

Observation on the Effect of Uterine Artery Embolization Combined with Hysteroscopy in the Treatment of Cesarean Scar Pregnancy

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Keywords: Cesarean scar pregnancy, Uterine artery embolization chemotherapy, Hysteroscopy.

Abstract: Objective To study the effect of uterine artery embolization (UAE) and methotrexate (MTX) combined with hysteroscopy in the treatment of cesarean scar pregnancy (CSP). **Methods:** 82 cases of cesarean scar pregnancy in the China-Japan Union Hospital of Jilin University were retrospectively studied between January, 2010 and January, 2016. They were divided into the two groups on the treatment method. The group A was offered prophylactic uterine artery embolization (UAE) and methotrexate (MTX) prior to uterine curettage with hysteroscopy method. The group B was treated with mifepristone prior to uterine curettage with hysteroscopy as routine therapy. The effect of the two groups after treatment was analyzed and compared. **Results:** The blood loss of the group A (27.42 ± 15.31) mL was significantly lower than that of the group B, $P < 0.05$. The total effective rate of the group A was 97.24%, which was significantly higher than that of the group B of 69.86%, $P < 0.05$. The bleeding days in the group A were significantly shorter than those in the group B, $P < 0.05$. The surgical time of group A was significantly shorter than the group B. **Conclusion:** Uterine artery embolization combined with hysteroscopy in the treatment of cesarean scar pregnancy can significantly improve the bleeding situation and prognosis.

Introduction

Cesarean scar pregnancy (CSP) is a special form of ectopic pregnancy, in which the gestational sac is implanted in a scar of a previous cesarean section; 6.1% of ectopic pregnancies after cesarean section have been reported to be CSPs, with an incidence of 1 in 1800–3000 pregnancies [1]. It can lead to massive hemorrhage and the risk of uterine rupture. Cesarean scar pregnancy is becoming common all over the globe with the increasing prevalence of cesarean section (CS) birth. There are 2 types of CSPs. Type I is caused by implantation of the amniotic sac on the scar with progression toward either the uterine cavity or the cervicoisthmic space. Type II is caused by implantation deeply into a previous CS, which is defect with infiltrating growth into the uterine myometrium and bulging from the uterine serosal surface. Type II may result in uterine rupture and severe bleeding during the first trimester of pregnancy [2]. Since 2010 in China-Japan Union Hospital of Jilin University, 82 type II CSP patients underwent transvaginal surgery to remove cesarean scar pregnancy;

all patients had a satisfactory therapeutic outcome while remaining fertile. Our experiences were reviewed and shared below.

Materials and Methods

General Information

Review from January 2010 to January 2016, the patients have been diagnosed as cesarean scar pregnancy by transvaginal ultrasound for the fine-detail evaluation of the gestational sac in relation to the scar. They were divided into two groups on the treatment method. The group A was offered prophylactic uterine artery embolization (UAE) and methotrexate (MTX) prior to uterine curettage with hysteroscopy method. The group B was treated with mifepristone prior to uterine curettage with hysteroscopy as routine therapy. The observation group (group A) aged 23 to 31(27.97±1.06) years old, the gestational weeks was 35 to 58 (46.78±0.22) , the size of the nidus was 2.2-4.8(3.1±0.6)cm, The value of bloodβ-HCG was 16025.6 to 19235.7 (17709.21±527.9) U/L. The control group(Group B) aged 24 to 33(28.54±1.12) years old, the gestational days was 32 to 57 (47.06±0.19) , the size of the nidus was 1.9-4.6(2.9±0.7)cm, the value of bloodβ-HCG was 17528.4 to 19458.7 (17236.53±516.8) U/L. There was no statistically significant difference in the general data such as age, gestational days, nidus size and β-HCG between the two groups of patients (P>0.05). **Table 1**

Table 1. General information of patients in two groups.

Group	Case number	Age (years)	Gestational days (days)	Size of the nidus (cm)	No of previous caesarean section(time s)	B-HCG (U/L)
Group A	47	27.97±1.06	46.78±0.22	3.1±0.6	1.36±0.63	17709.21±527.9
Group B	35	28.54±1.12	47.06±0.19	2.9±0.7	1.47±0.74	17236.53±516.8

Methods

The group A was offered prophylactic uterine artery embolization (UAE) and methotrexate (MTX 40mg) prior to hysteroscopy method. The group B was treated with mifepristone (100mg) prior to hysteroscopy as routine therapy. In the process of treatment, the effect of the two groups after treatment was analyzed and compared.

