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补肾活血方剂与曼月乐治疗围绝经期功血的疗效及血清激素水平的改善情况比较*

岳明明^{1,2} 郑琳¹ 沙塔娜提·穆罕默德^{2Δ} 李丹¹ 王芳¹

(1 新疆医科大学第四附属中医医院妇科 新疆 乌鲁木齐 830000; 2 新疆医科大学中医学院 新疆 乌鲁木齐 830000)

摘要 目的:比较补肾活血方剂与曼月乐治疗围绝经期功血的疗效及血清激素水平的改善情况。**方法:**选择 2013 年 7 月至 2016 年 11 月我院妇科收治的围绝经期功血患者 92 例为研究对象,随机分为 A 组和 B 组,每组各 46 例。A 组口服补肾活血方剂,B 组宫内放置曼月乐,两组均持续治疗 3 个周期。观察两组的疗效及不良反应发生率,检测两组的血清激素水平及子宫内膜厚度(ET)、血红蛋白(Hb)水平。血清激素指标包括促卵泡生成素(FSH)、黄体生成素(LH)、孕酮(P)及雌二醇(E2)。**结果:**两组的总有效率比较差异无统计学意义($P>0.05$)。治疗后,两组的血清 FSH、LH、E2、P、ET 和 Hb 水平均较治疗前显著降低($P<0.01$),且 B 血清 FSH、LH、E2、P 和 ET 水平均显著低于同期的 A 组($P<0.01$),两组的 Hb 水平比较差异无统计学意义($P>0.05$)。B 组(15.22%)的不良反应发生率显著高于 A 组(0%)($P<0.01$)。**结论:**补肾活血方剂与曼月乐对围绝经期功血的疗效相当,但曼月乐对血清激素水平及子宫内膜增厚的改善作用更强,补肾活血方剂的安全性更高。

关键词:功能失调性子宫出血;围绝经期;补肾活血方剂;曼月乐

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Comparison of the Clinical Effects and Improvement of Serum Hormone Levels of Kidney Tonifying and Blood Circulation Recipe and Mirena in the Treatment of Perimenopausal Dysfunctional Uterine Bleeding*

YUE Ming-ming^{1,2}, ZHENG Lin¹, Shatanati·Mohamed^{2Δ}, LI Dan¹, WANG Fang¹

(1 Department of Gynecology, the Fourth Affiliated Hospital of traditional Chinese medicine, Xinjiang Medical University, Xinjiang, Urumqi, 830000, China; 2 School of Chinese medicine, Xinjiang Medical University, Xinjiang, Urumqi, 830000, China)

ABSTRACT Objective: To compare the clinical effects and improvement of serum hormone levels of kidney tonifying and blood circulation recipe and mirena in the treatment of perimenopausal dysfunctional uterine bleeding. **Methods:** 92 cases of perimenopausal patients with dysfunctional uterine bleeding in our hospital from July 2013 to November 2016 were selected and divided into group A and group B with 46 cases in each group. Group A was orally administered with kidney tonifying and blood circulation recipe, and group B was administered with mirena. Both groups were treated for 3 periods. The efficacy and incidences of adverse effect in two groups were observed. The levels of serum hormones and hemoglobin (Hb), and endometrial thickness (ET) were detected in two groups. The indices of serum hormone included follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone (P) and estradiol (E2). **Results:** No significant difference was found in the total effective rate between two groups ($P>0.05$). After treatment, the levels of serum FSH, LH, E2 and P as well as ET and Hb in both groups were all significantly lower than those before treatment ($P<0.01$), and the levels of serum FSH, LH, E2 and P as well as ET of group B were significantly lower than those of group A ($P<0.01$), no significant difference in the Hb level between two groups ($P>0.05$). The incidence of adverse reactions of group B (15.22%) was significantly higher than that of group A(0%) ($P<0.01$). **Conclusions:** The kidney tonifying and blood circulation recipe had similar effect as mirena in the treatment of perimenopausal dysfunctional uterine bleeding, while mirena had strong improving effect in serum hormone level and ET, kidney tonifying and blood circulation recipe had higher security.

Key words: Dysfunctional uterine bleeding; Perimenopausal period; Kidney tonifying; Mirena

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前言

功能失调性子宫出血(dysfunctional uterine bleeding)简称

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作者简介:岳明明(1975-),博士,副主任医师,主要从事中医药防治妇科病等方面的研究,电话:13565870169,

E-mail: yuemingming76@163.com

Δ 通讯作者:沙塔娜提·穆罕默德(1973-),博士,副教授,研究方向:经方在妇科病中的应用

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功血,常见于围绝经期女性^[1,2]。围绝经期功血临床主要表现为月经周期失调,经量过多及不规则出血等,严重者甚至切除子宫,严重影响女性患者的生活质量及健康^[3]。围绝经期功血的治疗方法主要包括刮宫、激素及子宫内膜切除甚至子宫切除等^[4]。手术治疗创伤较大,并发症较多,目前的药物治疗以激素类药物为主,常用的有宫内放置曼月乐。

