doi: 10.13241/j.cnki.pmb.2017.13.026

桂枝茯苓胶囊对卵巢囊肿剥除术患者卵巢储备功能的影响 *

张 坤[1] 田 艺[1] 左 侠[1] 任小苗[1] 姜 锋[2]

（1 西安市第四医院 妇产科 陕西 西安 710004；2 第四军医大学第二附属医院唐都医院 妇产科 陕西 西安 710038）

摘要 目的：探究桂枝茯苓胶囊对卵巢囊肿患者囊肿剥除术后卵巢储备功能的影响。**方法：**选择我院收治的卵巢囊肿已行囊肿剥除术的患者 59 例，将其随机分为实验组及对照组。实验组 31 例予桂枝茯苓胶囊治疗，对照组予孕三烯酮治疗。对比两组患者治疗前及治疗后 12 周血清雌激素、抗苗勒氏管激素(AMH)、血清脂质结合唾液酸(LSA)、促卵泡激素(FSH)及基础窦卵泡数(AFC)水平及临床疗效。**结果：**实验组的有效率(96.8%)显著高于对照组(71.4%)，差异有统计学意义(P<0.05)。治疗 12 周后，两组患者血清雌激素、AMH、AFC 水平均较治疗前显著升高，而血清 FSH、LSA 水平均明显降低(P<0.05)，差异存在有统计学意义；与对照组比较，实验组患者的血清雌激素、血清 AMH 及 AFC 水平较高，血清 FSH、LSA 水平较低(P<0.05)，差异有统计学意义。**结论：**桂枝茯苓胶囊可以改善卵巢囊肿剥除术后患者的卵巢的储备功能，提高临床疗效。

关键词：桂枝茯苓胶囊；卵巢囊肿；囊肿剥除术；雌激素；抗苗勒氏管激素；脂质结合唾液酸；促卵泡激素；基础窦卵泡数

中图分类号：R711.75 **文献标识码：**A **文章编号：**1673-6273(2017)13-2502-03

Effects of Guizhi Fuling Capsule on the Ovarian Reserve Function of Patients with Ovarian Cyst after Oophorocystectomy*

ZHANG Kun[1], TIAN Yi[1], ZUO Xia[1], REN Xiao-miao[1], JIANG Feng[2]

(1 Department of Obstetrics and Gynecology, the fourth hospital of Xi'an, Xi'an, Shaanxi, 710004, China; 2 Department of Obstetrics and Gynecology, Tangdu Hospital, Second Affiliated Hospital of The Fourth Military Medical University, Xi'an, Shaanxi, 710038, China)

ABSTRACT Objective: To investigate the effects of Guizhi fuling capsule on the ovarian reserve function of patients with ovarian cyst after oophorocystectomy. **Methods:** 59 patients with ovarian cyst after oophorocystectomy who were treated in our hospital were selected and randomly divided into the the experimental group and the control group. 31 cases in the experimental group were treated with Guizhi fuling capsule, 28 cases in the control group were treated with gestrinone. The serum estrogen, eAnti-Mullerian hormone (AMH), follicle stimulating hormone(FSH), sinus follicle number(AFC) and serum lipid sialic acid (LSA) levels and the clinical efficacy of two groups of patients before treatment and 12 weeks after treatment were compared. **Results:** The effective rate of experimental group (96.8%) was significantly higher than that of the control group (71.4%)(P<0.05). At 12weeks after treatment, the serum estrogen, AMH, AFC levels were significantly increased than those before treatment, while the LSA, FSH levels were significantly decreased (P<0.05), compared with the control group, the serum estrogen, AMH, AFC levels of experimental group were higher, the serum FSH, LSA levels were lower (P<0.05). **Conclusions:** Guizhi fuling capsule could effectively improve the ovarian reserve function and enhance the clinical efficacy of patients after oophorocystectomy.

