

documented at 6 weeks and viable demonstrated fetal heart activity past the first trimester.

Results: There were 26 transfers from donors with endometriosis vs 144 in donors without endometriosis. The mean ages were 30.7 vs 31.3. The clinical and viable PRs and implantation rates were 73.1%, 61.5%, and 37.8% for the endometriosis group vs 54.9%, 47.2%, and 29.5% ($p = \text{NS}$). There were 17 ETs into donors with endometriosis and 127 into donors without endometriosis. The clinical and viable PRs and implantation rates for donors with endometriosis per ET was 41.2%, 35.3%, and 20.4% vs 50.4%, 48.0% and 28.4% for donors without endometriosis ($p = \text{NS}$). The mean age of the donors was 30.5 vs 30.6 years.

Conclusions: These data clearly show that endometriosis does not seem to adversely affect oocyte quality. Though no significant differences were found in donors with or without endometriosis in any parameters, there did appear to be a trend for lower PRs in those with endometriosis. Possibly a much larger study may show that endometriosis may have a mild negative adverse effect on uterine environment. Nevertheless, an implantation rate of 20.4% for donors with endometriosis is not indicative of a severe implantation disorder. These data suggest that if mild to moderate endometriosis does reduce fecundity, IVF seems to overcome the defect to a great extent.

P-261

Differential modulation of cyclooxygenase-2 and transforming growth factor-beta receptor gene expression following tumor necrosis factor treatment of endometrial cells from women with and without endometriosis. Donald P. Braun, Jianchi Ding, Fehr Shaheen, W. Paul Dmowski. Medical Coll of Ohio and Institute for the Study and Treatment of Endometriosis, Toledo, OH; Institute for the Study and Treatment of Endometriosis, Chicago, IL; Medical Coll of Ohio, Toledo, OH; Institute for the Study and Treatment of Endometriosis and Rush Medical Coll, Chicago, IL.

Objective: Previous studies from our laboratory have demonstrated that endometrial cells (EC) from women with endometriosis are resistant to apoptosis and to macrophage-mediated destruction in comparison to EC from women without endometriosis. This condition could favor the survival of EC in environments which contain inflammatory cytokines and activated macrophages as is found in pelvic and peritoneal cavities of women with endometriosis. The goal of the current study was to investigate the capacity of the inflammatory cytokine, TNF, to modulate the expression of genes with the capacity to regulate cell death and cell survival in EC from women with and without endometriosis

Design: In vitro cell culture of endometrial cells from women evaluated for endometriosis.

Materials/Methods: EC from women with and without endometriosis (3 control and 3 endometriosis specimens) were obtained from collagenase/DNase-treated eutopic endometrium, and cultured for 24 hours in the presence and absence of recombinant TNF. Total RNA was extracted, cDNA prepared, and mRNA for the following growth regulatory genes quantitated: heat shock proteins; BCL-xS and BCL-xL; ICAM-1; TNF; TNF-Receptor 1; TNF Receptor Associated Factor-4; Transforming growth factor beta receptor 1 (TGF-r1); cyclooxygenase-2 (COX-2) and TNF Associated Inhibitory Protein 1 (TNFAIP1). Levels of mRNA were quantitated relative to 1 million actin molecules by the STArt-pcr method.

Results: Basal expression of the genes varied amongst the specimens with no discernible level attributable to the presence of endometriosis. TNF treatment did not substantially alter expression of most genes (magnitude of difference was <2 fold in the presence vs absence of TNF). However, expression of mRNA for COX-2 in TNF-treated EC declined substantially in a control specimen obtained during the late secretory phase of the menstrual cycle (7 fold decrease) while the expression of mRNA for COX-2 increased substantially (4 fold increase) in an endometriosis specimen obtained during the same phase of the cycle. In addition, expression of mRNA for TGF-r1 decreased by 4 fold in response to TNF in the control specimen obtained during the late secretory phase while the same treatment had no effect on expression of this gene in the endometriosis specimen obtained during the same phase of the cycle

Conclusions: Preliminary results demonstrate differential effects of TNF on expression of COX-2 and TGF -r1 genes in EC from women with and without endometriosis. Reduced COX-2 and TGF-r1 in control EC treated with TNF could increase the sensitivity of these cells to spontaneous and immune-mediated apoptosis due to reduced cytoprotection by PGE₂ coupled with a decline in the receptor for the growth factor, TGF. In contrast,

increased expression of COX-2 mRNA as was seen in TNF-treated EC from an endometriosis specimen would be expected to increase resistance to immune-mediated destruction. The approach we have taken can elucidate regulatory mechanisms which favor survival of EC in inflamed, ectopic environments in women with endometriosis. The results may provide insight into new approaches for patient management.

