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## 宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连的临床研究 \*

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**摘要 目的:**探讨宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连的效果及对患者子宫内膜血流参数和血清基质金属蛋白酶-9(MMP-9)、转化生长因子- $\beta$ 1(TGF- $\beta$ 1)水平的影响。**方法:**选取 2017 年 3 月至 2019 年 3 月我院收治的宫腔粘连患者 106 例进行前瞻性随机对照研究,以随机数字表法将患者分为研究组( $n=53$ )和对照组( $n=53$ )。两组均采取宫腔镜下冷刀分离术,对照组术后置入 COOK 球囊,并在术后当天给予人工周期治疗,研究组在对照组基础上予以 P8 仿生物电刺激辅助治疗,均治疗 3 个月。对比两组疗效、月经改善情况、治疗后 1 年妊娠情况、粘连复发情况和治疗前、治疗 1 个月后、3 个月后粘连评分、子宫内膜容积、子宫内膜厚度、子宫内膜血流参数[阻力指数(RI)、搏动指数(PI)]、血清 MMP-9、TGF- $\beta$ 1 水平。**结果:**研究组治疗 3 个月后总有效率、月经改善率分别为 92.45%、94.34%,高于对照组的 75.47%、79.25%( $P<0.05$ );研究组治疗 1 个月后、3 个月后粘连评分和 RI、PI 低于对照组,子宫内膜容积、子宫内膜厚度高于对照组( $P<0.05$ );研究组治疗 1 个月后、3 个月后血清 MMP-9 水平高于对照组, TGF- $\beta$ 1 水平低于对照组( $P<0.05$ );研究组治疗后 1 年妊娠率 44.23%高于对照组 25.00%,粘连复发率 15.38%低于对照组 32.69%( $P<0.05$ )。**结论:**宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连可减轻宫腔粘连程度,改善子宫内膜容积、厚度、血流情况,调节血清 MMP-9、TGF- $\beta$ 1 表达,改善月经情况,进而提高疗效和妊娠率,减少粘连复发。

**关键词:**宫腔镜下冷刀分离术;P8 仿生物电刺激;宫腔粘连;血流参数;MMP-9;TGF- $\beta$ 1

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## Clinical Study of p8 Biomimetic Electrical Stimulation in Adjuvant Treatment of Intrauterine Adhesions after Hysteroscopic Cold Knife Separation\*

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**ABSTRACT Objective:** To investigate the effect of P8 biomimetic electrical stimulation for adjuvant treatment of intrauterine adhesions after hysteroscopic cold knife separation and its influence on endometrial blood flow parameters and the levels of serum matrix metalloproteinase-9 (MMP-9), and transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1). **Methods:** 106 patients with intrauterine adhesions in our hospital from March 2017 to March 2019 were selected for prospective randomized controlled study. The patients were divided into study group ( $n=53$ ) and control group ( $n=53$ ) by random number table. Both groups underwent hysteroscopic cold knife separation. The control group was implanted with a COOK balloon after operation, and was given artificial cycle treatment on the day after operation. The study group was given P8 biomimetic electrical stimulation for adjuvant treatment on the basis of the control group, all of them were treated for 3 months. The efficacy, menstrual improvement, pregnancy status, adhesion recurrence at 1 year after treatment, adhesion score, endometrial volume, endometrial thickness, endometrial blood flow parameters [resistance index (RI), pulse index (PI)], serum MMP-9, TGF- $\beta$ 1 levels before treatment, 1 month after treatment and 3 months after treatment were compared between the two groups. **Results:** The total effective rate and menstrual improvement rate in the study group at 3 months after treatment were 92.45% and 94.34%, respectively, which were higher than 75.47% and 79.25% in the control group ( $P<0.05$ ). The adhesion score and RI, PI in the study group were lower than those in the control group at 1 month and 3 months after treatment, and the endometrial volume, endometrial thickness were higher than those in the control group ( $P<0.05$ ). The level of serum MMP-9 in the study group was higher than that in the control group at 1 month and 3 months after treatment, and the level of TGF- $\beta$ 1 was lower than that in the control group ( $P<0.05$ ). The pregnancy rate at 1 year after treatment in the study group was 44.23% higher than 25.00% in the control group, and the adhesion recurrence rate was 15.38% lower than 32.69% in the control group ( $P<0.05$ ). **Conclusion:** P8 biomimetic electrical stimulation for adjuvant treatment of intrauterine adhesions after hysteroscopic cold knife separation can reduce the degree of intrauterine adhesions, and improve the volume, thickness and blood flow of the endometrium, regulate the expression of serum MMP-9, TGF- $\beta$ 1, improve menstruation status, and fur-

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ther improve the efficacy and pregnancy rate, and reduce the recurrence of adhesions.

