doi: 10.13241/j.cnki.pmb.2019.20.025

地屈孕酮联合醋酸曲普瑞林用于子宫内膜异位症术后的临床效果 *

王 婧 阿孜古丽·阿力木江 吐尔逊古丽·海木都拉 买买提·依斯热依力△ 陆 萍

(新疆维吾尔自治区人民医院妇产科门诊 新疆 维吾尔 830000)

摘要 目的:研究地屈孕酮联合醋酸曲普瑞林用于子宫内膜异位症术后的临床效果。**方法**:选择 2015 年 1 月～2017 年 12 月在我院接受腹腔镜手术治疗的 398 例子宫内膜异位症患者,根据患者入院的顺序编号,采用奇偶数法将其分为两组,每组各 199 例。对照组术后单纯口服地屈孕酮治疗,每次月经后的第 2 d 服用,1 片 / 次,2 次 /d,共服用药 6 个月。观察组术后采用地屈孕酮联合醋酸曲普瑞林治疗,即肌肉注射醋酸曲普瑞林,3.75 mg/ 次,1 次 / 月,共连续给药 6 次。比较两组的疗效、治疗前后血清学指标、痛经、盆腔痛及性交痛程度的变化。**结果**:治疗后,观察组的总有效率明显高于对照组 (*P<0.05*);两组的血清黄体生成激素(Luteinizing hormone,LH)和促卵泡生成素(Follicle-stimulating hormone,FSH)水平均未明显改变(*P>0.05*),而血清雌二醇(Estradiol,E_2)、糖类抗原 125(Carbohydrate antigen,CA125)和血管内皮生长因子(Vascular endothelial growth factor,VEGF)水平均较治疗前明显降低(*P<0.05*),且观察组以上指标均明显低于对照组(*P<0.05*)。两组治疗后痛经、盆腔痛及性交痛积分均较治疗前明显降低(*P<0.05*),且观察组明显低于对照组(*P<0.05*)。**结论**:子宫内膜异位症术后采取地屈孕酮联合醋酸曲普瑞林具有显著的治疗效果,能有效缓解患者的疼痛症状,并改善血清学相关指标,从而有效改善子宫内膜异位症术后的临床效果。

关键词:地屈孕酮;曲普瑞林;子宫内膜异位症;术后;疗效

中图分类号:R711.71 **文献标识码**:A **文章编号**:1673-6273(2019)20-3912-04

Effect of Progesterone Combined with Triptorelin Acetate in the Treatment of Endometriosis after operation*

WANG Jing, A Zi-gu-li·A LI MU JIANG, Tu Er-xun-gu-li·HAI MU DU LA, MAI Mai-ti·YI SI RE NONG LI△, LU Ping

(Gynecology and Obstetrics Department, People's Hospital of Xinjiang Uygur Autonomous Region, Uygur, Xinjiang, 830000, China)

ABSTRACT Objective: To analysis the clinical effect of progesterone combined with triptorelin acetate in the treatment of endometriosis. **Methods:** Selected 398 patients with endometriosis who were treated in our hospital from January 2015 to December 2017 were enrolled in the order of admission. They were divided into two groups according to the odd-even method, each group of 199 cases. The control group was given didrogesterone orally only after operation, one tablet per time, two times per day, for 6 months. The observation group was treated with desdrogesterone combined with triptorelin acetate after operation, i.e. intramuscular injection of triprillin acetate, 3.75 mg/time, once a month, for 6 consecutive times. The curative effect, serological index, dysmenorrhea, pelvic pain and degree of sexual intercourse pain before and after treatment were compared between the two groups. **Results:** After treatment, the total effective rate of the observation group was significantly higher than that of the control group (*P<0.05*). After treatment, the levels of luteinizing hormone (LH) and Follicle-stimulating hormone (FSH) did not change significantly in the two groups (*P>0.05*), while the levels of serum estradiol (E_2), carbohydrate antigen 125 (Carbohydrate antigen, CA125) and vascular endothelial growth factor (VEGF) were significantly lower than those before treatment (*P<0.05*). The scores of dysmenorrhea, pelvic pain and sexual pain in the two groups were significantly lower than those before treatment (*P<0.05*), and the observation group was significantly lower than the control group (*P<0.05*). **Conclusion:** Postoperative treatment of endometriosis with dydrogesterone combined with triptorelin acetate has a significant therapeutic effect, and can effectively alleviate the pain symptoms of patients, improve serum related indicators, and effectively improve endometriosis.

