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桂枝茯苓丸联合妇乐片对子宫内膜异位症的临床疗效*

杨 蕾¹ 黄志兰¹ 敬 源¹ 侯大乔¹ 谢婷婷²

(1 宝鸡市人民医院 妇科 陕西 宝鸡 721000; 2 第四军医大学第一附属医院西京医院 产科 陕西 西安 710032)

摘要 目的:探讨桂枝茯苓丸联合妇乐片对子宫内膜异位症患者血清甲胎蛋白(AFP)、血清脂质结合唾液酸(LSA)及临床疗效的影响。**方法:**选取我院确诊并治疗的子宫内膜异位症患者 68 例,按随机数字表法进行分组,每组 34 例。对照组患者予以妇乐片口服治疗;研究组患者在对照组用药基础上予以桂枝茯苓丸联合治疗,所有患者连续服药 6 个月。观察两组患者治疗前后血清甲胎蛋白(AFP)、血清 LSA、肿瘤坏死因子- α (TNF- α)及血管内皮生长因子(VEGF)水平的变化情况、临床疗效及不良反应发生率。**结果:**研究组治疗后临床有效率 91.18%,高于对照组治疗后临床有效率 70.59%,差异具有统计学意义($P < 0.05$);与对照组比较,研究组治疗后血清 AFP、LSA、TNF- α 、VEGF 水平降低,差异具有统计学意义($P < 0.05$);对照组不良反应发生率为 8.24%,研究组不良反应发生率为 5.88%,两组间不良反应发生率无统计学意义($P > 0.05$)。**结论:**采用桂枝茯苓丸联合妇乐片治疗子宫内膜异位症,能有效提高患者的临床疗效,推测其机制与降低血清 AFP、LSA、TNF- α 、VEGF 水平有关。

关键词:桂枝茯苓丸;妇乐片;子宫内膜异位症;AFP;LSA

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Effects of Guizhi Fuling Pills Combined with Fu Le Tablets on the Levels of Serum AFP and LSA in the Patients with Endometriosis and Its Clinical Efficacy*

YANG Lei¹, HUANG Zhi-lan¹, JING Yuan¹, HOU Da-qiao¹, XIE Ting-ting²

(1 Department of Gynecology, Shaanxi Baoji People's Hospital, Baoji, Shaanxi, 721000, China; 2 Department of Obstetrics, the First Affiliated Hospital of The Fourth Military Medical University, Xijing Hospital, Xi'an, Shaanxi, 710032, China)

ABSTRACT Objective: To investigate the effects of guizhi fuling pills combined with fu le tablets on the levels of serum AFP and LSA and its clinical efficacy for patients with endometriosis. **Methods:** 68 patients with endometriosis who were treated in our hospital were selected and randomly divided into experiment group and control group, with 34 cases in each group. The patients in the control group were treated with fu le tablets; the patients in the experiment group were treated on the base of the control group with guizhi fuling pills. The serum AFP (AFP), serum LSA, tumor necrosis factor α (TNF- α), vascular endothelial growth factor (VEGF) levels of the two groups were observed, and the clinical efficacy and adverse reactions was detected and compared. **Results:** After treatment, the clinical effective rate of the experiment group was 91.18%, significantly higher than 70.59% of the control group with statistical significance ($P < 0.05$); compared with the control group, the serum AFP, LSA, TNF- α and VEGF levels of the experiment group were decreased after treatment, and the differences were statistically significant ($P < 0.05$). The patients in two groups had no malignant adverse reactions, and incidence of the adverse reactions between two groups had no difference ($P > 0.05$). **Conclusions:** Guizhi fuling pills combine with fu le tablets can effectively improve the patient's clinical efficacy in the treatment of endometriosis, its mechanism might be related to reduction of the serum AFP, LSA, TNF- α and VEGF levels.