**Key words:** Hysteroscopic cold knife separation; P8 biomimetic electrical stimulation; Intrauterine adhesions; Blood flow parameters; MMP-9; TGF- $\beta$ 1

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## 前言

宫腔粘连是由于多种因素导致子宫内膜基底层受损,引起宫腔与宫颈间相互黏附,产生局部或者完全粘连的病症,患者临床表现为月经减少或闭经、下腹痛、继发性不孕等,影响适龄女性生育功能与生活质量<sup>[1-3]</sup>。宫腔镜下冷刀分离术为治疗宫腔粘连的有效术式,但研究报道表明,中重度宫腔粘连患者应用宫腔镜下宫腔粘连分离术后再粘连风险高,虽然能够恢复宫腔容积与解剖学形态,一定程度改善、修复子宫内膜,但患者术后受孕率低,妊娠成功率仅 22.5%~33.3%<sup>[4]</sup>。如何改善患者生殖预后、减少术后粘连复发一直是临床工作的研究重点。近期,有研究报道显示,对薄型子宫内膜应用电刺激治疗可明显增加子宫内膜厚度,改善子宫内膜血流灌注,提高预后妊娠率<sup>[5]</sup>,但电

刺激对由于粘连瘢痕、创伤造成的薄型子宫内膜的适用性尚不明确。本研究通过随机对照研究,首次分析宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连的效果及对患者子宫内膜血流参数和血清基质金属蛋白酶-9(MMP-9)、转化生长因子- $\beta$ 1(TGF- $\beta$ 1)的影响,现报道如下。

## 1 资料及方法

### 1.1 一般资料

选取 2017 年 3 月至 2019 年 3 月我院宫腔粘连患者 106 例进行前瞻性随机对照研究,以随机数字表法将患者分为研究组( $n=53$ )和对照组( $n=53$ )。两组一般资料(年龄、体质量指数(BMI)、孕次、月经改变时间、宫腔粘连程度、合并不孕症比例)均衡可比( $P>0.05$ ),见表 1。本研究经我院伦理委员会同意。

表 1 两组一般资料比较

Table 1 Comparison of general data between the two groups

| General dataeas                     | Study group( $n=53$ ) | Control group( $n=53$ ) | $t/\chi^2$ | $P$   |
|-------------------------------------|-----------------------|-------------------------|------------|-------|
| Age(years)                          | 27.72 $\pm$ 3.58      | 28.39 $\pm$ 3.26        | 1.007      | 0.316 |
| BMI(kg/m <sup>2</sup> )             | 20.48 $\pm$ 1.15      | 20.76 $\pm$ 1.34        | 1.154      | 0.251 |
| Pregnancies(times)                  | 2.64 $\pm$ 0.36       | 2.71 $\pm$ 0.28         | 1.117      | 0.266 |
| Change time of menstruation(months) | 12.75 $\pm$ 5.40      | 13.62 $\pm$ 5.86        | 0.795      | 0.429 |
| Degree of intrauterine adhesions(%) |                       |                         |            |       |
| Severe                              | 31(58.49)             | 29(54.72)               | 0.154      | 0.695 |
| Moderate                            | 22(41.51)             | 24(45.28)               |            |       |
| Combined with infertility(%)        | 41(77.36)             | 40(75.47)               | 0.052      | 0.819 |

### 1.2 纳入和排除标准

纳入标准:(1)经宫腔镜确诊为宫腔粘连;(2)宫腔粘连程度为中、重度;(3)存在刮宫术或其他宫腔操作手术史;(4)存在继发性闭经或者月经过少;(5)年龄 $<40$ 岁,有生育需求;(6)性生活正常;(7)排卵与性激素水平正常;(8)知晓本研究方案,签订知情同意书。排除标准:(1)由于男方因素导致不孕;(2)合并子宫畸形、子宫腺肌病、子宫肌瘤;(3)合并血栓性疾病、凝血功能异常、糖尿病;(4)合并肝、心、肾等脏器功能严重障碍;(5)合并生殖道畸形、炎症;(6)由于下丘脑性、垂体性、卵巢性造成的闭经;(7)乳腺超声检查示存在异常结节。

### 1.3 治疗方法

两组均采取宫腔镜下冷刀分离术,全麻或腰硬联合麻醉,膀胱截石位,常规消毒铺巾;以探针了解宫腔方向、深度,将宫腔镜置入宫腔,观察子宫情况,发现粘连后利用冷刀分离粘连。对照组术后置入 COOK 球囊,在球囊内注射 2 mL 生理盐水,术后 1 周取出球囊,并在术后当天给予人工周期治疗,予以戊酸雌二醇(法国 DELPHARM Lille S.A.S.,批准文号

