Türk Jinekoloji ve Obstetrik Derneği DERGİSİ

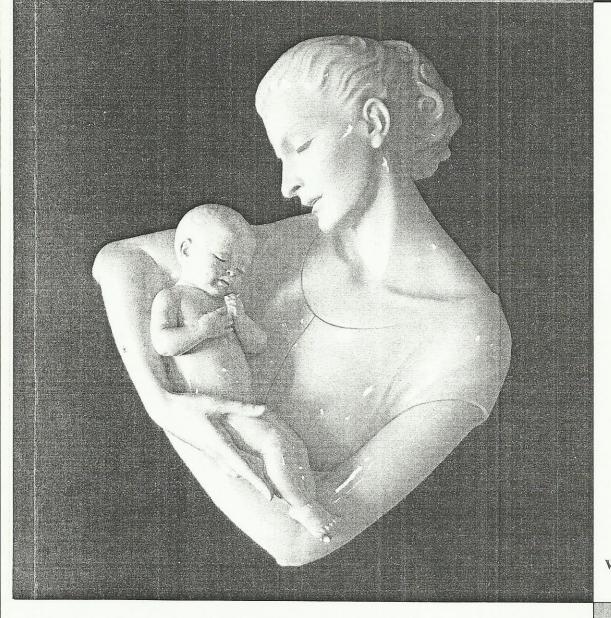
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Olgu Sunumu: 17 yaşında, bekar olarak ve primer amenoresi nedeniyle başvurdu. Anamnezinde 3 ay boyunca oral kontraseptif (Gynera tb, 1x1) kullandığı ancak menses olmadığı saptandı. Büyümesinin normal olduğu ve meme ve pubik kıllanma gelişiminin Tanner evre 4 olarak değerlendirildi. Yapılan kromozomal analiz sonucu 46, XX olarak rapor edildi. Laboratuar değerlerinden FSH, LH ve E2 normal olarak saptandı. Hastada müllerian agenezis ön tanısıyla yapılan transabdominal ultrasonografisinde ve pelvik magnetik rezonanas görüntülemede her iki over ve uterus izlenmedi şeklinde rapor edildi. Laparoskopi sırasında uterus orta hatta görülmekle birlikte unikornus yapıda idi. Rudimenter horn saptanmadı. Sol round ligament, tuba ve overler normal olarak izlendi. Sağ round ligament, tuba ve over izlenmedi. İntraabdominal endometriozise ait herhangi bir implantasyon odağı saptanmadı. Batın içinde mensese ait eski kanamaya ait bulgu izlenmedi. Postoperatif intra venöz pyelografi çekildi ve Postoperatif intra venöz pyelografi çekildi ve sağ böbrek izlenmedi, sol böbrek normalden büyük olarak rapor edildi. Hastaya oral kontraseptif başlanarak sonrasında histeroskopi altında vajinal ve/veya servikal agenezis açısından değerlendirilmesi planlanarak taburcu edildi. Sonuç: Nadir görülmeleri nedeniyle sebepleri tartışmalı da olsa müllerian kanalın kaudal kısmında ve genital kabartı bölgesinde lokalize bir defekt veya intrauterin dönemde adneksal torsiyon sonucunda oluşabilir.

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SPONTAN ABORTUS SPESİMENLERİNİN HİSTOPATOLOJİK BULGULARI İLE FETAL KARYOTİPİK DEĞİŞİKLİKLERİN KORELASYONU

Üreme Endokrinolojisi ve İnfertilite

Nesin Akdemir¹, Emre Okyay¹, Sait Tümer², Erdener Özer³, Bülent Gülekli¹,

¹Dokuz Eylül Üniversitesi Tıp Fakültesı, Kadın Hastalıkları ve Doğum Anabilim Dalı

