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不同治疗方案治疗瘢痕部位妊娠的临床疗效分析 *

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摘要 目的:探讨不同治疗方案治疗瘢痕部位妊娠(CSP)的临床疗效。**方法:**选取2010年1月至2017年9月西安交通大学第一附属医院妇产科收治的CSP患者89例,按治疗方案不同分为A、B、C三组。A组患者19例,采用药物甲氨蝶呤保守治疗;B组患者30例,行B超引导下人工流产术治疗;C组患者40例,行子宫动脉栓塞术联合清宫术治疗。比较三组患者的阴道出血情况以及治疗效果。**结果:**C组患者治愈率最高、血清β-HCG恢复至正常时间最短、治疗后阴道出血量最少,其次为B组,最后是A组,差异具有统计学意义($P<0.05$);治疗后第4d、7d,B、C两组血清β-HCG下降幅度显著高于A组($P<0.05$),尤其是C组在治疗后第7d的下降幅度最大;B组患者住院时间及住院费用均低于C组及A组,但输血率高,差异具有统计学意义($P<0.05$)。**结论:**子宫动脉栓塞术联合清宫术治疗CSP具有治愈率高、损伤小、术后恢复快等优势,在经济情况允许的情况下其临床疗效最佳。

关键词:瘢痕部位妊娠;甲氨蝶呤;人工流产术;清宫术;子宫动脉栓塞术;疗效

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Clinical Effect Analysis of Different Treatment Regimens in Treatment of Scar Site Pregnancy*

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ABSTRACT Objective: To investigate the clinical efficacy of different treatment regimens in the treatment of scar site pregnancy (CSP). **Methods:** A total of 89 patients with CSP, who were admitted to First Affiliated Hospital of Xi'an Jiao Tong University from January 2010 to September 2017, were selected and divided into three groups according to different treatments. Group A (n=19) was given drug methotrexate conservative treatment; group B (n=30) was treated with B-ultrasound guided abortion; group C (n=40) was treated with uterine artery embolization combined with uterine curettage. The vaginal bleeding and treatment of patients were compared among the three groups. **Results:** The treatment success rate of group C was the highest, the time of serum β-HCG descending to normal level was the lowest, and the amount of vaginal bleeding after treatment was the least; the second was group B, and the last was group A, the differences were statistically significant ($P<0.05$). The decrease of serum β-HCG in the group B and group C was significantly higher than that in group A 4d and 7d after treatment, the decrease of group C was the greatest 7d after treatment ($P<0.05$). The time of hospitalization and the cost of hospitalization in group B were lower than that of group C and group A, but the rate of blood transfusion was high, and the difference was statistically significant ($P<0.05$). **Conclusion:** Uterine artery embolization combined with uterine curettage in the treatment of CSP has the advantages of higher cure rate, less injury and quick recovery after operation. Its clinical efficacy is the best under the circumstances of economic conditions.

Key words: Cesarean scar pregnancy; Methotrexate; Artificial abortion; Uterine curettage; Uterine artery embolization; Curative effect

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前言

瘢痕部位妊娠(cesarean scar pregnancy, CSP)指受精卵着床于既往的子宫切口瘢痕处,是异位妊娠的一种特殊类型,最常见于有剖宫产病史的患者。CSP最早在1978年由Laren等人首次报道,其发病率较低,约1:1800~1:2216之间^[1-3]。近年来,随着国内剖宫产率逐年上升,B超、MRI等检查水平的不断提

高,我国CSP的诊断率逐渐提高^[4,5]。子宫瘢痕部位肌层薄弱、收缩力差,一旦妊娠物植入、穿透子宫肌层,治疗时如果盲目行人工流产术有可能导致子宫穿孔、大出血,甚至危及患者生命^[6,7]。目前CSP尚无统一规范的治疗标准,文献报道中常见治疗方法有药物保守治疗、经腹或腹腔镜局部病灶切除术治疗、经阴道局部病灶切除术治疗、宫腹腔镜联合病灶清除术治疗、清宫术治疗、子宫动脉栓塞术治疗等^[8-10],而子宫动脉栓塞术联合

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清宫术的治疗方案具有创伤小、出血少、术后恢复快、疗效显著等优点,受到临床医师的青睐^[11,12]。本研究回顾分析2010年1月至2017年9月西安交通大学第一附属医院妇产科收治的89例CSP患者的资料,旨在探索不同治疗方法的优缺点及有效性,为合理临床治疗提供一定的依据。

