Clinical efficacy analysis of different therapeutic methods in patients with cesarean scar pregnancy

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Research article

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Abstract

Background Cesarean scar pregnancy (CSP) is a rare form of ectopic pregnancy with a serious life-threatening situation. The purpose of this study is to analyze the clinical efficacy of five therapeutic strategies in patients with CSP.

Methods A total of 135 CSP patients were included in our research and divided into five groups based on the treatment they received, including transvaginal resection (Group A), laparoscopic resection (Group B), uterine arterial embolization (UAE) combined with hysteroscopic curettage (Group C), UAE combined with uterine curettage (Group D), and hysteroscopic curettage (Group E). To investigate the clinical efficacy of these strategies, intraoperative bleeding, serum $\beta$-hCG levels and recovery time, menstruation recovery time, hormone levels at 1 month after treatment, hospital stays and costs were analyzed.

Results The lowest postoperative serum $\beta$-hCG levels and the shortest serum $\beta$-hCG and menstruation recovery times were observed in group A, the next were in group B. Group C and D had small amount of blood loss. The hospital stays and costs were low in group E. In addition, no significant difference was performed at the sex hormone levels between the five groups.

Conclusions Our results indicated that resection surgery and UAE have good curative effects, but high hospital costs in CSP treatment. The selection of an optimal treatment regimen for CSP should be carried out based on specific conditions of the patients.

Introduction

Cesarean scar pregnancy (CSP) is a rare form of ectopic pregnancy with a serious life-threatening situation (1). It was first described in the study in 1978, and immediately becomes an important clinical challenge over the last 10 years (2). CSP is characterized by the gestational sac implantation at a previous scar site after cesarean section (3). The incidence of CSP is increasing in the recent decades, which mainly due to the elevated rate of cesarean section (4). Statistical data indicated that the cesarean section rate has increased from 5% in the early 1970s to more than 50% in the late 1990s in some developed countries (5). CSP is considered a long-term complication in the patients received a cesarean section. It is different from cervical, tubal or other types of ectopic pregnancies, and 1 case can be identified among 2500 ~ 8000 cesarean sections (6).

The most obvious symptom of CSP is vaginal bleeding at the early pregnancy (7). However, the diagnosis of CSP remains difficult, and some complications, such as hysterectomy, are presented if a false-negative diagnosis is performed (8). The pregnancy sac that implants on the thinned myometrium at the previous cesarean section line is hard to find, because its detection should be carried out when a cervix and an empty uterine cavity are observed (9).

With the increased incidence of CSP, several therapeutic strategies have been improved, such as uterine curettage, hysteroscopic curettage, uterine arterial embolization (UAE), surgical resection and some
combined methods (10–15). These advanced strategies have achieved considerably satisfactory results. However, the clinical responses of these techniques are variable in different CSP cases (16).

In the present study, we assessed the information of 135 CSP patients and compared the clinical efficacy of five therapeutic strategies: (1) transvaginal resection; (2) laparoscopic resection; (3) UAE combined with hysteroscopic curettage; (4) UAE combined with uterine curettage; and (5) hysteroscopic curettage.

**Methods**

**Patients and grouping**

A total of 135 patients were recruited in our research, who were diagnosed with CSP in Qingdao Hiser Medical Group between 2012 and 2016. All the patients were meet the following inclusion criteria: (1) history of amenorrhea; (2) history of cesarean section; (3) high $\beta$-hCG level compared with the normal value; (4) diagnosis of CSP using ultrasound based on the 1997 standard method (17) as follows: (i) gestational sac is not in the uterine cavity; (ii) gestational sac is not in the cervix; (iii) gestational sac locates in the long narrow section of the anterior uterine wall; (vi) a wall between the bladder and gestational sac is thin. The age range of the patients was 18–40 years, and the time duration of the most recent cesarean section time of the patients was 1–10 years. The demographics and clinical information were all recorded and listed in Table 1. The protocols of this study were approved by the Ethics Committee of The Affiliated Qingdao Hiser Hospital of Qingdao University (Qingdao Hospital of Traditional Chinese Medicine), and the written informed consent was received from each of the patient.

All these 135 patients were assigned into five groups based on the therapeutic strategies they received: transvaginal resection (Group A, n = 30); laparoscopic resection (Group B, n = 28); UAE combined with hysteroscopic curettage (Group C, n = 25); UAE combined with uterine curettage (Group D, n = 27); and hysteroscopic curettage (Group E, n = 25).