Key words: Progesterone; Triptorelin acetate; Endometriosis; Postoperative; Curative effect

Chinese Library Classification(CLC): R711.71 Document code: A

Article ID:1673-6273(2019)20-3912-04

前言

子宫内膜异位症是指机体具有生长功能的子宫内膜组织出现于子宫腔以外的部位,从而造成该位置产生与子宫内膜周

* 基金项目:新疆维吾尔自治区自然科学基金项目(2018D01C134)

作者简介:王婧(1981-),女,硕士,主治医师,研究方向:子宫内膜异位症,电话:15099555856,Email:wangjing198111@163.com

△ 通讯作者:买买提·依斯热依力(1984-),男,医学博士,医师,研究方向:肥胖代谢综合征,内分泌紊乱,心理压力相关疾病,心肾及胃肠道疾病的临床机制研究,电话:13699381985,E-mail:maimaiti727@sina.com

(收稿日期:2019-05-05 接受日期:2019-05-30)

期相应的临床变化特征，主要表现为月经失调、进行性痛经加重、不孕、慢性盆腔疼痛、性交痛等症状，有 25 %～35 %的不孕妇女患有此病[1-3]。手术虽然是首选的治疗方法，但是尚无法完全清除微小的异位内膜，而且很难消除病因，容易反复发作。术后通过服用性激素类药物可以提高治疗效果，使残留的病灶发生萎缩，减少复发。目前常用的性激素类药物主要有孕激素、短效避孕药及雄激素衍生物等[4-7]。

地屈孕酮可以抑制垂体和下丘脑促性腺激素分泌，进而达到抑制排卵的目的[8,9]；曲普瑞林能与促性腺激素释放激素竞争受体，可使黄体生成激素、促卵泡生成素等激素因敏感性降低而造成受体迅速减少，导致内膜萎缩、坏死。临床上尚未见将地屈孕酮与醋酸曲普瑞林联用的研究报道。鉴于此，本研究将地屈孕酮与醋酸曲普瑞林联合使用，以探讨其在子宫内膜异位症术后的应用效果。

1 资料与方法

1.1 病例资料

选择 2015 年 1 月～2017 年 12 月我院诊治的 398 例子宫内膜异位症患者，纳入标准：符合子宫内膜异位症诊断标准；采取腹腔镜子宫内膜病灶切除手术；近半年内未服用过任何激素类药物；肝、肾、心功肾功能和血脂正常；无本研究药物过敏史，能坚持配合治疗；排除肿瘤和糖尿病等疾病患者。根据患者入院的顺序编号，采用奇偶数法将其分为两组，每组各 199 例。观察组，年龄 25-51 岁，平均(36.74± 5.62)岁；经期 3-8 d，平均(5.73± 0.42)d；月经周期 25-36 d，平均(31.72± 1.34)d。对照组，年龄 25-52 岁，平均(37.18± 4.29)岁；经期 3-8 d，平均(5.64± 0.53)d；月经周期 25-36 d，平均(31.29± 1.48)d。两组基线资料比较差异均无统计学意义(*P>0.05*)，具有可比性。

1.2 治疗方法

对照组术后口服地屈孕酮(生产厂家：荷兰 Abbott Healthcare Products B.V，批号：H20110208)治疗，每次月经后的第 2 d 服用，1 片 / 次，2 次 /d，共服用药 6 个月。观察组在对照组治疗基础上，肌肉注射醋酸曲普瑞林(生产厂家：深圳翰宇药业股份有限公司，国药准字 H20054351)，3.75 mg/ 次，1 次 / 月，共连续给药 6 次。

1.3 观察指标

子宫内膜异位症的疗效评价标准如下：① 显效：患者症状基本消失，B 超检查显示包块已消失；② 有效：患者症状有所缓解，B 超检查显示包块缩小；③ 无效：患者症状和 B 超检查结果均无明显变化。

血清学指标：分别于治疗前和治疗 1 个月后采集 3 mL 肘静脉血，用 ELISA 法检测血清 VEGF 水平；放射免疫法检测 LH、FSH、E_2 水平；化学发光法检测 CA125 水平，试剂盒均购自上海恒远生化试剂有限公司。

疼痛程度：分别于治疗前和治疗 1 个月后采取视觉模拟评分(Visual analogue scale, VAS)法判断痛经、盆腔痛及性交痛程度，评分越高，疼痛越强。

1.4 统计学分析

数据采用 SPSS18.0 进行统计学分析，计量资料用($\bar{x}\pm s$)表示，组间比较行 t 检验；计数资料用%或率表示，组间比较行 x^2 检验，以 *P<0.05* 为差异有统计学意义。

2 结果

2.1 两组疗效对比

治疗后，观察组的总有效率为 96.98 %，明显高于对照组的 81.91 %(*P<0.05*)，见表 1。

表 1 两组疗效的对比[例(%)]

Table 1 Comparison of the clinical effect between the two groups[n(%)]

Groups	n	Effective	Valid	Invalid	The total effect rate
Control group	199	97(48.74)	66(33.17)	36(18.09)	163(81.91)
Observation group	199	113(56.78)	80(40.20)	6(3.01)	193(96.98)*

Note: Compared with the control group, *$P<0.05$.

