

## Analysis of oxidative stress and apoptosis in the ovary of rats treated with soybean isoflavones

R S Simoes (BR) [1], C P Teixeira (BR) [2], G R Sasso (BR) [3], C R Bertoncini (BR) [4], M C Baracat (BR) [5], J M Soares Junior (BR) [6], A A Carbonel (BR) [7]

Introduction: Ovarian aging is characterized by declining follicular reserve and decreased oocyte quality. Ovarian aging culminates in menopause, responsible for a number of disorders and chronic diseases, which seriously affect the quality of life of postmenopausal women. Oxidative stress appears to modulate fertility decline with age, inducing senescence and cellular apoptosis. Thus, antioxidants have been investigated to delay ovarian aging. Soy isoflavones are natural phenolic compounds that bind to estrogen receptors in target tissues, promoting biological activities that include antioxidant properties, relief of menopausal symptoms, inhibition of cell proliferation, and apoptosis. Objectives: To analyze ovarian follicle survival, apoptosis and oxidative stress modulation in the ovary of 3 and 12 month rats treated with soy isoflavones. Methods: Twenty-four Wistar rats divided into 4 groups and treated with soy isoflavone extract daily (150 mg / kg / day) or only with propylene glycol solution by gavage. After 8 weeks, the animals were euthanized and the ovaries removed. The right ovary was processed for morphological study (% of follicles) and evaluated for apoptosis by immunohistochemistry (caspase-3 cleaved and BCL-2). In the left ovary, the levels of reactive oxygen species, total antioxidant capacity and lipid peroxidation were analyzed as a biomarker of oxidative stress. The groups were compared by statistical analysis using the t-Student test (p?0.05). Results: In the histomorphometric analysis, a significant decrease was observed in the percentage of atresic follicles only in the 12-month rats that received isoflavones. There was also a significant decrease in the number of caspase-3 positive cells in the 3 and 12 month animals submitted to the isoflavones, whereas the BCL-2 immunopositivity was significantly increased only in the 12-month rats. Isoflavone treatment also promoted a significant increase in total antioxidant capacity, as well as a significant reduction in the levels of reactive oxygen species and lipid peroxidation in rats of 3 and 12 months. Conclusion: Soy isoflavones do not appear to interfere with follicular development but appear to reduce apoptosis and oxidative stress in ovarian cells.

GYNECOLOGICAL ENDOCRINOLOGY

<sup>[1]</sup> Medicine Faculty of University of Sao Paulo – FMUSP, Sao Paulo, Brazil, [2] Federal University of São Paulo, [3] Federal University of São Paulo, [3] Federal University of São Paulo, [4] Department of Gynecology, Paulista School of Medicine/Federal University of Sao Paulo – EPM/UNIFESP, Sao Paulo, [5] Medicine Faculty of University of Sao Paulo – FMUSP, Sao Paulo, Brazil, [6] Medicine Faculty of University of Sao Paulo – FMUSP, Sao Paulo, Brazil, [6] Medicine Faculty of University of Sao Paulo – FMUSP, Sao Paulo, Brazil, [7] Federal University of São Paulo