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桂枝茯苓胶囊对卵巢囊肿患者囊肿核摘除术后血清雌激素、AMH 及 LSA 水平的影响 *

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摘要 目的:探究桂枝茯苓胶囊对卵巢囊肿患者囊肿核摘除术后血清雌激素、抗苗勒氏管激素(AMH)及脂质结合唾液酸(LSA)水平的影响。**方法:**选择我院收治的已行囊肿核摘除术的卵巢囊肿患者 39 例,将其随机分为实验组及对照组。对照组 18 例予甲硝唑联合青霉素注射治疗;实验组 21 例予桂枝茯苓胶囊治疗。治疗后,对比两组的临床疗效及治疗前后血清雌激素、AMH 及 LSA 的水平。**结果:**治疗后,实验组总有效率(95.2%)显著高于对照组(72.2%),差异具有统计学意义($P<0.05$);治疗后,两组血清雌激素、AMH 水平均明显升高,血清 LSA 水平显著降低,差异均具有统计学意义($P<0.05$);与对照组比较,实验组治疗后血清雌激素、AMH 较高,而 LSA 水平较低,差异具有统计学意义($P<0.05$)。**结论:**桂枝茯苓胶囊可以有效提高行囊肿核摘除术卵巢囊肿患者的临床疗效,这可能与提高血清雌激素及 AMH 水平并降低血清 LSA 水平有关。

关键词:桂枝茯苓胶囊;卵巢囊肿;囊肿核摘除术;血清雌激素;抗苗勒氏管激素;脂质结合唾液酸

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Effects of Guizhi Fuling Capsule on the Serum Estrogen, AMH and LSA Levels of Patients with Ovarian Cyst after Laparoscopic Excision*

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ABSTRACT Objective: To investigate the effects of Guizhi fuling capsule on the serum levels of estrogen, AMH and LSA in patients with ovarian cyst after surgical removed the cyst nucleus. **Methods:** 39 patients with ovarian cyst after surgical removed the cyst nucleus who were treated in our hospital were selected and randomly divided into experiment group and control group. 18 cases in the control group were treated with metronidazole combined with penicillin, and another 21 cases in the experiment group were treated with Guizhi fuling capsule. Then the clinical efficacy and the serum levels of estrogen, anti miao le's tube hormone (AMH) and lipid sialic acid (LSA) in the two groups were observed and compared before and after the treatment. **Results:** The total effective rate of the experiment group was 95.2%, which was higher than 72.2% in the control group, and the difference was statistically significant ($P<0.05$); After treatment, the serum levels of estrogen and anti miao le's tube hormone (AMH) increased in the two groups, while the levels of serum lipid sialic acid (LSA) decreased, and the differences were statistically significant ($P<0.05$); Compared with the control group, the levels of estrogen and AMH of the experiment group were higher, and the LSA level was lower, and the differences were statistically significant ($P<0.05$). **Conclusion:** Guizhi fuling capsule can effectively relieve symptoms, strengthen the function of ovarian reserve, which may be relate to the increase of the estrogen and AMH, and the decrease of the LSA.

Key words: Guizhi fuling capsule; Ovarian cysts; Removed the cyst nucleus; Serum estrogen; AMH; LSA

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前言

卵巢囊肿是一种女性生殖系统常见的良性肿瘤,常单侧发生,也可双侧同时发生,易恶化^[1]。卵巢囊肿的早期多无明显症状,随着病情的进展,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]。当囊肿直径大于 5 厘米时,多需要手术治疗,卵巢囊肿核剥除术是一种常用的手术方式^[3]。通过对囊肿尽可能完整的分离和剥离,减少对卵巢组织的破坏,切除卵巢囊肿。卵巢囊肿好发于 20~50 岁的女性,越占女性生殖器肿

瘤的 30%^[4]。桂枝茯苓胶囊属于中医制剂,具有活血化瘀、调节内分泌等功效^[5]。本研究主要探讨了桂枝茯苓胶囊治疗卵巢囊肿核切除术后患者的临床疗效及其对血清雌激素、AMH 及 LSA 水平的影响,旨在为提高卵巢囊肿的临床疗效提供更多的参考。

