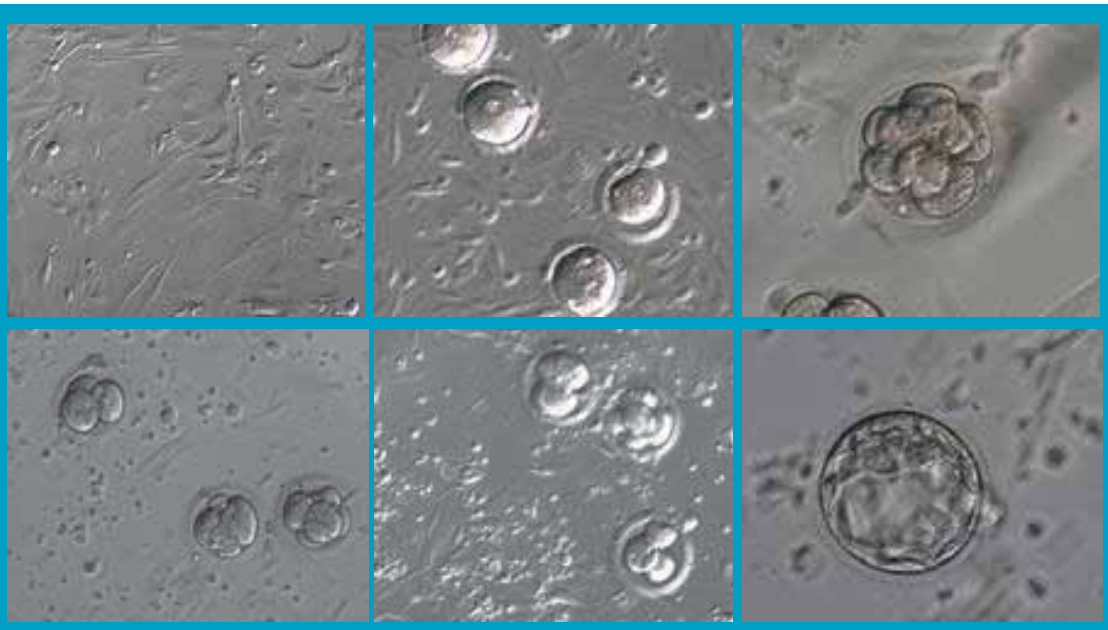
ISSN 1309-0399

TAJEV

TURKISH-GERMAN GYNECOLOGICAL EDUCATION and RESEARCH FOUNDATION

Journal of the Turkish-German Gynecological Association



Volume 11
Issue 2
June
2010

Original Investigations

Rectus fascia colpopexy for vault prolapse
Rajiv Mahendru; Haryana, India

PIVH in premature infants in China
Jing Liu et al.; Beijing, Wuhan, China

Knowledge of contraception among college students
Prachi Renjhen et al.; Melaka, Malaysia, Manipal, India

Fetal RhD detection in maternal blood
Tuba Günel et al.; İstanbul, Turkey

Ceruloplasmin and neural tube defects
Çağlar Yazıcıoğlu et al.; Gaziantep, Şanlıurfa, Turkey

Postpartum diabetes rates after gestational diabetes
Özlem Seçilmiş Kerimoğlu et al.; Ankara, Turkey

Shortening the second stage of labor?
Rajiv Mahendru; Haryana, India

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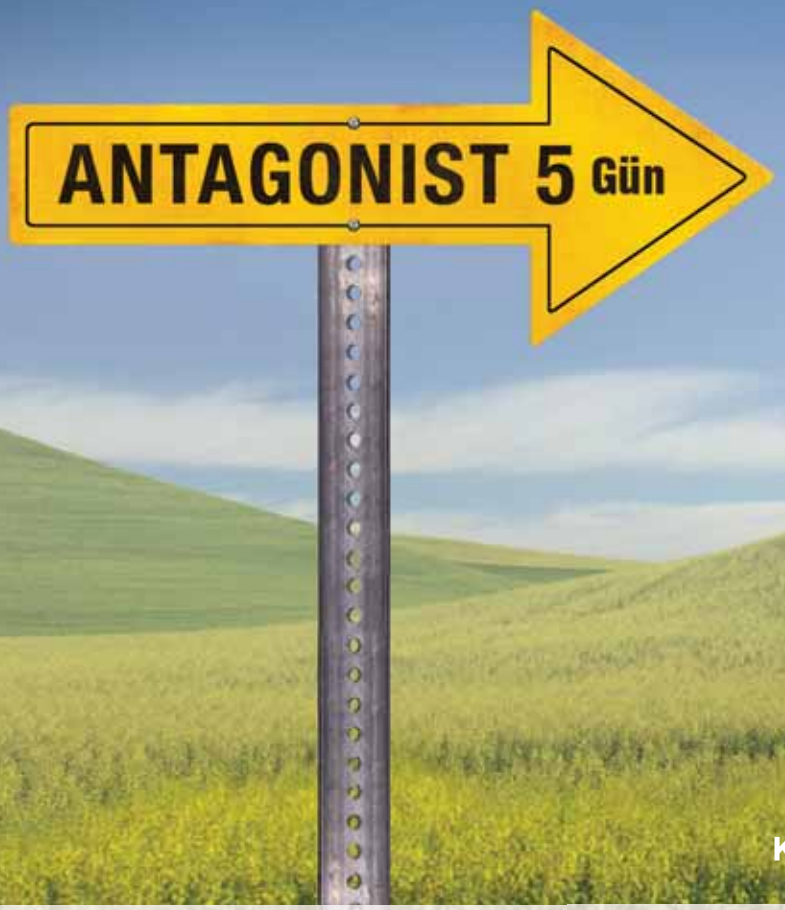
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Sadece 5 tedavi günü yüksek gebelik oranı sağlar[1-6]



Başarılı, kolay, kısa süreli tedavi,[1-6]

- Kanıtlanmış sonuçlar %38 devam eden gebelik oranı[1]
- Anlamlı derecede daha az sayıda enjeksiyon[4]
- Kullanıma hazır şırınga olarak sunulan tek GnRH antagonisti[7]
- Daha düşük OHSS riski[2,3]
- LH pikini önler[4,8,9]

Orgalutran®
ganirelix

Kanıtlanmış sonuçlar, Güvenilir deneyim.[6]

Referanslar: 1. Doody K, Witjes H, Mannaerts B, Gordon K. Success rates of a fixed rFSH/GnRH antagonist protocol are not affected by endogenous LH levels. Abstract presented at: the 25th Annual Meeting of the European Society of Human Reproduction and Embryology; June 28-July 1, 2009; Amsterdam, The Netherlands. **2.** Kolibianakis EM, Collins J, Tarlatzis BC, et al. Among patients treated for IVF with gonadotrophins and GnRH analogues, is the probability of live birth dependent on the type of analogue used? A systematic review and meta-analysis. Hum Reprod Update. 2006;12:651–71. **3.** Al-Inany HG, Abou-Setta AM, Aboulghar M. Gonadotrophin-releasing hormone antagonists for assisted conception (Review). Cochrane Database Syst Rev. 2006;3;CD001750. **4.** Fluker M, Grifo J, Leader A, et al. Efficacy and safety of ganirelix acetate versus leuprolide acetate in women undergoing controlled ovarian hyperstimulation. Fertil Steril. 2001;75:38–45. **5.** Devroey P, Aboulghar M, Garcia-Velasco J, et al. Improving the patient's experience of IVF/ICSI: a proposal for an ovarian stimulation protocol with GnRH antagonist co-treatment. Human Reprod. 2009;24(4):764-774. **6.** The European Orgalutran® Study Group; and Borm G, Mannaerts B. Treatment with the gonadotrophin-releasing hormone antagonist ganirelix in women undergoing ovarian stimulation with recombinant follicle stimulating hormone is effective, safe and convenient: results of a controlled, randomized, multicentre trial. Hum Reprod. 2000;15(7):1490-1498. **7.** Orgalutran SMPC. **8.** Lambalk CB, Leader A, Olivennes F, et al. Treatment with the GnRH antagonist ganirelix prevents premature LH rises and luteinization in stimulated intrauterine insemination: results of a double-blind, placebo-controlled, multicentre trial. Hum Reprod. 2006;21(3):632-639. **9.** European and Middle East Orgalutran Study Group. Comparable clinical outcome using the GnRH antagonist ganirelix or a long protocol of the GnRH triptorelin for the prevention of premature LH surges in women undergoing ovarian stimulation.

Hum Reprod. 2001;26:644-651.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 diller 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 diller advers olaylar, Orgalutran®'dan ziyade destekli üreme tekniklerine (ART) yönelik kontrollü over hiperstimülasyonu ile bağlantılıdır (örneğin kanın aşırısı, 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: Orgalütran® 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: Organon İlaçları A .Ş., PK. 120, 34673 Üsküdar-İstanbul Ruhsat tarihi: 23.09.2003 Ruhsat no. 114/76 Fiyat: 5'lik Paket: PSF (KDV Dahil) 362,42 YTL;(Eylül 2009) 1'lik Paket: PSF (KDV Dahil) 83,96 TL (Ağustos 2009)

WHOR0904-006

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FERPLEX® FOL

Demir Proteinsüksinilat + Kalsiyum Folinat

0'nu koruyun![1]



1) Pitkin R.M. Folate and neural tube defects. Am. J. Clin. Nutr. 2007;85 (suppl):285S - 8S

FORMULU: Her bir 15 ml'lik flakon etken madde olarak 40 mg. Fe3+ (üç değerlikli demir)'e eşdeğer demir proteinsüksinilat ve rezervuarlı kapak içerisinde, bastırmakla çözelti içerisine giren (0.185 mg. folinik asit'e eşdeğer) 0.235 mg. kalsiyum folinat pentahidrat içerir. **ENDİKASYONLARI:** Demir ve folik asit eksikliğinin tedavisi veya önlenmesi. **KONTRENDİKASYONLARI:** İçerdiği maddelerden herhangi birine karşı aşırı duyarlılıkta, hemokromatozis, hemosiderozisde, aplastik, hemolitik, sideroakrestik anemilerde, kronik pankreatit ve karaciğer sirozunda, kalıtımsal fruktoz intoleransı olanlarda kullanılmamalıdır. Pernisiyöz anemide eğer B12 vitamini ile beraber uygulanmıyorsa, kullanılmamalıdır. **UYARILAR/ÖNLEMLER:** Sürekli kanama, menoraji veya hamilelik durumları haricinde tedavi süresi 6 aydan uzun olmamalıdır. Süt proteinlerine duyarlılığı olanlarda, alkolizm, hepatit, aktif infeksiyoz durumlar, enterit, kolit, divertikülit ve ülseratif kolit, gibi intestinal sistemin enflamatuvar durumları, pankreatit ve peptik ülser durumlarında kullanımı dikkatle değerlendirilmelidir. **GEBELİK DÖNEMİNDE KULLANIMI:** Gebelik kategorisi A' dır. YAN **ETKİLER /ADVERS ETKİLER:** Alerjik belirtiler, diyare, bulantı, epigastrik ağrıya neden olabilir. Demir preparatlarının oral kullanımı ile birlikte feçes genellikle siyah bir renk alır. **İLAÇ ETKİLEŞİMLERİ:** Demir türevleri tetrasiklinler, bisfosfonatlar, kinolon grubu antiinfektif ilaçlar, penisilamin, tiroksin, levadopa, karbodopa, alfa-metildopa gibi ajanların emilimini ve biyoyararlanımını azaltabilir. Demir emilimi, 200 mg'ın üzerinde askorbik asitin eş zamanlı uygulaması ile artabilmekte veya antiasid kullanımı ile azalabilmektedir. Kloramfenikol demir tedavisine terapötik yanıtı geciktirebilir. Bitkiler, süt, kahve ve çay içerisinde yer alan ve demir ile kompleks yapan ajanlar (fosfat, fitat, oksalat gibi) demir emilimini baskılar. Bazı antineoplastik ve antilösemik ilaçlar, sülfamid ve trimetoprim gibi antibakteriyel ajanlarla ile birlikte kullanılmamalıdır. Süt ve yumurta ile birlikte kullanılması durumunda demirin emilimi engellenir. **KULLANIM ŞEKLİ VE DOZU:** FERPLEX FOL, **YETİŞKİNLERDE:** Günde 1-2 flakon iki eşit doza bölünmüş olarak ve tercihen yemeklerden önce alınır. **ÇOCUKLARDA:** Hekimin önerisine göre tercihen yemeklerden önce günde 1.5 ml./kg. şeklindeki dozaj 2 veya 3'e bölünerek uygulanır. **DOZ AŞIMI:** Demirin yüksek dozda alınımını izleyen 6 – 8 saat süresinde hastada abdominal ağrı, bulantı, kusma, diyare ve hematemez görülebilir. Beraberinde uyku hali, sararma siyanoz, şok ve koma hali de eşlik edebilir. Ipeka şurubu ile emesis oluşturulup; hasta komatoz ise sodyum bikarbonatla lavaj yapılır. Sıvı ve elektrolit dengesi sağlanır, ve asidoz için i.v. sodyum bikarbonat uygulanır. Antidotu deferoksamindir. **TİCARİ TAKDİM ŞEKLİ VE AMBALAJ MUHTEVASI:** Kutuda 15 mL'lik renkli cam flakon + rezervuarlı kapaklı ambalajlarda 10 adet **RUHSAT TARİHİ VE NUMARASI:** 12.11.2003 – 203/ 40 **RUHSAT SAHİBİ:** Italfarmaco S.p.A./İtalya lisansı ile Abdi İbrahim İlaç San. ve Tic. A.Ş. **İMAL YERİ:** Abdi İbrahim İlaç San. Ve Tic.A.Ş. Hadımköy-İstanbul **PERAKENDE SATIŞ FİYATI (KDV dahil):** 17,12 TL (Ocak 2010). Reçete ile satılır. Ayrıntılı bilgi için firmamıza başvurunuz. Abdica İlaç San. ve Tic. A.Ş. Kore Şehitleri Caddesi No:19 Zincirlikuyu-İstanbul T. +90 212 365 49 00 F. + 90 212 72 90 46

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Cover Picture: "Endometrium co-culture" Elif Gelenli, PhD., Kocaeli University

ISSN 1309-0399

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Basım Yeri: Görsel Dizayn Ofset Matbaacılık Tic. Ltd. Şti. - +90 212 671 91 00
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FORMÜLÜ: Beher vajinal tablet; 50 mg. Lactobacillus acidophillus, 0.03 mg. Estriol ve Laktoz içerir. **ENDİKASYONLARI:** Vajinal akıntı, Candida albicans ve Gardnerella vajinalis'ten oluşan vajinal enfeksiyonlar, antiseptik ajanlar ya da antibiyotiklerle, lokal ya da sistemik tedavi sonucu oluşan Döderlein florası bozulması, menopoz sonrası görülen Döderlein florası bozulması, örneğin; östrojen takviyesinde ilave tedavi olarak; tekrarlayan Candida enfeksiyonlarında; her menstruasyondan sonra Gynoflor ile proflaktik tedavi yapılması önerilir. **KONTRENDİKASYONLARI:** Meme ve vajende görülen malign değişiklikler, bilinmeyen orijinli vajinal kanamalar. Cinsel olgunluğa erişmemiş genç kızlar bu preparatı kullanmamalıdır. **UYARILAR/ÖNLEMLER:** Hamilelik ve emzirme döneminde kullanım: Gebelik kategorisi D'dir. Gynoflor, içeriğindeki estriolün düşük dozda olması nedeniyle fetüs üzerinde olumsuz bir etki yapması beklenmez. Ancak Gynoflor, gebeliğin sadece ilk trimesterinde (ilk üç ayında) sadece doktor muayenesi sonrasında ve yarar/zarar oranı dikkate alınarak kullanılmalıdır. Hamilelik sırasında kesinlikle gerekli olmadıkca verilmemelidir. Olası zararlar konusunda hastalar uyarılmalıdır. Gynoflor, emzirme sırasında kullanılabilir. **YAN ETKİLER/ADVERS ETKİLER:** Bugüne kadar bildirilmiş yan etki mevcut değildir. **İLAÇ ETKİLEŞMELERİ VE DİĞER ETKİLEŞMELER:** Döderlein bakterisi, antimikrobiyal ajanlara hassastır, Antimikrobiyal ajanlarla lokal ve sistemik tedavi Gynoflor'un etkisinde azalmaya neden olabilir. **KULLANIM ŞEKLİ VE DOZU:** 6-12 gün süre ile akşamları yatmadan önce vajen derinliğine 1-2 tablet yerleştirilir. Bu arada menstruasyon görülürse tedavi kesilir ve bitiminde tekrar devam edilir. Postmenopozal atrofik vajinitte başlangıçta 6-12 gün süre ile günde 1 vajinal tablet vajen derinliğine yerleştirilir. İdamesinde haftada 1-2 vajinal tablet olarak tedaviye devam edilir. **DOZ AŞIMI VE TEDAVİSİ:** Gynoflor herhangi bir toksikolojik risk taşımaz. **SAKLAMA KOŞULLARI:** 2°C - 8°C arasında buzdolabında saklayınız. Dondurmayınız. **TİCARİ TAKDİM ŞEKLİ VE AMBALAJ MUHTEVASI:** 12 vajinal tablet içeren blister ambalajlarda. **RUHSAT SAHİBİ:** ABDİ İBRAHİM İLAÇ PAZARLAMA A.Ş. Maslak/İstanbul **RUHSAT TARİH VE NO:** 11.12.1996 100/63 **İMAL YERİ:** MEDİNOVA–İsviçre lisansıyla Haupt Pharma Amareg GmbH Regensburg–Almanya. Reçete ile satılır. **PERAKENDE SATIŞ FİYATI (KDV DAHİL):** 23,69TL (12.01.2009) Daha geniş bilgi için firmamıza başvurunuz. Abdica İlaç Sanayi ve Ticaret A.Ş. Kore Şehitleri Cad. No: 19 Zincirlikuyu-İstanbul T.: 0 212 365 49 00 F.: 0 212 272 90 46

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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.

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ARVELES®

DEKSKETOPROFEN TROMETAMOL

AMPUL IM/IV TABLET

Hızlı etki başlangıcı

Olumlu **güvenlik** profili

Kanıtlanmış **etkinlik**

Analjezik tedavide

ilk tercih

olarak uygulanmasını desteklemektedir.[1]





REFERANSLAR 1- Barbanoj et al: Dexketoprofen trometamol: clinical evidence supporting its role as a painkiller, Expert Rev. Neurother. 8(11), 1625-1640 (2008)

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 kolitli olan hastalar • Şiddetli kalp yetmezliği olan hastalar •Orta veya şiddetli böbrek fonksiyon bozukluğu olan hastalar • Şiddetli karaciğer 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 güvenirliği 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 hastalarda, 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 enfeksiyöz 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 sülfonamidler; **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'dır, 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'ı 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 dönemle 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 ila 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 IV 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 ampüller (6 ampul). **RUHSAT SAHİBİNİN İSİM ve ADRESİ:** UFSA 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:* 29.12.2006-121/57. **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-ITALYA. / 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–ITALYA. 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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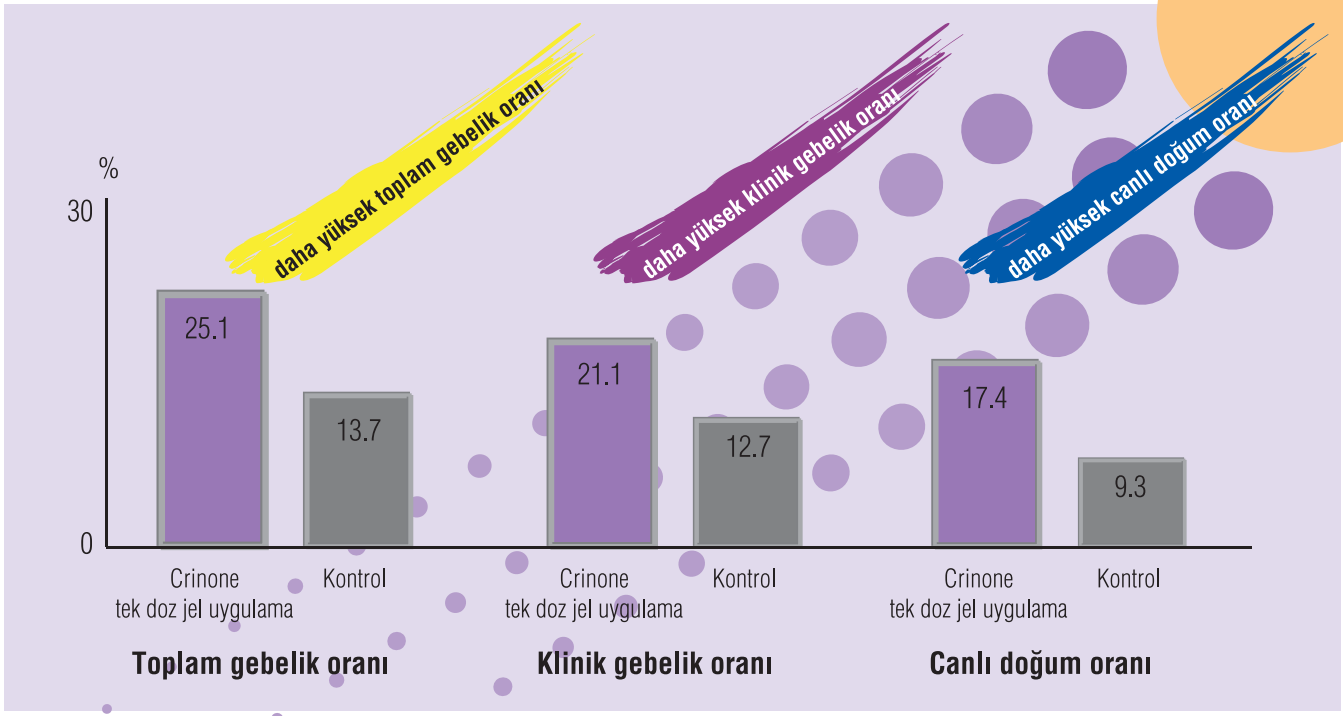
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İntra uterin inseminasyon (IUI) sikluslarında luteal faz desteği gebelik başarısını arttırır.[1]

Crinone Jel ile luteal faz desteği gebelik şansını yaklaşık **2 kat** arttırır.[1]





Referans
1. Ahmet Erdem, Mehmet Erdem, İsmail Guler, Songul Atmaca Fertility and Sterility August 2008 (Vol. 90, Issue 2, Pages 360-366)

CRİNONE® %8 (vajinal jel) Formülü: Her vajinal aplikatör aktif madde olarak 90 mg progesteron ve koruyucu madde olarak sorbik asit içerir. **Endikasyonlar:** 1. Estrojen replasman uygulamalarında ek tedavi. 2. Olası hormonal dengesizliğe bağlı bozukluklar - Premenstrual sendroma bağlı rahim krampları ve anormal / ağrılı kasılmalar. - Organik patoloji yokluğunda disfonksiyonel rahim kanaması - Estrojen tedavisi görenlerde sekonder amenore 3. İnfertilite tedavisi Progesteron eksikliği dokümante edilmiş veya progesteron eksikliğinden şüphelenilen kadınlarda, Yardımcı Üreme Teknikleri (ART) uygulamalarının bir bölümü olarak progesteron takviyesi veya progesteron replasmanı. **Kontrendikasyonları:** 1. Göğüste veya genital organlarda bilinen veya şüphelenilen malignansı. 2. Missed abortion (atlanmış düşük). 3. Teşhis edilmemiş rahim kanaması. 4. Aktif tromboflebit veya tromboembolik bozukluklar veya hormona bağlı bir tromboflebit veya tromboembolik bozukluklar geçmişi. 5. Karaciğer fonksiyon bozukluğu veya karaciğer hastalığı. 6. Crinone® formülasyonunun bileşenlerinden herhangi birine karşı bilinen hipersensitivite. **Uyarılar/önlemler:** Crinone® ile trombotik bozukluklar bildirilmemiştir. Bununla birlikte, bazı araştırmalarda, hormon replasman tedavisine bağlı olarak tromboflebit ve/veya tromboembolik bozukluklarda bir artış riski bildirilmiştir. Hormon replasman tedavisi sırasında hekim, trombotik bozukluklar (tromboflebit, retinal tromboz, serebral embolizm ve pulmoner embolizm dahil) olasılığına karşı dikkatli olmalı ve bunların erken belirtilerine karşı hazır bulunmalıdır. Bunlardan herhangi birinin meydana gelmesi veya şüphelenilmesi halinde hormon replasman tedavisi hemen kesilmelidir. Trombotik bozukluklara ilişkin risk faktörü taşıyan hastalar dikkatle gözlenmelidir. Tedavi öncesi ve sırasında periyodik muayenelerde tıbbi anamnez ve fiziki muayenede özellikle göğüsler ve pelvik organlar üzerinde durulmalı ve bir Papanicolaou smear alınmalıdır. Progestojenler bir ölçüde sıvı tutulmasına neden olabilecekleri için bu faktörden etkilenebilecek epilepsi, astım, migren ve kalp veya böbrek fonksiyon bozukluğu gibi hastalıkları olan kadınların dikkatle gözlem altında tutulması gerekir. Bütün düzensiz vajinal kanama vakalarında olduğu gibi ara kanama vakalarında, organik hastalığın bulunup bulunmadığını değerlendirmek üzere diyagnostik uygulamalar gerekli olabilir. Depresyon geçmişi olan hastalar dikkatle gözlenmeli ve depresyon ciddi bir ölçüde tekrar ortaya çıkarsa Crinone® kesilmelidir. Progestojenlerle tedavi, postmenopozal semptomların ortaya çıkışını maskeleyebilir. Progestojenlerin endometriyum gibi organların yapısında ve patolojisindeki etkisi nedeniyle ilgili numuneler verilen patologlara, progestojen tedavisi uygulandığı söylenmelidir. Progestojenler önceden mevcut porfirya belirtilerini kötüleştirebilir. Bu nedenle, bu gibi hastalarda Crinone® kullanılması önerilmez. **Yan etkiler/advers etkiler:** Crinone® genellikle iyi tolere edilmektedir. Klinik araştırmalarda, Crinone® tedavisi sırasında aşağıdaki advers etkiler bildirilmiştir: Bütün vücutta - karın, sırt, eklem, bacak ağrısı veya perineal ağrı; şişkinlik, göğüslerde şişkinlik/hassasiyet, yorgunluk, sıcak basması, laktasyon, su tutulması. Gastrointestinal sistem - konstipasyon, diyare, dispepsi, geğirti, flatülans, mide ağrısı, mide bulantısı, kusma. Genitoüriner sistem - cinsel arzunun azalması, dismenore, disparoni, sık idrara çıkma, lökore, noktüri, vajinal kaşıntı/ iritasyon, vajinal kanama ve lekelenme, vajinal sekresyonda artma. Sinir sistemi - baş dönmesi, depresyon, ruhsal durumda değişkenlik, başağrısı, uykusuzluk, iritabilite, sinirlilik, somnolans. Cilt - akne, genital prürit. Yukarıdaki bütün olaylarla Crinone® tedavisinin ilişkisi bilinmemektedir. Çoğu yan etki hafif ve geçicidir ve Crinone® tedavisinin sürdürülmesi ile ortadan kalkmaktadır. **İlaç etkileşmeleri ve diğer etkileşmeler:** Diğer ilaçlarla hiç bir etkileşim bildirilmemiş olmakla birlikte Crinone®'un diğer intravajinal preparatlarla birlikte kullanılması önerilmemektedir. Hastaya intravajinal antifungal bir tedavi uygulanıyorsa oral tedaviye geçilmesi önerilir. Laboratuvar testleri etkileşimleri: Crinone®'un laboratuvar testleri üzerinde herhangi bir etkisinin olup olmadığı bilinmemektedir. **Kullanım şekli ve dozu:** Crinone® ile intravajinal tedavi, spesifik endikasyona ve her hastanın terapötik cevabına göre ayarlanmalıdır. En düşük etkin doz uygulanmalıdır. Crinone®'un, endometriyumda sekretuar bir transformasyonu endüklemek üzere vajinal yoldan uygulanması ancak endometriyum endojen veya eksojen estrojen ile yeterli ölçüde hazırlanmışsa endikedir. Bu gibi vakalarda, gebelik meydana gelmemişse Crinone® tedavisinin kesilmesinden sonraki 3-7 gün içinde kesilme kanaması meydana gelir. Crinone®, temin edilen aplikatörle intravajinal olarak uygulanır. Crinone® her gün aynı zamanda uygulanmalıdır. Bir Crinone® dozunu unuttuğunuzu hatırlar hatırlamaz, o dozu hemen uygulayın ve önceki programa göre uygulamaya devam edin. Önerilen günlük dozdan fazlasını uygulamayın. Olağan Doz Aralığı: Crinone® %4 (45 mg) veya Crinone® %8 (90 mg). Dozaj programında, bir menstruel siklusun veya estrojen siklusların 28 gün olduğu ve 1. günün, kanamanın veya siklik estrojen tedavisinin ilk günü olduğu kabul edilmektedir. ESTROJEN REPLASMAN UYGULAMALARINDA EK TEDAVI: 28 günlük her bir estrojen tedavisinin son 12 gününde, gün aşırı (6 uygulama) bir vajinal Crinone® uygulaması. OLASI HORMONAL DENGESİZLİKLERLE İLGİLİ BOZUKLUKLAR: Estrojen verilerek hazırlanmış kadında, tercihen sabahları olmak üzere toplam 6 doza kadar gün aşırı bir vajinal Crinone® uygulaması. İNFERTİLİTE TEDAVİSİ – ART UYGULAMASINDA PROGESTERON TAKVİYESİ VEYA REPLASMANI: Progesteron eksikliğinden şüphelenilen, normal olarak ovülasyon görülen kadınlarda progesteron takviyesi olarak, dokümante edilen ovülasyondan sonra başlamak üzere günde bir veya iki kez Crinone® %8 (90 mg) uygulaması. Çoğu kadında günde 90 mg ile cevap alınır. Gebelik meydana gelirse tedavi 12 haftaya kadar devam edebilir. Luteal faz eksikliği gibi bir progesteron eksikliğinden şüphelenilen, normal olarak ovülasyon görülen kadınlarda daha düşük dozlar kullanılabilir. Bir ART rejiminin bir bölümü olarak endometrial takviye için günde bir veya iki kez Crinone® %8 (90 mg) ile uygulamaya başlanır. Çoğu kadında günde 90 mg ile cevap alınır. Bununla birlikte bazı kadınlarda günde iki kez 90 mg gerekli olabilir. Gebelik kesinleşirse, 12 haftaya kadar Crinone® %8 (90 mg)'a devam edilir. Crinone® %8 (90 mg) her gün aynı zamanda uygulanmalıdır. %4'lük jelden doz artışının, ancak %8'lik jel kullanılarak gerçekleştirilebileceği unutulmamalıdır. Uygulanan %4'lük jelin hacminin artırılması, absorbe olan progesteron miktarını artırmamaktadır. **Saklama koşulları :** 25°C'nin altındaki oda sıcaklığında saklayınız. **Ticari takdim şekli :** Crinone® v %8, 15 aplikatör içeren ambalajlarda sunulmaktadır. **Ruhsat sahibi:** Merck İlaç Ecza ve Kimya Tic. A.Ş. Kayışdağı Cad. Karaman Çiftliği Yolu Kar Plaza Kat 7 34752 İçerenköy-İstanbul **İmal yeri :** Central Pharma Ltd. Ingiltere **Ruhsat tarihi :** 10.11.2000 **Ruhsat no:** 109/16 **Perakende satış fiyatı :** 74,01 TL. (04.12.2009). **Reçete ile satılır. Daha geniş bilgi için firmamıza başvurunuz.**

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H. Alper Tanrıverdi (Aydın, Turkey)
Cemil Yaman (Linz, Austria)

The manuscript, figures and tables, prepared under "Microsoft Office Word program", double spaced on one side of A4 sized page, with margins of at least 25 mm should be submitted. Original articles should not exceed 15 pages including the tables and figures. Brief reports should not exceed 5 pages including one figure and/or maximum two tables. As the journals policy only online submissions of manuscripts are accepted after May 2005.