J20171038)2 mg/次,2 次/d,连续服用 21 d,后 10 d(即第 12~21 d)加用地屈孕酮(荷兰 Abbott Biologicals B.V.,批准文号 H20170221)10 mg/次,2 次/d,停药后出现撤退性出血;在下次月经第 5 d 起重复以上人工周期用药治疗,连续治疗 3 个月。研究组在对照组基础上予以 P8 仿生物电刺激辅助治疗:以法国 VIVALNS 公司生产的 P8 仿生物电刺激治疗仪进行治疗,将放置于体部电极与阴道探头,分为两个程序,每个程序 20 min,首先为血流动力激活阶段,电流频率 2 Hz,脉冲宽度 3 ms;其次为血流动力加速阶段,电流频率 3 Hz,脉冲宽度 3 ms;具体操作为:患者取膀胱截石位,在阴道中放置探头,体部置平滑肌刺激通道 4 对;刺激点分别是两侧腹股沟、两侧足背血管搏动显著处、耻骨联合上 1 cm 处和对应的腰骶部位置、背部对应位置、脐上 1.5 cm 处各放置两个电极片(规格 5 cm $\times$  5 cm),1 次/d,每次治疗时间为 40 min,视患者耐受与病情状态适当调整,并调节对应刺激通道电流情况,最大电流 $<16$  mA,以有循环、敲打感为宜;在术后每月阴道流血干净后采取连续治疗,共治疗 3 个月。

#### 1.4 观察指标

(1)对比两组疗效,治疗3个月后进行疗效评价<sup>[6]</sup>,月经量较治疗前未见改善或有一定程度改善但粘连复发为无效;月经量明显增加,宫腔形态基本恢复正常,但存在轻微宫腔粘连为有效;月经量与宫腔形态恢复正常,无宫腔粘连为治愈,总有效率=(有效+治愈)/总例数 $\times 100\%$ 。(2)对比两组月经改善情况,月经改善率=(月经增多+闭经恢复)/总例数 $\times 100\%$ 。(3)评价两组治疗前、治疗1个月后、3个月后宫腔粘连程度,依据粘连范围、粘连类型、月经状况进行评分,粘连范围: $>2/3$ 计4分,处于 $1/3\sim 2/3$ 之间计2分, $<1/3$ 计1分;粘连类型:致密肌性计4分,纤维性计2分,薄膜计1分;月经状况:闭经计4分,月经过少计2分,正常计1分,分值越高表明宫腔粘连程度越高<sup>[7]</sup>。(4)记录两组治疗前、治疗1个月后、3个月子宫内腔容积、子宫内膜厚度、子宫内膜血流参数[阻力指数(RI)、搏动指数(PI)],应用阴道超声测定。(5)分别在治疗前、治疗1个月后、3个月后采集患者4 mL清晨空腹静脉血样,应用离心机以

3000 r/min 转速离心 10 min,采集上层血清,放置到  $-20\text{ }^{\circ}\text{C}$  冰箱内冻存待检;应用酶联免疫吸附法测定血清 MMP-9、TGF- $\beta 1$  水平,操作严格按试剂盒说明书进行。(6)治疗后以门诊复查、电话随访等方式随访 1 年,统计两组妊娠情况与粘连复发情况。

#### 1.5 统计学处理

所得数据录入 SPSS21.0 软件处理,计量资料以  $(\bar{x} \pm s)$  表示,组间比较采取独立样本 t 检验,组内比较采取配对 t 检验;计数资料以  $n(\%)$  表示,组间比较采取  $\chi^2$  检验; $P < 0.05$  为差异有统计学意义。

### 2 结果

#### 2.1 疗效比较

研究组治疗3个月后总有效率高于对照组( $P < 0.05$ )。见表2。

#### 2.2 月经改善情况比较

研究组月经改善率高于对照组( $P < 0.05$ )。见表3。

表2 两组疗效比较 [n(%)]

Table 2 Comparison of curative effect between the two groups [n(%)]

| Groups        | n  | Invalid   | Effective | Cure      | Total effective rate |
|---------------|----|-----------|-----------|-----------|----------------------|
| Study group   | 53 | 4(7.55)   | 30(56.60) | 19(35.85) | 49(92.45)            |
| Control group | 53 | 13(24.53) | 28(52.83) | 12(22.64) | 40(75.47)            |
| $\chi^2$      |    |           |           |           | 5.675                |
| $P$           |    |           |           |           | 0.017                |

表3 两组月经改善情况比较 [n(%)]

