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## 中西医结合保守治疗异位妊娠的十年回顾性分析研究\*

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**摘要 目的:** 回顾性分析我院十年来中西医结合保守治疗异位妊娠的病历资料, 总结治疗该病的最佳用药方案。**方法:** 回顾性分析 2006 年 1 月至 2017 年 1 月在我院接受保守治疗 300 例的异位妊娠患者临床资料, 根据不同治疗方法分为 A、B、C 三组, 其中 A 组(115 例)予以 50 mg/次 甲氨蝶呤(MTX)+200 mg/d 米非司酮+中药治疗, B 组(92 例)采用 50 mg/次 MTX+100 mg/d 米非司酮+中药治疗, C 组(93 例)采用 200 mg/d 米非司酮+中药治疗。观察记录三组患者血清  $\beta$ -人绒毛膜促性腺激素( $\beta$ -HCG)下降至正常所需时间、盆腔内包块消失时间及住院天数, 记录三组患者临床疗效并统计不良反应发生情况。**结果:** 三组间血  $\beta$ -HCG 下降至正常时间、包块消失时间及住院天数比较差异有统计学意义( $P<0.05$ ), A 组患者血  $\beta$ -HCG 下降至正常时间、包块消失时间及住院天数均低于 B 组和 C 组, 有统计学差异( $P<0.05$ ), B 组和 C 组上述指标比较无明显差异( $P>0.05$ )。A 组、B 组、C 组患者治愈率分别为 96.52%、85.87%、86.02%, 三组患者治愈率整体比较差异有统计学意义( $P<0.05$ ), 且 A 组患者治愈率均高于 B 组和 C 组, 有统计学差异( $P<0.05$ ), B 组和 C 组治愈率比较无明显差异( $P>0.05$ )。A 组、B 组、C 组的不良反应发生率分别为 10.81%(12/111)、16.30%(15/92)、11.83%(11/93), 三组不良反应总发生率比较无统计学差异( $P>0.05$ )。**结论:** 中药联合 MTX 和大剂量米非司酮保守治疗异位妊娠疗效高, 疗程短, 且安全性良好, 值得推荐。

**关键词:** 异位妊娠; 保守治疗; 中西医结合治疗; 疗效; 不良反应

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## Retrospective Analysis of Conservative Treatment of Ectopic Pregnancy with Traditional Chinese and Western Medicine for Ten Years\*

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**ABSTRACT Objective:** To retrospectively analyze the clinical data of ectopic pregnancy treated with traditional Chinese and Western medicine in our hospital during the past 10 years, and summarize the best medication plan. **Methods:** The clinical data of 300 cases with ectopic pregnancy treated by conservative treatment in our hospital from January 2006 to January 2017 were analyzed retrospectively, who were divided into group A, group B and group C according to the different treatment methods. Group A (115 cases) was treated with 50 mg methotrexate (MTX), 200 mg/d mifepristone and Chinese medicine treatment. Group B (92 cases) received 50mg MTX, 100 mg/d mifepristone and Chinese medicine treatment. Group C (93 cases) used 200 mg/d mifepristone and Chinese medicine treatment. The decrease time serum  $\beta$ -human chorionic gonadotrophin ( $\beta$ -HCG) to normal, the disappearance time of pelvic mass and the time of hospitalization were observed and recorded between the three groups. The clinical efficacy and the incidence of adverse reactions between the three groups were recorded. **Results:** There were significant differences in the decrease time serum  $\beta$ -HCG to normal, the disappearance time of pelvic mass and the time of hospitalization between the three groups ( $P<0.05$ ). The decrease time serum  $\beta$ -HCG to normal, the disappearance time of pelvic mass and the time of hospitalization in group A were lower than that in group B and group C, the differences were statistically significant ( $P<0.05$ ). There was no significant difference above indicators between group B and group C ( $P>0.05$ ). The cure rate in group A, group B and group C were 96.52%, 85.87%, 86.02% respectively, there were significant differences between the three groups ( $P<0.05$ ). The cure rate in group A were higher than that in group B and group C, the differences were statistically significant ( $P<0.05$ ). There was no significant difference of the cure rate between group B and group C ( $P>0.05$ ). The incidence of adverse reactions in group A, group B and group C were 10.81% (12/111), 16.30% (15/92), 11.83% (11/93) respectively, there was no significant difference of the total incidence of adverse reactions between the three groups ( $P>0.05$ ). **Conclusion:** Chinese medicine treatment combined with MTX and large dose of mifepristone in the conservative treatment of ectopic pregnancy has high curative effect, short course and good safety, it is worth recommending.