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DECAPEPTYL® 0.1 mg Ürün Kısa Prospektüs Bilgisi

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.l 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.l 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.

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MENOPUR® Ürün Kısa Prospektüs Bilgisi

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. Erneklerde; 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. Erneklerde: Menopur® tedavisi sırasında bazen jinekomasti, göğüste ağrı, mastit, bulantı, anormal lipoprotein traksiyonu, 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 (oliguri), kan basıncında düşme (hipotansiyon) ve kan pıhtısıyla kan damarlarının tıkanması (tromboembolik olay) olabilir. Aşırı uyarılmanın ilk belirtileri ortaya çıkığında tedavi hemen durdurulmalıdır. Gebelikle beraber bu yan etkiler şiddetlenebilir ve uzun süre devam eder; hayati 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 erneklerde 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 follikullerin 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 follikullerde 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. Erneklerde 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.

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State concisely the purpose and rationale for the study and cite only the most pertinent references as background.

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State the importance and significance of your findings but do not repeat the details given in the Results section. Limit your opinions to those strictly indicated by the facts in your report. Compare your finding with those of others. No new data are to be presented in this section.

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Ertan AK, Tanriverdi HA, Schmidt W. Doppler Sonography in Obstetrics. In: Kurjak A, Chervenak FA, editors. Ian Donald School Textbook of Ultrasound in Obstetrics and Gynecology. New Delhi, India: Jaypee Brothers; 2003. p. 395-421.
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Journal of the
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Contents

Original Investigations

69 Rectus fascia colpopexy for post-hysterectomy vault prolapse: a valid option
Rajiv Mahendru, Haryana, India

73 General information on periventricular-intraventricular hemorrhage in premature infants in mainland China
Jing Liu, Li-wen Chang, Qi Wang, Gui-lian Qin, Beijing, Whuan, China

78 A study on knowledge, attitude and practice of contraception among college students in Sikkim, India
Prachi Renjhen, Ashwini Kumar, Sanjay Pattanshetty, Afrin Sagir, Charmaine Minoli Samarasinghe, Melaka, Malaysia, Manipal, India

82 Detection of fetal RhD gene from maternal blood
Tuba Günel, İbrahim Kalelioğlu, Hayri Ermiş, Kılıç Aydınlı, İstanbul, Turkey

86 The relationship of ceruloplasmin and neural tube defects
Çağlar Yazıcıoğlu, Fatma Bahar Cebesoy, Özcan Balat, Ebru Dikensoy, Hakim Çelik, Özcan Erel, Gaziantep, Şanlıurfa, Turkey

89 Incidence of diabetes mellitus at postpartum six to twelve months following the diagnosis of gestational diabetes mellitus
Özlem Seçilmiş Kerimoğlu, Serdar Yalvaç, Deniz Karçaaltınçaba, Ömer Kandemir, Ankara, Turkey

95 Shortening the second stage of labor?
Rajiv Mahendru, Haryana, India

Review

99 The rationale behind collecting umbilical cord blood
Nicolas H. Zech, Nikolas Broer, Iris Ribitsch, Mathias H. Zech, Karl-heinz Broer, Kubilay Ertan, Karl-heinz Preisegger, Graz, Austria, Cologne, Düsseldorf, Leipzig, Leverkusen, Germany

Case Reports

102 Laparoscopic surgery of interstitial (cornual) pregnancy, a case report
Ziya Günenç, Banu Bingöl, Aygen Çelik, Serpil Bozkurt, Ümit Özekici, İstanbul, Turkey

105 Successful management of uterine prolapse during pregnancy with vaginal pessary: a case report
Esra Esim Büyükbayrak, Gülden Yılmazer, Ayşe Gül Özyapı, Bülent Kars, Ayşe Yasemin Karageyim Karşıdağ, Cem Turan, İstanbul, Turkey

107 Herlyn-Werner-Wunderlich syndrome (uterus didelphys, blind hemivagina and ipsilateral renal agenesis)-a case report
İlker İnan Arıkan, Müge Harma, Mehmet İbrahim Harma, Ülkü Bayar, Aykut Barut, Zonguldak, Turkey

110 Incomplete androgen insensitivity (reifenstein syndrome) - a case report
Volkan Turan, Özgür Yeniel, Mete Ergenoğlu, Coşan Terek, Murat Ulukuş, İzmir, Turkey

113 Calcified pure uterinelipoma mimicking myoma
Arghya Bandopadhyay, Sailes Ray, Pranati Bera, Mimi Gangopadhyay, Indranil Chakrabarti, Biswajit Dey, Darjeeling, India

Brief Communication

115 Atypical preeclampsia and eclampsia: report of four cases and review of the literature
Mustafa Albayrak, İsmail Özdemir, Yavuz Demiraran, Süber Dikici, Düzce, Turkey

Letter to Editor

118 The characteristics of sexual behaviour and extent of condom usage among sexually active Croatians from Eastern Croatia, letter to the editor
Emre Karaşahin, Cihangir Mutlu Ercan, İbrahim Alanbay, İskender Başer, Ankara, Turkey

Quiz

119 Pulmonary atresia
Özlem Özdeğirmenci, Metin Kaplan, Ankara, Turkey

Journal of the
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Editorial

Dear Colleagues,



This issue of the Journal of the Turkish – German Gynecological Association (JTGGA) is introduced with plenty of meritorious scientific studies. Our objective is to collect more research studies from Turkey and the international gynecology and obstetrics community in the near future.

The second quarter of 2010 was a very beneficial and effective period for the Turkish-German Gynecological Education and Research Foundation as we organized two important activities. The first one was the 1st Symposium on Controversies in Infertility which we have co - organized with Istanbul Branch of the Turkish Association of Gynecology and Obstetrics on April 17th - 18th, 2010. More than two hundred fifty participants have been present at the symposium even if some foreign participants could not join us because of the volcano eruption in Iceland. The major topics in this meeting were the most actual subjects of In Vitro Fertilization (IVF) such as Minimal Ovarian Stimulation, Single Embryo Transfer (SET) and Cypropreservation.

The other organization was the 2nd Social Responsibility Project of the Turkish-German Gynecological Education and Research Foundation called “Just For Me”. The Social Responsibility Project has been organized at two destinations, Şanlıurfa and Birecik between 27th and 29th of May, 2010 with the support of the local government and municipalities, the Ministry of Health, Harran University and local hospitals. The Project was intended for the benefit of two target groups. Sessions directed to local health care professionals has been followed by many doctors, nurses and midwifes working in the area. The other sessions was intended for the benefit of the public. There was a high interest in these sessions by the local people, more than 250 participants in Şanlıurfa and 150 participants in Birecik. Servical Smear Screening for the public and some difficult operations has been performed in cooperation with the regional health professionals. We believe this Social Responsibility Project was a great honour for us to serve our country.

Kind regards,

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

Rectus fascia colpopexy for post-hysterectomy vault prolapse: a valid option

Histerektomi sonrası vajinal apikal prolapsus için rektus fasya kolpopeksisi: geçerli bir seçenek

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Abstract

Objective: Considering the great variety of techniques and disagreement about the ideal route, there is a need for a safe, simple and effective method for the management of apical prolapse.

Material and Methods: Twenty seven cases of post- hysterectomy vault prolapse (twenty four following vaginal and three after total abdominal hysterectomy) were treated surgically by anterior abdominal wall colpopexy with autogenous rectus fascia strips.

Result: Except for minor complaints like- vomiting, fever and urinary retention in 3.7% cases each (n=1), no major complications were encountered. Moreover, no recurrence, on follow-up thus far.

Conclusion: Using autogenous rectus fascia strips in anterior abdominal wall colpopexy is not only a simple, cheap and effective method of treating vault prolapse but is also devoid of any serious complications such as described with other techniques.

(J Turkish-German Gynecol Assoc 2010; 11: 69-72)

Key words: Vault Prolapse, rectus fascia, enterocoele

Received: 3 February, 2010 **Accepted:** 21 March, 2010

Özet

Amaç: Değişen birçok teknik ve yaygın kabul görmüş bir yöntem olmaması nedeniyle, apikal prolapsuslarda basit, güvenli ve etkin bir yönetime ihtiyaç vardır.

Gereç ve Yöntemler: Yirmi yedi post-histerektomi vajinal apeks prolapsusu olan (24 tanesi vajinal histerektomi, 3 tanesi de abdominal total histerektomi sonrası) vaka otolog rektus fasya şeriti kullanılarak abdominal kolpopeksi yöntemi ile opere edildiler.

Bulgular: Kusma, ateş, %3.7 vakada (n=1) üriner retansiyon gibi minor yakınmaların yanında herhangi bir mjor komplikasyon gözlenmedi. Dahası, şu ana kadar izlemde herhangi bir rekürrens de görülmedi.

Sonuç: Otolog rektus fasyası kullanılarak uygulanan apikal prolapsus tedavisi sadece basit, ucuz ve etkin değil, aynı zamanda diğer yöntemlerde bildirilen major komplikasyonların görülmemesi nedeniyle tercih edilmesi gereken bir yöntemdir.

(J Turkish-German Gynecol Assoc 2010; 11: 69-72)

Anahtar kelimeler: Vajinal apikal prolapsus, rektus fasyası, enterosel

Geliş Tarihi: 03 Şubat 2010 **Kabul Tarihi:** 21 Mart 2010

Introduction

Post-hysterectomy apical (vault) prolapse is referred to as the descent of the vaginal vault/cuff scar below a point that is 2 cm less than the total vaginal length above the plane of the hymen (1). This condition is shown to follow 11.6% of hysterectomies performed vaginally for prolapse and 1.8% of those performed abdominally for other indications (2). Several surgical procedures have been described for the treatment of vault prolapse and, given the available evidence of complications and limitations of each, it is difficult to recommend one technique over the other (3). Regarding vault suspension to the anterior abdominal wall, the number of studies available are insufficient to assess its efficacy.

Material and Methods

In the period between Dec.2002 to Apr. 2005, 27 cases of vaginal vault prolapse were treated by the innovative technique described hereunder. 88.89% (n=24)had had undergone vaginal hysterectomy for genital prolapse and the remaining 11.11% (n=3) had apical prolapse developing after abdominal hysterectomy for the indications of leiomyoma uteri in two cases and dysfunctional uterine bleeding in the other case. The mean time which elapsed from the previous surgery was 27 months, with the shortest being 11 months and the longest being 50 months. Two of these cases in the vaginal hysterectomy group had undergone prior surgery for vault prolapse-one had sacrocolpopexy 13 months previously, and the other had some vaginal procedure 27 months previously, for which there is no record available, but both of these developed recurrence. Mean age of our patients was 56.3 years, with the youngest and oldest being 33&67 years respectively. 19 patients belonged to a lower socio- economic strata out of which, 17 were labour class manual working women and two were routine housewives as also were five of the other group of 8 of middle income group. The remaining 3 were field health workers (n=2) and school teacher (n=1). Based on the quality of life, complaints, history, clinical examination (with classification according to the POP-Q system)-a questionnaire was filled for each patient. Six of the patients had stress incontinence (all after vaginal hysterectomy). The previous history of one patient included Pulmonary Tuberculosis for which she had had a full course of anti-

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doi:10.5152/jtgga.2010.01

tubercular treatment and at present was symptom free. Prior to surgery, the presence of chronic cough & chronic constipation complaints were clearly addressed. Written informed consent was obtained from all the patients and the Institutional Ethical Committee approved the study. Clinical examination was conducted for the presence of enterocoele (n=6-all of vaginal hysterctomy), cystocole (n=9), rectocoele (n=23) and, genuine stress incontinence (n=6). Initially, bladder catheterisation was performed with a 16 french indwelling Foley's catheter followed by tight vaginal packing pre-operatively. Technique employed: transverse skin incision (Pfannenstiel) about 8 cm long at the level of the anterior superior iliac spine. The rectus sheath was exposed by separating the subcutaneous adipose tissue from its surface for the entire length of the incision and about 2 cm in breadth. An approximately 1cm longitudinal incision was made in the rectus sheath in the midline and laterally this incision extended transversely about 3-4 cm on either side superiorly as well as inferiorly beyond the lateral margin of the rectus muscle. Thus two strips of the rectus fascia were produced (Figure 1) with free medial margins which were secured with silk no.1 with the thread kept long on both the sides. Peritoneal cavity was approached in the usual way and abdominal packing done followed by identification of the vault (Figure 2: made easy because of vaginal packing initially) which was then held with Allis' forceps at both of its angles. Peritoneum between these Allis' forceps over the vault was incised. A long curved artey forceps was used to make a track retroperitoneally,parallel to the erstwhile round ligament, exercising utmost care so as to avoid the ureter on the way. On reaching lateral to the rectus muscle the medial margin of the ipsilateral carved rectus sheath strip was held and brought to the angle of the vault, ensuring that no twisting occured. A similar procedure was performed on the opposite side. Once done, the silk threads (kept long earlier), were tied on to the vault with optimal tension (Figure 3). Reperitonisation was done by suturing the incised peritoneum on the vault. Patients with an enterocoele were treated by the Moschowitz operation (4). In those six patients having stress incontinence, concomitant pubovaginal sling repair was carried out. Abdomen was closed in layers after securing haemostasis and removing the sponge pack. Sub-cuticular sutures were applied in all cases. Vaginal packing done prior to surgery was removed. In cases with a rectocele, perineorrhaphy with levator myorrhaphy was done followed by vaginal packing for 24 hrs in such cases. Intravenous fluids were continued for 24 hours and Injectable antibiotics for 36 hours. Oral Fluids were offered after 24 hours. Patients were made ambulatory 24-36 hours following surgery. The catheter was removed after 24 hours, except in patients who also underwent anti-incontinence repair when it was taken out after 5 days post-operatively.

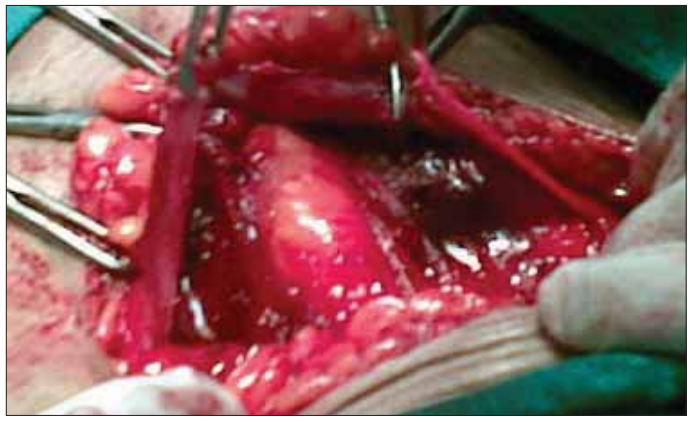


Figure 1. Rectus fascia strips



Figure 2. Vault as seen in the abdominal cavity (easily identified due to pre-op intravaginal packing)



Figure 3. Pulled-up vault after repair with retroperitoneal rectus fascia strips

Observations

Mean operating time was approximately 50 minutes. In those cases in whom only anterior abdominal wall colpopexy was done the procedure was accomplished in 45 minutes, but in those cases in whom additional surgical procedures were required, such as Moschowitz/ Burch/perineorrhaphy, an extra 15 minutes were taken but the duration of surgery never extended beyond 70 minutes. Intraoperative difficulties encountered were not very serious: 3 cases had omental and 1 had small gut adhesions on the vault. Amount of intraoperative blood loss was between 200 to 450 ml (more loss in cases where perineorrhaphy was also done); nevertheless no blood transfusion was required in any of the cases either intra-op. or post-operatively In the post-operative period ,one patient (3.7%) had vomiting on the 2nd day, another (3.7%) had fever. 33% (n=9) of patients felt

slight tightness in the abdomen but not amounting to discomfort or concern.One patient (3.7%) who had a simultaneous urinary anti-incontinence operation had urinary retention following removal of the indwelling catheter on the 5th post-operative day and had to be re-catheterised for another 48hrs and toning-up of the bladder carried out.One patient had bleeding from the perineorrhaphy wound on removal of the vaginal pack but not such as to cause concern. 21 patients were discharged 3 days after surgery, those six cases who had concomitant a pubo-vaginal sling for stress incontinence were discharged 5 days after surgery and all the patients were recalled on the 7th day for removal of sub-cuticular abdominal wound stitches. One patient who had retention of urine was re-admitted for 72hrs. At discharge, per-speculum examination was conducted and the success criteria considered was That, on straining, the vault which was pre-operatively prolapsing was seen to be pulled up/retracting. 18 (66%) patients are under regular follow-up, (longest follow-up-6yrs 8 months and shortest follow-up of 4yrs 4 months), 9 patients were lost after initial follow-ups and all these patients confirm the success of the procedure. None of the patients showed recurrence of the symptoms.

Discussion

The incidence of vault prolapse is uncertain but appears to be increased five fold after vaginal hysterectomy (5). The incidence in our institute appears to be marginally better than the quoted one (2), being about 7.8% of hysterectomies performed vaginally for prolapse and 1.2% of those performed abdominally for other indications Conservative measures include pelvic floor exercises and different type of pessaries.There is no evidence to suggest that pelvic floor exercises are helpful in vault prolapse (6). Conservative measures may be used to treat this condition in women unfit for surgery or those who require symptomatic relief while awaiting surgery (5). Correction of apical defect remains a surgical challenge-suspension of the vaginal apex is the keystone of surgical repair for pelvic organ prolapse.There are many surgical procedures for treating post-hysterectomy vaginal vault prolapse. The treatment route may be vaginal or abdominal (7). Anterior and posterior vaginal wall repair along with obliteration of the enterocoele sac are inadequate for post-hysterctomy vaginal vault prolapse: this standard repair operation does not support the vaginal vault, and there are risks of vaginal narrowing and shortening and thus dyspareunia (8). Vaginal repair often results in a narrowed and shortened vagina with diminished function (9). Moreover, posterior vaginal sling experience in elderly patients yields poor results (10). The established surgical options lie between a vaginal sacrospinous fixation or an abdominal procedure such as sacrocolpopexy or vault suspension operation (5). Complications of sacrospinous fixation included blood loss, bladder injury, rectovaginal haematoma and vaginal pain, and that of sacrocolpopexy blood loss, bladder injury, incisional hernia, mesh rejection, and wound infection (11). In another study sacrospinous fixation was associated with significantly more intraoperative blood loss, longer catheterisation and hospital stay and more sexual dysfunction (12). Moreover it has a higher failure rate (13). There is a significantly higher incidence of recurrent vault prolapse and recurrent stress incontinence in the vaginal group (14). In anterior abdominal wall colpopexy using autogenous strips of rectus fascia to repair post-hyst prolapse of the vaginal vault, preservation of a physiologically useful vagina and vaginal caliber and depth were secured and no recurrence arose (15). Successful use of rectus sheath tendon flap was performed in 20 patients with vaginal vault prolapse with minimal complications (16). A comparative study of abdominal colpopexy using rectus fascia and sacral fixation for the treatment of prolapsed vagina following hysterectomy was performed-the abdominal approach yields better results (17). Although augmentation by foreign material is not altogether a new concept, the introduction of commercial kits make mesh procedures more standardized but not necessarily technically easier to perform (18). Recently, a study was carried out involving hitching the vault with a synthetic tape inserted along the lines of the round ligaments and fastened to the external oblique aponeurosis (19). However, use of mesh is associated with infection (20). In patients who are additionally incontinent, an anti-incontinence procedure such as Burch colposuspension or pubo-vaginal sling is usually performed at the same time (20). The role of prophylactic surgery for occult stress incontinence is unclear (21). All pelvic floor defects should be identified to enable surgical repair of significant and potential defects (22). The great variety of techniques described indicate that there is disagreement about the ideal route or technique to be used (7).

Conclusion

No doubt greater awareness at the time of the original hysterectomy may be the better solution in reducing the incidence of vault prolapse. Nevertheless, anterior abdominal wall colpopexy using autogenous strips of rectus fascia is a simple operation,for repair of post-hysterectomy prolapse of the vaginal vault providing the desirable result of preserving a physiologically useful vagina with normal caliber and depth; moreover,there is no recurrence in follow-up. This anterior abdominal wall colpopexy is a safe operation with low morbidity and longstanding good results with patient satisfaction and can be recommended for sexually active women.

Conflict of interest

Authors declare that there is no conflict of interest.

Acknowledgement

M.M. Educational Trust

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General evaluation of periventricular-intraventricular hemorrhage in premature infants in mainland China

Çin'de prematür infantlardaki periventriküler-intraventriküler hemorajiler hakkında genel bilgiler

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Abstract

Objective: To explore the incidence and analyze the high risk factors of PIVH in premature infants in mainland China.

Materials and Methods: A total of 1122 premature infants at <37 weeks gestation were enrolled in this study. All the infants received intracranial ultrasound examinations within 1 week after birth,and the perinatal data were recorded to analyze the high risk factors for PIVH.

Results: The results showed that the incidence rate of PIVH was 55.2% in mainland Chinese population. Among these cases, mild degrees of PIVH accounted for 82.2% and severe degrees of PIVH accounted for only 17.8%. The most important risk factors related to PIVH were low gestational age, low birth weight, low Apgar score and ventilatory treatment, etc.

Conclusions: It suggested that there were many high risk factors related to PIVH in premature infants and a screening cutoff point of 2000 g appeared to be more adequate for China.

(J Turkish-German Gynecol Assoc 2010; 11: 73-7)

Key words: Periventricular-intraventricular hemorrhage, premature infant, risk factors, Chinese population

Received: 6 December, 2009 **Accepted:** 4 February, 2010

Özet

Amaç: Çin'de prematur infantlardaki PIVH insidansını araştırmak ve analiz etmek.

Gereç ve Yöntemler: Otuzyedi hafta öncesinde doğmuş 1122 prematur infant çalışmaya dahil edildi. Tüm bu bebekler doğumdan 1 hafta sonra intrakranial ultrasonografi incelemesine tabii tutuldu ve perinatal bilgileri PIVH için risk faktörlerinin analiz etmek için kaydedildi.

Bulgular: Ana Çin populasyonunda PIVH insidansı %55.2 olarak saptandı. Bu olgularda hafif PIVH oranı %82.2, ağır PIVH ise %17.8 olarak saptandı. PIVH için en önemli risk faktörleri erken gebelik haftaları, düşük doğum kilosu, düşük Apgar skoru ve ventilatuar tedaviler vb. olarak belirlendi.

Sonuç: Öyle görünmektedir ki prematur infantlardaki PIVH gelişimi için birçok risk faktörü bulunmaktadır. Çin'de PIVH taraması için 2000 g bebek ağırlığı eşik değer olarak uygundur.

(J Turkish-German Gynecol Assoc 2010; 11: 73-7)

Anahtar kelimeler: Periventriküler-intraventriküler hemoraji, prematur infant, risk faktörleri, Çin populasyonu

Geliş Tarihi: 06 Aralık 2009 **Kabul Tarihi:** 04 Şubat, 2010

Introduction

Periventricular-intraventricular hemorrhage (PIVH) is a common disease in premature infants and one of the most important causes of mortality and disabilities, including cerebral palsy and neurodevelopmental delay, even in patients with milder grades of PIVH (1-3). Although the incidence of PIVH has declined over the past two decades from 30-40% in the early 1980s to <20% in the 1990s in developed countries (4-8), there is a lack of general data concerning PIVH in China, the largest developing country. The aims of the present study were to explore the incidence of PIVH and analyze its high risk factors in premature infants, and to suggest a working protocol for PIVH diagnosis, prevention and treatment in newborn infants at risk.

Materials and Methods

Patients

This study was a cohort prospective study involving 1122 premature infants (594 males; 528 females) delivered at <37 and >26 weeks of gestation at the Beijing Obstetrics & Gynecol-

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doi:10.5152/jtgga.2010.02

ogy Hospital and Qinhuangdao Maternity and Infants' Hospital from January 2002 to June 2005. Among all the newborn infants, the mean gestational age was 31.9±2.1 weeks and the mean birth weight was 1997±523 g.

Ultrasound criteria

Ultrasound examinations were carried out during the first week after birth. Intraventricular hemorrhage was diagnosed sonographically,based on the classification by Papile (9) as follows: Grade I, germinal matrix hemorrhage with no or minimal intraventricular hemorrhage; Grade II: intraventricular hemorrhage without ventricular dilatation; Grade III: intraventricular hemorrhage with primary ventricular dilatation; Grade IV: intraventricular hemorrhage and intraparenchymatous hemorrhage. Mild degrees of hemorrhage were defined as Grades I and II, while severe degrees of hemorrhage were defined as Grades III and IV.

Clinical data collection

The study recorded various kinds of perinatal data including maternal complications (pregnancy-induced hypertension, chronic hypertension, diabetes, anemia, etc.), premature rupture of fetal membranes, fetal distress, mode of delivery, gestational age, asphyxia, Apgar score, birth weight, sex, multiple birth, body temperature of ≤35.5°C, antenatal corticosteroid use, presence of respiratory distress and need for ventilatory treatment, anemia, blood pH≤7.20, SaO_2<85%, $PaCO_2$≥7.33 kPa, serum osmolality, hyperlactacidemia and platelet parameters.

Pregnant women at high risk for preterm birth at a gestational age of <35 weeks were randomly divided into two groups according to their in-patient registration numbers of theBeijing Military Region General Hospital. Pregnant women in the vitamin K_1 group received antenatal injections of vitamin K_1 at 10 mg/day intramuscularly or intravenously for 2 to 7 days. Women in the control group were not given vitamin K_1 injections. The women in the two groups had similar ages, domestic economic statuses, prenatal complications and routes of delivery. Besides, the infants were divided into phenobarbital and non-phenobarbital groups as well according to the in-patient registration number after birth. The infants in the phenobarbital group received an intravenous injection of phenobarbital at 20 mg/kg within 2 hours after birth, followed by injections at 5 mg/kg every 12 hours for 3 days. The infants in the non-phenobarbital group did not receive any phenobarbital injections after birth. And the study protocol was approved by the research committee of the Beijing Military Region General Hospital.

To understand the blood count data, 50 healthy term infants without PIVH or any other diseases were selected as healthy controls. Their data were compared with the platelet parameters of the premature infants with PIVH to clarify whether abnormal platelet parameters have an influence on PIVH.

Statistical analysis

Data analyses were conducted with SPSS12.0 for Windows. Differences among the incidences of PIVH between the groups were assessed with χ^2 tests, one-way ANOVA or *t*-tests.