Key words: Guizhi fuling pills; Fu le tablet; Endometriosis; AFP; LSA

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前言

子宫内膜异位症是指子宫内膜组织在子宫腔被覆盖内膜及子宫以外的部位出现、生长、浸润,反复出血,继而引发疼痛、不孕及结节或包块等。流行病学调查显示,本病发病率较高,约为 10%~15%,对孕龄妇女的身心健康造成了严重影响^[1,2]。随

着研究不断深入,中医药在子宫内膜异位症的治疗方面具有独特的优势,妇乐片临床上主要用于治疗子宫内膜炎、子宫内膜异位症等,具有清热凉血,消肿止痛的功效^[3]。桂枝茯苓丸是东汉时期《金匮要略》中的名方,具有消癥、活血化瘀的作用,广泛应用于子宫内膜异位症患者的临床治疗中^[4]。本次研究选取我院 68 例子宫内膜异位症患者作研究对象,为确立桂枝茯苓丸

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作者简介:杨蕾(1982-),女,本科,主治医师,研究方向:妇科临床,电话:13379185440

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联合妇乐片治疗该病的优势提供依据,现报告如下。

1 资料与方法

1.1 临床资料

选取自 2013 年 3 月到 2015 年 5 月来我院确诊并治疗的子宫内异症位症患者 68 例,按美国生育协会修正分期法分期: I 期 8 例, II 期 18 例, III 期 28 例, IV 期 14 例。均符合 2015 年中华医学会妇产科学分会子宫内膜异位症协作组拟定的《子宫内膜异位症诊治指南》中的诊断标准,经我院伦理委员会审核通过,排除子宫肌瘤、子宫腺肌症患者,排除宫颈病变及宫腔粘连等子宫病变患者,排除高血压、糖尿病、冠心病等严重器质性疾病患者,排除合并严重心、脑、血液以及免疫等系统疾病者,排除对研究所涉及药物的用药禁忌症及药物过敏者,患者或家属签字同意,参照随机数字表法分成 2 组,每组 34 例。对照组 34 例患者年龄 20~43 岁,平均年龄(28.12±4.01)岁,病程 5~27 个月,平均病程(18.45±2.63)个月,给予妇乐片治疗;研究组 34 例,患者年龄 21~42 岁,平均年龄(27.95±3.99)岁,病程 6~26 个月,平均病程(18.26±2.60)个月,予以桂枝茯苓丸联合妇乐片治疗。两组间基本资料具有可比性(P>0.05)。

1.2 方法

两组患者均予以常规对症治疗,在此基础上对照组 34 例患者予以妇乐片(陕西东泰制药有限公司,国药准字 Z20073057)口服治疗,2.5 g/次,2 次/日,连续用药 6 个月;研究组 34 例患者在予以常规对症治疗基础上予以桂枝茯苓丸(亚宝药业大同制药有限公司,国药准字 Z14020280)联合妇乐片(陕西东泰制药有限公司,国药准字 Z20073057)治疗,桂枝茯苓丸用法,6 g/次,2 次/日,连续用药 6 个月;在治疗期间,除研究药物以外,不再服用其他药物。

1.3 观测指标

1.3.1 观测指标 观察两组患者治疗前后血清甲胎蛋白(AFP)、血清 LSA、肿瘤坏死因子-α(TNF-α)、血管内皮生长因子(VEGF)、临床疗效、血/尿常规、肝肾功能、血脂血糖、心电图、脑电图、不良反应。

1.3.2 血清甲胎蛋白(AFP)、血清 LSA 测定 由专业人员于治疗前后晨起空腹抽取所有患者肘静脉血 5 mL,置于抗凝真空

管中,静置在 3000 r/s 条件下离心 15 min 后取上清液,-70 ℃的冰箱中保存待测,采用酶联免疫吸附试验法测定 AFP 及 LSA,应用多功能酶标仪(香港伯齐科技有限公司提供,型号 CLARIOstar)AFP、LSA 血清试剂盒均由上海乔羽生物科技有限公司提供,完全按照试剂盒要求进行操作。

1.3.3 肿瘤坏死因子-α(TNF-α)、血管内皮生长因子(VEGF)测定 由专业人员于治疗前后晨起空腹抽取所有患者肘静脉血 5 mL,置于抗凝真空管中,静置在 3000 r/s 条件下离心 15 min 后取上清液,-70 ℃的冰箱中保存待测,采用双蛋白抗体夹心法测定 TNF-α 水平,采用免疫发光法测定 VEGF 水平,应用全自动化学发光免疫分析仪(有索灵诊断医疗设备有限公司提供,型号 LIAISON?)进行检测,TNF-α、VEGF 试剂盒均北京盛齐扬恒生物科技有限公司提供,完全按照试剂盒要求进行操作。