²Dokuz Eylül Üniversitesi Tıp Fakültesi, Tıbbi Biyoloji ve Genetik Anabilim Dalı

³Dokuz Eylül Üniversitesi Tıp Fakültesi, Patoloji Anabilim Dalı

Giriş ve Amaç: Anormal karyotip saptanan ilk trimester spontan abortus olgularında fetoplasental histolojinin çeşitli farklılıklar gösterdiği öne sürülmüş ve karyotip anormallikleri ile ilişkili histopatolojik değişiklikler saptanmaya çalışılmıştır. Çalışmamızın amacı, tekrarlayan gebelik kaybı öyküsü olan 1. trimester spontan abortus olgularında, histopatolojik bulguların sitogenetik korelasyonunu belirlemek ve histolojik incelemenin tanısal önemini ortaya koymaktır. Gereç ve Yöntem: Dokuz Eylül Üniversitesi Tıp Fakültesi Uygulama ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Anabilim Dalı' nda Ekim 2001 ve Nisan 2006 yılları arasında spontan abortus nedeniyle gebeliği sonlanan ve sitogenetik inceleme yapılmış 20 olgunun sitogenetik vepatolojik kayıtları retrospektif olarak incelendi. Bulgular: Çalışmaya dahil edilen 20 olguda anne yaşı 20-42 arasında değişmekte ve median yaş: $32.65 \text{ (} \pm 6.54 \text{ SD)}$ idi. Median anne yaşı normal fetal karyotip saptanan 13 olguda 30.46 ($\pm\,5.88{\rm SD}$) iken, anormal fetal karyotip bulgusu izlenen 7 olguda 36.71 ($\pm\,6.07~\mathrm{SD}$) idi. Yaş göze alındığında iki grup arasındaki farklılık istatistiksel olarak anlamlı bulundu (p=0.03). Şiddetli desidual nekroz bulgusunun anormal karyotip saptanan olgularda, normal gruba kıyasla daha yüksek oranda olduğu izlendi (% $57\ vs\ \%$ 8) ve bu bulgu istatistiksel olarak anlamlıydı (p=0.03). Şiddetli desidual nekroz dışındaki histopatolojik inceleme kriterlerinde ise her iki grup arasında istatistiksel farklılığın olmadığı saptandı. Sonuç ve Yorum: Spontan abortuslarda fetal karyotip ile plasental histoloji arasındaki ilişki tartışmalıdır. Karyotipik yapıya bağlı spesifik histolojik değişikliklerin belirlenememesi, farklı karyotipe sahip olgularda histopatolojik benzerlikler bulunması ve normal karyotipli olgulara ait kesin histolojik özelliklerin belirlenmemesine bağlı olabilir.

PS. 310

COMBATING ENDOMETRIOSIS BY BLOCKING PROTEASOME AND NUCLEAR FACTOR-KAPPAB PATHWAYS Üreme Endokrinolojisi ve İnfertilite

Önder Çelik¹, Seyma Hasçalık¹, M.Emin Tağluk², Koray Elter³, Bilgin Gurates⁴, N: Engin Aydın⁵

¹Department of Obstetrics and Gynecology, Inonu University School Of Medicine, Malatya

²Department of Electric and Electronic Engineering, Inonu University, Malatya

³Eurofertil Center for Human Reproduction, Istanbul

⁴Department of Obstetrics and Gynecology, Firat University School of Medicine, Elazig

⁵Department of Pathology, Inonu University School of Medicine, Malatya, Turkey

Introduction: Endometriosis is associated with systemic subclinical inflammation. NuclearFactor-kappaB (NF-κB) is a ubiquitously expressed transcription factor that causes inflammation in endometriotic cells. The inhibition of NF-κB within the endometrial implant may be achieved either by NF-κB inhibitors or by prevention of releasing of NF-κB precursors using proteasome inhibitors. The objective of this study was to investigate the effect of pyrrolidine dithiocarbamate (PDTC; an NF-κB inhibitor) and bortezomib (velcade; a proteasome inhibitor) on the development of experimental endometriotic implants in rats.

Material and Methods: Endometriosis was surgically induced in 30 rats using the method of vernon and Wilson. Three weeks later the viability and volume of the implants were recorded and classified as described by Ingelmo. Six of 30 rats were not considered satisfactory because the implants of four were nonviable and of two were covered by omentum. Other remaining rats were put into three groups with equal numbers: the control (0.1 mL of isotonic saline/day per rat, i.p), the PDTC (100 mg/kg of body weight, i.p) and the bortezomib (0.2 mg/kg of body weight, i.p) groups. Seven days after treatment, a third laparotomy was done and the volume of implants was measured again using the ellipsoid formula. The animals were then sacrificed, and the implants were processed for microscopic examination. Five micrometer sections of paraffin blocks were stained with hematoxylin and eosin, Masson's trichrome, Ki67 which is expressed in the cells during M, G1, S and G2 phases of cell cycle, proliferating cell nuclear antigen (PCNA), a nuclear protein whose expression peaks during the S phase of the cell cycle and CD34 a stain used for endothelial cells. Histologic changes of the implants, vascularity, PCNA, Ki67 and CD34 immunoreactivity was assessed under light microscopy and scored using a semi-quantitative grading system.

