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GENERAL GYNECOLOGY

Evaluation of the frequency of G-765C polymorphism in the promoter region of the *COX-2* gene and its correlation with the expression of this gene in the endometrium of women with endometriosis

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Abstract

Objective To evaluate the frequency of polymorphism G-765C (rs20417) of the *COX-2* gene and the expression of this gene in the endometrium of women with endometriosis.

Study design This is a case–control study of 365 women with endometriosis (251 infertile and 114 fertile) submitted to laparoscopy/laparotomy with histological confirmation of endometriosis. The control group was composed of 522 fertile women without endometriosis. Of these, 37 patients from the endometriosis group and 47 from the control group were submitted to biopsy of the endometrium for analysis of the expression of the *COX-2* gene. The genotypes were determined using analysis by High-Resolution Melt. Gene expression was measured by qRT-PCR with TaqMan methodology using the GAPDH gene as normalizer of the reactions.

Results The distribution of the genotypes and alleles in the group of fertile women with moderate/severe endometriosis showed a statistically significant difference, demonstrating association of the ancestral allele, −765G, with increased risk of endometriosis ($p = 0.028$; OR 0.53; CI 0.32–0.90). The mean expression of the *COX-2* gene (mRNA PTGS2) in the group of women with endometriosis was statistically higher compared to the control group (3.85 versus 2.84, $p = 0.028$).

Conclusion The present study identified that in Brazilian women the presence of the ancestral allele, −765G, of the *COX-2* gene is associated with an increased risk for development of moderate/severe endometriosis associated with fertility, and that the eutopic endometrium of women with endometriosis showed increased expression of *COX-2* when compared to the control group.

Keywords Endometriosis · Infertility · Polymorphism · Gene expression · *COX-2* gene

Introduction

Endometriosis is a chronic inflammation that represents one of the most common benign gynecological diseases. It is a steroid-dependent condition in which tissue histologically similar to the endometrium with glands and stroma grows outside the uterine cavity by implanting itself in other tissues and organs such as Fallopian tubes, ovaries, peritoneum, colon, rectovaginal region, and bladder, causing dysmenorrhea, pelvic pain, and infertility. It affects between 3 and 10 % of women in their reproductive phase and 20–50 % show alterations in fertility [1–3].

Despite the high prevalence of endometriosis, the exact mechanisms of its pathogenesis in causing infertility are varied. But it is known that there is a multifactorial mechanism involving anatomy, immunology, genetics, and environmental factors [4–6].

The COX-2 enzyme, also known as prostaglandin synthetase-2 (PTGS2), was isolated in 1976 and is the key in prostaglandin biosynthesis, starting from Arachidonic Acid. There are two classes of prostaglandins: COX-1 that is constitutive and is involved in the production of prostaglandins for cell maintenance functions, and the mitogen-inducible COX-2, associated with biological events such as lesion, inflammation, and proliferation. COX-2 is not

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