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ORIGINAL ARTICLE

Pituitrin Injection before Hysteroscopic Curettage for Treating Type I Cesarean Scar Pregnancy in Comparison with Uterine Artery Embolization: A Retrospective Study

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Abstract

Background The effectiveness and safety of pituitrin injection coupled with hysteroscopy and suction curettage as treatment for type I cesarean scar pregnancy (CSP) have not been studied enough in the literature, by comparing it to uterine artery embolization (UAE) followed by suction curettage we aim to determine its efficacy.

Materials and Methods Data of 53 patients (the PIT group) with type I CSP treated with pituitrin injection combined with hysteroscopic suction curettage and 137 patients (the UAE group) with type I CSP treated with UAE followed by suction curettage were collected in retrospect. The clinical data were analyzed statistically to compare the efficacy and safety between the two groups.

Results The PIT group had a shorter duration of postoperative vaginal bleeding, postoperative hospitalization, and overall hospitalization length ($P < 0.05$). The PIT group had lower overall hospitalization costs and a lower rate of adverse events than the UAE group ($P < 0.05$). There was no significant difference between the two groups in terms of treatment success rate, the average length of operation, blood loss during the procedure, time when serum β-hCG returned to normal range, and menstrual recovery time after hospital release ($P > 0.05$).

Conclusion UAE and pituitrin injection followed by hysteroscopic suction curettage are good choices for type I CSP treatment. However, pituitrin injection with hysteroscopic suction curettage outperforms UAE followed by suction curettage. Thus, pituitrin injection may be an option of high priority for type I CSP.

Keywords Cesarean scar pregnancy · Hysteroscopy · Pituitrin · Suction curettage · Uterine artery embolization

Introduction

Cesarean scar pregnancy (CSP) is a rare ectopic pregnancy in which the fertilized egg is implanted in a prior cesarean section scar [1]. The incidence of CSP is 1:1800–1:2216 in early pregnancy [2]. An increase in rates of CSP is seen due to the increased rate of cesarean section deliveries in recent years [3].

There are two types of CSP: type I—grows toward the uterine cavity, and type II—grows toward the bladder and abdominal cavity, known as endogenic and exogenic, respectively. Our study is concerned with type I endogenic CSP, when the gestational sac develops toward the uterine cavity after implantation on the scar site [4]. Management of CSP is mainly focused on removing the gestational sac, excising trophoblastic tissue, homeostasis, and preserving fertility [5]. Among commonly used treatment modalities for type I CSP is uterine artery embolization (UAE) combined with dilatation and curettage (D&C) [6]. But UAE has certain limitations, it may cause uterine adhesions and affect ovarian function and fertility [7, 8]. Researchers recently are trying to avoid the bilateral UAE before the evacuation of the conceptus. Pituitrin is injected instead at the junction of the cervix and vagina for hemostasis before uterine curettage and suction.

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Only a few studies have focused on the advantages of pituitrin in gynecological procedures, especially CSP management. This study aimed to retrospectively analyze the clinical curative efficacy of pituitrin injection followed by hysteroscopic suction curettage compared to UAE followed by suction curettage and expand on prior research and provide sufficient evidence that the former is an effective and cost-efficient treatment choice for type I CSP.

Materials and Methods

Study Groups

The data were collected retrospectively from January 2013 to April 2020 in the Department of Gynecology at Jiangsu Province Hospital. After obtaining informed consent from all the patients and clearance from the ethics committee (2019-NT-24), 190 patients were recruited for this study. The clinical data were analyzed to compare the efficacy and safety between the groups.

Inclusion criteria

1. History of cesarean section.
2. History of amenorrhoea, serum beta-human chorionic gonadotropin (β-hCG) level increased, or urine pregnancy test positive.
3. Diagnosed as type I CSP as per diagnostic criteria of CSP; the expert consensus on diagnosis and treatment of CSP after cesarean section in 2016 [9]. According to the imaging data of the patients, classified as type I because gestational sac was implanted in the uterine scar, located in the uterine cavity, and the thickness of myometrium between gestational sac and bladder was more than 3 mm.
4. No cardiopulmonary, liver, kidney dysfunction or hematological disorders.
5. Postoperative pathology was per the pathological features of CSP; trophoblast and villous structures were seen in the myometrium of the scar.