Outcome Measures

(1) volume of bleeding: volume method and weight method were used to calculate the amount of vaginal bleeding. The two groups were recorded the amount of vaginal bleeding

during the operation and the first 24h after the operation. (2) time for serum β -HCG levels return to normal.(3) the operation time.(4)time for normal menstrual cycle recovery.(5)the hospitalization days.

Statistical Methods

All data using SPSS 21.0 statistical software for processing, measurement data using mean and standard deviation ($X\pm S$) to represent. And paired t test for data comparison between two groups, $P < 0.05$ considered statistically significant.

Result

Comparison of Therapeutic Effect

The total effective rate of group A was 100%, and no invalid patients were found. The total effective rate of group B was 91.4%, there were 3 patients bleeding heavily and underwent laparotomy and removed the embryonal tissue. There was a statistically significant difference between two groups in blood loss volume ,operation time, menstrual cycle recovery and the days for β -HCG levels return to normal ($P < 0.05$). There was no statistically significant difference between two groups in the hospitalization days ($P > 0.05$), **Table 2**

Table 2. Comparison between the two groups.

Group	hospitalization days (days)	Blood loss volume (mL)	Operation time(min)	Menstrual cycle recovery (days)	β -HCG levels return to normal (days)
Group A	7.76 \pm 1.35	17.81 \pm 5.15	23.43 \pm 9.08	36.39 \pm 5.03	28.82 \pm 6.55
Group B	7.81 \pm 1.38	41.76 \pm 7.89	24.71 \pm 6.24	37.23 \pm 5.90	29.75 \pm 6.97
P Value	0.136	0.008	0.012	0.002	0.018

Discussion

CSP is a rare form of ectopic pregnancy that may lead to life-threatening heavy bleeding and uterine rupture due to abnormally adherent placenta. The etiology of CSP is unclear, but it is generally thought that CSP occurs when a blastocyst is implanted on fibrous scar tissue within a wedge-shaped myometrial defect in the anterior lower uterine segment at the site of a prior caesarean scar [3, 4]. The common presenting symptoms are vaginal bleeding and abdominal pain, but at least one-third of patients are asymptomatic [5, 6]. Due to the rate of cesarean deliveries and the severity of complications, it is important to diagnose CSP as early as possible. Transvaginal sonography is a useful tool for such purpose [2, 7] and has been

used in this study to confirm the CSP of the 82 patients, besides considering their clinical symptoms such as menopause, elevated serum β -HCG, vaginal bleeding, etc. Upon the diagnosis of CSP, termination of the pregnancy during the first trimester is strongly recommended due to the risk of uterine rupture associated with life-threatening hemorrhage. The goals of treatment are termination of pregnancy, reduction of hemorrhage, and prevention of uterus rupture. Two different types of CSP have been proposed [2]. The first type is an implantation on the prior scar with progression towards the cervico-isthmic space or the uterine cavity. Such a pregnancy may progress to viability with the risk of massive haemorrhage. The second type is a deep implantation into the caesarean scar defect growing towards the bladder and abdominal cavity and more prone to scar rupture [8,9]. The hysterectomy rate in these cases is 71% because of the increased risk of placental previa/accreta and massive hemorrhage [2,8,9,10]. Termination of the diagnosed cases by surgical or medical means may improve the outcomes by allowing preservation of the uterus and future fertility. It is anticipated that delay in treatment of scar pregnancies can lead to uterine rupture, hysterectomy and significant maternal morbidity [11]. Various medical and surgical treatments have been attempted, however, there is no consensus on the optimal mode of treatment [12]. Many medical and surgical approaches have been attempted with the aim of eliminating the gestational sac and preserving fertility, including systemic MTX. The surgical methods included dilatation and curettage, UAE, hysteroscopic resection, laparoscopic resection or even hysterectomy. Local, systemic and combined treatments with MTX have been described. However, fibrous tissue within the scar around the gestational sac can delay systemic MTX absorption into the sac [13]. Local injection of embryocides under sonographic guidance may decrease the need of additional interventions compared to systemic MTX [9, 10, and 11]. However, close monitoring of the patient after intervention is required as hemorrhage may still occur. Therefore, bilateral UAE should be considered [4,14]. Surgical management with laparoscopy or laparotomy with excision of the pregnancy may be optimal for women who do not respond to conservative medical treatments or are late to present for medical attention [13]. However, surgery carries the risk of postoperative adhesions that may impair future fertility, increased size of surgical wounds, a longer hospital stay and recovery and possibly an increased risk of future placental previa/accreta [9, 13, and 15]. Dilation and curettage should not be considered as the first choice of therapy. This is because the majority of the villi are implanted in the myometrium and it seems unlikely that the gestational sac can be expelled by curettage without perforating the uterine wall or damaging the urinary bladder and may also cause life-threatening hemorrhage [9, 11]. Previous findings suggest that selective UAE can temporarily block uterine perfusion and minimize hemorrhage and they have used this technique before or after curettage [16]. UAE treatment of CSP was first reported in 1999 and has been used widely to control hemorrhage and preserve the uterus [17, 18]. However, isolated UAE without eliminating the gestational sac results in the gradual decrease of serum β -HCG levels and irregular menstrual bleeding [11, 12]. Therefore, uterine curettage should be performed after UAE. Gelfoam appears to promote clotting via physical effects by supporting thrombus development. Vascular occlusion with gelfoam causes acute necrotizing arteritis. This inflammatory process eventually leads to breakdown of the gelfoam within 1-3 weeks after embolization, with subsequent vascular recanalization [19]. Because of its temporary nature, uterine curettage should be carried out as soon as possible. In published studies, uterine curettage was usually carried out within 24-72 h after UAE [13]. In accordance with our study, the results

