

Effect of palmitoylethanolamide in endometriosis in rats: histological evidence

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Endometriosis (EMS) is a chronic inflammatory disease that occurs when tissue resembling endometrium (i.e. glandular and stromal elements) grows in other places outside the uterine cavity, such as the fallopian tubes, ovaries or along the pelvis. Symptoms of endometriosis include dysmenorrhoea, dyspareunia, abdominal pain and infertility. Several reports demonstrate that high numbers of activated mast cells are present in EMS sites contributing to the development of endometriotic lesions (D'Cruz et al., 2007).

It is well known that palmitoylethanolamide (PEA) and its derivatives negatively modulate the inflammatory process by inhibiting mast cells activation (De Filippis et al., 2013).

The aim of the present study was to investigate the effect of PEA in a rat model of EMS. Experimental endometriosis was induced in female rats by autotransplantation of small pieces of uterus on arteries of mesenteric plexus, ovary, and abdominal wall; endometrial autografts produced fluid-filled cysts. The animals were treated with PEA (10mg/kg *per os*) or vehicle (carboxymethylcellulose) for 26 days. After this time, the cysts were removed and processed for histological analysis. Our results demonstrated that PEA reduced the dimension of cysts without affecting their number, as compared to vehicle-treated animals; this effect correlated, at least in part, with a reduction of mast cells activation. In fact histological analysis of cysts stained with toluidine blue (which allows us to discriminate between degranulated-light blue and not degranulating-deep blue mast cells), demonstrated that only the number of mast cells was reduced in tissues obtained from PEA-treated rats compared with tissues from vehicle-treated rats, while we did not observe any variation in mast cells degranulation in both tissues.

Furthermore, chronic PEA administration reduced angiogenesis as calculated by counting the number of blood vessel in endometriotic cysts, as compared to vehicle-treated animals.

In conclusion our study suggests that PEA administration is useful for treating endometriosis thanks to its ability to modulate mast cells behaviour and the release of their stored mediators.

D'Cruz et al., (2007) *Am J Reprod Immunol*; 58:75–97

De Filippis et al. (2013) *CNS Neurol Disord Drug Targets*. 12(1):78-83.