Preoperative Preparation and Procedure

Patients were informed of risks and alternative treatment options once diagnosed. All routine examinations were obtained. Blood transfusion, Foley catheter, and an open venous line were also prepared. Preparations made for UAE or hysterectomy if necessary.

UAE Combined with Suction Curettage

Local anesthesia was injected 2 cm below the right inguinal ligament, and the right femoral artery was punctured using the modified Seldinger method. Under digital subtraction angiography (DSA), a catheter sheath was inserted through the internal iliac artery. Gelatin particles were injected via the catheter for embolization. Once the angiography showed occlusion of the uterine arteries, the catheter was removed, and the right femoral artery was bandaged and compressed. Bed rest for 24 h while vital signs were monitored. After 24–72 h of embolization, the patient underwent direct curettage or hysteroscopic suction curettage.

Pitutrin injection followed by suction and curettage

In the bladder lithotomy position after anesthesia, 6 U of pituitrin and 10 ml of normal saline were injected through the anterior fornix of the vagina at the junction of the cervix just prior suction curettage to remove fetal tissue under negative pressure of 400 mm Hg (53 k Pa). Hysteroscopy was done for residual tissue.

Efficacy judgment

1. Postoperative serum β-hCG level recovered to normal.
2. No residual fetal tissue in the uterine cavity.
3. Second intervention not required (UAE, laparoscopic surgery, open surgery or hysterectomy).
4. No complications.

Criteria for treatment failure

1. Postoperative serum β-hCG level does not drop or rise.
2. The mass on the scar is enlarged.
3. Internal bleeding in the abdomen, severe abdominal pain that required surgery, drugs or UAE intervention.

Observation index

1. Amount of bleeding during the procedure.
2. Duration of the procedure.
3. The procedure was successful or not (cure rate).
4. Duration of postoperative vaginal bleeding.
5. Total hospital stay.
6. Total hospital expenses.
7. Postoperative decrease in hemoglobin.
8. The time needed for postoperative β-hCG to return to normal levels.
9. Menstrual recovery time after the procedure.
10. Menstrual changes.

11. Adverse reactions (nausea and vomiting, lower abdomen or pelvic pain, fever, numbness and weakness of the lower limbs).

Postoperative Follow-up

All patients required to be on strict contraception for at least one year postoperatively and were monitored for a period of three months after discharge from hospital for β-hCG levels and US. Follow-up was done via telephone post-procedure to check for adverse reactions, menstrual recovery, and changes.

Statistical Analysis

All statistical analyses were performed with the SPSS 23.0 software. If the normal distribution was met, continuous data were expressed as mean ± standard deviation ($x \pm s$), and an independent t-test was used to analyze differences. If the normal distribution was not met, continuous data were represented as median [interquartile range], and Mann–Whitney U test was done for comparison. The Chi-squared test was used to compare categorical data. A $P \leq 0.05$ level of significance was considered statistically significant.

Results

Preoperative Clinical Data of the Two Groups

Patients ranged from ages 22 to 45 years with a mean age of 30.3 ± 0.72 years. The number of pregnancies ranged from 1 to 8, with 3 being the median. The number of miscarriages ranged from 0 to 6. In the past, 140 cases had only one cesarean section, and the remaining 50 cases had two cesarean sections. All patients had a history of c-section delivery, with a median time interval of 5 years since the last cesarean section (range 1–20 years). In 184 cases, CSP had occurred for the first time, and 6 cases were recurrent CSP.

Comparison of Cure Rate and Adverse Reactions Between the Two Groups

The average duration of postoperative vaginal bleeding in the PIT group was 5.20 ± 3.00 days, and the total hospital stay was 5.63 ± 3.25 days. The UAE group's average was 10.12 ± 14.51 days and 7.87 ± 3.56 days. PIT group's time of postoperative vaginal bleeding, postoperative hospital stay and total hospital stay was considerably shorter than those of the UAE group. The difference was statistically significant ($P < 0.05$, Table 1). The average total hospitalization expenses of the PIT group (6720.98 ± 1893.55 RMB), which was lesser than

