

论著

### GnRH II与GnRH I对子宫内膜异位症患者间质细胞分泌VEGF作用的比较

黄凤英<sup>1</sup>, 刘秋红<sup>2</sup>, 王焕萍<sup>1</sup>, 邹颖<sup>1</sup>

1.中南大学湘雅二医院妇产科, 长沙 410011; 2.湖南省人民医院妇产科, 长沙 410003

摘要:

目的: 测定GnRH II与GnRH I对子宫内膜异位症(EMs)患者离体培养子宫内膜间质细胞分泌血管内皮生长因子(VEGF)的影响, 探讨GnRH II对EMs患者可能的作用。方法: 给予原代培养的EMs患者在位及异位子宫内膜间质细胞不同浓度的GnRH II, GnRH I类似物(戈舍瑞林, goserelin)处理, 同时设对照组(不加GnRH), 采用酶联免疫吸附法(ELISA)测定培养液中VEGF浓度, 并进行比较。结果: EMs患者离体培养的异位子宫内膜间质细胞经48 h培养, 能分泌VEGF, 分泌量与在位子宫内膜间质细胞的相近, 两者比较差异无统计学意义( $P>0.05$ )。不同浓度的GnRH II对EMs患者离体培养的在位和异位子宫内膜间质细胞VEGF的分泌有明显的抑制作用, 呈剂量依赖性( $P<0.05$ ), 且较GnRH I类似物(戈舍瑞林)的作用更强( $P<0.05$ )。不同浓度的GnRH II对EMs患者离体培养的异位子宫内膜间质细胞VEGF分泌的抑制作用明显强于在位( $P<0.05$ )。结论: EMs患者的异位子宫内膜间质细胞具有分泌VEGF的功能, 分泌量与在位子宫内膜的相近, 这对EMs的形成和发展可能起重要作用。GnRH II呈剂量依赖性地抑制异位内膜间质细胞分泌VEGF, 其抑制作用明显强于在位, 且GnRH II明显强于GnRH I, 为寻找EMs抗血管形成方面的新药治疗提供了新的依据。

关键词: 子宫内膜异位症 II型促性腺激素释放激素 I型促性腺激素释放激素激动剂 血管内皮生长因子 内膜间质细胞

### Effect of GnRH II and GnRH I on secretion of VEGF by eutopic and ectopic endometrial stromal cells of endometriosis patients

HUANG Fengying<sup>1</sup>, LIU Qihong<sup>2</sup>, WANG Huanping<sup>1</sup>, ZOU Ying<sup>1</sup>

1.Department of Obstetrics and Gynecology, Second Xiangya Hospital, Central South University, Changsha 410011;  
2. Department of Obstetrics and Gynecology, People's Hospital of Hunan Province, Changsha 410003, China

Abstract:

Objective To determine the effect of GnRH I and GnRH II on the secretion of VEGF by eutopic and ectopic endometrial stromal cells cultured in vitro, and to provide theoretical basis for exploring new treatments for endometriosis (EMs). Methods Eutopic and ectopic endometrium stromal cells cultured in vitro were treated with different concentrations of GnRH II and a GnRH I (goserelin), and a control group was not treated by GnRH II and GnRH I. Enzyme linked immunosorbent assay (ELISA) was used to measure the content of vascular endothelial growth factor (VEGF) protein in the medium of the above 2 groups. Results (1) There was no difference in the VEGF protein secreted by eutopic and ectopic stromal cells in the medium after being cultured in vitro for 48 h ( $P>0.05$ ). (2) 10<sup>-10</sup>, 10<sup>-8</sup>, and 10<sup>-6</sup> mol/L GnRH II dose dependently reduced VEGF protein secreted by endometrial stromal cells ( $P<0.05$ ), and the inhibition effect was stronger than that of GnRH I ( $P<0.05$ ). (3) The inhibition effect of GnRH II on VEGF in ectopic stromal cells was stronger than that of eutopic stromal cells ( $P<0.05$ ). Conclusion (1) Ectopic stromal cells cultured in vitro can secrete VEGF, which has no difference from the eutopic stromal cells, and which may play an important role in the formation and development of EMs. (2) GnRH II can dose dependently reduce VEGF protein secreted by ectopic and eutopic endometrial stromal cells cultured in vitro, and the inhibition effect is stronger than that of GnRH I, providing theoretical basis for exploring new treatments for EMs.