Results

Total incidence of PIVH in premature infants

The total incidence of PIVH in the study population was 55.2% (619/1122). Among the 619 cases, low degrees of PIVH accounted for 82.2% and severe degrees of PIVH accounted for 17.8%.

Correlation between gestational age and the incidence of PIVH

The incidences of PIVH were 78.5% (197/251) among infants at <32 gestational weeks, 57.1% (287/503) among infants at <32~35 gestational weeks and 36.7% (135/368) among infants at <35~37 gestational weeks. These data indicated that lower gestational ages were associated with higher incidences of PIVH. Among the 110 cases with severe PIVH, 79 were at <32 weeks, 27 at <35 weeks and only 4 at ≥35 weeks. These data indicated that lower gestational ages were associated with more severe degrees of PIVH.

Correlation between birthweight and the incidence of PIVH

As shown in Table 1, lower birthweights were associated with higher incidences of PIVH, and the incidences were especially high among infants with birthweights of <2000 g.

Correlation between mode of delivery and the incidence of PIVH

The incidences of PIVH were 52.7% in the cesarean section group and 57.2% in the vaginal delivery group. These data indicated that delivery mode was not associated with PIVH (χ^2=1.15, p=0.283).

Correlation between multiple births and the incidence of PIVH

The incidences of PIVH were 57.4% in the multiple birth group and 54.8% in the single birth group. These data indicated that multiple births did not significantly increase the incidence of PIVH (χ^2=0.11, p=0.740).

Correlation between use of antenatal corticosteroids and the incidence of PIVH

Use of antenatal corticosteroids significantly reduced the incidence of PIVH in infants at <35 weeks, but had no marked influence on infants at ≥35 weeks (Table 2).

Effect of postnatal administration of phenobarbital on the incidence of PIVH

During the study, we examined the effect of postnatal administration of phenobarbital on the incidence of PIVH. Among 112 pre-

Table 1. Incidences of PIVH among infants with different birthweights

birthweight (g)	n	PIVH (n)	incidence rate (%)
≤1250	102	77	75.5
~1500	138	94	68.1
~2000	308	192	62.3
~2500	379	189	49.9
>2500	195	67	34.4
χ^2= 28.96, p<0.001			

term infants, 50 were divided into a phenobarbital-treated group and 62 were divided into a control group. Administration of phenobarbital was carried out at <2 hours after birth. Although the total incidences of PIVH were 52.0% in the phenobarbital group and 56.4% in the non-phenobarbital group ($\chi^2=0.221$, $p=0.638$), the incidence of severe PIVH was markedly decreased in the phenobarbital group (4.0% vs. 17.7%, $\chi^2=5.09$, $p=0.024$).

Influence of maternal perinatal complications on the incidence of PIVH

Maternal complications in the perinatal period significantly increased the incidence of PIVH among infants at <35 weeks, but not among infants at ≥35 weeks (Table 3).

Influence of fetal distress and birth asphyxia on the incidence of PIVH

The incidences of PIVH were 67.4% and 49.0% in preterm infants with and without fetal distress and birth asphyxia, respectively ($\chi^2=5.52$, $p=0.019$).

Mechanical ventilation and the incidence of PIVH

Mechanical ventilation significantly increased the incidence of PIVH from 52.2% to 82.2% ($\chi^2=13.79$, $p<0.001$).

Hypoglycemia and the incidence of PIVH

The incidence of PIVH was much higher in infants with hypoglycemia than in infants without hypoglycemia (61.0% vs. 51.7%, $\chi^2=5.99$, $p=0.014$).

Serum osmolality and the incidence of PIVH

The serum osmolalities in the groups with and without PIVH were 292.7±9.77 and 293.9±8.83 mOsm/L, respectively, and showed no significant difference ($t=1.01$, $p=0.335$).

Hypoxia, acidosis and hypercapnia and the incidence of PIVH

The incidence of PIVH was much higher in infants with hypoxia (SaO_2<85%) than in infants without hypoxia (61.8% vs. 53.3%, $\chi^2=4.095$, $p=0.043$). Acidosis (blood pH≤7.20) significantly increased the incidence of PIVH in preterm infants from 49.9% to 58.5% ($\chi^2=5.206$, $p=0.023$). Hypercapnia ($PaCO_2$≥7.33 kPa) was also a high risk factor for PIVH, and increased the incidence of PIVH from 51.9% to 61.0% ($\chi^2=3.837$, $p=0.05$).

Correlation between hyperlactacidemia and the incidence of PIVH

The incidences of PIVH were 61.7% and 50.1% in the hyperlactacidemia and normal serum lactic acid groups, respectively ($\chi^2=9.173$, $p=0.002$).

Correlation between premature rupture of fetal membranes and the incidence of PIVH

The incidences of PIVH were 60.2% and 49.9% in infants with and without premature rupture of fetal membranes, respectively ($\chi^2=9.380$, $p=0.002$).

Hypothermia and the incidence of PIVH

Hypothermia (body temperature of ≤35.5°C) increased the incidence of PIVH in preterm infants from 54.1% to 65.1% ($\chi^2=5.87$, $p=0.017$).

Maternal antenatal administration of vitamin K_1 and the incidence of PIVH

Maternal antenatal administration of vitamin K_1 decreased the incidence of PIVH in preterm infants from 54.0% to 32.5% ($\chi^2=4.16$, $p=0.041$).

Correlations between platelet parameters and the incidence of PIVH

The platelet parameters examined included platelet counts (PLT; $\times10^9$/L), thrombocytocrit (PCT; %), mean platelet volume (MPV; fl) and platelet distribution width (MPV; %). These parameters were determined in 100 premature infants with PIVH, 60 premature infants without PIVH and 50 healthy term

Table 2. Correlation between antenatal corticosteroid use and PIVH

Groups	gestational age<35wks			gestational age≥35wks		
	n	PIVH	incidence (%)	n	PIVH	incidence (%)
corticosteroid use	155	82	52.9	51	17	33.3
non corticosteroid use	597	399	66.8	319	121	37.9
χ^2			4.30			0.180
P			0.038			0.671

Table 3. Correlation between maternal perinatal complications and PIVH

Groups	gestational age<35weeks			gestational age≥35weeks		
	n	PIVH	incidence (%)	n	PIVH	incidence (%)
MPC	187	138	73.8	117	46	39.3
Non-mpc	567	346	61.0	251	89	35.5
χ^2			4.31			0.380
P			0.038			0.540

infants (HTI). The results showed that changes in platelet parameters may be involved in the pathogenesis of PIVH in premature infants (Table 4).

Discussion

The results of the present study indicate that the incidence of neonatal PIVH in China is much higher than previously reported incidences in developed countries (4-10). The lower the birthweights, the higher is the incidence rate in PIVHs, especially for those infants with birthweights of <2000 g. This maybe mainly because the lower birthweight, the lower gestational ages the babies have, and accordingly the more premature in subependymal germinal matrix. Thus we think the screening cutoff point of a birth weight of 2000 g seems to be more adequate than 1500 g which was commonly used in China. PIVH in premature infants is an important cause of mortality and is associated with long-term morbidity including neurodevelopmental problems such as hydrocephalus, cerebral palsy, learning disabilities, language barrier, delayed mental development, severe behavioral problems and so on. Particularly in those infants with high grade hemorrhage, early onset PIVH is also likely to be severe and to progress to a higher grade. According to the results of this study, low gestational age, low birth weight, mechanical ventilation, hypoxia, acidosis, hypercapnia, hypothermia, hypoglycemia, hyperlactacidemia, maternal perinatal complications, fetal distress and birth asphyxia were the most important risk factors for PIVH. Premature rupture of fetal membranes (PROM) is also a common cause of PIVH which may be correlated with conditions of ascending intrauterine infection caused by PROM, and it is well known that inutero exposure to bacterial infection increases the incidence of PIVH in immature newborn infants (11), and the inflammation and cytokines play an important role in the pathogenesis of brain damages (11,12). The more premature infants have a higher incidence, experiencing more severe PIVH, may be mainly because of low use of steroids, more premature in subependymal germinal matrix and Choroid Plexus Capillaries, etc. Serum osmolality, multiple births and cesarean section were not significantly correlated with the incidence of PIVH in premature infants. Maternal antenatal administration of vitamin K_1 or corticosteroids can significantly decrease the incidence of PIVH (13, 14), and can be used routinely for women at risk of premature birth at <35 weeks of gestation. Antenatal supplementation with vitamin K_1 may significantly increase the plasma activities of factors II, VII and X, and consequently decrease the incidence of PIVH and lower the severity of hemorrhage. The immaturity of subependymal germinal matrix is the basic cause of PIVH in premature infants, when there is no intact basement membrane or only a basement-like material. Previous study showed use of antenatal corticosteroid can improve the maturation of subependymal germinal matrix (15). Thus, the incidence and the degree of PIVH in preterm infants before 35 weeks gestational age can be decreased significantly.

The present study also found that changes in platelet parameters, especially low platelet counts and a low thrombocytocrit, may be involved in the pathogenesis of PIVH in premature infants. It is important to monitor the changes in these platelet parameters in premature infants after birth.

Postnatal administration of phenobarbital for the prevention of PIVH has been used for more than two decades, but its effects have remained controversial. A previous meta-analysis revealed no differences between a phenobarbital-treated group and a control group for PIVH incidence, severe PIVH, posthemorrhagic ventricular dilatation, severe neurodevelopmental impairment and death before hospital discharge (16). Therefore, this strategy cannot be recommended as a prophylactic procedure for preventing PIVH in preterm infants and was found to be associated with an increased need for mechanical ventilation (16). Our present results showed that, although the total incidence of PIVH did not differ between the phenobarbital-treated and control groups, phenobarbital administration appeared to be effective for decreasing the severity of PIVH in preterm infants delivered at <35 weeks of gestation. Hence, we believe that phenobarbital administration may still have some benefits for the prevention of PIVH in premature infants.

In conclusion, many high risk factors were involved in the incidence of PIVH in preterm infants. The incidence of PIVH in preterm infants in China was much higher than the previously reported incidences in developed countries, especially for infants with birthweights of <2000 g. Therefore, we suggest that a new cutoff point of 2000 g, rather than 1500 g, should be used in China to assess the risk of PIVH based on birthweight. The present investigation provides a working protocol for PIVH diagnosis, prevention and treatment in premature newborn infants at risk.

Conflict of interest

None declared

Table 4. The correlation of the parameters of platelet and the incidence of PIVH (X±S)

Groups	n	PLT (×10⁹/L)	PCT (%)	MPV (fl)	PDW (%)
HTI	50	299.6±80.5	0.254±0.09	8.55±1.32	17.5±0.83
Non-PIVH	60	239.5±86.5	0.189±0.09	8.27±1.15	17.6±1.04
PIVH	100	175.7±78.8	0.139±0.06	8.46±1.17	17.7±1.26
F		31.84	28.64	0.70	0.46
p		<0.001	<0.001	0.497	0.632

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A study on knowledge, attitude and practice of contraception among college students in Sikkim, India

Hindistan, Sikkim'deki kolej öğrencilerinin kontrasepsiyon hakkındaki bilgileri, tavırları ve uygulamaları konusundaki bir çalışma

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Abstract

Objective: To assess the knowledge, attitude and practice of contraception among the college students.

Materials and Methods: A cross sectional study was conducted in the Government College, Gangtok, Sikkim, during the month of April 2009 to evaluate the knowledge, attitude and practice of contraception among 156 students enrolled in the first year bachelor course. Descriptive statistics was used for data analysis.

Results: 98% (153/156) of the students had knowledge about family planning and 86% (134/156) of them had heard about contraceptives. Most of them knew about condoms (85%) and contraceptive pills (40%) but knowledge about permanent methods and Cu-T was poor (average 12%). Most students thought contraceptives were to be used to prevent unwanted pregnancy (35%) and for birth spacing (30%). 11% of students had used some form of contraceptive in the past and 7% were currently users. The most commonly used contraceptives were condoms, followed by combined use of OCP and condom.

Conclusion: The study highlights the need to motivate the youth for effective and appropriate use of contraceptives when required and arrest the trend towards unwanted pregnancy.

(J Turkish-German Gynecol Assoc 2010; 11: 78-81)

Key words: Family planning, contraception, knowledge, practice

Received: 5 March, 2010 **Accepted:** 16 April, 2010

Özet

Amaç: Kolej öğrencilerinin kontrasepsiyon haklkındaki bilgi, tecrübe ve tavırlarını değerlendirmek.

Gereç ve Yöntemler: Sikkim, Gangtok'taki devlet kolejinde okuyan 156 ilk yıl öğrencisinin kontrasepsiyon hakkındaki bilgi, tecrübe ve davranışlarını belirlemek için Nisan 2009'da kesitsel bir çalışma yürütüldü. Betimleyici istatistik analizleri kullanıldı.

Bulgular: Öğrencilerinin %98'i (153/159) aile planlamısını biliyordu ve %86'sı (134/156) kontrasepsiyonu duymuştu. Çoğu kondommu biliyor (%85) ve doğum kontrol hapları hakkında fikir sahibi (%40) iken, kalıcı yöntemler ve bakırlı rahim içi araçlar hakkında bilgisi olan azdı (ortalama %12). Çoğu kontraseptiflerin istenmeyen gebeliği önlemek için (%35) veya doğum sayısını azaltmak için (%30) kullanıldığını biliyor ve öğrencilerin %11'i geçmişte bazı yöntemleri uygularken,%7 kadar şu an herhangi bir yöntemi kullanıyordu. En sık uygulanan yöntem Kondom ve onu doğum kontrol hapları takip ediyordu.

Sonuç: Çalışmamız, gençleri etkin ve uygun kontraseptif kullanımı hakkında bilgilendirmeye, motive etmek ve istenmeyen gebelik oranını düşürmeye dikkat çekmiştir.

(J Turkish-German Gynecol Assoc 2010; 11: 78-81)

Anahtar kelimeler: Aile planlaması, kontrasepsiyon, bilgi, uygulama

Geliş Tarihi: 05 Mart 2010 **Kabul Tarihi:** 16 Nisan 2010

Introduction

The global population today stands at over 6 billion, one-sixth of which is in India. Uncontrolled population growth is recognized as the single most important impediment to national development. Despite the fact that India was the first country in the world to implement a national population control programme in 1952, the country is still struggling to contain the baby boom. A lot of efforts and resources have gone into the National Family Welfare Programme but the returns are not commensurate with the inputs. The programme has targeted eligible couples in its efforts to control the population.

The United Nations Fund for Population Activities (UNFPA) notes that future population trends will hinge on the fertility decisions of today's men and women aged 15-24 years and on their ability and freedom to act on those decisions (1). Concern about adolescent fertility arises from its health implications both for the mother and the child, its demographic implications in societies with rapid population growth and its social development implications. Because of the young age-structure of India's population, the reproductive attitude and behaviour of teenagers are likely to have an important impact on overall reproductive health, demographic and social outcome. Adolescent sex and exposure to the risk of pregnancy has attracted considerable research attention to understand its magnitude and address it as a problem. Studies in developed countries have shown a high level of such exposure (2-5), as also in Latin America (6, 7), China (8) and some African countries like Uganda and Nigeria (9-11), South Africa (12-14) and India (15, 16).

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doi:10.5152/jtgga.2010.03

These facts warrant an investigation into the knowledge and attitude of this age-group regarding fertility control and contraception.

Material and Methods

A cross sectional study was conducted in the Government College, Gangtok, the capital town of Sikkim, a small state in north-east India. A Knowledge Attitude Practice (KAP) study was conducted among 156 students during the month of April 2009.
The inclusion criteria: Students enrolled in the first year bachelor course, who were willing to participate in the study.

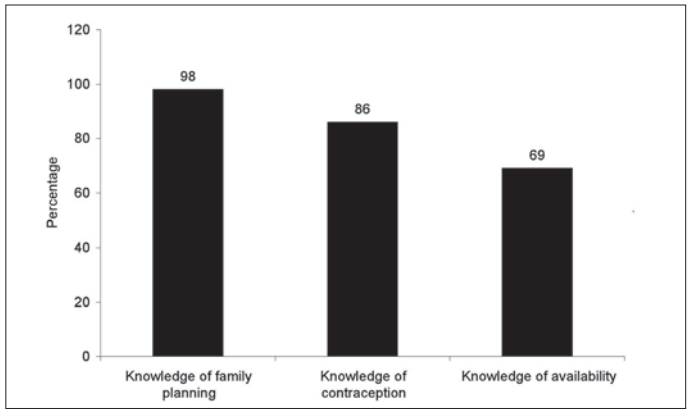


Figure 1. Knowledge of Family planning methods & Contraception among college students (N=156)

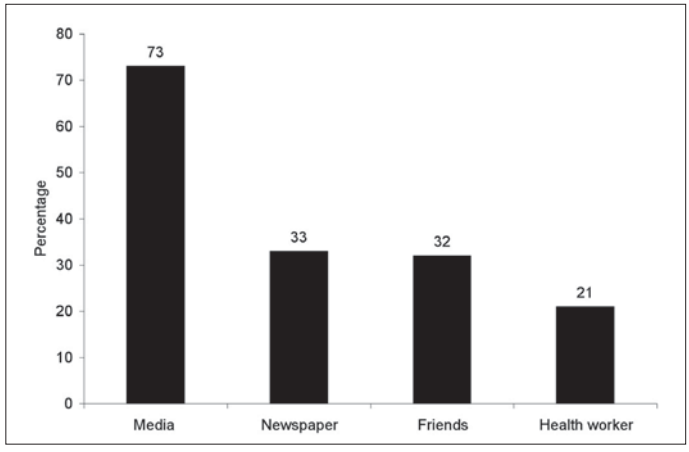


Figure 2. Source of Knowledge regarding Family planning and contraception among college students (N=156)

Table 1. Attitude towards use of contraception (N=156)

Attitude	N=156	%
Contraceptive beneficial	111	71
Contraceptive not beneficial	21	13
Adopt Family Planning	122	78
Use Contraceptive in future	81	52
Not Use Contraceptive	21	17
No Response	47	30

The exclusion criteria: Those students who were not willing to participate in the study.
Purposive Sampling with snowball technique was used. The questionnaire was designed by the authors after an extensive review of available literature, and the questionnaire was pretested. After obtaining written informed consent, the questionnaire was administered for data collection on general information, knowledge and attitude regarding family planning methods, and contraceptive practices.
Ethical committee clearance and permission from the principal of Government College was obtained. The students were assured regarding the confidentiality and secrecy of the information provided by them. The data was collected through the questionnaire which was voluntarily filled out by the students.
Variables were knowledge, attitude, and practice of students regarding family planning and contraception.
Descriptive statistics was used for data analysis. The collected data was analyzed with regard to the information given by the subjects according to the set questionnaire items and the analyzed data is presented in the following tables.

Results

The study showed that 98% (153/156) of the students had knowledge about family planning and 86% (134/156) of them had heard about contraceptives. and 69% knew about the source of availability of contraceptives.
73% (115/ 156) had gained information about family planning and contraception from the media, 33% from newspapers, 32% from friends and 21% from health personnel.

Awareness regarding various methods of contraception

The majority of the students (85%) knew about condoms but only 40% had knowledge about contraceptive pills. However, knowledge about permanent methods and intra-uterine devices was poor (average 12%).

Concept regarding contraceptive use

Most students thought that contraceptives were used to prevent unwanted pregnancy (35%) and for birth spacing (30%). 26% thought that the contraceptives could be used to have a child when required and about 23% thought that they could be used to prevent infections. 71% (111/156) of students thought that contraceptive use was beneficial, 13% (21/156) thought otherwise. 78% of students wanted to adopt family planning in the future but only 52% (81/156) were willing to use some contraceptive method in the future.

Reasons for not using contraceptives, N=21

The most common reasons (23%) cited for not using contraceptives were that it was against their religious beliefs to use a contraceptive and that it would interfere with sexual pleasure. However 19% felt that use of contraceptives may cause weakness and nearly 10% felt that it may lead to obesity.

The most preferred contraceptive method among the college students
The most common methods of contraception used by the students were condoms (past users 70% and current users 81%), followed by combined OC pills and condoms (17%). Of those students who had used some method of contraception, 6% had used OC pills; however in the current user group about 9% were using OC pills.

Discussion

Many studies have been conducted all over the world to study the knowledge, attitude and practice of contraception in adolescent and young adults. A study conducted among 991 senior students (15-17 years) in North Gondar in 1995 by Fantahun MI et al showed the level of knowledge of contraception to be 75% (17). Another study conducted in Nigeria itself in 1998 by Araoye et al in randomly selected 971 males and females aged 18-24 years in a Nigerian tertiary institution showed that 97.7% of males and 98.4% females respectively knew at least one method of contraception (18). Adinma JI et al. conducted two studies in 1995 and 1999 and reviewed contraception in 498 Nigerian Tertiary School Girls-228 from the Medical Discipline (MD) of study and 270 from the Non-Medical Discipline (NMD) in 1995 and in 314 teenage Nigerian school girls comprising 128 students at secondary and 186 at tertiary levels of institution in 1999. The overall mean awareness of contraception was 70.9% in the first group, however the mean level of contraceptive awareness for the various methods of contraception was 38.2% for the second survey group: 22.6% for the secondary school girls and 54.4% for the tertiary school girls (19, 20).
In India, two such studies have been carried out in Delhi and Ludhiana in the past. Aggarwal O et al. in Delhi (21) conducted the survey in 500 undergraduate students of the medical colleges of Delhi and reported the knowledge regarding, contraception to be 83.5%, which was comparable to the study conducted in Ludhiana by Benjamin (22) et al. among 527 senior secondary school children, where 87% were aware of contraception. Similar results were reported by Arowojolu AO (23) et al. from Nigeria, where a survey of 2388 Nigerian undergraduate students showed the contraceptive knowledge level to be 87.5%.
In the present study group 86% of the college students had knowledge of contraception and 69% knew about the source of availability
The source of knowledge about contraception in most of the studies, like that of Fantahun MI et al. in North Gonder by Adinma JI in Nigeria and Aggarwal O et al. in Delhi, was from school and friends respectively, whereas in the present study it was the media which had played the most important role in spreading awareness about contraceptive methods among the students. In the study done by Fantahun MI et al. among 991 senior high school students in north Gonder, the most common reason for not using modern contraceptive methods among sexually active respondents was little or lack of knowledge of contraceptives followed by no access to contraceptives and harmful effects of contraceptives. In the present study the most common reasons (23%) cited for not using contraceptives were that it was against their religious beliefs to use contraceptives and that their sexual life would not be happy respectively. However, 19% felt that use of contraceptives would result in weakness, and nearly 10% felt that it would result in obesity. Arowojolu AO et al. surveyed 2388 Nigerian undergraduate students and reported that 87% had experienced sex but only 34% had used some method of contraception. In the study done by Fantahun et al. about 30% of students had experienced sex but only 17% had used contraception .The two studies done by Adinma JI et al. also had similar results, where the number of students who experienced sex was 57% and 26.8% and the use of contraceptive was 23.5% and 17% respectively. Lowes et al. from USA reported that 68% of 283 unmarried school students (at average 19 years of age) had experienced sex and 44% had used contraception, which is the highest among all the studies documented so far (24). In the present study experience of sex was not analysed but the use of contraceptives was the lowest, being only 17%, which was the same as that of the study conducted by Fantahun MI et al. in North Gonder in 1995 and Adinma et al in Nigeria.
The most preferred method of contraception in young adults was the condom followed by OCPs as reported in the study conducted by Fantahun MI in North Gonder in 1995 and by Araoye MO et al. in Nigeria in 1998. However, OCPs were the most preferred method of emergency contraception (43.9%) in a study conducted by Tamire W (25) in Ethiopia in 2007. In the present study the condom was the most preferred method of contraception used by the students (past users 70% and current users 81%).
In India also there is evidence from studies amongst senior secondary school students that adolescents are becoming increasingly sexually active. A study in four public and two government schools of South Delhi conducted in 1992 showed that 63.3% of boys and 37.4% of girls were of the opinion that students of their age had sex; 17% boys and 9% girls agreed to take the risk of AIDS rather than miss the chance of having sex with an attractive stranger (15). In another study conducted in four senior secondary schools in rural Delhi (in 1992), 23.4% boys and 15.1% girls admitted to having had sex, while 5.7% boys and 9.6% girls did not deny it (16).

Conclusion

The use of contraceptives among adolescents is significantly different from that of older married couples, and it is influenced by educational, developmental, social, and psychological factors.
The study highlights that knowledge and awareness do not always lead to a positive attitude towards the use of contraceptives. Although in the present study the actual number of sexually active young adults was not known, there appears a need for continuing education about sexuality and contraception. Also there is a need to motivate the youth for effective and appropriate use of contraceptives and arrest the trend towards unwanted pregnancy and increase in population. The media as we see has played a pivotal role in spreading awareness among

the college students regarding contraceptives in the state of Sikkim. This can thus be used for motivating the young adults to adopt family planning methods and use of contraception.

Conflict of interest

None declared

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Detection of fetal RhD gene from maternal blood

Maternal kandan fetal RhD tayini

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Abstract

Objective: Hemolytic disease of the newborn (HDN) is a clinic phenomenon which occurs during pregnancy due to the Rhesus (Rh) D alloimmunization between a Rh (-) pregnant woman, who has become sensitive to RhD antigens, and her Rh (+) fetus. As a result of the attack of maternal RhD antibodies on fetal RhD antigens, fetal anemia, HDN and fetal death may occur. % 40 of Rh (-) pregnant women carry Rh (-) fetus. However, all Rh (-) pregnant women are offered anti-D Immunoglobulin (Anti-D Ig) at 28 weeks' gestation in case of fetomaternal haemorrhage, so the pregnant women carrying Rh (-) fetus are exposed to blood products unnecessarily. Although the RhD of fetus can be detected, methods used for prenatal diagnosis recently are invasive tests and they can result in abortion in a certain percentage . The discovery of circulating cell-free fetal nucleic acids in maternal plasma has opened up new possibilities for non invasive prenatal diagnosis. The aim of this study was to detect prenatal RhD by analysing the presence of the RhD gene of fetal DNA in maternal blood.

Material and Methods: Total free DNA was isolated from the blood of 19 Rh (-) pregnant women, who had RhD alloimmunization with their husbands, in the 11-14 th week of their pregnancy. The existence of a gene in isolated DNA was investigated with TaqMan prob and "Real-time PCR" method by using primers belonging to exon 7 of RhD gene.

Results: Using a quantitative real-time PCR assay, the presence of RhD gene sequences was evaluated in the serum of patients at the onset of pregnancy. We have analyzed 19 Rh (-) pregnant women. Twelve of them were Rh (-) and the rest of them were 7 Rh (+). After birth the baby's blood groups were concordant with our results.

Conclusion: The results obtained by RhD primer were analysed. The possibility of detection of fetal RhD gene in maternal blood contributed to noninvasive prenatal diagnosis.

(J Turkish-German Gynecol Assoc 2010; 11: 82-5)

Key words: Fetal DNA, RhD gene, real-time PCR

Received: 2 January, 2010 **Accepted:** 20 April, 2010

Özet

Amaç: Yeni doğanın hemolitik hastalığı, daha önce "Rhesus" (Rh) D antijenleri ile duyarlı hale gelmiş Rh (-) anne ile Rh (+) çocuğu arasındaki RhD uyumsuzluğuna bağlı olarak hamilelik sürecinde ortaya çıkan klinik bir tablodur. Maternal RhD antikorlarının fetal RhD antijenlerini yok etmesiyle, fetusta kansızlık, yenidoğanda sarılık veya fetal ölüm gerçekleşebilir. Rh (-) gebelerin yaklaşık % 40'ı Rh (-) fetus taşımaktadır. Buna rağmen tüm gebelere olası bir fetal kanama riskine karşı hamileliklerinin 28. haftasında anti D immünglobulin (Anti-D Ig) uygulanmakta ve Rh (-) fetus taşıyan gebeler gereksiz aşı ürününe maruz kalmaktadır. Doğum öncesi tanı ile fetusun RhD tayini yapılabilse de, günümüzde kullanılan doğum öncesi tanı metodları girişimsel tetkikler olup belli oranlarda gebelik kayıplarına neden olabilmektedir. Anne kanında fetusa ait nükleik asitlerin hücre dışında serbest dolaşabileceklerinin keşfi noninvazif prenatal tanı için yeni olanaklar açmıştır. Bu çalışmada da maternal kandan fetal DNA'da RhD geninin varlığına bakılarak doğum öncesi RhD tayini yapılabilmesi amaçlanmıştır.

Gereç ve Yöntemler: 11-14. gebelik haftalarında bulunan ve eşleriyle aralarında RhD uyumsuzluğu olan 19 Rh (-) gebeden kan alınarak total serbest DNA izolasyonu yapılmıştır. İzole edilen DNA'larda RhD geninin ekson 7 bölgesine ait primerler kullanılarak, TaqMan prob yöntemi ile ve "Real-time PCR" aracılığıyla genin varlığı araştırılmıştır.

Bulgular: "Real-time PCR" kullanılarak gebeliklerinin başında olan hastaların serumlarında RhD gen dizilerinin varlığı değerlendirildi. Analiz edilen 19 Rh (-) gebenin 12'sinin (Rh-), 7'sinin Rh (+) olduğu belirlendi. Doğum sonrasında bebeklerin kan grupları ile bizim sonuçlarımız birebir uyumlu çıkmıştır.