1 资料与方法

1.1 一般资料

选取2010年1月~2017年9月西安交通大学第一附属医院妇产科收治的89例CSP患者,纳入标准:患者均符合CSP的诊断标准;排除标准:(1)选择开腹或腹腔镜治疗CSP的患者;(2)存在治疗禁忌症者;(3)入院时生命体征不平稳者(4)随访时失访者。按治疗方案不同分为A、B、C三组,A组患者19例,采用药物甲氨蝶呤保守治疗;B组患者30例,行B超引导下人工流产术治疗;C组患者40例,行子宫动脉栓塞联合清宫术治疗。三组患者一般资料比较差异无统计学意义($P>0.05$),具有可比性,见表1。患者或家属对本研究知情同意并签署知情同意书,本研究经西安交通大学第一附属医院伦理委员会审核批准。

1.2 诊断标准

根据患者既往剖宫产术病史、停经史、血β-人绒毛膜促性腺激素(β-human chorionic gonadotrophin, β-HCG)、腹部彩超或经阴道彩超检查结果明确诊断。B超诊断标准^[13]:①宫腔内及宫颈管内未见孕囊,或仅见部分妊娠囊;②子宫峡部瘢痕处可见孕囊附着;③膀胱壁及孕囊之间的瘢痕处肌层连续性中断,肌层变薄;④彩色多普勒血流现象提示孕囊周围可见胎盘循环。

1.3 治疗方法

A组患者给予甲氨蝶呤保守治疗,具体治疗方法为甲氨蝶

呤肌肉注射50 mg/m²,用药后第4d、7d复查血β-HCG及B超,如血β-HCG下降小于15%则重复使用甲氨蝶呤,此后每周复查血β-HCG直至阴性;B组患者确诊后采用B超引导下人工流产术治疗,利用负压吸刮的方式清除瘢痕处绒毛组织及孕囊;C组患者先行双侧子宫动脉栓塞术,术后24h~48h内实施清宫术,出血量只计算清宫术时的出血量。

1.4 疗效评价

治愈:血β-HCG进行性下降,并于治疗2月内降至正常水平,复查B超未见子宫峡部异常回声或包块。治疗失败:血β-HCG无明显下降或治疗后反而升高,复查B超未见包块缩小反而增大,需要追加额外治疗;或在治疗过程中出血或大出血,需开腹或腹腔镜下行子宫切除术或次全子宫切除术。

1.5 观察指标

(1)统计并对比治疗后三组患者的阴道出血情况;(2)统计并对比三组患者血清β-HCG下降幅度及恢复正常时间、治愈率、输血率、住院时间、住院费用。

1.6 统计学方法

运用SPSS19.0软件进行数据处理,符合正态分布的计量资料以($\bar{x}\pm s$)表示,两组比较采用t检验,偏态分布的计量资料比较使用Kruskal-Wallis检验,计数资料以率(%)表示,采用卡方检验,多组间比较采用单因素方差分析, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 三组患者一般情况比较

A、B、C三组患者年龄、孕次、产次、距离上次剖宫产时间、妊娠停经时间、孕囊大小及治疗前血β-HCG值比较差异均无统计学意义($P>0.05$),见表1。

表1 三组患者一般情况比较

Table 1 Comparison of preoperative clinical data among three groups

| Indexes | Group A(n=19) | Group B(n=30) | Group C(n=40) | Hc/F | P |
|---|------------------|------------------|------------------|-------|-------|
| Age(years old) | 30.51±1.71 | 36.40±4.24 | 32.79±4.10 | 6.484 | 0.547 |
| Times of pregnancy(times) | 3(2-4) | 3(2-4) | 2(2-4) | 3.585 | 0.169 |
| Delivery time(times) | 1(1-2) | 1(1-2) | 1(1-2) | 0.731 | 0.690 |
| Distance from the last cesarean section time(years) | 3.5(2.5-5.5) | 6(2.0-10.5) | 5.0(3.0-6.0) | 1.377 | 0.300 |
| Time of pregnancy menopause(d) | 50.52±15.56 | 47.50±6.70 | 50.98±13.81 | 2.523 | 0.987 |
| Size of gestation sac(cm) | 2.53±1.76 | 2.64±0.85 | 2.50±1.10 | 0.447 | 0.870 |
| Before treatment serumβ-HCG(mIU/mL) | 39745.54±2200.33 | 37591.67±8961.40 | 46010.01±9657.04 | 2.580 | 0.081 |

2.2 三组患者阴道出血情况比较

A组患者给予药物治疗后,在等待血β-HCG下降过程中阴道出血时间较长,阴道出血量最多,为120(30-300)mL。B组患者中有5例在清宫术中出现阴道大出血,失血约2000 mL,紧急行经腹次全子宫切除术,另有4例患者在清宫术中出血量约1000 mL,紧急行腹腔镜下子宫局部病灶切除术,这9例患者术中均给予输入同型红细胞800-1200 mL对症治疗;其余的