1.3.4 疗效判断标准 完全缓解:患者出现的各类疼痛(子宫内异症引起)情况均消失;部分缓解:患者出现的各类疼痛(子宫内异症引起)情况均较治疗前减轻,但仍出现持续或间断疼痛症状;无效:患者出现的各类疼痛(子宫内异症引起)情况均为改变或加重。注:有效率=(完全缓解例数+部分缓解例数)/总例数×100%。

1.3.5 不良反应 治疗过程中测定血/尿常规、肝肾功能、血脂血糖、心电图、脑电图等,记录两组间不良反应状况。

1.4 统计学分析

所有统计数据均统一整理,采用 SPSS17.0 软件包进行分析,符合正态性的计量资料采用均数±标准差表示,两组治疗前后血清 AFP、LSA、TNF-α、VEGF 水平及临床疗效对比予以配对样本 t 检验,两组间血清 AFP、LSA、TNF-α、VEGF 水平及临床疗效对比予以独立样本 t 检验,临床疗效计数资料采用百分率(%)表示,予以 RxC 卡方检验,P<0.05 存在统计学意义。

2 结果

2.1 两组患者治疗过程中临床疗效对比

研究组患者治疗后临床有效率为 91.18%(31/34),对照组患者治疗后临床有效率为 70.59%(24/34),研究组高于对照组,具有统计学意义(P<0.05)。

表 1 两组患者治疗过程中临床疗效对比(例,%)

Table 1 Comparison of the clinical curative effect in the treatment process in two groups(n,%)

Groups	Case	Complete remission	Partial remission	Invalid	Total effective rate
Control group	34	13(38.24%)	11(32.35%)	10(29.41%)	24(70.59%)
Experiment group	34	17(50.00%)	14(41.18%)	3(8.82%)	31(91.18%)
X ²					4.660
P					0.031

2.2 两组患者治疗前后血清 AFP 水平对比

与治疗前比较,两组患者治疗后血清 AFP 水平均下降,研究组治疗后血清 AFP 水平显著低于对照组,具有统计学意义(P<0.05)。

2.3 两组患者治疗前后 LSA 水平对比

与治疗前比较,两组患者治疗后 LSA 水平均下降,研究组

治疗后 LSA 水平显著低于对照组,具有统计学意义(P<0.05)。

2.4 两组患者治疗前后 TNF-α、VEGF 水平对比

与对照组比较,两组患者治疗后 TNF-α、VEGF 水平降低,研究组治疗后 TNF-α、VEGF 水平低于对照组,具有统计学意义(P<0.05)。

表 2 两组患者治疗前后血清 AFP 水平对比($\bar{x} \pm s$)
Table 2 Comparison of the serum AFP level in two groups($\bar{x} \pm s$)

Groups	Case	Time point	AFP ($\mu\text{g/L}$)
Control group	34	Before treatment	57.23 $\pm$ 8.17
		After treatment	43.22 $\pm$ 6.17*
Experiment group	34	Before treatment	57.41 $\pm$ 8.20
		After treatment	35.08 $\pm$ 5.01*#
t1		7.979	
t2		13.550	
t3		5.972	

Note: Compared with before treatment,* $P < 0.05$. Compared with the control group after treatment, # $P < 0.05$; t1: comparison of the control group before and after treatment; t2: comparison of the experiment group before and after treatment; t3: comparison of the two groups after treatment.

表 3 两组患者治疗前后 LSA 水平对比($\bar{x} \pm s$)
Table 3 Comparison of the LSA level in two groups before and after treatment($\bar{x} \pm s$)

Groups	Case	Time point	LSA (mg/dL)
Control group	34	Before treatment	15.35 $\pm$ 2.19
		After treatment	11.02 $\pm$ 1.57*
Experiment group	34	Before treatment	15.51 $\pm$ 2.21
		After treatment	8.12 $\pm$ 1.15*#
t1		9.370	
t2		17.296	
t3		8.689	

Note: Compared with before treatment,* $P < 0.05$. Compared with the control group after treatment, # $P < 0.05$. t1: comparison of the control group before and after treatment; t2: comparison of the experiment group before and after treatment; t3: comparison of the two groups after treatment.

