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宫腔镜电切术联合左炔孕酮宫内节育系统对子宫内膜息肉患者性激素、炎症因子及复发的影响*

陈红霞 方春丽 王 辉 胡菲菲 应小燕

(南京医科大学第二附属医院妇产科 江苏 南京 210011)

摘要 目的:探讨宫腔镜电切术联合左炔孕酮宫内节育系统(LNG-IUS)对子宫内膜息肉患者炎症因子、性激素及复发的影响。**方法:**选取2016年4月到2018年4月期间我院收治的98例子宫内膜息肉患者,分为对照组与联合组,各49例。对照组予以宫腔镜电切术治疗,联合组予以宫腔镜电切术联合LNG-IUS治疗,比较两组性激素、炎症因子及复发情况,记录两组不良反应发生情况,观察两组月经周期、月经量、子宫内膜厚度。**结果:**术后6个月,两组月经周期、月经量、子宫内膜厚度均较术前降低,且联合组低于对照组($P<0.05$)。两组术前、术后6个月卵泡生成激素(FSH)、黄体生成激素(LH)、雌二醇(E2)比较无显著性差异($P>0.05$)。术后6个月,两组白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、C反应蛋白(CRP)均较术前降低,且联合组低于对照组($P<0.05$),白介素-4(IL-4)升高,且联合组高于对照组($P<0.05$)。两组不良反应发生率对比未见显著性差异($P>0.05$)。联合组复发率低于对照组($P<0.05$)。**结论:**宫腔镜电切术联合LNG-IUS治疗子宫内膜息肉患者,可有效阻止息肉生长,降低复发率,对性激素水平影响较小,其作用机制可能与抑制炎症反应有关。

关键词:宫腔镜电切术;左炔孕酮宫内节育系统;子宫内膜息肉;性激素;炎症因子;复发

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Effect of Hysteroscopic Resection Combined with Levonorgestrel Intrauterine Contraceptive System on Sex Hormones, Inflammatory Factors and Recurrence in Patients with Endometrial Polyps*

CHEN Hong-xia, FANG Chun-li, WANG Hui, HU Fei-fei, YING Xiao-yan

(Department of Obstetrics and Gynecology, The Second Affiliated Hospital of Nanjing Medical University,

Nanjing, Jiangsu, 210011, China)

ABSTRACT Objective: To investigate the effect of hysteroscopic resection combined with levonorgestrel intrauterine contraceptive system (LNG-IUS) on sex hormones, inflammatory factors and recurrence in patients with endometrial polyps. **Methods:** 98 patients with endometrial polyps in our hospital from April 2016 to April 2018 were selected, and randomly divided into control group and combined group, 49 cases in each group. The control group was treated with hysteroscopic resection, and the combined group was treated with hysteroscopic resection combined with LNG-IUS. The sex hormones, inflammatory factors and recurrence of the two groups were compared, and the incidence of adverse reactions in the two groups was recorded. The menstrual cycle, menstrual volume and endometrial thickness of the two groups were observed. **Results:** 6 months after operation, the menstrual period, menstrual volume and endometrial thickness of the two groups were lower than those before operation, and those of the combined group were lower than those of the control group ($P<0.05$). There were no significant differences in follicle-generating hormone (FSH), luteinizing hormone (LH), estradiol (E2) between the two groups before and 6 months after operation ($P>0.05$). 6 months after operation, the interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), C-reactive protein (CRP) in the two groups were lower than those before operation, and those of the combined group were lower than those of the control group ($P<0.05$), and the interleukin-4 (IL-4) increased, and that of the combined group was higher than that of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). The recurrence rate of the combined group was lower than that of the control group ($P<0.05$). **Conclusion:** Hysteroscopic resection combined with LNG-IUS in the treatment of endometrial polyps can effectively prevent the growth of endometrial polyps, reduce the recurrence rate, and have little effect on the levels of sex hormones. The mechanism may be related to the inhibition of inflammatory reaction.

