin levels and neonatal birthweight (11). Insulin resistance, hyperinsulinism and hyperleptinemia exist in infants of diabetic mothers and the trend of higher leptin levels in infants of diabetic mothers than in infants of non-diabetic mothers shows that leptin could be related to insulin resistance in these infants. Also glucose levels were found to be lower in large-for-gestational-age infants of both diabetic and non-diabetic mothers (12).

Ergin et al. found similarities in terms of patient characteristics between GDM patients and patients with single value abnormality as a result of OGTT test. Also, taking fasting insulin levels and insulin resistance as 2 separate criteria of analysis, patients with a single value abnormality were found to be indistinguishable from patients with GDM; both groups were significantly different from the normal oral glucose tolerance test group. It was observed that that mean insulin secretion increased from normal oral glucose tolerance test to impaired glucose tolerance and GDM (4). It was suggested that a single abnormal test value in an oral glucose tolerance test should be regarded as a pathologic finding and patients with glucose intolerance might also be treated as GDM patients (4).

Some studies in the literature suggest that plasma leptin levels in diabetic subjects are not different from non-diabetic ones and they are related to adiposity (13, 14). McGregor et al. found no difference in leptin levels between diabetic and non-diabetic subjects (13). In obese subjects, the defective leptin receptors in pancreatic β cells alter the regulation of this adipoinsular axis, leading to hyperinsulinemia and diabetes (15). Leptin is also found to be significantly high in obese subjects due to leptin resistance. The most important factor affecting the leptin level is found to be the amount of adipose tissue (16, 17).

In this study, no statistically significant correlation between maternal leptin level and BMI was observed. The maternal leptin level increases in the first and second trimester of pregnancy and it peaks around 22-27 gestational weeks (18). Leptin level correlates strongly and positively with maternal body weight and BMI in the first and second trimester of pregnancy but such a relationship cannot be revealed in the third trimester of pregnancy (19). The BMI in pregnancy is also an imprecise measure of the amount of fat stores and relates fetal weight as well as placental size, amniotic fluid and maternal fluid expansion (20).

In the literature, it is estimated that GDM patients are older and more obese than normal subjects (21, 22). The measurements of body fat percentage calculated from skinfold thickness were higher in GDM group compared to those of subjects with normal glucose levels (9). It is also shown that 60-80% of GDM patients are obese (23). In this study the BMI of patients with GDM and glucose intolerance were significantly higher than the patients with normal glucose levels, suggesting that obesity is a risk factor for the development of GDM. Also the development of GDM in the previous pregnancies and a family history of GDM are risk factors. For the early diagnosis and treatment of GDM, these risk factors should also be taken into consideration and, if a single value abnormality is detected in 100 gram OGTT in high risk patients, the physician needs to be alert for the development of GDM.

Finally, since there are controversial conclusions drawn from different studies about leptin, and the pathophysiology of hyperleptinemia is not exactly understood to this date, further studies are necessary to better evaluate the mechanism and exact relationship between leptin and insulin.

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The effects of maternal anxiety prior to amniocentesis on uterine and fetal umbilical blood flow

Amniosentez öncesi maternal anksiyetenin uterin ve fetal umblikal kan akımı üzerine etkileri

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Abstract

Objective: To investigate the mothers' anxiety levels and determine its effect on fetomaternal circulation in pregnant women undergoing genetic amniocentesis.

Material and Methods: A prospective case-control study was conducted regarding the assessment of maternal anxiety levels by means of the Spielberger State-Trait Anxiety Inventory in 60 pregnant women having genetic amniocentesis and 60 control cases having their early second trimester ultrasonographic screening, 30 minutes before and immediately after the procedure. Additionally, maternal-fetal hemodynamic changes and Doppler ultrasonographic measurements of fetoplacental circulation were recorded in both groups.

Results: The maternal anxiety state scores were found to be significantly higher in the amniocentesis group ($p<0.001$). Maternal heart rate was significantly higher in the amniocentesis group ($p<0.05$), while the fetal heart rate was significantly lower ($p<0.05$) compared to the control group. Uterine artery Doppler measurements were comparable in the two groups but umbilical artery resistance index ($p<0.05$) and S/D ratio ($p<0.05$) were significantly higher in the amniocentesis group. Regression analysis revealed that the time which elapsed from offering amniocentesis until it was performed is the main predictor of fetal umbilical artery S/D ratio measured prior to amniocentesis in the amniocentesis group ($\beta=0.66$, $p<0.001$) and maternal anxiety state scores ($\beta=0.04$, $p=0.003$) are the main predictors of fetal umbilical artery S/D ratio measured prior to amniocentesis or ultrasonography in the two groups. The education of the patient in years decreased ($\beta=-0.13$, $p=0.04$), while the amniocentesis procedure ($\beta=1.44$, $p=0.02$) and the time which elapsed in days from offering amniocentesis or ultrasonography up to its performance ($\beta=0.41$, $p=0.04$) increased the S/D ratio measured after the procedures.

Conclusion: Our study provides the evidence that maternal anxiety and its duration has effects on the fetal blood flow. Early booking and patient support may help to overcome undesired consequences of an invasive prenatal procedure.

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Key words: Maternal anxiety, genetic amniocentesis, Doppler ultrasonography

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Özet

Amaç: Amniyosentez öncesi maternal anksiyete düzeylerinin araştırılması ve genetik amniosentez uygulanacak gebelerde fetomaternal dolaşım üzerine etkilerinin değerlendirilmesi.

Gereç ve Yöntemler: Genetik amniosentez uygulanan 60 gebe kadın ve erken ikinci trimester ultrasonografik incelemesi yapılan 60 kontrol vakasına, işlemden 30 dakika önce ve hemen sonrasında maternal anksiyete seviyesinin Spielberger Durumluk ve Sürekli Anksiyete Ölçeği ile değerlendirildiği prospektif bir vaka control çalışması uygulandı. Ek olarak, maternal-fetal hemodinamik değişiklikler ve fetoplasental dolaşımın Doppler ultrasonografik ölçümleri her iki grupta kayıt edildi.

Bulgular: Maternal durumluk anksiyete skoru amniosentez grubunda belirgin olarak daha yüksek saptandı ($p<0.001$). Maternal kalp hızı amniosentez grubunda belirgin olarak daha yüksek ($p<0.05$) ve kontrol grubu ile karşılaştırıldığında fetal kalp hızı belirgin olarak daha düşük ($p<0.05$) olarak saptandı. Uterin arter Doppler ölçümleri her iki grup arasında benzer iken, umblikal arter rezistans indeks ($p<0.05$) ve S/D oranı ($p<0.05$) amniosentez grubunda belirgin olarak yüksek ölçüldü. Regresyon analizinde amniosentez önerilmesinden uygulanmasına kadar geçen sürenin amniosentez öncesi ölçülen fetal umblikal arter S/D oranının öngörülmesinde amniosentez grubu için esas belirteç olduğu ($\beta=0.66$, $p<0.001$) ve maternal durumluk anksiyete skorlarının ($\beta=0.04$, $p=0.003$) amniosentez ya da ultrasonografi öncesi ölçülen fetal umblikal arter S/D oranının öngörülmesinde her iki grup için esas belirteçler olduğu sonucuna varılmıştır. Yıl olarak hasta eğitim süresi işlem sonrası ölçülen S/D oranlarını azaltırken ($\beta=-0.13$, $p=0.04$), amniosentez işlemi ($\beta=1.44$, $p=0.02$) ve amniosentez ya da ultrasonografi önerilmesinden uygulanmasına kadar geçen süre ($\beta=0.41$, $p=0.04$) bu oranı arttırmaktadır.

Sonuç: Çalışmamızda, maternal anksiyete ve süresinin fetal kan akımı üzerine etkileri olduğu sonucuna varılmıştır. Erken döneme randevu verilmesi ve hastalara yeterli destek sağlanması bu tipte invaziv prenatal bir işlemin istenmeyen sonuçlarının engellenmesine yardımcı olacaktır.

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Anahtar kelimeler: Maternal anksiyete, Genetik amniosentez, Doppler ultrasonografi

Geliş Tarihi: 01 Şubat 2009 **Kabul Tarihi:** 10 Ağustos 2009

Introduction

The main concerns of the clinicians regarding invasive procedures such as amniocentesis are the diagnostic accuracy and a variety of fetal complications (1). Although the psychological impact of these procedures is of great importance, less extensive attention has been paid to psychological distress associated with invasive prenatal diagnostic procedures and

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various modulating parameters (2). Some authors reported a significantly higher maternal anxiety preceding genetic amniocentesis, while some others found an equal level of anxiety to that of women undergoing just a routine ultrasonographic scan (3, 4). In studies where a raised anxiety level was demonstrated to be clearly associated with amniocentesis, this anxiety was at its highest level just prior to the procedure (5). The results are difficult to compare due to differences regarding how and when anxiety is measured. It is important to quantify such concerns as amniocentesis has become a common procedure. Few studies addressed the possible negative influence of maternal anxiety due to invasive procedures on the fetoplacental circulation. Maternal stress in late pregnancy was reported to influence uteroplacental circulation and thus fetal cerebral circulation (6, 7). Abnormal uterine blood flow in anxious pregnant women is suggested to be related to adverse obstetric outcome, particularly fetal growth restriction and preeclampsia (7). It is not clear whether this relation exists earlier in pregnancy, when uterine artery resistance is usually measured and the opportunity to intervene in time to protect the fetus from any harmful effects of anxiety is greatest.

The present study was conducted to assess the maternal anxiety prior to and following genetic amniocentesis by using Spielberger's State-Trait Anxiety Inventory (STAI). Additionally, we aimed to demonstrate whether maternal distress evoked by this invasive intervention leads to altered Doppler ultrasonographic measurements of fetoplacental circulation, namely uterine arteries and fetal umbilical arteries. Consequently, emphasis has been placed on identifying potential predictors of Doppler ultrasonographic examination results.

Materials and Methods

This prospective case-control study was conducted on 60 pregnant women with singleton gestation undergoing genetic amniocentesis and 60 control cases having their routine 16-20-week ultrasonographic scan (USG). Subjects were recruited consecutively among pregnant women who were referred for either amniocentesis or routine USG between January 2004 and October 2006 at a University Hospital Department of Obstetrics and Gynecology. All subjects gave their written informed consent prior to inclusion and an approval from the local ethics committee was obtained.

Maternal anxiety levels of the subjects were measured by means of Spielberger's State-Trait Anxiety Inventory (STAI) 30 minutes before and immediately after the procedure (amniocentesis or USG). STAI is a widely used self-rating instrument for the assessment of the current (state) and inherent (trait) level of anxiety and has been extensively used in research and clinical practice (8). It is designed as a 40 item-scale; 20 items for evaluation of state anxiety and the other 20 for measurement of trait anxiety level. S-anxiety score demonstrates how anxious the patient feels in response to a defined situation while T-anxiety score points out how the individual generally feels. T-anxiety score seems to be the reflection of an inherent anxious personality that is not altered significantly secondary to a certain condition. Each item scores one to four. Total scores of STAI range between 20-80. STAI is also validated for Turkish speaking populations (9).

Hemodynamic variables and Doppler ultrasonographic measurements both preceding and following the procedure were determined. The same sonographer (EC) recorded the Doppler flow velocity waveforms using a Siemens versaplus ultrasonograhy machine with 3.5-7 MHz transabdominal probe. Colour Doppler imaging was used to identify bilateral uterine and umbilical arteries after placing the Doppler gate in an optimal manner over the defined vessels. The Doppler gate was located over the entire diameter of the uterine artery 1 cm distal to the crossover of external iliac artery and main uterine artery. Measurements with an angle of insonation $<60^{\circ}$ were accepted. Pulsatility index and resistance index of flow velocity waveforms were calculated from five consecutive uniform waveforms and a diastolic notch was looked for. Since the insonation angle could not be reliably determined due to the tortuous nature of the umbilical artery, the highest possible Doppler shifts were recorded. Maternal and fetal heart rates, Doppler ultasonography measurements of bilateral uterine arteries and umbilical arteries were determined in all study subjects before and just after the genetic amniocentesis. The same recordings were performed in control cases before and after the ultrasonographic scan.

Additionally, sociodemographic and clinical parameters such as age, education, employment, tobacco use, parity, obstetric history and gestational age were recorded. The couples were offered amniocentesis and this was performed whenever the couples decided to have it.

Pearson correlation analysis was performed to find out the relation between anxiety scores and hemodynamic variables measured prior to the amniocentesis or ultrasonography procedures such as heart beat and Doppler measurements. A regression model was built to determine possible predictors of fetal umbilical artery S/D ratio measured prior to the procedures (amniocentesis in the case group and ultrasonography in the control group). A model was built using backward linear logistic regression analysis where the group was included as a dichotomous variable (women in the amniocentesis group or control group), together with the presence or absence of tobacco use, education of the women in years, age of women in years, time elapsed in days from offering amniocentesis until performance, state anxiety and trait anxiety scores. The resulting β coefficient indicates the amount of change in the dependent variable which is the umbilical artery S/D ratio measured prior to the procedures. The β coefficient indicates the amount of change in the dependent variable for a one unit change in the independent variable, controlling for the variables in the model. The values of the β coefficient are in units of the independent variable. It is useful for assessing the practical magnitude of the effect of an independent variable, because variables can be statistically significant without having a substantially practical effect. In order to evaluate the effect of needle insertion during

the amniocentesis we also built a model using the same independent variables in addition to the localization of the placenta; anterior, posterior and lateral localizations.

The statistical analysis of the data was performed using the Statistical Package for Social Sciences for Windows (SPSS, Chicago, IL, USA). Results were reported as mean ± standard deviation or numbers and percentages. Differences between the groups were assessed using chi-square test or Fisher's exact test for categorical data whenever appropriate. Independent samples t test was used in order to detect the differences of continuous variables between the groups and paired samples t- test was used to assess within group changes of continuous variables measured prior to or after the procedures. Probability (p) <0.05 was considered statistically significant for all comparisons.

Results

Amniocentesis was performed for advanced maternal age in 14 (23.3%) women and for positive triple screen risk <1/ 250 in 46 (76.7%) women. In the amniocentesis group, the placenta was attached to the anterior uterine wall in 37 (61%) women, posterior wall in 17 (28.3%) and right lateral wall in 6 (10%). None of the fetuses had cardiac anomalies and two cases were diagnosed as trisomy 21.Demographic variables of the couples were similar in the two groups in terms of age, education, employment, tobacco use, parity, previous abortion, curettage and gestational age (Table 1).

The mean time which elapsed from offering until performing amniocentesis was 2.9±1.5 days (Range:0-7 days), and the time which elapsed from offering until performing detailed second trimester ultrasonography was 1.1±0.7 days (Range: 0-3 days, $p<0.001$). Patient state anxiety scores were significantly higher in the amniocentesis group (48.9±11.8) compared to the control group (33.5±6.5, $p<0.001$) ,while patients' trait anxiety was similar in the two groups (46.4±7.3, 45±5.1, $p=0.2$ respectively). In the amniocentesis group the state anxiety scores of patients with positive triple screen test and advanced maternal age as indications of amniocentesis were similar ($p=0.2$).