**Transvaginal resection (Group A)**

The patients assigned into group A were placed in a dorsal lithotomy position and received i.v. anesthesia. 10 mL epinephrine (0.6 $\mu$g/mL) was injected locally through the cervicovaginal gap except for the cases with hypertension history. The bladder was moved down appropriately, and the peritoneum was opened. An incision was made and the pregnancy tissue was exposed. Then the scar tissue and pregnancy tissue were all removed. To decrease bleeding, 2 U pituitrin was injected into the cervix. Suction curettage was subsequently carried out through the incision with the guidance of B-mode ultrasound. The incision was sutured using 1–0 absorbable sutures (Polysorb GL182; Covidien, Ltd.).

**Laparoscopic resection (Group B)**
The patients in group B were placed in lithotomy position to create conventional CO2 pneumoperitoneums. A laparoscope was used to detect the anterior wall of the uterine isthmus, and the relationship between the cesarean section scar and bladder, the CSP mass size and the adhesion status were evaluated. The adhesiolysis was conducted if there was adhesion. The bladder was moved down appropriately, and 10 mL hypophysin (0.1 U/mL) was infected around the lesion. After the uterine contents were all removed, a catheter was advanced into the uterine cavity through the cervix, and a balloon filled with 15 mL saline was placed in the cervical isthmus. The resection using laparoscopy was carried out as per the method presented in the study by Donnez et al. (18). The scar was opened after bipolar coagulation at the lesion, then the lesion tissues were excised until the normal myometrium was exposed. The incision was sutured using 1–0 absorbable sutures (Polysorb GL182; Covidien, Ltd.).

UAE combined with hysteroscopic curettage (Group C)

UAE was carried out following the conventional method. The patients were placed in supine position and the bilateral inguinal canal was disinfected. After the local anesthesia, femoral artery puncture was performed under 2 cm of the right inguinal ligament. The catheter and wire guide were then advanced to perform the left iliac arteriography. We injected 75 mg methotrexate into the uterine artery after the uterine artery orifice was observed, and the embolism was achieved using 700 ~ 900 μm microspheres. The embolism of the heterolateral uterine artery was performed with the same method. According to the arteriography, the uterine artery was entirely blocked. The puncture site was pressurized and bandaged after the treatment. After 48 h, the hysteroscopic curettage was performed. Briefly, the patients were placed in the bladder lithotomy position and received i.v. anesthesia. The uterine cavity was inflated using a distending media. Then a hysteroscope was used to evaluate the relationship between the gestational sac and the incision site. The pregnancy tissues were removed by curettage, and no residual tissue was found by ultrasound. The residual pregnancy tissues were all removed by biopsy forceps until the scar site was smooth.

UAE combined with uterine curettage (Group D)

The patients in group D were received UAE combined with uterine curettage. UAE was performed as the method as above. After the 48 h of UAE, uterine curettage was carried out for the patients. The patients with full bladders were placed in the bladder lithotomy position. The pregnancy tissues were removed using biopsy forceps with the guidance of B-mode ultrasound. The curettage was finished until the scar site was smooth under the ultrasound detection.

Hysteroscopic curettage (Group E)

The patients in group E were treated with uterine curettage by hysteroscopy. The procedures of this strategy were given in the method of group C.
Observational indexes

To evaluate the therapeutic effects of the five treatment methods above, we collected and analyzed several indicators of the patients with CSP. The intraoperative bleeding, serum β-hCG levels and recovery time, menstruation recovery time, hormone levels at 1 month after treatment, hospital stays and hospital costs.

Follow-up

Each of the patient was enrolled in a 1 year follow-up survey after discharged from hospital.

Statistical analysis

All statistical analyses were performed using SPSS 18.0 software (SPSS Inc., Chicago, IL). Data were analyzed using Student’s t test and ANOVA analysis. A result with a $P < 0.05$ was considered statistically significant.

Results

Preoperative conditions of the CSP patients

All the demographics and clinical information of the patients with CSP were summarized in Table 1. The 135 patients with CSP with age range of 18–40 years ($33.26 \pm 4.23$) were divided into five groups according to the different therapeutic strategies. Their amenorrhea time was 48–86 days, thickness of scar was 0.8–3.9 mm, and levels of serum β-hCG was 485–38,452 mIU/mL. No obvious significance was found between the five groups at age, pregnancy history, amenorrhea time, the thickness of scar and serum β-hCG levels (all $P > 0.05$).