Key words: Hysteroscopic resection; Levonorgestrel intrauterine contraceptive system; Endometrial polyps; Sex hormones; Inflammatory factors; Recurrence

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作者简介:陈红霞(1968-),女,本科,副主任医师,研究方向:妇科腔镜,E-mail:chx2215@163.com

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前言

子宫内膜息肉是由于局灶性子宫内膜增生过度的良性病变,可引发不规则阴道出血、不孕、月经异常、贫血等临床症状,严重影响女性生命健康及生活质量^[1-3]。青春期后所有年龄层女性均可发病,以更年期前后及生育期女性的发病率最高^[4]。现临床针对症状不明显或体积偏小息肉者,可暂时不给予治疗,针对症状明显且体积较大的息肉者,主要采取手术治疗^[5,6]。宫腔镜电切术是治疗子宫内膜息肉的常用术式,具有安全性高、定位准确等优点,但其术后复发率较高一直是困扰临床医生的主要难题之一^[7,8]。左炔孕酮宫内节育系统(LNG-IUS)可在患者宫腔内稳定、缓慢释放低剂量左炔诺孕酮,使宫腔局部维持较高浓度的孕激素,达到抑制子宫内膜增生效果^[9,10]。本次研究通过比较单纯宫腔镜电切术与宫腔镜电切术联合 LNG-IUS 治疗子宫内膜息肉的疗效,以期临床治疗提供参考。

1 对象与方法

1.1 研究对象

选取 2016 年 4 月到 2018 年 4 月期间我院收治的子宫内膜息肉患者 98 例,纳入标准:(1)病理证实为子宫内膜息肉,超声提示子宫内膜息肉,双侧附件无异常;(2)均符合手术指征,手术操作由同一组医师团队完成;(3)自愿参与本次研究,并签署知情同意书;(4)均完成随访;(5)对本次研究所用药物耐受。排除标准:(1)全身或内外生殖器官器质性病变导致的子宫异常出血者;(2)伴其他子宫内膜疾病者;(3)子宫畸形者;(4)伴精神性疾病者;(5)术前合并盆腔急性或亚急性炎;(6)合并严重糖尿病、高血压或重要器官功能不全等内科慢性疾病者。本研究经我院伦理委员会批准。采用随机分层抽样法将患者分为对照组与联合组,各 49 例。对照组与联合组一般资料对比无显著差异($P>0.05$),见表 1。

表 1 两组患者一般资料对比
Table 1 Comparison of general data between the two groups

Groups	n	Age(years)	Disease course (days)	Disease type		Body mass index (kg/m ²)
				Single shot	Multiple	
Control group	49	36.49± 5.17	24.38± 1.02	28	21	23.97± 1.15
Combined group	49	36.12± 4.96	24.43± 1.13	30	19	24.19± 1.37
χ^2/t	-	0.362	0.230	0.168		0.861
P	-	0.719	0.819	0.861		0.391

1.2 方法

均实施宫腔镜电切术。步骤:取膀胱截石位,腰硬联合麻醉,将宫颈扩张至 7 号,选用生理盐水作为膨宫液,设置电凝、双极汽化电切功率均为 70 W,膨宫压力维持在 80~100 mmHg。探查宫腔内部,了解息肉的位置、数目及大小,沿着息肉蒂部进行切割,切除组织送病理诊断。联合组在对照组的基础上于术后第一次月经来潮时第 4~7 d 置入 LNG-IUS [批准文号 H20140237, Bayer Oy, 规格:含左炔诺孕酮 52 mg/ 个(20 微克/24 小时)],通过探针对宫腔深度进行测量,当宫腔深度不超过 90 mm 时则将 LNG-IUS 置于宫底,经 B 超检测位置是否正确。

1.3 评价指标

(1)记录两组术前、术后 6 个月的月经周期、月经量、子宫内膜厚度。月经量嘱患者使用相同品牌及规格的卫生巾,通过月经失血图法记录。子宫内膜厚度行超声测量时记录。(2)记录两组术前、术后 6 个月的性激素、炎症因子水平,于上述时间段抽取患者空腹肘静脉血 4 mL,室温下静置 30 min,经常规离心处理(3600 r/min 离心 12 min,离心半径 16 cm)分离上清液,置于 -30℃ 冰箱中待测。应用电化学发光法检测卵泡生成激素(FSH)、黄体生成激素(LH)、雌二醇(E2),应用酶联免疫吸附试验法检测白介素-4(IL-4)、白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、C 反应蛋白(CRP)水平,试剂盒分别购自北京拜尔迪生物技术有限公司、上海桑戈生物工程有限公司,严格遵守试剂盒说明书步骤进行检测。(3)记录两组术后不良反应发生率。(4)对所有患者随访 2 年,随访方式为门诊复查。以宫腔镜

检查结果为标准,比较两组复发率。复发标准为子宫内膜息肉重新出现。

1.4 统计学方法

采用 SPSS19.0 统计学软件分析数据,以比或率的形式表示计数资料,经 χ^2 检验处理,以($\bar{x} \pm s$)的形式表示计量资料,经 t 检验处理,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组月经周期、月经量、子宫内膜厚度比较