Keywords: endometriosis; gonadotropin releasing hormone II (GnRH II); GnRH Ia (goserelin); vascular endothelial growth factor (VEGF); endometrial stromal cell

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参考文献:

- [1] 丰有吉, 沈铿. 妇产科学 [M]. 北京: 人民卫生出版社, 2008:357 365.
- FENG Youji, SHEN Keng. Obstetrics and Gynecology [M]. Beijing: People Health Press, 2008:357 365.
- [2] Enomoto M, Endo D, Kawashima S, et al. Human type II GnRH receptor mediates effects of GnRH on cell proliferation [J]. Zool Sci, 2004,21(7): 763 770.
- [3] Grundker C, Gunthert A R, Millar R P, et al. Expression of gonadotropin releasing hormone II (GnRH II) receptor in human endometrial and ovarian cancer cells and effects of GnRH II on tumor cell proliferation [J]. J Clin Endocrinol Metab, 2002,87(3):1427 1430.
- [4] Wang A F, Li J H, Maiti K, et al. Preferential ligand selectivity of the monkey type II gonadotropin releasing hormone(GnRH) receptor for GnRH 2 and its analogs [J]. Mol Cell Endocrinol, 2003,209(1/2): 33 42.
- [5] 韩利伟, 姜卫国. GnRHa对子宫内异位症内膜间质细胞生长增殖及血管形成的影响 [J]. 现代妇产科进展, 2008, 17(10):737 739.
- HAN Liwei, JIANG Weiguo. The effect of GnRHa on endometrial stromal cell proliferation and angiogenesis in endometriosis [J]. Progress in Obstetrics and Gynecology, 2008, 17(10):737 739.
- [6] 陈建林, 林秋华, 方小玲, 等. 孕酮对异位子宫内间质细胞MMP 2和MMP 9表达的影响 [J]. 中南大学学报: 医学版, 2005, 30 (3): 307 311.
- CHEN Jianlin, LIN Qiuhua, FANG Xiaoling, et al. The effect of Progesterone on the ectopic endometrial stromal cells in expression of MMP 2 and MMP 9 [J]. Journal of Central South University. Medical Science, 2005, 30 (3):307 311.
- [7] Morimoto C, Osuga Y, Yano T, et al. GnRH II as a possible cytostatic regulator in the development of endometriosis [J]. Hum Reprod, 2005, 20(11):3212 3218.
- [8] 方小玲, 夏晓梦, 林秋华. 子宫内异位症患者腹腔液和在位子宫内皮细胞因子表达的研究 [J]. 湖南医科大学学报, 2003, 28 (3): 288 290.
- FANG Xiaoling, XIA Xiaomeng, LIN Qiuhua. The expression of vascular endothelial growth factor in peritoneal fluid and eutopic endometrial in patients with endometriosis [J]. Bulletin of Hunan Medical University, 2003, 28 (3):288 290.
- [9] 吴献青, 方小玲, 林秋华, 等. 腹腔液中巨噬细胞产生血管内皮细胞生长因子及其受体的表达 [J]. 细胞与分子免疫学杂志, 2003, 19(5):462 465.
- WU Xianqing, FANG Xiaoling, LIN Qiuhua, et al. The expression of vascular endothelial growth factor and its receptor in peritoneal fluid macrophages [J]. Journal of Cellular and Molecular Immunology, 2003, 19 (5):462 465.
- [10] 吴献青, 林秋华, 陶光实, 等. 异种血管内皮细胞疫苗治疗Lewis大鼠子宫内异位症的动物模型 [J]. 中南大学学报: 医学版, 2004, 29(1):39 43.
- WU Xianqing, LIN Qiuhua, TAO Guangshi, et al. The study of heterogeneous vascular endothelial cell vaccine for treating endometriosis Lewis rat animal model [J]. Journal of Central South University. Medical Science, 2004, 29 (1):39 43.
- [11] 杨梅, 曲银娥, 王毅峰. 血管内皮生长因子在子宫内异位症中的表达 [J]. 中国煤炭工业医学杂志, 2007, 10 (6): 646 647.
- YANG Mei, QU Yine, WANG Yifeng. The expression of vascular endothelial growth factor in endometriosis [J]. Journal of China Coal Industry Medicine, 2007, 10 (6):646 647.
- [12] Eun H S, Young L J, Hye Sung M, et al. Angiopoietin 1, angiopoietin 2 and Tie 2 expression in eutopic endometrium in advanced endometriosis [J]. Molecular Human Reproduction, 2006, 12(7):421 426.
- [13] Millar R P. GnRH II and type II GnRH receptors [J]. Trends Endocrinol Metab, 2003, 14 (1):35 43.
- [14] Cheon K W, Lee H S, Parhar I S, et al. Expression of the second isoform of gonadotrophin releasing hormone (GnRH II) in human endometrium throughout the menstrual cycle [J]. Mol Hum Reprod, 2001, 7(5):447 452.
- [15] Borroni R, Di Blasio A M, Gaffuri B, et al. Expression of GnRH receptor gene in human ectopic endometrial cells and inhibition of their proliferation by leuprolide acetate [J]. Mol Cell Endocrinol, 2000, 159 (1/2): 37 43.
- [16] Imai A, Takagi A, Tamaya T. Gonadotropin releasing hormone analog repairs reduced endometrial cell apoptosis in endometriosis in vitro [J]. Am J Obstet Gynecol, 2000, 182 (5): 1142 1146.
- [17] Kupker W, Schultze Mosgau A, Diedrich K. Paracrine changes in the peritoneal environment of women with endometriosis [J]. Hum Reprod Update, 1998, 4 (5): 719 723.
- [18] Meresman G F, Bilotas M A, Lombardi E, et al. Effect of GnRH analogues on apoptosis and release of interleukin 1beta and vascular endothelial growth factor in endometrial cell cultures from patients with endometriosis [J]. Hum Reprod, 2003, 18(9):1767 1771.