In the amniocentesis group the mean maternal pulse rate, fetal umbilical artery resistance index and systole/diastole were significantly higher than the control group, while the mean fetal heart rate was significantly lower (Table 2). After the procedures (amniocentesis for the study group, ultrasonography for the controls) the mean maternal pulse rate decreased significantly within the groups whereas the mean fetal heart rate increased only in the amniocentesis group (Table 2). There was a trend for increase in umbilical artery S/D due to amniocentesis with a borderline significance. The state and trait anxiety scores did not correlate with any of the maternal and fetal Doppler measurements and heart beat in the control group, while the state anxiety score correlated positively with the fetal umbilical artery S/D ratio, prior to ($r=0.32$, $p=0.01$) and after ($r=0.35$, $p=0.007$) amniocentesis and negatively correlated with the fetal heart beat after the amniocentesis ($r=-0.26$, $p=0.04$)

A regression model was built to determine possible predictors of fetal umbilical artery S/D ratio. The ages of the couples, anxiety scores of patients and husbands, gestational age, maternal serum alpha fetoprotein levels, nulliparity, the presence of prior abortions or curettages, the time elapsed since amniocentesis was offered up to performance, couples' education years and tobacco use were all included in the model. Regression analysis revealed that the time elapsing in days from offering amniocentesis or ultrasonography until performance ($\beta=0.66$, $p<0.001$) and every increase in maternal state anxiety scores ($\beta=0.04$, $p=0.003$) are the main predictors of fetal umbilical artery S/D ratio measured prior to the procedures (amniocentesis in the case group and ultrasonography in the control group). When independent variables that predict umbilical artery S/D ratio measured after the procedures were evaluated the education of the patient in years decreased ($\beta=-0.13$, $p=0.04$), while amniocentesis procedure ($\beta=1.44$, $p=0.02$) and the time elapsing in days from offering amniocentesis or ultrasonography until performance ($\beta=0.41$, $p=0.04$) increased the S/D ratio.

There was no case of absent end-diastolic flow. Two cases had umbilical artery PI>2SD in the control group and also in

Table 1. Selected couple variables according to the groups. Data are presented as mean ± standard deviation or numbers (percentages)

Variable	Amniocentesis Group (n=60)	Control Group (n=60)	P
Maternal age (year)	31.2±6.6	29.7±6.2	0.2*
Patient Education (year)	7.9±3.6	8.3±3.7	0.5*
Women unemployed	38 (63)	42 (70)	0.4**
Tobacco use	5 (8.3)	6 (10)	0.7**
Nulliparous	34 (56.7)	40 (66.7)	0.2**
Previous abortion ≥1	13 (21.7)	8 (13.3)	0.2**
Previous d&c≥ 1	7 (11.7)	8 (13.3)	0.7**
Gestational age (weeks)	18.7±1.6	18.9±1.4	0.6*

*Not significantly different ($p>0.05$), independent samples t-test
**Not significantly different, ($p>0.05$), chi-square test

Table 2. Maternal fetal hemodynamic changes and Doppler measurements before and after amniocentesis or before and after ultrasound examination in the control group. The data is given as means and 95% confidence intervals of the mean in parenthesis

Variable	Amniocentesis Group (n=60)		p	Control Group (n=60)		p
	Before	After		Before	After	
Maternal heart rate (beats/min)	95.8 (91.2-100)[a]	92.8 (89-96.2)[b]	0.02*	88.3 (86-90)	82.6 (80.6-84.5)	<0.001*
Fetal heart rate (beats/min)	147 (145.7-150.2)[a]	151 (148.8-154.4)	0.004*	152 (150.5-154.5)	152 (150-153.9)	0.5
Umblical artery PI	1.3 (1.19-1.44)	1.29 (1.22-1.35)[b]	0.6	1.2 (1.1-1.3)	1.17 (1.13-1.22)	0.2
Umblical artery RI	0.75 (0-73-0.78)[a]	0.77 (0.74-0.80)[b]	0.3	0.69 (0.68-0.70)	0.69 (0.68-0.71)	0.8
Umblical artery S/D	4.9 (4.2-5.6)a	5.7 (4.7-6.8)[b]	0.05	3.4 (3.2-3.6)	3.5 (3.3-3.7)	0.1
Right uterine artery PI	1.1 (0.98-1.21)	1.09 (0.99-1.19)	0.8	1 (0.96-1.13)	1.05 (0.96-1.13)	0.2
Right uterine artery RI	0.63 (0.59-0.66)	0.63 (0.60-0.66	0.7	0.60 (0.58-0.63)	0.60 (0.58-0.62)	0.5
Right uterine artery S/D	3.4 (2.6-4.1)	3.2 (2.7-3.78)	0.6	2.7 (2.5-2.9)	2.7 (2.55-2.90)	0.5
Left uterine artery PI	1.1 (1-1.2)	1.3 (1.12-1.47)	0.3	1.2 (1.09-1.45)	1.26 (1.09-1.44)	0.3
Left uterine artery RI	0.66 (0.60-0.72)	0.66 (0.63-0.68)	0.3	0.64 (0.61-0.67)	0.66 (0.63-0.69)	0.1
Left uterine artery S/D	3.2 (2.8-3.5)	3.2 (2.94-3.6)	0.8	3.2 (2.8-3.6)	3.5 (3.19-3.87)	0.1

PI: Pulsatility Index, RI: Resistance Index, S/D: Systole/diastole
*Significantly different (p<0.05), paired samples t-test
[a]Significantly different than the corresponding before measurement in the control group (p<0.05), independent samples t-test
[b]Significantly different than the corresponding after measurement in the control group (p<0.05), independent samples t-test

the amniocentesis group prior to and after ultrasonography and amniocentesis. IUGR developed in 8 (13.3%) cases in the amniocentesis group and 5 (8.3%) cases in the control group (p=0.3). Preeclampsia developed in 6 (10%) and 4 (6.7%) cases respectively (p=0.5). When umbilical artery S/D values were compared, no difference was found in cases diagnosed to have IUGR or not (p=0.3) and preeclampsia or not (p=0.09) later during pregnancy.

Discussion

Assessment of the psychological consequences of invasive prenatal diagnostic procedures is still a neglected area of research. We demonstrated that patient state anxiety scores were significantly raised due to amniocentesis in accordance with most of the previous studies (4, 5, 10-12). Although there are a number of studies reporting acute fetal hemodynamic changes secondary to anxiety associated with amniocentesis, such changes were not found to have a significant clinical relevance (3, 5, 13, 14). On the other hand, the newborns of the stressed or anxious women are reported to be small for gestational age and have a tendency to premature birth (15-17). Some experimental studies provided confirmation of those findings as they also indicated that birth weight was reduced and fetal behaviour was found to be influenced by maternal anxiety, possibly through a variety of hormonal mechanisms (18-20).

Teixeria and colleagues concluded that pregnant women with high state anxiety scores at STAI interviewed at their 28-32 weeks of gestation appeared to have significantly abnormal patterns of blood flow through uterine arteries with elevated resistance index values and faster maternal heart rates, although not significant (7). Impaired uterine artery blood flow is considered to be mostly due to a chronic phenomenon such as defective trophoblastic invasion in early pregnancy which is known to be predictive of preeclampsia and intrauterine fetal growth restriction. However short term changes such as transiently altered hormonal concentrations, invasive or noninvasive therapeutic interventions and exercise may probably lead to uterine artery blood flow changes (21-24). Likewise noradrenaline infusion is shown to diminish uterine blood flow in a number of studies, and in addition, reproductive tissues are found to be more sensitive to vasoconstrictive effects of noradrenaline than are other organs (21, 25). Based on these recent findings, elevated noradrenaline concentrations in women with high state anxiety levels suggest that the hypothalamus-hypophysis-adrenal axis may be responsible for abnormal uterine artery blood flow patterns (26).

It is uncertain whether altered uterine artery blood flow can be observed earlier in pregnancy. Kent and colleagues investigated the association between maternal anxiety using Hospital Anxiety Depression Scale (HADS) and uterine artery waveform patterns at 20 weeks of gestation and concluded that there was no significant association between maternal anxiety scores and uterine artery Doppler indices (13). Different population samples and the use of different questionnaires to assess anxiety levels and the time of gestation when the study was conducted

may explain why those studies achieved such different results.
In our study, uterine artery indices did not indicate significant changes when compared with the controls, and maternal anxiety was not found to be correlated with any of the uterine artery Doppler indices. On the other hand, mean maternal heart rate, fetal umbilical artery resistance index and umbilical artery systole/diastole were demonstrated to be significantly higher, while fetal heart rate was significantly lower in the amniocentesis group. Additionally, maternal anxiety scores were positively correlated with umbilical artery S/D before and after amniocentesis, while anxiety scores were significantly correlated inversely with fetal heart rate after the procedure. We used the same anxiety scale as Texieria et al, who found an association between anxiety and uterine artery Doppler measurements, but the gestational weeks of our study populations were earlier (7). We performed the study at similar gestational weeks with Kent and colleagues who found no association between anxiety and uterine artery Doppler, as we did (13).
Sjöström and colleagues demonstrated that women with higher trait anxiety scores had higher umbilical artery pulsatility index and lower middle cerebral artery (MCA) pulsatility index values at 37-40 weeks of gestation (6). Those measurements indicated increased resistance in the placental vascular bed and decreased vascular resistance in the fetal brain, leading to redistribution of fetal blood flow with increased cerebral blood flow, called the brain sparing effect. Again, humoral factors such as stress hormones, namely cortisol and noradrenaline, were suggested to be responsible for altered fetal hemodynamics in women who tend to have high trait anxiety scores (27).
In our study, umbilical artery RI and S/D measurements were significantly higher in the amniocentesis group in comparison with the controls and there was a trend for an increase in umbilical artery S/D due to amniocentesis, although not statistically significant. The state anxiety score correlated positively with the fetal umbilical artery S/D ratio before and after amniocentesis and the maternal state anxiety score was one of the main predictors of fetal umbilical artery S/D ratio in the amniocentesis group who displayed higher anxiety. All the se findings at the early second trimester stage were in accordance with most of the findings of Sjöström (6).
Our findings point to an increased anxiety response in the mother before an invasive procedure, which has prominent effects on fetal umbilical artery blood flow as the time to performance of amniocentesis since offered increases. Another interesting finding is that the normal fetal heart beat increase response after amniocentesis is reversed in mothers with high anxiety scores. These findings suggest that increased maternal anxiety may act through decreasing placental blood flow which causes an uncompensated response by the fetus in an acute stress setting caused by the amniocentesis procedure.
We conclude that high maternal anxiety may have profound effects on fetal umbilical artery blood flow as the time of onset increases. Counseling and immediate scheduling for amniocentesis may decrease the maternal stress response to an invasive procedure.

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Thyroid hormones in pregnancy and preeclampsia

Gebelikte ve preeklampside tiroid hormonları

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Abstract

Objective: There is a state of hypothyroxinemia in normal pregnancy and in preeclampsia, when biochemically raised TSH occurs. Identification of changes in thyroid hormones in preeclampsia might be of help in preventing the occurrence of preeclampsia.

Material and Methods: The present study was carried out in a hundred women with preeclampsia, 100 age- and parity matched normotensive pregnant women and 50 age-matched healthy non-pregnant women. Thyroid hormones [total T3,T4 and TSH], serum albumin and uric acid were analyzed in these subjects.

Results: Women with preeclampsia had higher TT3, TT4 levels as compared to non pregnant women [$p<0.05$], but preeclamptic TT3,TT4 levels were lower compared to normotensive pregnant women [$p<0.05$, $p<0.01$]. TSH levels were higher in both preeclamptic & normotensive pregnant women compared to nonpregnant women [$p<0.001$] and levels were lower in normotensive pregnant women as compared to nonpregnant women [$p<0.001$]. A significant negative correlation was observed between birth weight and TSH levels [$r=-0.296$, $p<0.001$] serum albumin and TSH levels in preeclamptic women [$r=-0.781$, $p<0.01$]. Also, a significant positive correlation was observed between birth weight and albumin [$r=0.298$, $p<0.001$]; birth weight and serum uric acid levels [$r=-0.46$, $p<0.01$], and serum albumin and TT3 & TT4 levels [$r=0.409$ & $r=0.35$, $p<0.01$ respectively].

Conclusion: These findings indicate that there is state of hypothyroxinemia in normal pregnancy and in preeclampsia. Identification of changes in thyroid hormones in preeclampsia might be of help in preventing the occurrence of preeclampsia.

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Key words: Preeclampsia, thyroid, pregnancy, thyroxine, uric acid, albumin

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Özet

Amaç: Gebelikte ve preeklampside TSH yükselmesi görüldüğünde ortaya çıkan bir hipotiroksinemi durumu vardır. Gebelikte tiroid hormonlarının değişiminin saptanması preeklampsi gelişiminin engellenmesine yardım edebilir.

Gereç ve Yöntemler: Bu çalışma preeklamptik 100 gebe ve yaş eşleştirmesi yapılmış tansiyonu normal 100 gebe ve 50 gebe olmayan kadın karşılaştırılarak yapıldı. Tiroid hormonlar [total T_3,T_4 and TSH], serum albumin and urik asid düzeyleri analiz edildi.

Results: Preeklamptik hastalar gebe olmayanlar ile karşılaştırıldığında daha yüksek TT_3, TT_4 düzeylerine sahiptiler [$p<0.05$], fakat preeklamptiklerin TT_3,TT_4 düzeyleri normotansif gebelerinkinden daha düşük idi [$p<0.05$, $p<0.01$]. TSH düzeyleri preeklamptiklerde ve normal gebelerde gebe olmayan gruba göre daha yüksek idi [$p<0.001$], fakat TSH düzeyleri normotansif gebelerde gebe olmayanlara göre daha düşük idi [$p<0.001$]. Preeklamptik gebelerde doğum kilosu ile TSH arasında [$r=-0.296$, $p<0.001$] ve serum albumini ile TSH arasında ($r=-0.781$, $p<0.01$] anlamlı bir negatif korelasyon saptandı. Ayrıca doğum kilosu ile serum albumini arasında [$r=0.298$, $p<0.001$]; doğum kilosu ile serum ürik asid düzeyleri arasında ($r=-0.46$, $p<0.01$], ve serum albumin ile TT_3 ve TT_4 arasında [$r=0.409$ & $r=0.35$, $p<0.01$) anlamlı bir pozitif korelasyon saptandı.