Table 3 Comparison of menstrual improvement between the two groups [n(%)]

| Groups        | n  | Menstrual   |           | Amenorrhoea |           | Menstrual improvement |
|---------------|----|-------------|-----------|-------------|-----------|-----------------------|
|               |    | No increase | Increase  | No increase | Increase  |                       |
| Study group   | 53 | 3(5.66)     | 37(69.81) | 0(0.00)     | 13(24.53) | 50(94.34)             |
| Control group | 53 | 11(20.75)   | 30(56.60) | 0(0.00)     | 12(22.64) | 42(79.25)             |
| $\chi^2$      |    |             |           |             |           | 5.267                 |
| $P$           |    |             |           |             |           | 0.022                 |

#### 2.3 粘连评分比较

两组治疗前粘连评分相比,差异无统计学意义( $P > 0.05$ );两组治疗后粘连评分均下降,研究组治疗1个月后、3个月后粘连评分低于对照组( $P < 0.05$ )。见表4。

#### 2.4 子宫内腔容积、子宫内膜厚度比较

两组治疗前子宫内腔容积、子宫内膜厚度相比,差异无统计学意义( $P > 0.05$ );两组治疗后子宫内腔容积、子宫内膜厚度均升高,研究组治疗1个月后、3个月后子宫内腔容积、子宫内膜厚度高于对照组( $P < 0.05$ )。见表5。

#### 2.5 子宫内膜血流参数比较

两组治疗前 RI、PI 相比,差异无统计学意义( $P > 0.05$ );两组治疗后 RI、PI 下降,研究组治疗1个月后、3个月后 RI、PI 低于对照组( $P < 0.05$ )。见表6。

#### 2.6 血清 MMP-9、TGF- $\beta 1$ 水平比较

两组治疗前血清 MMP-9、TGF- $\beta 1$  水平相比,差异无统计学意义( $P > 0.05$ );两组治疗后血清 MMP-9、TGF- $\beta 1$  与治疗前比较存在显著性差异( $P < 0.05$ ),研究组治疗1个月后、3个月后血清 MMP-9 水平高于对照组,TGF- $\beta 1$  水平低于对照组( $P < 0.05$ )。见表7。

#### 2.7 妊娠和粘连复发情况比较

经1年随访,研究组、对照组各脱落1例。研究组治疗后1年妊娠率高于对照组,粘连复发率低于对照组( $P < 0.05$ )。见表8。

### 3 讨论

临床对存在月经过少或闭经、不孕症状且有生育需求的宫腔粘连患者常推荐采取手术治疗,治疗目的为促进子宫内膜修复与再生,改善月经与生育功能<sup>[8-10]</sup>。宫腔镜下冷刀分离术为治疗宫腔粘连的首选术式,可针对性分离与切除宫腔粘连,促进

表 4 两组治疗前后的粘连评分比较( $\bar{x} \pm s$ , 分)Table 4 Comparison of adhesion scores between the two groups before and after treatment( $\bar{x} \pm s$ , scores)

| Time                     | Groups        | n  | Adhesion range          | Adhesion type           | Menstruation status     | Total score             |
|--------------------------|---------------|----|-------------------------|-------------------------|-------------------------|-------------------------|
| Before treatment         | Study group   | 53 | 3.59± 0.34              | 3.61± 0.28              | 3.32± 0.35              | 10.52± 1.34             |
|                          | Control group | 53 | 3.63± 0.31              | 3.65± 0.33              | 3.36± 0.39              | 10.64± 1.27             |
|                          | t             |    | 0.633                   | 0.673                   | 0.556                   | 0.473                   |
|                          | P             |    | 0.528                   | 0.503                   | 0.580                   | 0.637                   |
| 1 month after treatment  | Study group   | 53 | 2.42± 0.23 <sup>a</sup> | 2.37± 0.24 <sup>a</sup> | 2.28± 0.26 <sup>a</sup> | 7.08± 1.02 <sup>a</sup> |
|                          | Control group | 53 | 2.75± 0.26 <sup>a</sup> | 2.69± 0.29 <sup>a</sup> | 2.60± 0.31 <sup>a</sup> | 8.04± 1.27 <sup>a</sup> |
|                          | t             |    | 6.921                   | 6.189                   | 5.758                   | 4.291                   |
|                          | P             |    | <0.001                  | <0.001                  | <0.001                  | <0.001                  |
| 3 months after treatment | Study group   | 53 | 1.94± 0.17 <sup>a</sup> | 2.02± 0.15 <sup>a</sup> | 1.83± 0.20 <sup>a</sup> | 5.79± 0.85 <sup>a</sup> |
|                          | Control group | 53 | 2.28± 0.20 <sup>a</sup> | 2.31± 0.18 <sup>a</sup> | 2.14± 0.23 <sup>a</sup> | 6.73± 0.92 <sup>a</sup> |
|                          | t             |    | 9.430                   | 9.011                   | 7.404                   | 5.464                   |
|                          | P             |    | <0.001                  | <0.001                  | <0.001                  | <0.001                  |