1 资料与方法

1.1 病历选择

收集我院收治的卵巢囊肿患者 39 例,将其随机分为实验

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组及对照组。对照组 18 例,年龄 31~45 岁,平均(39.2± 4.3)岁,其中浆液性囊腺瘤 11 例,成熟畸胎瘤 7 例;实验组 21 例,年龄 28~41 岁,平均(38.9± 4.1)岁,其中浆液性囊腺瘤 13 例,成熟畸胎瘤 8 例。两组患者的年龄、病程等对比,差异没有统计学意义($P>0.05$)。符合 8 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;行肿瘤标志物检测已排除卵巢恶性肿瘤的患者;没有性激素使用史;年龄位于 20 至 50 岁之间的女性。本次研究获得我院伦理委员会的批准,告知患者患者且已经签署了知情同意书。排除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。

1.2 方法

两组患者均在手术前禁食补液及营养支持治疗,由同一组治疗组对患者在全麻下,行腹腔镜下卵巢囊肿核摘除术进行治疗。术后禁食过辣过咸、过热或过冷的食物。术后 1 天两组患者开始服药。对照组给予甲硝唑氯化钠注射液(赤峰源生药业有限公司,国药准字 H20123229)250 mL,注射用青霉素钠(天津药业焦作有限公司)480 万 U 注入 250 mL 注射液中,静脉滴注每日一次,连续治疗 2 周,后隔一日进行一次注射;实验组予桂枝茯苓胶囊(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。12 周为一个疗程。治疗前后在患者空腹时,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。

1.3 检测方法

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。

1.4 疗效评价

根据临床症状及血清 AMH 水平将结果化为痊愈、显效和无效三个等级。痊愈:患者的临床症状与体征消失,血清 AMH 水平升高 ≥ 1 ng/mL;显效:临床症状及体征基本消失,血清 AMH 水平升高 ≥ 0.5 ng/mL;无效:患者仍存在临床症状及体征或自觉加重,B 超或影像学检查显示复发,血清 AMH 水平未有明显改善。总有效率=(痊愈+显效)/ $\times 100\%$ 。密切关注所有对象在服药治疗期间出现的不良反应,并予以对症治疗。

1.5 统计学方法

使用统计学软件 SPSS 19.0 分析数据,通过 " $\bar{x} \pm s$ " 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 $P<0.05$ 时为结果差异具有统计学意义。

2 结果

2.1 两组患者临床疗效的比较

实验组的总有效率(95.2%)显著高于对照组(72.2%),差异具有统计学意义($P<0.05$)。见表 1。

表 1 两组患者治疗后临床疗效的比较 n(%)

Table 1 Comparison of the clinical curative effect between two groups after treatment n(%)

Groups	Cases	Cure	Effective	Invalid	Clinical curative effect rate
Control group	18	6(33.3)	7(38.9)	5(27.8)	13(72.2)
Experimental group	21	11(52.4)	9(42.9)	1(4.8)	20(95.2)*

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

治疗后,两组患者血清雌激素、AMH 水平均升高,血清 LSA 水平均降低($P<0.05$),差异具有统计学意义($P<0.05$);与对

照组比较,实验组血清雌激素、AMH 水平较高,LSA 水平较低($P<0.05$),差异具有统计学意义。见表 2。

表 2 两组患者血清雌激素、AMH 及 LSA 水平比较($\bar{x} \pm s$)

Table 2 Comparison of the clinical effect of estrogen, serum AMH and LSA levels between two groups($\bar{x} \pm s$)

Groups	Cases	(IU/L)Estrogen		AMH(ng/mL)		LSA(mg/dL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	18	42.8± 5.4	46.6± 5.9*	5.2± 0.7	6.3± 0.8*	12.5± 1.6	10.9± 1.4*
Experimental group	21	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 before treatment, * $P<0.05$. Compared with the control group, # $P<0.05$.