Sonuç: Bu bulgular normal gebelikte ve preeklampside bir hipotiroksineminin varlığını teyit eder. Gebelikte tiroid hormonlarındaki değişimlerin saptanması preeklampsi gelişiminin öngörüsünde fayda sağlayabilir. (J Turkish-German Gynecol Assoc 2009; 10: 168-71)

Anahtar kelimeler: Preeklampsi, tiroid, gebelik, tiroksin, ürik asid, albumin

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Introduction

During normal pregnancy, changes in thyroid function are well-documented, but information about thyroid function in complicated pregnancy is scanty. During pregnancy, there is an increased thyroid demand and increased iodine uptake and synthesis of thyroid hormones. Estrogen induces a rise in serum TBG and the placenta releases several thyroid stimulatory factors in excess e.g. hCG. Alpha subunit of hCG is identical to that of TSH and has weak thyrotropic activity (1). Hypothyroidism has been listed as one of the causes of high blood pressure (2). In preeclampsia, there is failure of estrogen production due to placental dysfunction resulting in lowering of TBG, TT_3, TT_4 along with growth retardation of the fetus (3). Increasing evidence suggests that oxidative stress and altered endothelial cell function may have a role in preeclampsia (4-6). Also, oxidative stress has been proposed as another contributing source of the hyperuricemia noted in preeclampsia apart from renal dysfunction (8). In preeclampsia, an increase in the superoxide anion, which

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may inactivate NO, leading to reduced relaxation and increased vasoconstriction (6, 7). Experimental studies have indicated that release of NO is altered in hypothyroidism and the resulting endothelial cell dysfunction might be a pathogenetic mechanism for hypothyroidism in preeclampsia (9).

The present study was undertaken to evaluate thyroid hormones in preeclamptic women as compared to normotensive pregnant women and healthy non pregnant controls.

Methods

The present study was carried out on 100 women with preeclampsia admitted to or attending the Outpatient Department of Obstetrics and Gynecology in Pt. BDS PGIMS, Rohtak, between August 2005 to October 2006. Hundred age & party-matched normotensive pregnant women and fifty age-matched, healthy non-pregnant women served as controls. Inclusion criteria of preeclampsia were blood pressure of ≥ 140/90 mmHg on at least two occasions, six hours apart and/or proteinuia. Exclusion criteria were: history of chronic hypertension, any renal disease, any metabolic disorder or medication known to affect thyroid function. The preeclampsia group was sub-divided into two groups namely, mild preeclampsia (n=50) and severe preeclampsia (n=50). Study samples were drawn before starting any treatment and serum was separated for assay for thyroid hormones (T_3, T_4,TSH) by radioimmunoassay (RIA) (10), albumin and uric acid (8). The data so obtained was analyzed statistically and student's t-test and regression analysis was carried out.

Results

Table 1 shows clinical characteristics of women in the study and control groups. There was a significant difference in TT_3(total T_3)levels in normotensive pregnancy as compared to healthy non-pregnant women ($p < 0.001$, Table 2). Women with preeclampsia had higher TT_3 levels as compared to non pregnant women ($p < 0.05$), but, the TT_3 levels were slightly lower in preeclamptic women as compared to normotensive pregnant women ($p > 0.05$).

TT_4 (total T_4) levels were raised significantly in both preeclamptic and normotensive pregnant women as compared to non-pregnant women ($p < 0.01$ and $p < 0.001$ respectively). TT_4 levels were significantly higher in normotensive women as compared to preeclamptic women ($p < 0.01$).

TSH levels were higher in preeclamptic women as compared to nonpregnant control ($p < 0.001$)and they were lowered significantly in normotensive pregnant women as compared to non-pregnant women ($p < 0.001$, Table 2). No significant influence of age and parity on thyroid hormonal levels could be observed in any of the three groups. A significantly higher number (78%) in the severe preeclampsia group had raised TSH levels than in the mild preeclampsia group (35%) ($p < 0.001$). On the other

Table 1. Clinical Characteristics (mean +SD)

	Preeclampsia		Normotensive Non Pregnant		
	Total	Mild	Severe		
Age (years)	23.07 + 2.75	23.08+ 3.01	23.01+2.28	23.04+ 2.17	23.50 + 2.01
Gestational age (weeks)	37.77 + 1.7	38.67+ 0.81	36.87 + 1.90	39.09 + 1.3	-
Birth weight (kg)	2.32 + 0.43	1.55 + 0.22	2.09 + 0.46	2.74 + 0.24	-
Placental weight(g)	438.25+56.90	472.5 + 34.71	404 + 54.24	502.50 + 50.81	-
Serum albumin(g/l)	3.38+0.2	3.52 + 0.19	3.24 + 0.22	-	-
Serum uric acid (mg/dl)	6.54+ 1.15	5.42 + 0.79	7.66 + 1.51	2.31+0.81	2.02 + 0.71

Table 2. Thyroid hormone levels in various groups (mean + SD)

	Preeclampsia		Normotensive Non Pregnant pregnant		
	Total (n=100)	Mild (n=50)	Severe (n=50)	(n=100)	(n=50)
TT_3 (ng/dl)	128.23^{+} ± 36.53	136.82 ± 36.82	119.64 ± 34.48^{b}	134 ± 34.56*	115.88 ± 22.89
TT_4 (μg/dl)	10.12$^{++,a}$ ± 2.64	10.84 ± 2.53	9.39 ± 2.57	12.14 ± 2.49*	7.9 ± 1.40
TSH (μIU/ml)	4.52 $^{++,a}$ ± 2.30	3.42 ± 1.61	5.63 ± 2.37	2 ± 1.18	*2.67 ± 1.24

$^{+}$compared to non pregnant $p < 0.05$
$^{++}$compared to non pregnant $p < 0.001$
preeclampsia
i. compared with mild $p < 0.05$
ii. compared with mild $p < 0.01$
iii.compared with mild $p < 0.001$
a compared to normotensive pregnant $p < 0.01$
* compared to normotensive pregnant $p < 0.001$

hand, the level of TT_3 and TT_4 was not statistically significant amongst these two subgroups.

Severe preeclamptic women had higher uric acid levels and low serum albumin levels as compared to mild preeclamptic ones ($p<0.001$ in both cases, Table 2). A significant negative correlation was observed between birth weight and TSH levels in preeclamptic women ($r=-0.296$, $p<0.001$), and significant positive correlation between birth weight and albumin levels ($r=0.298$, $p<0.001$). Also, a highly significant correlation of birth weight with serum uric acid levels ($r=0.46$, $p<0.01$) was noted in preeclampsia.

Serum uric acid levels showed a positive correlation with TSH levels ($r=0.507$, $p<0.01$) and a negative correlation with TT_4 levels ($r=-0.204$, $p<0.05$) in preeclampsia. No significant correlation could be observed between serum uric acid levels and TT_3 levels in preeclampsia.

A highly significant positive correlation was observed between serum albumin and TT_3 & TT_4 levels in preeclampsia ($r=0.409$ & $r=0.356$ respectively, $p<0.01$), while there was a significantly negative correlation between serum albumin levels and TSH levels ($r=-0.781$, $p<0.01$) in preeclampsia (fig 1). No significant correlation was observed between birth weight and thyroid hormone levels in normotensive controls.

Conclusion

In the present study, TT_3 levels were significantly higher in normotensive pregnant women as compared to nonpregnant women ($p<0.001$). The TT_3 levels were slightly lower in preeclampsia as compared to normotensive pregnant patients ($p>0.05$, table 2). This fall was observed only in the severe form of preeclampsia and not in the mild form of preeclampsia. These findings are in agreement with those reported in the literature (11).

On the other hand, lower TT_3 levels in preeclampsia as compared to normotensive pregnant have been reported in the literature (12-14).

During preeclampsia, there is involvement of the liver and kidney that may lead to decreased peripheral conversion of T_4 to T_3, hence decreasing the T_3 levels. Also, "low T_3 syndrome" has been reported in preeclampsia (13-15). In addition to this, there is loss of proteins and protein-bound hormones in the urine in preeclampsia which may also contribute to low TT_3 levels in preeclampsia as compared to controls (12). Also, it may be a reflection of an inability to compensate for increased fetal demand, increased thyroid break-down by the placenta and transfer of maternal T_4 to fetus. TT_4 levels were significantly higher during preeclampsia and normotensive pregnant women as compared to non pregnant women ($p<0.001$, Table 2) and the levels were lower in preeclamptic women when compared with normotensive pregnant women ($p<0.01$). Conflicting reports are available in the literature regarding TT_4 levels (9-12). A few reports have observed lower TT_4 levels in preeclampsia (11, 12) while others have reported higher TT_4 levels (14) . This may again be due to high TSH (Table 2)and low free thyroxine index along with concurrent loss of proteins in preeclampsia.

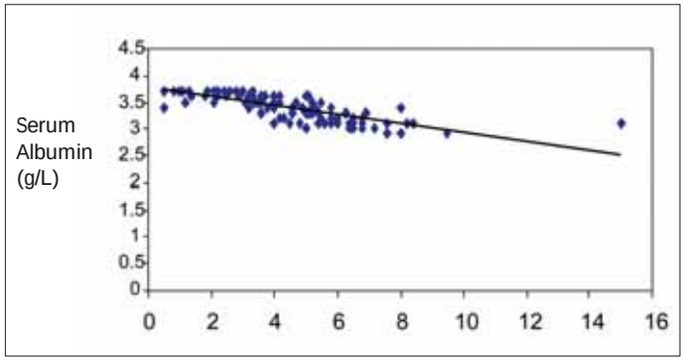

Figure 1. Correlation between tsh and serum albumin in preeclampsia group

In the present study, high TSH levels were observed in preeclamptic women as compared to controls (Table 2). Our findings lend support to earlier reports where preeclamptic women were observed to have a higher incidence of biochemical hypothyroidism compared with normotensive pregnant women (11, 12, 15, 17). In contrast, Qublan et al reported no significant difference in TSH levels between these two groups (18).

Pregnancy is generally associated with hypothyroxinemia and the degree of hypothyroxinemia might reflect the severity of preeclampsia. In the present study, a highly significant negative correlation between birth weight and TSH levels was observed in preeclampsia ($r=0.296$, $p<0.01$). However, no correlation between birth weight and thyroid hormones in normotensive pregnant women was observed. In the present study, preeclamptic women with lower birth-weight babies had a higher degree of hypothyroxinemia and higher TSH levels and this may be explained by placental dysfunction in preeclamptic patients. Placental dysfunction may cause failure in estrogen production, leading to a decrease in TBG, TT_3 and TT_4 levels with simultaneous growth failure of the fetus (12). TBG is reported to be lower in unsuccessful pregnancies indicating placental function deterioration in pregnancy (13). Also, low TBG, TT_4 and TT_3 levels have been reported in preeclampsia, which was attributed to placental dysfunction in preelamptic women (3).

In the present study, a significant inverse correlation of serum uric acid with TT_4 levels in preeclampsia ($r=-0.204$, $p<0.05$)and a positive correlation with TSH levels ($r=0.507$, $p<0.01$) was observed, suggesting that a state of biochemical hypothyroidism is related to preeclampsia. However, no correlation was observed between uric acid levels and TT_3 levels ($r=0.119$, $p>0.05$). Our findings are in agreement with those reported in the literature (11).

Albumin levels also showed a positive correlation with both TT_3 & TT_4 levels ($r=0.409$ & $r=0.356$ respectively, $p<0.01$) and a negative correlation with TSH levels ($r=0.781$, $p<0.01$) in preeclampsia. Our studies are in agreement with other reports (11, 15). Reduced serum albumin and hyperuricemia observed in preeclampsia along with their significant correlation reflects the severity of fetal involvement in preeclampsia with TT_4,TT_3 & TSH, while hyperuricemia reflects the severity of fetal involvement in preeclampsia, and serum albumin was reduced due to proteinuria occurring in preeclampsia. In the present study, a significant positive correlation of birth weight with albumin levels

(r=0.298), p<0.01)and negative correlation of birth weight with serum uric acid levels was observed in preeclampsia (r=-0.46, p< 0.01). Many workers have observed low TT_4, TT_3 levels in women with preeclampsia who had small -for -gestational age babies as compared to women with appropriate- for -gestational age infants, thus reflecting the severity of preeclampsia (11, 17).
Raised TSH levels in preeclampsia with a concomitant decrease in TT_3 & TT_4 levels have been correlated with the severity of preeclampsia and high levels of endothelin. Since endothelial dysfunction has been implicated in widespread vasospasm and poor perfusion of many organs, including the fetoplacental unit in preeclampsia, nitric oxide has been implicated in the pathophysiologic mechanisms of preeclampsia (18). Experimental studies have shown that release of nitric oxide is altered in hypothyroidism in animals (19). Altered release of nitric oxide in endothelial cell dysfunction might be a pathogenetic mechanism for hypothyroidism in preeclampsia (9, 18, 19).
There is a state of hyperthyroxinemia in normal pregnancy and in preeclampsia, a biochemical hypothyroidism (raised TSH) occurs. Thyroid hormonal levels correlated with the severity and outcome of preeclampsia. Thyroid hormones are known to regulate neurodevelopment, probably from early fetal life onwards and may be responsible for preterm birth in preeclampsia. Large scale multicentic studies may discover the association and mechanism of thyroid abnormality in preeclamptic women. Identification of thyroid hormones and thyroid screening during pregnancy might be of help in preventing the occurrence and instituting timely intervention and appropriate measures in terms of possible thyroid hormone administration in preterm infants in future. The changes in thyroid hormones in preeclampsia merit further studies in order to assess the severity of the conditions.

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Ruptured tubal hydatidiform mole

Tubal mol hidatiform rüptürü

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Abstract

Objective: Ruptured ectopic gestation is a life threatening medical emergency especially in developing countries. However, the occurrence of hydatidiform mole in ruptured tubal pregnancy is uncommon.

Material and Methods: A consecutive analysis of patients with hydatidiform mole in ruptured tubal gestation over a 9-year period in a tertiary hospital.

Results: Of a total of 101 females with ectopic gestations, only five had ruptured tubal hydatidiform mole. The ages ranged from 20-37years and they all presented with acute abdominal symptoms which necessitated emergency surgical intervention. Intra-operative findings revealed ruptured/ leaking tubal gestation. The excised tissue specimens showed hydatidiform mole characterized by circumferential trophoblastic proliferation, hydropic degeneration and stromal karyorrhexis. Patients' serial HCG levels were monitored before discharge.

Conclusion: Ruptured tubal hydatidiform mole is uncommon and strict histologic criteria are important in diagnosis. Serial HCG levels must be monitored in individual patients to forestall development of malignant trophoblastic disease.

(J Turkish-German Gynecol Assoc 2009; 10: 172-4)

Key words: Choriocarcinoma, Hydatidiform mole, Tubal pregnancy

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Özet

Amaç: Ektopik gebeliğin rüptürü özellikle gelişmekte olan ülkelerde hayatı tehtid eden bir durum olmaya devam etmektedir. Rüptüre ektopik gebeliklerde mol hidatiform gelişimi nadirdir.

Gereç ve Yöntemler: Tersiyer bir merkezde 9 yıl boyunca meydana gelen rüptüre ektopik gebelikler arasında mol gebeliklerin araştırılması.

Bulgular: Ektopik gebeliği olan 101 gebenin sadece 5 tanesinde rüptüre mol hidatiforma rastlandı. Yaşları 20-37 arasında değişen bu vakaların tümü cerrahi girişim gerektiren bir acil durum ile hastaneye müracaat etmişlerdi. Ameliyat bulguları rüptüre ektopik gebelik ile uyumlu idi. Eksize edilen dokularda hidatiform mol karakterleri olan çevresel trofoblastik proliferasyon, hidropik dejenerasyon ve stromal karyoreksiz içeriyordu. Hastalara operasyon sonrası seri beta hCG takibi yapıldı.