Sonuç: RhD primeri ile alınan sonuçlar analiz edilmiştir. Fetüse ait RhD geninin maternal kanda belirlenebilmesi girişimsel olmayan doğum öncesi tanı için önemli bir katkı sağlamıştır.

(J Turkish-German Gynecol Assoc 2010; 11: 82-5)

Anahtar kelimeler: Fetal DNA, RhD gen, gerçek zamanlı PZR

Geliş Tarihi: 02 Ocak 2010 **Kabul Tarihi:** 20 Nisan 2010

Introduction

Hemolytic disease of newborn (HDN) is a clinic phenomenon evidenced in children due to the rhesus (Rh) blood group incompatibility between maternal and paternal blood groups. The RhD antigens encoded by the RhD gene on the chromosome 1 determine the RhD blood group (Rh-, or Rh+) of people, and in case of incompatibility between maternal and paternal RhD blood group, this may result in intrauterine fetal death, fetal anemia or neonatal icterus (1). The Rhesus (Rh) blood group system is a very polymorphic system. RhD and RhCE are located in the region of p36.13-p34.3 on chromosome 1, and they are 97% homologous to each other. Each of these genes consists of 10 exones, and they contain 69 kb of DNA. The regions of exone 7 and exone 10 within the RhD gene are the areas of focus. In all positive results, the RhD blood group has also been found positive (2). The bi-sidal flow from the placenta during pregnancy has been presented

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doi:10.5152/jtgga.2010.04

in many studies (3). Free fetal DNAs stemming from the destruction of fetal cells in earlier weeks of pregnancy transport to the maternal blood via the bi-sidal flow through the placenta (4). 3%-6% of free DNAs in the plasma of pregnant women have been found to be fetal in origin (5). When the properties brought by the the fetal DNA as a genetic substance has been considered, many studies putting forward the assumptions of the possibility of recognizing some of the genetical diseases during pregnancy and the emphasis of the issue at prenatal diagnosis have been subject to questioning. However, as the purifying can be applied to have an access to total free DNA, the particularity that belongs to the fetus does not have to be found in the mother (the chromosomal disorders and gender) and has to be inherited by a single gene (thalassemia and cystic fibrosis) (6).

The determination of the free fetal DNA and RhD gene in maternal blood make it possible to detect the RhD sitiuation of baby via a non-invasive method. Studies put more emphasis on this area (7). Unnecessary application of Anti D Ig can be prevented for pregnant women who carry a Rh - fetus, also this results in a better follow-up of pregnant women who carry a Rh+ fetus with the detection of RhD genotype of fetus in maternal plasma at the first trimester of pregnancy.

Lately, widely used methods of prenatal genetic diagnosis are invasive examinations that may lead to specific rates of pregnancy loss. Therefore, prenatal diagnosis should be applied to high risk pregnant women rather than all pregnant women. Despite applying some prenatal screening methods to constitute the so-called risk group, these screening results cannot provide an accurate result (8). With the help of developing noninvasive prenatal diagnostic techniques, prenatal diagnostic methods giving certain results can be applied to all pregnant women without any screening. Therefore, the need of the invasive procodures, such as amniocentesis and chorion villus sampling to get fetal cells for the resources of fetal DNA, has to be replaced (9).

Horizons of prenatal diagnosis expand continuously, and the methods which are faster, less costly and harmful for the baby, as well as mothers are being developed in order to put into practice.

Material and Methods

5 ml blood was taken from each 19 Rh (-) pregnant woman having Rh incompatibility with their husbands who came to 11-14 week controls to the Istanbul University Faculty of Medicine, Department of Gynecology and Obstetrics, and Istanbul University Cerrahpasa Medical Faculty, Department of Gynecology and Obstetrics. The day blood was taken, they were centifuged 15' at 4100 g, and saved at -80° until the day of the isolation of upper fluid. The total free DNA isolation was performed according to free DNA isolation procedures of High Pure PCR Template Preparation Kit" (Roche Applied Science Kat. No: 11 796 828 001). The samples that were saved at-80° were first centrifuged at 13000 rpm for 10' and upper fluids were taken. 200 μl "Binding Buffer" and 40 μl "Proteinase K" were put in each sample, and they were kept at 70° in a water bath for 10'. 100 μl isopropanol were also added to them and the mixtures were taken to strainer eppendorf and centrifuged until all of the liquid passed to the bottom. 500 μl "Inhibitor Buffer" was added to eppendorfs and centrifuged. Two cetrifuges were then also formed by adding 500 μl "Wash Buffer" each time. Next, 50 μl "Elution Buffer" was added to strainer eppendorfs, the sub- tube which had free DNA after centrifugation was taken to -20° until the day of "Real Time PCR" would be conducted. With the content on Table 1 and at the conditions on Table 2, "Real Time PCR" for gene detection was perfomed by using the specific primers (5'-CTC CAT CAT GGG CTA CAA-3', 5'-CCG GCT CCG ACG GTA TC-3') for region exon 7 which belongs to RhD and TaqMan prob (5'-FAM AGC AGC ACA ATG TAG ATG ATC TCT CCA TAMRA-3'); FAM [6 carboxyfluorescein] and TAMRA [6 carboxytetrametthylrhodamine] were the fluorescent reporter dye and quencher dye, respectively. The tubes which contained RhD genes were used for positive control, and the tubes that were known not to contain RhD gene were used for negative control. The tubes containing the NTC (PCR mixture without DNA) reaction mixture was used for the determination of contamination.

Results

The total DNA of 19 pregnant women that were known to be Rh-, was analyzed with positive and negative controls by NTC "TaqMan prob" method, negative control, NTC. 12 samples were found to be RhD (-) and positive control, and 7 samples were found to be RhD (+) (Table 3).

Discussion

After the discovery of free fetal DNA (10), tremendous progress has been made in prenatal diagnosis. The detection of prenatal fetal gender, and fetuses having single gene disorders that are paternally inherited and hemolytic diseases are actualized by

Table 1. Components of amplification mixture

Component	Volume (μl)	Final amount
TaqMan Probes	0.6	25nM
Forward Primer	3	300nM
Reverse Primer	3	300nM
dH_2O	13.4	-
Template DNA	5	20ng
PCR Reaction Buffer	25	-

Table 2. Cycling parameters

	Segment 1	Segment 2
Temperature (°C)	95	95 60
Time	10 min	15 min 1 min
Cycles	1	50

Table 3. Results of RhD genotyping of fetuses of RhD negative women with the use of RhD Real-time PCR assay and serologic RhD typing of the newborns

Samples values	CT results	Real-Time PCR Rh phenotypes	Newborn
NTC (No template control)	-	-	-
Positive control	25.63	Rh (+)	Rh (+)
Negative control	-	Rh (-)	Rh (-)
1	-	Rh (-)	Rh (-)
2	-	Rh (-)	Rh (-)
3	-	Rh (-)	Rh (-)
4	-	Rh (-)	Rh (-)
5	34.83	Rh (+)	Rh (+)
6	-	Rh (-)	Rh (-)
7	34.25	Rh (+)	Rh (+)
8	-	Rh (-)	Rh (-)
9	34.65	Rh (+)	Rh (+)
10	35.52	Rh (+)	Rh (+)
11	32.31	Rh (+)	Rh (+)
12	34.56	Rh (+)	Rh (+)
13	-	Rh (-)	Rh (-)
14	-	Rh (-)	Rh (-)
15	34.19	Rh (+)	Rh (+)
16	-	Rh (-)	Rh (-)
17	-	Rh (-)	Rh (-)
18	-	Rh (-)	Rh (-)
19	-	Rh (-)	Rh (-)

the researches conducted during this period. The accuracy rates between 98%-100% of researches shows that recently, fetal RhD detection can be applied routinely to Rh (-) women, and the use of human anti -D can be significantly reduced (9). Fetal DNA can be identified from the 5th week of pregnancy in maternal blood and is rapidly destroyed immediately after birth. However, only 3%-6% of total DNA in maternal blood is welded fetal origin (11). Genes inherited from the mother are pressured by excessive quantities of free maternal DNA. This situation prevents only prenatal diagnosis of X-linked or recessive inherited diseases. The sensitivity of the studies that have been recently carried out by the devoleped PCR techniques has been increased, but the greatest difficulty encountered is the isolation of pure and high scale fetal DNA. By doing this isolation, the need of invasive procedures, such as amniocentesis will largely be eliminated (9).

The complete disappearance of invasive procedures can be made possible by putting studies into practice that begin with the discovery of fetal mRNA transcripts. The discovery can open a new array in the field of detection of chromosomal disorders, which cannot be determined by free DNA and follow-up fetal maturing (9).

In the study, the reality of results were confirmed by postnatal tests and after birth the baby's RhD blood groups were concordant with the results. There have been no nonunderstood amplifications and contaminations found in the samples. Only 7 of the 19 pregnant women that are known as Rh (-) samples have been found with RhD gene. 40% of Rh (-) pregnant women were identified to have Rh (-) fetus (12). The low number of samples that was analyzed indicates higher results than expected. The higher rate expected from the society can be related to the higher number of heterozygote fathers than supposed and this can be changed by increasing the number of samples. The costs of use of unnecessary vacine products can be higher according to our results (13).

There are RhD variants in society that make no expression or low expression, and this causes false negative results. The RhDΨ pseudogene, which causes RhD negative phenotype in the African black population is exposed to too many mutations. As a result, it has variants that make low expression, which may in turn lead to false negative and false positive results (14).

The concordance of the results of "Real-Time PCR" analysis of region exon 7 belonging to RhD gene after the detection of fetal DNA from maternal plasma and the RhD blood group results of babies confirm the high sensitivity and reliability of the method. The study indicates toe need to work on the regions of exon 7 and exon10 together for more sensitive and reliable applications (14, 15).

Conflict of interest

None declared

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The relationship of ceruloplasmin and neural tube defects

Seruloplasmin ve nöral tüp defektleri arasındaki ilişki

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Abstract

Objective: To compare the levels of ceruloplasmin (cp) in the amniotic fluids and maternal bloods of second trimester fetuses with and without neural tube defects (NTD).

Materials and Methods: 66 pregnant women were included in the study. Amniocentesis was performed in 32 women in a patient group diagnosed as NTD or anencephaly and 34 pregnants in a control group with positive Down Syndrome screening test. Maternal bloods were also taken. Cp was measured with Erel's ceruloplasmin measurement method.

Results: The cp levels of the amniotic fluid of patients and controls were not statistically different ($p>0.05$). The cp levels of the maternal bloods were not different in two groups ($p>0.05$).

Conclusion: As an antioxidant, no relation was found between cp and NTD.

(J Turkish-German Gynecol Assoc 2010; 11: 86-8)

Key words: Ceruloplasmin, Antioxidant, Neural tube defect

Received: 5 February, 2010 **Accepted:** 24 March, 2010

Özet

Amaç: Bebeklerinde intrauterin nöral tüp defekti (NTD) olan ve olmayan ikinci trimesterdeki gebe kadınlarda amnion sıvısı ve anne kanındaki seruloplasmin değerlerinin karşılaştırılması.

Gereç ve Yöntem: Çalışmaya 66 kadın dahil edildi. NTD veya anensefali tanısı konulan hasta grubundaki 32 gebe ile Down sendrom taraması pozitif olan 34 gebe kadına amniosentez yapıldı ve anne kanları alındı. Amnion sıvıları ile anne kanlarında Erel'in metodu ile seruloplasmin bakıldı.

Bulgular: Hasta ve kontrol grubunun amnion sıvısı ile anne kanlarındaki seruloplasmin seviyeleri arasında anlamlı fark saptanmadı ($p>0.05$).

Sonuç: Antioksidan olarak seruloplasmin ve NTD arasında herhangi bir ilişki saptanamamıştır.

(J Turkish-German Gynecol Assoc 2010; 11: 86-8)

Anahtar kelimeler: Seruloplasmin, Antioksidan, Nöral tüp defekti

Geliş Tarihi: 05 Şubat 2010 **Kabul Tarihi:** 24 Mart 2010

Introduction

Ceruloplasmin (Cp) is an acute phase response protein with two important potential functions: first; transportation of copper to the tissue sites; and second; functions such as oxidase activity of aromatic amines and serum antioxidation. In this setting, Cp acts as an extracellular scavenger of free radicals and superoxide ions, and then endogenously modulates inflammatory responses and so synthesis and secretion of Cp can be markedly increased during inflammation, infection, and in diseases such as diabetes, cancer, and cardiovascular disease, as well as during pregnancy (1, 2).

Neural tube defects (NTD) are a group of heterogenous and complex congenital anomalies of the central nervous system (CNS). Commonly included in this group are anencephaly, spina bifida and encephaloceles (3). The exact etiology of NTD is rather complex and poorly understood. Recently, oxidative metabolism was considered to be related with congenital anomalies including CNS (4, 5).

This study aims to compare the levels of cp in the amniotic fluids and maternal bloods of second trimester fetuses with and without NTD.

Materials and Methods

66 pregnant women admitted to Obstetrics and Gynecology Clinic of Gaziantep University Faculty of Medicine were included in the study. In addition to the local ethics board approval, the informed consent form was obtained from all the parcipitants of the study.

Design of Study: The Patient Group consisted of 32 women, diagnosed with NTD or anencephaly by ultrasonography, in the 16-20th gestational week and termination of pregnancy was decided on. Amniocentesis was performed using a 22 gauge spinal needle by ultrasound guidance before the termination of the pregnancy. 5 cc amniotic fluid was taken during the procedure. Simultaneously, 5 cc maternal blood sample was taken from the antecubital vein.

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doi:10.5152/jtgga.2010.05

The Control Group consisted of 34 pregnants with positive screening of first and second trimester biochemical test results (>1/250 for trisomy 18 and/or trisomy 21) but having normal ultrasonografic findings. In this group, during the amniocentesis procedure which was performed for chromosomal analysis, similar to the patient group's procedure, an extra 5 cc amniotic fluid was taken. Simultaneously, a 5 cc blood sample was also taken from the antecubital vein.

Maternal serum samples and amniotic fluid samples were stored at-80^0 C.

Ceruloplasmin measurement: Erel's ceruloplasmin measurement method was used. This method is automated, colorimetric, and based on the enzymatic oxidation of ferrous ion to ferric ion. The results were expressed in milligrams per deciliter, and the precision of this assay is within 3% (6, 7).

Apparatus: A Cecil 3000 spectrophotometer with a temperature controlled cuvette holder (Cecil) and an Aeroset automated analyzer (Abbott) were used (6).

Statistical Analysis: Statistical analyses (t test) were performed by using commercial program SPSS (Statistical Package for Social Sciences) 11.0. Values of $p<0.05$ were considered to be significant.

Results

The mean ages of the patients and controls were 28.59 (±5.09), and 30.17 years (±5.65) respectively. The mean value of BMI were patients and controls were 25.16 (±1.20) and 24.72 (±0.37). Mean gestational ages of the patients and controls were 17.7 (±1.3), 17.8 weeks (±1.4) respectively. The two groups were similar according to age, BMI and gestational age ($p>0.05$).

The ceruloplasmin levels of the amniotic fluid of patients and controls were 304.96 (±20.1) mg/dl and 305.31 (±14.9)mg/dl. There were no statistical differences between the groups ($p>0.05$).

The ceruloplasmin levels of the maternal bloods were 888.20 (±99.3) and 853.14 (±119.21) mg/dl for the patients and controls respectively. The value of the ceruloplasmin in maternal bloods were not found to be statistically different in the two groups ($P>0.05$).The results were summarized in Table 1.

Discussion

Ceruloplasmin is one of the most important acute phase response proteins of the organism. The oxidation of aromatic amines is the important activity of cp in terms of antioxidation (1, 2).

Despite years of intensive epidemiological, clinical and experimental research, the exact etiology of NTD remains rather complex and poorly understood. Genetic and environmental factors contribute to NTD. However, it is generally agreed that most NTD cases are of multifactorial origin, having a significant genetic component in their etiology that interacts with a number of environmental risk factors (3, 8, 9).

Many physical agents (e.g. X-irradiation, hyperthermia, stress), drugs (e.g. thalidomide, folate antagonists, androgenic hormones, antiepileptics ,hypervitaminosis A), chemical agents (e.g. organic mercury, lead), airborned chemicals (polyvinyl chloride) and maternal infections (e.g. rubella, cytomegalovirus, *Toxoplasmo gondii*, syphilis), are capable of causing congenital malformations of the central nervous system structures (3).

These factors are probably affecting the closure mechanisms of NTD at gene level. Also, most of these chemical and physical agents are also effective in the production of oxidative stress, which can effect the CNS. At this point antioxidation mechanisms become an important activity of the organism in order to prevent biofunctional disorders.

In the light of previous datas about the etiology of CNS anomalies, they seem to be related to oxidant chemical and physical agents (3-5, 10). Ceruloplasmin was considered to be effective as an antioxidant in NTD.

However, in a study Jenkins et al. have found that pregnancies that went successfully to term were associated with increased levels of ceruloplasmin early in the first trimester. This change was thought to offer the cell protection from the damage caused by the increased oxidative stress associated with pregnancy (11).

In our study we investigated whether there is a relation between the NTD and Cp. We could not find a significant relationship between Cp and NTD. The limitation of our study is the gestational week of the parcipitants. Although it was documented that NTD was a very early onset anomaly (early first trimester), the patients in our study were in the second trimester. On the other hand, cp is only one of the many antioxidants in the body. Maybe the other antioxidants, but not cp,are effective in NTD development. This is an other aspect in order to investigate the probable etiology of NTD, and different studies about these antioxidants need to be planned.

Also, a study evaluating a larger patient group in early first trimester may document significant cp values related with NTDs.

Table 1. Results of the patient ant control groups

	Patient group	Control group	P*
MaternalAge	28.59 (±5.09)	30.17 (±5.65)	>0.05
Gestational age	17.7 (±1.3)	17.8 (±1.4)	>0.05
BMI	25.16 (±1.20)	24.72 (±0.37)	>0.05
Cp values of amniotic fluid (mg/dl)	304.96 (±20.1)	305.31 (±14.9)	>0.05
Cp values of maternal blood (mg/dl)	888.20 (±99.3)	853.14 (±119.21)	>0.05

*p>0.05 is not statistically significant

In summary; according to this study, cp is not a marker related with NTD yet. However, this result does not mean that cp and other antioxidants are definitely not effective on NTD. Larger and well structured studies are needed for more accurate results.

Conflict of interest
None declared

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Incidence of diabetes mellitus at postpartum six to twelve months following the diagnosis of gestational diabetes mellitus

Gestasyonel diyabetes mellitus tanısı sonrasında postpartum 6-12. aylarda diyabetes mellitus saptanma oranları

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Abstract

Objective: The aim of this study was to research the rates of diabetes mellitus (DM) and the risk factors that may play a role in the prediction of this condition by evaluating patients with the diagnosis of gestational diabetes mellitus (GDM) at the 6th-12th postpartum months.

Material and Method: Among 109 cases who had been invited to the hospital for oral glucose tolerance test (OGTT) at the 6th-12th postpartum months, 84 cases (77%) were enrolled in the study. To the 78 patients that were found to be appropriate according to the study criteria, 75 gr OGTT was administered. Patients who had new pregnancies during the period of postpartum screening, and those with previously diagnosed DM were excluded from the study.

Results: While the results of 23 cases (29.5%) included in the study were normal, 27 cases (34.6%) were diagnosed with DM and 28 cases (35.9%) were diagnosed as having an impaired glucose tolerance and /or impaired fasting glucose (IGT/IFG). Among patients diagnosed with DM, the history of DM in the first degree relatives (n=21, 77.8%, p=0.018), body mass index before pregnancy (mean=30.1±4.4, p=0.009) and insulin requirement for the treatment of GDM (n=25, 92.6%, p<0.05) were determined at higher rates. In the logistic regression analysis, multiparity (OR=2) and insulin requirement during pregnancy (OR: 7.27) were found to be the predictive factors in the development of postpartum DM.

Discussion: In this study, the determination of high rates of DM development in the postpartum period after GDM demonstrates the necessity of augmentation in efforts to increase the screening rates after delivery and to increase the patients' acknowledgement of this topic.

(J Turkish-German Gynecol Assoc 2010; 11: 89-94)

Key words: Gestational diabetes mellitus, postpartum, OGTT

Received: 20 February, 2010 **Accepted:** 11 April, 2010

Özet

Amaç: Bu çalışmada gestasyonel diyabetes mellitus (GDM) tanısı alan hastaların postpartum 6-12.aylar arasında değerlendirilmesi sonucunda diyabetes mellitus (DM) saptanma oranları ve bu durumun öngörülmesine katkısı olabilecek risk faktörlerini araştırmak amaçlanmıştır.

Gereç ve Yöntemler: Postpartum 6-12. aylar arasında oral glikoz tolerans testi (OGTT) için hastaneye davet edilen 109 hastadan 84 (%77) olgu çalışmaya başvurdu, çalışma kriterlerine uygun 78 hastaya 75 gr OGTT uygulandı. Postpartum tarama zamanında tekrar gebelik tespit edilen veya daha önce DM tanısı alan hastalar çalışma dışı bırakıldı.

Bulgular: Çalışma kapsamındaki hastalardan 23 (%29.5) olgunun sonuçları normalken; 27 olguya (%34.6) DM, 28 (%35.9) olguya bozulmuş glikoz toleransı ve/veya bozulmuş açlık glikozu tanısı konuldu. DM tanısı alan hasta grubunda 1.derece akrabalarda DM öyküsü (n=21, %77.8, p=0.018), gebelik öncesi vücut kitle indeksi (ortalama=30.1±4.4, p=0.009) ve GDM tedavisi için insülin gereksinimi (n=25, %92.6, p<0.05) daha fazla oranda tespit edildi. Yapılan lojistik regresyon analizi sonucunda multiparite (OR=2) ve gebelikte insülin tedavisi gereksiniminin (OR: 7.27) postpartum DM gelişimi için öngörü faktörleri olarak değerlendirilebileceği tespit edildi.

Sonuçlar: Bu çalışmada GDM sonrası postpartum dönemde yüksek oranlarda DM gelişiminin tespit edilmesi, doğum sonrası tarama oranlarının artırılması ve hastaların bu konuda bilgilendirilmesi için daha çok çaba sarf edilmesinin gerekli olduğunu göstermektedir.

(J Turkish-German Gynecol Assoc 2010; 11: 89-94)

Anahtar kelimeler: Gestasyonel diyabetes mellitus, postpartum, OGTT

Geliş Tarihi: 20 Şubat 2010 **Kabul Tarihi:** 11 Nisan 2010

Introduction

Gestational diabetes mellitus (GDM) is defined as the carbohydrate intolerance that first develops or is recognized during pregnancy (1). It develops due to impairment in the mechanisms physiologically compensating the increased insulin resistance and decreased insulin sensitivity during pregnancy, and the prevalence of GDM has been reported to vary between 1-14% in many studies, depending on the population characteristics and diagnostic criteria (2). In Turkey, the prevalence of GDM has been reported as 4.48% in a study using the diagnostic criteria of Carpenter and Coustan (3, 4). In a great majority of patients with GDM, glucose tolerance returns to normal in the postpartum period. However, if pregnancy, which is a diabetogenic period itself, becomes complicated with GDM, the mother will be in the high risk group

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doi:10.5152/jtgga.2010.06

for the development of type 2 diabetes mellitus (DM) in the long term. In the postpartum period, the rate of type 2 DM development among GDM patients varies, depending on the ethnicity and follow-up period, and it is interesting that a prolongation in the follow-up period increases this rate. DM is a chronic disease that negatively affects the quality of life and continues progressively to destruction. For this reason, important targets in the postpartum follow-up of patients with GDM should include education of patients about their risks and what they could do to prevent or delay the development of DM (5).

In this study, it was aimed to investigate the rate of DM and the risk factors that may have a role in the prediction of this condition at the 6th-12th postpartum months, following the diagnosis of GDM.

Material and Method

The records of 335 patients who had been diagnosed with GDM and hospitalized for treatment between the dates of 1st of January 2005 and 31st of December 2007 were investigated for this study. Afterwards, the patients were contacted by telephone. One hundred and nine patients reached were informed about the study and the patients were invited to the hospital for screening of DM with 75 gr OGTT. Twenty-five of the patients were not admitted to the hospital, while 6 of the patients were excluded since they were pregnant on admission. As a result, 78 patients at the postpartum 6th-12th months who had been admitted to the hospital and agreed to be included to the study were enrolled.

This study was approved by the local ethics committee. In our hospital, GDM screening is performed by a two step method. To all pregnant women, 50 gram glucose loading test in 1 hour is administered at the 24th-28th weeks of gestation. 100 gram OGTT in 3 hours is administered to patients, whose plasma glucose (PG) levels are ≥140 mg/dl (2). The diagnosis of GDM is based on the Carpenter and Coustan criteria (4).

The variables of the patients included in the study were interrogated after having been classified for 3 periods. The variables before pregnancy were regarded as; history of DM in first degree relatives, body mass index (BMI) and GDM history in previous pregnancies; while the variables during pregnancy were; age, number of pregnancies, polyclinic control number, treatment modality (diet, insulin), total number of hospitalization days and weight gain during pregnancy. The variables of the postpartum period were; BMI on admission and at the time of lactation. A BMI [weight (kg)/height ^{2}(m^2)] below 25 kg/m² was defined as normal, while 25-29.9 kg/m² was perceived as overweight and above 30 was considered as obese. In this study, patients were investigated after having been grouped according to their BMI values as below 25 kg/m², between 25-29.9 kg/m² and above 30 kg/m².

Diagnoses of type 2 DM, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) were made with 75 gram OGTT based on the suggestions of the World Health Organization (WHO) (6). The patients were divided into 3 groups according to their final diagnoses following 75 gram glucose loading test: (1) *Normal glucose tolerance* (NGT) group (Patients with fasting plasma glucose (FPG) of <110 mg/dl and the other normal OGTT measurement results); (2) *IGT/IFG* group (Patients with an FPG value of between 110-125 mg/dl and following the loading, when at the second hour the PG was between 140-199 mg/dl); (3) *Type 2 DM* group (Patients with FPG of ≥126 mg/dl or following the loading, when at the second hour the PG was ≥ 200 mg/dl).

PG concentrations were measured using the standard glucose oxidase method from venous plasma samples (Glucose Analyzer II, Beckmann-Coulter).

Statistical analysis

All data were recorded and evaluated using the SPSS (Statistical Package for Social Sciences) program. χ^2 analysis was used for the categorical data. The Mann-Whitney U test was used in the comparison of the 2 groups, and the Kruskall-Wallis test was used in the comparison of 3 or more groups. Furthermore, logistic regression analysis was performed for the calculation of risk coefficients. The significance level was set as $p<0.05$.

Results

In the evaluation of patients with 75 gram OGTT, while the results of 23 cases (29.5%) were normal, the results of 28 cases (35.9%) were compatible with IGT/IFG, and in 27 cases (34.6%), DM was determined (Figure 1). The clinical and laboratory data of patients included in the study have been summarized in Table 1 under the headings of variables of before pregnancy, during pregnancy and the postpartum period. In the investigation of patients regarding the presence of risk factors before pregnancy, the presence of DM in first degree relatives was at the rate of 77.8% (n=21) in patients diagnosed with DM, 64.3% (n=18) in patients with IGT/IFG, and 39% (n=9) in patients with NGT, and the presence of DM in the family history was statistically significantly higher than in other groups of patients diagnosed with DM (p=0.018).

In the evaluation of the medical histories of patients, a GDM

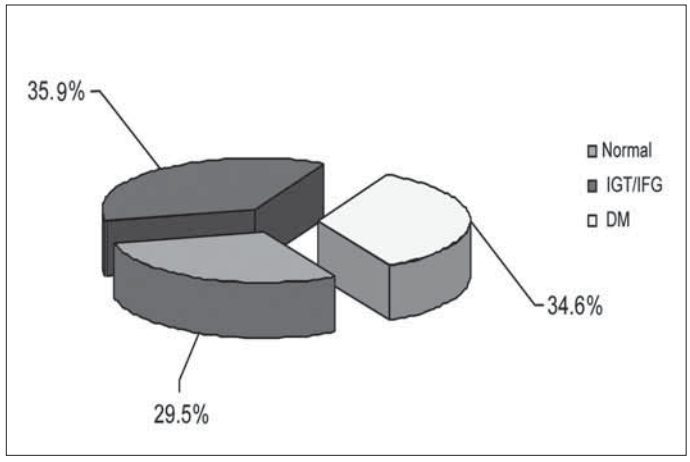


Figure 1. The evaluation rates with 75 g OGTT at the 6th - 12th postpartum months

Table 1. Patients' clinical and metabolic characteristics [mean ± SD or %(n)]

	NGT (n=23)	IGT/IFG (n=28)	DM (n=27)	p
Variables before pregnancy				
Presence of family history	39% (9)	64.3% (18)	77.8% (21)	p=0.018
BMI before pregnancy (kg/m²)	25.7±4.6	27.4±4.9	30.1±4.4	p=0.009
GDM history in previous pregnancies	8.7% (2)	14.3% (4)	0	*
Variables during pregnancy				
Age (year)	23±3.5	33.3±5.4	37±2.8	P<0.05
Parity Primiparous	8.7% (2)	35.7% (10)	7.4% (2)	p=0.02
Multiparous	91.3% (21)	64.3% (18)	92.6% (25)	
Insulin treatment	8.7% (2)	57.1% (16)	92.6% (25)	p<0.05
Weight gain during pregnancy (kg)	10.2±5.6	10.1±7	9.2±4.4	p>0.05
Total days of hospitalisation	10.5±9.4	12.9±10	12.9±10.8	p>0.05
Polyclinic control number (0-9)	47.8% (11)	35.7% (10)	44.4% (12)	p>0.05
(10-20)	52.2% (12)	64.3% (18)	55.6% (15)	
Variables of the postpartum period				
Postpartum BMI (kg/m²)	28.3±5.3	29±4.3	30.7±5.2	p>0.05
Lactation < 6ay	43.4% (10)	14.3% (4)	14.8% (4)	p>0.05
≥ 6ay	56.5% (13)	85.7% (24)	85.2% (23)	

NGT: Normal glucose tolerance, IGT/IFG: Impaired glucose tolerance/ Impaired fasting glucose, DM: Diabetes mellitus, BMI: Body mass index
*Statistical analysis could not be performed, since the number of cases was insufficient

history in previous pregnancies was questioned. However, since this was the first pregnancy in 14 patients and in 21 multiparous patients, results of GDM in previous pregnancies in only 43 patients could be accessed. In those patients, 6 (7.7%) had received the diagnosis of GDM in previous pregnancies, but due to the low number of cases, statistical analysis could not be performed.