两组术前月经周期、月经量、子宫内膜厚度比较无差异($P>0.05$),术后 6 个月,两组月经周期、月经量、子宫内膜厚度均较术前降低,且联合组低于对照组($P<0.05$),见表 2。

2.2 两组性激素水平比较

两组术前、术后 6 个月 FSH、LH、E2 比较无显著性差异($P>0.05$),见表 3。

2.3 两组炎症因子水平比较

两组术前 IL-4、IL-6、TNF- α 、CRP 比较无显著性差异($P>0.05$),术后 6 个月,两组 IL-6、TNF- α 、CRP 均较术前降低,且联合组低于对照组($P<0.05$),IL-4 升高,且联合组高于对照组($P<0.05$),见表 4。

2.4 两组不良反应发生率比较

两组不良反应发生率对比未见显著性差异($P>0.05$),见表 5。

表 2 两组月经周期、月经量、子宫内膜厚度比较($\bar{x} \pm s$)Table 2 Comparison of menstrual cycle, menstrual volume and endometrial thickness between the two groups($\bar{x} \pm s$)

Groups	Menstrual cycle (d)		Menstrual volume (mL)		Endometrial thickness (mm)	
	Before operation	6 months after operation	Before operation	6 months after operation	Before operation	6 months after operation
Control group (n=49)	9.54 $\pm$ 1.09	7.23 $\pm$ 1.84*	368.89 $\pm$ 21.34	263.54 $\pm$ 19.41*	11.45 $\pm$ 1.38	8.39 $\pm$ 1.31*
Combined group (n=49)	9.48 $\pm$ 1.25	5.11 $\pm$ 1.63*	367.75 $\pm$ 20.49	194.28 $\pm$ 15.33*	11.49 $\pm$ 1.42	5.46 $\pm$ 1.25*
t	0.253	6.037	0.270	19.602	0.141	11.327
P	0.801	0.000	0.788	0.000	0.888	0.000

Note: compared with before operation, * $P < 0.05$.表 3 两组性激素水平比较($\bar{x} \pm s$)Table 3 Comparison of levels of sex hormones between the two groups($\bar{x} \pm s$)

Groups	FSH (IU/mL)		LH (IU/mL)		E2 (pg/mL)	
	Before operation	6 months after operation	Before operation	6 months after operation	Before operation	6 months after operation
Control group (n=49)	5.45 $\pm$ 0.78	5.49 $\pm$ 0.84	6.23 $\pm$ 0.43	6.28 $\pm$ 0.55	92.53 $\pm$ 5.24	92.67 $\pm$ 6.26
Combined group (n=49)	5.43 $\pm$ 0.69	5.52 $\pm$ 0.73	6.27 $\pm$ 0.39	6.31 $\pm$ 0.69	92.59 $\pm$ 6.37	92.72 $\pm$ 8.35
t	0.134	0.189	0.482	0.238	0.051	0.034
P	0.893	0.851	0.631	0.831	0.979	0.973

表 4 两组炎症因子水平比较($\bar{x} \pm s$)Table 4 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	IL-4 (ng/L)		IL-6 (ng/L)		TNF- α (ng/L)		CRP (mg/L)	
	Before operation	6 months after operation	Before operation	6 months after operation	Before operation	6 months after operation	Before operation	6 months after operation
Control group (n=49)	53.54 $\pm$ 7.09	74.23 $\pm$ 9.84*	418.89 $\pm$ 29.34	326.54 $\pm$ 36.41*	66.45 $\pm$ 5.38	42.39 $\pm$ 4.31*	26.45 $\pm$ 3.38	18.59 $\pm$ 3.31*
Combined group (n=49)	53.36 $\pm$ 6.96	90.51 $\pm$ 7.63*	418.05 $\pm$ 33.49	261.28 $\pm$ 35.32*	66.81 $\pm$ 5.42	31.46 $\pm$ 5.35*	26.23 $\pm$ 4.40	12.18 $\pm$ 3.24*
t	0.127	9.152	0.132	9.006	0.330	11.137	0.278	9.687
P	0.899	0.000	0.895	0.000	0.742	0.000	0.782	0.000

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

表 5 两组不良反应发生率比较 例 (%)

Table 5 Comparison of the incidence of adverse reactions between the two groups n (%)

Groups	Infected	Vaginal bleeding	Intrauterine adhesions	Total incidence rate
Control group (n=49)	3 (6.12)	2 (4.08)	2 (4.08)	7 (14.29)
Combined group (n=49)	2 (4.08)	3 (6.12)	1 (2.04)	6 (12.24)
χ^2				0.089
P				0.766

