SR-16234, a selective estrogen receptor modulator, represses development of endometriosis-like lesions in rat model.

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Objective: Endometriosis is a common estrogen-dependent disorder. Medical treatments consist of GnRH agonists, oral contraceptives, and progestins, however, neither is fully effective and entail side effects. Selective estrogen receptor modulators (SERM) have tissue-selective actions. SR-16234, is a newly developed SERM, which has an estrogen receptor (ER) alpha pure antagonist and ER beta partial agonist activity. We investigate the efficacy of SR16234 for the treatment of endometriosis in the rat model.

Method: All rats (7 weeks, Crl: CD rat: n=36) were ovariectomized, and then the lumen of right uterine horn was opened longitudinally and divided into 2 pieces. Two everted segments of each uterine horn were sutured to the parietal peritoneum. A rat endometriosis model was established by transplanting autologous endometrial tissue. E2 was administered subcutaneously throughout from ovariectomy to resection of endometriosis-like lesions. After 4 weeks of oral SR-16234 (0.1-1 mg/kg/day) treatment, the endometriosis-like lesions, left uterus, pituitary, and right femur were excised to evaluate. Gene expression ER alpha, ER beta, PR (progesterone receptor), VEGF (vascular endothelial growth factor), IL (interleukin)-6, MCP (monocyte chemotactic protein) -1 and PEDF (pigment epithelium-derived factor) in the lesions were analyzed by real-time RT-PCR.

Result: Oral administration of SR-16234 decreased dose-dependently the weight of the endometriosis-like lesions. Maximal dose (1mg/kg) of this drug completely inhibited the formation of lesions. SR-16234 showed tendency to decrease the weight of eutopic uterine tissues. E2 administration increased the weight of pituitary and SR-16234 inhibited this increase. SR-16234 did not affect the weight of femur. By E2 treatment, IL-6 and MCP-1, PEDF mRNA expression in the lesions were upregulated. Among them, SR-16234 repressed E2-induced IL-6 mRNA expression, and showed tendency to increase ER beta, PR, and PEDF mRNA expression. SR-16234 did not affect ER alpha, VEGF, and MCP-1 mRNA expression.

Conclusion: SR16234 had a regressive effect on the development of rat endometriosis-like lesions.

Mots clés : estrogen receptor, rat endometriosis model
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