曼月乐是一种T型宫内节育器,含有左炔诺孕酮,能够释放孕激素从而提高局部孕激素浓度达到治疗目的^[5]。然而研究表明^[6],曼月乐治疗虽然可以取得一定的疗效,但存在恶心呕吐、下腹痛等诸多不良反应,患者的耐受性差,甚至有致癌的风险^[7]。中医认为围绝经期功血是由肾虚封藏失职、精血失固所致,可采用补肾活血方剂加以治疗,且中药无明显的毒副作用,具有较明显的优势。因此,本研究比较了补肾活血方剂与曼月乐对围绝经期功血患者的疗效,以期对围绝经期功血的临床治疗提供更多的参考。

1 资料与方法

1.1 一般资料

选择2013年7月-2016年11月于我院妇科诊治的92例围绝经期功血患者作为研究对象,并随机分为两组,A组和B组,每组各46例。其中,A组年龄41-59岁,平均年龄(49.3±6.1)岁;病程为2-11个月,中位病程为6.0个月;子宫内膜单纯型增生38例,增殖期子宫内膜8例。B组年龄42-57岁,平均年龄(47.9±6.5)岁;病程为1-13个月,中位病程为6.5个月;子宫内膜单纯型增生37例,增殖期子宫内膜9例。两组患者的年龄、病程、病理类型等差异比较均无统计学意义($P>0.05$),具有可比性。

1.2 排除标准

① 生殖系统炎症、生殖器官肿瘤或感染导致的子宫出血;② 全身血液系统或肝、肾等重要脏器疾病导致的出血;③ 异物或节育器引发的子宫不规则出血。

1.3 治疗方法

A组服用补肾活血方剂,补肾方剂主要组成:菟丝子、枸杞子、女贞子、旱莲草、鹿角胶(烊化)、沙苑及黄芪各15g,炒香附、巴戟天、当归各12g。水煎温服,1剂/d,2次/剂,时间为上午9:00-10:00及下午3:00-4:00,连服7d。活血方剂:五灵脂、益

母草、生蒲黄、泽兰各15g,桃仁12g,艾叶、炮姜各10g,1剂/d,于睡前服用,连服4d;止血后单服补肾方剂。连续服用3个周期。B组患者于刮宫术后第5d宫内放置曼月乐(拜耳医药保健有限公司,德国;批准文号:国药准字J20140088)。连续治疗3个周期。

1.4 疗效判定和安全性

疗效判定^[8]标准:有效:治疗期间闭经或月经规律、经量少;无效:治疗期间或停药后仍然月经不规律或经量增多。观察两组治疗期间出现的不良反应并做好记录。

1.5 观察指标

所有患者均于治疗3个周期后检测下列指标:① 血清激素水平:取空腹静脉血检测促卵泡生成素(follicle-stimulating hormone,FSH)、黄体生成素(luteinizing hormone,LH)、孕酮(progestone,P)及雌二醇(estradiol,E2);② 血红蛋白(hemoglobin,Hb)水平:取空腹静脉血,通过血常规检查检测Hb水平;③ 子宫内膜厚度(endometrial thickness,ET):通过阴道B超检查并测量ET。

1.6 统计学分析

应用统计学软件SPSS19.0对数据进行统计分析,计量资料用平均数±标准差($\bar{x} \pm s$)表示,组间比较采用t检验,计数资料采用 χ^2 检验,以 $P<0.05$ 认为差异具有统计学意义。

2 结果

2.1 两组临床疗效比较

患者经治疗后1年内,A组绝经30例(65.22%),月经稀发5例(10.87%),月经规律10例(17.39%),3例(6.52%)治疗3个月无效改用其他治疗方案,有效率为93.48%;B组绝经27例(58.70%),月经稀发7例(15.22%),月经规律10例(21.74%),2例(4.35%)治疗3个月无效改用其他治疗方案,有效率为95.65%。两组的总有效率比较差异无统计学意义($P>0.05$)。

2.2 两组患者治疗前后血清激素水平比较

治疗前,两组的FSH、LH、E2和P水平比较差异无统计学意义($P>0.05$)。治疗后,两组的FSH、LH、E2和P水平均较治疗前显著性降低($P<0.01$),且B组的上述指标水平均显著低于同期的A组($P<0.01$)。见表1。

表1 两组患者治疗前后血清激素水平比较($\bar{x} \pm s$)

Table 1 Comparison of serum hormone levels before and after treatment between two groups($\bar{x} \pm s$)

Groups	n	Time	FSH (mIU/mL)	LH (mIU/mL)	E2 (pg/mL)	P (pg/mL)
Group A	46	Before treatment	20.73± 3.41	19.85± 2.96	97.31± 6.80	1.19 ± 0.32
		After treatment	12.27± 2.82*	11.28± 2.51*	51.43± 5.79*	0.91 ± 0.25*
Group B	46	Before treatment	21.11± 3.25	20.03± 3.12	99.72± 8.17	1.11 ± 0.40
		After treatment	9.10± 1.99* [#]	7.96± 2.14* [#]	39.15± 4.13* [#]	0.59 ± 0.16* [#]

Note: compared with before treatment, * $P<0.01$; compared with A group after treatment, [#] $P<0.01$.