Results: In 80.0 % of implanted rats vesicle at the sutures region was observed; the vesicle diameters were <2 mm (grade 2) in 41.6 %, between 2 mm and 4.5 mm (grade 3) in 33.3 % and >4.5 mm (grade 4) in 25.0 %. After treatment with PDTC or bortezomib these percentages were decreased in grade 3 and grade 4, and increased in grade 1 and 2. In the control group, on the contrary, these percentages increased in grade 4 and decreased in grade 2. The implant volumes were 72.5±28.7 mm3, 64.6±24.7 mm3 and 67.3±35.1 mm3 before treatment, which did not show a statistically significant difference (P>0.05), and were 80.4±30.1 mm3, 31.9±20.0 mm3 and 32.8±20.1 mm3 after the treatment in the control, PDTC and bortezomib groups, respectively. After the treatment, while the volumes in the control group were higher then others (P<0.000 and P<0.000), the volumes in the PDTC and bortezomib groups remained comparable (P=0.798). As the pre- and post-treatment volumes were compared in each group, the posttreatment volumes were decreased in the PDTC and bortezomib groups (P<0.002 and P<0.001), and slightly increased in the control group (P=0.279). Immunohistochemical stainings for PCNA, Ki67

and CD34 has revealed an intense proliferation of stromal, glandular and endothelial cells in implants of control animals, but only a minor proliferation of this cells which were mainly localized within the endometrial stroma in implants of PDTC and bortezomib groups. In PDTC and bortezomib groups, CD34, PCNA and Ki67 expressions were similar but were significantly reduced as compared to control group (P<0.05). Also the mean score of vascularity, stromal and glandular tissue in the PDTC and bortezomib groups were lower than in the control group (P<0.05)

Conclusions: Selective NF-κB inhibition induces regression on endometriotic implants in rats. Accordingly, PDTC and bortezomib may represent a novel therapeutic strategy for treatment of endometriosis.

PS. 311

INFLUENCE OF RESVERATROL (3,5,4'-TRANS-TRIHYDROXYSTILBENE) AND PYRROLIDINE DITHIOCARBAMATE (NUCLEAR FACTOR-KAPPAB INHIBITOR) ON PMSG-LNDUCED OVULATION RATE Üreme Endokrinolojisi ve İnfertilite

Önder Çelik¹, Haydar Bağış², Seyma Hasçalık¹, Arzu Taş², N. Engin Aydın³

¹Department of Obstetrics and Gynecology, Inonu University School of Medicine, Malatya

²Tubitak Mrc, Genetic Engineering Biotechnology Institute Transgenic Core Facility, Kocaeli