3 讨论

卵巢囊肿属于女性生殖器官的常见肿瘤,有多种类型,包括巧克力囊肿、畸胎瘤、浆液性上皮囊肿、功能性囊肿等,多发

于年轻女性具有恶变可能性^[6]。卵巢囊肿的发生多与雌激素分泌过量、饮食结构不良等因素相关,早期时并没有明显症状,仅表现为下腹不适及下坠感^[7]。后会出现月经异常、白带增多等症状,按压患者腹部时患者自觉腹痛或可触及坚实肿块,发生囊

肿蒂扭转引起患者严重腹胀腹痛及恶心呕吐等症状^[8]。囊肿变大后会影影响受精卵的正常运行,导致患者不孕、诱发流产,导致内分泌失调,甚至危及患者生命^[9]。而且卵巢囊肿较易并发卵巢肿瘤、破裂穿孔及感染等并发症对患者的生命造成威胁,因此应于病变早期对患者进行确诊及治疗^[10]。对于囊肿直径大于 5 cm 的患者需进行手术治疗。卵巢囊肿核切术常用于治疗囊肿直径小于 10 cm 的患者,在腹腔镜下对囊肿进行分离和剥脱,可以减少术中出血^[11]。在剥除囊肿时应注意保证被膜的完整,减少对创口的损伤及对卵巢功能的损伤^[12]。剔除卵泡的同时造成正常组织的破坏,损害已储备的卵泡,对育龄女性的卵泡储存功能造成影响。

桂枝茯苓胶囊主要成分包括茯苓、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,拥有抗肿瘤抗癌细胞及提高机体免疫力的作用^[15]。桂枝味辛属中等大乔木,有温经通脉、助阳化气的功能,现代医学认为桂枝具有抗炎作用,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,现代医学的研究显示^[16]牡丹皮能够抗炎抑菌、增强免疫力。桂枝茯苓胶囊通过各个中药的配伍来发挥功效,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,减小血液粘滞度,抑制血小板的聚集,提高巨噬细胞的吞噬功能,加强炎症的吸收。

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,受神经和体液双重调节^[18]。当人体内的雌激素分泌出现异常时,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,促使雌激素下降。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]。在实施卵巢囊肿核摘除术后,由于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。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。

本研究结果所示实验组总有效率 (95.2%) 高于对照组 (72.2%),表明桂枝茯苓胶囊能够有效恢复患者卵巢功能,降低体内血液粘度,促进细胞功能的修复及平衡体内激素水平,维持体内正常内分泌功能。而两组患者血清雌激素、AMH 水平均升高,LSA 水平均降低($P<0.05$),与对照组对比,实验组雌激素、血清 AMH 较高,LSA 水平较低。这说明患者在治疗后体内激

素的水平都得到明显改善了改善,但桂枝茯苓胶囊在平衡雌孕激素水平、修复改善创口细胞等方面的功能及疗效更好。

综上所述,桂枝茯苓胶囊可以有效提高行囊肿核摘除术卵巢囊肿患者的临床疗效,这可能与其提高血清雌激素及 AMH 水平并降低血清 LSA 水平有关。

参考文献(References)