Sonuç: Rüptüre Mol hidatiform yaygın değildir. Tanı için katı histopatolojik kriterler gereklidir. Seri beta hCG ölçümü malign potansiyeli dışlamak için yapılmalıdır.

(J Turkish-German Gynecol Assoc 2009; 10: 172-4)

Anahtar kelimeler: Koryokarsinoma, mol hidatiform, tubal gebelik

Geliş Tarihi: 23 Mart 2009 **Kabul Tarihi:** 01 Temmuz 2009

Introduction

Ectopic gestation is a common phenomenon with an incidence rate of 4.5/1000 to 16.8/1000 pregnancies and the fallopian tube is the commonest location in 1/200 to 1/300 pregnancie. (1-3). The rupture of an ectopic tubal gestation is a life threatening medical emergency and an important cause of maternal mortality in developing countries (4-7) Molar gestation is an uncommon complication of pregnancy characterized by the presence of abnormal trophoblastic tissue proliferation and can be differentiated into partial, complete and invasive types (8, 9) Its occurrence in ruptured tubal pregnancy is a rarity and less than fifty cases have been reported in the literature (10,11) We present five females with ruptured tubal hydatidiform mole.

Materials and Method

All consecutive patients diagnosed with tubal gestation and hydatidiform mole from January 2000 to December 2008 in the Pathology laboratory of a tertiary hospital were analyzed. A total of one hundred and one (101) ectopic gestations were seen. All were located in the fallopian tube except for two cases, which occurred in the ovary. There were one hundred and fifty two (152) diagnosed gestational trophoblastic disease cases. Of these, one hundred and nine (109) had hydatidiform mole comprising the complete, partial and invasive types while choriocarcinoma accounted for the remaining forty-three (43) cases. Patients' tissue biopsies from salpingectomy or endometrial curettage were fixed in 10% formalin and processed with paraffin wax. Histology slides stained with haematoxylin and eosin were studied.

The diagnostic criteria of tubal pregnancy and rupture were the histological presence of chorionic villi, expanded eodematous tubal wall and inflammatory cells. Tubal hydatidiform mole was diagnosed by the presence of chorionic villi with circumferential trophoblastic hyperplasia, hydropic swelling and absence of foetal vessels and parts (11). Only cases which fulfilled these diagnostic criteria of ruptured tubal hyda-

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tidiform mole were presented. Human chorionic gonadotropin (HCG) levels were monitored weekly for 3 consecutive weeks, then monthly for 6 consecutive months. The monthly monitoring was done on an out- patient basis. Statistical analysis was done using SAS/STAT.

Result

One hundred and one (101) patients with ectopic gestation and one hundred and fifty-two (152) gestational trophoblastic disease (GTD) cases were seen in the department during the study period. All the ectopics occurred in the fallopian tubes except for two cases in the ovary. Of the GTDs, 109 were hydatidiform mole comprising 29 complete, 28 partial, 2 invasive and 50 unclassified moles. The remaining 43 GTDs were choriocarcinoma cases.
Only five patients aged 20, 28, 33, 35 and 37years fulfilled the diagnostic criteria of tubal hydatidiform mole. Four of the patients presented with acute abdominal symptoms of pain associated with tenderness, vomiting, vaginal bleeding and varying periods of amenorrhoea which necessitated emergency surgical intervention. The fifth patient who presented with menorrhagia and a 14-week uterine size was diagnosed as a case of uterine fibroid. Three were nulliparous and none of the patients gave a history of previous abortion.
Intra-operative findings revealed ruptured and or leaking tubal gestation in all five and multiple intramural uterine fibroids in the fifth patient. All five patients had salpingectomy by laparotomy and the fifth also had myomectomy.
The excised tissue specimens sent for histology showed a ruptured and expanded tubal wall, chorionic villi of varying sizes exhibiting circumferential and polar trophoblastic proliferation, hydropic degeneration and stromal karyohexis (Fig. 1).
Serial urinary human chorionic gonadotropin (bHCG) levels of patients were monitored weekly for 3 weeks before discharge. Three of the patients were lost to follow up within three months after hospital discharge, while two were followed up for a year without recurrence or elevated HCG level.

Discussion

Hydatidiform mole represents a malformation of the placenta due to genetic aberration of the villous trophoblast characterized by cystic swelling and varying degree of trophoblastic proliferation (8-10). It is an uncommon complication of pregnancy and the most frequent GTD within the reproductive age of 13-49 years (9, 12, 13). However, a rare postmenopausal case has been reported (14). The common age of presentation from varying reports in our geographic region is the 3rd and 4th decade with a mean age of 28 years (15, 16). Our five cases fall within this age category.
The incidence of hydatidiform mole is variable for regions worldwide and ranges from 1 per 1000 to 1200 pregnancies in the United States to 10 per 1000 in Indonesia (8, 17, 18). Ectopic pregnancy accounts for one in 150 pregnancies and is unquestionably a major influence on increasing maternal mortality in developing countries, with an incidence of 1 per 114 deliveries, and also accounts for 14.4% of all gynaecologic and 19.28% of pregnancy related specimens (4, 7, 8, 19, 20).

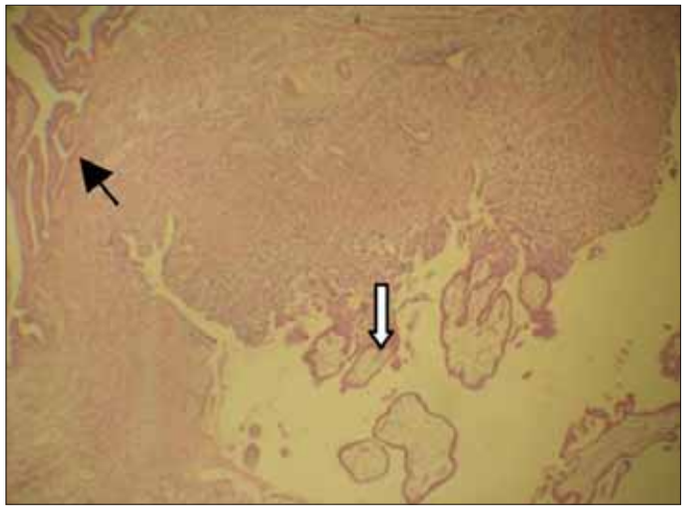

Figure 1. Tubal fimbriae (black arrow) and hydropic villi with trophoblastic hyperplasia (white arrow)

Molar gestation commonly develops within the uterus but may also occur in sites of ectopic pregnancy (8). However, tubal ectopic hydatidiform moles are rare and less than 50 cases have been reported (11, 21, 22). Predisposing risk factors to development of tubal hydatidiform mole include nulliparity, pelvic inflammatory disease, oral contraceptive use, low socioeconomic status, prior hydatidiform mole and advanced or young maternal age (15,18).
It is important to monitor the HCG level of patients serially until it becomes undetectable using the recommended protocol of weekly for 3 consecutive weeks, then monthly for 6 consecutive months, to forestall recurrence and to aid in the early diagnosis of persistent trophoblastic disease or its malignant choriocarcinoma (12, 23- 27). However, one single undetectable HCG level after evacuation is sufficient follow-up in partial moles (28).
The frequency of choriocarcinoma is higher with complete mole (8, 10, 24). Its incidence is higher in areas where hydatidiform mole and ectopic gestation are prevalent as in our setting (10). This would explain the high number of choriocarcinoma cases recorded within the study period. Other pertinent reasons are patients' late hospital presentation, ignorance and poverty.
Ruptured tubal hydatidiform mole is uncommon and the histologic criteria for its diagnosis conform to the complete mole type where foetal parts and vessels are absent (11, 29). Accurate pathologic diagnosis can also be achieved by flow cytometry to determine ploidy (30, 31). The presence of hydropic villi alone without trophoblastic proliferation is a feature of early placentation or hydropic abortion when seen in the tubes and should not be confused with molar gestation (11). Serial HCG levels must be monitored in individual patients to forestall development of choriocarcinoma.

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Prolonged Survival (>48 months) in a Squamous Cell Carcinoma of the Cervix After Late Skin Metastasis (>5 year) to Incision Site: A Case Report

Geç cilt metaztazı (>5 yıl) yapmış squamoz hücreli serviks kanserinde uzamış sürvi (>48 ay): bir vaka sunumu

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Abstract

Metastasis to the incision site of squamous cervical cancer (SCC) is an extremely rare entity which is strictly related with extremely poor prognosis. The vast majority of the reported cases died in a year due to distant recurrences, whereby skin metastases were predominantly observed close to the primary tumor site. A SCC with skin metastasis which was diagnosed 5 years after the radical surgery and postoperative radiotherapy which involved the midline incision site was reported. Large surgical excision of the metastasis with remaining surgical free margins (>2 cm) and combined chemo-radiotherapy with single agent (cisplatinum) was performed. The patient did not show any recurrences for 4 years follow-up. Apparently, palliative combined chemo-radiotherapy along with large excision seems favorable for controlling symptoms and progression of skin metastasis of squamous cervical cancer. (J Turkish-German Gynecol Assoc 2009; 10: 175-7)

Key words: Cervical cancer; Skin metastasis; Prolonged Survival; Chemotherapy; Radiotherapy

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Özet

Servikal skuamoz hücreli kanserde insizyon alanına metaztaz oldukça seyrek görüllür ve kötü prognoz ile ilişkilidir. Bildirilen vakaların çoğunda hasta özellikle uzak metaztazlardan sonraki 1 yıl içerisinde yaşamını yitirmiştir. Beş yıl önce cerrahi ve radyoterapi görmüş servikal skuamoz kanserli bir hastada geç dönmede ortaya çıkan insizyon yeri metaztazı bildirildi. Metaztazın geniş lokal ekziyonu ve tek ajan (sisplatin) kemoradyoterapi kombinasyonu ile hasta tedavi edildi. Operasyon sonrası 4 yıl hasta rekürrens göstermedi. Göründüğü kadarıyla cilde metaztaz yapmış skuamoz hücreli kanserin en uygun tedavisi geniş eksizyona kombine edilmiş kemoradyoterapidir.

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Anahtar kelimeler: Serviks kanseri, cilt metaztazı, uzamış sürvi, kemoterapi, radyoterapi

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Background

Carcinoma of the cervix, the second most common gynecological malignancy, metastasizes mainly to the lung, bone, and liver (1,2). Involvement of skin in cervical cancer is a rare entity (0.1 to 2%), especially diagnosed in advanced stages, and is closely related with extremely poor prognosis (3,4). Adenocarcinomas are the most common histological type rather than squamous cell carcinomas (SCC) in cases with skin metastases (3). The vast majority of the SCC with skin metastases are observed in the abdominal wall, vulva, anterior chest wall or lower extremities, respectively (4). Herein, a SCC case of the cervix with skin metastasis to the midline incision site which was treated with a combined chemo-radiotherapy with single chemotherapeutic agent and large excision of lesion was reported.

Case

A 32 year-old woman, was referred to the Ankara University Faculty of Medicine, Department of Gynecological Oncology for the evaluation of postcoital bleeding and leucorrhea. The initial gynecological examination revealed a 4cm cervical lesion extending to the upper part of vagina and a 4x4 cm solid mass at the cervical site was confirmed both by transvaginal ultrasonography (with intrauterine hypoechogenity) and by computerized tomography . The cervical biopsy revealed an undifferentiated SCC. Intravenous pyelography showed no abnormality on each kidney. Examination under anesthesia along with cystourethroscopy and sigmoidoscopy verified a FIGO stage II A lesion. After preoperative tests the patient underwent radical hysterectomy type III and pelvic-periaortic lymph node dissection. On histological examination, involvement of the lmyphovascular space was diagnosed and three of the sampled pelvic and periaortic lymph nodes (left 3/6, right 0/9, periaortic 0/5) were found to be positive for metastasis. Subsequently, radiotherapy was performed and the patient received 6000 CGy of external beam irradiation in 30 sessions over 6 weeks.

Postoperatively, the control visits of the patient were uneventful for five years. However, a 3x2 cm deep subcutaneous mass with a 1,5x1 cm fixed-nodular skin lesion located on

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the lower abdominal wall, just adjacent to the midline incision, was noticed after five years of disease free follow up. The fine needle biopsy revealed a metastasis of undifferentiated SCC. Computed tomography of the abdomen and pelvis showed a 4x4 cm mass on the anterior abdominal wall adjacent to the surgical incision site, without any extensions to the abdominal cavity or other recurrences at the primary surgical sites or lung and liver (including vaginal cuff and pelvic organs). Examination of the chest was normal. Surgical excision of the mass by leaving a >2 cm surgically free zone at all surgical borders was performed and confirmed by the frozen sections intraoperatively. The macroscopic and microscopic pathological findings confirmed the skin metastasis of undifferentiated SCC (Figures 1 and 2). Chemotherapy along with radiotherapy was subsequently planned and six courses of chemotherapy with Cisplatinium (50 mg/m^2) every 3 weeks after 3000-CGy external beam irradiation in 10 sessions (cobalt) over 2 weeks were given to the patient, sequentially. The patient was then followed by control visits with 6 monthly intervals comprising transabdominal and transvaginal ultrasonography, biochemical tumor markers (CEA, Ca 19-9, CA 15-3, CA 125), direct anterior-posterior chest X ray, and ALP, as well as annually performed computerized tomography, bone scintigraphy and mammography. On the last visit after 4 years of disease free follow up, she had respiratory complaints and on the chest X ray pulmonary edema and on computerized tomography a suspicious nodule in the left pulmonary apex was diagnosed which was thought to be a recurrence. She had no recurrences at the primary or secondary operation sites. Nevertheless, she died in a few months due to cardiopulmonary arrest.

