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宫腔镜子宫内膜电切术治疗功能失调性子宫出血的疗效 及对患者性激素水平的影响*

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摘要 目的:探讨宫腔镜子宫内膜电切术治疗功能失调性子宫出血的疗效及对患者性激素水平的影响。**方法:**从本院 2016 年 7 月-2017 年 7 月收治的围绝经期功能失调性子宫出血患者中选取 94 例,按随机数字表法分为对照组和观察组,各 47 例。对照组采用曼月乐进行治疗,观察组采用宫腔镜子宫内膜电切术治疗。比较两组治疗后 3 个月、6 个月、12 个月的治疗效果,检测两组治疗前、治疗后 3 个月、6 个月、12 个月血红蛋白(Hb)含量及血清垂体催乳素(PRL)、孕酮(P)、促卵泡生成素(FSH)、促黄体生成素(LH)、睾酮(T)、雌二醇(E₂)水平。随访 1 年,观察两组患者的不良反应发生情况。**结果:**观察组治疗后 3 个月、6 个月、12 个月的总有效率分别为 100.00%、95.74%、95.74%,均分别高于对照组的 93.62%、89.36%、87.23%,但两组各时期比较差异无统计学意义($P>0.05$)。两组患者治疗后 3 个月、6 个月、12 个月的 Hb 含量均高于治疗前,且观察组治疗后 3 个月、6 个月、12 个月的 Hb 含量均明显高于对照组($P<0.05$)。治疗后 6 个月、12 个月,对照组的 PRL、P、FSH、LH、T 水平均高于治疗前和观察组,而 E₂ 水平低于治疗前和观察组($P<0.05$)。观察组治疗后 3 个月、6 个月、12 个月的各项性激素指标水平与治疗前比较差异均无统计学意义($P>0.05$)。观察组不良反应发生率为 4.26%,低于对照组的 21.28%($P<0.05$)。**结论:**宫腔镜子宫内膜电切术治疗功能失调性子宫出血疗效确切,能明显改善患者贫血状况,且对性激素水平无明显影响,具有较好的安全性。

关键词:宫腔镜;子宫内膜电切术;功能失调性子宫出血;疗效;性激素

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The effects of Hysteroscopic Endometrial Resection on the Treatment of Dysfunctional Uterine Bleeding and the Sex hormone Levels in Patients*

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ABSTRACT Objective: To investigate the effects of hysteroscopic endometrial resection on the treatment of dysfunctional uterine bleeding and its influence on sex hormone levels. **Methods:** 94 patients with dysfunctional uterine bleeding in perimenopausal period who were admitted to our hospital from July 2016 to July 2017 were selected, they were divided into control group and observation group according to random number table method, they were 47 cases in each group. The control group was treated with intrauterine device, and the observation group was treated with hysteroscopic endometrial resection. The therapeutic effects of the two groups were compared at 3, 6 and 12 months after treatment. The hemoglobin (Hb), serum prolactin (PRL), progesterone (P), follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T) and estradiol (E₂) levels were compared between the two groups at 3, 6 and 12 months after treatment. Follow up for 1 year, the incidence of adverse reactions were observed in the two groups. **Results:** The total effective rates of the observation group were 100.00%, 95.74% and 95.74% respectively at 3, 6 and 12 months after treatment, which were higher than those of the control group (93.62%, 89.36% and 87.23% respectively), but there were no significant differences between the two groups at all stages ($P>0.05$). The levels of Hb in the two groups were higher than those before treatment at 3, 6 and 12 months after treatment, and the levels of Hb in the observation group at 3, 6 and 12 months after treatment were significantly higher than those in the control group ($P<0.05$). At 6 and 12 months after treatment, the levels of PRL, P, FSH, LH and T in the control group were significantly higher than before treatment and observation group, while the levels of E₂ were significantly lower than before treatment and observation group ($P<0.05$). There were no significant differences in the sex hormone levels between the observation group at 3, 6 and 12 months after treatment and before treatment ($P>0.05$). The incidence of adverse reactions in the observation group was 4.26%, which was significantly lower than that in the control group (21.27%) ($P<0.05$). **Conclusion:** Hysteroscopic endometrial resection is effective in the treatment of dysfunctional uterine bleeding, it can significantly improve the anemia status of patients, and it has no significant effect on the sex hormone levels, it has better security.

