Modulatory effect of Metformin on AMPK/Sirt1/PGC-1α/Sirt3 pathway in the heart of mouse model of endometriosis

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Introduction
Endometriosis is a gynecological disease defined by the presence of endometrial tissue outside its normal location, also associated with an increased risk of cardiovascular events.1 An imbalance in antioxidant defenses in the serum and organs of women with endometriosis has been reported.2 Metformin is a widely used antidiabetic drug with anti-oxidative properties that have positive effects on endometriotic tissue.3 As such, by mimicking energy restriction, metformin could have a role in the prevention of cardiovascular events, by modulating oxidative stress defenses, in particular the AMPK/Sirt1/PGC-1α/Sirt3 pathway.

Objective: To investigate alterations in the AMPK/Sirt1/PGC-1α/Sirt3 pathway involved in oxidative stress response in the heart of a mouse model of endometriosis.

Methods
36 female B6CBA/F1 mice were divided into 4 groups: Control (C; sham-operated), surgically induced endometriosis treated with orally administered 50mg/kg/day Metformin for 3 months (EM), Endometriosis (E) and Metformin (M). Levels of pAMPK, AMPK, Sirt1, PGC-1α, Sirt3, SOD2 and GPX1, were assessed in heart tissue by Western Blotting.

Results

Discussion
All proteins were detected in all experimental groups. An increase in pAMPK in the EM group (compared to C) was found. A parallel trend was seen for total AMPK, but not for pAMPK/AMPK, partly due to the similar increases in both total and phosphorylated AMPK. However, the increase in enzyme expression is congruent with a response to oxidative stress.

No differences among groups in expression of Sirt1, PGC-1α, Sirt3 and SOD2 were observed. However, GPx1 expression was increased in EM (compared to C). An increasing trend was observed in EM group relatively to M and E groups, suggesting that metformin’s effect in GPX1 expression is higher in endometriosis individuals than in controls.

Further studies are required to fully understand the role of oxidative stress in endometriosis– associated cardiovascular disease and to identify new therapeutic agents for its control.