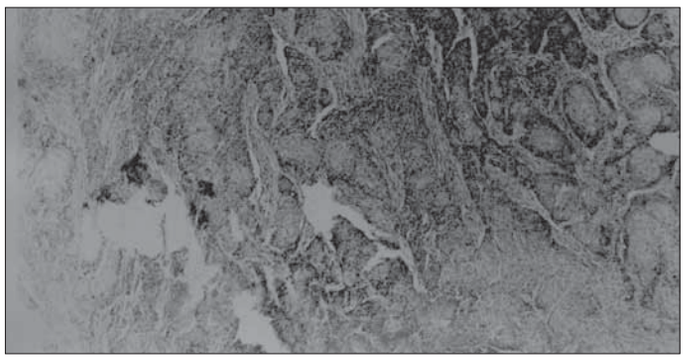

Figure 1. Microscopic view showing squamous cell islets of metastatic squamous cell carcinoma adjacent to vascular and lymphatic structures in incisional scar (x40, hematoxylene–eosin stain)

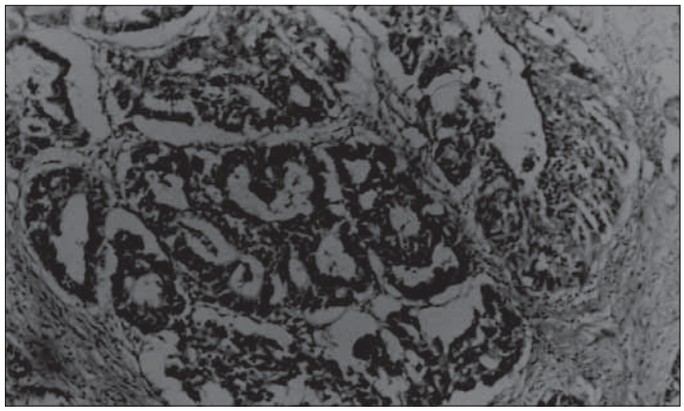

Figure 2. High microscopic view showing clumps of metastatic squamous cell carcinoma in incisional scar (x100, hematoxylene-eosin stain)

Discussion

The usual route of metastatic spread to the skin in cervical cancer is via the lymphatic system (5). The cutaneous metastases were reported to be caused by retrograde spread of the tumor secondary to lymphatic obstruction. The tumor cells can be demonstrated in dilated lymphatics of the skin lesions.[5,6] However, the frequency of unusual metastatic sites such as surgical scars in reported cases again raised reasonable concerns about possible direct implantation of tumor cells, or hematogenous metastasis (7-10)

It has been suggested that the incidence of skin metastasis tends to be increased by the advancement of clinical stage and was determined in 1,2 % of stages II-III whereby an incidence of 20 % was defined in undifferential carcinomas (6). The vast majority of the reported cases were SCC especially those that metastasize to surgical scars (9). However, there are also some reports of metastasis to surgical sites such as episiotomy scars with adenocarcinomas.[11]

The mean interval between the diagnosis of cervical cancer and skin metastasis was reported in a range of 1 to 70 months.[5-8] However, there are a few reports about late recurrence or onset of skin metastasis (5-8). Nevertheless, interval to diagnosis seemed to have no negative influence on the prognosis regardless of the clinical stage and/or histological type whereby extremely poor prognosis has been reported in almost all of the cases (6-8)

The mean survival of these patients with skin metastasis was indicated as 3 to 12 months (6-8, 12). However a prolonged survival, more than a year, was reported in just two cases (8, 12) In the current case disease free survival for 48 months was obtained. Possible synchronous primary cervical cancer and primary skin cancer cannot be excluded and molecular genetic techniques for identifying human papillomavirus genes may have a beneficial role.

Cisplatinium is still accepted as the single and most active agent for palliative treatment of recurrent cervical cancer, however palliative radiation is also regarded as helpful in controlling the symptoms of recurrence (13) A combined treatment with single agent chemotherapy and radiotherapy was reported to be favorable in prolongation of survival in another SCC case (FIGO stage IIIB, >1 year) previously reported by Khalil et al (14). In our case, we used combined radiotherapy and chemotherapy sequentially and this application for skin metastases of cervical cancer seems to be successful.

In conclusion, predominance of surgical scars in skin metastasis of cervical cancer raises questions concerning the reported lymphatic metastasis route. Besides this, according to the literature, the histological type of SCC has predominance in contrast to current beliefs. Particularly, a combined regimen based on sequenial chemotherapy and radiotherapy and large excision of the lesion might prolong the expected survival in such cases.

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Expectant management of partial ureteral angulation: a case report

Parsiyel üreteral açılanmanın yönetimi: bir vaka bildirimi

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Abstract

Urinary tract injuries are one of the most serious complications of pelvic surgery and its incidence is about 0.1-1.5%. A 28 year-old woman who had delivered by emergency cesarean section in the second stage of labour presented at the emergency department with pain commencing on the fifth day of the birth. The diagnosis was left ureteral angulation due to deep myometrial suturing during surgery. The patient was regularly followed-up by ultrasonography once a week until the left pelvic ectasia disappeared. Medical therapy is given when necessery. The aim of this report is to evaluate expectant management for the treatment of ureteral angulation that is diagnosed in the early period after ceasarean section.

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Özet

Uriner sistem komplikasyonları pelvik cerrahi girişimlerin en ciddi komplikasyonlarıdır ve yaklaşık olarak %0.1-1.5 sıklıkta görülür. Sezaryen ile 5 gün önce doğum yapmış ve acile karın ağrısı ile gelen 28 yaşındaki bir vaka sunuldu. Tanı derin myometriyal sütüre bağlı oluşan sol üreteral açılanma olarak değerlendirildi. Hasta pelvik konjesyonu gerileyene kadar haftalık ultrasonlarla takip edildi. Bu vaka, erken dönemde tanı konulan vakalarda bekle gör tedavisinin yeri olduğunu göstermek için sunuldu.

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Introduction

Urinary tract injuries during surgery are one of the most serious complications of pelvic surgery and occur more commonly in the left ureter (1-3). The incidence is about 0.1-1.5% (2, 4). Emergency operations are one of the most important risk factors in ureteral injuries (5-7).

Intraoperatively, the ureters can be damaged by suture ligation, sharp incision or transection, avulsion, devascularization, and heat or cryoablative therapy. Intraoperative recognition of ureteral injury is difficult and the diagnosis rate is about 33% (2). Urinary tract injury can be detected postoperatively by an intravenous pyelogram (IVP) or retrograde x-ray studies. The management of ureteral injury can be simple and successful when is recognized early. However, there is still controversy regarding the management of ureteral injuries.

We aimed to present the result of expectant management for the treatment of left ureteral angulation which was diagnosed in the early period after cesarean section.

Case

A 28 year-old woman, who had been delivered by emergency cesarean section with indications of repeated cesarean sections and on the patient's request in the second stage of labor. applied to the emergency department with complaints of left upper flank pain commencing on the fifth day after birth. Bimanual pelvic examination and vital signs were within normal limits, but in the physical examination evident pain was detected in the left upper posterolateral abdominal wall during deep palpation. While the hemogram results revealed mild anemia (hemoglobin 10.5gr/dl, hematocrit 32.4%, leucocytes 14500/cc), the other laboratory test results were within normal limits (such as BUN 16mg/dl, creatine 0.8mg/dl). First degree ectasia of the left renipelvic was shown in ultrasonography. Thereupon, IVP and retrograde pyelography under scopy was performed. Delay in the left renal filling and dilatation on the upper part and mid-ureter of the left urinary tract due to the left ureteral angulation was shown (Figure 1a). The patient was regularly followed-up by ultrasonography once a week until the left renipelvic ectasia disappeared and the control IVP was performed. The control IVP was within normal limits (Figure 1b). Meanwhile, medical therapy was given when necessary.

Discussion

Urinary tract injuries are one of the most serious and frequent complications encountered during gynecologic pelvic surgery

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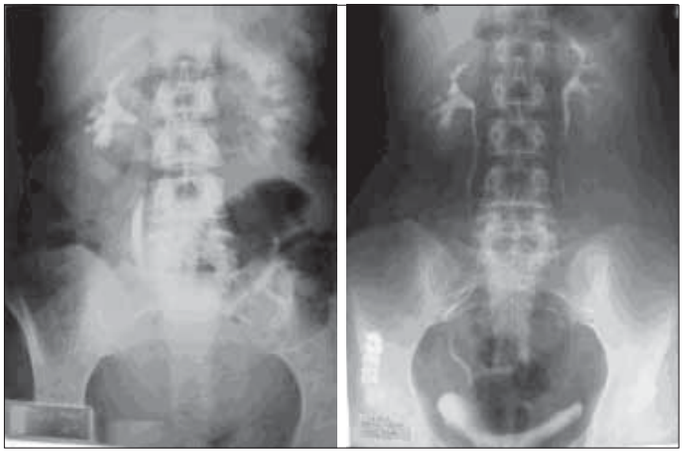

Figure 1. Postoperative early and late IVP

at Departments of Obstetric and Gynaecology (1, 2). The genital and urinary tracts are in close relationship both embryologically and anatomically. The ureter, approximately 25-30 cm in length, lies in its course from the renal pelvis to the bladder. Because of the close relationship, ureteral injury during gynecologic pelvic surgery is more frequent than other organ injuries (2, 5). Left ureteral injury occurs more frequently than right ureteral injury since the left ureter is closer to the cervix than the right ureter (3). The ureteral injuries due to gynecologic pelvic surgery occur frequently at the level of the uterine artery (1, 2). Even in the hands of the most experienced gynecologic surgeon, ureteral injury may be almost unavoidable. Fortunately, such injuries are uncommon and the incidence is 0.1-1.5% (2, 4, 8).

Ureteral injury is more common in gynecologic surgery than obstetric surgery (2). In the past 20 years, a marked rise in the proportion of cesarean section delivery has occured and has steadily increased from about 5% to more than 20% (6, 9, 10). The rising number of elective repeat cesarean sections has been one of the principal reasons for the steady increase in the cesarean delivery rate. In general, cesarean section is a safe delivery procedure and the surgery risks related to cesarean section have been reduced in the course of time but not completely eliminated (6). Particularly, the intraoperative maternal complication rate is higher in the urgent cesarean sections compared to elective procedures (5-7). Risk factors for ureteral injury during gynecologic pelvic surgery or cesarean section may be enumerated as; large uterus, urgent operations, pelvic organ prolapse, surgery performed because of malignant tumor, history of previous irradiation, pelvic adhesions due to prior pelvic surgery and skill of the operator (6). Our patient is also a case of left partial ureteral injury which occured during emergency cesarean section.

Intraoperatively, the ureters may be damaged by suture ligation, sharp incision or transection, avulsion, devascularization, heat or cryoablative therapy. The majority of ureteral injuries during cesarean section is the obstructive type caused by hemostatic sutures placed for bleeding control. Less frequently, ureters may be directly damaged due to extending an uterine incision (3, 6). Hemostatic sutures placed to control bleeding may lead to partial or complete ligation of the ureter or kinking because of periureteral edema or scarring in the ureter. Complete recovery of renal function after relief of obstruction is dependent on several factors such as the duration and location of the obstruction, whether it is partial or complete, and the presence of intercurrent infection (2, 11-13). In general, such minor ureteral injuries may heal without sequelae as an advantage of a blood supply to the ureters from multiple sources. Depending on pelvic pressure caused by the enlarged uterus in pregnancy, minimal ureteral obstruction may be seen and renal function may be affected temporarily. In the same way, an ureteral calculus may also lead to partial or complete ureteral obstruction. Our patient is a case of partial ureteral injury occuring due to the deep hemostatic suture placed near to the ureter because of an extending left side uterine incision. The suture placed is a synthetic absorbable suture that is known as polyglactin 910 and the time for complete absorption of this suture is 56 -72 days. Namely; after absorption of the suture, the obstruction may be relieved. Due to these factors, we would prefer an expectant management rather than an invasive procedure and then a close follow-up.

Key factors for obtaining optimal results in the management of urological injuries are the early recognition and immediate repair of damage (1). The surgical management of ureteral injuries is simple and successful when they are promptly recognized (1). But, when there is a delay in diagnosis or it is not repaired, ureteral injury may lead to hydroureter, hydronephrosis, and/or loss of kidney function (1, 11, 14). The indications for determining the loss of kidney function due to ureteral injury are few. There is no relation between the degree of ureteral injury and complaints of the patient. The most common complaints are flank pain, nausea, vomiting and fever if secondary urinary infection devolops. So, the intraoperative recognition rates in the literature for ureteral injury range from 11% to 33% (2). For example, Newell first drew attention to previously ligated ureters at autopsy in an autopsy study in 1939. In none of these cases were injury suspected in the ureters before autopsy. In this respect, both intraoperative and postoperative evaluation of the ureters in patients with suspected ureteral damage would prevent delay in the diagnosis. Diagnostic procedures are urography, renal ultrasonography, retrograde pyelography with cystoscopy, computerized tomography, and magnetic resonance imaging scan. Particularly, retrograde urography is a powerful tool for evaluating ureteral functioning in the critically ill patients. If necessary, the peritoneum should be opened during or after surgery and the surgeon may see the ureters along the lateral pelvic wall if the anatomy is normal. In our case too, there was left flank pain complaint commencing in the early postoperative period and diagnosis of partial ureteral injury was confirmed by ultrasonography, IVP and retrograde pyelography with cystoscopy.

Gynecologic surgeons must be knowledgeable about common intraoperative and postoperative complications in order to decrease the risk of patient morbidity and understand the anatomy and physiology of the ureter. Diagnostic tests should be made if necessary. However, the most important aspect of ureteral injury is prevention of the injury. The best way to

prevent ureteral injury is to identify the ureters by palpation in paracervical tissues before placement of a suture or clamp.The results of ureteral injury may not always be as expected and kidney function may not return to normal completely with or without any clinical signs and symptoms.

In conclusion, if the ureter is ligated by suture, the suture should be removed or, if the ureter is serious damaged, the ureter should be repaired. If necessary also, a ureteral catheter (double-J ureteral stent) may be placed. The earliest reports in repair of ureteral injury have been reported by Berard (1841) and Simon (1869). Since then, very many studies have been reported. Despite this, there is still controversy regarding the management of an ureteral injury among gynecologic surgeons, and the question of whether expectant management or invasive procedure is safer for such patients is often debated. Expectant management in suitable cases may be an alternative for the treatment of such partial ureteral injury which is diagnosed early after cesarean sections. Clearly, more studies regarding expectant management are needed.

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Huge solitary primary pelvic hydatid cyst presenting as an ovarian malignancy: case report

Over kaynaklı tümör ile karışan büyük bir pelvik hidatik kist: vaka sunumu

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Abstract

Hydatid disease is a zoonotic parasitic infection caused by Echinococcus granulosus. Echinococcus cysts are found mostly in the liver (60%) and lung (15%), but they can be located in any part of the body. However pelvic echinococcosis as the primary site is rarely seen. We report the case of a large echinococcal cyst localized in the lower pelvis. A 76-year-old woman was admitted to an emergency department with urinary retention for ten days. Ultrasonography and other imaging modalities revealed a mass with solid and cystic components in pelvic localization. This unusual presentation in an elderly postmenopausal woman was initially considered as an ovarian malignancy until surgical exploration and microscopic studies confirmed the diagnosis of echinococcosis. Antihelminthics were administered postoperatively and the patient is now being closely followed up. Gynecologists should be aware of the possibility of a primary hydatid cyst of the pelvic cavity and should be considered in the differential diagnosis of cystic pelvic masses, especially in areas where the disease is endemic.

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Key words: Hydatid cyst, echinococcal, pelvis

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Özet

Hidatik kist Ekinokokkus granulozus tarafından oluşturulan bir parazitik kisttir. Çoğunlukla karaciğer (%60) ve akciğerde (%15) yerleşir. Fakat vücudun herhangi bir bölgesinde de olabilirler. Pelvik hidatik kist oldukça nadir görülür. Burda 76 yaşındaki pelvik hidatik kisti olan bir vaka sunuldu. Hasta acile 10 gündür idrar yapamama yakınması ile müracaat etti. Hasta cerrahi yapılıp histopatolojik inceleme yapılana kadar over tümörü olarak değerlendirilmişti. Cerrahi sonrası antihelmintik tedavi başlandı. Jinekologlar özellikle de hastalığın endemik olduğu yöreleden gelen hastalarsdaki pelvik kitlelerde hidatik kisti de ayırıcı tanıda düşünmelidirler.