Supported by: Institute for the Study and Treatment of Endometriosis.

P-262

Matrix metalloproteinase and the tissue inhibitor of metalloproteinase expression in sera of women with endometriosis before and after gonadotropin-releasing hormone analog therapy. Wei-Chung Vivian Yang, Wei-Chen Lee, Chii-Ruey Tzeng. Taipei Medical Univ, Taipei, Taiwan; Taipei Medical Univ Hosp, Taipei, Taiwan.

Objective: It is believed that the extracellular matrix (ECM) remodeling is relevant to the progression of endometriosis. Tissue remodeling involving ECM turnover is regulated by the combined action of matrix metalloproteinases (MMPs) and the tissue inhibitors of MMPs (TIMPs). Gonadotropin-releasing hormone analog (GnRHa) has been used for the treatment of endometriosis. However, it still lacks specific markers for diagnosis of endometriosis. The purpose of this study is to find any useful marker in serum for early diagnosis of endometriosis.

Design: Sera from women with endometriosis, untreated and treated with GnRHa, pregnant, and infertile with the reasons other than endometriosis in the obstetrics and gynecology clinic at Taipei Medical University Hospital were obtained.

Materials/Methods: Equal amount of total protein from each serum sample was subjected onto SDS-PAGE. Followed by western blot analysis, the expression of variant MMP/TIMPs in serum was investigated respectively.

Results: The MMP/TIMP expression in sera from 10 women with endometriosis (stage 1 and 2) without receiving GnRHa treatment, 7 women diagnosed endometriosis with GnRHa treatment, 3 pregnant women, and 3 infertile women without endometriosis were analyzed. Surprisingly, nine out of the ten women with endometriosis not receiving GnRHa treatment, the free TIMP-1 was highly expressed in serum. Whereas the women with endometriosis receiving GnRHa treatment, pregnancy women, and infertile women, the free TIMP-1 expression was at non-detectable level. Additionally, a 122 kDa band appeared in most of the tested sera, suggesting a proMMP9/TIMP-1 complex was formed. The suspected proMMP9/TIMP-1 complex was later confirmed by another western blot analysis probed with MMP9 antibody. The expressed TIMP-1 may bind to proMMP9 and inhibit MMP9 activation.

Conclusions: Based on the western blot analysis, we reported that the expression of free form of TIMP-1 in serum from the patients with endometriosis was significantly increased. After GnRHa treatment, the expression level of TIMP-1 in serum was decreased. These results were in contradiction to another report using a heterologous competitive equilibrium RIA method, which could not distinguish free form of TIMP-1 from the other, only to measure the total TIMP-1 concentration. TIMP-1 may bind to pro-MMP9 and inhibit its activity. Instead of using the indirect method to measure the concentration of TIMP-1, we use the anti-TIMP-1 antibody with high specificity to monitor the expression of TIMP-1 in serum. It appears that both free and complex forms of TIMP-1 present in serum. The increasing expression of free TIMP-1 in the patients with endometriosis may result from a regulatory mechanism of inhibiting the increasing MMP expression during the progression of endometriosis. This study supports important information that the expression of TIMP-1 in serum could be detected, and further, the expression of free form of TIMP-1 in serum can be a useful marker for early diagnosis of endometriosis.

Supported by: Taipei Medical University.

P-263

Effect of gonadotropin-releasing hormone analogs on the apoptosis and release of IL-1 and VEGF in endometrial cultures from patients with endometriosis. Gabriela F. Meresman Jr., Mariela Bilotas Jr., Eduardo Lombardi Sr., Marta Tesone Sr., Carlos E. Sueldo Sr., Rosa Ines Baranao Sr. Inst de Biología y Medicina Experimental (IByME)-CONICET, Buenos Aires, Argentina; Inst de Biología y Medicina Experimental (IByME)-CONICET, Buenos Aires, Argentina; Inst de Ginecología y Fertilidad (IFER), Buenos Aires, Argentina.