- [1] Kwon S K, Kim S H, Yun S C, et al. Decline of serum antimüllerian hormone levels after laparoscopic ovarian cystectomy in endometrioma and other benign cysts: a prospective cohort study [J]. Fertility and sterility, 2014, 101(2): 435-441
- [2] Gundling N, Drews S, Hoedemaker M. Comparison of two different programmes of ovulation synchronization in the treatment of ovarian cysts in dairy cows [J]. Reproduction in Domestic Animals, 2015, 50 (6): 893-900
- [3] Jang W K, Lim S Y, Park J C, et al. Surgical impact on serum anti-Müllerian hormone in women with benign ovarian cyst: A prospective study[J]. Obstetrics & gynecology science, 2014, 57(2): 121-127
- [4] Maggiore U L R, Scala C, Venturini P L, et al. Endometriotic ovarian cysts do not negatively affect the rate of spontaneous ovulation[J]. Human Reproduction, 2015, 30(2): 299-307
- [5] Alletti S G, Rossitto C, Fanfani F, et al. Telelap ALF-X-assisted laparoscopy for ovarian cyst enucleation: report of the first 10 cases[J]. Journal of minimally invasive gynecology, 2015, 22(6): 1079-1083
- [6] Lind T, Hammarström M, Lampic C, et al. Anti-Müllerian hormone reduction after ovarian cyst surgery is dependent on the histological cyst type and preoperative anti-Müllerian hormone levels[J]. Acta obstetrica et gynecologica Scandinavica, 2015, 94(2): 183-190
- [7] Vorwergk J, Radosa M P, Nicolaus K, et al. Prophylactic bilateral salpingectomy (PBS) to reduce ovarian cancer risk incorporated in standard premenopausal hysterectomy: complications and re-operation rate [J]. Journal of cancer research and clinical oncology, 2014, 140 (5): 859-865
- [8] Legendre G, Catala L, Morinière C, et al. Relationship between ovarian cysts and infertility: what surgery and when?[J]. Fertility and sterility, 2014, 101(3): 608-614
- [9] Shah D K, Mejia R B, Lebovic D I. Effect of surgery for endometrioma on ovarian function [J]. Journal of minimally invasive gynecology, 2014, 21(2): 203-209
- [10] Sanchez A M, Viganò P, Somigliana E, et al. The distinguishing cellular and molecular features of the endometriotic ovarian cyst: from pathophysiology to the potential endometrioma-mediated damage to the ovary[J]. Human reproduction update, 2014, 20(2): 217-230
- [11] Jeengar K, Chaudhary V, Kumar A, et al. Ovarian cysts in dairy cows: old and new concepts for definition, diagnosis and therapy[J]. Animal Reproduction, 2014, 11(2): 63-73
- [12] Papic J C, Billmire D F, Rescorla F J, et al. Management of neonatal ovarian cysts and its effect on ovarian preservation[J]. Journal of pediatric surgery, 2014, 49(6): 990-994
- [13] Song M J, Lee S J, Yoo S H, et al. Single port gasless laparoscopy-assisted mini-laparotomic ovarian resection (SP-GLAMOR): Reasonable treatment for large cystic ovarian tumors with suspicion of malignancy[J]. Gynecologic oncology, 2014, 132(1): 119-124