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Anahtar kelimeler: Hidatik kist, ekinokkus, pelvis

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Introduction

Hydatid disease, or echinococcosis, is a parasitic infection caused by echinococcus larvae. Echinococcus granulosus is the most common type and is endemic in the Mediterranean, Middle East, Eastern Europe and South America. Although it may attack all the organs, primary involvement of the pelvic cavity is a very rare entity and patients usually present with pressure symptoms affecting the adjacent organs (1). Nearly 80% of all pelvic cases involve the genital area, the ovary being the most frequent location (2). These cases are usually secondary to the accidental rupture of a cyst in other areas of the body (2). In this case report, we present the rare occurrence of a primary pelvic hydatid cyst which manifested itself with urinary problems and mimicking an ovarian malignancy.

Case report

A 76-year-old, gravida 2, para 2 woman was admitted to our emergency department with urinary retention. She had been in menopause for 36 years. On bimanual examination, an intrapelvic adnexial mass extending anteriorly to the superior vaginal margins, approximately 100x120 mm in diameter, was palpated. Speculum examination was normal. Laboratory investigations including blood sugar, blood urea nitrogen, creatinine, liver enzymes, and urinalysis were normal. Chest radiograph was also normal. Although she had no previoushistory of hydatic disease, an indirect hemagglutination (IHA) test was found to be positive at a low dilution 1:160.

She was referred to radiology for an abdominal ultrasound (US) examination, which revealed a 104x71 mm round, heterogeneous mass with solid and cystic components located anterolaterally to the bladder in the pelvis . For further delineation of the mass and disease extension in the pelvic cavity, a computed tomography (CT) scan was performed that revealed a multiloculated, heteregeneous mass lesion approximately 126 x 104 x 89 mm in diameter in the pelvic cavity, extending to the right obturator space. It also revealed obliteration of the fatty tissue plane between the mass and bladder, right pubic wall and obturator canal. The liver and

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other abdominal organs were completely normal, both on US and CT examinations. The patient underwent pelvic magnetic resonance imaging (MRI) which demonstrated that the mass was a multiloculated cystic lesion originating close to the arm of the right ischium bone and reaching to the ischiorectalis, ischianalis and obturator spaces (Figure 1).

The patient underwent an exploratory laparotomy under general anesthesia for further diagnosis of the mass and to rule out genitourinary malignancy after obtaining informed consent. At operation, a cystic mass 110x105 mm in size was identified retroperitoneally, anterior to the bladder, extending to the right obturator area and adhering to the right pelvic side wall. Both uterus and bilateral ovaries were seen normal The cyst ruptured during exploration due to adhesions. All the contents were removed. The cystic cavity was irrigated with 3% sodium chloride solution to kill any remaining alive scolexes and aspirated. The wall of the cyctic sac was then totally excised.

The pathology report confirmed the diagnosis of cyst hydatic (Figure 2). The patient recovered uneventfully and was discharged on the 9th postoperative day. Albendazole (per oral 800 mg per day) as adjuvant therapy was administered for six months postoperatively. The patient was kept under regular follow-up.

Discussion

Echinococcus granulosus is a 5-mm long worm, with a lifespan of 5-20 month within the jejunum of dogs. When eggs are ingested, they enter the portal circulation, and are then trapped in the liver (3). If they escape the hepatic filter, the embryos enter the systemic circulation and settle in the lungs or, unusally, in other organs.

Hydatid disease located in the pelvis is very rare. In most cases, coexistent cysts are detected elsewhere, usually in the liver.

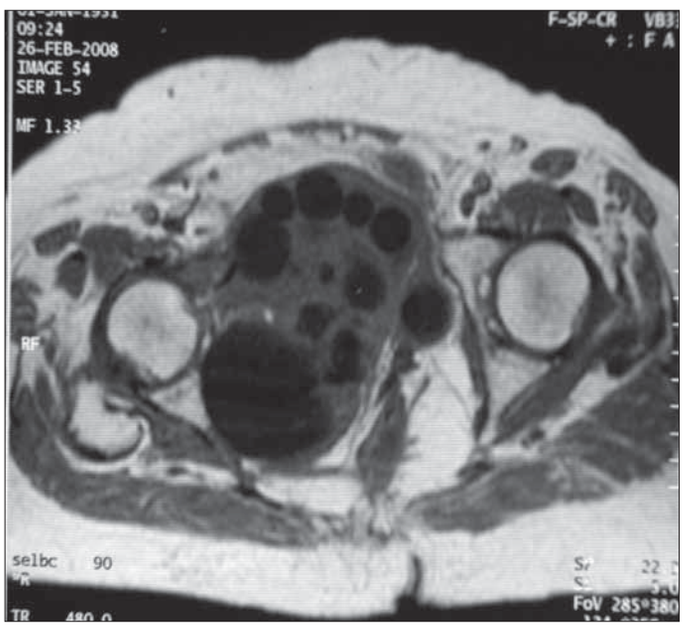

Figure 1. Sagittal MRI demonstrates lesion with solid and cystic components

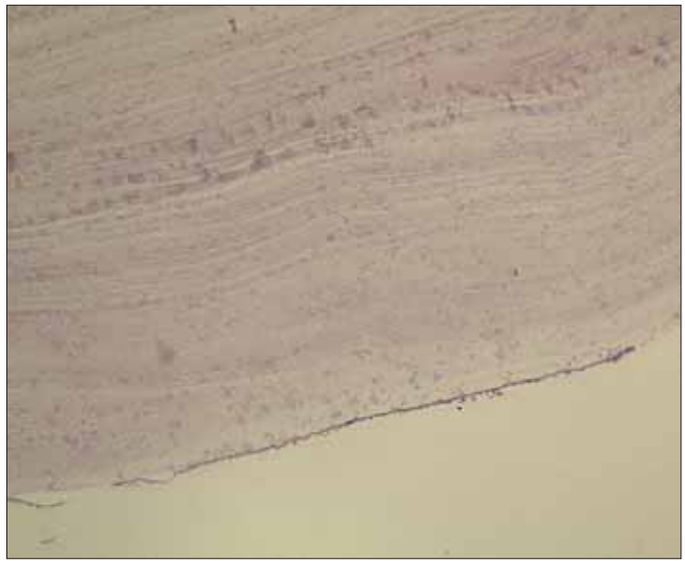

Figure 2. The wall of the hydatid cyst. Note the fibrolamellary membrane and the inner germinative layer. HE,X50

Only a few cases of primary pelvic hydatid cyst have been reported (1, 4-7) and primary pelvic involvement is exceedingly rare. In the presented case, the absence of cysts in other organs was clearly demonstrated by exploration of the abdomen and imaging techniques, and isolated pelvic hydatid cyst was confirmed. Additionally, in our case, as a unique finding, the patient was 76 years of age, older than the previously reported cases in the literature.

The symptoms of pelvic echinococcosis are not specific and may involve abdominal pain, swelling, menstrual irregularities, infertility, obstruction of labor and pressure symptoms from adjacent organs including the bladder and rectum (8). In our patient, the primary complaint was urinary retention.

Pelvic echinococcosis may simulate malignancies and mimick a multicystic ovary (9). In our case, the solid component of the cyst and the patient's advanced age also raised the possibility of malignancy. Also, the present case underlines the possibility of resemblance between the clinical and radiological manifestation of the hydatid cyst and malignant disease of the reproductive organs.

Ultrasound (US) is an important imaging modality for hydatid disease and may clearly demonstrate the floating membranes, and daughter cysts characteristically seen in purely cystic lesions. The ultrasonographic findings range from purely cystic lesions to a completely solid appearance (9). CT also confirms the diagnosis by revealing the presence of daughter cysts and plaque-like calcifications in the cystic wall.

Surgical intervention is the treatment for pelvic hydatid disease. Laparotomy should be the choice in order to avoid intraoperative rupture of the cyst. Surgical treatment can be either radical or conservative. Total cystectomy, whenever possible, is the gold standard (3). In other cases of pelvic hydatid cyst in the literature, cyst extirpation and aspiration with saline or other agents have been performed. It is very important to use a scolicidal agent in the operating field such as a NaCl solution

or a povidone-iodine solution. Mebendazole or albendazole should be used as an adjunct to surgery (3). In many studies the efficacy of preoperative administration of albendazole have been evaluated and these studies showed that the rates of recurrence decreased with antihelminthic therapy (10, 11). Use of albendazole preoperatively for 3 months and should be continued for at least 1 month after surgical treatment (11).

In our case, in order to eradicate the disease, total cystectomy was carried out with dissection of the bladder from the cyst wall and in this way the bladder was freed from compression, and urination was greatly improved postoperatively. Since the diagnosis of the pelvic lesion could only be made during the exploratory laparotomy in our case, we had no opportinity to use albendazole therapy in the preoperative period.

In conclusion, since hydatid disease can occur in various organs or systems, we believe that in cases such as our patient, the most important factor in diagnosis of hydatid disease of the pelvic cavity is the high index of suspicion about its possibility. The optimal treatment is total cystectomy regardless of the location or, when impossible, unroofing and drainage followed by adjuvant antihelminthic therapy is the suboptimal treatment of choice.

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Uterine prolapse in a 19 year old pregnant woman: a case report

Ondokuz yaşındaki bir gebede uterin prolapsus: bir vaka sunumu

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Abstract

It is well-known that multiparity and advanced age are major risk factors for pelvic organ prolapse which can rarely complicate pregnancy. We present the youngest case of uterine prolapse during pregnancy. She admitted with ruptured membranes at the 36th week of gestation and irreducible prolapse. As the edematous and thick, trapped and ulcerated cervix was not reducible, labor was obstructed due to cervical dystocia and a cesarean delivery was decided. A live male infant weighing 3100 gram was delivered. The prolapsed uterus recovered spontaneously following the cesarean operation. Uterine prolapse during pregnancy should be managed conservatively. It seems to be essential to perform elective cesarean section because of the risk of possible obstructed labor . We observed a rapid recovery of the anatomy, probably due to the young age.

(J Turkish-German Gynecol Assoc 2009; 10: 184-5)

Key words: Uterine prolapse, pregnancy, adolescence

Received: 8 May, 2009 **Accepted:** 17 June, 2009

Özet

Ileri yaş ve multiparitenin gebeliği nadiren komplike eden pelvik organ prolapsusu açısından önemli bir risk faktörü olduğu bilinmektedir. Bu vaka sunumunda gebelik esnasında uterus prolapsusu gelişen en genç hastayı sunmaktayız. Hasta gebeliğinin 36'ncı haftasında membran rüptürü ve redükte edilemeyen uterus prolapsusu ile hastanemize başvurdu. Ödemli, kalınlaşmış, sıkışmış ve ülsere serviks redükte edilemediğinden ve servikal distosi sebebiyle doğum engellendiğinden, sezaryen doğuma karar verildi. 3100 gram ağırlığında canlı bir erkek bebek doğurtuldu. Doğum sonrasında uterus prolapsusu kendiliğinden düzeldi. Gebelik esnasında gelişen uterus prolapsusu konservatif olarak takip edilmelidir. Doğum obstrüksiyonu ihtimali nedeni ile elektif sezaryen yapılması daha uygun gibi görülmektedir. Muhtemelen genç hasta yaşı nedeni ile anatominin hızla düzeldiği görülmüştür.

(J Turkish-German Gynecol Assoc 2009; 10: 184-5)

Anahtar kelimeler: Uterin prolapsus, gebelik, adolesan

Geliş Tarihi: 08 Mayıs 2009 **Kabul Tarihi:** 17 Haziran 2009

Introduction

Irreducible uterine cervical prolapse during pregnancy is unusual, with an estimated incidence rate of 1 per 10,000–15,000 deliveries (1). Only less than 10 cases have been reported during the last decade (2). Almost all cases have been issued third or/and fourth decade ages (2, 3, 6-8). This is the first case of the age of 19 years woman with uterine prolapse during pregnancy that simply benefits from of a conservative management.

Case Report

A 19-year-old pregnant woman (gravida: 2, para: 1) admitted to the hospital with premature rupture of the membranes in labor at 36^{+5} weeks' of gestation with an irreducible cervical prolapse. One year ago, she had no history of prolapse during the pregnancy which resulted in one uncomplicated spontaneous vaginal delivery at term. The weight of newborn was in the normal range, 3,250 g. The medical and obstetric history was unremarkable. There was neither history of pelvic trauma or prolapse nor any stress incontinence during or after the previous pregnancy. She had no antenatal care and reported that she complained of a sensation of vaginal fullness and a firm mass in the lower vagina, protruding through the vaginal introitus two weeks before.

Pelvic examination in the dorsal lithotomic position revealed a third-degree uterine prolapse. The elongated cervix was projecting through the vaginal introitus with the vagina being partly inverte and bloody secretions. Biophysical profile of the fetus was normal on ultrasonography evaluation. Fetus was at vertex presentation and with estimated fetal body weight of 3.200 g. Irregular and non effective uterine contractions and a normal fetal heart rate pattern were obtained by cardiotocography. As the edematous and thick, trapped and ulcerated cervix was not reducible, labor was obstructed due to cervical dystocia and a cesarean delivery was decided. A live male infant weighing 3.100 g was delivered. She was discharged in 4 days with no complaint and complete resolution of the cervical prolapse. A follow-up examination at 3 months postpartum revealed no evidence of uterine prolapse.

Discussion

We reported the youngest pregnant woman with cervical prolapse in the literature. Uterine prolapse is a rare complication of pregnancy despite it is a common condition in non-pregnant older women (3). Multiple studies have suggested that the prevalence of pelvic organ prolapse increases with age that a risk factor for the development of pelvic organ prolapse, a correlation between age and pelvic floor

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Figure 1. Uterine prolapse and cervical elongation at 36+5 weeks' of gestation

relaxation (4). Contrarily in the present case 19 years old and has second pregnancy.

There are well-known risk factors for pelvic organ prolapse, including aging, childbirth trauma, multiparity, congenital weakness, traumatic and prolonged labor and operative vaginal deliveries, chronic increases intra-abdominal pressure, genetic factor, smoking, prior surgery, myopathy and collagen abnormalities (5). The main cause of prolapse of the uterus and vaginal vault is failure of supportive ligaments of the uterus, such as Mackenrodt or cardinal ligaments (6). Often, a combination of these etiologic factors results in pelvic organ prolapse.

The situation is usually first well-known in the third trimester (7) and disappears after labor and delivery (6). Treatment options are very limited. Conservative management of antenatal uterine cervical prolapse is consisting of genital hygiene and bed rest in a slight. Trendelenburg position (7) should be considered the foremost treatment option. A suspensory pessary application to protect the prolapsed cervix from trauma and minimize the discomfort for the patient may be practical though it frequently falls out after a few days (8).

In conclusion, obstetricians also all included caregivers should be aware of this rare condition, as early diagnosis is very important for an uneventful gestation. Cesarean delivery is probably the safest mode of delivery (3). However, an individualized approach depending on the gestational age, the severity of the prolapse, the probable complications and the patient's preferences may ensure a successful pregnancy outcome. It is also should be concluded that prolapse is not a disease of the elderly.