Key words: Guizhi fuling capsule; Ovarian cysts; Removed the cyst nucleus; estrogen; anti-Mullerian hormone; Lipid Bound Sialic acid; Follicle-stimulating hormone; Antral Follicle count

Chinese Library Classification(CLC): R711.75 Document code: A

Article ID: 1673-6273(2017)13-2502-03

前言

卵巢囊肿是一种常见的女性生殖系统良性肿瘤，好发于 20~50 岁的女性，约占女性生殖器肿瘤的 30%[4]，常单侧发生，也可双侧同时发生，还存在恶变的倾向[1]。卵巢囊肿的早期多无明显症状，随着病情的进展，囊肿逐渐增大，患者会出现下腹部坠痛、月经紊乱、内分泌失调甚至不孕等症状[2]，还可能发生卵巢囊肿蒂扭转、破裂、继发感染等多种严重病变。长期不愈者影响妇女的生育功能和身心健康。关于卵巢囊肿的发病机理尚不明确，目前认为其发病与内分泌、环境、遗传等多种因素有关。当囊肿直径大于 5 厘米时，有手术治疗指征，可行囊肿剥除术。但手术治疗在切除囊肿的同时，对正常的卵巢组织亦造成损伤。桂枝茯苓胶囊属于中药制剂，通过各中药成分的配伍，具有活血化瘀、调节内分泌等功效[5]。本实验通过观察桂枝茯苓胶囊在治疗卵巢囊肿剥除术后患者时的临床疗效及血清雌激素、AMH、LSAFSH 及 AFC 的变化，来探究桂枝茯苓胶囊对卵巢囊肿剥除术患者卵巢储备功能的影响及临床效果。

* 基金项目：陕西省自然科学基金项目(2006c251)

作者简介：张坤(1980-)，女，硕士，主治医师，研究方向：妇科内分泌，电话：15229324381

(收稿日期：2016-11-11 接受日期：2016-11-30)

1 资料与方法

1.1 病例选择

选取我院 2014 年 10 月～2015 年 11 月因卵巢囊肿行腹腔镜囊肿剥除术的患者 59 例，将其随机分为实验组及对照组。对照组 28 例，年龄 31~45 岁，平均(39.2± 4.3)岁，卵巢单纯囊肿 11 例，浆液性囊腺瘤 10 例，成熟性畸胎瘤 7 例；实验组 31 例，年龄 28~41 岁，平均(38.9± 4.1)岁，卵巢单纯囊肿 8 例，浆液性囊腺瘤 14 例，成熟性畸胎瘤 9 例。两组患者的年龄、孕产史、BMI 等对比差异没有统计学意义(P>0.05)，具有可比性。

1.2 纳入及排除标准

纳入标准：符合第六版《妇产科学》中对卵巢囊肿的诊断标准；具有卵巢囊肿临床症状，可扪及一侧附件区有包块，且光滑、活动性好、有弹性；已行影像学检查 B 超显示一侧附件区出现回声团块、界限清晰完整、形态规整、内壁完整没有分隔，直径在 5~10 cm 之间者；月经规律正常者；肿瘤标志物检测排除卵巢恶性肿瘤，行卵巢囊肿核摘除术后病理检查为良性；没有性激素使用史；年龄位于 20 至 50 岁之间的女性。排除标准：生殖道畸形及妇科恶性肿瘤患者；卵巢子宫内膜异位囊肿；双侧附件病变；严重心脑血管疾病；严重肝肾功能损害患者；药物过敏者；依从性不好者；月经不规律者。

1.3 治疗方法

两组患者术前及术后均未服用任何激素类药物，均于月经结束 3-7 天在全身麻醉下，行腹腔镜下卵巢囊肿剥除手术，手术过程均顺利，无一例发生严重围手术期并发症，术后病理均为良性病变。实验组患者于术后 1 天开始予桂枝茯苓胶囊(江苏康缘药业股份有限公司，国药准字 Z10950005)0.31 g，每次 3 粒餐后口服，每日 3 次，对照组予孕三烯酮(秦皇岛紫竹药业有限公司，国药准字 H19980003)，每次 1 粒口服，手术后 1 天开始服用，3 天后第 2 次服用，以后每周在相同时间服药。12 周为一个疗程。

