23157 | Metformin treatment decreases placenta fibrosis in a murine model of surgically-induced endometriosis

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Endometriosis is a chronic inflammatory disease defined by ectopic endometrial-like tissue growing outside the uterus, causing fibrotic adhesions and constrictions. Dysmenorrhea and infertility are common manifestations of the disease. Endometriosis yet unclear pathophysiology limits treatment options, and its impact on placental function and pregnancy outcomes remains uncertain. This study examined whether metformin, a pregnancy-safe drug with anti-inflammatory and antioxidant properties, affects placental fibrosis (consequence of chronic inflammation) in mice with surgically-induced endometriosis. In this study, B6CBA/F1 mice (n=32) were divided into four experimental groups: Sham (S), Metformin (M) (50 mg/ml diluted in drinking water), Endometriosis (E), and Metformin/Endometriosis (ME). Placental tissues were stained with Hematoxylin-Eosin to analyze the decidua, junctional zone, labyrinth, myometrium, and chorionic plate. Fibrosis was quantified in sections after Picrosirius-Red staining, through morphometric analysis using Image-Pro Plus 6 software. The one-way ANOVA test was then performed to evaluate statistical differences. The morphometric analysis revealed that placenta sections from Endometriosis-mice exhibited the most extensive fibrosis area (37,78%) that significantly decreases with metformin treatment; Metformin/Endometriosis mice present 17.8% of fibrotic tissue ($p=0.0006$). Notably, the fibrosis area of Metformin/Endometriosis mice is equivalent to that found in the Sham group (22.26%;$p=0.0226$). Metformin-group showed the lowest level (12.92%;$p<0.0001$). Quantitative analysis showed increased placental fibrosis in endometriosis, which metformin alleviated to levels similar to healthy mice. These findings suggest metformin as a potential therapy to improve pregnancy outcomes in endometriosis, corroborating previous findings of the group.

Keywords: Endometriosis, metformin, mice model, placenta.

References:

[1] Martins et al. Biomedicines. 2022;10(11):2782.

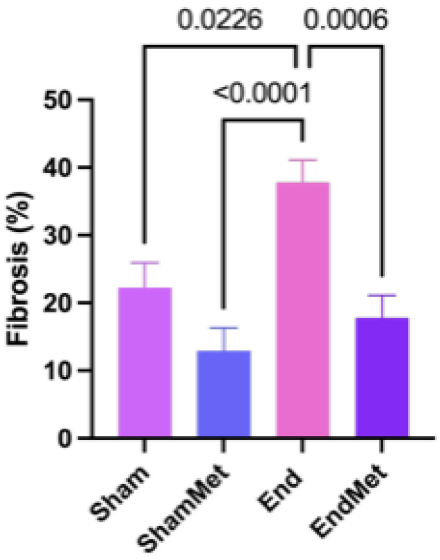

Figure 1: Fibrosis levels.