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Termination of pregnancy after positive result for fetal anomaly due to second trimester ultrasonography screening: an appraisal

İkinci trimester ultrasonografisine bulunan fetal anomaliye dayanarak gebeliğin sonlandırılması: bir değerlendirme

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Prenatal diagnosis is widely practiced in obstetrics. The main aim of such tests is early detect ion of the fetal anomaly so that proper management can be selected. One of the common diagnostic tools is second trimester ultrasonography screening.This technique has proved to be cost effective. For the positive cases of this screening technique, the termination of pregnancy is an important outcome. The termination of pregnancy depends on several factors including the medical, social and legal factors in each setting. The author hereby appraises the rate of termination of pregnancy after having derived positive results from second trimester ultrasonography screening in published papers from several settings. First, the specific literature search on second trimester ultrasonography screening for fetal anomaly detection was done using standard researching on referencing databases (PubMed, Scopus and SciCitationIndex). The includion is set as any reports published in English. The exclusion is set as any reports that lack complete data on prevalence (positivity) and termination of pregnancy rate. Metanalysis on derived data was done. ANOVA was used for assessing differences among settings. Statistically significant difference was set at P value equal to or less than 0.05

According to this work, there were 8 reports (1-8) on 75264 screenings. The reported prevalence (positivity) ranges from 043% to 3.0% without different among settings. Overall prevalence (positivity) is equal to 1.48%. The reported termination of pregnancy rate ranges from 0.141% to 0.61% without difference among settings. The overall rate of termination of pregnancy is 0.35%. The rate of termination of pregnancy in positive screening cases ranges from 4.8% to 55%, with a significant difference among settings. The author hereby found that the rates of abnormality (positivity) detected by the screening in studies reported are within the same range. In addition, the finalized termination of pregnancy rates also do not differ. However, it can be seen that the rates of termination of pregnancy in positive screened cases are highly variable. This also confirms that the decision on finalized management of detected fetal anomaly from screening is totally different depending on settings. Although the screening is useful, the finalized usefulness of screening results havsmany underlying factors. This is also concordant with the statement of Rasch et al on the effect of the socio-economic situation and country of birth on the termination of pregnancy (9).

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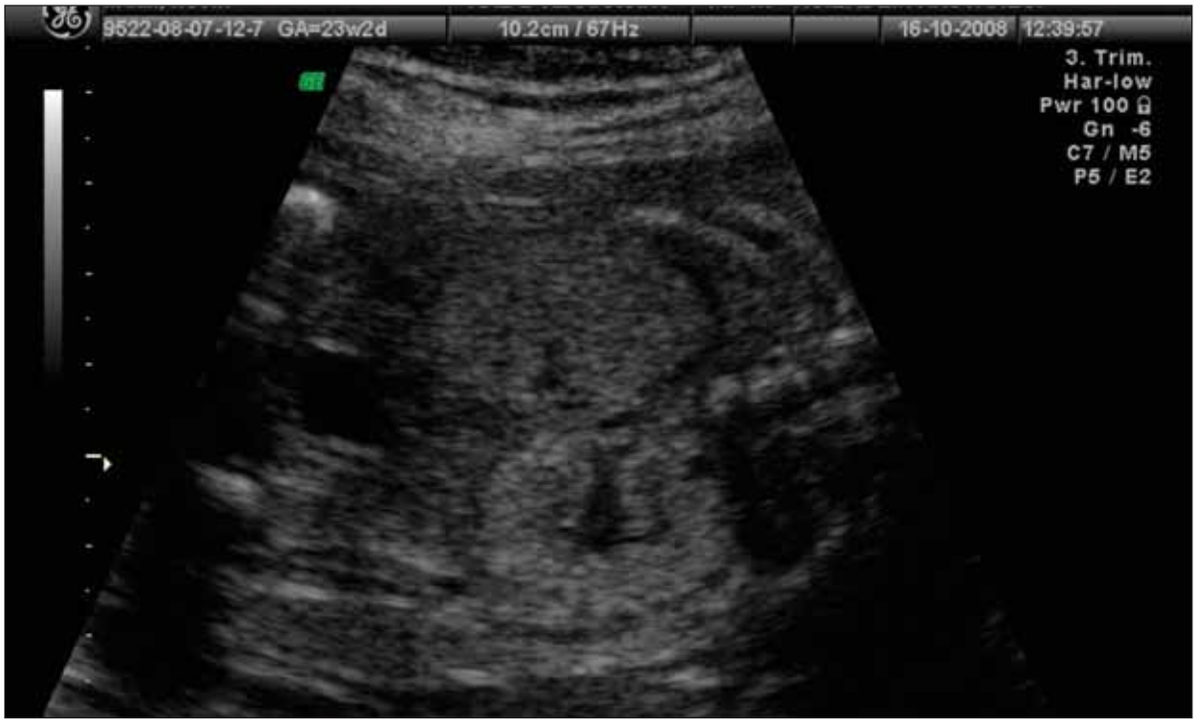
What is your diagnosis?



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Answer

Kidney hyperechogenicity is diagnosed after 17 week' s gestation when the kidneys appear more echogenic than the liver or the spleen (1). The presence of echogenic kidneys on the prenatal ultrasound is associated with a high incidence of renal problems. Such abnormal echogenicity can result from the presence of multiple microscopic cysts, dysplasia or tubular dilatation (2).

In the recent years hyperechogenic kidneys are diagnosed with increasing frequency. This sonographic finding may correspond to many kidney diseases including obstructive dysplasia, bilateral multicystic dysplasia, genetic inherited renal disease (autosomal recessive polycystic kidney diseases, autosomal dominant polycystic kidney diseases), genetic syndromes (Perlman syndrome, Beckwith- Wiedemann syndrome, Bardet-Biedl syndrome, Meckel syndrome), nephroblastomatosis, renal vein thrombosis, toxic injury, infections, ischemia, aneuploidy and in some cases may be a normal variant (3).

Fetal kidney length (expressed as standard deviation from the mean) must be measured and echogenic patern, corticomedullary differentiation (CMD), presence or absence of the of renal cyst, size of the collecting system, amniotic fluid volume and other abnormal sonographic findings must be analyzed and recorded for the differential diagnosis.

In the presented ultrasound image of a fetus at 23 weeks of gestation, moderately enlarged (1-2 SD> mean) kidneys were demonstrated. The medulla and cortex were both hyperechoic and CMD was absent as described by Brun et al. which was not specific but should be clue for consedering other sonographic features of the disease (4). The family history was consistent with autosomal dominant polycystic kidney diseases (ADPKD). The prenatal diagnosis was confirmed to be ADPKD with postnatal follow- up. This appearance differs from what is usually observed in cases of autosomal recessive polycystic kidney diseases (ARPKD) with very enlarged kidneys (4-6 SD), absent, decreased or reversed CMD, cysts and frequently reduced amniotic fluid.

Prenatal diagnosis of fetal nephropathies would provide adequate prenatal counseling to parents and would improve short and long-term outcome with appropriate multidisciplinary management of these cases.

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Picture of the cover page is a case of Cloacal Dysgenesis confirmed via fetal magnetic resonance imaging.
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Intensive Laparoscopic Suturing and Knot Tying and Step-by-Step Total and Supracervical Hysterectomy

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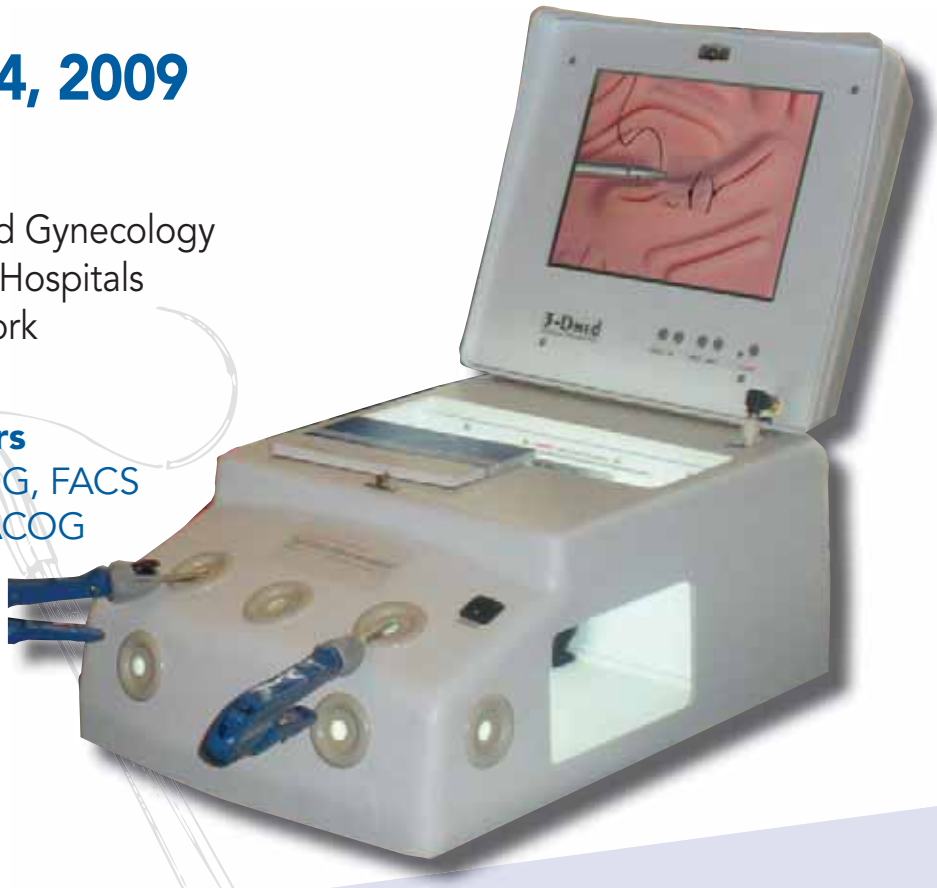

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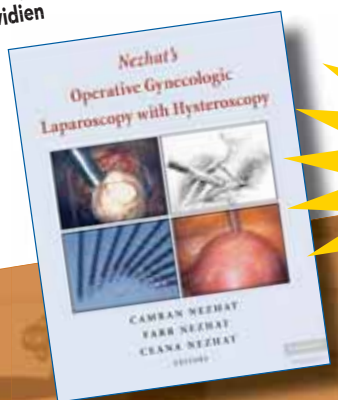

Three copies of Nezhat's Operative Gynecologic Laparoscopy with Hysteroscopy (2008) will be given to conference participants via a surprise drawing. All fully-paid attendees will be eligible to enter.

Intensive Laparoscopic Suturing and Knot Tying and Step-by-Step Total and Supracervical Hysterectomy

Course Directors
Farr Nezhat, MD, FACOG, FACS
Radha Syed, MD, FACOG

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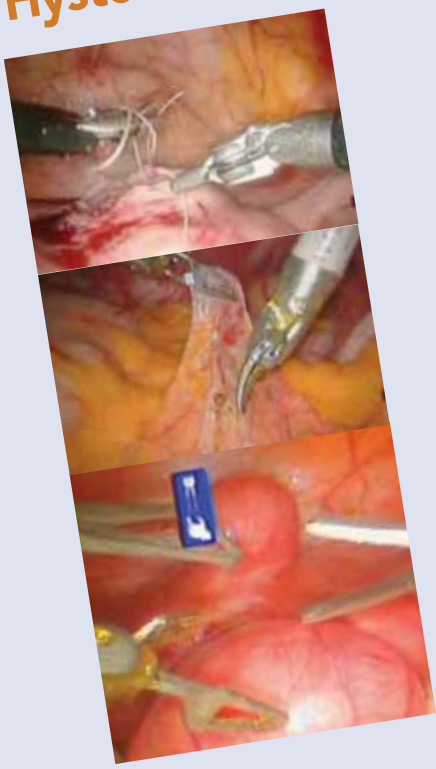

Course Description

The primary goal of this two-day postgraduate course is to educate gynecologic surgeons in the art and science of laparoscopic suturing and knot-tying. This will be done via six intensive, hands-on workshops using approximately 45 of the latest in pelvic-trainer stations. During workshop sessions, preceptors will supervise each station and guide each participant to achieve their desired goals. In addition, a variety of surgical-video presentations and didactic lectures by renowned guest faculty will clearly demonstrate step-by-step procedures for tackling easy to difficult laparoscopic hysterectomy, including the total, supracervical, and laparascopically-assisted vaginal procedures, with and without adnexectomy.

Suturing and knot-tying are essential tools for advancing your career as a laparoscopic surgeon. A deficiency in suturing skills has forced many an unnecessary conversion from laparoscopy to laparotomy, prolonged operating time, and/or increased postoperative morbidities. The course format entwines didactics with repetitive hands-on sessions to reaffirm the learnt skills.

Course Objectives

- Advance ability to perform all aspects of minimally-invasive surgery by strengthening suturing and knot-tying skills;
- Evaluate the treatment options for gynecological patients presenting for a minimally-invasive hysterectomy;
- Acquire the knowledge of experts in applying minimally-invasive surgery techniques to advanced gynecological procedures;
- Increase the self-confidence of gynecologic surgeons toward minimally-invasive surgery, thereby improving patient outcomes;
- Explore indications and techniques for use of the new vessel-sealing technologies;
- Identify early diagnosis and treatment options for gynecologic conditions;
- Identify newly-recognized complications of laparoscopic surgery that affect the diagnostic and management options for treating patients.

HANDS ON

TARGET AUDIENCE: Attending and resident obstetrician/gynecologists, fellows in gynecologic subspecialities, and PA's who function as surgical first assistants.