1. 黄凤英; 林秋华; 方小玲; 张志胜; 王新; .Bcl-2和Bax蛋白在子宫内膜异位症的表达[J]. 中南大学学报(医学版), 2003,28(2): 102-
2. 刘秋红, 黄凤英, 王焕萍, 邹颖.GnRH- II对子宫内膜异位症患者离体培养的子宫内膜间质细胞分泌VEGF的影响[J]. 中南大学学报(医学版), 2009,34(09): 926-932
3. 罗敏<sup>1</sup>,申东翔<sup>1</sup>,张宏斌<sup>1</sup>, 王捷<sup>1</sup>,宗利丽<sup>2</sup>,关婷<sup>1</sup>,何援利<sup>2</sup>.肿瘤坏死因子- $\beta$ 基因多态性对子宫内膜异位症患者血清中TNF浓度的影响[J]. 中南大学学报(医学版), 2007,32(04): 656-659
4. 龚斐, 唐奕, 张红, 卢光琇.

[EN]改良超长降调节方案改善不孕患者体外受精-胚胎移植的结局

[J]. 中南大学学报(医学版), 2009,34(03): 185-189

5. 方小玲; 夏晓梦; 林秋华; .子宫内膜异位症患者腹腔液和在位子宫内膜血管内皮生长因子表达的研究[J]. 中南大学学报(医学版), 2003,28(3): 288-
6. 范红\*, 方小玲 .环氧合酶-2在子宫内膜异位症子宫内膜组织中的表达[J]. 中南大学学报(医学版), 0,(): 92-95
7. 范红\*, 方小玲 .环氧合酶-2在子宫内膜异位症子宫内膜组织中的表达[J]. 中南大学学报(医学版), 2005,30(1): 92-95
8. 罗敏, 何援利\*, 彭冬先, 刘木彪, 陈燕英 .子宫内膜异位症患者血清TNF- $\alpha$ 和TNF- $\beta$ 的测定[J]. 中南大学学报(医学版), 2005,30(3): 304-306
9. 陈建林, 林秋华\*, 方小玲, 陶光实, 黄凤英 .孕酮对异位子宫内膜间质细胞MMP-2和MMP-9表达的影响[J]. 中南大学学报(医学版), 2005,30(3): 307-311
10. 魏晓强<sup>1</sup>,张怡<sup>1</sup>\*,唐猛<sup>2</sup>,彭丽秀<sup>1</sup>.子宫内膜异位症性不孕与瘦素的关系[J]. 中南大学学报(医学版), 2005,30(4): 487-488
11. 曾飞\*,薛敏.芳香化酶细胞色素P450及CA125联合检测对子宫内膜异位症的诊断价值[J]. 中南大学学报(医学版), 2005,30(6): 682-685
12. 张怡<sup>1</sup>, 彭丽秀<sup>1</sup>, 孟琳<sup>2</sup> .子宫内膜异位症患者腹腔液及血清IL-18水平测定[J]. 中南大学学报(医学版), 2005,30(6): 731-732
13. 吴献青\*, 林秋华, 陶光实, 方小玲, 黄凤英.异种血管内皮细胞疫苗治疗Lewis大鼠子宫内膜异位症的动物模型[J]. 中南大学学报(医学版), 2004,29(1): 39-43
14. 吴献青\*, 夏晓梦, 方小玲.子宫内膜异位症患者腹腔液中VEGF和Epo的变化及意义[J]. 中南大学学报(医学版), 2004,29(5): 604-605
15. 黄凤英<sup>1</sup>, 王焕萍<sup>2</sup>, 伍媚<sup>1</sup>, 殷团芳<sup>3</sup>.GnRHII与GnRH Ia对子宫内膜异位症患者离体间质细胞增殖抑制的影响[J]. 中南大学学报(医学版), 2011,36(6): 554-