Table 1 Comparison of postoperative clinical data of the two groups

Observation index	UAE group ($n = 137$)	PIT group ($n = 53$)	P-value
Successfully cured	127 (92.70)	48 (90.56)	0.850
Hospitalization time after the first evacuation (days)	03.06 ± 2.55	2.29 ± 1.51	0.042
Total length of hospital stay (days)	07.87 ± 3.56	5.63 ± 3.25	< 0.001
Total hospitalization expenses (ren min bi)	14,140.80 ± 4884.34	6720.98 ± 1893.55	< 0.001
Duration of procedure (minutes)	20.00 [17.00,30.00]	20.00 [15.00,25.00]	0.099
Blood loss during the procedure (ml)	10.00 [10.00,20.00]	10.00 [5.00,10.00]	< 0.001
Hb drop after procedure(g/L)	10.14 ± 8.18	11.70 ± 7.78	0.312
Duration of postoperative vaginal bleeding (days)	10.12 ± 14.51	5.20 ± 3.00	0.034
Postoperative serum β-hCG return to normal levels (days)	35.56 ± 16.86	26.64 ± 8.81	0.096
Postoperative recovery of menstruation(days)	41.78 ± 30.60	30.10 ± 8.77	0.239
Adverse reactions			
Fever	112(81.75)	15(28.30)	< 0.001
Abdominal Pain	75(54.74)	0	< 0.001
Nausea, vomiting	21(15.32)	0	0.006
Pain, weakness, and numbness in lower limbs	37(27.00)	0	< 0.001
Postoperative reduced menstruation (> 1/3 of previous menstrual volume)	82(59.85)	2(3.77)	< 0.001
Other adverse reactions	55(40.14)	3(5.66)	< 0.001

Data are represented as n (%) or mean ± SD or median [range]

Hb Hemoglobin, *β-hCG* beta-human chorionic gonadotropin, *PIT* pituitrin injection, *UAE* uterine artery embolization

the UAE group (14,140.80 ± 4884.34 RMB). As in Table 1 ($P < 0.05$), a significant difference was seen. The incidence of adverse reactions such as fever, lower abdomen or pelvic pain, nausea and vomiting, weakness and numbness of the lower extremities, menstrual reduction and any other side effects were lower in the PIT group when compared with the UAE group. PIT group had 15 patients (28.30%) with fever, all low grade, whereas 112 cases (81.75%) in the UAE group, the difference between the two groups was statistically significant ($P < 0.05$, Table 1). PIT group had no patients with abdominal pain, nausea and vomiting, weakness and numbness of the lower limbs, and 3 (5.66%) patients had other adverse reactions. A total of 75 patients in the UAE group (54.74%) had abdominal pain, 21 patients (15.32%) had nausea and vomiting, 37 cases (27.00%) had lower limb pain or numbness and weakness, and 55 cases (40.14%) had other adverse reactions such as allergies, changes in bowel movements, premature ovarian failure and deep vein thrombosis. This difference was statistically significant between the two groups ($P < 0.05$, Table 1). The number of patients with postoperative reduced menstruation in the PIT group was significantly lower than in the UAE group. The difference was statistically significant ($P < 0.05$, Table 1); only 2 patients (3.77%) in the PIT group had decreased menstruation in comparison with 82 patients (59.85%) in the UAE group. No statistically significant difference was recorded in the cure rate between the two groups ($P > 0.05$, Table 1). A total of 48 out of 53 patients in the PIT group did not require a second intervention (cure rate 90.56%); 127 out of 137 were successfully treated in the UAE group, whereas 9 patients required secondary intervention (cure rate 92.70%).

There was no statistically significant distinction between PIT and UAE groups regarding the duration of the procedure, amount of bleeding during suction curettage, postoperative decrease in hemoglobin levels, the time needed for postoperative β-hCG to return to normal levels, and duration of postoperative menstrual recovery.

Discussion

CSP was first reported by Larsen et al. in 1978 [10]. A study conducted found that the incidence of CSP was 0.15%, accounting for 6.1% of ectopic pregnancies among women with a history of cesarean section [11, 12]. Statistics from Peking Union Medical College Hospital in 2008 found that CSP incidence was 1:1 221, accounting for 1.05% of ectopic pregnancies [13]. The clinical early diagnosis rate of CSP has increased significantly with an increase in the rate of cesarean sections and the advancement of medical imaging technology [14]. CSP is a long-term complication of cesarean section, which can cause serious complications such as massive bleeding, placental implantation and uterine rupture. Therefore, the principle of diagnosis and treatment of CSP is early diagnosis, termination, and removal to preserve the patient's fertility [9].

