

## **Abstract**

**Research question:** Endoplasmic reticulum stress (ERS) is caused by the accumulation of the misfolded or unfolded proteins in the endoplasmic reticulum and induces the unfolded protein response (UPR). Peritoneal fluid is important in the pathogenesis of endometriosis. In this study, the role of UPR associated with ERS in endometriosis, and peritoneal fluid, were investigated.

**Design:** Normal, eutopic and ectopic endometrium tissues were divided into menstrual cycle phases, and endometrial stromal cells (ESC) were treated with 10-20% concentration of control peritoneal fluid and peritoneal fluid obtained from women with endometriosis for 10, 30 and 60 min, and 24 and 48 h. The UPR signalling proteins were analysed immunohistochemically and immunocytochemically. Data were compared statistically.

**Results:** p-IRE1 was increased in ectopic glandular and stromal cells in the early proliferative phase compared with normal and eutopic endometrium. p-PERK increased in ectopic glandular and stromal cells in the late proliferative phase compared with normal endometrium. ATF6 was increased in ectopic glandular epithelium compared with normal endometrium in the proliferative phases, versus eutopic endometrium in the late secretory phase. p-IRE1 and p-PERK were increased in high concentrations of ESC treated with peritoneal fluid obtained from women with endometriosis for 10, 30 and 60 min compared with controls. In ESC treated with peritoneal fluid from women with endometriosis, p-IRE1 decreased at 24-48 h compared with 30 min.

**Conclusions:** In endometriosis, UPR pathways are activated as highly dependent on cell type and phase. Also, p-PERK and p-IRE1 increased because of exposure to high-dose peritoneal fluid from women with endometriosis in stromal cells. Our findings provide a basis for further studies searching for a potential biomarker for the diagnosis of endometriosis.