Clinical observation of hysteroscopic surgery combined with ectopic pregnancy ii decoction and methotrexate in the treatment of cesarean scar pregnancy

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1. Introduction

Cesarean Scar Pregnancy (CSP) refers to the ectopic pregnancy where the fertilized egg is implanted in the scar of the uterus of the previous cesarean section[1]. It is a long-term complication of cesarean section. With the increase of cesarean section rate in recent years, the rate of cesarean section is increasing year by year. CSP has poor contractility due to weak myometrium attached to pregnancy sac and too much fibrous tissue in scar. Some embryo sac myometrial coverage and peripheral blood supply is very easy to occur in the curettage of uterine rupture, bleeding, peripheral organ damage. Or even hysterectomy during the operation of uterine clearing is very high, which is a serious threat to a woman’s reproductive health and life. Because of the clinical risk of the disease, clinical diagnosis should have an early diagnosis, early termination and early removal. CSP treatment more, including drug treatment, hysteroscopic surgery, uterine artery chemoembolization interventional therapy, laparotomy, etc., but there is no standard treatment[2-4]. Hysteroscopic surgery for the treatment of CSP can completely and accurately heal the pregnancy sac, which can effectively stop bleeding and retain fertility function. However, due
to the relatively large operation difficulty, there are other risks of other complications caused by the failure of the operation, so there are certain limitations in the treatment of CSP alone[5]. Studies have shown that preoperative drug pretreatment can improve the surgical efficacy of CSP, reduce the amount of intraoperative bleeding, avoid complications, ensure fertility, and improve the safety of surgery[6]. Currently the most commonly used clinical drug is methotrexate (MTX). It is found that the effect of MTX alone may not be ideal, and some of the drugs need to be used repeatedly. There may be damage to liver and kidney function. Bone marrow suppression will occur in severe cases, and some patients will still have massive bleeding and the possibility of embryo residue in the course of operation[7]. Ectopic Pregnancy II decoction prescription used in ectopic pregnancy medicine conservative treatment has remarkable effect. The combination of Ectopic Pregnancy II decoction prescription before hysteroscopic resection can improve the efficacy of killing embryo activity on the one hand and reduce the toxic side effects of repeated use of MTX on the other. Therefore, in this study, I observed the use of Ectopic Pregnancy II and MTX pretreatment combined with hysteroscopic electrosurgical treatment of CSP. The aim is to provide reference for clinical treatment of CSP and the research results are reported below.

2. Materials and methods

2.1. General Information

A total of 80 cases of CSP patients admitted to obstetrics and gynecology department of Haikou Hospital of Traditional Chinese Medicine from January 2014 to March 2017. They are divided into observation group and control group according to their different treatment methods, 40 cases in each.

2.2 Inclusion criteria and exclusion criteria

Inclusion criteria: The study refers to Consensus of Experts on Diagnosis and Treatment of Uterine Scar Pregnancy after Cesarean Section formulated by Chinese Medical Association of Obstetrics and Gynecology Branch Family Planning Group in 2016[1]: on the basis of the history, menopause, blood β-HCG level, combing with the clear vaginal ultrasound joint diagnosis, (1) in line with the diagnostic criteria of uterine scar pregnancy after cesarean section; (2) menopause within 8 weeks; (3) little or no vaginal bleeding; (4) uterine scar thickness ≥2 mm. These are all with the patient’s consent. Chinese medicine diagnosis are in line with “Chinese medicine gynecology” in the second edition of the relevant diagnostic criteria: (1) menopause with early pregnancy reaction, blood β-HCG test was positive; (2) vaginal irregular bleeding or no bleeding, lower abdominal pain; (3) the tongue is reddish or dark, the coated tongue is white, the pulse is slippery, etc. Exclusion criteria: (1) MTX contraindications; (2) combined with liver and kidney dysfunction or other serious diseases; (3) incomplete data; (4) cannot cooperate with the examination of the treatment.

The study was approved by our hospital ethics committee.

2.2.1 Comparison of general conditions between two groups

The results shows that 52 patients (65.0%) had more than 2 cesarean sections in 80 patients with CSP, and the last cesarean section was 1-8 years from this pregnancy, with an average of (3.87±2.13). The comparison between the two groups shows that the observation group is from 25 to 40 years old and the menopause time is 33 to 71 d. The control group is from 27 to 38 years old and the menopause time is 35 to 72 d.

2.3 Treatment

2.3.1 Improvement of various examinations after admission

(1) ECG, coagulation six, liver and kidney function, blood, blood β-HCG levels. (2) vaginal color doppler ultrasound examination, recording the size of pregnancy mass.