Note: Compared with before treatment in this group, <sup>a</sup>P<0.05.表 5 两组治疗前后的子宫内膜容积、子宫内膜厚度比较( $\bar{x} \pm s$ )Table 5 Comparison of endometrial volume and endometrial thickness between the two groups before and after treatment ( $\bar{x} \pm s$ )

| Groups        | n  | Endometrial volume (cm <sup>3</sup> ) |                         |                          | Endometrial thickness (mm) |                         |                          |
|---------------|----|---------------------------------------|-------------------------|--------------------------|----------------------------|-------------------------|--------------------------|
|               |    | Before treatment                      | 1 month after treatment | 3 months after treatment | Before treatment           | 1 month after treatment | 3 months after treatment |
| Study group   | 53 | 1.52± 0.71                            | 3.79± 0.68 <sup>a</sup> | 4.54± 0.61 <sup>a</sup>  | 4.68± 1.09                 | 7.08± 1.30 <sup>a</sup> | 8.34± 1.38 <sup>a</sup>  |
| Control group | 53 | 1.56± 0.75                            | 3.15± 0.77 <sup>a</sup> | 3.58± 0.82 <sup>a</sup>  | 4.74± 1.16                 | 5.70± 1.24 <sup>a</sup> | 6.46± 1.29 <sup>a</sup>  |
| t             |    | 0.282                                 | 4.536                   | 6.838                    | 0.274                      | 5.592                   | 7.245                    |
| P             |    | 0.779                                 | <0.001                  | <0.001                   | 0.784                      | <0.001                  | <0.001                   |

Note: Compared with before treatment in this group, <sup>a</sup>P<0.05.表 6 两组治疗前后子宫内膜血流参数比较( $\bar{x} \pm s$ )Table 6 Comparison of endometrial blood flow parameters between the two groups before and after treatment( $\bar{x} \pm s$ )

| Groups        | n  | RI               |                         |                          | PI               |                         |                          |
|---------------|----|------------------|-------------------------|--------------------------|------------------|-------------------------|--------------------------|
|               |    | Before treatment | 1 month after treatment | 3 months after treatment | Before treatment | 1 month after treatment | 3 months after treatment |
| Study group   | 53 | 0.57± 0.08       | 0.46± 0.06 <sup>a</sup> | 0.41± 0.05 <sup>a</sup>  | 0.93± 0.20       | 0.72± 0.18 <sup>a</sup> | 0.66± 0.14 <sup>a</sup>  |
| Control group | 53 | 0.60± 0.11       | 0.53± 0.08 <sup>a</sup> | 0.47± 0.06 <sup>a</sup>  | 0.95± 0.23       | 0.81± 0.20 <sup>a</sup> | 0.74± 0.17 <sup>a</sup>  |
| t             |    | 1.606            | 5.096                   | 5.593                    | 0.478            | 2.435                   | 2.645                    |
| P             |    | 0.111            | <0.001                  | <0.001                   | 0.634            | 0.017                   | 0.009                    |

Note: Compared with before treatment in this group, <sup>a</sup>P<0.05.表 7 两组治疗前后血清 MMP-9、TGF-β1 水平比较( $\bar{x} \pm s$ )Table 7 Comparison of the levels of serum MMP-9 and TGF-β1 between the two groups before and after treatment( $\bar{x} \pm s$ )

| Groups        | n  | MMP-9 (μg/mL)    |                          |                          | TGF-β1 (μg/L)    |                          |                          |
|---------------|----|------------------|--------------------------|--------------------------|------------------|--------------------------|--------------------------|
|               |    | Before treatment | 1 month after treatment  | 3 months after treatment | Before treatment | 1 month after treatment  | 3 months after treatment |
| Study group   | 53 | 21.02± 2.47      | 46.29± 4.36 <sup>a</sup> | 52.78± 5.48 <sup>a</sup> | 54.72± 6.43      | 37.26± 4.30 <sup>a</sup> | 32.59± 3.75 <sup>a</sup> |
| Control group | 53 | 21.36± 2.61      | 38.95± 3.87 <sup>a</sup> | 43.73± 5.04 <sup>a</sup> | 55.61± 6.25      | 45.27± 5.64 <sup>a</sup> | 38.03± 4.42 <sup>a</sup> |
| t             |    | 0.689            | 9.166                    | 8.849                    | 0.723            | 8.222                    | 6.832                    |
| P             |    | 0.493            | <0.001                   | <0.001                   | 0.472            | <0.001                   | <0.001                   |

Note: Compared with before treatment in this group, <sup>a</sup>P<0.05.