Serum β-hCG levels in different groups

The levels of serum β-hCG in different groups were measured after the treatment. As shown in Table 2, we analyzed the β-hCG levels before and after the therapies and found that serum β-hCG levels were significantly downregulated in each of group before the surgery compared with preoperative serum β-hCG levels (all $P < 0.05$). Moreover, the levels of serum β-hCG were variational between the five groups with significant differences ($P < 0.05$), and the lowest serum β-hCG was observed in group A (Figure 1).

Intraoperative bleeding in different groups
The operative procedures were remarkably different between the five groups. Thus, the amount of blood loss during the surgery was compared for the five treatment groups. From the data shown in Figure 2, we found that the intraoperative bleeding was dramatically high in group A and group B, while it was low in group C and group D. Among all these five groups, group C had the lowest amount of blood loss during the operation \((P < 0.05)\).

**Hormone levels in different groups**

Given the important roles of sex hormones in biological processes of the female reproductive system, we examined the levels of follicle stimulating hormone (FSH), estradiol (E2) and luteinizing hormone (LH) in the patients at 1 month after the surgery. The analysis results indicated that the levels of FSH, E2, and LH had no significant difference between the five groups (all \(P > 0.05\), Figure 3).

**Postoperative findings**

In addition to the changes in serum \(\beta\)-hCG, intraoperative bleeding, and hormone levels, the recovery times of serum \(\beta\)-hCG and menstruation, hospital stays and hospital costs after the surgery were assessed in this study. The data in Table 3 revealed that the shortest recovery times of serum \(\beta\)-hCG and menstruation were detected in group A, and the next were in group B \((P < 0.05)\). However, the hospital stays and costs were significantly high in group A and group B compared with the other groups \((P < 0.05)\).

**Prognosis**

A 1-year follow-up survey was carried out for the patients after hospital discharge. There was no severe complication detected in the patients and the levels of serum \(\beta\)-hCG maintain at the normal value after treatment. The menstruation was recovered to normal at 2–9 months after therapy in 132 patients, and three patients were amenorrhea at the end of the survey. In addition, the enclosed mass was disappeared at 3–11 months after the treatment.

**Discussion**

CSP is a kind of heterotopic pregnancy, which is characterized by the implantation of gestational sac in the scar of a previous cesarean section, leading to life-threatening complications (19). The risk of hysterectomy and hematorrhea was increasing along with the growth and development of the embryo in the patients with CSP (20). The implantation of gestational sac is occurred due to the invasion of the myometrium via a microscopic fistula or the direct implantation of fertilized ovum at the invaginated cesarean scar (21, 22). Data in the previous studies reported that multiple cesarean section history, hysteromyoma decollement, and uterine curettage history are the common risk factors for the occurrence
of CSP. The uterine incision abnormal healing and the inflammation after the surgeries above promote the formation of scar and thus increase the rate of CSP (23). Currently, the diagnosis of CSP mainly depends on high-resolution transvaginal color Doppler ultrasonography. Also, magnetic resonance imaging (MRI) is considered an assistant examination for ultrasonography, which can measure the volume of the lesion and provide the lesion location information during the surgery (24). Since the necessity of cesarean section in clinical practices, it is impossible to avoid the occurrence of CSP. Thus, suitable treatment programs are needed for the patients diagnosed with CSP.

It is generally considered that the therapeutic purpose for CSP is to remove the embryo, reduce the amount of bleeding, and recover the fertility of the patients. Some therapeutic strategies have been improved currently, including medical therapy, UAE, hysteroscopic curettage, hysteroscopic resection, laparoscopic resection and transvaginal resection. To select the most appropriate treatment regimen, the clinical characteristics of the patients need to be sufficient assessed (25, 26). Although the available therapeutic methods have been applied in the clinical practices, their treatment effects still need to be further analyzed and compared due to the limitations of these strategies (27). Therefore, our study was carried out to assess the clinical efficacy of five therapeutic methods, including transvaginal resection, laparoscopic resection, UAE combined with hysteroscopic curettage, UAE combined with uterine curettage, and hysteroscopic curettage, in 135 patients with CSP.