2.3 两组治疗前后患者子宫内膜厚度和血红蛋白水平的比较

治疗前,两组的ET和Hb水平比较差异无统计学意义($P>0.05$)。治疗后,两组的ET和Hb水平均较治疗前显著降低($P<0.01$),B组的ET显著低于同期的A组($P<0.01$),两组的Hb水平比较差异无统计学意义($P>0.05$),见表2。

2.4 两组不良反应发生情况的比较

A组连续3个周期的治疗没有出现明显的不适;B组治疗期间有5例(10.87%)患者轻度恶心,2例(4.35%)患者乳房胀痛,不良反应发生率为15.22%。两组的不良反应发生率差异比较具有统计学意义($P<0.01$),B组较A组显著升高。

表 2 两组患者治疗前后子宫内膜厚度和血红蛋白的比较($\bar{x} \pm s$)

Table 2 Comparison of the endometrial thickness and hemoglobin before and after treatment between two groups($\bar{x} \pm s$)

Groups	Number	Time	ET (mm)	Hb (g/L)
Group A	46	Before treatment	11.32± 2.15	79.86± 11.37
		After treatment	6.74± 2.82*	102.44± 13.65*
Group B	46	Before treatment	11.83± 2.69	81.29± 13.50
		After treatment	4.93± 1.17* [#]	105.28± 15.31*

Note: compared with before treatment, *P<0.01; compared with A group after treatment, [#]P<0.01.

3 讨论

围绝经期功血的发生主要是由于下丘脑 - 垂体对性激素的正反馈调节的反应敏感性降低所致^[9],造成敏感性降低的原因是多方面的,包括机体内部及诸如精神高度紧张、恐惧等的外界因素,可导致患者黄体功能不足,继而停止排卵,雌激素水平降低。而长期的低雌激素持续引发子宫内膜腺体及血管,并出现内膜脱落周期紊乱,引发功血^[10-12]。目前,对该病的治疗秉持着止血、调整月经周期的原则。

曼月乐是含有 52 mg 左炔诺孕酮的 T 型宫内节育器,具有向宫腔保持恒定速率释放恒定剂量孕激素(左炔诺孕酮,20 μg/d)的作用^[13],其治疗原理是通过局部高浓度孕激素抑制子宫内膜的发育,从而减弱血管生成及内膜厚度^[14];此外,还可以抑制雌激素受体的合成,降低子宫内膜对雌二醇的敏感性,导致子宫内膜萎缩甚至退化^[15,16]。既往研究表明曼月乐治疗围绝经期的疗效肯定,但还存在一定的不良反应(恶心呕吐、下腹痛、头痛等)。因此,本研究尝试从中医角度探讨围绝经期功血的治疗方案。

围绝经期功血隶属中医学“崩漏”范畴,临床常见于肾虚血瘀型。中医学认为崩漏是由肝肾亏虚,肝不藏血,脾气虚弱,脾不统血,气不摄血而统摄无权所致^[17,18]。故本研究采用补肾活血方剂治疗。补肾方中的鹿角霜、巴戟天及沙苑具有温补肾阳的功効,旱莲草、枸杞子、女贞子等具有甘润滋补肾阴以填精的効用,两者相合阴阳双补。辅以活血方剂的益母草、五灵脂等,起到破血逐瘀,促进子宫内膜脱落的作用,同时艾叶、炮姜温经止血,甘草调和药性。诸药合用,起到补肾固冲,活血止血的功効^[7]。本研究结果显示两组的总有效率比较差异无统计学意义,说明补肾活血方与曼月乐治疗围绝经期功血疗效相当。此外,补肾活血方和曼月乐对患者的激素水平紊乱及子宫内膜增厚均有明显的改善作用,且曼月乐的改善程度更为明显。曼月乐的作用机理为宫内释放的左炔诺孕酮促使子宫内膜基质蜕膜化,导致内膜萎缩变薄;同时,通过对雌激素受体的负调节,阻断雌激素的效能,进而引发子宫内膜萎缩、退化^[19,20],而局部高浓度的孕激素也导致患者机体分泌产生的孕激素减少。曼月乐持续稳定释放的左炔诺孕酮对抑制内膜增厚及降低血清激素水平的作用更强、起效更快。补肾活血方可能也有类似左炔诺孕酮对激素水平及子宫内膜影响的作用,只是作用更弱。此外,服用补肾活血方的患者并没有出现明显的不良反应,而采用曼月乐治疗的部分患者出现了不良反应,这提示补肾活血方对围绝经期患者的安全性更高。

综上,补肾活血方剂与曼月乐对围绝经期功血的疗效相当,但曼月乐对血清激素水平及子宫内膜增厚的改善作用更强,补肾活血方剂的安全性更高。

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