**Key words:** Ectopic pregnancy; Conservative treatment; Combined treatment of Chinese and Western medicine; Effect; Adverse reaction

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## 前言

异位妊娠指受精卵在子宫腔外着床发育,是妇科常见急腹症之一,也是引发孕妇妊娠早期死亡的主要因素<sup>[1,2]</sup>。阴道B超、腹腔镜以及血清 $\beta$ -人绒毛膜促性腺激素( $\beta$ -human chorionic gonadotrophin, $\beta$ -HCG)是检查异位妊娠的常用方法,近年来,随着检验医学及影像技术的进步,特别是临床医师对疾病认识的不断提高,多数异位妊娠均可在早期明确诊断,这就为保守治疗创造了条件<sup>[3-5]</sup>。保守治疗是患者要求保留生殖能力早期输卵管妊娠的主要治疗手段,其中包括手术治疗和药物治疗,手术切除是一种应用较广的治疗方式,但手术治疗对患者损伤大、并发症多,且对生育功能影响较大,且治疗成功后均可能形成局部粘连或疤痕,从而影响输卵管功能或通畅情况,降低妊娠率,增加异位妊娠的可能性,严重者则有不孕等不良情况的发生,对患者影响较大<sup>[6-8]</sup>。目前临床上多采用甲氨蝶呤(methotrexate, MTX)、米非司酮等西药治疗异位妊娠,但疗程较长、副作用多,患者不易接受<sup>[9,10]</sup>。中西医结合治疗以疗程短、疗效高等优势受到临床医生及患者的普遍认可,但何种用药方

案对患者获益最大仍是一个值得探讨的重要问题<sup>[11]</sup>。鉴于此,本研究回顾性分析了本院10年来中西医结合保守治疗异位妊娠的病历资料,总结治疗该病的最佳用药方案,为临床合理用药提供理论依据,现报道如下。

## 1 资料和方法

### 1.1 一般资料

选入2006年1月至2017年1月在我院接受保守治疗的异位妊娠患者300例,纳入标准:(1)符合输卵管妊娠诊断标准<sup>[12]</sup>;(2)常规检测正常、生命体征平稳、腹痛现象不明显者;(3)B超检查未发现活动性腹腔出血症状者;(4)要求保守治疗,以求保留生育功能者。排除标准:(1)不符合输卵管妊娠者;(2)严重心、肝、肾功能障碍者;(3)病历资料不完整影响疗效判断者。根据患者的治疗方法将其分为A、B、C三组,其中A组115例,B组92例,C组93例,三组患者年龄、孕龄、包块最大直径、血清 $\beta$ -人绒毛膜促性腺激素( $\beta$ -human chorionic gonadotrophin, $\beta$ -HCG)含量等基本情况进行比较无明显差异( $P>0.05$ ),均衡可比。见表1。

表1 三组基本情况比较

Table 1 Comparison of the basic situation of the three groups

| Groups           | n   | Age(years)       | Gestational age(d) | Nulliparous/multi-parous | Maximum diameter of block(cm) | $\beta$ -HCG(U/L)    |
|------------------|-----|------------------|--------------------|--------------------------|-------------------------------|----------------------|
| Group A          | 115 | 30.17 $\pm$ 7.06 | 41.26 $\pm$ 3.15   | 71/44                    | 3.34 $\pm$ 0.91               | 1185.82 $\pm$ 337.21 |
| Group B          | 92  | 30.06 $\pm$ 6.94 | 41.50 $\pm$ 3.22   | 55/37                    | 3.31 $\pm$ 0.87               | 1159.32 $\pm$ 297.53 |
| Group C          | 93  | 30.25 $\pm$ 7.18 | 41.73 $\pm$ 3.34   | 57/36                    | 3.29 $\pm$ 0.96               | 1201.06 $\pm$ 315.28 |
| F/x <sup>2</sup> |     | 0.019            | 0.395              | 0.087                    | 0.079                         | 0.413                |
| P                |     | 0.982            | 0.674              | 0.957                    | 0.924                         | 0.662                |