The mean BMI before pregnancy was calculated as 30.1±4.4 kg/m² in patients diagnosed with DM, 27.4±4.9 kg/m² in patients with IGT/IFG, and 25.4±4.6 kg/m² in the NGT group. The mean BMI before pregnancy was statistically significantly higher than that in other groups in patients diagnosed with DM (p=0.009). The mean BMI before pregnancy was re-evaluated after having been grouped, as below 25 kg/m², between 25-29.9 kg/m², and above 30 kg/m². This evaluation revealed that the development of DM in the postpartum period in patients with a BMI higher than 30 kg/m² before pregnancy was significantly higher than that of the other 2 groups (p<0.05) (Figure 2).

In the investigation of variables during the pregnancy period, the mean age during pregnancy was 37±2.8 years in patients diagnosed with DM, 33.3±5.4 in patients diagnosed with IGT/IFG, and 23.5±3.5 in patients with NGT. The mean age was observed to be lower than the DM group in patients diagnosed with NGT and IGT/IFG (p<0.05).

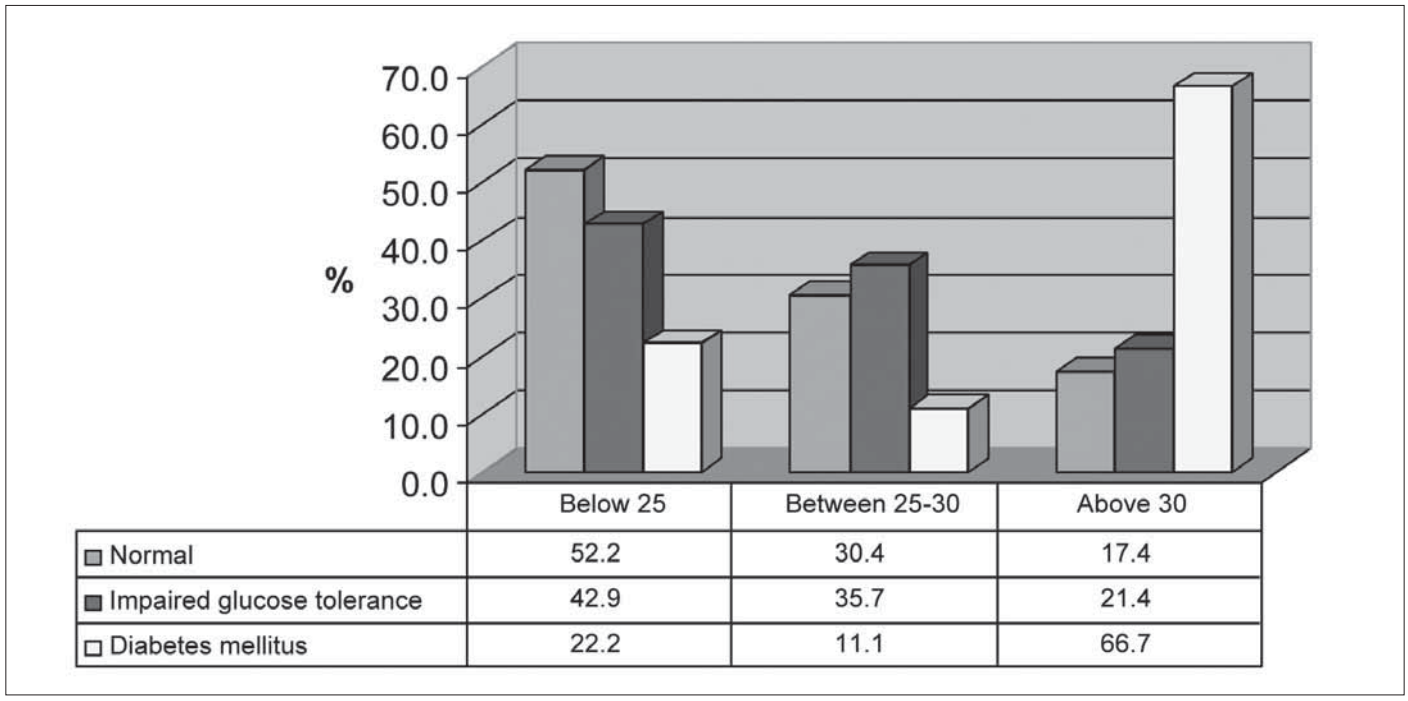
Sixty-four (82%) cases included in the study were multiparous, while 14 (18%) cases were primiparous. In the analysis of the effects of parity on the diagnosis of postpartum DM, 92.6% of the patients diagnosed with DM were multiparous. In the logistic regression analysis among patients diagnosed with DM (n=27) and other patients (n=51), multiparity was found as a significant factor affecting the model (p < 0.05, OR=2).

The insulin treatment rate for GDM was found as 92.6 % (n=25) in patients diagnosed with postpartum DM, 57.1% (n=16) in patients with IGT/IFG, and 8.7% (n=2) in patients with NGT. Among patients diagnosed with DM, the insulin treatment rate during pregnancy was found to be statistically significant (p<0.05). In the logistic regression analysis, an increase in the rate of insulin use increased the risk of development of DM development 7.27-fold (p<0, 05 OR=7, 27).

The total number of hospitalization days for blood glucose regulation and the number of polyclinic outpatient admission days were similar in all 3 groups.

The effects of lactation, which is one of the postpartum period variables, on the postpartum glycemic status were investigated after having been divided into 2 groups as shorter than 6 months, or longer than 6 months; however, no significant effects of lactation on the postpartum glycemic status was observed.

Postpartum BMI, calculated at the time of enrolment in the study was not different between the 3 groups. The cases were also investigated for postpartum BMI parameters after having been grouped as: lower than 25 kg/m², between 25-29.9 kg/m², and above 30 kg/m²; however, no statistically significant difference was determined (Figure 3).



	Below 25	Between 25-30	Above 30
Normal	52.2	30.4	17.4
Impaired glucose tolerance	42.9	35.7	21.4
Diabetes mellitus	22.2	11.1	66.7

Figure 2. **The association of BMI before pregnancy with postpartum glycemic status (%, kg/m²)**

Discussion

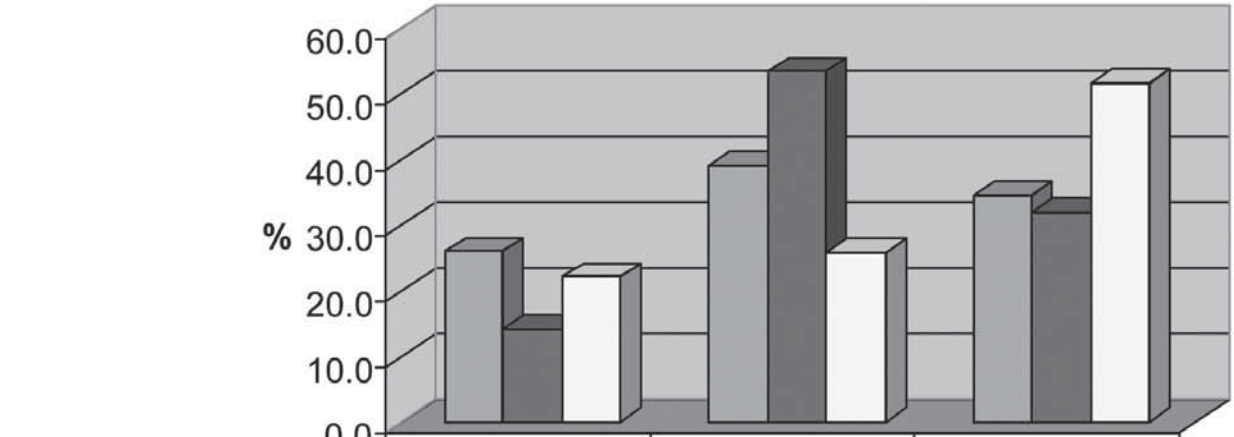
In this study, in the evaluation of patients with GDM in the postpartum 6th-12th months, IGT/IFG was determined at a rate of 35.9% and DM was determined at a rate of 34.6%. There are many studies reporting the results of screening of postpartum DM development among women who had GDM in their pregnancies. In the evaluation of these studies, which determined the results up to the end of the first year after delivery, similar to our study, the reported type 2 DM development rate was between 2% and 38%, and the IGT development rate changed between 7-21% (7-11). In our study, the higher rates of DM and IGT/IFG development than that in the literature may be due to differences in populations and follow-up periods of studies, variations in patient populations, and/or diagnostic criteria, as well as the limitations of this study.

The lack of determination of diabetes and glucose intolerance in the included patients before pregnancy is one of the limitations of this study. The possibility of the presence of diabetes or impaired glucose tolerance before pregnancy among patients diagnosed with GDM may explain these high rates in the postpartum period. Another limitation of this study is that auto-antibodies defining the presence of type DM were not determined. Hence, this high rate includes all DM cases. However, since the rate of type 1 DM among all patients diagnosed with DM is as low as 2.3%-9.3% in studies with follow-up periods ranging between 1-10 years in the literature, the high rate of DM we determined in the postpartum first year cannot be explained with this factor alone (16-19).

In the study of Costa et al. on the Spanish population, the prevalence of type 2 DM at the 2nd -12th postpartum month period was determined as 2%, which is lower than that in the literature and in our study. The reason for this may be ethnic origin, as well as the use of the 1985 WHO criteria to diagnose DM with OGTT in this study (11). In the study of Lam on the Chinese population, in the postpartum first year, the rate of DM diagnosis following GDM was reported as 5%, and the rate for IGT diagnosis was found to be 8%. The differentiation of this study from our study and other studies and the reason for the low DM prevalence in this study was probably the exclusion of cases with normal results on the first glycemic status evaluation at the sixth week after delivery (9).

Despite the presence of studies reporting that ethnic origin does not have primary importance, there are studies associating the prevalence of postpartum type 2 DM they determined following GDM, directly with de novo type 2 DM development rates in the population study (5, 12-14). In our country, there is no specific screening program for DM except for the pregnancy period. A few years ago, in the Turkish Diabetes Epidemiology study (TURDEP), the DM prevalence in our adult population was defined as 7.2% and the IGT prevalence was defined as 6.7, and they have been reported more commonly in women than men (15). When the 7.2% DM prevalence reported in TURDEP is considered, the high rates of postpartum type 2 DM development in our patient population cannot be associated with de novo type 2 DM development.

As in many studies, we also demonstrated the increased risk of postpartum DM development following GDM in patients with DM in first degree relatives (7, 9, 10, 20). Although the history of GDM in previous pregnancies was not a clearly evaluated variable in our study, many researchers have defined this variable as a predicting factor for development of DM in the future (21-23).



	Below 25	Between 25-30	Above 30
Normal	26.1	39.1	34.8
Impaired glucose tolerance	14.3	53.6	32.1
Diabetes mellitus	22.2	25.9	51.9

Figure 3. **The association of BMI after delivery with postpartum glycemic status (%, kg/m²)**

When the clinical features of patients in our study were evaluated, it could be stated that the age of the patients diagnosed with DM at the postpartum period during index pregnancies were significantly higher than that of other patients. Older age has been described as a classic risk factor in the development of postpartum DM in many studies, and has also been confirmed in our study and the importance of cautious follow-up of pregnant women who are in an older age group and with obesity has been emphasized (21, 24).

In many studies in the literature, the association of parity with glycemic status after delivery could not be demonstrated (9, 20, 23, 25, 26). However, in our study, it has been determined that multiparity increases the risk of DM development; but up to 82% of the patient population in our study was multiparous, which may be the reason for this difference from that in the literature ($p<0.05$ OR=2).

In this study, the rate of incidence of postpartum DM development in the first year among patients treated with insulin for GDM was found to be higher than that of other patients ($p<0.05$ OR=7.27). The necessity of insulin use during pregnancy was also defined as a factor with high predictive value for the development of DM in the future in the literature (9, 21, 28-30).

The total number of hospitalisation days and polyclinic control were evaluated since they consequently show poor glycemic control and the necessity of more common assessment, but there was no significant difference between patients diagnosed with DM and those not diagnosed with DM.

Nowadays, one of the most important factors affecting human health all over the world is obesity. Supporting many previous studies in the literature, in this study, the BMI before pregnancy was found to be significantly higher among patients diagnosed with postpartum DM (16, 21, 29, 31). However, similar to the literature, there was no significant difference between patients diagnosed with DM and the other patients with regard to weight gain during pregnancy and BMI calculated on admission to the study, but it was noteworthy that the mean of this variable for all patients was 29.4 kg/m². In the studies performed, since the development of DM depends on many different mechanisms, it has been suggested that obesity cannot be solely blamed as the responsible factor in the etiology (25, 32).

In our study, lactation did not have a significant effect on postpartum glucose tolerance. Similarly, in the literature, although the positive effects of lactation on the glycemic status of the mother could not be clearly demonstrated, there are studies demonstrating that it decreases the high feeding rates in babies, and the rate of these babies being overweight-obese is lower and consequently lactation should be supported in these patients (2, 33-35).

Cumulative incidence of postpartum DM shows a fast rise in GDM patients in the first 5 years, and in the 5-10-year period, and although the increase continues, the acceleration decreases (5). These patients should be followed-up for a longer duration in order to contribute to the public data. If the results of this study, that 1 in every 3 GDM patients receives the diagnosis of DM in the first year after delivery and similarly 1 in every 3 patients also receives the diagnosis of IGT, which is a risk factor for DM, are taken into account, the most important health target for a GDM-diagnosed pregnant woman in the postpartum period is the prevention of DM development, which is a chronic disease that negatively affects the quality of life, has an expensive treatment and severe complications.

Conflict of interest
None declared

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Shortening the second stage of labor?

Travayın ikinci evresinin kısaltılması

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Abstract

Objective: To evaluate the benefits and risks of using uterine fundal pressure in shortening the second stage of labor and on the obstetrical outcome.

Material and Methods: A pilot study comprising 209 primigravidae between 37 and 40 gestational weeks with singleton fetus in cephalic presentation admitted to the delivery suite were considered and were randomly allocated into two groups: I (n=101) and II (n=108), with or without manual fundal pressure, respectively, during the second stage of labor. Main observation measures considered were: duration of the second stage of labor was the primary outcome measure and the secondary outcome measures were severe maternal morbidity/mortality, neonatal trauma, admission to neonatal intensive care unit, and neonatal death.

Results: There were no significant differences in the mean duration of the second stage of labor and secondary outcome measures. Significant adverse findings having no mention in the earlier literature, were noticed which were: one case each of retained placenta and uterine prolapse besides increased evidence of maternal exhaustion and perineal injuries (including one case of complete perineal tear) in the group where fundal pressure was exercised.

Conclusion: Application of uterine fundal pressure in a delivering woman was not only ineffective in shortening the second stage of labor but added to the risks during parturition.

(J Turkish-German Gynecol Assoc 2010; 11: 95-8)

Key words: Fundal pressure, second stage, perineal injuries

Received: 26 January, 2010 **Accepted:** 21 March, 2010

Özet

Amaç: Doğumun ikinci evresinde uterin fundal baskı uygulamanın fayda ve risklerini ve obstetrik getiri üzerindeki etkisini araştırmak.

Gereç ve Yöntemler: Otuzyedi-kırk hafta arasında sancıları başlamış bebeği tekil ve baş ile gelen 209 primigravid gebe doğumhaneye alındı ve fundal bası uygulanacak olan (n=101) ve uygulanmayacak olan (n=108) olarak iki gruba alloke edildi. Doğumun ikinci evresinin süresi primer getiri, ciddi maternal mortalite ve morbidite, neonatal travma, yenidoğan yoğun bakı ünitesine giriş ve yenidoğan ölümü sekonder getiriler olarak belirlendi.

Bulgular: Doğumun ikinci evresi veya sekonder getiriler açısından iki grup arasında anlamlı fark saptanmadı. Ancak, şu ana kadar literaturde bildirilmeyen önemli bir bulguya rastlandı: fundal bası uygulanan gruptaki bir hastada plasenta retansiyonu ve uterin prolapsus ve diğer bir hastada da perineal yaralanma (komplet perineal yırtık) görüldü.

Sonuç: Doğumun ikinci evresinde fundal bası yapmak süreyi kısaltmada etkisiz olmasının yanında aynı zamanda doğumu riskli bir hale getirir.

(J Turkish-German Gynecol Assoc 2010; 11: 95-8)

Anahtar kelimeler: Fundal bası, ikinci evre, perineal yaralanma

Geliş Tarihi: 26 Ocak 2010 **Kabul Tarihi:** 21 Mart 2010

Introduction

Uterine fundal pressure is an age old practice and is applied by some health workers including resident and native doctors and traditional birth attendants to women in labor with the belief that it helps to increase expulsive efforts in labor (1). It comprises of the application of external force to the uppermost part of the uterus in the caudal direction in the second stage of labor in an attempt to shorten its duration and to help expedite the delivery. A large majority of centers, including the U.S, also use fundal pressure, although many fail to document the practice in medical records (2). The use of this practice to assist the second stage of labor has been controversial throughout (3). Studies of how fundal pressure might speed delivery are lacking.

The present study was conducted to determine the effect of uterine fundal pressure on shortening the second stage of labor and on the fetal outcome.

Material and Methods

A review based on 209 vaginal deliveries, during the period between 19th Mar. 2007 to 5th Sept. 2008 in the Maharishi Markendeshwar Institute of Medical Sciences and Research, Mullana, (Ambala, India) was evaluated.

Written informed consent was obtained and the department Ethical Committee approved the study. Being a pilot study, sample size calculation was not required. Those included were healthy primigravidae patients (aged 20-27 years) with a singleton fetus in cephalic presentation, having spontaneous onset of labour at-term, between 37-40 weeks, with the pelvis being average adequate gynaecoid with no clinical evidence of cephalo- pelvic disproportion. Exclusion criteria considered were women with a previously scarred uterus, uterine anomalies, previous instrumental abortion, clinical or sonographic evidence of intra-uterine growth restriction,

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doi:10.5152/jtgga.2010.07

induction of labor, inappropriate prostaglandin and oxytocin usage, vacuum extraction/ forceps delivery or intrauterine manipulations and caesarean sections.Two hundred and forty two women were enrolled for the study but 33 of these did not meet the inclusion criteria (non-cephalic presentation n=9, use of oxytocics for augmentation of labour n=13, signs of fetal distress n=11). Allocation of the remaining 209 patients was done into two groups by using a randomized table of numbers. Index cards with the random assignment were prepared and placed in sealed envelopes and a researcher who was blinded to the baseline examination findings opened the envelope, approximately at the onset of the second stage of labour, and the proceedings were done according to the group assignment. As depicted in Figure 1, two groups were assigned: group-I (n=101), where manual pressure was applied to the uterine fundus during the second stage of labour, and group-II (n=108), in whom no fundal pressure was executed. All participants were in active labour at-term and the women remained alert and responsive throughout. During the course of labor, neither oxytocin nor prostaglandin augmentation was administered to any of the patients in both groups.

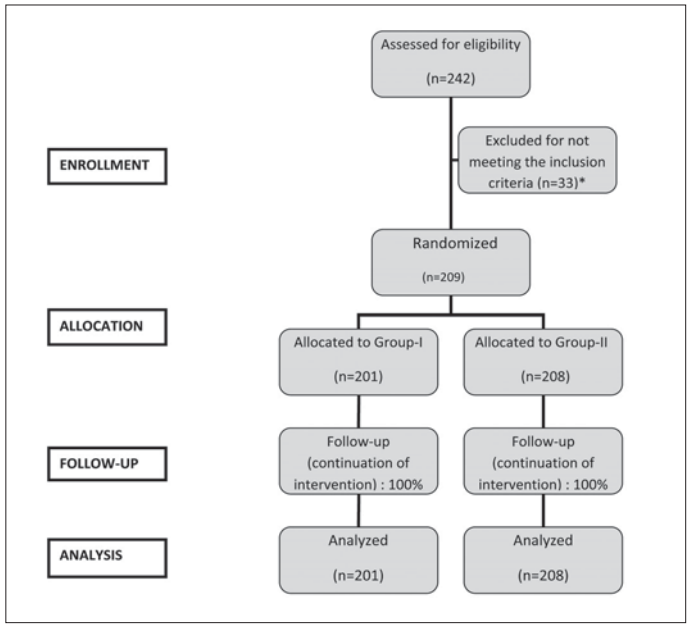


Figure 1. The CONSORT Flow Diagram showing the progress of participants at each stage of the study. *(non-cephalic presentation n=9, use of oxytocics for augmentation of labour n=13, signs of fetal distress n=11)

Fundal pressure was applied manually at a 30-to 40-degree angle to the spine in the direction of the pelvis by the same doctor and three applications at the most in group-I patients after the clinical confirmation of full cervical dilatation with the vertex below the level of the ischial spines (plus-station) and occipito- anterior position. To observe uniformity, right mediolateral episiotomy was employed at the instance of crowning of the vertex in all the cases and the placenta was delivered by modified Brandt- Andrew's technique (controlled cord traction) at the clinical confirmation of its separation following delivery of the baby.

All the observations were given consideration along with perioperative complications in both the groups. The data were tabulated and analyzed. Summary statistics such as mean, standard deviation were estimated. Chi-square and Fisher's exact tests were used for categorical data. For continuous data like age, weight and duration of the second stage, student's t -test was utilised. The significance was seen after applying log transformation and stastical significance was set at $P<0.05$.

Observations

The main objective was to note the difference in the duration of the second stage of labour and secondary areas of concern were mother's condition and findings from postpartum examination, complications like perineal injuries, Apgar score of the babies, any neonatal complications, or any other unforeseen eventualities in either of the groups.

The profile of the patients constituting both the groups is depicted in Table 1 and apparently the difference in the two groups was not statistically significant. Birth weight of the babies in the two groups was also not significantly different.

No appreciable difference was noted in our primary outcome concern of this study, as the average duration of the second stage in group-I was 34-55 minutes (mean being 49 minutes),and in group-II 33-53 minutes (mean 48 minutes), Table 2. The table also illustrates the perineal injuries sustained such as: extension of episiotomy in 5 cases of group-I, while only one woman had this eventuality in group-II. One case in group-I had complete perineal tear and this was repaired following the delivery of the placenta. Significant adverse findings happened only in group-I, where one case of retained placenta was encountered and had to undergo manual removal under general anaesthesia. In this patient, fundal pressure or uterine manipulation after the delivery of the baby and active management of the third stage, along with the possibility of adherent placenta (by sonography and color dop-

Table 1. Patient Profile and Birth weight

	GROUP - I (n=101) Mean (Range)	GROUP - II (n=108) Mean (Range)	P - VALUE
PATIENT PROFILE			
AGE (years)	21.6 (20.2-26.7)	22.3 (20.0-26.9)	>0.05
WEIGHT (kg)	58.41 (43.4-76.4)	57.92 (42.5-77.0)	>0.05
BIRTH WEIGHT (kg)	2.86 (2.52-3.32)	2.91 (2.50-3.48)	>0.05

pler) which might have precipitated the placenta to be retained, were ruled out and thus this could be attributed to the application of fundal pressure during the second stage.

One patient in this group developed uterine prolapse in the post-partum period and this persisted even six months after delivery. The past history of this patient did not reveal any precipitating factor for such an eventuality.

Other significant findings noted were that, in group I, maternal exhaustion during and immediately after parturition was apparently more, and a subjective feeling of pain as evidenced by the requirement of injectable analgesic (Diclofenac, besides routine oral anti-spasmodic drugs) within 36 hours post-delivery, was also in higher proportions, Table 3.

One patient in this group had post-natal retention of urine for which bladder decompression was done twice with a disposable catheter and on recurrence had to be put on indwelling Foley's catheter for 72 hours. This was removed after toning up the bladder with clamping and intermittent release when the patient felt the desire to micturate.

In none of the two groups was a severely asphyxiated baby born and the Apgar score was also no different, being between 7 and 9 at 1 and 5 minutes respectively. No case of neonatal trauma and/or neonatal death was reported, the probable reason being that cases with intra-uterine growth restriction, vacuum extraction or forceps delivery, and intrauterine manipulations were excluded from the study.

Discussion

Fundal pressure is the application of steady pressure on the fundus of the uterus and is considered among the most controversial maneuvers used in the second stage of labor since no confirmed benefit of the procedure has been documented, albeit a few adverse events have been reported in association with its execution (3). A scientific justification for its use is yet to be made. In their study, Api et al. concluded that application of fundal pressure on a delivering woman was ineffective in shortening the second stage of labor (4) while, Cosner in 1996 (5) reported that its use to assist the second stage has been found to cause a longer second stage of labor instead. Moreover, it has been associated with a number of complications (6) ranging from higher incidence of third and fourth degree perineal lacerations (4, 7) to several reports of uterine rupture (8, 9) in those women where application of fundal pressure is practiced in labor. Pan et al. (10) reported a case of uterine rupture due to traumatic fundal pressure in a primigravid woman with an unscarred uterus . However, Wei et al encountered this complication in a case where fundal pressure was applied because of coexistent shoulder dystocia (11). Kurduglu et al. (12) have cautioned against the use of uterine fundal pressure, particularly in conditions like shoulder dystocia: if applied in this circumstance, besides the risk of uterine rupture, the shoulder will be further impacted and increase the chances of injury to the baby (3).

Uterine rupture is a rare but serious complication in obstetrical practice resulting in maternal and fetal jeopardy. In an unscarred uterus it is seen much more rarely, with an estimated occurrence of one in 8000-15000 deliveries, but the incidence increases when fundal pressure is applied on the uterus during active labor (10), more so in cases with previous cesarean section, inappropriate prostaglandin and oxytocin usage, previous instrumental abortion, vacuum extraction delivery and intrauterine manipulations. All these, besides obstructed labor and grandmultiparity, are considered as risk factors for uterine rupture if fundal pressure is applied (13). These cases were excluded from our study. This practice of applying uterine

Table 2. Duration of Second Stage, Perineal Injuries and other Significant Findings

FINDINGS	GROUP - I	GROUP - II	P - VALUE
DURATION OF SECOND STAGE			
Mean(range)	49 (34-55) minutes	48 (33-53) minutes	>0.05
PERINEAL INJURIES			
Extension of episiotomy	5 (4.95%)	1 (0.92%)	<0.05
Complete Perineal tear	1 (0.99%)	- (0.0%)	
SIGNIFICANT FINDINGS			
Retained placenta	1 (0.99%)	- (0.0%)	
Uterine prolapse	1 (0.99%)	- (0.0%)	

Table 3. Injectable analgesic requirement within 36 hours post-natal

Injection Diclofenac (in 36 hours post-delivery)	GROUP - I (n=101) No. of patients (%)	GROUP - II (n=108) No. of patients (%)	P - VALUE
Single dose	21 (20.79)	5 (4.63)	<0.05
Two doses	9 (8.91)	3 (2.77)	<0.05
Three doses	4 (3.96)	- (0.0)	

fundal pressure is also associated with acute puerperal uterine inversion (14, 15).

These conditions are life threatening to the mother and in the case of ruptured uterus, to the baby too. Fundal pressure in labor also reportedly precipitated uterovaginal prolapse (1) as also happened in one of our cases. According to Buhimschi et al. (2), such fundal thrust can substantially augment intrauterine pressure in some parturients and this hypothesis may be a reason behind its adversities**.** In the present study, although no major life threatening complications were encountered, uterine fundal pressure application was found to be fraught with increased evidence of maternal exhaustion with enhanced rate of extension of episiotomy and even a case of complete perineal tear. A case of retained placenta was also seen in this group attributable to the fundal pressure maneuvre. Our study also noticed a case of uterovaginal prolapse, possibly due to the practice of applying fundal pressure during labour: this being the second such case encountered as per review of the literature (1).

