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Natural therapies assessment for the treatment of endometriosis.

Ricci AG[1], Olivares CN, Bilotas MA, Bastón JI, Singla JJ, Meresman GF, Barañao RI.

Author information

Abstract

STUDY QUESTION: Can resveratrol and epigallocatechin-3-gallate (EGCG) inhibit the growth and survival of endometriotic-like lesions in vivo in a BALB/c model of endometriosis, and in vitro in primary cultures of human endometrial epithelial cells (EECs)?

SUMMARY ANSWER: Resveratrol and EGCG exerted a potent inhibitory effect on the development of endometriosis in a BALB/c murine model and on the survival of EECs.

WHAT IS KNOWN ALREADY: Endometriosis is a common condition associated with infertility and pelvic pain in women of reproductive age. Resveratrol and EGCG are two polyphenols with anticarcinogenic and antioxidant properties that have been proposed as natural therapies to treat endometriosis.

STUDY DESIGN, SIZE, DURATION: Fifty-six 2-month-old female BALB/c mice underwent surgical induction of endometriosis. Treatments with resveratrol or EGCG started 15 days post-surgery and continued for 4 weeks. Human biopsies were taken with a metal Novak curette from the posterior uterine wall from 16 patients with untreated endometriosis and 15 controls who underwent diagnostic laparoscopy for infertility.

MATERIALS, SETTING, METHODS: After the treatments, animals were sacrificed and lesions were counted, measured, excised and fixed. Immunohistochemistry for proliferating cell nuclear antigen and CD34 was performed for cell proliferation and vascularization assessment in the lesions. The terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick-end labeling (TUNEL) technique was performed for apoptosis evaluation. Peritoneal fluid was collected to analyze vascular endothelial growth factor levels. Human EECs were purified from proliferative-phase endometrial biopsies and cultured. The effect of both

polyphenols on cell proliferation was determined by a colorimetric assay using the CellTiter 96®AQueous One Solution Cell Proliferation Assay kit and on apoptosis by the TUNEL technique, using an In Situ Cell Death Detection Kit with Fluorescein.

MAIN RESULTS: In the mouse model, both treatments significantly reduced the mean number ($P < 0.05$ versus control) and the volume of established lesions ($P < 0.05$ versus control). Treatments consistently statistically significantly diminished cell proliferation (resveratrol $P < 0.01$ and EGCG $P < 0.05$, versus control), reduced vascular density (resveratrol $P < 0.01$ and EGCG $P < 0.001$, versus control) and increased apoptosis within the lesions (resveratrol $P < 0.01$ and EGCG $P < 0.05$, versus control). Both compounds induced reduction in human EEC proliferation ($P < 0.05$ versus basal) and increased apoptosis ($P < 0.05$ versus basal) in primary cultures.

LIMITATIONS: In vitro studies were only carried out in epithelial cells from human eutopic endometrium.

WIDER IMPLICATIONS OF THE FINDINGS: The present findings are promising and will assist the development of novel natural treatments for endometriosis.

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