### 1.2 治疗方法

A组予以米非司酮(上海新华制药有限公司,国药准字:H10950131)200 mg/d,1次/d,口服;MTX(浙江海正药业股份有限公司,国药准字:H20055198)50 mg/次,臂深部肌肉注射,1次为1疗程;中药组方(宫外孕二号方加双柏散):宫外孕二号方成分如下:紫草、天花粉各30 g,当归、丹参、赤芍、三棱、莪术各15 g,川芎、桃仁各10 g,蜈蚣2条,随症加减:伴恶心、呕吐者加吴茱萸5 g,伴腹泻者加茯苓15 g、白术10 g;以水煎煮,1剂/d,分早晚两次口服;双柏散成分如下:生大黄20 g,侧柏叶20 g,泽兰20 g,黄柏20 g,薄荷20 g,用法:穴位冷敷。B组采用米非司酮50 mg/次,2次/d,口服,MTX和中药方用量和用法同A组。C组采用米非司酮200 mg/d,1次/d,口服;中药用法、剂量等与A组一致。三组均连续治疗5 d。治疗后每5 d复查1次孕三项、阴道B超、肝肾功、血常规,根据检查结果决定下一步治疗方案:若血清 $\beta$ -HCG含量下降 $\geq$ 15%,说明治疗有效,继续原方案不变,每5 d复查1次上述项目,直至 $\beta$ -HCG降到正常为止;若血 $\beta$ -HCG下降不足15%,且B超提示盆腔包块较前明显增大或出现盆腔积液增多,则需调整治疗方案;

若保守治疗期间出现剧烈腹痛及出血,需转急诊行手术治疗。

### 1.3 疗效判定

(1)治愈:下腹痛、阴道出血等临床症状消失,血 $\beta$ -HCG含量低于3.1 U/L;妇科B超检查提示妊娠包块缩小或消失;(2)失败:治疗期间腹痛加剧、内出血增多,血 $\beta$ -HCG含量不断上升或居高不下,包块不缩小或增大而改行手术治疗。

### 1.4 观察指标

观察记录三组患者血 $\beta$ -HCG下降至正常所需时间、盆腔内包块消失时间及住院天数,记录三组患者临床疗效并统计不良反应发生情况。

### 1.5 统计学方法

采用SPSS 20.0进行统计分析,包块消失时间等计量资料表示为( $\bar{x} \pm s$ )的形式,多组间比较采用单因素方差分析,两两比较采用t检验,计数资料表示为率(%)的形式,采用 $\chi^2$ 检验。检验标准设置为 $\alpha=0.05$ 。

## 2 结果

### 2.1 三组患者临床指标比较

三组间血  $\beta$ -HCG 下降至正常时间、包块消失时间及住院天数比较差异有统计学意义 ( $P<0.05$ ), A 组患者血  $\beta$ -HCG 下降至正常时间、包块消失时间及住院天数均低于 B 组和 C 组, 有统计学差异 ( $P<0.05$ ), B 组和 C 组上述指标比较无明显差异 ( $P>0.05$ )。见表 2。

表 2 三组患者临床指标比较( $\bar{x}\pm s, d$ )Table 2 Comparison of observation indexes of the three groups( $\bar{x}\pm s, d$ )

| Groups  | n   | The decrease of blood $\beta$ -HCG to normal time | Block disappearance time        | Time of hospitalization         |
|---------|-----|---------------------------------------------------|---------------------------------|---------------------------------|
| Group A | 115 | 16.20 $\pm$ 8.87 <sup>△ #</sup>                   | 32.86 $\pm$ 9.51 <sup>△ #</sup> | 15.98 $\pm$ 7.46 <sup>△ #</sup> |
| Group B | 92  | 22.46 $\pm$ 11.34                                 | 37.05 $\pm$ 10.34               | 23.94 $\pm$ 10.07               |
| Group C | 93  | 25.28 $\pm$ 12.15                                 | 39.27 $\pm$ 12.19               | 26.06 $\pm$ 9.73                |
| F       |     | 19.820                                            | 9.796                           | 36.462                          |
| P       |     | 0.000                                             | 0.000                           | 0.000                           |

