Influence of angiogenic agents (cabergoline) on rat-induced endometriosis

Autors: Giovana da Gama Fortunato, Julio Cesar Silva e Rosa, Juliana Meola Lovato

Institution: Federal University of Mato Grosso, College Medicine de Ribeirão Preto- São Paulo University, Brasil

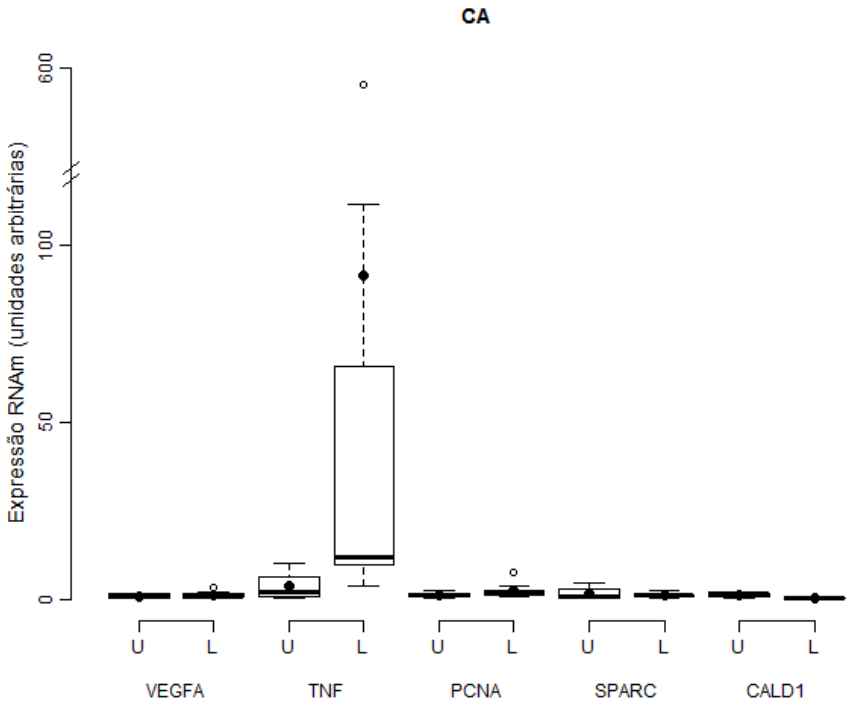
Contact: gife@terra.com.br

Introduction : Endometriosis is a benign gynecological disease , estrogen - dependent , which affects 10-15 % of women of reproductive age. Its pathogenesis can not be understood by only a theory , and there are several hypotheses that seek to elucidate it . The presence of endometrial epithelial cells with dhesion characteristics, deployment, growth and angiogenesis, peritoneal fluid associated with obstructed menstrual flow and endometriosis corroborate that this is the most accepted theory. Recently it was proposed that angiogenesis is an important step in this process, since, similar to metastatic tumors, endometrial implants depend on neovascularization for their, implantation, invasion and expression. This finding suggests that suppression of blood vessel development through inhibition of specific angiogenic factors may be a new therapeutic opportunity in endometriosis approach. **Objectives:** To evaluate the antiangiogenic effect of two doses of cabergoline on lesions induced endometriosis in rats. To this end, we studied the effect of this drug on markers of differentiation, invasion, cell proliferation and apoptosis and also genes such as VEGF, CALD1 PCNA, TNF and SPARC, that are involved in adhesion, motility and angiogenesis of endometriotic lesions through the extraction of total RNA, cDNA synthesis, and quantification by real time PCR.

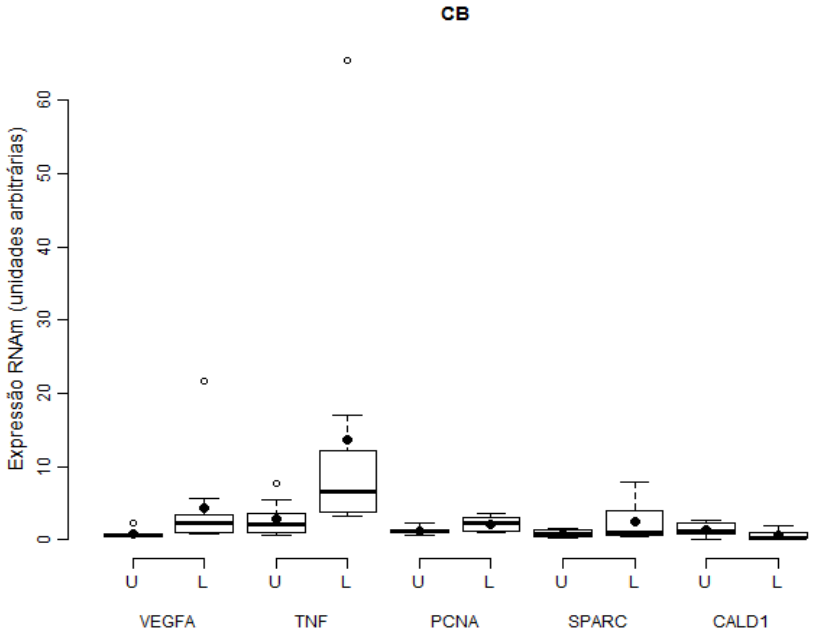
Materials and Methods: This experimental animal study 30 adult rats New Zealand, virgin females and undergoing laparotomy for injury induction of endometriosis being used by resection of a uterine horn and fixation of the pelvic peritoneum 5mm fragment. The rats were divided into three groups of 10 animals, and the animals of group 1 (control = 10) were sacrificed after 4 weeks of induction of ectopic endometrial lesions and the two lower dose groups (n = 10) and the high (n =