2.5 两组复发率比较

两组均随访 2 年,对照组中有 9 例复发,复发率为 18.37% (9/49);联合组中有 2 例复发,复发率为 4.08% (2/49);联合组复发率低于对照组($\chi^2=5.018, P=0.012$)。

3 讨论

子宫内膜息肉的病因目前尚无定论,考虑其发病与局部内膜炎症、内分泌紊乱、雌激素水平升高等因素存在密切联系,且与遗传、炎症刺激等因素也有一定关联^[11-13]。上述因素相互作用于子宫内膜,引起子宫内膜增殖过多,最后发展为有蒂肉质瘤体,单发较小的子宫内膜息肉可无临床症状,大型息肉或突入颈管的息肉,易继发感染、坏死,引起患者不孕症,且随病情发

展,存在恶变的风险,严重影响患者生命健康^[14-16]。宫腔镜是诊断子宫内膜息肉的"金标准",宫腔镜电切术是子宫内膜息肉患者的首选治疗手段,宫腔镜下手术可直接观察到子宫内膜息肉的大小、位置、形态及其与周围组织间的联系,切除位置能达到患者的息肉基底部,可准确切除息肉,避免伤及子宫内膜周围正常组织^[17-19]。同时宫腔镜电切术中采用环形电极电切内膜息肉,可有效降低手术创伤^[20]。尽管宫腔镜电切术优势显著,但由于子宫内膜自身具备再生功能,手术仅仅只能切除已存在的息肉、周围内膜,无法从根本上改变子宫内环境,并未彻底对子宫内膜息肉的致病因素进行干预,故术后仍存在复发可能^[21]。

为提高手术疗效,降低术后复发,我院对收治的子宫内膜息肉患者在宫腔镜电切术的基础上联合 LNG-IUS 治疗,结果显示,术后 6 个月,联合组子宫内膜厚度小于对照组,月经量、月经周期少于对照组,与张蓉等学者^[22]的研究结果基本相似。LNG-IUS 是一种 T 型宫内节育器,有效期长达 5 年,含有 52 mg 左炔诺孕酮,置于人体后可持续释放左炔诺孕酮药物,使得左炔诺孕酮在局部子宫内膜中的浓度提升,提高患者体内孕酮含量,促进子宫内膜萎缩、蜕膜化,阻止其进一步增生,发挥长久避孕的效果,有效调节月经周期^[23-25]。同时,LNG-IUS 还可作用于子宫内膜的间质、腺体,增强子宫肌层收缩功能,萎缩子宫内膜组织,缩小子宫内膜厚度^[26]。此外,左炔诺孕酮可启动内源、外源两种凝血路径,减少月经量^[27]。通过比较两组复发率可知,联合组复发率低于对照组,且两组性激素水平无明显差异,再一次证实宫腔镜电切术联合 LNG-IUS 治疗可有效改善患者预后,且对机体性激素影响较轻。进一步深入分析宫腔镜电切术联合 LNG-IUS 治疗的作用机制,既往研究结果显示^[28],子宫内膜息肉患者体内存在较强的炎症反应,炎症反应在该病发生、发展过程中发挥重要作用。IL-6 是促溶酶体酶及超氧化物释放的炎症因子,IL-4 是抗炎症细胞因子,二者失衡可体现机体炎症病理损伤程度;CRP 是一种急性时相反应蛋白,扩大炎症级联化;TNF- α 可促进多种白细胞介素的释放及 IL-6、CRP 的合成。本研究中联合组的 IL-4、IL-6、TNF- α 、CRP 等指标水平改善效果明显优于对照组,可能是因为 LNG-IUS 可减少血管形成,萎缩子宫内膜组织,从而抑制增生内膜组织释放炎症因子,而炎症因子水平的降低又可促使疾病往良性方向发展进展,促进患者转归^[29]。本研究中两组不良反应发生率对比无差异,而马鸿云等学者^[30]报道却显示,宫腔镜电切术联合 LNG-IUS 治疗可有效降低子宫内膜息肉患者的不良反应发生率。与本次研究结果存在一定的差异,可能与两项研究样本量及患者病情存在差异有关,后续研究中将采取增加样本量,增加不同病情患者分组的措施以期获取更为准确的数据。

综上所述,宫腔镜电切术联合 LNG-IUS 治疗子宫内膜息肉患者,可有效阻止息肉生长,安全性高,且不易复发,对性激素水平影响较小,其作用机制可能与抑制炎症反应有关。

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