Note: Comparison with group B, <sup>△</sup>  $P<0.05$ ; Comparison with group C, <sup>#</sup>  $P<0.05$ .

## 2.2 三组患者临床疗效比较

A 组、B 组、C 组患者治愈率分别为 96.52%、85.87%、86.02%，三组患者治愈率整体比较差异有统计学意义 ( $P<0.05$ )，且 A 组患者治愈率均高于 B 组和 C 组，有统计学差异 ( $P<0.05$ )，B 组和 C 组治愈率比较无明显差异 ( $P>0.05$ )，保守治疗失败者均转为急诊手术。见表 3。

表 3 三组患者临床疗效比较  $n[(\%)]$ Table 3 Comparison of the clinical efficacy of the three groups  $n[(\%)]$ 

| Groups   | n   | Cure                      | Fail                   |
|----------|-----|---------------------------|------------------------|
| Group A  | 115 | 111(96.52) <sup>△ #</sup> | 4(3.48) <sup>△ #</sup> |
| Group B  | 92  | 79(85.87)                 | 13(14.13)              |
| Group C  | 93  | 80(86.02)                 | 13(13.98)              |
| $\chi^2$ |     | 8.814                     |                        |
| P        |     | 0.012                     |                        |

Note: Comparison with group B, <sup>△</sup>  $P<0.05$ ; Comparison with group C, <sup>#</sup>  $P<0.05$ .

## 2.3 三组患者不良反应比较

治疗期间,三组患者均未出现肝肾功能异常、骨髓抑制等严重不良反应,21 例患者(A 组 7 例,B 组 9 例,C 组 5 例)有恶心呕吐反应,17 例(A 组 5 例,B 组 6 例,C 组 6 例)出现口腔溃疡,均为轻症,患者可耐受,停药后可逐渐恢复正常。A 组、B 组、C 组的不良反应发生率分别为 10.81%(12/111)、16.30%(15/92)、11.83%(11/93),三组不良反应总发生率比较无统计学差异 ( $\chi^2=1.480, P=0.477$ )。

## 3 讨论

随着人们生活压力的增加、无规律生活的循环以及性观念的开放,异位妊娠的发病率不断上升,且表现出年轻化的趋势<sup>[13-15]</sup>。因此,要求保留生育能力的异位妊娠患者不断增多,药物保守治疗成为主要手段。目前,MIX 和米非司酮是西医常用药物,前者是一种抗叶酸类抗肿瘤药,可通过抑制二氢叶酸还原酶产生细胞毒作用,干扰 DNA、RNA 以及蛋白质的合成,具有抑制胚胎滋养细胞分裂、破坏绒毛的作用,使胚胎组织坏死、脱落及吸收<sup>[16,17]</sup>。米非司酮是一种强抗孕激素,可竞争性结合于孕酮受体,产生抗孕酮效应,发挥抗着床、促宫颈成熟、终止早孕等作用,同时可与糖皮质激素受体结合,诱发妊娠的绒毛组织及蜕膜变性,降低黄体生成素,释放内源性前列腺素,进而引起