Hysteroscopic curettage has been extensively applied in clinical practices for it is one of the minimally invasive surgeries for patients with CSP (28). It can be used to clean and monitor the uterine cavity and give the precise data of gestational sac size and incision status, and thus contributes to the uterine curettage with the accurate position. The rates of uterine perforation and hemorrhage can be reduced by using hysteroscopic curettage in CSP treatment. UAE is a procedure where an interventional radiologist used a catheter to deliver small particles that block the blood supply to the uterine body (29). According to this method, blood flow to the gestational sac is stopped, leading to atrophy of the sac. This interventional method can block the arterial lumen but has no damaging effects on the capillary network. The application of UAE combined with uterine curettage or with hysteroscopic curettage has been widely used in recent years, which facilitates to better outcomes for the patients with CSP (30). The results of our study also revealed that the amount of blood loss was dramatically low in the patients received UAE combined with uterine curettage or with hysteroscopic curettage compared with those received other therapies. Resection of lesions is the basic principle for CSP treatment, and it can be achieved by transvaginal resection or laparoscopic resection, which represent two extensively used resection operations for CSP patients (14, 31). These methods can completely resect the pregnancy tissues, shorten the recovery time of β-hCG and protect the fertility of the patients with better prognosis. In our research, we also demonstrated that the patients received transvaginal resection or laparoscopic resection had low postoperative serum β-hCG levels and short recovery time. To further understand the clinical efficacy of these therapeutic strategies, the outcomes of CSP patients were evaluated and compared.
The intraoperative bleeding, postoperative serum β-hCG levels and recovery time, menstruation recovery time, hormone levels at one month after treatment, hospital stays and costs of the patients with CSP were investigated in this present study. After the treatment, the serum β-hCG levels were significantly decreased compared with the preoperative levels, and the most rapid decline in serum β-hCG levels was observed in patients received transvaginal resection, and the next was detected in patients with laparoscopic resection treatment. However, these two methods led to a large amount of blood loss compared with the other strategies. Inversely, we found that the patients received UAE had obviously low intraoperative bleeding, which is one of the attractive advantages of UAE (25). Also, the postoperative recovery times at serum β-hCG levels and menstruation was also analyzed. The results indicated that the shortest recovery times were detected in transvaginal resection group, and the next was in laparoscopic resection group. However, the hospital stays and costs were markedly high in both two groups. Moreover, the sex hormone levels were examined at one month after the surgery and showed no significant difference between the five groups. According to the 1 year follow-up survey, no severe complication was found in these patients, and the serum β-hCG levels and menstruation were recovered to normal in most of the patients at the end of the follow-up.

Taken together, our results revealed that transvaginal resection and laparoscopic resection in CSP treatment have advantages of shorter time to serum β-hCG and menstruation normalizing and high success rates, that UAE is characterized by its small intraoperative amount of blood loss. However, their hospital costs are relatively high. Therefore, the selection of an optimal treatment regimen for CSP should be carried out based on specific conditions of the patients.

Declarations

Abbreviations

CSP: Cesarean scar pregnancy

UAE: uterine arterial embolization

Ethics approval and consent to participate

The protocols of this study were approved by the Ethics Committee of The Affiliated Qingdao Hiser Hospital of Qingdao University (Qingdao Hospital of Traditional Chinese Medicine), and the written informed consent was received from each of the patient.

Consent for publication

Written informed consent for publication was received from each of the patient.
Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

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Authors’ contributions

YW and YG initiated and designed the study. YW, LS and YS carried out the study and collected important background information. YW, XL and YG carried out literature search, data analysis and manuscript preparation. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References


### Tables

#### Table 1 Demographics and clinical information of the patients with CSP

<table>
<thead>
<tr>
<th>Features</th>
<th>Group A (n = 30)</th>
<th>Group B (n = 28)</th>
<th>Group C (n = 25)</th>
<th>Group D (n = 27)</th>
<th>Group E (n = 25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.42 ± 4.55</td>
<td>32.54 ± 3.81</td>
<td>34.27 ± 4.25</td>
<td>33.82 ± 4.16</td>
<td>32.93 ± 3.95</td>
<td>0.42</td>
</tr>
<tr>
<td>Pregnancy history (times)</td>
<td>1-2</td>
<td>1-2</td>
<td>1-2</td>
<td>1-2</td>
<td>1-2</td>
<td>0.68</td>
</tr>
<tr>
<td>Amennorhea time (days)</td>
<td>61.45 ± 5.24</td>
<td>62.52 ± 5.26</td>
<td>63.14 ± 5.39</td>
<td>62.42 ± 5.18</td>
<td>62.75 ± 5.32</td>
<td>0.47</td>
</tr>
<tr>
<td>Thickness of scar (mm)</td>
<td>1.25 ± 0.51</td>
<td>1.21 ± 0.58</td>
<td>1.22 ± 0.50</td>
<td>1.28 ± 0.56</td>
<td>1.24 ± 0.53</td>
<td>0.34</td>
</tr>
<tr>
<td>Serum β-hCG (mIU/mL)</td>
<td>28,418 ±</td>
<td>25,457 ±</td>
<td>28,732 ±</td>
<td>25,147 ±</td>
<td>29,783 ±</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>1,038.49</td>
<td>1,189.75</td>
<td>1,284.12</td>
<td>1,345.74</td>
<td>1,410.26</td>
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</tr>
</tbody>
</table>