Conclusion

The purpose for which uterine fundal pressure is primarily employed i.e. shortening the second stage of labour, is disapproved by this study. However, when there is delay in the second stage of labor, efforts should be made to determine the reasons and appropriate corrective measures be put in place. Since fundal pressure is associated with several complications, both orthodox and traditional health practitioners should avoid applying it.

Acknowledgements
Maharishi Markendeshwar Educational Trust.

Conflicts of interest
it is declared that there are no conflicts of interest

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The rationale behind collecting umbilical cord blood

Umbilikal kordon kanı toplanmasının altında yatan gerçek

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Abstract

Umbilical cord blood (UCB) is an increasingly important and rich source of stem cells. These cells can be used for the treatment of many diseases, including cancers and immune and genetic disorders. For patients for whom no suitable related donor is available, this source of hematopoietic stem cells offers substantial advantages, notably the relative ease of procurement, the absence of risk to the donor, the small likelihood of transmitting clinically important infections, the low risk of severe graft-versus-host disease (GVHD) and the rapid availability of placental blood for transplantation centers. Even though almost 80 diseases are treatable with cord blood stem cells, 97 percent of cord blood is still disposed of after birth and lost for patients in need! To improve availability of stem cells to a broader community, efforts should be undertaken to collect cord blood and expectant parents should be properly informed of their options with regard to cord blood banking.

(J Turkish-German Gynecol Assoc 2010; 11: 99-101)

Key words: Stem cell, umbilical cord blood, collection, allogeneic, autologous, transplantation

Received: 26 November, 2009 **Accepted:** 31 December, 2009

Özet

Umbilikal kordon kanı kök hücre zengin bir kök hücre kaynağıdır ve önemi gittikçe artmaktadır. Bu hücreler kanser, immun ve genetik birçok hastalığın tedavisinde kullanılmaktadırlar. Uygun donor bulunamayan hastalar için bu hemopoetik kök hücre kaynağı birçok avantajlar sunar. Bunlar; işleme için kolaylık, donor bulunmama riskinin ortadan kalkması, klinik önemi olan enfeksiyon hastalıklarının bulaşma oranının düşük olması, greft reddi oranının az olması ve plasenta kanının tarnsplantasyon merkezlerine kolayca ulaştırılması gibi. Kordon kanındaki kök hücreler ile şu an yaklaşık olarak 80 kadar hastalık tedavi edilebilirken, ne yazık ki kordon kanlarının %97'si hala atılmakta ve hastalar tedavi şanslarını yitirmektedirler. Kök hücrelerin bulunabilirliğini arttırmak ve tüm topluma ulaştırmak için, kordon kanını toplamak ve çiftleri kordon kanı bankacılığı hakkında yeterli bilgilendirmek için çaba harcanmalıdır.

(J Turkish-German Gynecol Assoc 2010; 11: 99-101)

Anahtar kelimeler: Kök hücre, umbilikal kord kanı, toplama, allojenik, otolog, transplantasyon

Geliş Tarihi: 26 Kasım 2009 **Kabul Tarihi:** 31 Aralık 2009

Introduction

Bone marrow (BM) and peripheral blood (PB) stem cell (SC) transplantations from human leukocyte antigen (HLA)-identical sibling donors have been used for many years in the treatment of hematological malignancies, BM failure syndromes, selected hereditary immunodeficiencies and metabolic disorders. A higher probability of successful engraftment and a reduction in the risk of potentially fatal graft-versus-host disease (GVHD) is conferred with close matching. Unfortunately, there is only a 25-30% chance of identifying a full sibling donor HLA match (1, 2). An alternative to a related donor involves seeking unrelated HLA-matched adult allogeneic donors outside the family. Today more than 13 million potential unrelated volunteer adult donors are registered in the Bone Marrow Donor Worldwide registry (3). However, more than 50% of all patients are unable to find a suitable adult donor in a timely manner (4) and only 30-40% of donor searches result in unrelated donor SC transplantation (5). Non-caucasians have an overall lower chance of identifying a fully matched unrelated adult donor because of genetic heterogeneity and under-representation of non-white donors in the registries (6).

Umbilical cord blood transplantation for children and adults

Umbilical cord blood (UCB) has been evaluated by clinical investigators as an alternate source for SC transplantation in an attempt to increase the availability of suitable donors and reduce the morbidity and mortality associated with allogeneic BM- and PB-SC transplantation (7-11). Many patients who are unable to identify a BM- or PB-SC donor can now benefit from a partially or fully matched UCB due to advances in the clinical practice of cord blood transplantation. Initially, UCB-SC

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doi:10.5152/jtgga.2010.08

transplantation using allogeneic UCB was performed in small children. However, in the meantime it has been proven that older children, adolescents, and adults can also be successfully transplanted with unrelated allogeneic UCB (12) In fact, almost 50% of the transplanted allogeneic UCB units facilitated by the National Marrow Donor Program in 2008 were for adults (13). Furthermore, recently, the first child with leukaemia was successfully treated with her own UCB (14).

Umbilical cord blood for regenerative medicine

Additionally, SC from UCB may serve as a stem cell source for future cellular therapy for tissue repair and tissue regeneration. In particular, promising results from in- vitro studies using cord blood for engineering blood vessels and heart valves (15) point in this direction (16). Furthermore, in human and animal studies, such cells seem to provide disease-ameliorating effects in conditions such as urinary stress incontinence (17), Alzheimer's disease (18), Huntington's disease (19), amyotrophic lateral sclerosis (20), spinal cord injury (21) diabetes (22, 23) myocardial infarction (24-27), to name just a few. The value and power of UCB-SC and the potential they possess for medical treatment and cures is creating a new paradigm for the future. There are already more than 138 clinical trials listed in the U.S under the National Institute of Health for various diseases (28). To date, more than 73 diseases were successfully treated using adult SC (29) with more than 20.000 UCB-SC transplants performed for a variety of malignant and non-malignant diseases, mainly due to the fact that they are a rich and readily available source of adult SC (30). The number of children who have received autologous CB treatment is more than 100 to date (31). The developments in the direction of autologous UCB treatments for diseases, which have a much higher incidence than those requiring allogeneic donors, is supported by research and clinical trials in areas such as neurological disorders (32) and diabetes (33). In contrast to the increasing use of SC such as from UCB to treat various diseases, not a single clinical application is currently available for embryonic stem cells.

Cord blood has advantages over bone marrow

Advantages of UCB over SCs from the BM or PB of related or unrelated donors include the fact that it is readily available, carries less risk of transmission of blood-borne infectious diseases, and is transplantable across HLA barriers with a diminished risk of GVHD (34, 35).

Despite the high value of SC from UCB for clinical applications as well as for research, more than 97 percent are still being discarded. The reasons are manifold, most prominent because their therapeutic potential is still underestimated and undervalued even though they show better results for allogeneic use compared with SC from BM or PB (36-38). Additionally, autologous clinical applications are underrepresented, because most potential recipients are still in their infancy and severe diseases in this phase of life are relatively rare.

Furthermore, most patients who could potentially benefit from an autologous or allogeneic stem cell treatment have no chance to receive their own UCB or UCB from a donor. This is mainly due to the fact that doctors are still reluctant to tell pregnant women of the possibility of storing their child's UCB in a private family bank or to donate it to a public bank.

Conclusion

It has been estimated that the lifetime probability of undergoing an autologous or allogeneic UCB-SC transplantation is almost 1:200 if only 50% of all haematopoietic diseases, which are treatable with SC, were treated with UCB-SC (not including all other potential non-hematopoietic conditions!) (39). Considering this perspective it seems that all expectant parents should be advised properly by their doctors with complete and up-to-date information, thus helping the parents to make a sound decision regarding whether to store the CB of their baby in a private family bank or to donate it to a public bank. The only wrong decision that actually can be made is throwing away this life saving material.

Conflict of interest

None declared

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Laparoscopic surgery of interstitial (cornual) pregnancy, a case report

İntertisyel (kornual) gebeliğin laparoskopik tedavisi, vaka sunumu

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Abstract

We report a successful laparoscopic management of an interstitial pregnancy of a 24- year-old single woman, treated by cornuostomy. The patient was first managed with methotrexate treatment. After the 2. methotrexate administration, the patient suffered from low abdominal pain, and intraabdominal bleeding signs were reported by transvaginal ultrasonograpy. The hemoglobin level was decreased from 12.8 gr/dl to 11.8 gr/dl and the beta hCG level was increased from 8,314 mIU/l to 11,541 mIU/l. The laparoscopic approach to interstitial pregnancy was presented and other management strategies such as medical treatment and laparotomy have been reviewed.

(J Turkish-German Gynecol Assoc 2010; 11: 102-4)

Key words: Interstitial (cornual) pregnancy, laparoscopy, methotrexate, cornuostomy

Received: 24 June, 2009 **Accepted:** 17 September, 2009

Özet

24 yaşında bekar bir bayan hastada görülen intertisyel (kornual) ektopik gebelik vakasının laparoskopik kornuostomi uygulanarak, başarılı bir şekilde tedavisi sunulmuştur. Tanı konulmasını takiben; önce metotreksat tedavisine alınan hastada, 2. metotreksat uygulaması sonrası gelişen kasık ağrısı şikayeti nedeniyle yapılan transvajinal ultrasonografide, intraabdominal kanama bulguları görülmüştür. Hemoglobin seviyesinin 12.8 gr/dl'den 11.8 gr/dl'ye düşmesi ve beta hCG düzeyinin 8,314 mIU/ml'den 11,541 mIU/ml'ye yükselmesi üzerine, hasta laparoskopiye alınmıştır. Bu makalede intertisyel gebeliklerde laparoskopik uygulamalar ve diğer tedavi seçenekleri (medikal tedavi ve laparotomi) irdelenmiştir.

(J Turkish-German Gynecol Assoc 2010; 11: 102-4)

Anahtar kelimeler: İntertisyel (kornual) gebelik, laparoskopi, metotreksat, kornuostomi

Geliş Tarihi: 24 Haziran 2009 **Kabul Tarihi:** 17 Eylül 2009

Introduction

Interstitial pregnancy is a rare form of ectopic pregnancy that can lead to catastrophic events. As the cornua are the vascular confluence region, a ruptured cornu can trigger a life-threatening hemorrhage and may lead to rupture of the uterus in a subsequent pregnancy (1). It comprises 2% of all ectopic pregnancies (2). The gold standard was to treat interstitial pregnancy by laparotomy with cornual resection, but sometimes difficult hemostasis needs hysterectomy or hypogastric artery ligation to be performed. Current trends in treatment are mostly conservative with the objective of minimizing morbidity and preserving fertility. These conservative methods may be medical or surgical, such as intramuscular methotrexate administration (3), local injection of methotrexate or potassium chloride (4) with or without systemic, multidose methotrexate (5), laparoscopic cornuotomy using a temporary tourniquet suture and diluted vasopressin injection (6). The terms cornual and interstitial pregnancy are used synonymously to define pregnancy implanted in the interstitial part of the fallopian tube which is the proximal portion that is embodied within the muscular wall of the uterus. We present our case to raise awareness of this rare pathology which has a different diagnosis and to highlight the recent advances in fertility preserving treatments.

Case report

A 24-year-old woman Gravida:3, Para:0 with 2 artificial abortions was admitted to our hospital with 6 weeks of amenorrhea, spotting and lower abdominal pain. On examination, her internal os was closed and she had tenderness in the left fornix. The uterus was hypertrophic, and there was a little vaginal bleeding. Transvaginal ultrasonography scan showed a heterogeneous mass of 3 cm which has a 14 mm gestational sac situated in the left cornual region. The endometrial thickness was 14 mm, no fetal pole or yolk sac was seen. The endometrial biopsy using abdominal ultrasonography guidance showed that the gestational sac was not interfering with endometrial cavity and the material did not have chorionic villi. The beta hCG level was 8314 mIU/ml, hemoglobin (Hb) level was 12.8 gr/dl, and the patient was hemodynamically stable. We administered the first dose of methotrexate (1 mg/kg) and folinic asid (0.1 mg/kg) therapy. On the third day after

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doi:10.5152/jtgga.2010.09

the second methotrexate therapy, the patient suffered from lower abdominal pain. A transvaginal ultrasonography revealed fluid in the Douglas pouch, and the myometrial thickness was as thin as 3 mm in the left cornual region. The laboratory results were as follows; Hb: 11.8 gr/dl, beta hCG: 11,541 mIU/ml. A laparoscopy that immediately followed revealed the presence of an enlarged left cornua (Figure 1), and intraabdominal bleeding (from the tubal ostium). A successful laparoscopic cornuostomy operation was performed.

Surgical technique

After endotracheal intubation and general anesthesia in a dorsolithotomy position, a Veress needle was inserted through the umbilicus, and the abdomen was inflated with CO2. In the laparoscopic exploration, the left enlarged cornua was seen. Bipolar coagulation was performed on the cornual region as far away as possible from the tube. Monopolar cauterisation was used to make a vertical incision. The gestational sac was emptied with grasping forceps and suction irrigation under the magnified view provided by the laparoscope. Again, bipolar coagulation was used for the hemostasis. After hemostasis, the cornua was stitched with Vicryl sutures using the intracorporeal technique (Figure 2). Strict hemostasis and hemoperitoneal evacuation were performed and a Hemovac drain was inserted into the abdominal cavity, which was expelled after 12 hours. The serum beta-hCG level returned to within normal range approximately 5 weeks postoperatively.

Discussion

The incidence of interstitial ectopic pregnancy is 2.8% of all ectopic pregnancies and 1 in 2035 live births (7). Early diagnosis is the most important part of the management and outcome of the patients. With the advances in high-resolution transvaginal ultrasonography and the sensitive beta-hCG assay, it is now possible to diagnose interstitial pregnancy at an earlier time. The cornual mass is the most common ultrasound scan finding in the definitive diagnosis of a cornual (interstitial) pregnancy. Timor-Tritsch et al. (8) described three diagnostic criteria for cornual pregnancy: 1) an empty uterine cavity, 2) a chorionic sac seen separately and >1 cm from the most lateral edge of the uterine cavity, 3) a thin myometrial layer surrounding the gestational sac. Our patient's findings were consistent with all the criteria reported above. The traditional treatment of interstitial pregnancy was hysterectomy or cornual resection by laparotomy. Today to the experience of most of the gynecological operations can be performed laparoscopically. In experienced hands Laparoscopic techniques involve cornual resection, cornuostomy.

The most important point in laparoscopic cornual operations is fertility preserving surgery and hemostasis. During hemostasis, we prefer to use bipolar coagulation by using saline solution to maintain electrolytes in the operative field. Also, if bipolar coagulation was not enough for hemostasis, we used monopolar coagulation in the cutting mode with 30-40 watts. Monopolar coagulation with high voltage and coagulation mode can result in myometrial end endometrial damage, which may affect future conceptions. Hemostasis may also be achieved with vasopressin but because the vascularization is high, it may pass to the systemic circulation in a very short time; and therefore the dose must be controlled. Laparoscopic suturing techniques are also very important in these operations. We prefer to perform a figure of eight with vicryl suture by using intracorporeal suturing technique.

Most authors will concur that the size of the cornual pregnancy determines the best laparoscopic approach. Tulandi et al. (9) reported that cornuostomy is appropriate for gestations <3.5 cm, whereas Grobman and Milad (10) recommended cornual wedge resection for gestation >4 cm. In our case the dimension of the cornual gestation was about 3 cm. In some cases,

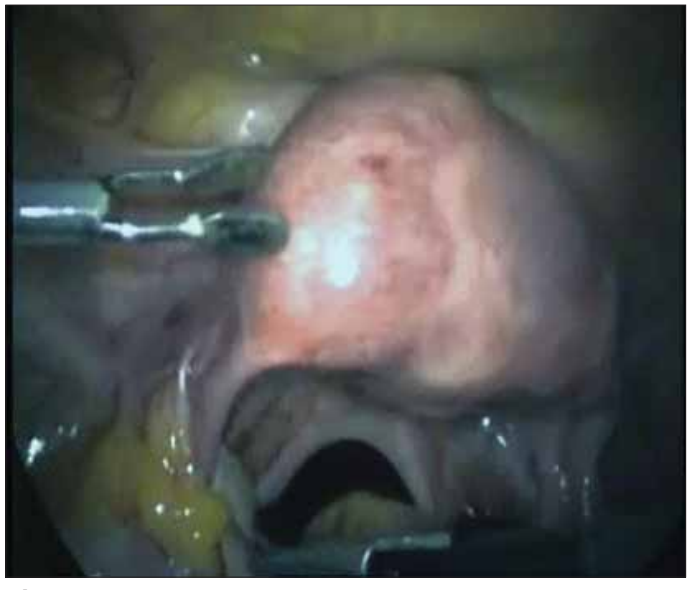


Figure 1. Cornual (interstitial) pregnancy before laparoscopy



Figure 2. The intraabdomial view after laparoscopy

post-surgical methotrexate treatment or guided potassium chloride injection to the amniotic sac is needed to succeed in termination of the pregnancy (4).

In conclusion, interstitial (cornual) pregnancy remains a challenging and dangerous pathology, and early diagnosis and treatment is paramount. The treatment choice depends on various parameters; laparoscopy allows the diagnosis and treatment together. When managing an interstitial pregnancy, experience of the surgeon plays an important role. The surgeon must be competent in suturing and coagulation techniques. In experienced hands, laparoscopy is a safe and effective treatment for interstitial pregnancy.

Conflict of interest

None declared

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CONGRESS CALENDAR

27-30 June 2010	**ESHRE,** *Rome, Italy* http://www.eshre.com
30 June-2 July 2010	**Gynecological Endoscopy Education Days,** *İzmir-Turkey* www.egelaparoskopi.org
25-29 September 2010	**12. Gynecological Oncology Congress,** *Antalya, Turkey* www.jineonko2010.org
26-29 September 2010	**7th National Congress of Turkish Maternal Fetal Medicine and Perinatology Association,** *İstanbul, Turkey* www.tmftpkongre2010.org
2-5 October 2010	ESIDOG, *Trieste, Italy* www.esidogtrieste.eu
7-10 October 2010	**4th National Congress on Reproductive Endocrinology and Infertility, TSRM 2010,** *Antalya, Turkey* www.tsrm.org.tr
23-27 October 2010	**ASRM,** *Denver, Colorado, USA* http://www.asrm.org
27-31 October 2010	**7th Congress of Obstetric and Gynecological Ultrasound, Harbiye Military Museum,** *İstanbul, Turkey* www.usgkongre2010.org
6-10 April 2011	**AAGL 5th International Congress on Minimally Invasive Gynecology,** *İstanbul, Turkey* www.tsge2011.org
4-8 May 2011	**9th Congress of the Turkish-German Gynecology Foundation,** *Antalya, Turkey* www.tajev.org
25-29 May 2011	**19th International Pelvic Pain Society Annual Scientific Meeting,** *İstanbul, Turkey* www.ipps2011.org

Successful management of uterine prolapse during pregnancy with vaginal pessary: a case report

Gebelikte uterin prolapsusun vajinal pesser ile başarılı yönetimi; vaka sunumu

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Abstract

We present a case of uterine prolapse complicating a second trimester pregnancy which was managed successfully with a vaginal pessary.

Case: A 19 year-old primigravid woman referred to the obstetric emergency unit at the 16th week of gestation complaining of uterine prolapse. A silicone ring-shaped middle-size vaginal pessary was placed into the vagina. On each control visit, when the vaginal pessary was removed , the uterine prolapse still persisted until birth. The patient gave birth at 38th week by spontaneous vaginal delivery to a healthy baby. After birth, with uterine contractions, uterine prolapse regressed progressively.

Conclusion: The management and treatment of uterine prolapse in pregnancy should be individualized depending on the patient's preference. A vaginal pessary may be helpful to avoid complications of this condition and should be considered during patient counseling.

(J Turkish-German Gynecol Assoc 2010; 11: 105-6)

Key words: Uterine prolapse, pregnancy, vaginal pessary

Received: 7 July, 2009 **Accepted:** 13 October, 2009

Özet

Gebeliğin ikinci trimesterinde izlenen uterin prolapsus durumunun vajinal pesser ile başarıyla yönetildiği bir olgu sunulmuştur.

Vaka: 19 yaşında, 16 haftalık gebeliği bulunan primigavid hasta kliniğimiz obstetrik polikliniğine rahim sarkması şikâyetiyle başvurmuştur. Orta boy, yuvarlak, silikon pesser vajene yerleştirilerek prolapsus redükte edilmiştir. Her kontrolde vajinal pesser çıkarıldığında prolapsus halinin doğuma kadar sebat ettiği izlenmiştir. 38'inci gebelik haftasında spontan vajinal doğum ile sağlıklı bir bebek doğurtulmuştur. Doğum sonrasında uterin kontraksiyonlarla prolapsus hali progresif olarak gerilemiştir.

Sonuç: Gebelikte gelişen uterin prolapsusun yönetiminde ve komplikasyonlarından korunmada vajinal pesser uygulaması faydalıdır ve hasta değerlendirilirken göz önünde tutulmalıdır.

(J Turkish-German Gynecol Assoc 2010; 11: 105-6)

Anahtar kelimeler: Uterin prolapsus, gebelik, vajinal pesser

Geliş Tarihi: 07 Temmuz 2009 **Kabul Tarihi:** 13 Ekim 2009

Introduction

Uterine prolapse during pregnancy is a rare condition with an estimated incidence of 1 per 10,000-15,000 deliveries (1). Complications of this condition are patient discomfort, cervical desiccation and ulceration, urinary tract infection, acute urinary retention, abortion, preterm labor, fetal and maternal sepsis, and maternal death (2). The management varies from a conservative approach to laparoscopic treatment (3).

A vaginal pessary for uterine prolapse during pregnancy was first used in 1949. There are various shapes and sizes of pessaries. The silicone coated ring pessary is amenable for self-removal and insertion by the patient (4).

We present a case of uterine prolapse complicating a second trimester pregnancy which was managed successfully with a vaginal pessary.

Case

A 19 year-old primigravid woman was referred to the obstetric emergency unit at the 16th week of gestation complaining of uterine prolapse. There was no history of pelvic trauma, stress urinary incontinence or uterine prolapse before pregnancy. On pelvic examination the cervical os was closed and the entire cervix was lying outside of the vulva (Figure 1). The cervix was enlarged, edematous and ulcerated but not desiccated. The obstetric ultrasonography revealed a 16 weeks live, apparently normal fetus with a normal amniotic fluid index. A Papanicolaou smear test was taken on her first visit and reported inflammatory changes.

We recommended antibiotherapy (amoxicillin clavulonate treatment for seven days) for cervicovaginal infection and a vaginal pessary to reduce prolapsed uterus. Bed rest was not recommended and the patient was told to continue her routine daily activities. A silicone ring-shaped middle-size vaginal pessary was placed in the vagina and the patient was taught how to place the vaginal pessary herself. After insertion of the pessary, the cervix remained totally intravaginal and there was no urinary retention complaint by the patient (Figure 2). The patient was then controlled weekly and at each control visit the vaginal pessary was removed, disinfected with baticon and replaced in the vagina until the 20th week. The patient was followed up monthly until the 32nd week, twice a month until the 36th week and then weekly until birth. The antepartum follow-up was unremarkable and no further complications occurred during pregnancy. The patient adjusted herself to the pessary perfectly and there was no complaint of the pessary falling out. There was no vaginal ulceration due to vaginal pessary usage and cervical ulceration healed because the cervix remained intravaginal with the vaginal pessary. On each control visit, when we took the vaginal pessary out, uterine prolapse still persisted up to birth.

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doi:10.5152/jtgga.2010.010



Figure 1. Uterine prolapsus in pregnancy



Figure 2. Cervix remained intravaginal after insertion of vaginal pessary

The patient gave birth at 38th week by spontanous vaginal delivery to a healthy 3200 gr, 50 cm baby with Apgar scores of 8 and 10. After birth, with uterine contractions, the uterine prolapse regressed progressively. On the first postpartum day, the uterine prolapse was completely resolved and the patient was discharged on the second postpartum day. The puerperial period was uneventful. A control examination at the second postpartum month revealed no evidence of uterine prolapse.

Discussion

Uterine prolapse in pregnancy is a rare condition. The main causes may be childbirth trauma, obstetric history of difficult deliveries or large babies, congenital connective tissue disorders, obesity, increased intraabdominal pressure, physiologic changes of pregnancy causing cervical elongation, hypertrophy and relaxation of the supportive ligaments (5). In this case uterine prolapse occurred in a first pregnancy and in the second trimester. Since there was no history of trauma or obstetric complications, we considered that this condition could be due to physiologic changes of pregnancy (hormonal changes especially progesterone and relaxin effect causing growth and softening of the cervix). Another possible cause was congenital connective tissue disorders, but we could not attempt to do a serious diagnostic workup due to the patient's refusal.

The management strategies reported in the literature are conservative management, use of vaginal pessary, laparoscopic uterine suspension and concomitant cesarean hysterectomy with abdominal sacrocolpopexy (3, 5-7). Conservative management consists of gyneacological hygiene and bed rest in a slight Trandelenburg position and this is reported to be successful (5). In 1949, Klawans and Kanter advised continual use of the Smith-Hodge pessary throughout the pregnancy for women with late occurrence of prolapse (6). Vaginal pessaries can be obtained and applied easily. Vaginal discharge, odor, mucosal erosion and abrasions of vagina, urinary retention are common complications of vaginal pessaries (4). In this patient, we did not encounter any of this complications. Different types of vaginal pessary have been used but this management was reported as unsuccessful since pessaries frequently fall out after a few days. Contrary to the literature, this case was managed successfully with a pessary. The ring pessary and its size was perfectly fitted to the patient. The patient was taught how to use the pessary and she performed the proceedure perfectly. Thus, selection of pessary shape and its size and the patient's congruity to the treatment are the touchstones of success of this management. When conservative management fails and prolonged bed rest is impossible, another treatment choice may be laparoscopic uterine suspension during early pregnancy. However, this procedure should be performed in experienced hands since several failed laparoscopic uterine suspension cases have been reported (3). An alternative choice for women who have completed their family might be concomitant cesarean hysterectomy with abdominal sacrocolpopexy (7). Management strategies should be targeted to reduce complications of patient discomfort, urinary tract infections, urinary retention, cervical laceration, preterm labor, fetal and maternal infections and death. In this case we managed uterine prolapse successfully with a pessary and avoided all these complications.

In conclusion, the management and treatment of uterine prolapse in pregnancy should be individualized depending on the patient's preference. Vaginal pessary may be helpful to avoid complications of this condition and should be considered during patient counseling.

Conflict of interest

None declared

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Herlyn-Werner-Wunderlich syndrome (uterus didelphys, blind hemivagina and ipsilateral renal agenesis) - a case report

Herlyn-Werner-Wunderlich Sendromu (uterus didelphys, kör hemivajen ve ipsilateral renal agenezi) - vaka sunumu

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Abstract

Uterovaginal duplication with obstructed hemivagina and ipsilateral renal agenesis is referred to as the Herlyn-Werner-Wunderlich (HWW) syndrome. A 17 year old woman presented with right pelvic pain and dysmenorrhea, present since menarche at 13 and worsening over the past year. Ultrasound examination revealed a right pelvic mass (5x5 cm), double endometrial echoes, and hematocolpos. A right pelvic mass, agenesis of the right kidney, double uterus, and blind hemivagina with hematocolpos were detected by magnetic resonance imaging and intravenous pyelography. A right tubo-ovarian abscess with dense adhesions and a double uterus were observed on diagnostic laparoscopy. Adhesiolysis was carried out and purulent material irrigated. After a course of antibiotics, a vaginal septum resection was performed and the pyocolpos drained. She remained symptom free after four months of follow-up. Prompt and accurate diagnosis and treatment of this syndrome can significantly improve the lives of sufferers and prevent future complications.

(J Turkish-German Gynecol Assoc 2010; 11: 107-9)

Key words: Blind hemivagina, Herlyn-Werner-Wunderlich syndrome, Müllerian duct anomaly, Pyocolpos, Uterus didelphys

Received: 13 November, 2009 **Accepted:** 16 December, 2009

Özet

Kör hemivajen ile beraber olan uterovajinal duplikasyon ve ipsilateral renal agenezi Herlyn-Werner-Wunderlich (HWW) Sendromu olarak tanımlanır. 17 yaşındaki hasta; 13 yaşında gördüğü ilk adetinden itibaren olan ve son bir yılda şiddeti artan sağ kasık ağrısı ve dismenore şikayetleri ile acil servise başvurdu. Ultrasonda; sağ pelvik kitle (5x5 cm), çifte endometrial eko ve hematokolpos tespit edildi. Yapılan magnetik rezonans görüntülemesi ve intravenöz pyelografisinde; sağ pelvik kitle, sağ böbrek agenezi, çifte uterus, ve hematokolposla beraber olan kör hemivajen tespit edildi. Yapılan diagnostik laparoskopide; kalın yapışıklıklarla olan sağ tubaovaryen abse ve çift uterus tespit edildi. Abse drene edildi ve yapışıklıklar açıldı. Hastaya antibiyotik tedavisi verildikten sonra tekrar opere edildi ve vajinal septum eksize edilerek pyokolpos drene edildi. Hastanın takiplerinde herhangi bir şikayeti olmadı. Bu sendromun erken ve doğru tespit ve tedavisi, bu problemi yaşayan hastaların refahını belirgin olarak artırabilir ve yaşanabilecek komplikasyonları engelleyebilir.