表 8 两组妊娠情况和粘连复发情况比较 [n(%)]

Table 8 Comparison of pregnancy status and adhesion recurrence status between the two groups [n(%)]

| Groups        | n  | Pregnancy status |                   |                 | Adhesion recurrence |
|---------------|----|------------------|-------------------|-----------------|---------------------|
|               |    | IVF-ET pregnancy | Natural pregnancy | Total pregnancy |                     |
| Study group   | 52 | 8(15.38)         | 15(28.85)         | 23(44.23)       | 8(15.38)            |
| Control group | 52 | 5(9.62)          | 8(15.38)          | 13(25.00)       | 17(32.69)           |
| $\chi^2$      |    |                  | 4.248             |                 | 4.265               |
| P             |    |                  | 0.039             |                 | 0.039               |

Note: exfoliation cases have been excluded.

子宫正常形态恢复,改善月经过少或闭经情况,促进预后妊娠,且术中应用的冷刀操作系统可防止内膜热损伤,降低电切术后创面渗血,对正常内膜的损伤相对较小<sup>[11-13]</sup>。但有研究报道指出,单纯应用宫腔镜下宫腔粘连分离术治疗无法修复损伤子宫内膜,术后粘连复发风险较高,且预后妊娠情况仍需进一步改善<sup>[14-16]</sup>。

宫腔粘连术后预防粘连复发的措施包括宫腔支撑球囊、雌激素等<sup>[17-19]</sup>,研究证实,在宫腔镜下宫腔粘连分离术后应用 COOK 球囊结合雌孕激素序贯人工周期治疗能够显著改善月经情况,降低再粘连风险<sup>[20]</sup>。本研究中对照组术后应用 COOK 球囊辅助人工周期治疗,患者月经改善率为 79.25%,与侯安丽<sup>[20]</sup>等人的研究相近。分析原因,COOK 球囊的置入可有效隔离宫腔创面贴附,引流宫腔中渗血渗液,有利于月经、宫腔形态改善,且人工周期治疗能改善雌激素表达,调节月经状况,一定程度改善妊娠情况<sup>[21-23]</sup>。

宫腔粘连术后粘连复发、妊娠情况与子宫内面积密切相关,有效增加子宫内面积避免粘连复发、改善妊娠率的重要途径<sup>[24-26]</sup>。电刺激疗法为一种物理治疗手段,曾彩霞<sup>[27]</sup>研究证实,对宫腔粘连患者在人工周期基础上联合盆底肌肉电刺激治疗后总有效率达 91.84%,且可有效改善子宫内厚度,减少复发率。本研究发现,研究组治疗 3 个月后总有效率、月经改善率达 92.45%、94.34%,且治疗 1 个月后、3 个月后粘连评分、RI、PI 和治疗后 1 年粘连复发率低于对照组,子宫内厚度、子宫内厚度和治疗后 1 年妊娠率高于对照组。表明应用宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连可减轻宫腔粘连程度,改善子宫内厚度、厚度、血流及月经情况,进而提高疗效和妊娠率,减少粘连复发。考虑原因为 P8 仿生物电刺激可刺激盆底和盆腔血管平滑肌松弛、收缩,促进盆腔血液循环与淋巴回流,阻止成纤维细胞与胶原纤维产生,抑制细胞外基质沉积,减少粘连复发,并可改善子宫与卵巢血液循环,增加子宫内厚度,加速子宫内厚度修复与生长,增加子宫内厚度,提高子宫内厚度容受性,为胚胎着床提供有利微环境,提升疗效和妊娠率<sup>[28]</sup>;此外,基础实验研究指出,电刺激治疗也能调节性激素水平,改善卵巢发育状况<sup>[29]</sup>。

有关研究报道指出,子宫内厚度受损后血清 MMP-9、TGF- $\beta$ 1 异常表达可加速子宫内厚度纤维化,阻止子宫内厚度增长,加剧宫腔粘连情况<sup>[30-32]</sup>。本研究发现,研究组治疗 1 个月后、3 个月后血清 MMP-9 水平高于对照组,TGF- $\beta$ 1 水平低于对照组。表明宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连可调节血清 MMP-9、TGF- $\beta$ 1 表达,也从侧面证实应用该方案治

疗可促进子宫内厚度修复、生长。推测原因与应用 P8 仿生物电刺激治疗可调节雌激素受体水平,一定程度调节 MMP-9、TGF- $\beta$ 1 在子宫内厚度腺上皮细胞与间质细胞中表达有关,但具体机制仍有待进一步探讨。

综上所述,宫腔镜下冷刀分离术后 P8 仿生物电刺激辅助治疗宫腔粘连可降低宫腔粘连程度,改善子宫内厚度容受性、厚度、血流情况,调节血清 MMP-9、TGF- $\beta$ 1 表达,促进月经恢复,进而提升疗效和妊娠率,减少粘连复发。