³Department of Pathology, Inonu University School of Medicine, Malatya

Objective: It was proposed that ovulation is one type of localized physiological inflammatory reaction. Since that time, several inflammatory cytokines and reactive oxygen species (ROS) have been characterized and also linked to the process of ovulation. NF-kB is a transcription factor, which induces the expression of many genes that participate in inflammatory responses. Pyrrolidine dithiocarbamate (PDTC) is an antioxidant and NF-kB inhibitor. Resveratrol (RSV; 3,5,4'-trans-trihydroxystilbene), a natural phytoalexin present in grapes, peanuts, and red wine, has various pharmacological effects including anti-inflammatory and antioxidant properties. Its anti-inflammatory effect is related to inhibiting oxidation, leukocyte priming and suppression of several transcription factors such as NF-κB. The present study in this perspective was undertaken to evaluate the efficacy of PDTC and RSV on ovulation stimulated by PMSG and hCG. Materials and Methods: Animal care and use procedures were in accordance with the International Guide for the Care and Use of Laboratory Animals and were approved by the Animal Ethics Committee of Inonu University. The 21 weight and age matched female mice were randomly put into three groups with 7 mice in each group: [1] the control group subject to ovulation iduction with PMSG (10 IU) and 48 hours later hCG (7.5 IU, i.p.); [2] the PDTC group was subject to a similar ovulation induction protocol but 4 hours before hCG injecton, PDTC was given intraperitoneally (100 mg/kg body weight); [3] the RSV group was administrated with RSV perorally (10mg/kg body weight) seven days before a similar ovulation induction. Briefly, female mice were superovulated by intra-peritoneal administration of 10 IU pregnant mare serum gonadotropin (PMSG) and 48 hr later by intra-peritoneal administration of 7.5 IU hCG (Pregnyl; Organon). Approximately 18 h after administration of hCG, mices were killed by cervical dislocation. The oviducts of superovulated females were removed and the ampullae of the oviducts were ripped open with dissecting needles. Cumulus-oocyte complexes (COCs) were released from oviductal ampullae and transferred into drops of M2 medium containing hyaluronidase (80 IU/ml) for a short time, then embryos were washed three times in M2 medium.. Results: In present study, the numbers of ovulations were decreased both in the control and PDTC treated mices $(6.5\pm0.20 \text{ and } 6.2\pm0.35)$ and a lower number of neutrophils were seen in the ruptured follicles. However, a significant increase in the ovulation rate in RSV-treated animals (9.0±0.48) when compared to control and PDTC groups (P<0.05). No significant difference in ovulation rate between PDTCtreated and the control groups (P=0.363). Histological examination of ovary demonstrated that there was a considerable number of perifollicular extravasated white blood cells at the time of ovulation. The leukocytes were seen both in the stroma and in the follicle wall, where they were intermingled with the theca interna cells. To determine whether the increase in ovulation rate seen after RSV treatment was due to the improving of follicular rupture or a increase in the number of preovulatory follicles that developed, the total number of follicles of preovulatory size and corpora lutea were counted in H&E sections of both the ovaries from each group. When ovaries were collected after ovulation, there were more corpora lutea and fewer preovulatorysized unruptured follicles in the RSV-treated ovaries than in the PDTC and control groups. The most remarkable change observed in PDTCtreated ovaries was the failure of the cumulus complex to detach from the mural granulosa layer and to undergo full expansion. None of these findings were observed in the RSV and control groups. Conclusion: Inhibition of NF-kB pathway with PDTC does not affect the ovulation rate. RSV has been successfully employed in the current study to generate data that suggest that antioxidant treatment has a role in stimulating the growth of follicles to the preovulatory stage of development and in increasing follicular rupture. Treatment with RSV before ovulation induction can be used to achieve a increase in ovulation rate. Knowledge about the activity of RSV in ovulation may be important to be able to pharmaceutically modify the ovulatory process in a stimulatory way to increase ovulation number.

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TÜM POLİKİSTİK OVER SENDROMLU HASTALARA RUTİN ORAL GLUKOZ TOLERANS TESTİ GEREKLİ MİDİR? Üreme Endokrinolojisi ve İnfertilite

Elif Esra Uyar¹, Mithat Erenus², Gülfem Şişmanoğlu²,

¹Tokat Doğum ve Çocuk Bakımevi Hastanesi

²Marmara Üniversitesi Tıp Fakültesi Hastanesi, Kadın Hastalıkları ve Doğum Anabilim Dalı

Giriş ve Amaç: Zayıf ve obez polikistik over sendromu (PKOS) hastalarını diyabet riski açısından incelemek ve tüm PKOS hastalarına oral glukoz tolerans testi (OGTT) ile rutin tarama yapmanın gerekliliğini araştırmaktır.

Gereç ve Yöntem: Mart 2004-Şubat 2006 tarihleri arasında Marmara Üniversitesi Hastanesi Jinekoloji ve Hirsutizm polikliniklerine adet düzensizliği ve/veya kıllanma şikayetleri ile başvuran hastalardan Rotterdam kriterlerine göre PKOS tanısı alan toplam 57 olmak üzere, 43 zayıf PKOS (VKİ < 25 kg/m2) ve 14 aşırı kilolu ve obez PKOS (VKİ ≥25 kg/m2) hastası prospektif olarak çalışmaya alındı. Kontrol grubu olarak Marmara Üniversitesi Hastanesi çalışanlarından ve Marmara Üniversitesi Tıp Fakültesi öğrencilerinden PKOS hastaları ile benzer yaşta olan 15 kişi çalışmaya dahil edildi. Zayıf ve obez PKOS hastalarına ve sağlıklı kontrol grubuna pelvik ultrasonografi yapılarak polikistik over görüntüsü araştırıldı. PKOS hastalarının erken foliküler dönemdeki hormon seviyeleri değerlendirildi, Ferriman-Gallwey skorları belirlendi. Zayıf ve obez PKOS hastalarına ve kontrol grubundaki olgulara 75gr glukoz ile 2 saatlik OGTT yapıldı. İnsülin rezistansının değerlendirmek amacıyla HOMA, QUİCKİ, AUC.insülin, AKŞ/insülin oranları hesaplandı.

Bulgular: Ortalama VKİ değerleri; PKOS, zayıf PKOS, obez PKOS ve kontrol grubu için sırasıyla; 21.1 ± 2.5 , 23.2 ± 4.1 , 21.3 ± 1.9 , 28.8