胚胎死亡<sup>[18-20]</sup>。但西药治疗疗程长、副作用多,患者不易接受而影响治疗效果。

中医理论认为,异位妊娠属“经闭”、“经漏”、“停经腹痛”等范畴,其发病机理与宿有少腹瘀滞,房劳不慎、情志不遂、起居不慎以及外感风寒湿邪、或先天肾气不足等有关,故治疗以活血化瘀、消癥杀胚为其主要目的<sup>[21]</sup>。宫外孕二号方中,丹参、赤芍具有活血祛瘀、通经止痛之效<sup>[22]</sup>;当归补血和血,调经止痛,同时提高机体的免疫力;桃仁具有抗凝及一定的溶血作用,可改善血流阻滞、血行障碍;三棱、莪术破血行气、消积止痛,然前者偏于破血,后者偏于破气,二者配伍,气血兼顾<sup>[23]</sup>;川芎可行气开郁,活血止痛;紫草清热解毒,活血凉血;花粉生津止渴,消肿排脓;蜈蚣熄风止痉,解毒散结。诸药联用,发挥活血化瘀、消结理气等作用,缩小血肿包块、防止附件粘连、减少再次发生异位妊娠的风险。此外,以宫外孕二号方为基础,根据患者的不同症状加入相应的药材,形成个体化的治疗方案,不仅可提高治疗效果,减少不良反应的发生,更是中医辨证施治优势的体现<sup>[24]</sup>。此外,双柏散中生大黄逐瘀通经、凉血解毒,侧柏叶凉血止血,泽兰活血化瘀、消肿通络,黄柏清火清湿热,薄荷则可发挥扩散、渗透的作用,诸药联用,发挥活血化瘀、清热解毒的功效。本研究回顾性分析了本院 10 年来中西医结合保守治疗异位妊娠的病历资料,结果发现,A 组患者血  $\beta$ -HCG 下降至正常时

间、包块消失时间及住院天数均低于 B 组和 C 组( $P<0.05$ ), B 组和 C 组上述指标比较无明显差异, 说明中西医结合能有效改善患者的临床症状。中西医结合疗法是治疗异位妊娠的主要方式, 其优于单纯中药或单纯西药治疗, 整体调节、标本兼顾、优势互补, 是当前比较认可的一种趋势。其中中药具有活血化瘀、清热解毒、消肿散结的作用, 消除局部淤滞, 使血流通畅, 促使炎症吸收, 改善输卵管的正常蠕动, 从而起到有效的治疗作用<sup>[25,26]</sup>。本研究三组患者均在中药治疗基础上加用不同剂量的 MTX 和米非司酮治疗, 结果显示, A 组患者治愈率均高于 B 组和 C 组( $P<0.05$ ), B 组和 C 组治愈率比较无明显差异( $P>0.05$ ), 说明大剂量(200 mg/d)米非司酮联合 MTX 治疗异位妊娠的临床疗效优于小剂量(100 mg/d)米非司酮联合 MTX 及单纯应用米非司酮的临床效果, 杨仁美等<sup>[27]</sup>回顾性分析了天花粉、甲氨蝶呤、米非司酮、MTX 加米非司酮、天花粉加 MTX 加米非司酮在异位妊娠患者保守治疗中的临床效果, 结果显示天花粉加 MTX 加米非司酮治疗有效率为 94.0%, 显著高于其他治疗方法, 单纯应用米非司酮效果最差, 但三种药物联合应用不良反应发生率较高, 达 48.0%, 这是由于该研究直接应用天花粉进行治疗, 而天花粉较易导致患者过敏, 通过与其他药物配伍可显著降低不良反应<sup>[28]</sup>。有研究比较了 50 mg/m<sup>2</sup> MTX 和 25 mg/m<sup>2</sup> MTX 治疗异位妊娠的临床效果, 大剂量临床疗效好于小剂量, 但大剂量组不良反应发生率高于小剂量组<sup>[29,30]</sup>。本研究结果还显示, A 组、B 组、C 组的不良反应发生率分别为 10.81%、16.30%、11.83%, 三组不良反应总发生率比较无统计学差异( $P>0.05$ ), 说明大剂量米非司酮组不良反应发生率与其他两组无显著差异, 提示大剂量米非司酮安全性较高, 且无严重不良反应。

综上所述, 中药联合大剂量米非司酮和 MTX 治疗异位妊娠的临床疗效优于小剂量米非司酮联合 MTX 及单纯应用米非司酮的临床效果, 改善临床症状, 缩短住院时间, 治愈率也较高, 并且无严重不良反应, 值得临床推广应用。

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