2.2 两组治疗前后血清学指标对比

治疗后，两组血清 E_2、CA125 和 VEGF 均较治疗前明显降低，且观察组更低(*P<0.05*)，而两组治疗前后 LH 和 FSH 水平比较无显著改变(*P>0.05*)。见表 2。

表 2 两组治疗前后的血清 LH、FSH、E_2、CA125 和 VEGF 水平的对比($\bar{x}\pm s$)

Table 2 Comparison of serum LH, FSH, E_2, CA125 and VEGF levels before and after treatment between the two groups ($\bar{x}\pm s$)

Groups	n		LH(U/L)	FSH(U/L)	E_2(pmol/L)	CA125(U/mL)	VEGF (pmol/mL)
Control group	199	Before treatment	6.69± 1.34	4.77± 1.34	253.49± 14.27	42.76± 6.39	185.34± 16.27
		After treatment	6.57± 1.43	4.75± 1.26	167.48± 12.51#	25.63± 5.42#	129.73± 11.46#
Observation group	199	Before treatment	6.67± 1.28	4.76± 1.38	251.76± 15.42	43.85± 7.14	186.29± 17.38
		After treatment	6.52± 1.49	4.73± 1.24	134.69± 10.38*#	13.49± 3.27*#	96.34± 10.25*#

Note: Compared with the control group, *$P<0.05$; compared with before treatment, #$P<0.05$.

2.3 两组治疗前后疼痛程度对比

治疗后，两组各疼痛 VAS 评分均较治疗前明显降低，且观察组明显更低(*P>0.05*)，见表 3。

表 3 两组治疗前后的痛经、盆腔痛和性交痛评分的对比($\bar{x}\pm s$,分)

Table 3 Comparison of the dysmenorrhea, pelvic pain and sexual intercourse pain scores between the two groups before and after treatment ($\bar{x}\pm s$, scores)

Groups	n		dysmenorrhea	pelvic pain	sexual intercourse pain
Control group	199	Before treatment	4.73± 0.62	4.26± 0.54	5.13± 0.72
		After treatment	2.32± 0.75#	3.17± 0.63#	2.28± 0.83#
Observation group	199	Before treatment	4.71± 0.59	4.23± 0.49	5.11± 0.64
		After treatment	1.49± 0.76*#	1.36± 0.74*#	1.35± 0.92*#

Note: Compared with the control group, *$P<0.05$; compared with before treatment, #$P<0.05$.

3 讨论

子宫内膜异位症是由子宫内膜间质以及腺体生长于宫体肌层和子宫腔被覆面以外,引发出血和浸润,导致包块和结节的形成,从而引起不孕、痛经、盆腔疼痛、性交困难等症状[10-13]。临床对于子宫内膜异位症主要采取手术治疗,但只能去除表面的病灶,可能会遗留病灶,术后在甾体激素的作用下,残存的微小病灶会因此而复发,造成病情反复发作,因此,在手术后必须使用药物辅助治疗[14-17]。

地屈孕酮能促进子宫内膜转变为完全的分泌相,有效预防由雌激素导致的子宫内膜增生以及癌变,且对脂代谢无显著影响,且不引起发热[18-20]。腹腔镜术后肌肉注射醋酸曲普瑞林可以有效降低雌性激素水平,抑制病灶活动和卵巢功能,使残存、微小的以及肉眼难以检测到的病灶得到显著退化或控制,进而有效避免子宫内膜异位症的复发[21-23]。研究显示醋酸曲普瑞林的安全性明显优于其他药物, 分析原因为使用醋酸曲普瑞林时,通过采取 " 反向添加 " 治疗,给予患者合理剂量的孕激素及雌激素,可以有效降低骨质丢失量,减轻疼痛程度,改善围绝经期症状[24,25]。本研究结果显示地屈孕酮联合醋酸曲普瑞林治疗可以显著提高疗效。

CA125 作为监测卵巢上皮癌的指标,分布于卵巢上皮等体腔上皮化生组织的细胞膜表面[26,27]。VEGF 在子宫内膜的增殖过程中,能有助于促进血管的形成[28-30]。子宫内膜异位症的发生机制与雌激素紧密相关,主要表现为雌激素依赖性、侵袭性和复发性,当卵巢分泌的雌激素水平正常时,子宫内膜异位症的病情会随着每次月经来潮而呈现加重的趋势,典型病理特征包括周期性出血、纤维组织粘连以及增生[31-33]。本研究结果表明表明二者联用能更有效地降低子宫内膜异位症术后的血清肿瘤标志物水平,改善血清性激素水平。疼痛是该病最常见的表现,会严重影响患者的日常生活及工作[34]。本研究结果表明地屈孕酮联合醋酸曲普瑞林可以显著缓解性交痛、痛经和盆腔痛程度,可以有效的改善疼痛情况,进一步体现了其临床应用价值。

综上所述,子宫内膜异位症术后采取地屈孕酮联合醋酸曲普瑞林具有显著的治疗效果, 且能有效缓解患者的疼痛症状,并改善血清学相关指标,从而有效的改善子宫内膜异位症术后的临床效果与预后。

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