ACCREDITATION STATEMENT
Beth Israel Medical Center and St. Luke's and Roosevelt Hospitals are accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION
Beth Israel Medical Center designates this educational activity for a maximum of *18 AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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Intensive Laparoscopic Suturing and Knot Tying and Step-by-Step Total and Supracervical Hysterectomy

Thursday, December 3, 2009
Ball Room, Park Central Hotel

7:00 a.m.	**Continental Breakfast and Registration**
7:30 a.m.	**Opening Remarks and Welcome** Oded Langer, MD, PhD, Chairman, Department of Obstetrics and Gynecology St. Luke's and Roosevelt Hospital Center; F. Huntington and Dorothy D. Babcock Professor of Obstetrics and Gynecology, Columbia University College of Physicians and Surgeons
	MODERATOR: Farr Nezhat, MD
7:35 a.m.	**Introduction to the Course; Announcements**
7:40-8:15	**How to Suture and Tie Knots: Demonstration of Intracorporeal, Extracorporeal, and New Methods** Farr Nezhat, MD
8:15-8:45	**Normal Pelvic Anatomy in Laparoscopic Surgery: Trocar Placement for Optimum Performance and Suturing** Ceana Nezhat, MD
8:45-9.15	**Total Laparoscopic Hysterectomy, Easy Case: How to Develop Bladder Flap; Discussion of Abnormal Anatomy** Gabrielle Gossner, MD
9:15-9:30	**Q&A on Knot Tying; Coffee Break**
9:30-10:45	**Hands-On Session I: Pelvic Trainer/Suture Lab/Knot Tying** Directors: Radha Syed, MD, and Ceana Nezhat, MD With Preceptors Maximum 3 participants per trainer
10:45-11:15	**Laparoscopic Supracervical Hysterectomy, Moderate-Sized Uterus:** Utilization of Blood-Vessel Sealing Devices; Morcellation Techniques Ceana Nezhat, MD
11:15-11:45	**Total Laparoscopic Hysterectomy for Severe Endometriosis, Difficult Case: Step-by-Step Description** Camran Nezhat, MD
11:45-12:00	**Q&A on Hysterectomy**
12:00-1:00	**Lunch and Exhibits**
	MODERATOR: Radha Syed, MD
1:00-1:45	**Laparoscopically-Assisted Vaginal Hysterectomy With Pelvic Reconstruction** Anne Hardart, MD
1:45-2:10	**Laparoscopic Radical Hysterectomy and Pelvic/Para-Aortic Lymph Node Dissection** Farr Nezhat, MD
2:10-2:30	**Nonsurgical Hemostasis With Pelvic Surgery and Hysterectomy** Jacques Moritz, MD
2:30-2:45	**Q&A on Radical Hysterectomy and Pelvic Reconstruction; Coffee Break**
2:45-4:00	**Hands-On Session II: Pelvic Trainer/Suture Lab/Knot Tying** Directors: Radha Syed, MD, and Ceana Nezhat, MD With Preceptors Maximum 3 participants per trainer
4:00-4:30	**Management of Vascular Complications in Laparoscopy; Recognition of Timing of Laparotomy** Ceana Nezhat, MD
4:30-5:00	**Anesthesia Considerations of Laparoscopy: Educating Anesthesiologists To Put Patient in Deepest Trendelenberg** Camran Nezhat, MD
5:00-5.10	**Break and Stretch**
5:15-6:30	**Hands-On Session III: Pelvic Trainer/Suture Lab/Knot Tying** Directors: Radha Syed, MD, and Ceana Nezhat, MD With Preceptors Maximum 3 participants per trainer
6:30	**Adjourn**

Intensive Laparoscopic Suturing and Knot Tying and Step-by-Step Total and Supracervical Hysterectomy

Friday, December 4, 2009
Ball Room, Park Central Hotel

7:30-8:00	**Continental Breakfast and Registration**
	MODERATOR: Radha Syed, MD
8:00-8:30	**Laparoscopic Hysterectomy for Large Myoma: Step-by-Step Myomectomy With Abdominal and Vaginal Morcellation** Ceana Nezhat, MD
8:30-9:00	**Abdominal Hysterectomy: Indications and How to Stay Out of Trouble** Lisa Anderson, MD
9:00-9:30	**Alternative to Hysterectomy, Endometrial Ablation: The Old and the New** Robert Neuwirth MD
9:30-10:00	**Laparoscopic Repair of Bladder and Transected Ureter:** Step-by-Step Description Farr Nezhat, MD
10:00-10:15	**Coffee Break, Exhibits and Q&A**
10:15-10:45	**Laparoscopic Repair of Bowel Perforation** Camran Nezhat MD
10:45-11:45	**Hands-On Session IV: Pelvic Trainer/Suture Lab/Knot Tying** Directors: Radha Syed, MD, and Ceana Nezhat, MD With Preceptors Maximum 3 participants per trainer
11:45-12:00	**Q&A and Panel Discussion**
12:00-1:00	**Lunch and Exhibits**
	MODERATOR: Farr Nezhat, MD
1:00-1:30	**Laparoscopic Hysterectomy via the da Vinci Robot: When and How** Camran Nezhat, MD
1:30-2:00	**The Role of Robotic Radical Hysterectomy in Treatment of Cervical Cancer** Pedro Ramirez, MD
2:00-2:30	**Surgical Video Session I: Challenging Cases, Including Pelvic-Wall Dissection for Difficult Hysterectomies** Ceana Nezhat, MD
2:30-3:30	**Hands-On Session V: Pelvic Trainer/Suture Lab/Knot Tying** Directors: Radha Syed, MD, and Ceana Nezhat, MD With Preceptors Maximum 3 participants per trainer
3:30-4:00	**Surgical Video Session II: Treatment of Different Stages of Endometrioisis** Camran Nezhat MD; Coffee Break as desired
4:00-5:00	**Hands-On Session VI: Pelvic Trainer/Suture Lab/Knot Tying** Directors: Radha Syed, MD, and Ceana Nezhat, MD With Preceptors Maximum 3 participants per trainer
5:00-5:30	**Q&A and Panel Discussion**
5:30	**Adjourn**

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Director, MISGR Fellowship Program
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CONFERENCE DATES: December 3 and 4, 2009

REGISTRATION FORM
Registration fee entitles you to all meals and breaks, all didactic and hands-on sessions, all surgical video sessions, exhibits, and a CD of the syllabus material.

Tuition:

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Email: cbellamy@chpnet.org
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Tabletler normal siklusun ilk günü (kanamanın ilk günü) alınmaya başlanmalıdır. **Kontrendikasyonlar:** Kombine oral kontraseptifler aşağıdaki koşulların varlığında kullanılmamalıdır ve ilk kez kombine oral kontraseptif kullanımı sırasında bunlardan herhangi biri ortaya çıkacak olursa, tedavi hemen kesilmelidir. ▪Venöz veya arteriyel trombotik/tromboembolik olayların (örn. derin ven trombozu, pulmoner emboli, miyokard enfarktüsü) veya serebrovasküler bir olayın varlığı ya da öyküsü, ▪Tromboz prodromu varlığı veya öyküsü (örn. geçici iskemik atak, angina pektoris), ▪Fokal nörolojik belirtili migren öyküsü, ▪Vasküler tutulumlu diabetes mellitus, ▪Venöz veya arteriyel tromboz için ciddi olan tek, ya da birden fazla risk faktörünün varlığı da bir kontrendikasyon oluşturabilir (bkz. Uyarılar/Önlemler), ▪Ağır hipertrigliseridemi ile bağlantılı pankreatit veya pankreatite benzer öykü, ▪Karaciğer fonksiyon değerleri normale dönmedikçe, ciddi karaciğer hastalığı öyküsü veya varlığı, ▪Ağır veya akut böbrek yetmezliği, ▪Karaciğer tümörü varlığı veya öyküsü (iyi veya kötü huylu), ▪Eğer seks steroidlerinden etkileniyorsa genital organların veya memenin bilinen ya da şüpheli malign hastalıkları, ▪Tanı konulmamış vaginal kanama, ▪Bilinen gebelik veya şüphesi ▪Etkin ya da yardımcı maddelerden herhangi birine aşırı duyarlılık hali. **Özel kullanım uyarıları ve önlemleri:** Özel kullanım uyarıları: Aşağıda belirtilen durumlardan herhangi birinin ortaya çıkması durumunda kombine oral kontraseptiflerin kullanımına ait yararlar olası risklere karşı tartılmalı ve tedaviye başlamadan önce kullanacak olan kadınla birlikte tartışılmalıdır. Dolaşım bozuklukları: Epidemiyolojik çalışmalar, kombine oral kontraseptif kullanımıyla miyokard enfarktüsü, inme, derin ven trombozu ve akciğer emboli gibi arteriyel ve venöz trombotik/tromboembolik hastalıkların risk artışı arasında bir ilişki bulunduğunu belirtmektedirler. Bu olaylar ender olarak ortaya çıkmaktadır. Derin ven trombozu ve/veya pulmoner emboli şeklinde ortaya çıkan venöz tromboemboli (VTE) tüm kombine oral kontraseptiflerin kullanımı sırasında ortaya çıkabilir. Tümörler: Servikal kanser için en önemli risk faktörü süregelen human papilloma virüs (HPV) enfeksiyonudur. Bazı epidemiyolojik çalışmalarda uzun süre kombine oral kontraseptif kullanımının servikal kanser riskinde artışa neden olabileceği bildirilmiştir ancak bu bulguların kombine oral kontraseptif kullanımının hangi etkilerine bağlı olabileceği (servikal inceleme, hormonal olmayan kontraseptif kullanımı dahil olmak üzere seksüel davranış) halen tartışılmaktadır. 54 epidemiyolojik çalışmayı kapsayan bir meta-analiz sonuçlarına göre halen kombine oral kontraseptif kullanan kadınlarda meme kanseri teşhis edilmesi bağıl riskinde (bağıl risk = 1.24) hafif bir artış olduğu rapor edilmiştir. Bu risk artışı kombine oral kontraseptif kullanımının kesilmesiyle birlikte 10 yıl içinde göreceli olarak ortadan kalkar. Diğer uyarılar: Böbrek yetmezliği olan hastalarda potasyum atılım kapasitesi sınırlı olabilir. Hipertrigliseridemisi olan ya da bu şekilde bir aile öyküsüne sahip bulunan kadınlarda, kombine oral kontraseptif kullanımıyla pankreatit gelişimi riskinde artış ortaya çıkabilir. Kombine oral kontraseptif alan kadınların çoğunda kan basıncında hafif artış görüldüğü bildirilmesine rağmen, klinik olarak anlamlı artış enderdir. Drospirenon, antimineralokortikoid etkisinden dolayı diğer kombine oral kontraseptifleri kullanan normal tansiyonlu kadınlarda etinilestradiol'e bağlı gelişen tansiyon yükselmesini olumlu yönde etkileyebilir. Bununla beraber, kombine oral kontraseptif kullanımı sırasında ortaya çıkan klinik olarak belirgin bir hipertansiyon gelişiminde, hekimin kombine oral kontraseptif kullanımını kesmesi ve hipertansiyon tedavisine başlaması gerekir. Kolestaza bağlı sarılık ve/veya kaşıntı, safra taşı oluşumu, porfiri, sistemik lupus eritematozus, hemolitik üremik sendrom, Sydenham koresi, herpes gestationis, otoskleroza bağlı işitme kaybı gibi durumların gebelik ve kombine oral kontraseptif kullanımı sırasında ortaya çıktığı ya da kötüleştiği bildirilmişse de, bunların kombine oral kontraseptiflerle olan ilişkisi kesinlik kazanmamıştır. Ailesel anjiyoödemi olan kadınlarda egzojen estrogenler anjiyoödem belirtilerinin ortaya çıkmasına veya alevlenmesine yol açabilirler. Karaciğer fonksiyonlarında görülen akut ve kronik değişiklikler, kombine oral kontraseptif kullanımının fonksiyon testi değerleri normale dönene dek kesilmesini gerektirebilir. Gebelik sırasında ilk kez ortaya çıkan ya da daha önce seks steroidlerinin kullanıldığı sırada görülmüş olan kolestatik sarılığın nüks etmesi kombine oral kontraseptif kullanımının kesilmesini gerektirir. Crohn hastalığı ve ülseratif kolit kombine oral kontraseptif kullanımı ile ilişkilendirilmiştir. Özellikle kloazma gravidarum öyküsü olan kadınlarda daha belirgin olmak üzere kloazma ortaya çıkabilir. Azalmış etkinlik: Kombine oral kontraseptiflerin etkinliği tablet alımı unutulduğunda (bkz. Tablet alımı unutulduğunda), mide-bağırsak bozuklukları olması halinde (bkz. Mide-bağırsak bozuklukları durumunda), ya da eş zamanlı ilaç tedavilerinde (bkz. İlaç etkileşmeleri) azalabilir. Azalmış siklus kontrolü: Tüm kombine oral kontraseptiflerde, özellikle kullanımın ilk aylarında düzensiz kanamalar (lekelenme veya kırılma kanamaları) gelişebilir. Bu nedenle herhangi bir düzensiz kanamanın araştırılması yaklaşık 3 sikluslık bir adaptasyon süresinden sonra anlamlıdır.Etkileşimler:Oral kontraseptifler ve diğer ilaçlar arasındaki etkileşimler kırılma kanamalarına ve/veya kontraseptif başarısızlığa yol açabilirler. Aşağıdaki etkileşimler literatürde bildirilmiştir. Hepatik metabolizma: Mikrozomal enzimleri etkileyen ilaçlarla (örn. fenitoin, barbitüratlar, primidon, karbamazepin, rifampisin ve muhtemelen okskarbazepin, topiramat, felbamat, griseofulvin ve "St. John's wort (Sarı kantaron)" içeren ürünler) olan etkileşimler, seks hormonlarının klerensinin artması ile sonuçlanabilir. Gebelik kategorisi X'dir. YAZZ® 24+4 gebelik döneminde uygulandığı takdirde ciddi doğum kusurlarına yol açmaktadır, YAZZ® 24+4 gebelik döneminde kontrendikedir. YAZZ® 24+4 film kaplı tabletlerin kullanımı sırasında gebelik meydana gelmesi durumunda kullanım durdurulmalıdır. Laktasyon, anne sütünün miktarında azalmaya ve bileşiminde değişikliğe yol açabileceğinden, kombine oral kontraseptifler tarafından etkilenebilir. **İstenmeyen etkiler:** Kombine oral kontraseptiflerin kullanımıyla ilişkilendirilen en ciddi yan etkiler "Uyarılar/önlemler" bölümünde ele alınmıştır. Aşağıdaki diğer yan etkiler kombine oral kontraseptif kullanıcılarında bildirilmiş ve ilişkileri ne doğrulanmış ne de yanlışlığı kanıtlanmıştır. **Göz:** Seyrek: Kontakt lense toleranssızlık **Gastrointestinal sistem:** Yaygın: Bulantı, batında ağrı, Yaygın olmayan: Kusma, diyare **İmmün sistem bozuklukları:** Seyrek: Hipersensitivite **İncelemeler:** Yaygın: Kiloda artış, Seyrek: Kiloda azalma **Metabolizma ve beslenme:** Yaygın olmayan: Sıvı tutulumu **Sinir sistemi:** Yaygın: Baş ağrısı, Yaygın olmayan: Migren **Psikiyatrik düzensizlikler:** Yaygın: Depresif duygu durumu, duygu durum değişiklikleri Yaygın olmayan: Libido azalması, Seyrek: Libido artışı **Üreme sistemi ve meme:** Yaygın: Meme ağrısı, meme hassasiyeti, Yaygın olmayan: Memede hipertrofi, Seyrek: Vaginal akıntı, memede akıntı **Cilt ve cilt altı:** Yaygın olmayan: Döküntü, ürtiker, Seyrek: Eritema nodozum, eritema multiforme. Ailesel anjiyoödemi olan kadınlarda egzojen estrogenler anjiyoödem belirtilerinin ortaya çıkmasına veya alevlenmesine yol açabilirler. **Raf ömrü:** 48 ay. **Saklamaya yönelik özel tedbirler:** 25 C'nin altında oda sıcaklığında saklayınız. **Ambalajın niteliği ve içeriği:** PVC/Alüminyum blister'de etkin madde içeren 24 adet ve etkin madde içermeyen 4 adet film kaplı tablet. **Ruhsat Sahibi:** Bayer Türk Kimya San. Ltd. Şti., Çakmak Mah. Balkan Cad. No:53 34770 Ümraniye – İstanbul Tel: (0216) 528 36 00 Faks:(0216) 538 37 40 **Ruhsat Numarası:** 126/93 **Ruhsat Tarihi:** 02.03.2009 Fiyatı: KDV dahil perakende satış fiyatı: 21.53 TL Ayrıntılı bilgi için Firmamıza başvurunuz.

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