#### 参考文献(References)

- [1] Cao M, Pan Y, Zhang Q, et al. Predictive value of live birth rate based on different intrauterine adhesion evaluation systems following TCRA[J]. *Reprod Biol Endocrinol*, 2021, 19(1): 13
- [2] Abbott J, Deans R. Accelerating the Science After 125 Years of Treating Intrauterine Adhesions [J]. *J Minim Invasive Gynecol*, 2021, 28(2): 151-152
- [3] Cheng M, Chang WH, Yang ST, et al. Efficacy of Applying Hyaluronic Acid Gels in the Primary Prevention of Intrauterine Adhesion after Hysteroscopic Myomectomy: A Meta-Analysis of Randomized Controlled Trials[J]. *Life (Basel)*, 2020, 10(11): 285
- [4] 刘嘉, 司景革, 齐歆, 等. 宫腔镜下宫腔粘连分离术后患者妊娠情况调查分析[J]. *临床和实验医学杂志*, 2018, 17(2): 203-206
- [5] 葛伟平, 楚蔚昕, 陈龙, 等. PHENIX 8 仿生物电刺激治疗薄型子宫内厚度临床研究[J]. *中国计划生育和妇产科*, 2019, 11(4): 78-81
- [6] 胡丽莉, 杨菁, 闫文杰, 等. 中重度宫腔粘连宫腔镜术后低频神经治疗仪辅助治疗效果观察 [J]. *武汉大学学报 (医学版)*, 2018, 39(5): 826-829
- [7] 汤懿懿, 刘恒炼, 白殊同, 等. 补肾活血方联合宫腔灌注治疗对宫腔粘连相关机制 TGF- $\beta$ 1、Smad2 和 Smad3 的影响分析[J]. *重庆医科大学学报*, 2020, 45(5): 660-666
- [8] Chawla L, Prateek S, Bahadur A, et al. Intrauterine adhesions with secondary amenorrhea: A notable indicator of endometrial tuberculosis [J]. *Indian J Tuberc*, 2020, 67(4): 575-577
- [9] Lee DY, Lee SR, Kim SK, et al. A New Thermo-Responsive Hyaluronic Acid Sol-Gel to Prevent Intrauterine Adhesions after Hysteroscopic Surgery: A Randomized, Non-Inferiority Trial [J]. *Yonsei Med J*, 2020, 61(10): 868-874
- [10] 马晓旻, 郑萍, 卢丹, 等. 不同剂量戊酸雌二醇治疗宫腔粘连的临床效果[J]. *现代生物医学进展*, 2015, 15(30): 5886-5888
- [11] Li C, Cong L, Wang W. Two cases of larger cornual residual villi, treated by the hysteroscopic cold knife [J]. *J Obstet Gynaecol Res*, 2020, 46(11): 2430-2434
- [12] 汪期明, 史春波. 宫腔镜下冷刀分离联合 COOK 球囊治疗中重度