(J Turkish-German Gynecol Assoc 2010; 11: 107-9)

Anahtar kelimeler: Kör hemivajen, Herlyn-Werner-Wunderlich sendromu, Müllerian kanal anomalisi, Pyokolpos, Uterin didelfus

Geliş Tarihi: 13 Kasım 2009 **Kabul Tarihi:** 16 Aralık 2009

Introduction

Uterine malformations, including such minor malformations as a hypoplastic and arcuate uterus, are seen among all women, with an incidence of 7-10%. However, complex malformations of the female genital tract are rare and often incorrectly identified, inappropriately treated, and sometimes incorrectly reported (1). In most cases, the etiologic factors are unknown, but may include an insult during the first trimester or polygenic/multifactorial inheritance (2).

The Wolffian (mesonephric) ducts and the Mullerian (paramesonephric) ducts are the two paired urogenital structures from which the internal genital organs and the lower urinary tract derive (3). The fallopian tubes, uterus, and the upper two-thirds of the vagina develop from the bilateral Mullerian Ducts (4). As a result of any interruption in the development of this embryological event, different types of uterine anomalies can arise, such as agenesis, hypoplasia, unicornuate, didelphys, bicornuate, arcuate, and septate uterus (3). The American Society of Reproductive Medicine has classified these malformations under seven groups (5), while Acien et al have more recently proposed a clinical embryological classification of all genital tract malformations (1).

Finally, the lower third of the vagina develops from the joining of the Mullerian ducts and the urogenital sinus (6). Vaginal anomalies, such as aplasia, hypoplasia, septa or duplication, may exist alone or accompany the Mullerian anomalies, due to the different embryological origins (3).

Uterovaginal duplication with obstructed hemivagina and ipsilateral renal agenesis is referred to as the Herlyn-Werner-Wunderlich (HWW) syndrome (3). Embryological arrest at 8 weeks of gestation is the cause of uterine didelphys with

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doi:10.5152/jtgga.2010.011

renal agenesis, and in the general population the reported incidence for this anomaly is 0.1-3.8% (2, 7). A complete vaginal septum is present in 75% of women with uterine didelphys (8). Most of the patients present at menarche with symptoms of pelvic pain secondary to hematocolpos, fever, and abcess formation (2). Unfortunately, making the diagnosis of HWW syndrome is not always simple . The experience with HWW syndrome was definitely limited, consisting of case reports. Resection of the vaginal septum mostly relieves the pain and prevents further complications. In this case report, we wish to emphasize the need for early and accurate diagnosis for the correct treatment of this entity.

Case History

A 17-year-old woman presented to the Emergency Unit with complaints of right pelvic pain and dysmenorrhea. The symptoms had become more intense over the past year, and she had used non-steroidal anti-inflammatory drugs (NSAIDs) prescribed by her primary care physician for the last six months, but her condition had not improved. She had experienced menarche when she was 13 years old and had a history of regular menses with cyclic pelvic pain.

Tenderness in the right lower abdomen, and normal vulva, anus and hymen were noted at her first clinical examination. Her ultrasound examination revealed a right pelvic mass (5x5 cm), double endometrial echoes, and hematocolpos. Because she was a virgin, traditional issues prevented a vaginal examination. A right pelvic mass, agenesis of the right kidney, double uterus, and blind hemivagina with hematocolpos were detected by magnetic resonance imaging (MRI) (Figure 1) and intravenous pyelography (IVP) (Figure 2).

Diagnostic laparoscopy was performed, and a right tuba-ovarian abscess with dense adhesions and a double uterus were observed. Adhesiolysis was carried out and purulent material irrigated. The patient was treated with oflaxacin 400 mg/day + metronidazole 1.5 g/day for 14 days in preparation for operation. After we received the informed consent of the patient, we performed a vaginal septum resection and detected a pyocolpos, which was drained. Both cervixes were also explored.

After the operation, her pain improved and she was discharged from the hospital on the 11th post-operative day. Her follow up was symptom-free at the 4th postoperative month.

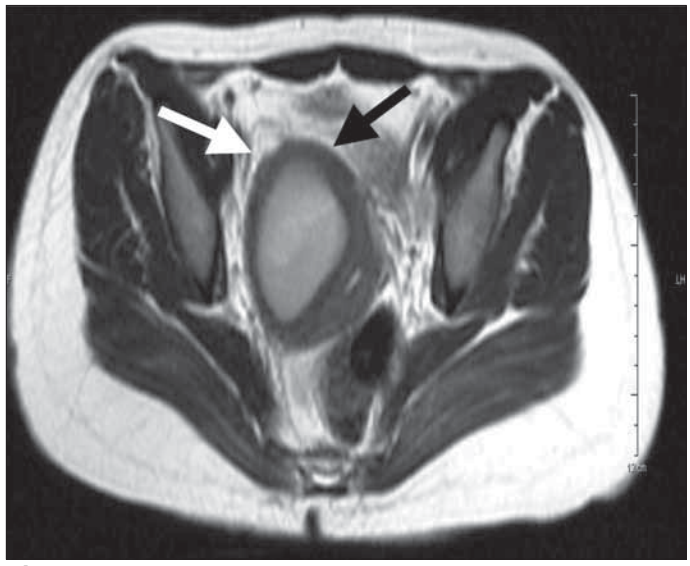


Figure 1. Right hemivagina with pyocolpos



Figure 2. Intravenous pyelography, absent right kidney

Discussion

The exact etiology and pathogenesis of HWW syndrome are still not known (3, 9, 10), but are probably related to the fact that the Wolffian ducts play an important role in the precise development of internal genital organs as well as giving rise to the kidneys (3, 4, 9). They are inductor elements for adequate Mullerian ducts fusion. For this reason, embryologic anomaly of one Wolffian ducts may cause unilateral renal agenesis associated with imperforate hemivagina (4, 11). This hypothesis is supported by Gruenwald's experiment in chick embryos, where ipsilateral renal and Mullerian duct anomalies were produced following the destruction of the caudal portion of the mesonephros (12). On the affected side, Mullerian ducts cannot fuse, resulting in a didelphic uterus, and cannot come into contact with the urogenital sinus centrally, forming two separate vaginas with one obstructed (3).

The syndrome usually presents with progressive and recurrent pelvic pain after the menarche. It is not initially diagnosed, because of the regular menstrual flow from the unobstructed vagina. Some time after menarche, the retention of menstrual blood in the obstructed hemivagina leads to the formation of a haematocolpos, which is usually clinically detected as a pelvic mass. A right sided prevalence of the obstructed system has been mentioned in the literature (7, 12, 13). Diagnosis may be further delayed if a communication between the two vaginas exists (3). Not only a dilated hemivagina but also a dilated uterine cavity and fallopian tube may be present at the time of diagnosis. Especially in delayed cases, bleeding into the peritoneal space may occur as a consequence of retrograde menstruation. Endometriosis can also be formed in these patients (7, 8, 13).

Ultrasonography and MRI are widely and effectively used in the diagnosis of genitourinary anomalies, with even 100% accuracy being reported for MRI because of its high accuracy and detailed elaboration of uterovaginal anatomy (14, 15). However, since 1981 laparoscopic exploration has been regarded as the gold standard (2, 7).

Renal malformations are now usually detected at the perinatal period and in the case of a renal agenesis or multicystic dysplastic kidney, detected in female newborn. The Mullerian system should also be checked for a malformation (16).

It is the least common but has the best prognosis of Mullerian duct anomalies (17). The definitive treatment of HWW syndrome is the resection of as much of the obstructing vaginal septum as possible. This rapidly relieves the symptoms and prevents complications related to chronic cryptomenorrhae, such as endometriosis, pelvic adhesions, and infectious collections (2, 3, 10, 13). Candiani et al. have suggested marsupializing the vaginal margins after excision of the septum to allow ample drainage of the purulent material and better expose the cervix (7). Fertility is preserved with this surgery, which is not significantly decreased in women with a didelphic uterus (3).

Conclusion

The prompt and accurate diagnosis of female reproductive tract disorders, including HWW syndrome, is necessary to prevent complications and preserve future fertility. The cooperation of pediatricians, pediatric surgeons, radiologists, and gynecologists is essential to avoid complications due to diagnostic delay. In conclusion, early recognition of this relatively rare syndrome would lead to the immediate, proper surgical intervention. Laparoscopy provided additional information beyond radiologic tests regarding pelvic anatomy. This approach should retrieve affected cases, which would otherwise face a rather discouraging future.

Conflict of interest
None declared

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Incomplete androgen insensitivity (Reifenstein syndrome) - a case report

İnkomplet androjen insensitivitesi-reifenstein sendromu

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Abstract

We report a 20 year old case of partial androgen insensitivity syndrome, referred to our clinic with complaints concerning external genital organs and left undescended testicle. The phenotypically male case was first evaluated for secondary sex development. Axillary hair was scanty and no pubic hair was found. There was no breast development. In the gynecological examination, the clitoris was hypertrophic (4.6 cm) and a blind vagina with intact hymen was seen. Abdominopelvic ultrasonography revealed the absence of an uterus and adnexes which was supported by magnetic resonance imaging (MRI). There was a palpable mass in the left inguinal canal (cryptorchism), seen as atrophic tissue under the skin in MRI. Although the other testis was in the labioscrotal fold, it was atrophic. The Karyotype was 46 XY after genetic investigation.

(J Turkish-German Gynecol Assoc 2010; 11: 110-2)
Key words: Reifenstein syndrome, testicular malignancy
Received: 5 October, 2009 **Accepted:** 3 November, 2009

Özet

Yirmi yaşında erkek fenotipli hasta, polikliniğimize dış genital organlardaki farklılık ve sol inguinal bölgede ele gelen kitle şikayetiyle başvurdu. Olgu ilk olarak sekonder sex karekterleri açısından değerlendirildi. Pubik kıllanma olmamasına karşın seyrek aksiller kıllanma mevcuttu. Meme gelişimi yoktu. Jinekolojik muayenede hipertrofik klitoris (4.6 cm), intakt hymen ve kör vajen saptandı. Abdominopelvik ultrasonda uterus ve adneksler izlenmedi. Bunun üzerine hastaya MR çekildi ve sol inguinal bölgede kriptorşizm ile uyumlu testiküler doku cilt altında atrofik olarak izlendi. Diğer testis ise labioskrotal foldun içinde olup, atrofikti. Genetik inceleme yapıldı, karyotip 46 XY olarak saptandı.

(J Turkish-German Gynecol Assoc 2010; 11: 110-2)
Anahtar kelimeler: Reifenstein sendromu, testiküler malignite
Geliş Tarihi: 05 Ekim 2009 **Kabul Tarihi:** 03 Kasım 2009

Case report

A 20-year-old boy was referred to our clinic with complaints concerning the external genital organs and left undescended testicle. He was raised as a girl up to the age of 17. The phenotypically male case was first evaluated for secondary sex development. Axillary hair was scanty and no pubic hair was found. There was no breast development. In the gynecological examination, the clitoris was hypertrophic. (4.6 cm), a blind vagina with intact hymen and also perineal hypospadias was seen. Abdominopelvic ultrasonography revealed the absence of an uterus and adnexes which was supported by magnetic resonance imaging. There was a palpable mass in the left inguinal canal (cryptorchism) which was seen as atrophic tissue under the skin in MRI. Although the right testis was in thelabioscrotal fold it was atrophic (Figure 1). Human chorionic gonadotropin, alfa fetoprotein (AFP) and lactate dehydrogenase (LDH) levels were detected for the risk of cancer which is associated with testicular tissue. (0.01 mIU/ml, 3.85 ng/ml, 299 U/l respectively) All values were normal. The reactivity of 5α reductase and 21α hydroxylase were also normal. Follicle stimulating hormone (FSH), luteinizing hormone (LH) and free testesterone levels were high.(36.01 mIU/ml, 13.92 mIU/ml, 10.3 pg/ml respectively) Other androgens, 17- hydroxyprogesterone and cortisol levels were normal. Karyotype was determined as 46 XY on chromosomal analysis. The patient had undergone inguinal herniotomy five years earlier and had an penoscrotal hypospadias reparation two years earlier. There was no familial history of ambiguity.

Introduction

Congenital genital anomalies are very complex pathologies. The androgen insensitivity syndrome (AIS) is an X-linked disorder which can be seen in 46XY individuals with normal androgen production and metabolism. AIS is estimated to be present in 1: 20,000-64,000 male births (1, 2), and variable phenotypic expression has allowed the classification of AIS into complete (CAIS) and partial forms (PAIS). PAIS is the most common form. Partial androgen insensitivity syndrome (PAIS) includes syndromes that were once thought to represent separate entities: Reifenstein, Gilbert-Dreyfus, Rosewater

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doi:10.5152/jtgga.2010.012

and Lub syndromes. In the differential diagnosis of AIS, congenital adrenal hyperplasia and 5α-reductase deficiency must be considered. In the present report, we describe a case who is 20 years-old, and presented at our polyclinic with complaints concerning the external genitalia and an undescended testicle, diagnosed after a thorough investigation (establishment of karyotype, investigation of hormones and their derivates and radiological examination) as PAIS similar to Reifenstein syndrome.

Case report

A 20-year-old boy was referred to our clinic with complaints concerning his external genital organs and left undescended testicle. He was raised as a girl until the age of 17. The phenotypically male case was first evaluated for secondary sex development. Axillary hair was scanty and no pubic hair was found. There was no breast development. In the gynecological examination, the clitoris was hypertrophic. (4.6 cm), a blind vagina with intact hymen and also perineal hypospadias was seen. Abdominopelvic ultrasonography revealed the absence of uterus and adnexes and was supported by magnetic resonance imaging. There was a palpable mass in the left inguinal canal (cryptorchism) which was seen as atrophic tissue under the skin in MRI. Although the right testis was in the labioscrotal fold it was atrophic. (Figure 1) Human chorionic gonadotropin, alfa fetoprotein (AFP) and lactate dehydrogenase (LDH) levels were detected for the risk of cancer associated with testicular tissue. (0.01 mIU/ml, 3.85 ng/ml, 299 U/l respectively) All the values were normal. The reactivity of 5α reductase and 21α hydroxylase were normal also. Follicle stimulating hormone (FSH), luteinizing hormone (LH) and free testesterone levels were high. (36.01 mIU/ml, 13.92 mIU/ml, 10.3 pg/ml respectively) Other androgens, 17- hydroxyprogesterone and cortisol levels were normal.The Karyotype was determined as 46 XY on chromosomal analysis. He had undergone inguinal herniotomy five years earlier and had had a penoscrotal hypospadias reparation two years earlier. There was no familial history of ambiguity.

Discussion

Diagnosis is usually established either during inguinal herniotomy or application of a patient at puberty with absence of menstruation. During the definition of genital ambiguity, it is important to assess nutritional status, arterial blood pressure, the presence of pubic hair, acne and signs of puberty. External genitalia should be assessed to classify the degree of virilization, analyze the size of the phallus, position of the urethral meatus, presence of vaginal introitus or urogenital sinus opening, degree of fusion, symmetry and wrinkling of the labioscrotal folds, presence of inguinal masses and location and size of the gonads. Hormonal tests and karyotyping should be performed at specialist services, as should be the imaging of the uterus, gonads, prostate and urogenital sinus, which is necessary, but not always conclusive. The most frequently used studies are

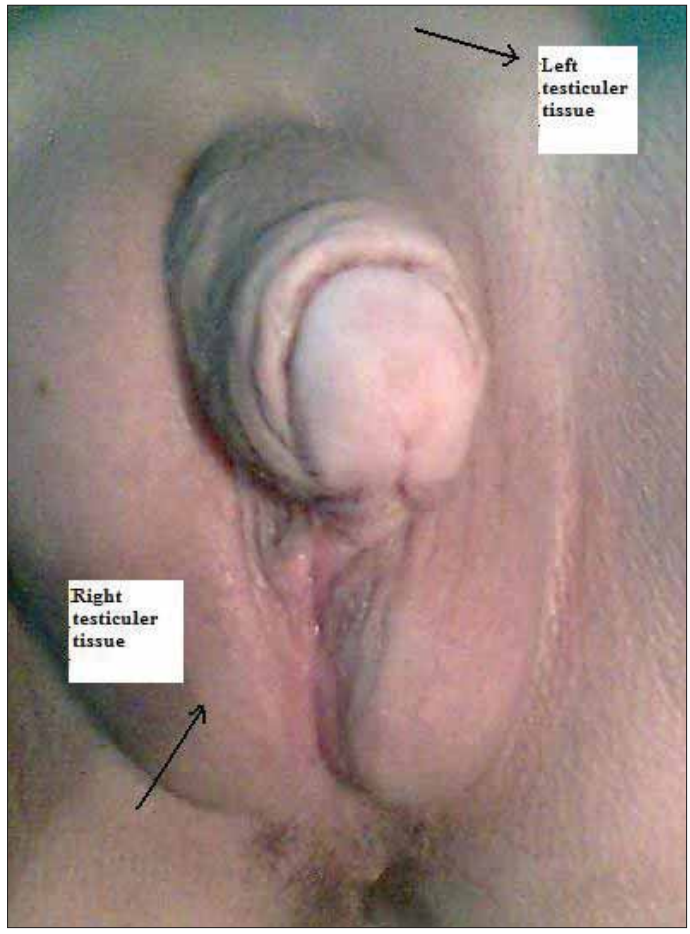


Figure 1. **The sites of testicular tissues**

ultrasound in association with genitourinary imaging and, less frequently, computerized tomography or magnetic resonance imaging of the pelvic region. During the radiologic examination urinary system anomalies should be considered.

The most frequent cause of virilization (around 80 to 90% of cases) with female genetic gender (46,XX) is congenital adrenal hyperplasia. It can manifest in two clinical forms, simple virilization (SV) or a salt wasting form (SW). The SV form accounts for 20 to 30% of cases and causes ambiguous genitalia in female newborn infants. When untreated, it leads to progressive postnatal virilization in both sexes, with signs and symptoms of early pseudopuberty. In the SW form, the clinical manifestations include, in addition to the prenatal virilization of females and postnatal virilization of both sexes, a range of forms, from the severe cases of hyponatremic and hyperkalemic dehydration, vomiting, metabolic acidosis, hypovolemic shock and death, if treatment is not given. If the genetic gender is male, the diagnosis can be 5α-reductase deficiency or androgen insensitivity syndrome (AIS). With 5α-reductase deficiency there is genital virilization, although not always with adequate penile growth, absence of gynecomastia and hypoplasia or absence of the prostate. Thus, in this situation a genetically 46XY individual has more female features. On considering the types of AIS, Baron (3) reported that in the CAIS there was absent or very scarce

pubic hair in 100% of the cases, normal development of breasts in 97% of the cases, blind vagina of mean length 5.0 +/- 2.3 cm in 97% of the cases and inguinal hernia in 30% of the cases. In PAIS, normal breasts occured in 62.5%, public hair in 50%, complete absence of vagina in 62.5%, blind vagina of mean length 2.5 cm in 37.5%, inguinal hernia in 75% and hypertrophy of clitoris of mean length 2.0 +/- 1.0 cm in 62.5% of the cases. In the incomplete form, surgery for inguinal hernia was necessaryin 87.5% of the patients (studied in 41 AIS patient). Our patient 's external genitalia exhibits hypertrophic clitoris, perineal hypospadias and cryptorchism, also called Reifenstein syndrome.

Ahmed et al. (4) compared children, known as AIS, to the sex of rearing from birth. The median mascularization score was used for this. The median masculinization score of 3 was higher in the group reared as boys than in the group of girls, who had a median masculinization score of 2.5. However, there was no significant difference between the scores on analysis. Although the present case was raised as a girl, after 17 years he has feelings and attitudes of a male and his masculinization score is 4 (Table 1).

A common practice is to remove the testes after puberty when feminization of the affected individual is complete, since feminization occurs partly by testicular estrogen and partly by peripheral conversion of androgen to estrogen. The reason for the postpubertal gonadectomy is the risk of testicular malignancy, which rarely occurs before puberty. The malignant development may first be carcinoma in situ, later gonadoblastoma, which if untreated may develop into malignant germinoma or seminoma (5). Although our patient has normal markers for testicular malignancy, absolute testicular tissue must be extirpated with an operation. Because of this we referred him to an urology doctor for testicular tissue extirpation.

Table 1. Criteria for the masculinization score

Scrotal Fusion	Micro Phallus	Urethral Meatus	Right Gonad	Left Gonad	
YES	YES	Normal			3
		Glandular			2
			Scrotum	Scrotum	
		Penile	Inguinal	Inguinal	1
			Abdominal	Abdominal	
NO	NO	Perineal	Absent	Absent	0

At present more than 100 mutations at the androgen receptor gene are known (6). The incomplete forms are more common but also more difficult to diagnose. The appearance of those individuals might range from almost normal female to nearly male. Early and correct diagnosis requires adequate medical attention in order to make it possible to establish prognosis of puberty, fertility and malignancy. This reduces the risk of psychological and social problems. Depending on their age and ability to understand, the patient can contribute to defining their own sex. The sex of rearing depends on genetic and physiologic criteria and on the prognosis of life quality in the future. Surgical and medical treatment is applied to emphasize or encourage the development of the appropriate sex features, attempting to avoid anatomical discrepancy and helping to confirm psychological identity.

Conflict of interest

There is no conflict of interest

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Calcified pure uterine lipoma mimicking myoma

Leiomyomu taklit eden kalsifiye uterus lipomu

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Abstract

Pure lipoma of the uterus is a rare entity and only a few cases have been reported in the literature. Clinical symptoms and signs are similar to those found in leiomyoma and create preoperative diagnostic confusion. The histogenesis is still unclear. We report the case of a 70 year-old woman with pure lipoma of the uterus with calcification.

(J Turkish-German Gynecol Assoc 2010; 11: 113-4)

Key words: Lipoma, uterus, calcification

Received: 11 October, 2009 **Accepted:** 3 November, 2009

Özet

Uterusun saf lipomu seyrek görülen bir hadisedir ve literaturde sadece birkaç vaka bildirilmiştir. Klinik semptomları ve yakınmaları leiomyomdaki gibi olduğundan preoperatif tanıda konfüzyon yaratır. Hala histogenezisi netleştirilememiştir. Biz burda 70 yaşında saf lipoması olan ve uterusu kalsifiye olmuş bir vakayı bildirdik.

(J Turkish-German Gynecol Assoc 2010; 11: 113-4)

Anahtar kelimeler: Lipoma, uterus, kalsifikasyon

Geliş Tarihi: 11 Ekim 2009 **Kabul Tarihi:** 03 Kasım 2009

Introduction

Lipomatous neoplasms of the uterus are rare and received little attention in the literature. It is difficult to diagnose these tumors preoperatively because its clinical presentation similar to that of uterine leiomyoma (1). There is no consensus as to the histogenesis or nomenclature of uterine fatty tumors. (2, 3). Pure fatty tumors of the uterus are extremely rare and usually develop in post menopausal women (4).

We report a case of isolated pure uterine lipoma with calcification diagnosed postoperatively by histopathological examination.

Case Report

A 70 year-old postmenopausal, multiparous woman presented with a sense of heaviness in the lower abdomen. On abdominal examination a suprapubic mass was palpable which was about 14 weeks gravid uterine size. The mass was firm and non tender with well defined margins. Per vaginal examination revealed an irregularly enlarged uterine corpus. Routine investigations revealed hemoglobin of 9.8 gm/dl with no other significant findings. Ultrasonography (USG) of the abdomen showed a large calcified mass measuring 61.2 x 59.4 mm, arising from the fundus and posterior to the urinary bladder. Endometrial echo was thin and pushed posteriorly. Sonological diagnosis was calcified intramural myoma (Fig. 1). Total abdominal hysterectomy with bilateral salpingo-oophorectomy was carried out and the postoperative period was uneventful. Grossly, the uterus and cervix together measured 13×8.5×9 cm. in size. The cut section showed a well circumscribed yellowish intramural mass with punctate white areas measuring 6.5×6.5cm (Fig. 2). Multiple sections were taken and stained with hematoxylin and eosin. The sections showed lobules of mature adipocytes separated by thin vascular connective tissue. The myometrium was pushed to the periphery forming a pseudocapsule along with fibrous tissue (Fig. 3). There was linear calcification at the periphery, and blotchy calcification within the fatty tissue. The endometrium was atrophic. Von-Kossa stain proved the white blotchy areas to be calcification.

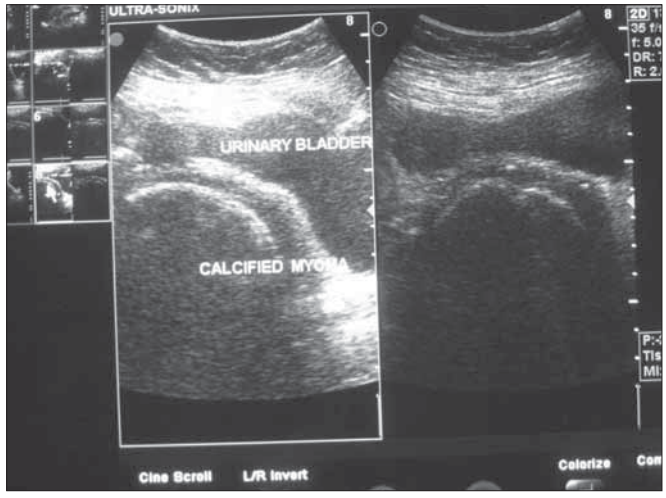


Figure 1. **USG diagnosing the mass as calcified myoma**

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doi:10.5152/jtgga.2010.013

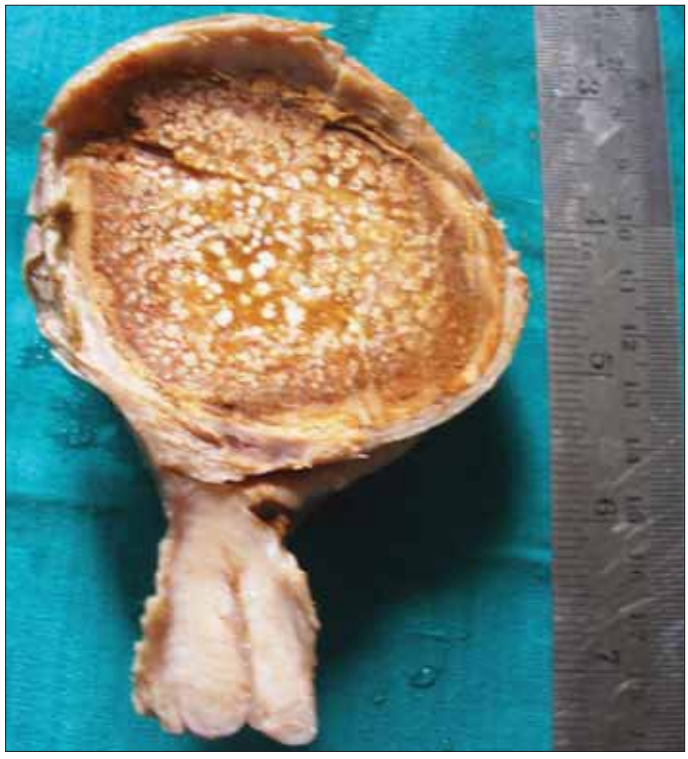


Figure 2. Gross appearance showing circumscribed yellowish uterine mass with punctate white areas

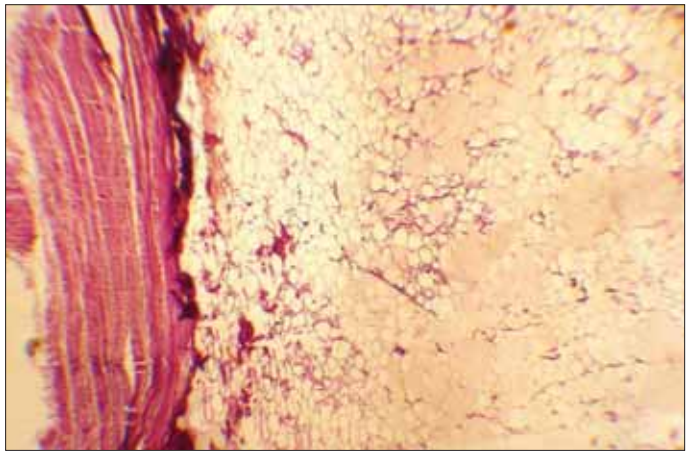


Figure 3. Section showing compressed myometrium along with adipose tissue, H&E, ×40

Discussion

Fatty uterine tumors may be defined as tumors composed entirely or in part of adult type adipose tissue. Smooth muscle and fibrous tissue are usually intermixed (5). These fatty tumors include pure lipoma and mixed lipoma such as myolipoma, lipofibroma, lipomyoma, and fibromyolipoma (6). Some of the pure lipomas are co-incidentally associated with other lesions. Dey and Dhar in 1993 reported a case of uterine lipoma in association with struma ovarii (7), DiGesu'G et al. in 1998 found pure uterine lipoma with endometrial carcinoma (8), Dilek TU reported a case of pure uterine lipoma with cervical carcinoma (9). Strikingly, very few cases of isolated pure lipoma of the uterus with calcification were reported. The incidence of uterine fatty tumors varies from 0.03 to 0.2 % (10).