表 4 两组患者治疗前后 TNF- α 、VEGF 水平对比($\bar{x} \pm s$)
Table 4 Comparison of the TNF- α and VEGF levels in two groups before and after treatment($\bar{x} \pm s$)

Groups	Case	Time point	TNF α (pmol/L)	VEGF (ng/mL)
Control group	34	Before treatment	46.32 $\pm$ 6.61	41.11 $\pm$ 5.87
		After treatment	38.49 $\pm$ 5.49*	36.54 $\pm$ 5.22*
Experiment group	34	Before treatment	45.95 $\pm$ 6.56	40.92 $\pm$ 5.70
		After treatment	32.25 $\pm$ 4.60*#	30.47 $\pm$ 4.35*#
t1		5.313		3.392
t2		9.970		8.498
t3		5.080		5.209

Note: Compared with before treatment,* $P < 0.05$. Compared with the control group, # $P < 0.05$. t1: comparison of the control group before and after treatment; t2: comparison of the experiment group before and after treatment; t3: comparison of the two groups after treatment.

2.5 两组患者治疗过程中不良反应状况分析

两组患者治疗期间均无恶性不良反应出现,患者治疗后血/尿、肝肾功能、心电图等指标均未出现明显异常,对照组治疗期间不良反应发生率为 8.24 % (3/34),其中 2 例恶心患者,1 例头晕;研究组治疗期间不良反应发生率为 5.88 % (2/34),其中 1 例乏力,1 例腹泻,在给予及时对症处理后,上述不良反应症状均可消失。两组间不良反应发生率无统计学意义($P > 0.05$)。

3 讨论

子宫内膜异位症产生的病理原因是子宫内膜和宫颈腔被覆盖引起,患有子宫内膜异位症的患者均会伴有不同程度的小腹疼痛,痛经等症状,其疼痛会随病情变化而变化,有时会呈现出继发性,严重者会出现不孕,严重影响女性身心健康^[6-7]。妇乐片是由蒲公英、大青叶、大黄、牡丹皮、甘草、大血藤、忍冬藤、延胡索、川楝子、赤芍等药物有效成分精制而成,具有清热凉血、消肿止痛的功效^[8]。桂枝茯苓丸最早出现于东汉张仲景所著的《金匮要略妇女妊娠病》,其组成为桂枝、茯苓、牡丹、芍药、桃仁

各等分炼蜜和丸,主要治疗子宫内位症^[9];妇人素有癥病;经断未及三月,而得漏下不止,胎动在脐上者^[10]。

甲胎蛋白(AFP)是一种多功能糖蛋白,其诊断的敏感性较低,特异性较高。肿瘤坏死因子- α (TNF- α)主要担当免疫调节反应和多向性炎症反应的介导作用,其特点为生物学效应较为广泛^[11]。TNF- α 大部分作用于生殖系统参与生殖系统免疫^[12]。TNF- α 的异常增加,导致血管功能障碍和血管内皮损坏,从而导致合成血管内皮的功能降低及血管内皮的释放功能损伤^[13]。VEGF是在血管生成过程中起到关键作用,VEGF的过度表达,会引起血管生成增加,促进异位内膜细胞的粘附及种植生长,为其提供营养物质及充分的氧分^[14-16],新生血管的产生会分泌多种细胞生长因子,加速异位内膜的浸润粘附,且新生血管内皮细胞的扩增增加了异位内膜向远处转移条件^[17-19]。本实验结果显示,与对照组比较,研究组治疗后血清APF、LSA、TNF- α 、VEGF水平降低,具有统计学意义($P < 0.05$)。桂枝茯苓丸中桂枝温通血脉,丹皮、芍药凉血散瘀,行血,寒热并用,不耗伤阴血,降低子宫内位症带给患者的疼痛,减少炎症发生,从而降低血清APF、LSA、TNF- α 、VEGF水平。这与《子宫内位症的诊治指南》中血清APF、LSA、TNF- α 、VEGF水平降低这一结果一致。

本研究发现研究组治疗后临床有效率为91.18%,高于对照组治疗后临床有效率70.59%,具有统计学意义($P < 0.05$),说明桂枝茯苓丸联合妇乐片可以有效提高子宫内位症患者的临床疗效,减少疼痛。不良反应发生率方面,对照组治疗期间不良反应发生率为8.24%,研究组治疗期间不良反应发生率为5.88%,说明桂枝茯苓丸联合妇乐片在治疗子宫内位症方面副作用小,用药安全^[20]。

综上所述,桂枝茯苓丸联合妇乐片治疗子宫内位症效果显著,能有效降低血清APF、LSA、TNF- α 、VEGF水平。

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