10) of cabergoline sacrificed after 14 days of treatment. The lesion was excised for histological analysis along with the uterine horn contralateral, proving the presence of endometrial glandular and stromal tissue. Reactions immunohistochemical markers of differentiation, invasion, cell proliferation and apoptosis and molecular biology were performed in eutopic and ectopic endometrial tissue through the genes *VEGF A, CALD1*, *PCNA, TNF and SPARC*, which are involved in adhesion, motility and angiogenesis of lesions of endometriosis.

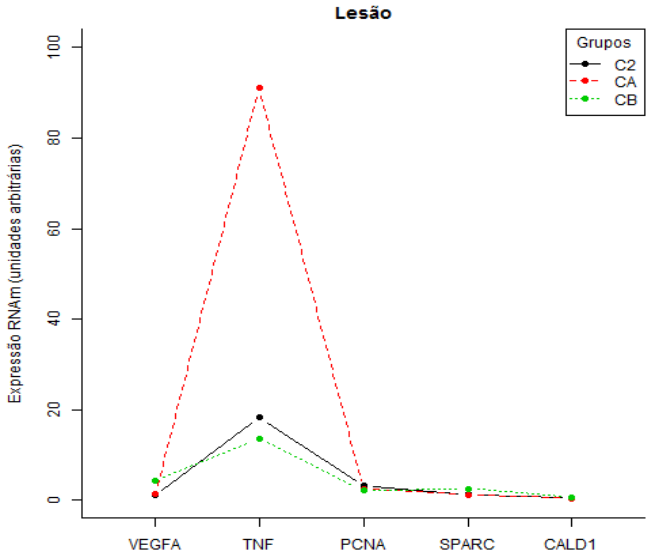
Results: Immunohistochemical study we found no differences between the study groups compared with the control, however when comparing each group of injury and uterus separately with each gene, we can detect results of statistical significance in gene expression, particularly those associated with angiogenesis and better therapeutic response in the high dose group.



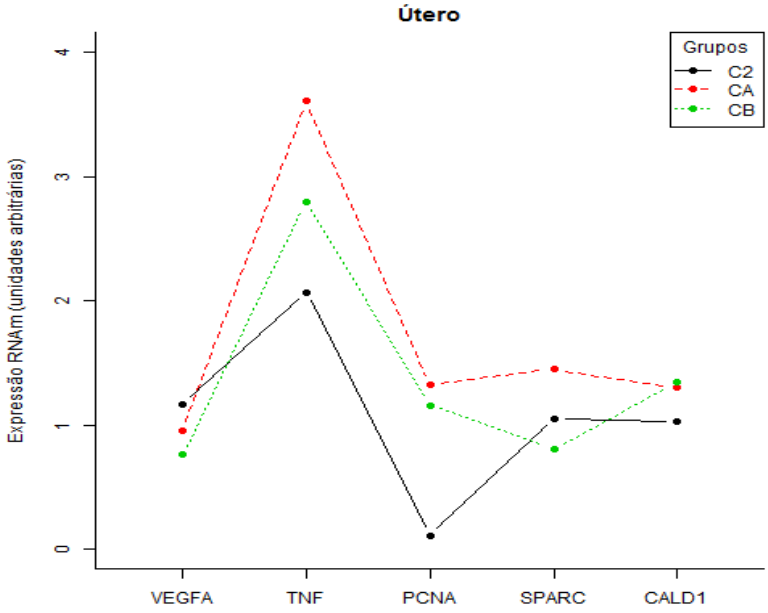
Expressão relativa de RNAm de cada gene alvo estudado no tecido útero (U) e lesão (L) do grupo CA. * p<0,05.