B组患者清宫术的平均出血量为50 mL,在清宫术后的阴道出血量仅为30(20-39)mL。C组15例患者中有13例在清宫术中出血量均小于50 mL,仅有2例患者病情特殊:1例停经63d的患者在清宫术中出血约500 mL,术中输血400 mL,另有1例停经85d的患者行子宫栓塞术后自诉每日阴道出血量仍多于100 mL,在充分了解病情后自愿选择腹腔镜下子宫局部病灶清除术,其余C组患者清宫术后的阴道出血量为25(5-35)mL,A

组患者治疗后的阴道出血量高于 B 组和 C 组 ($U_c=3.105$ 、 4.658 , $P=0.008$, 0.000), B 组、C 组治疗后的阴道出血量比较无统计学差异 ($U_c=1.211$, $P=0.389$)。

2.3 三组患者治疗效果比较

三组患者均在治疗后第 4、7d 复查血 β -HCG, 并随访至其下降到正常水平, 结果显示: 治疗后第 4d、7d, B、C 两组其下降幅度显著高于 A 组 ($P<0.05$), 尤其是 C 组在治疗后第 7d 的下

降幅度最大; 对于血 β -HCG 恢复至正常时间而言, C 组最短, 其次为 B 组, 最后为 A 组, C 组与其他两组相比差异有统计学意义 ($P<0.05$); C 组的治愈率最高, 其次为 B 组, 最后是 A 组, 组间比较差异有统计学意义 ($P<0.05$); 输血率 B 组最高, 其次为 A 组, 最低为 C 组, C 组输血率低于其他两组 ($P<0.05$); 住院时间 B 组最短, C 组其次, A 组最长, 住院费用 B 组最低, A 组其次, C 组最高, 组间比较差异具有统计学意义 ($P<0.05$)。

表 2 三组患者治疗效果比较

Table 2 Comparison of postoperative conditions among three groups

| Indexes | Group A(n=19) | Group B(n=30) | Group C(n=40) | Hc/F | P |
|--|------------------|-------------------|---------------------|--------|-------|
| Cure rate [n(%)] | 11(57.89) | 23(76.67)* | 36(90.00)*# | 7.732 | 0.029 |
| Blood transfusion rate [n (%)] | 4(21.05) | 9(30.00) | 2(5.00)*# | 2.265 | 0.041 |
| The decrease of β -HCG in 4d after treatment(mIU/mL) | 35.37± 16.37 | 62.91± 11.96* | 55.42± 17.24* | 4.195 | 0.030 |
| The decrease of β -hCG in 7d after treatment(mIU/mL) | 63.23± 16.14 | 81.53± 11.79* | 86.25± 10.29* | 6.480 | 0.015 |
| Recovery of β -HCG to normal time (d) | 42.41± 16.50 | 30.72± 12.42* | 27.51± 9.83* | 8.431 | 0.037 |
| Hospitalization time(d) | 18.91± 6.40 | 5.40± 2.80* | 7.34± 2.60*# | 3.421 | 0.040 |
| Hospitalization expenses(yuan) | 8152.63± 8992.24 | 6870.83± 6146.99* | 16643.22± 8481.23*# | 10.492 | 0.000 |

Note: Compared with the group A, * $P<0.05$; compared with the group B, # $P<0.05$.

3 讨论

CSP 是异位妊娠的特殊类型, 占异位妊娠的 6% 左右, 也是剖宫产远期严重并发症之一。随着国内二胎政策的开放, CSP 的发生率呈上升趋势^[14]。目前 CSP 的发病机制尚未明确, 大多数学者认为剖宫产等手术造成手术部位的子宫肌层及内膜层的连续性中断, 愈合后子宫肌层及内膜层可能形成与宫腔相通的微小窦道或憩室, 当再次妊娠时受精卵通过宫腔时未具备着床能力, 到达既往手术瘢痕部位时绒毛组织易侵入切口瘢痕处甚至肌层, 从而发生 CSP^[15,16]。CSP 患者早期症状无特异性, 主要以停经史、少量阴道出血为主, 甚至有部分患者无任何症状, 仅在早期 B 超检查时发现^[17,18]。目前 CSP 的诊断主要依靠经阴道彩色多普勒超声显示孕囊位置、大小、血流情况、瘢痕处肌层情况及孕囊种植处与周围组织的关系情况^[19]。由于子宫峡部的肌层薄弱, 既往手术切口处瘢痕组织收缩能力差, 孕中晚期可导致胎盘植入、子宫破裂、大出血甚至危及生命的风险, 因此 CSP 一经诊断, 应该尽早终止妊娠、去除病灶, 防止发生子宫破裂等严重并发症, 以保留患者安全及生育功能^[20,21]。目前 CSP 的临床治疗有很多种, 尚无统一的治疗标准, 针对每个患者如何选择最佳的治疗方案, 是目前妇产科医师面临的一个挑战。