#### Table 2 Preoperative and postoperative serum β-hCG in the patients with CSP

<table>
<thead>
<tr>
<th>Status</th>
<th>Group A (n = 30)</th>
<th>Group B (n = 28)</th>
<th>Group C (n = 25)</th>
<th>Group D (n = 27)</th>
<th>Group E (n = 25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperation (mIU/mL)</td>
<td>28,418 ±</td>
<td>25,457 ±</td>
<td>28,732 ±</td>
<td>25,147 ±</td>
<td>29,783 ±</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>1,038.49</td>
<td>1,189.75</td>
<td>1,284.12</td>
<td>1,345.74</td>
<td>1,410.26</td>
<td></td>
</tr>
<tr>
<td>1 week after operation</td>
<td>21,845 ±</td>
<td>22,453 ±</td>
<td>23,115 ±</td>
<td>23,982 ±</td>
<td>25,487 ±</td>
<td>0.15</td>
</tr>
<tr>
<td>(mIU/mL)</td>
<td>1,047.25</td>
<td>1,021.32</td>
<td>1,125.24</td>
<td>9,58.52</td>
<td>1,147.85</td>
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<tr>
<td>2 weeks after operation</td>
<td>9,238 ±</td>
<td>11,856 ±</td>
<td>14,286 ±</td>
<td>15,869 ±</td>
<td>18,954 ±</td>
<td>0.028</td>
</tr>
<tr>
<td>(mIU/mL)</td>
<td>552.14</td>
<td>641.28</td>
<td>685.45</td>
<td>692.14</td>
<td>742.18</td>
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#### Table 3 Postoperative observation of the patients with CSP
<table>
<thead>
<tr>
<th>Features</th>
<th>Group A (n = 30)</th>
<th>Group B (n = 28)</th>
<th>Group C (n = 25)</th>
<th>Group D (n = 27)</th>
<th>Group E (n = 25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum β-hCG recovery time (days)</td>
<td>18.79 ± 3.48</td>
<td>20.42 ± 3.87</td>
<td>28.52 ± 4.28</td>
<td>31.89 ± 4.56</td>
<td>46.27 ± 5.21</td>
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</tr>
<tr>
<td>Menstruation recovery time (days)</td>
<td>25.78 ± 5.42</td>
<td>29.52 ± 5.13</td>
<td>34.52 ± 5.84</td>
<td>37.25 ± 5.47</td>
<td>68.24 ± 6.85</td>
<td>0.041</td>
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<tr>
<td>Hospital stays (days)</td>
<td>7.52 ± 1.98</td>
<td>8.87 ± 2.12</td>
<td>6.81 ± 1.87</td>
<td>4.12 ± 1.74</td>
<td>9.05 ± 1.68</td>
<td>0.018</td>
</tr>
<tr>
<td>Hospital costs (RMB)</td>
<td>12,074.47 ± 512.47</td>
<td>1,365.58 ± 584.34</td>
<td>8,245.68 ± 657.25</td>
<td>5,845.62 ± 687.29</td>
<td>3,895.62 ± 254.17</td>
<td>0.027</td>
</tr>
</tbody>
</table>

**Figures**
Figure 1

Preoperative and postoperative Serum β-hCG in patients with CSP. The levels of serum β-hCG were variational between the five groups, and the lowest serum β-hCG was observed in group A.
Figure 2

Intraoperative bleeding in the CSP patients. The amount of blood loss was relatively low in group C and group D.
Figure 3

Postoperative hormone levels in the patients with CSP. No significant difference was detected at sext hormone levels between the five groups. FSH, follicle stimulating hormone; E2, estradiol; LH, luteinizing hormone.