2.3.2 Control group

Improve various examinations after admission. After exclusion of contraindications, use MTX 50 mg/m² to an intramuscular injection; On the 7th day, the size of pregnancy mass is recorded again by transvaginal color Doppler ultrasonography, and hysteroscopy is performed on the 8th day. Surgical methods: patients take bladder lithotomy position, with conventional anesthesia, disinfection of the vagina, cervix. After expanding to 9.5, hysteroscopy is placed and the location, size and shape of the lesion are observed under direct vision, the lesion is respected by electric ring, and the bleeding is stopped by electric coagulation. After the operation, the routine anti-infective and rehydration support are treated.

2.3.3 Observation group

All the patients admitted to hospital are excluded from the treatment contraindications. On the basis of the control group, 100 mL decoction of Ectopic pregnancy II are added (10 g of Salvia miltiorrhiza, 10 g of Radix Paeoniae Rubra, 10 g of Peach Kernel, 10 g of Sanleng, 10 g of Curcuma) 1 dose per day, 2 times after meals, used for 7 d; On the 7th day, the size of pregnancy mass was recorded again by transvaginal color Doppler ultrasound; The operation method was the same as that of the control group, and the operation was completed by the same doctor. The doctor completed the operation. After the operation, the routine anti-infective and rehydration support are treated, continued to use ectopic pregnancy II until the blood HCG decreased to normal.
2.4 Observation indexes and evaluation of therapeutic effect

2.4.1 Observation indicators

(1) Observe the two groups' blood HCG levels before and after on the 4th, 7th and 11th day, and the size and adverse reactions of pregnancy masses on the 7th day.

(2) After operation, the recovery time, vaginal bleeding time, hospitalization time, menstrual cramps interval and follow-up recovery time of all patients are statistically analyzed.

(3) Observe and record all the patients' intraoperative bleeding, gastrointestinal adverse reactions and bone marrow suppression complications.

2.5 Statistical methods

Using SPSS 20.0 statistical software to process the data, we first analyze the distribution of measurement data. \( \chi^2 \) test is used to measure the data of normal distribution, and paired t-test is used to measure the data of non-normal distribution. \( P<0.05 \) indicates that the difference is statistically significant.

3. Result

3.1 Comparison of clinical data between two groups of patients

By comparing the two groups' serum \( \beta \)-HCG recovery time, vaginal bleeding time, hospitalization time, menstrual interval time and follow-up recovery time, we have found that the observation groups' serum \( \beta \)-HCG recovery time is (17.5±2.5) d, which is less than the control group (36.5±5.0); the duration of vaginal bleeding is (6.0±1.5) d, which is less than the control group (9.5±2.5); but the hospitalization time, menstrual interval time, recovery time are no significant difference between the two groups.

3.2 Comparison of serum HCG levels between two groups before and after treatment on the 4th, 7th and 11th day

Before treatment, there is no significant difference in blood \( \beta \)-HCG levels between the two groups \((P>0.05)\). The levels of \( \beta \)-HCG in the two groups are significantly lower than those before treatment, and gradually decreased. The observation group is lower than the control group, the difference is statistically significant \((P<0.05 \text{ or } P<0.01)\). See Table 1 for details.

3.3 Comparison of the size of pregnancy mass between the two groups

Before treatment, the size of pregnancy mass in the observation group (3.42±0.15) cm and the control group (3.46±0.25) cm are recorded by vaginal color Doppler ultrasonography; after pretreatment with different drugs, the size of pregnancy mass are measured on the 7th day. The mass of the pregnancy group (1.58±0.06) cm in the observation group is significantly lower than that of the control group (3.18±0.14) cm.

3.4 Comparison of the incidence of adverse reactions

Adverse reactions are compared between the two groups. In the observation group, there are 2 patients with massive bleeding during the operation, no gastrointestinal adverse reactions and bone marrow suppression, the total incidence of adverse reactions is 5%; in the control group, there are 5 patients with massive bleeding, 2 patients with gastrointestinal adverse reactions, 1 patient with bone marrow suppression, and the total incidence of adverse reactions is 20%. The overall incidence of adverse reactions in the control group is significantly lower than that in the control group.