1.4 检测指标和方法

两组患者在月经来潮的第 2 至 5 天，采集 5 mL 肘静脉血，把已经采集好的血液置于充有 EDTA 的抗凝采血管中，依转速 3000 r/min 离心 10 min，取上层血清入 EP 管中，置于 -20℃冰箱中保存备用。测定治疗前后血清中的雌激素，AMH 及 LSA 等指标。

采用双抗体夹心酶联免疫吸附法 (ELISA) 检测血清雌激素、AMH 及 LSA 水平。雌激素及 FSH 的测定选用由上海广锐生物科技有限公司生产的试剂盒。AMH 的测定采用深圳欣博盛生物科技有限公司提供的试剂盒进行检测，LSA 选用由上海江莱生物科技有限公司生产的试剂盒检测，严格按照盒上操作说明及步骤进行检测。

选择 GE 三维超声仪经阴道测量双侧卵巢的基础窦卵泡数(AFC)。AFC 的测定方法固定两名经验丰富的超声科医生，各自测定双侧卵巢内直径 2-9 mm 的窦卵泡之和取均值，再将两名超声科医生测得结果取均值即可。

1.5 疗效评价

根据血清 AMH 水平将结果化为显效和无效两个等级。显效：血清 AMH 水平升高≥ 0.5 ng/mL；无效：血清 AMH 水平未有明显变化。有效率 = 显效 / 总病例数× 100%。

1.6 统计学方法

使用统计学软件 SPSS 19.0 分析数据，通过 "$\bar{x}$± s" 表述正态数据结果，行 t 检验，以率(%)来计数资料，数据的差异比较选择卡方检验，以 P<0.05 时认为差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

实验组有效率(96.8%)显著高于对照组(71.4%)，差异有统计学意义(P<0.05)。见表 1。

表 1 两组患者临床疗效比较[例(%)]

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

Groups	Cases	Cure	Effective	Invalid	Clinical curative effect rate
Control group	28	0(0%)	20(71.4)	8(28.6)	
Experimental group	31	0(0%)	30(96.8)*	1(3.2)	

注：与对照组比较，*P<0.05。

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

2.2 两组患者治疗前后血清雌激素、AMH 及 LSA 水平的比较

治疗 12 周后，两组患者血清雌激素、AMH、AFC 水平均较治疗前显著升高，血清 FSH、LSA 水平均明显降低(P<0.05)，差异存在有统计学意义；与对照组比较，实验组雌激素、AMH、AFC 水平较高，FSH、LSA 水平较低(P<0.05)，差异具有统计学意义。见表 2 及表 3。

表 2 两组患者治疗前后血清雌激素、AMH 及 LSA 水平的比较($\bar{x}$± s)

Table 2 Comparison of the serum estrogen, AMH and LSA levels between two groups before and after treatment($\bar{x}$± s)

Groups	Cases	Estrogen(IU/L)		AMH(ng/mL)		LSA(mg/dL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	28	42.8± 5.4	46.6± 5.9*	5.2± 0.7	6.3± 0.8*	12.5± 1.6	10.9± 1.4*
Experiment group	31	43.1± 5.2	52.3± 5.9*#	5.1± 0.7	7.5± 0.8*#	12.4± 1.6	9.1± 1.2*#

注：与本组治疗前相比，*P<0.05；与对照组相比，#P<0.05。

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

表 3 两组患者血清 FSH 及 AFC 水平的比较($\bar{x}\pm$ s)

Table 3 Comparison of the serum FSH and AFC levels between two groups before and after treatment($\bar{x}\pm$ s)

Groups	Cases	AFC(n)		FSH(IU/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	28	9.3± 1.2	10.6± 1.1*	8.6± 0.9*	8.2± 0.9
Experiment group	31	9.1± 5.2	13.6± 1.7*#	9.2± 1.1*#	8.1± 0.8