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前言

功能失调性子宫出血多发于围绝经期女性,其临床表现为月经不规律、经期延长、经期出血量增多等,严重者可继发贫血、感染等,对患者生活造成不良影响^[1-3]。治疗功能失调性子宫出血传统非手术方法主要包括诊断性刮宫治疗和口服激素类药物等,但这些治疗方法存在患者依从性差、治疗后容易复发等问题^[4-6]。此外,有报道认为^[7],心血管疾病、乳腺癌、子宫内膜癌的发病率与长期口服激素类药物存在一定的相关性,因此药物治疗功能失调性子宫出血的远期效果并不理想。手术疗法中,子宫切除术可从根本上解决患者的月经问题,但其创伤大、患者恢复慢、并发症多,多数患者存在恐惧心理,术后易出现一系列心理问题^[8,9]。因此,寻找一种既能克服药物治疗弊端,又无需切除子宫的治疗方法具有重要的临床意义。随着微创技术的不断发展,妇科内镜诊疗技术被广泛应用于妇科疾病的诊疗中。宫腔镜子宫内膜电切术具有微创、安全、术后恢复快的特点,并且能完整保留子宫,在临床中受到妇产科医师及功能失调性子宫出血患者的青睐^[10,11]。本研究探讨宫腔镜子宫内膜电切术治疗功能失调性子宫出血的疗效及对患者性激素水平的影响,为临床提供数据支持。现整理报道如下。

1 资料与方法

1.1 一般资料

从本院 2016 年 7 月-2017 年 7 月收治的围绝经期功能失调性子宫出血患者中选取 94 例进行本次研究。纳入标准:① 患者经诊断均符合第 8 版《妇产科学》^[12]中关于功能失调性子宫出血的诊断标准;② 患者经 B 超诊断,卵巢未见病变,大小正常;③ 患者年龄不高于 55 岁;④ 患者已生育且均无再生育需求;⑤ 对本研究知情同意,且签署知情同意书。排除标准:① 合并严重心、肝、肾功能障碍者;② 合并内分泌疾病、血液系统疾病者;③ 合并恶性肿瘤者;④ 近半年内有激素服用史者;⑤ 合并急性生殖道感染者;⑥ 合并宫颈病变者。所有患者按随机数字表法分为对照组和观察组,各 47 例。对照组年龄 38-55 岁,平均(47.32±4.86)岁,产次 1-4 次,平均(1.89±0.51)次,病程 4 个月-3 年,平均(1.32±0.44)年,血红蛋白(Hemoglobin, Hb)含量为(74.35±8.27)g/L。观察组年龄 39-54 岁,平均(47.67±4.57)岁,产次 1-3 次,平均(1.73±0.56)次,病程 5 个月-3 年,平均(1.41±0.52)年, Hb 含量为(75.62±8.83)g/L。两组一般资料比较无统差异($P>0.05$)。研究已获本院伦理会批准。

1.2 治疗方法

对照组于月经干净后的 5-7d,采用左炔诺孕酮宫内节育系统(曼月乐, Bayer Oy 公司, 国药准字: J20140088, 规格: 含左炔诺孕酮 52 mg/ 个)置入阴道内进行治疗。观察组术前 12h 口服米索前列醇片(浙江仙琚制药股份有限公司, 国药准字: H20084598, 规格: 0.2 mg/ 片) 0.2 mg, 于月经干净后的 3-5d 行宫腔镜下子宫内膜电切术: 静脉全麻后取截石位, 常规消毒后

采用 Hegar 扩张器 10 号扩张宫颈, 插入宫腔镜全面观察宫腔情况, 若患者内膜肥厚, 则先撤出宫腔镜予以吸宫薄化内膜后再插入宫腔镜。采用环形切割电极自宫底至宫颈解剖学内口上下约 0.5 cm 处, 对子宫底、后壁、前壁及两侧壁子宫内膜依次实施切除。切割深度包括子宫内膜全层及其下方肌层约 2-3 mm。采用滚球电极电凝内膜和宫角及其它电切难以到达的位置进行止血。手术完成后将切除的组织送病理检查。

1.3 观察指标

1.3.1 治疗效果^[13] 于治疗后 3 个月、6 个月、12 个月根据患者术后月经量对两组的治疗效果进行评价: 治愈: 经治疗后闭经; 显效: 经过治疗后存在点滴量月经, 每周期卫生巾使用量为 1-2 块; 有效: 经过治疗后存在少量月经, 每周期卫生巾使用量为 3-5 块; 无效: 相比于治疗前, 患者月经量无明显变化。总有效率 = 治愈率 + 显效率 + 有效率。

1.3.2 Hb 及性激素水平 所有患者均于治疗前及治疗后 3 个月、6 个月、12 个月进行血常规检测, 统计 Hb 含量; 化验室抽取 2 mL 外周静脉血, 采用放射免疫法测定性激素水平, 包括血清垂体催乳素(Pituitary prolactin, PRL)、孕酮(Progesterone, P)、促卵泡生成素(Follicle-stimulating hormone, FSH)、睾酮(Testosterone, T)、促黄体生成素(Luteinizing hormone, LH)和雌二醇(Estradiol, E₂)。

