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PREMATÜR OVARYEN YETMEZLİĞİN NEDEN OLDUĞU OSTEOPOROZ ENGELLENEBİLİR Mİ?

Üreme Endokrinolojisi ve İnfertilite

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Giriş: Prematür ovaryan yetmezliği (POF) olan kadınlarda kemik mineral dansitometrisini (KMD) değerlendirmek ve olası osteoporozun önüne geçmek.

Gereç ve Yöntem: Karyotip olarak normal olan, sistemik ve metabolik bir hastalığı bulunmayan, 40 yaşın altında, anamnez ve labaratuvar parametreleri kullanılarak kliniğimizde prematür ovaryan yetmezlik tanısı konmuş 75 kadın değerlendirmeye alındı. POF tanı kriteri olarak; ≥ 6 ay amenore, 0, 1 ve 2 ay ara ile saptanan FSH düzeyleri >40 mIU/ml kabul edildi. L1-L4 ve femur neck-total kemik mineral dansitometri değerleri saptandı. Menstrüel siklusu düzenli ve paritesi olan 50 kadın kontrol grubu olarak çalışmaya alındı.

Bulgular: POF olan kadınlarla kontrol grubunun yaşları arasında fark yoktu ($p>0.05$). POF olan kadınların ortalama yaşı 30,4 (18-39) ve prematür menopoz tanısı ortalama 3,2 (0,6-8) yıl idi. Yetmiş beş kadının 6'sı (%8) hormon replasman tedavisi almıştı ve bu hastalar (femur neck: 0.831 ± 0.29 , femur total: 0.698 ± 0.25 , L1-L4 total: 1.098 ± 0.29) ile kontrol grubu (femur neck: 0.843 ± 0.31 , femur total: 0.706 ± 0.24 , L1-L4 total: 1.112 ± 0.21) arasında KMD yönünden istatistiksel açıdan anlamlı fark bulunmadı ($p>0.05$). POF nedeniyle önceden hiç tedavi görmemiş 69 kadının ise KMD değerleri; femur neck: 0.658 ± 0.33 , femur total: $0.0.614 \pm 0.22$, L1-L4 total: 0.901 ± 0.21 idi. Mevcut bulgularla kontrol grubu ile POF olan kadınların arasında KMD yönünden anlamlı derecede fark vardı ($p<0.001$).

Sonuç: Turner sendromu başta olmak üzere kromozomal anormallikler, otoimmün ve metabolik hastalıklar, ooforektomi, sitotoksik kemoterapotikler ile ilişkilidir. Nadiren idiopatik olarak tanı konur ve 40 yaş altında, hipergonadotropik hipogonadizm şeklinde kendini gösterir. Otuz yaşından küçük kadınlarda 1/10.000 sıklıkta iken, 40 yaş civarında 1/100 oranında görülür. POF'teki uzun vadedeki en önemli sorunlarından biri erken kemik kaybı ve dolayısı ile erken osteopeni-osteoporozdur. Bu kadınların kemik kaybını minimum düzeyde tutmak için hormon replasman tedavisi vermek, erken osteopeni-osteoporoz ile mücadelenin bir yolu olabilir.

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FEASIBILITY OF XENOGENEIC PORCINE SMALL INTESTINAL SUBMUCOSA FOR OVARIAN DEFECT REPAIR, MAINTANING OVARIAN RESERVE AND RENEWAL OF PRIMORDIAL FOLLICLES

Üreme Endokrinolojisi ve İnfertilite

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Introduction: Porcine small intestinal submucosa (SIS) is an exciting material, which has been shown to provide temporary support for regenerative process of native tissues. The purpose of this study is to

investigate the feasibility of porcine SIS as a scaffold for ovarian defect repair and possibility of follicle renewal in an in situ xenograft model.

Material and Methods: Fourteen female rabbits were put into two subgroups: Group 1 rabbits whose unilateral ovarian defect was repaired with SIS graft, and Group 2 rabbits whose unilateral ovarian defect was repaired with 7-0 vicryl as the controls. Contralateral ovary of each animal was assigned as a local control to its pair. The animals were killed at 4, 8, 12, 16, 20, 24 and 28 weeks following the repair. During laparotomy, the extent and severity of adhesions in the operation site and contralateral nongrafted site were evaluated using Mazuji's scoring system. Afterwards, bilateral ovaries were removed and their volumes were measured using ellipsoid formulae. The graft site, along with the adjacent ovarian tissue was dissected and processed for microscopic examination. The sections were stained with hematoxylin and eosin, Masson's trichrome and also proliferating cell nuclear antigen (PCNA) and inhibin- α subunit immunohistochemistry. Microscopic images of these sections were further processed for filtering and identification of tissue using image-processing techniques.

Results: The ovarian volumes where SIS graft was applied were found of similar size compared to the volumes of contralateral ones (140.25 ± 8.78 mm³ vs. 151.21 ± 9.96 mm³, $P>0.05$). In contrast, in the control group, the volume of the operated ovary was small compared to the volume of contralateral one (109.14 ± 8.15 mm³ vs. 238.30 ± 8.97 mm³, $P<0.05$). The total volumes of the SIS grafted ovary was found as larger than the volume of damaged ovaries of control group ($P<0.05$), and the adhesion was lower in SIS grafted rabbits (1.14 ± 0.14 vs 3.85 ± 0.26 , $P<0.001$). Until 4 weeks, the response of host tissue to the SIS graft involved hemorrhage and polymorphonuclear leukocytes infiltration, but this is rapidly diminished to a negligible level by the next time point of evaluation (8 weeks). From 12 to 16 weeks the SIS graft and ovarian tissue were well organized and the primordial follicles were accumulated about the boundary of the SIS-ovary. Most of the primordial follicles appeared to be dragging out from the ovarian site toward adjacent SIS graft. However, there also were some isolated primordial follicles showing no apparent connection to the adjacent normal ovarian tissue. These primordial follicles were stained by PCNA and interestingly both primordial follicles and some cells that could be of stromal cells in the SIS graft were stained by inhibin- α . Being staining with inhibin- α and PCNA raises the possibility of these cells being of pre-granulosa cells, which are rendering signs of follicle formation. At 24-28 weeks the primordial follicles collaborated in the majority of the SIS graft and organized alike ovarian structure so that the SIS material could not be identified under light microscopy. Epithelization in SIS graft was partial till 16 weeks, around %75 at 20 weeks and completed by 28 weeks. Interestingly at 28 weeks, control animals showed incomplete epithelization. Granulation tissue had resolved in SIS group by 16 weeks but it was still present in control animals at 28 weeks. Signs of graft rejection were not found in tissue samples of the SIS grafted ovary.

Conclusions: This study provided favorable results that indicate that porcine SIS can confidently be used as a reliable scaffold for repairing of ovarian defect. SIS graft remodeled into the native ovarian tissue and demonstrated primordial follicles that are probably newly formed.