More than thirty treatment methods are suggested for CSP, most done under ultrasound guidance, including D&C, D&C and UAE, D&C and intramuscular methotrexate, laparoscopic excision, laparoscopy and hysteroscopy, hysteroscopic, transabdominal, transvaginal or laparoscopic excision and uterine repair [15]. Ultrasound and Doppler imaging are used for diagnosing CSP. If the same treatment is adopted for patients with different types of CSP, the clinical prognosis is not the same, so the classification of CSP is of great significance for the choice of treatment options [10].

The endogenous scar pregnancy proposed by Vial is further divided into type I and type II [16]. Among them, type I CSP refers to a scar pregnancy with gestational sac mainly located in the uterine cavity, partially implanted in the uterine scar, and the thickness of the anterior uterine wall muscle layer is greater than 3 mm [7].

The commonly used treatment for type I CSP is UAE combined with uterine evacuation, but UAE has certain limitations [8]. Reports indicate that UAE may affect ovarian function and endometrial blood supply and cause intrauterine adhesions, postoperative thrombosis in lower limbs or complications such as vulvar pain [8, 17, 18]. In this study, patients with type I CSP showing stable vital signs and no high-risk factors for significant bleeding, we injected pituitrin at the squamocolumnar junction of the cervix instead of performing UAE before hysteroscopic suction curettage as a treatment plan for uterine purgation. The advantage of hysteroscopic curettage compared to blind curettage is apparent in the treatment of CSP. Hysteroscopy can directly observe the gestational tissue's position, size, and blood supply in the uterine cavity. The presence of residual tissue can be detected under direct vision with the help of a hysteroscope. It can reduce the risk of bleeding and aid in treating abnormal uterine cavity conditions such as intrauterine adhesions or mediastinal uterus, conducive to pregnancy [19].

Pituitrin is a water-soluble component extracted from pigs, cattle and other mammals' posterior pituitary glands, and it contains oxytocin and vasopressin. Oxytocin has a strong contraction effect on uterine smooth muscle, whereas vasopressin constricts small arteries and capillaries. Therefore, as a quick and effective hemostatic agent, pituitrin is widely used in gynecological surgery [20]. It can effectively reduce intraoperative bleeding in the treatment of CSP. Pituitrin is cheap and easy to obtain. However, intensive monitoring is required when using pituitrin during surgery.

The administration of pituitrin can contract the smooth muscles in the blood vessels throughout the body, which can cause adverse reactions such as increased blood pressure, angina pectoris and decreased urine output [21]. In recent years, pituitrin injection before suction curettage as a treatment for CSP has been gaining popularity, especially in China.

The probable reason for a decreased postoperative hospital stay in the PIT group is that as long as the patients do not have pituitrin contraindications, the pituitrin injection does not require additional preoperative preparations. In addition, hospital stay after UAE is prolonged as patients tend to have abdominal pain, fever and other adverse reactions. The risk of residual tissue was significantly reduced as the gestational tissue in the PIT group was located by ultrasound before curettage, and hysteroscopy was performed. In the UAE group, curettage included direct curettage under ultrasound monitoring or hysteroscopic guided curettage. Direct curettage may lead to residual tissue, long-term intrauterine bleeding after surgery, and require a second curettage.

Until recently, there was no literature comparing pituitrin pretreatment with UAE. Our research is one of the initial studies shedding light on this comparison. The latest study by Jianing Wang et al. suggests similar findings as our study considering using pituitrin instead of UAE before the evacuation procedure [22]. However, their sample size is smaller and included all three types of CSP, while our study focused on type I CSP that could undergo suction curettage.

Conclusion

Pituitrin with hysteroscopic suction curettage and UAE with suction curettage are safe and effective treatments for type I CSP. However, with pituitrin injection, the patient's duration of hospital stay and postoperative vaginal bleeding time is significantly reduced. The cost of treatment and the incidence of complications are relatively low. In combination with hysteroscopic suction curettage, pituitrin warrants recognition, clinical implementation, and further research. Thus, this mode of therapy is worthy of clinical promotion.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical Standard The study was approved by the institutional local ethics committee of Jiangsu Province Hospital (2019-NT-24) and informed consent was also obtained from the patients.

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