1.3.3 不良反应情况 治疗后通过电话询问或门诊复查等方式随访 1 年, 观察两组患者的不良反应发生情况。

1.4 统计学方法

采用 SPSS23.0 软件对数据进行分析。治疗效果及不良反应发生情况以率表示, 采用 χ^2 检验; Hb 含量、性激素水平等计量资料以“均数±标准差”的形式表示, 行双侧 t 检验。检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组治疗效果比较

观察组治疗后 3 个月、6 个月、12 个月的总有效率分别为 100.00%、95.74%、95.74%, 均分别高于对照组的 93.62%、89.36%、87.23%, 但两组各时期比较差异无差异($P>0.05$)。见表 1。

2.2 两组患者 Hb 含量变化情况

两组患者治疗后 3 个月、6 个月、12 个月的 Hb 含量均高于治疗前, 差异有统计学意义($P<0.05$)。观察组治疗后 3 个月、6 个月、12 个月的 Hb 含量均明显高于对照组($P<0.05$)。见表 2。

2.3 两组患者性激素水平变化情况

治疗后 6 个月、12 个月, 对照组的 PRL、P、FSH、LH、T 水平高于治疗前和观察组, 而 E₂ 水平低于治疗前和观察组($P<0.05$)。观察组治疗后 3 个月、6 个月、12 个月的各项性激素指标水平与治疗前比较差异均无统计学意义($P>0.05$)。见表 3。

2.4 不良反应情况

随访 1 年, 对照组出现下腹坠胀痛 3 例, 阴道不规则流血 6 例、环位下移 1 例, 不良反应发生率为 21.28%(10/47); 观察

表 1 两组治疗总有效率比较[n(%)]

Table 1 Comparison of the total effective rates between the two groups[n(%)]

Groups	n	3 months after treatment	6 months after treatment	12 months after treatment
Control group	47	44(93.62)	42(89.36)	41(87.23)
Observation group	47	47(100.00)	45(95.74)	45(95.74)
χ^2	-	3.099	1.389	2.186
P	-	0.078	0.239	0.139

表 2 两组患者 Hb 含量比较($\bar{x} \pm s$, g/L)Table 2 Comparison of Hb content between the two groups ($\bar{x} \pm s$, g/L)

Groups	n	Before treatment	3 months after treatment	6 months after treatment	12 months after treatment
Control group	47	74.35 $\pm$ 8.27	101.43 $\pm$ 8.51*	111.09 $\pm$ 9.42*	113.69 $\pm$ 7.84*
Observation group	47	75.62 $\pm$ 8.83	109.32 $\pm$ 10.04*	118.95 $\pm$ 8.32*	124.73 $\pm$ 7.13*
t	-	0.720	4.110	4.287	7.142
P	-	0.474	0.000	0.000	0.000

Note: compared with before treatment,* $P<0.05$.

表 3 两组患者性激素水平比较($\bar{x} \pm s$)Table 3 Comparison of sex hormone levels between the two groups ($\bar{x} \pm s$)

Groups	n	Times	PRL(ng/ml)	P(ng/ml)	FSH(mIU/ml)	LH(mIU/ml)	T(ng/dl)	E2(pg/ml)
Control group	47	Before treatment	11.61 $\pm$ 2.36	0.28 $\pm$ 0.09	14.16 $\pm$ 3.12	12.71 $\pm$ 1.81	54.92 $\pm$ 2.64	48.36 $\pm$ 2.87
		3 months after treatment	11.38 $\pm$ 2.62	0.30 $\pm$ 0.12	14.78 $\pm$ 3.43	13.24 $\pm$ 1.93	55.39 $\pm$ 2.87	47.92 $\pm$ 2.41
		6 months after treatment	13.94 $\pm$ 2.85*	0.36 $\pm$ 0.10*	17.35 $\pm$ 3.27*	14.83 $\pm$ 1.67*	61.35 $\pm$ 3.82*	44.39 $\pm$ 2.67*
		12 months after treatment	14.82 $\pm$ 3.28*	0.37 $\pm$ 0.11*	18.24 $\pm$ 3.67*	15.29 $\pm$ 1.84*	63.15 $\pm$ 4.28*	43.27 $\pm$ 2.93*
Observation group	47	Before treatment	11.84 $\pm$ 2.41	0.27 $\pm$ 0.10	14.28 $\pm$ 3.72	12.41 $\pm$ 1.93	55.17 $\pm$ 2.39	48.89 $\pm$ 2.55
		3 months after treatment	11.98 $\pm$ 2.37	0.29 $\pm$ 0.07	14.73 $\pm$ 3.68	12.64 $\pm$ 1.82	54.81 $\pm$ 2.37	48.43 $\pm$ 2.62
		6 months after treatment	12.12 $\pm$ 2.52 [#]	0.29 $\pm$ 0.09 [#]	14.13 $\pm$ 3.82 [#]	12.92 $\pm$ 2.03 [#]	55.22 $\pm$ 2.61 [#]	48.37 $\pm$ 2.36 [#]
		12 months after treatment	11.62 $\pm$ 2.31 [#]	0.28 $\pm$ 0.10 [#]	14.52 $\pm$ 3.39 [#]	12.54 $\pm$ 1.77 [#]	55.49 $\pm$ 2.52 [#]	49.63 $\pm$ 2.88 [#]