- Rates and Graft Outcome in Kidney Transplantation for End-Stage Renal Disease Due to Reflux Nephropathy Versus Chronic Glomerulonephritis[J]. Transplant Proc, 2016, 48(6): 2065-2071
- [3] Ding SY, Zheng PD, He LQ, et al. The Research on Xiaochaihu Decoction Improving the Inflammation of Chronic Glomerulonephritis Patients and Relieving the Proteinuria[J]. Chinese Journal of integrated traditional Chinese and Western Medicine, 2013, 33(01): 21-26
- [4] Zatelli A, Roura X, D'Ippolito P, et al. The effect of renal diet in association with enalapril or benazepril on proteinuria in dogs with proteinuric chronic kidney disease[J]. Open Vet J, 2016, 6(2): 121-127
- [5] Nie WQ, Yu XQ, Wang LM, et al. Study on the treatment of acute kidney injury in elderly patients with renal Kang Injection[J]. Pharmacology and Clinics of Chinese Materia Medica, 2014, 30(01): 136-139
- [6] Wang HY. Nephrology [M]. Third Edition. Beijing, People's Medical Publishing House, 2008: 937
- [7] Zhen XY. Clinical guiding principle of traditional Chinese medicine in the treatment of chronic nephritis (Trial)[S]. Beijing: The Medicine Science and Technology Press of China, 2010: 29
- [8] Tashiro M, Sasatomi Y, Watanabe R, et al. IL-1 β promotes tubulointerstitial injury in MPO-ANCA-associated glomerulonephritis[J]. Clin Nephrol, 2016, 86(10): 190-199
- [9] Sahutoglu T, Atay K, Caliskan Y, et al. Comparative Analysis of Outcomes of Kidney Transplantation in Patients With AA Amyloidosis and Chronic Glomerulonephritis [J]. Transplant Proc, 2016, 48(6): 2011-2016
- [10] Shen P, Yang X, He L. Effect of Astragali and Angelica particle on proteinuria in Chinese patients with primary glomerulonephritis [J]. J Tradit Chin Med, 2016, 36(3): 299-306
- [11] Generali JA, Cada DJ. Benazepril: Nephropathy (Non-diabetic)[J]. Hosp Pharm, 2016, 51(4): 293-295
- [12] Chu JY. Review on the pharmacology and clinical research progress of Shen Kang Injection [J]. Research and Practice of Chinese Medicines, 2014, 28(02): 76-78
- [13] Deng JH, Zhang FL, Wang DY, et al. Meta analysis on Shengkang Injection in treatment of chronic renal failure [J]. Modern drugs and clinical, 2015, 30(05): 595-599
- [14] Feng Z, Niu K, Liu B, et al. Effect of Shen Kang Injection Combined with benazepril on proteinuria in patients with idiopathic membranous nephropathy[J]. Hebei Medical Journal, 2013, 35(04): 547-548
- [15] Ma LQ, Wang L, Fu RG, et al. Clinical control study on the treatment of diabetic nephropathy with renal Kang Injection Combined with Benner Pury [J]. Laboratory medicine and clinical, 2013, 10(23): 3162-3163
- [16] Stangou M, Bantis C, Skoularopoulou M, et al. Th1, Th2 and Treg/T17 cytokines in two types of proliferative glomerulonephritis [J]. Indian J Nephrol, 2016, 26(3): 159-166
- [17] Zhou YJ, Li P, Zhang LJ, et al. The variation and its clinical significance of Th1/Th2 and CD28+cells from peripheral blood in patients with chronic glomerulonephritis [J]. Laboratory Medicine, 2015, 30(02): 141-144
- [18] 刘奇, 许焱, 王兆星, 等. 肾炎康复片对慢性肾小球肾炎患者血清 FN、IL-2 及胱抑素 C 水平的影响 [J]. 现代生物医学进展, 2016, 16(10): 1915-1918
- Liu Qi, Xu Yan, Wang Zhao-xing, et al. Effect of Nephritis Rehabilitation Tablets on the Serum FN, IL-2 and Cystatin C Level in Patients with Chronic Glomerulonephritis [J]. Progress in Modern Biomedicine, 2016, 16(10): 1915-1918
- [19] He L, Peng Y, Liu H, et al. Th1/Th2 polarization in tonsillar lymphocyte form patients with IgA nephropathy [J]. Ren Fail, 2014, 36(3): 407-412
- [20] Krebs CF, Turner JE, Paust HJ, et al. Plasticity of Th17 Cells in Autoimmune Kidney Diseases[J]. J Immunol, 2016, 197(2): 449-457
- (上接第 2476 页)
- [14] Moscarini M, Milazzo G N, Assorgi C, et al. Ovarian stripping versus cystectomy: recurrence of endometriosis and pregnancy rate [J]. Archives of gynecology and obstetrics, 2014, 290(1): 163-167
- [15] Nahum G G, Kaunitz A M, Rosen K, et al. Ovarian cysts: presence and persistence with use of a 13.5 mg levonorgestrel-releasing intrauterine system[J]. Contraception, 2015, 91(5): 412-417
- [16] Pilny A. Ovarian cystic disease in guinea pigs [J]. Veterinary Clinics of North America: Exotic Animal Practice, 2014, 17(1): 69-75
- [17] Schreiber L, Raanan C, Amsterdam A. CD24 and Nanog identify stem cells signature of ovarian epithelium and cysts that may develop to ovarian cancer[J]. Acta histochemica, 2014, 116(2): 399-406
- [18] Madeddu C, Gramignano G, Kotsonis P, et al. Ovarian hyperstimulation in premenopausal women during adjuvant tamoxifen treatment for endocrine dependent breast cancer: A report of two cases [J]. Oncology letters, 2014, 8(3): 1279-1282
- [19] Alborzi S, Keramati P, Younesi M, et al. The impact of laparoscopic cystectomy on ovarian reserve in patients with unilateral and bilateral endometriomas[J]. Fertility and sterility, 2014, 101(2): 427-434
- [20] Cattaneo L, Signorini M L, Bertoli J, et al. Epidemiological description of cystic ovarian disease in Argentine dairy herds: risk factors and effects on the reproductive performance of lactating cows[J]. Reproduction in Domestic Animals, 2014, 49(6): 1028-1033