Metformin effect in ectopic endometrium histological features in a mice-model of endometriosis

Botelho M, Rodrigues AR, Gouveia AM, Almeida H, Neves D, Neto AC.

Department of Biomedicine - Experimental Biology Unit, Faculty of Medicine of the University of Porto, 4200-319 Porto, Portugal
Instituto de Investigação e Inovação em Saúde (i3S), 4200-135 Porto, Portugal

Introduction
Endometriosis is a gynecological inflammatory disease and one of the major causes of infertility.\(^1,2\) It is characterized by ectopic vascularized endometrial tissue growth mainly in the pelvic cavity, which provokes pain and infertility.

Metformin is widely used for diabetes type-2 treatment, reducing glucose, oxidative stress and inflammation. It also induces regression of endometrial implants in an endometriosis rat model.

Aim: characterize the ectopic endometrium tissue on a mouse-model of endometriosis treated with metformin

Methods
In 4 groups of B6CBA/F1 mice: S–sham; M–metformin (50mg/Kg/day/3months); E–endometriosis; EM–endometriosis with metformin, histological characterization of ectopic endometriosis was carried out by hematoxylin and eosin (H&E), Masson’s trichrome stain (TM), and immunolabelling of proliferating cell nuclear antigen (PCNA) and 17α-hydroxylase (CYP17a) proteins, markers of cell proliferation and estrogen secretion, respectively.

Results

![Images of histological sections comparing different groups](image1)

Figure 1. Histological similarities were observed between the ectopic tissue and uterus. It is possible to observe that the ectopic endometrium layer is thinner in the EM group compared with the E group. In untreated animals, the cavity of ectopic tissue has more flaking cells (black arrow) than in animals with metformin treatment. Images 10x.

![Images of immunolabelling](image2)

Figure 2. PCNA and CYP17A1 labeling was present in the same cells of eutopic and ectopic endometrium, with an apparent lower frequency in the ectopic tissue in the EM group. PCNA and CYP17A1 are green marked, and DNA in the nucleus is blue marked.

Conclusions
In sum, metformin seems to have a positive role in the control of cell proliferation and estrogen production of ectopic endometrium, but more results are needed to elucidate the effect of metformin in endometriosis-associated infertility.

References