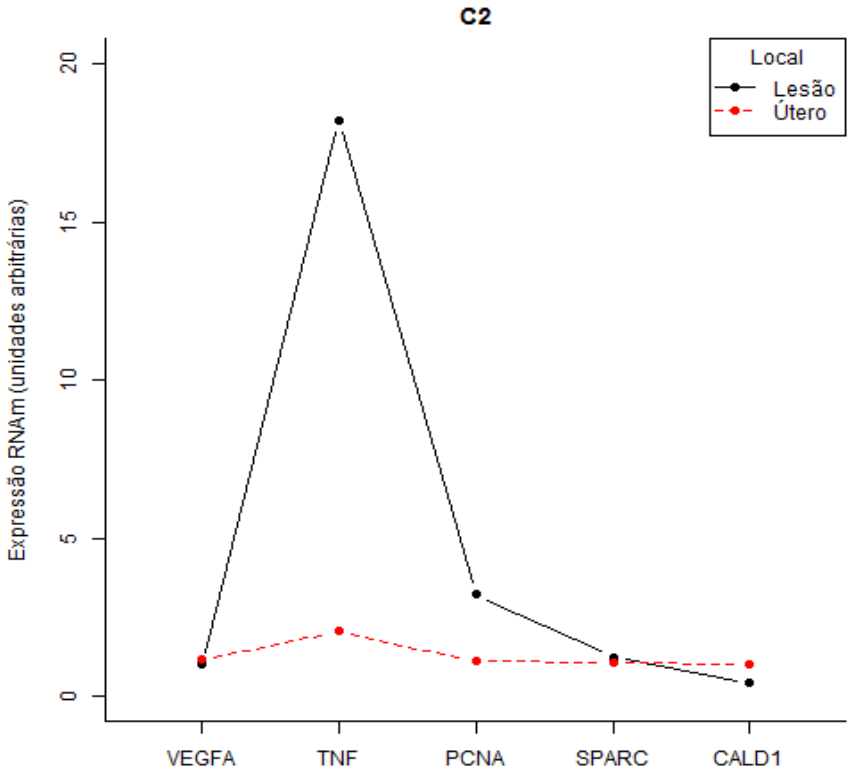
Expressão relativa de RNAm de cada gene alvo estudado no tecido útero (U) e lesão (L) do grupo CB. * p< 0,05.



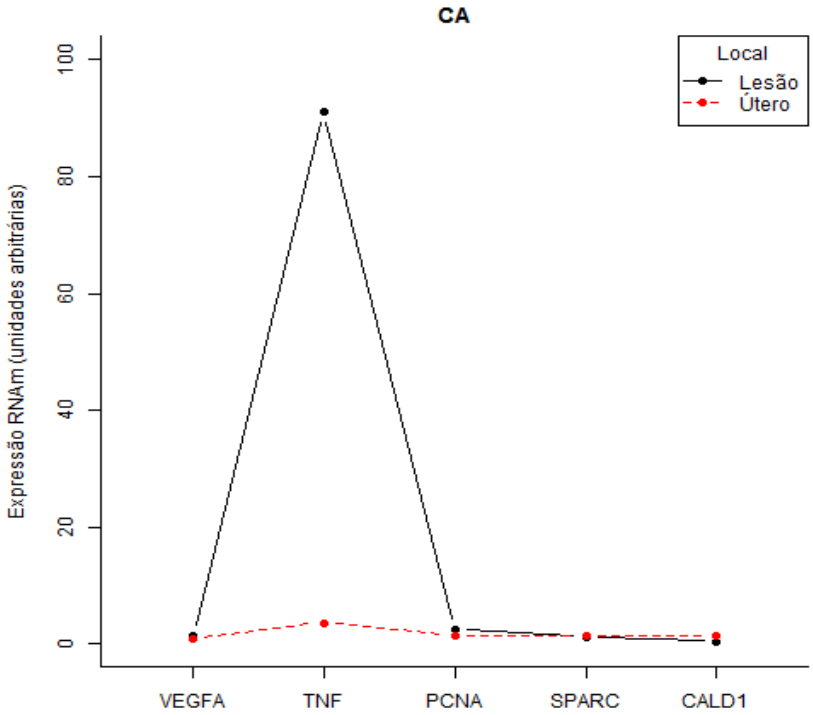
Expressão gênica de todos genes e os grupo s do tecido lesão



Expressão gênica de todos genes e os grupos do tecido útero



Expressão gênica de todos genes e os grupo controle do tecido útero e lesão



Expressão gênica de todos genes e os grupo alta dose do tecido útero e lesão

Conclusion: Treatment with antiangiogenic drugs offers new prospects for therapeutic approach for patients with endometriosis.

Keywords: experimental endometriosis, cell proliferation, apoptosis, angiogenesis, cabergoline, rats

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