Effects of 17b-estradiol on the release of monocyte chemotactic protein-1 and MAPK activity in monocytes stimulated with peritoneal fluid from endometriosis patients

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목적: Hormones and inflammation have been implicated in the pathological process of endometriosis. Therefore, we investigated the combined effects of 17b-estradiol (E2) and peritoneal fluid obtained from patients with endometriosis (ePF) or a control PF (cPF) obtained from patients without endometriosis on the release of monocyte chemotactic protein-1 (MCP-1) by monocytes and the role of signaling pathways.

방법: Monocytes were cultured with ePF and cPF in the presence of E2 and the MCP-1 levels in the supernatants were then measured by ELISA. In addition, MAPK activation was measured by western blotting of phosphorylated proteins.

결과: E2 down-regulated MCP-1 release by LPS- or cPF-treated monocytes but failed to suppress its release by ePF-treated monocytes. The release of MCP-1 by ePF- and cPF-treated monocytes was efficiently abrogated by p38 MAPK inhibitors. However, the MCP-1 release by cPF-treated monocytes, but not by ePF-treated monocytes was blocked by MEK inhibitor. In addition, E2 decreased the phosphorylation of p38 MAPK, but not ERK1/2 in ePF-treated monocytes. However, E2 decreased the phosphorylation of p38 MAPK, ERK1/2, and JNK in cPF-treated monocytes.

결론: The ability of E2 to modulate MCP-1 production is impaired in ePF-treated monocytes, which may be related to regulation of MAPK activity. These findings suggest that the failure of E2 to suppress ePF-treated production of MCP-1 may be involved in the pathogenesis of endometriosis.

Non-steroidal anti-inflammatory drug-activated gene-1 (NAG-1) expression and apoptosis induction in endometrial cells of patients with endometriosis by trichostatin A or 5-aza-2'-deoxycytidine

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목적: The aim of this study was to evaluate the effect of trichostatin A (TSA) or 5-aza-2'-deoxycytidine (5-aza-dC) on Non-steroidal anti-inflammatory drug-activated gene-1 (NAG-1) expression and apoptosis of endometrial cells in patients with endometriosis.

방법: Endometrial samples were obtained during surgery from patients with and without endometriosis. Real-time PCR was used to quantify NAG-1 mRNA levels. To investigate the effects of TSA or 5-aza-dC, endometrial stromal cells (ESCs) were isolated and cultured with different concentrations of TSA or 5-aza-dC. Apoptosis was assessed by flow cytometry.

결과: The DNA demethylating agent 5-aza-dC did not increase apoptosis in cultured ESCs. However, TSA induced NAG-1 mRNA levels and apoptosis in cultured ESCs. TSA did not synergistically act with 5-aza-dC to induce apoptosis. Small interfering RNA experiments link NAG-1 expression to apoptosis induced by TSA.

결론: Endometriosis appears to be an epigenetic disease and TSA may be a promising therapeutic agent. In addition, NAG-1 may be a therapeutic target for endometriosis.