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

组出现下腹坠胀痛 2 例,不良反应发生率为 4.26%(2/47),低于对照组,差异有统计学意义($\chi^2=6.114$, $P=0.013$)。

3 讨论

目前认为,功能失调性子宫出血与内分泌系统功能紊乱密切相关^[14]。围绝经期是女性的卵巢功能衰退到最后一次月经出现后 1 年的一段生理变化时期^[15]。研究表明^[16],围绝经期女性的下丘脑-垂体-卵巢系统调节功能较易出现紊乱,体内激素水平出现明显变化,导致处于这一时期的女性较易出现功能失调性子宫出血。围绝经期功能失调性子宫出血治疗原则是止血并调整月经周期、积极纠正贫血、防止子宫内膜癌变等^[17,18]。药物治疗及宫腔镜子宫内膜电切术均是临床中治疗功能失调性子宫出血的常用方法,但关于其治疗效果的优劣,目前仍存

在争议。

本研究中,观察组治疗后各时期的治疗总有效率均高于对照组,但两组比较无统计学差异($P>0.05$),表明两种治疗方法均能较为有效地治疗功能失调性子宫出血。曼月乐又名左炔诺孕酮宫内节育系统,其主要成分左炔诺孕酮可直接作用与宫腔内部,通过下调雌、孕激素受体的表达水平,达到降低子宫内膜对雌、孕激素的敏感性,进一步达到减少月经量的目的^[19,20]。宫腔镜子宫内膜电切术则是通过宫腔镜下高频电刀的作用,对子宫内膜基层、功能层进行切割,使子宫内膜形成瘢痕并纤维化,进一步阻止子宫内膜增生,达到止血效果^[21]。观察两组患者 Hb 含量变化发现,治疗后两组患者的 Hb 含量均高于治疗前,且观察组患者的 Hb 含量均明显高于对照组,提示两组患者的贫血状况在经过治疗之后均得到了纠正,但宫腔镜子宫内膜电

手术纠正贫血的效果优于曼月乐。推测其原因,可能与曼月乐放置后其有效成分释放较为缓慢有关,而宫腔镜子宫内电切术具有微创的特点,术后子宫内膜瘀痕形成快,出现纤维化后功能失调性子官出血复发可能性较低,从而可促使患者 Hb 含量的回升^[22-24]。

为分析曼月乐与宫腔镜子宫内膜电切术对卵巢功能的影响,本研究还观察了两组患者性激素水平变化情况,结果发现,治疗后对照组的PRL、P、FSH、LH、T水平均高于治疗前和观察组,而E₂水平低于治疗前和观察组,但观察组的各项性激素指标无明显变化。表明宫腔镜子宫内膜电切术对卵巢功能的影响较小。究其原因,宫腔镜子宫内膜电切术在宫腔镜下完成,手术过程医生的视野开阔清晰,可有效避免一些不必要的手术损伤,同时这一手术也能完整保留子宫及卵巢的解剖结构,从而改善患者生殖预后^[25-27]。此外,观察组不良反应发生率低于对照组,提示宫腔镜子宫内膜电切术具有较高的安全性。曼月乐是一种节育系统,与普通节育器一样,易出现下腹坠胀痛、环位下移等不良反应,而阴道不规则流血的出现,则可能与曼月乐放置后宫腔内的药物浓度不均匀有关^[28,29]。宫腔镜子宫内膜电切术在手术过程中可能出现宫腔积血、气体栓塞等情况,进一步导致下腹坠胀痛的出现,同时宫腔镜子宫内膜电切术不影响为卵巢供血的卵巢动脉及子宫动脉巢支,且对卵巢功能影响小,因此能减少部分不良反应的发生^[30]。

综上所述,宫腔镜子宫内膜电切术治疗功能失调性子宫出血安全有效,可改善患者贫血状况,且对性激素水平无明显影响。值得一提的是,行宫腔镜子宫内膜电切术后,患者容易出现人为闭经,因此较为适宜在围绝经期功能失调性子宫出血患者中推广使用。

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- 切术纠正贫血的效果优于曼月乐。推测其原因,可能与曼月乐放置后其有效成分释放较为缓慢有关,而宫腔镜子宫内电切术具有微创的特点,术后子宫内瘢痕形成快,出现纤维化后功能失调性子宫出血复发可能性较低,从而可促使患者Hb含量的回升^[22-24]。
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