Expression and possible role of non-steroidal anti-inflammatory drug-activated gene-1 (NAG-1) in the human endometrium and endometriosis

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Background: Non-steroidal anti-inflammatory drug (NSAID)-activated gene-1 (NAG-1) is involved in cellular processes such as inflammation, apoptosis and tumorigenesis. However, little is known about the expression and function of NAG-1 in the endometrium. This study aimed to evaluate the expression of NAG-1 in the endometrium and in the absence or presence of endometriosis and to investigate the effect of celecoxib, a selective cyclooxygenase (COX)-2 inhibitor, on NAG-1 mRNA levels and apoptosis in human endometrial stromal cells (HESCs).

Methods: Eutopic endometrial samples were obtained during surgery from 40 patients with, and 40 patients without, endometriosis. Real-time PCR was used to quantify NAG-1 mRNA levels and immunohistochemistry was used to localize NAG-1 protein in the endometrium. To investigate the effects of celecoxib, HESCs were isolated and cultured with different concentrations of celecoxib or with 100 µM celecoxib at different times. Apoptosis was assessed by flow cytometry.

Results: NAG-1 mRNA levels and immunoreactivity showed cyclical changes through the menstrual cycle, increasing during the late secretory and menstrual phases. NAG-1 mRNA and protein levels were significantly lower in patients with endometriosis, compared with the control group. Celecoxib induced NAG-1 mRNA levels and apoptosis in cultured HESCs, with the effects dependent on drug concentrations and duration of treatment. Celecoxib treatment had no effect on prostaglandin E2 levels in the culture supernatants.

Conclusions: NAG-1 may be important in maintaining homeostasis in the normal endometrium and alterations in NAG-1 expression may be associated with the establishment of endometriosis. NAG-1 might be a therapeutic target for endometriosis.

Key words: NAG-1; Endometrium; Endometriosis; Apoptosis