注:与本组治疗前相比,*P<0.05;与对照组相比,#P<0.05。

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

3 讨论

卵巢储备功能是指卵巢中的卵泡生长发育形成可受精卵母细胞的能力,包括卵泡的数量和质量。卵巢储备功能降低将导致生育力下降、不孕、月经紊乱、卵巢早衰或过早绝经等等。随着医学知识的普及与保健意识的增强,卵巢良性肿瘤的确诊率有所提升,对患卵巢良性肿瘤的妇女实施手术已成为年轻患者的首选,尤其是腹腔镜下手术。但无论是卵巢囊肿疾病本身,还是手术剥除,均会造成卵巢储备功能降低。对于育龄期女性,如何在治病的同时保护卵巢功能受到了越来越多的关注。

桂枝茯苓胶囊为妇科之名方,其主要成分包括茯苓、桂枝及牡丹皮等,具有活血化瘀功效,常用于妇科疾病的治疗[13]。茯苓属于拟层孔菌科,味甘淡平,是真菌茯苓的干燥菌核,具有利水健脾的作用[14]。现代医学证明茯苓内含有大量的茯苓聚糖,能够抑制癌细胞的 DNA 合成而发挥作用[15]。桂枝味辛属中等大乔木,有温经通脉、助阳化气的功能,具有抗炎作用,而其中的桂皮醛则具有抗肿瘤的作用。牡丹皮味苦微寒,能够活血化瘀,抗炎抑菌、增强免疫力[16]。桂枝茯苓胶囊通过各个中药的配伍发挥功效,能够抑制酶蛋白的新发损害,同时对子宫颈癌细胞可以起到抑制作用[17]。桂枝茯苓胶囊通过调整体内促黄体生成素释放激素的水平,维持雌激素与孕激素的平衡,改善体内雌激素的异常水平。

促卵泡激素(FSH)由脑垂体合成并分泌,在女性卵巢内能够促进未成熟卵泡进行生产。雌激素是由卵巢和胎盘生成的女性激素,主要用于维持女性身心健康,受被神经和体液双重调节[18]。人体内的雌激素分泌出现异常会增加雌激素依赖性妇科疾病发生的可能性,如卵巢囊肿等。桂枝茯苓胶囊通过有效平衡患者体内的激素水平,刺激囊肿创面的修复。血清抗苗勒氏管激素(AMH)主要由次级卵泡生成,当卵泡进行发育后,AMH 水平逐渐降低,其水平与卵泡数目呈相关性,反映了卵巢的储备功能[19]。在实施卵巢切除术后,电凝等的影响会对卵巢的卵泡储备功能造成破坏,使血清 AMH 水平降低。服用桂枝茯苓胶囊后,通过改善体内微循环缓解创口卵巢损伤,达到提升血清 AMH 水平,恢复卵巢储备功能的目的。基础窦卵泡数(AFC)可以协助评价卵巢功能储备情况,通过对窦卵泡的计数评估来反应经卵巢囊肿核除术后卵巢的功能。血清脂质结合唾液酸(LSA)是一种肿瘤标志物,主要与神经节苷脂结合,在血液及乳汁粘液中的含量较高,具有多种生物学活性[20]。正常人体中的 LSA 水平甚少,只有在细胞发生恶变后,细胞膜的构成发生变化,细胞表面的负电荷增多,同时生成大量 LSA 复合物,导致 LSA 大量释放入血,阻断机体内的免疫防御系统的识别功能,利于肿瘤的繁殖与播散。卵巢囊肿核摘除术后 LSA 水平明显降低,说明了桂枝茯苓胶囊对机体内血液粘度的改善功能及对细胞功能的修复作用。本实验结果显示经过 12 周的治疗后,实验组有效率(96.8%)高于对照组(71.4%),说明桂枝茯苓胶囊能够有效恢复患者卵巢功能。此外,两组患者体内激素的水平都得到改善,但桂枝茯苓胶囊在在改善卵巢储备功能方面疗效显著,说明其干预治疗效果更好。

综上所述,桂枝茯苓胶囊可以改善卵巢囊肿剥除术后患者的卵巢的储备功能,提高临床疗效。

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