Ninety percent of fatty tumors of the uterus occur in patients over the age of 40 years (5) and their clinical presentation is similar to uterine leiomyomas and diagnosed rarely by USG or X ray. The age of our patient was 70 years and the mass was misdiagnosed as a case of calcified myoma. For preoperative diagnosis MRI is the best modality of radiological investigation (4).

The uterine fundus is the typical site for uterine fatty tumors. This is comparable with our case. The tumor may be located at the cervix and less commonly in the subserosal location (5).

There are no accepted criteria for distinction of a pure lipoma from a mixed lipoma/leiomyoma. According to D.J. Pounder (5) the diagnosis of pure lipoma of the uterus should only be made when any smooth muscle cells present, are confined to the periphery of the tumor. Histopathology showed purely adipose tissue interspersed with fibrous septa in our case. One of the unique features in our case was the presence of dystrophic calcification. Only a few cases of pure lipoma with calcification are reported.

Theories on histogenesis lay emphasis on explaining the presence of adipose tissue, an element not usually found in the uterine corpus. According to Bride et al. (6) fatty degeneration of connective tissue of the myometrium may be responsible for differentiation into fatty tissues. A morphologic and histogenic analogy has been drawn between uterine fatty tumors and renal angiolopomas (2). It has been suggested that uterine fatty tumors are hamartomas or most recently choriostomas. It is also believed these tumors, or even the rarer pure uterine lipiomas, result from adipose tissue metaplasia in leiomyoma (5).

Conflict of interest
None declared

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Atypical preeclampsia and eclampsia: report of four cases and review of the literature

Atipik preeklampsi ve eklampsi: dört vaka bildirimi ve literatürün gözden geçirilmesi

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Abstract

Classically, most women who develop preeclampsia (hypertension and proteinuria) present some time after 20 weeks of gestation up to 48 h postpartum;and this is especially true in otherwise healthy, nulliparous pregnancies. Recent data suggest that in some women, preeclampsia and even eclampsia may develop in the absence of hypertension or proteinuria. Here, we report four atypical cases: eclampsia in the absence of hypertension and proteinuria (case 1), a partial seizure following eclampsia with antecedent proteinuria, but no hypertension (case 2), a case presenting with fetal distress, but no hypertension (case 3), and a case with unusually rapid progression and massive proteinuria that was unresponsive to therapy (case 4). Problems with atypical forms of eclampsia lie in its unpredictable onset; timely diagnosis and management are critical in avoiding complications. The purpose of this review is to increase the awareness of atypical forms of hypertensive disorders during pregnancy.

(J Turkish-German Gynecol Assoc 2010; 11: 115-7)

Key words: Atypical preeclampsia, atypical eclampsia

Received: 24 December, 2009 **Accepted:** 26 January, 2010

Özet

Klinik olarak preeklampsi (hipertansiyon ve proteinüri) geliştiren çoğu kadında bulgular 20 gebelik haftasından postpartum 48 saate kadar ortaya çıkar ve bu özellikle diğer yönlerden sağlıklı nullipar gebelerde böyledir. Son bazı çalışmalarda preeklampsi ve hatta eklampsinin hipertansiyon ve proteinüri olmadan gelişebileceği gösterilmiştir. Burda biz dört atipik vaka takdim ettik: proteinüri ve hipertansiyon olmadan eklampsi (olgu 1), hipertansiyon olmaksızın proteinüriyi takip eden parsiyel eklampsi nöbeti (olgu 2), fetal distresle gelen ancak hipertansiyon olmayan bir vaka (olgu 3) ve hızlı gelişen tedaviye yanıt vermeyen masif proteinüri vakası (olgu 4). Atipik eklampsideki problem tahmin edilemeyen ortaya çıkışıdır, o nedenle zamanında tanı ve müdahale komplikasyonları engellemek için elzemdir. Bu yazının amacı gebelikteki atipik hipertansif durumlar hakkındaki bilinci arttırmaktır.

(J Turkish-German Gynecol Assoc 2010; 11: 115-7)

Anahtar kelimeler: Atipik preeklampsi, atipik eklampsi

Geliş Tarihi: 24 Aralık 2009 **Kabul Tarihi:** 26 Ocak 2010

Introduction

The classic triad of preeclampsia is hypertension, proteinuria, and edema. Today, edema is no longer considered an important part of this condition, because it is a common finding in normal pregnancy, and approximately one-third of eclamptic women do not develop edema (1). In recent years, the new term “atypical preeclampsia-eclampsia” has been used to describe non-classical forms of hypertensive disorders arising during pregnancy (1-3). Although there is no strict definition of atypical preeclampsia-eclampsia, it has come to include cases with minimal or no proteinuria, but with hypertension, or proteinuria with no or marginally elevated blood pressure (BP), or without hypertension or proteinuria. Presentations before 20 weeks or more than 48 h postpartum, those resistant to $MgSO_4$ therapy, and hemolytic anemia, elevated liver enzymes, and low platelets (HELLP) syndrome and its variants are also included in the atypical category (4) (Table 1).

Atypical eclampsia constitutes about 8% of eclamptic cases (5). Problems with the atypical forms are their unpredictable onset and thus the difficulty in making a timely diagnosis to initiate management, which is critical in avoiding complications. We present four cases of atypical preeclampsia/eclampsia and discuss the challenges with these atypical forms, with an overview of the literature.

Case 1

A 20-year-old primigravida was hospitalized at 37 weeks with regular contractions. She had had irregular antenatal visits, which revealed no abnormality. She had a blood pressure (BP) between 130/80 and 100/60 mmHg on admission. Laboratory findings were unremarkable (hemoglobin 12 mg/dL, hematocrit: 37.2%, thrombocyte: 122000/mm³, glucose: 70 mg/dL, creatinine: 0.58, ALT: 31 U/L, AST: 35 U/L, LDH: 519 U/L), with a trace of proteinuria in the urinalysis. She had no prodromes suggestive of hypertensive disease. She delivered a healthy female baby vaginally a few hours later, uneventfully. At 4 h after delivery, she developed a generalized convulsion, lasting 23 min, despite being normotensive, and soon after this she had two other seizures. $MgSO_4$ was given (loading dose of 46 g over 1520 min, followed by a

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doi:10.5152/jtgga.2010.014

Table 1. Atypical preeclampsia (4)

Gestational hypertension plus
Mild symptoms of preeclampsia
Thrombocytopenia
Elevated liver enzymes
Proteinuria plus
Hemolysis
Thrombocytopenia
Elevated liver enzymes
Early preeclampsia at <20 weeks
Late postpartum preeclampsia/eclampsia
HELLP, ELLP, and EL syndromes

maintenance dose of 2 g/h as a continuous intravenous infusion). Following the seizures, her BP ranged between 140/90 and 100/60 mmHg. Slight increases in the liver function tests and LDH values and slight decreases in hemoglobin and platelets were detected (hemoglobin 10.3 mg/dL, hematocrit 31.5%, platelets 91,000/mm^3, alanine aminotransferase (ALT) 35 U/L, aspartate transaminase (AST) 66 U/L, lactate dehydrogenase (LDH) 932 U/L). Computed tomography (CT) was completely normal. Subsequently, she had three more seizures and another 2-g bolus of $MgSO_4$ was infused over 35 min and continued for the following 24 h, during which she suffered no further convulsion. The next day, a 24 h urine sample revealed 330 mg proteinuria; cranial magnetic resonance imaging (MRI) showed no abnormality.

Case 2

A 20-year-old nulligravida was admitted with regular contractions at 37 weeks gestation. All her prenatal visits had been normal, including BP, which was recorded as 120/80 to 110/70 mmHg. There was no prodrome of hypertensive disease and no laboratory abnormality, including platelet count, liver enzymes, LDH, electrolytes, and glucose, although proteinuria (3+) on dipstick was noticed on admission. She delivered a 2800-g male fetus vaginally, uneventfully. Following the delivery, her BP increased suddenly to 150/100 to 140/100 mmHg. Then, she had a generalized seizure lasting 5-10 s. Then, 2 h later, she developed sudden blindness, an occipital headache, and myoclonic seizures, particularly involving the right upper extremity. The postictal BP was around 160/120 mmHg. $MgSO_4$ was given for 24 h as the patient seemed to have atypical eclampsia. She had no seizure subsequently. Her BP remained high for a few days, ranging between 150/100 and 140/90 mmHg and normalized on postpartum day 3, with 930 mg/dL proteinuria in the 24 h urine collected postpartum. Cranial MRI was unremarkable. On postpartum day 4, she was discharged with her baby.

Case 3

A 31-year-old multipara presented with contractions at 33 weeks gestation with the cervix 2 cm dilated and 40% effaced. Her BP was 110/70 to 110/60 mmHg on admission. Her CBC, routine biochemical tests, and coagulation studies were normal, but she had a dipstick proteinuria of 3+. On admission, the intrapartum fetal heart rate recording revealed poor variability and late decelerations. An emergency Cesarean delivery was performed for fetal distress and a male fetus weighing 1900 g was delivered with APGAR scores of 4 and 6 at 1 and 5 min, respectively. The baby was admitted to the intensive care unit for respiratory distress syndrome. The placenta was atrophic, but not abrupted. Then, 2 h postoperatively, the mother became hypertensive, with a BP of 160/100 to 150/100 mmHg, a severe headache and visual blurring. A $MgSO_4$ infusion was started with a loading dose 4.5 g over 20 minutes, followed by a maintenance dose of 2 g/h as a continuous intravenous infusion for 24 h. Three days later, she became normotensive and her complaints resolved. She was discharged on the 4^{th} postoperative day.

Case 4

A 24-year-old primigravida patient was admitted at 30 weeks gestation with suspected preeclampsia. She had 1+ proteinuria on dipstick and a BP of 110/70 to 140/90 mmHg. Her 24 h proteinuria was 440 mg/dL. She was discharged 2 days later with a diagnosis of mild preeclampsia, to be followed as an outpatient. Four days later, she was readmitted with a BP of 190/120 mmHg measured at home. On readmission, her BP ranged between 120/90 and 170/110 mmHg, with most values below 140/90 mmHg. She had 3+ proteinuria, a reactive non-stress test, and normal amniotic fluid volume and Doppler indexes. She had no symptom or laboratory abnormality. On the day of readmission, she had eclampsia and the fetus was lost in utero. Labor was induced with a 50 mcg misoprostol intravaginally, but 6 h later she had nine convulsions despite the $MgSO_4$ infusion. Subsequently, she underwent delivery by Cesarean section under general anesthesia, due to failure of induction, and she was anesthetized for 24 h in the intensive care unit postoperatively. She had normal CT and a calculated proteinuria of 36 g/24 h. After weaning from the ventilator on the second day, she continued to convulse in the intensive care unit. However, she had no further convulsions from 48 h after awakening and was transferred to a normal ward and discharged 6 days later.

Discussion

The classic teaching that eclampsia is the end point of a disease process, starting subclinically and proceeding to mild preeclampsia and then severe preeclampsia implies that hypertension and proteinuria should precede the onset of eclampsia. In contrast to this paradigm, eclampsia can potentially be encountered at the beginning of the disease process before hypertension and proteinuria develop. Consequently, the term 'preeclampsia' has been criticized as misleading (6). In classic cases, the disease usually first involves the arteries and kidneys, manifesting as hypertension and proteinuria before other organ systems are involved. In atypical cases, however, the organ involvement may start with other systems, such as cerebral involvement, which presents initially as eclampsia. In our first, second, and third cases, the first mani-

festation of the preeclampsia before hypertension or proteinuria was cerebral, renal, and placental involvement, respectively. This indicates that signs and symptoms of organ system involvement should be sought vigilantly in the absence of hypertension or proteinuria in suspected cases. Thus, these women should be seen frequently, at least twice weekly (4). Rather than relying solely on the presence of hypertension or proteinuria, the patient history, physical examination, and laboratory and imaging studies may be critical in not missing atypical forms (7). Suspicious findings may include marginally elevated BP or liver enzymes, fetal distress, blurred vision, and headache. The initial diagnosis should be atypical preeclampsia and eclampsia when suspected; time-consuming diagnostic investigations for a differential diagnosis should be deferred until the patient is stabilized. A management plan should be started immediately for atypical forms, rather than searching for a rare disease in a differential diagnosis (Table 2) (8). Even a minor sign, such as the trace proteinuria in our first case, should not be overlooked and could be alarming in the absence of overt hypertension and proteinuria. In the second case, if the proteinuria per se had alarmed us earlier, despite the absence of hypertension, the patient could have been watched more closely for a postpartum rise in BP and pain management might have prevented the sudden increase in BP that provoked the convulsion. The absence of classic features results in unnecessary consultations and investigations or a delay in diagnosis and $MgSO_4$ infusion. This is especially true for healthcare providers unfamiliar with atypical forms of eclampsia.

The rapidly progressive case of eclampsia in our fourth case was another example of an atypical form. She progressed to severe preeclampsia in four days and had resistant eclampsia, unresponsive to anticonvulsive therapy. This patient is a typical case of non-preventable eclampsia, because her convulsions could not be predicted or prevented even under hospital care.

Sibai et al. reported that 56 of 179 cases of eclampsia were potentially unavoidable, despite proper antenatal care and management. Of the 56 patients, 24 convulsed, despite a recent prenatal visit with no previous hypertension, proteinuria, or symptoms suggestive of the forthcoming eclampsia (9). The extension of this series to 254 eclamptic cases found that 80 patients (32%) did not have edema, 58 (23%) had minimal or no hypertension, and 49 (19%) did not have proteinuria at the time of convulsions (10). In a comprehensive study of 383 eclamptic women in the United Kingdom, 38% of the eclamptic convulsions occurred before the documentation of proteinuria and hypertension and 75% developed in hospital, while under supervision (6). These findings reflect the challenges in the early recognition and management of atypical presentations.

The most common cause of convulsions in association with hypertension or proteinuria during pregnancy or immediately postpartum is eclampsia. However, late postpartum eclampsia is defined as eclampsia that occurs more than 48 h, but less than four weeks, after delivery (2). All patients with atypical-onset eclampsia should undergo a neurological evaluation to rule out the presence of neurologic causes of seizures (Table 2). Cerebral imaging is indicated for patients with focal neurologic signs, such as hemiparesis, an unconscious state, and prolonged coma. Additionally, cerebral imaging may be helpful in patients who have an atypical presentation of eclampsia (onset before 20 weeks or more than 48 h after delivery, refractory to magnesium sulfate therapy, and recurrent seizures).

Table 2. Differential diagnosis of eclampsia (8)

Cerebrovascular accidents
Hemorrhage
Ruptured aneurysm
Arterial embolism or thrombosis
Cerebral venous thrombosis
Hypoxic ischemic encephalopathy
Angiomas
Hypertensive encephalopathy
Seizure disorders
Previously undiagnosed brain tumors
Metastatic gestational trophoblastic disease
Metabolic diseases
Reversible posterior leukoencephalopathy syndrome
Thrombophilia
Thrombotic thrombocytopenic purpura
Postdural puncture syndrome
Cerebral vasculitis

In conclusion, the absence of hypertension or proteinuria should not preclude diagnosing preeclampsia/eclampsia. Eclampsia or fetal distress may be an unusual presenting scenario in atypical cases before the detection of overt hypertension or proteinuria. Even minor clues in diagnoses, such as a marginally elevated BP or trace proteinuria, may be critical for appropriate, timely management. Obstetricians should be aware of atypical presentations, maintain a high level of suspicion, and be ready to take immediate steps. Moreover, valuable time should not be spent conducting detailed investigations.

Conflict of interest

None declared

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The characteristics of sexual behaviour and extent of condom usage among sexually active Croatians from Eastern Croatia, letter to the editor

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

Emre Karaşahin, Cihangir Mutlu Ercan, İbrahim Alanbay, İskender Başer
Gulhane Military Medical Academy Department of Obstetrics and Gynecology, Ankara, Turkey

Dear Sir,

We have read "The characteristics of sexual behaviour and extent of condom usage among sexually active Croatians from Eastern Croatia" by Miskulin et al (1), in the J Turkish-German Gynecol. Assoc. 2009, 10; 142-7 with interest.

The authors have put considerable efforts into their study and they draw attention to the risky sexual behaviour of a certain Croatian population and stated their study was the first attempt in this aspect.

They have used a 20 question questionnaire to collect data for their study. While this questionnaire provided valuable data, the question number 12, "I have NEVER in my lifetime involved myself in sexual activities combined with drug or alcohol abuse without condom: a) yes b) no" is a CRITICAL question in this questionnaire.

As far as we are concerned, the answers of the subjects to this question have not been mentioned in the text of the article. Gender differences notwithstanding, the qualitative data generally suggest that alcohol use before sex leads to uninhibited sexual behavior, including increased sexual arousal, increased likelihood for participating in casual sex, and increased confidence and flirtation with the opposite sex in both men and women. Furthermore, the situational use of alcohol was found to be related to inconsistent or non-use of condoms and increased difficulty to implement condom use (2).

We believe authors should have presented their data about risky sexual behaviour associated with alcohol and/or drug use in their manuscript. However, this could also, be another topic to be discussed separately.

Another interesting data would have been the association of risky sexual behaviour with Hepatitis B, which is also found in the questionnaire, but has not been mentioned in the text. Hepatitis B is classified as a sexually transmitted infection (3). It would be interesting to learn about the Hepatitis B immune or non immune people's sexual behaviour and preferences, since Hepatitis B is a major health concern in some parts of the world.

The authors mentioned risky sexual behaviour but have not defined what should be considered as risky sexual behaviour. For convenience, a definition would be: Unprotected intercourse without male or female condom use, except in a long-term, monogamous relationship, unprotected mouth-to-genital contact, except in a long-term monogamous relationship, early sexual activity, especially before age 18, having multiple sex partners, having a high-risk partner (one who has multiple sex partners or other risk factors), having anal sex or a partner who does, except in a long-term, monogamous relationship, having sex with a partner who injects or has ever injected drugs, exchange of sex (sex work) for drugs or money (4).

We would like to thank the authors for sharing their valuable data with us.

Sincerely

Conflict of interest

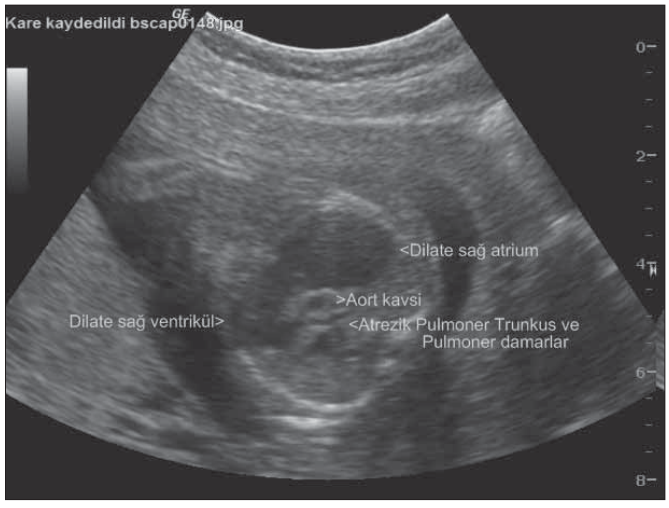
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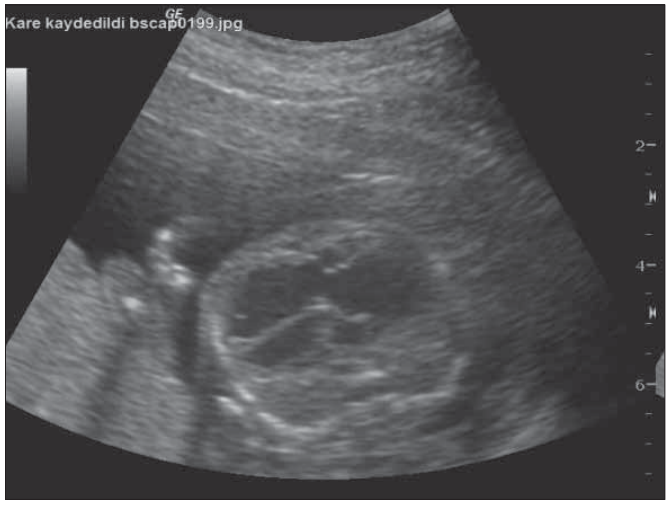
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What is your diagnosis ?







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doi:10.5152/jtgga.2010.016

Answer

Pulmonary atresia (PA) is a congenital malformation of the pulmonary valve in which the valve fails to develop. The incidence of PA with IVS is 4.5 per 100.000 live births (1). It is associated with a broad spectrum of anatomic variability. PA can occur either with an intact ventricular septum (IVS) or with ventricular septal defect.

Two types of pulmonary atresia with an intact ventricular septum have been described (2). In type I disease, a combination of pulmonary valvular atresia, competence of the tricuspid valve, and an intact ventricular septum result in massive right ventricular hypertrophy and chamber obliteration with suprasystemic pressures. In type II disease, proximal pulmonary arterial atresia and an intact ventricular septum are present, but tricuspid incompetence allows retrograde flow of blood from the right ventricle into the right atrium and across an atrial septal defect. Thus, in type II disease, the right ventricle is either normal or dilated.

Demonstration of reversal of blood flow through the ductus is virtually always present in pulmonary atresia with an intact ventricular septum. The tricuspid valve orifice is usually proportional to the size of the right ventricular cavity. The valve leaflets are often dysplastic, which results in varying degrees of insufficiency or stenosis. A dilated right atrium is another finding commonly associated with this disorder. The degree of dilation is dependent on the amount of tricuspid regurgitation present or the inability of blood to enter the right ventricle.

The outcome for infants born with pulmonary atresia and an intact ventricular septum is poor. They are dependent on a patent ductus arteriosus for survival in the neonatal period. Administration of prostaglandin E1 at birth is essential to maintain patency until surgery can be performed (3, 4).

In the presented ultrasound image of a fetus at 18 weeks of gestation, pulmonary atresia with intact ventricular septum is visualized. Imaging demonstrated marked dilatations of the right atrium and ventricle. A small pulmonary artery was seen with an atretic pulmonary valve. The tricuspid valve was present and tricuspid insufficiency was confirmed by color Doppler indicated by an arrow in the figure.

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0.5 ml İM Enjeksiyon İçin Süspansiyon İçeren Kullanıma Hazır Enjektör
[Human Papillomavirüs Tip 16 ve 18 Rekombinant AS04 adjuvanlı Aşı]

Formülü: Human Papillomavirüs Tip 16 ve 18 Rekombinant AS04 adjuvanlı Aşı, rekombinant DNA teknolojisi ile üretilen ve alimünyum hidroksit ile absorbe edilmiş infeksiyöz olmayan virüs benzeri partikül (VLP'ler) formunda L1 proteinini içerir. 0.5 ml dozu, 20 mikrogram İnsan Papillomavirüs Tip 16 L1 proteini ve 20 mikrogram İnsan Papillomavirüs Tip 18 L1 proteini içerir. **Endikasyonları:** Cervarix® aşısı, 10 yaş ile 25 yaş arası kız çocukları ve kadınlarda Human Papilloma Virüs (HPV) Tip 16 ve 18 ile nedensel ilişkisi olan yüksek gradeli servikal intraepitelyal neoplazilerin (CIN grade 2 ve 3) ve servikal kanserin önlenmesi için endikedir. **Kontrendikasyonları:** Cervarix®'in içeriğinde bulunan maddelere ve aşının kendisine duyarlı olan kişilerde yan etkilere neden olabilir. **Uyarılar/Önlemler:** Eğer sizde veya çocuğunuzda aşağıdaki durumlardan herhangi biri varsa: Aşının içerdiği maddelerden herhangi birine karşı gelişen aşırı duyarlılık (yardımcı madde listesine bakınız). Aşının bir dozunu aldıktan sonra gelişen aşırı duyarlılık. Aşırı duyarlılık belirtileri: Kaşıntılı deri döküntüsü, nefes darlığı ve yüz veya dilde şişme olarak sıralanabilir. Kanama bozukluğu olanlarda dikkatle yapılmalıdır. Bu uyarılar geçmişteki herhangi bir dönemde dahi olsa, sizin veya çocuğunuz için geçerliyse lütfen doktorunuza danışın. Bütün diğer enjektabl aşılarda olduğu gibi, aşının uygulanmasının ardından seyrek olarak anafilaktik reaksiyon görüldüğü takdirde gerekli olabilecek tıbbi tedavi olanakları hazır bulundurulmalıdır. Cervarix® 10 yaş altı çocuklarda kullanılmaz. **Gebelik ve Emzirme Döneminde Kullanımı:** Gebelik Kategorisi: C. Bu aşının hamilelik dönemindeki güvenliliği henüz tam olarak belirlenmiş değildir. Hamilelik sırasında bu aşıyı kullanıp kullanmamanıza doktorunuz karar verecektir. Cervarix®'in anne sütüne geçip geçmediği bilinmemektedir. Bu nedenle, emziriyorsanız doktorunuzu bilgilendiriniz. Emzirmenin durdurulup durdurulmayacağına ya da Cervarix® kullanımının durdurulup durdurulmayacağına ilişkin karar verilirken, emzirmenin çocuk açısından faydası ve Cervarix® kullanımının emziren anne açısından faydası dikkate alınmalıdır. Cervarix® gerekli olmadıkça gebelik döneminde kullanılmamalıdır. Aşı kesinlikle damar içine uygulanmamalıdır. **Yan Etkiler/Advers Etkiler:** Tüm ilaçlar gibi, Cervarix®'in içeriğinde bulunan maddelere ve aşının kendisine duyarlı olan kişilerde yan etkilere neden olabilir. Aşı uygulama yerinde bölgesel olarak ağrı, kızarıklık, şişlik hissedebilirsiniz. Bu belirtiler genel olarak tüm aşılarda aşılamaya bağlı olarak görülen hafif yan etkilerdir ve uzun süreli değildir. Baş ağrısı, egzersiz ile ilişkili olmayan kas ağrısı, yorgunluk, 38°C ve daha yüksek ateş, bulantı, kusma, ishal ve karında ağrı, baş dönmesi, eklem ağrısı, deride döküntü, kaşıntı diğer bildirilen yan etkilerdir. **İlaç Etkileşmeleri:** Cervarix® bağışıklık sistemini baskılayan diğer ilaçlarla birlikte kullanıldığında beklenen etkisini en iyi şekilde gösteremeyebilir. Klinik çalışmalar, Cervarix® ile elde edilen korunmanın ağızdan alınan doğum kontrol ilaçlarıyla azalmadığını göstermiştir. **Kullanım Şekli ve Dozu:** Optimal koruma sağlamak amacıyla üç intramüsküler enjeksiyon olacak şekilde 0, 1 ve 6 aylık uygulama şeması kullanılmalıdır. Cervarix® intramüsküler olarak uygulanmalıdır. Cervarix® intravenöz yoldan kesinlikle uygulanmamalıdır. **Aşırı Dozaj:** Uygulanamaz. **Saklama Koşulları:** Aşı +2°C ile +8°C arasında saklanmalıdır. Aşıyı kesinlikle dondurmayınız. Eğer aşı donmuşsa kullanmadan atınız. **Ruhsat Sahibinin Adı ve Adresi:** GlaxoSmithKline İlaçları Sanayi ve Ticaret A.Ş., 1.Levent/İstanbul. **Ruhsat Tarih ve Numarası:** 28.12.2007 - 4 Reçete ile satılır. 25.01.10 tarihi itibarıyle perakende satış fiyatı KDV dahil (%8) 129,37 TL'dir. **Kullanma Talimatı Onay Tarihi:** 28.12.2007 **Kullanma talimatı Kodu:** Cervarix_KT_PFS.10/19.12.07/v.2/C Cervarix® GlaxoSmithKline şirketler grubunun tescilli markasıdır.

CE/IL/02.10/01



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Cervarix®
Human Papillomavirüs Tip 16 ve 18 Rekombinant, AS04 adjuvanlı aşı



YAZZ 24 +4 KISA PROSPEKTÜS

YAZZ® 24+4 film kaplı tablet: Herbiri 3 mg drospirenon ve 0.02 mg etinilestradiol içeren 24 film kaplı tablet ve bunları takip eden 4 plasebo tablet. **Terapötik endikasyonlar:** ▪Gebeliği önleyici etkisinin yanısıra antimineralokortikoid ve antiandrogenik etkileri sayesinde, hormona bağlı su tutulması ve buna bağlı belirtiler gösteren kadınlarda, ▪Oral kontrasepsiyon isteyen hastalarda akne vulgaris tedavisi, ▪Premenstruel disforik bozukluk (PMDD; Premenstrual Dysphoric Disorder) semptomlarının tedavisinde endikedir. **Pozoloji/uygulama sıklığı, süresi ve şekli:** Tabletler paketin üstünde gösterildiği yönde, hergün yaklaşık aynı zamanda bir miktar su ile alınmalıdır. Tablet alımı süreklidir. Birbirini izleyen 28 gün boyunca hergün bir tablet alınır. Her bir sonraki pakete önceki kutudaki son tablet alımının ertesi günü başlanır. 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, anjina 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 embolisi 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 siklusluk 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 sonuclanabilir. 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/Aluminyum 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.

R-VH-04-09-0121-TR

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