在 CSP 的药物保守治疗中, 最常用的药物即为米非司酮及甲氨蝶呤, 主要通过抑制滋养细胞增生、破坏绒毛、使蜕膜组织坏死、脱落来降低妊娠组织的活性^[22-24], 但并不是每例患者均能取得成功。本研究结果显示, A 组仅仅使用甲氨蝶呤治疗, 在治疗后第 4d 及第 7d 血 β -HCG 下降缓慢, 患者治疗后最终 HCG 恢复正常时间及阴道出血量均大于 B、C 两组, 差异具有

统计学意义 ($P<0.05$), 且 A 组患者住院时间最长, 明显多于 B、C 两组, 但其住院费用介于 B、C 两组之间。因此, 药物治疗虽然有一定的疗效, 但是对于血 β -HCG 较高的 CSP 患者而言, 其治愈率较低、住院时间长、住院费用不低, 等待 β -HCG 下降过程中大出血风险相对较高, 并非首选的治疗方案。

B 超引导下直接清宫术也是 CSP 常见的治疗手段之一^[25], 但是其价值存在争议。盲目的清宫术易导致子宫穿孔、难以控制的大出血, 甚至危及生命, 因此中华医学会发布的指南中不推荐其单独直接使用。在 B 超监护下清宫术的优点是在 B 超监护下进行手术, 可以直接将绒毛负压吸除、减少残留, 手术操作更直观, 可评估性更强^[26]。本研究结果显示, B 超引导下直接清宫术后阴道出血量同 C 组比较无明显差异, 但是明显低于 A 组 ($P<0.05$); 血 β -HCG 下降幅度及恢复时间均同 C 组比较无明显差异, 但明显高于 A 组, 其住院时间、住院费用均低于其他 2 种方法, 差异具有统计学意义 ($P<0.05$)。B 组的治愈率达 76.67%, 介于 A、C 组之间, 其 23.33% 的失败患者均因术中大出血接受了紧急输血, 甚至手术治疗, 可见在 B 超引导下清宫术在治疗 CSP 上虽然有一定的优越性, 但需要根据患者的孕周、血 β -HCG 值、病灶大小、B 超评估的瘢痕部位子宫肌层厚度、CSP 的类型等因素来综合评估清宫术中的出血风险, 尤其是早期 CSP 患者。

子宫动脉栓塞术通过直接阻塞子宫动脉血供从而减少清宫术中的出血, 同时可使瘢痕部位妊娠物因局部缺血缺氧导致滋养细胞坏死、萎缩, 最早在 2002 年由 Ghezzi 等首次报道其在治疗 CSP 上具有良好的疗效, 目前已广泛应用于子宫肌瘤、产后出血的抢救等方面^[27,28]。但是单纯的子宫动脉栓塞治疗

CSP 的成功率偏低,治疗时间长,不少学者建议采用子宫动脉栓塞术联合清宫术和或甲氨蝶呤药物灌注治疗 CSP^[29,30]。本研究中采用子宫动脉栓塞术联合清宫术治疗 CSP,结果发现在血 β-HCG 下降幅度、恢复正常时间方面均高于其他两组,且成功率达 90%,仅有 2 例患者行腹腔镜下病灶切除术,无任何患者需行子宫切除术。另外 C 组清宫术后阴道出血量最少,输血率仅为 5%,明显低于其他两组,说明子宫动脉栓塞术对于减少清宫术中出血、降低手术风险效果良好。患者入院确诊后,我们需联系周围血管科进行子宫动脉栓塞术,并于术后 24-48h 行清宫术,故该组患者的平均住院时间介于 A 组及 B 组之间,但其住院费用最高。因此我们认为子宫动脉栓塞后清宫比 B 超引导下清宫更安全、高效,但其缺点是治疗费用高。在有条件开展介入治疗的医院,临床医师充分评估 CSP 患者的病情,对于高危患者,尤其是 III 型 CSP 患者推荐使用子宫动脉栓塞术联合清宫术的治疗方案。

综上所述,本研究三种治疗方案对子宫 CSP 均有不同程度的疗效,其中子宫动脉栓塞联合清宫术具有安全、高效、创伤小的优点,在经济情况允许的情况下是最为理想的治疗方案。

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