4. Discussion

According to statistics[8], the rate of cesarean section is more than 50 percent a year in China, which is a serious threat to patients' fertility and physical and mental health. In view of the high incidence and high risk of CSP, its correct diagnosis and treatment in clinical work is very important. There are many causes of CSP, mainly related to multiple cesarean section, breech presentation cesarean section, suture technique, etc. Due to the lack of specific clinical manifestations of CSP patients, it is difficult to differentiate between gestational trophoblastic diseases, cervical pregnancy and early intrauterine pregnancy, which is easy to misdiagnose, resulting in poor therapeutic effect[9,10].

Studies have shown that the pathogenesis of CSP may be related to inadequate repair of the endometrium of the myometrium, excessive scar contracture around the incision of the isthmus or the chemotaxis of fertilized eggs by some invasive inflammation in the incision of the uterus. The results of this study show that in 80

Table 1.

Comparison of serum HCG levels between two groups before and after treatment on the 4th, 7th and 11th day (mIU/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Before Treatment</th>
<th>The 4th Day after Treatment</th>
<th>The 7th Day after Treatment</th>
<th>The 11th Day after Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Observation Group ((n=40))</td>
<td>38 957.8±2 883.6</td>
<td>33 880.5±2 145.2 (^*)</td>
<td>32 721.1±1 596.4 (^*)</td>
<td>1 152.9±354.2 (^*)</td>
</tr>
<tr>
<td>The Control Group ((n=40))</td>
<td>32 547.2±2 015.6</td>
<td>30 254.2±2 154.4 (**)</td>
<td>30 151.6±1 306.9 (**)</td>
<td>1 668.1±583.5 (**)</td>
</tr>
</tbody>
</table>

Attention: Compared with prior treatment, \( ^*P<0.05 \); compared with the control group, \( ^*P<0.01 \).
cases of CSP patients, there are 52 cases with more than 2 cesarean sections, accounting for 65.0%. Although some scholars believe that the occurrence of CSP has nothing to do with the number of cesarean section, but I believe that many cesarean section will lead to increased scar area, lower anterior wall of the uterus fibrosis and wound repair defects, the formation of scar tissue or sinus road, and fertilized eggs are implanted in the myometrium of the scar of cesarean incision, leading to the occurrence of CSP. It is found that the previous cesarean section is 1 to 8 years from this pregnancy time, with an average of (3.87±2.13) years; CSP can occur in more than a few years after cesarean section, but also can occur within 1 year of cesarean section, but at present the relationship between the length of the last cesarean section and the onset of CSP is not yet clear. In summary, to reduce the cesarean section without indications and improve vaginal delivery rate, and do a good job in the propaganda and education of the patients, and at least 2 years of contraception after cesarean section can reduce the incidence of CSP.

CSP early pregnancy has no specific clinical manifestations, or only similar to the performance of threatened abortion, such as vaginal bleeding, mild abdominal pain and so on. 80 cases of this study are mostly postmenopausal vaginal bleeding. Among them, 8 cases are admitted to hospital because of massive vaginal bleeding, the analysis is due to the lack of clear CSP clinical diagnosis, blind uterine clearance resulted in massive bleeding. If the treatment is not timely and severe, the disseminated intravascular coagulation may be caused, and even the life of the patient is compromised. The warning to clinicians is that the disease needs to be well understood, diagnosed and properly managed to avoid serious complications.

In recent years, with the continuous research of CSP clinically, there are several kinds of treatment methods reported at home and abroad, but no matter what treatment, there is the possibility of bleeding at any time, which leads to rescue passively. So far, there is still no clear and unified treatment plan[11]. Pregnancy should be terminated immediately after CSP diagnosis[12]. Cesarean alone should not be the preferred method of CSP[13], especially for patients with gestational sac convex to the bladder, curettage is absolutely contraindicated[14].

At present the main methods are drug embryo killing, surgical treatment and uterine artery cheemoembolization interventional therapy, etc. Commonly used drugs are mainly MTX and mifepristone, the purpose of both are to induce pregnancy to accelerate its death. However, the use of simple drug therapy is rarely used. The study shows that MTX alone is not ideal for the decline of blood β-HCG level, and the treatment time is long. It can lead to the formation of hematoma after the necrosis of trophoblastic cells. The local lesions may be enlarged in the short term, and there is a risk of massive bleeding caused by uterine rupture[15]. In recent years, uterine arterial cheemoembolization interventional treatment for CSP vaginal bleeding is suitable for the conservative treatment of patients with CSP vaginal bleeding requiring urgent hemostasis and retention of reproductive function. It can accelerate the death of gestational sac, kill trophoblast cells, but due to cost and conditions, clinical promotion and application of limited, and postoperative complications easily lead to puncture site infection, severe intrauterine adhesions or infertility, which affect the patients' fertility[16,17]. Therefore, it is not suitable to use it as the first choice in the treatment of CSP. Hysteroscopy, laparoscopy and vaginal surgery are commonly used for surgical treatment. Hysteroscopic surgery is a reasonable and reliable mode of minimally invasive surgery, which can not only clearly observe the internal environment of the uterine cavity, determine the location and size of the lesion, but also possible to determine the blood supply and vascular distribution at the site of the lesion implantation, greatly reduce the incidence of injury, adhesion, perforation and massive hemorrhage to other sites[18]. There are reports of experts and research suggests that preoperative drug pretreatment can effectively reduce the operative time and the bleeding, enhance the curative effect, also can promote the recovery of patients fertility[19,20]. Therefore, through this study, we hope to find a reliable, wide indication and safe treatment scheme.