demonstrated that UAE and methotrexate (MTX) prior to uterine curettage with hysteroscopy method may be an effective and safe treatment for CSP. In the pathological sample of CSP, trophoblast cells were found to have invaded the myometrium, adhered, implanted and even penetrated the myometrium [4]. For this reason, 40 mg of MTX was given by infusing the arterial catheter to manage the possibility of residual villi in the scar tissue. Previous studies reported that MTX alone followed by suction curettage requires more hospitalization time and causes greater bleeding volumes compared with UAE [4]. Therefore, laparoscopy-guided curettage after UAE combined with MTX (40 mg) is a safe and effective means of treating CSP. Compared with laparoscopy-guided curettage after having mifepristone, hospitalization days showed no significant difference, while the blood loss volume, the operation time, the days for menstrual cycle recovery and the days for β -HCG levels return to normal showed significant difference. The blood loss volume during laparoscopy-guided curettage after UAE combined with MTX was only 17.81 ± 5.15 (ml), the operation time was 23.43 ± 9.08 (mins), the days for menstrual cycle recovery was 36.39 ± 5.03 (days), the time for serum β -HCG normalization was 28.82 ± 6.55 (days) after the UAE combined with MTX. This study showed that all CSP patients under the UAE combined with MTX had much less bleeding and short time during curettage, and also had less days for menstrual cycle recovery and for β -HCG levels return to normal.

However, it needs to be emphasized that no invasive procedure is risk-free. Associated complications consist of pain, fever, nausea and vomiting, and are most transient symptoms. Because UAE blocked temporary uterine arterial blood flow, there is also a concern about whether ovarian perfusion is affected, which is directly connected to patient's reproductive future. Zhang et al. [20] found that the normal menstrual cycle resumed two or four months after performing UAE in association with local MTX, and a normal pregnancy occurred in 50% of the patients within one year. In our research, 47 CSP patients recovered their menstruation 1-4 months after UAE and 4 patients were pregnant again within one year. It has been estimated that once the blood vessel has been embolized with gelatin sponge particles, it reopens its course after around 2-3 weeks, which helps the recovery of the reproduction system [21, 22]. Until now, few reports have addressed the potential impact of UAE combined with MTX infusion on fertility. MTX is a FDA Pregnancy Category X medication, so patients should be informed about the associated risks and use contraception for at least 3 months after MTX infusion [20, 23].

In summary, accurate early diagnosis of pregnancy within cesarean scar and its effective management is important to preserve the fertility of patients and reduce maternal mortality. This study suggests that UAE combined with intra-arterial MTX infusion is a safe and effective treatment for CSP patients. Further studies with a larger sample size are necessary to confirm our findings.

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