- 宫腔粘连的临床效果[J]. 现代实用医学, 2020, 32(7): 816-819
- [13] Lavie M, Shamir-Kaholi N, Lavie I, et al. Outcomes of ultrasound and physical-exam based cerclage: assessment of risk factors and the role of adjunctive progesterone in preventing preterm birth-a retrospective cohort study[J]. Arch Gynecol Obstet, 2020, 301(4): 981-986
- [14] 李莉, 王敏. 阿司匹林联合芬吗通对重度宫腔粘连术后预后的影响[J]. 河北医科大学学报, 2020, 41(2): 158-162
- [15] 张晓兴, 陈云燕. 宫腔粘连分离术后不同方法预防再粘连的效果[J]. 江苏医药, 2018, 44(3): 348-349
- [16] 陈欢, 洛若愚, 李梦如, 等. 不同方法在宫腔粘连分离术后的治疗疗效分析[J]. 中国性科学, 2018, 27(8): 58-62
- [17] Wei C, Pan Y, Zhang Y, et al. Overactivated sonic hedgehog signaling aggravates intrauterine adhesion via inhibiting autophagy in endometrial stromal cells[J]. Cell Death Dis, 2020, 11(9): 755
- [18] Ma H, Liu M, Li Y, et al. Intrauterine transplantation of autologous menstrual blood stem cells increases endometrial thickness and pregnancy potential in patients with refractory intrauterine adhesion [J]. J Obstet Gynaecol Res, 2020, 46(11): 2347-2355
- [19] Xiao Y. CircPlekha7 plays an anti-fibrotic role in intrauterine adhesions by modulating endometrial stromal cell proliferation and apoptosis[J]. J Reprod Dev, 2020, 66(6): 493-504
- [20] 侯安丽, 刘慧兰, 周秀英. COOK 球囊联合雌孕激素序贯治疗预防宫腔镜下宫腔粘连分离术后宫腔再粘连的临床效果观察[J]. 实用妇产科杂志, 2019, 35(8): 601-604
- [21] Du H, Zhang N, Xiao CY, et al. Effectiveness of Dinoprostone and Cook's Balloon for Labor Induction in Primipara Women at Term[J]. Curr Med Sci, 2020, 40(5): 951-959
- [22] Duro-Gómez J, Garrido-Oyarzún MF, Rodríguez-Marín AB, et al. Efficacy and safety of misoprostol, dinoprostone and Cook's balloon for labour induction in women with foetal growth restriction at term[J]. Arch Gynecol Obstet, 2017, 296(4): 777-781
- [23] 曾薇薇, 苏圣梅, 阎恺, 等. COOK 球囊放置时长对重度宫腔粘连疗效的影响[J]. 医学研究生学报, 2020, 33(6): 618-622
- [24] Zhou Q, Shi X, Saravelos S, et al. Auto-Cross-Linked Hyaluronic Acid Gel for Prevention of Intrauterine Adhesions after Hysteroscopic Adhesiolysis: A Randomized Controlled Trial [J]. J Minim Invasive Gynecol, 2021, 28(2): 307-313
- [25] Wang YQ, Song XH, Wu SL, et al. Comparison of Autocross-Linked Hyaluronic Acid Gel and Intrauterine Device for Preventing Intrauterine Adhesions in Infertile Patients: A Randomized Clinical Trial[J]. Gynecol Minim Invasive Ther, 2020, 9(2): 74-80
- [26] Zhang LP, Wang M, Shang X, et al. The incidence of placenta related disease after the hysteroscopic adhesiolysis in patients with intrauterine adhesions[J]. Taiwan J Obstet Gynecol, 2020, 59(4): 575-579
- [27] 曾彩霞. 人工周期联合盆底肌肉电刺激治疗轻中度宫腔粘连的临床效果[J]. 中国现代药物应用, 2020, 14(12): 63-65
- [28] 韦红兰, 林忠, 吴秀芬, 等. P8 仿生物电刺激联合球囊子宫支架对中、重度宫腔粘连患者术后的疗效研究 [J]. 广西医科大学学报, 2020, 37(1): 72-77
- [29] 周建勇, 张小月, 于美玲, 等. 经皮穴位电刺激对多囊卵巢综合征大鼠激素及卵巢甾体激素代谢酶表达的影响 [J]. 针刺研究, 2016, 41(01): 11-17
- [30] Chen JX, Yi XJ, Gu PL, et al. The role of KDR in intrauterine adhesions may involve the TGF- $\beta$ 1/Smads signaling pathway [J]. Braz J Med Biol Res, 2019, 52(10): e8324
- [31] Liu L, Yang H, Guo Y, et al. The impact of chronic endometritis on endometrial fibrosis and reproductive prognosis in patients with moderate and severe intrauterine adhesions: a prospective cohort study[J]. Fertil Steril, 2019, 111(5): 1002-1010.e2
- [32] 徐新亚, 张科群. 补肾逐瘀汤对宫腔粘连分离术后肾虚血瘀证患者的疗效及对 TGF- $\beta$ 1、PAI-1、MMP-9 水平的影响 [J]. 中药材, 2019, 42(1): 222-225

(上接第 1945 页)

- [25] Schaefer B, Behrends S. Translocation of heme oxygenase-1 contributes to imatinib resistance in chronic myelogenous leukemia[J]. Oncotarget, 2017, 8(40): 67406-67421
- [26] Schillingmann DA, Riese SB, Vijayan V, et al. Inhibition of Heme Oxygenase-1 Activity Enhances Wilms Tumor-1-Specific T-Cell Responses in Cancer Immunotherapy [J]. Int J Mol Sci, 2019, 20(3): 113-119
- [27] Varol F, Uzunoğlu R, Erbaş H, et al. VEGFR-1, Bcl-2, and HO-1 Ratios in Pregnant Women With Hypertension [J]. Clin Appl Thromb Hemost, 2015, 21(3): 285-288
- [28] Zhe N, Chen S, Zhou Z, et al. HIF-1 $\alpha$  inhibition by 2-methoxyestradiol induces cell death via activation of the mitochondrial apoptotic pathway in acute myeloid leukemia[J]. Cancer Biol Ther, 2016, 17(6): 625-634
- [29] Hörl S, Banki Z, Huber G, et al. Complement factor H-derived short consensus repeat 18-20 enhanced complement-dependent cytotoxicity of ofatumumab on chronic lymphocytic leukemia cells [J]. Haematologica, 2013, 98(12): 1939-1947
- [30] Oostindie SC, Van Der Horst HJ, Lindorfer MA, et al. CD20 and CD37 antibodies synergize to activate complement by Fc-mediated clustering[J]. Haematologica, 2019, 104(9): 1841-1852