

CYP2C19 polymorphism increases the risk of endometriosis

Denise Maria Christofolini · Aline Amaro ·
Fernanda Mafra · Amanda Sonnewend · Bianca Bianco ·
Caio Parente Barbosa

Received: 14 July 2014 / Accepted: 23 September 2014 / Published online: 18 November 2014
© Springer Science+Business Media New York 2014

Abstract

Purpose Estrogen metabolizing gene mutations can be associated with defective hormonal signaling leading to disease processes. Endometriosis is an estrogen dependent that can be influenced by defective signaling in the estrogen pathway.

Objectives To evaluate the association of A/G 85952 *CYP2C19* and A/G 937 *HSD17B1* gene polymorphisms with endometriosis through the investigation of a large Brazilian sample of women with endometriosis and a fertile control group.

Methods Five hundred women with endometriosis and 500 women without endometriosis were tested for *CYP2C19* and

Capsule In a case-control study comprising 500 women with endometriosis and 500 women without the disease we were able to demonstrate a statistically difference considering genotype and allelic frequency of *CYP2C19* polymorphism (rs11592737). Comparing endometriosis cases classified as stages I/II and III/IV with control group for the *CYP2C19* we observed that the polymorphism is more frequent in the cases with stages I/II. Regarding *HSD17B1* polymorphism no association was also found. We concluded that *CYP2C19* polymorphism is associated to endometriosis in Brazilian women and can be considered a potential biomarker of the disease.

D. M. Christofolini (✉)

Instituto Ideia Fertil de Saúde Reprodutiva, Morphology Department, FMABC, Avenida Príncipe de Gales, 821, Ed. CEPES, 2o. floor, room 101, Santo André, SP, Brazil
e-mail: denise.christofolini@fmabc.br

A. Amaro · F. Mafra · A. Sonnewend · B. Bianco · C. P. Barbosa
Instituto Ideia Fertil de Saúde Reprodutiva, Collective Health Department, FMABC, Avenida Príncipe de Gales, 821, Ed. CEPES, 2o. floor, room 101, Santo André, SP, Brazil

A. Amaro
e-mail: aline.amaro.santos@hotmail.com

F. Mafra
e-mail: mafra.fe@gmail.com

A. Sonnewend
e-mail: amandasonnewend@gmail.com

B. Bianco
e-mail: bianca.bianco@hotmail.com

C. P. Barbosa
e-mail: caiopb@uol.com.br

HSD17B1 polymorphisms, by *TaqMan* Real Time PCR. The results were statistically analyzed by chi-square, logistic regression and tested for Hardy-Weinberg equilibrium.

Results The comparison of genotype and allelic frequency of *CYP2C19* polymorphism (rs11592737) in patients with endometriosis and control group showed a statistically significant difference ($p=0.0203$) and for the *HSD17B1* polymorphism (rs605059) differences were not significant ($p=0.0687$). Comparing the stages I/II and III/IV endometriosis with the control group for the *CYP2C19* we observed $p=0.0133$ and $p=0.0564$, respectively, and for *HSD17B1* the values for $p=0.4319$ and $p=0.0667$.

Conclusion We observed that *CYP2C19* polymorphism is associated with endometrisis in Brazilian women and can be considered a potential biomarker of the disease.

Keywords Endometriosis · *CYP2C19* · *HSD17B1* · Infertility · Molecular biomarker

Introduction

Endometriosis is a steroid-dependent condition recognized as the most common cause of female infertility [1, 2]. The disease is defined by the presence of endometrial glands and/or stroma outside the uterine cavity.

The estrogen-dependent growth of endometrial tissue is mediated by aromatase, that is the key of local estrogenic biosynthesis, promoting the conversion of androstenedione to estrone and from testosterone to estradiol [3].

Genetic polymorphisms in genes associated to the estrogen synthesis pathway, as receptors and metabolizing enzymes of the hormone have been associated to interindividual variation in the levels of circulating estrogen [4].

CYP2C19 is an important gene of cytochrome p450 family and encodes an aromatase associated by the estrogen metabolism, including the conversion of estradiol in estrone and the