In recent years, Chinese medicine awareness of the disease has gradually been clinically valued. CSP is a special form of ectopic pregnancy, traditional Chinese medicine that the pathological mechanism of juvenile abdomen with stasis, Chong Ren improper, or lack of kidney, abnormal pregnancy and pregnancy position, blockage of Qi and blood stagnation caused by blood clotting, pain plot is not formed into mass; blood left in the uterus, the blood runs sluggish, less common disease is less bloating full of stinging, evil blood dripping net. Comprehensive CSP pulse evidence for the evil of blood stasis less abdominal evidence. Therefore, treatment must get rid of evil blood, governance heat and cooling blood, Zhu Yu eliminate embryo. Therefore, we selected classic prescription medicine of the treatment of ectopic pregnancy-Ectopic Pregnancy II decoction. Studies have shown that[21], the prescription medicine may be through the destruction of mitochondria in the structure of the mitochondrial synthesis of ATP to reduce, leading to cell dysfunction and promote inflammatory cell infiltration, affecting the normal trophoblast physiological metabolism and promote apoptosis, necrosis, Lost nutrition support embryos, which play a role in killing embryos. Modern pharmacological studies also found that ectopic pregnancy on the 2nd can dilate blood vessels, reduce vascular resistance and improve blood circulation, blood stasis is conducive to absorption, but also increase vascular permeability and promote the absorption of hematoma mass[22], while Tissue around the mass of clots and embryonic tissue becomes soft and dissipate, is conducive to MTX play a role.

Therefore, by observing Ectopic Pregnancy II combined with Hysteroscopic Surgery on the treatment of CSP, we find that the two groups’ blood β-HCG levels are significantly lower than the same group before treatment and gradually decreased. The observation group is lower than the control group, the differences are statistically significant. After pretreatment with different drugs,
the sizes of two groups of pregnancy mass are measured on the 7th day, and it is found that the observation group is significantly smaller than the control group. The results show that ectopic pregnancy group I combined with MTX drug preconditioning could reduce the incidence of massive bleeding during hysteroscopic electroresection. After ectopic pregnancy group II combined with MTX drug pretreatment after hysteroscopic resection, the incidence of intraoperative bleeding is low, no serious side effects during treatment, less postoperative vaginal bleeding time, blood β-HCG recovery time is short, normal menstrual complex tide. In summary, ectopic pregnancy II combined with MTX pretreatment hysteroscopic electrosurgical treatment of CSP has a significant clinical effect, it can control intraoperative bleeding, reduce MTX side effects, reduce the physical and psychological burden on patients. It gives full play to the western medicine combined strengths, plays a synergistic and complementary role in promoting postoperative recovery of the body and fertility, shortening the hospital stay, thereby reducing hospitalization costs and save medical resources to avoid uterine artery chemotherapy embolization interventional treatment of the palace cavity adhesions, infections and other side effects This is an economical, safe, simple and effective treatment which is worth popularizing in clinic.

The shortcomings of this study is the lack of data comparison of large samples due to the limited number of CSP cases. In addition, during the traditional Chinese medicine prescription medication process, it needs further dialectical additions and subtractions. For example, after using MTX, on the one hand, due to the abundant local blood flow of pregnancy, hormone level has not been reduced to normal, we should continue to promote blood circulation and eliminate blood stasis, on the basis of eliminating disease and killing embryo, add the medicine of replenishing qi and blood, in order to help the healthy qi. In the latter part, after the local blood flow disappears and the hormone level drops to normal, attention should be paid to regulating qi and blood, restoring menstruation and strengthening the follow-up work of patients after discharge. These will be of guiding significance to the clinical and scientific research work in the future.

References


