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Is methotrexate administration needed for the treatment of caesarean section scar pregnancy in addition to suction curettage?

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ABSTRACT **Objective** This study evaluated the clinical outcomes and safety of treating caesarean scar pregnancy (CSP) by means of suction curettage followed when required by Foley tamponade, with or without methotrexate (MTX) therapy preceding the curettage.

Methods Twenty-five patients with CSP were identified between August 2008 and April 2012. The first team of doctors treated Group A patients ($n = 11$) with systemic MTX followed by dilatation and suction curettage whereas the second team of doctors carried out only a suction curettage on women of Group B ($n = 14$). If uncontrolled vaginal bleeding occurred in either group during or after the operation, a Foley catheter, guided by real time transabdominal ultrasound, was placed in the uterine cavity against the site where the CSP had been implanted.

Results Clinical outcomes in the two groups – including mean estimated blood loss, major complication rate, and hospital length of stay – were comparable. Surgeons used Foley catheter balloons for tamponade in six of the 11 patients in Group A and in seven of the 14 patients in Group B. Treatment was successful in ten of 11 cases in group A and 13 of 14 cases in group B. Group B's mean duration of treatment (2.36 ± 0.49 days) was significantly shorter than that of Group A (14.45 ± 4.96 days; $p < 0.001$).

Conclusion Suction curettage, followed when needed by Foley catheter tamponade, is an effective treatment for CSP.

KEY WORDS Caesarean scar pregnancy; Suction curettage; Foley catheter; Methotrexate

INTRODUCTION

A blastocyst may implant in the fibrous scar tissue of a prior caesarean section^{1,2}. Larsen and Solomon were the first to report on a caesarean scar pregnancy (CSP), in 1978³. Since then, the number of caesarean sections has dramatically increased worldwide, and so has the incidence of CSP. Jurkovic *et al.*⁴ and Seow *et al.*⁵ estimated that the prevalence of CSP among women receiving early pregnancy assessment in their setting was 1:1800 and 1:2216, respectively. This prevalence constitutes 6% of all cases of ectopic pregnancy among women with a history of at least one prior caesarean delivery⁶. In the meantime, improvements in early pregnancy assessment standards and the general use of Doppler transvaginal ultrasound have led to early intervention and significant gains in favourable outcomes for patients with CSP.

Despite improvements in the care and treatment of CSP, the lack of universally accepted therapeutic management protocols means that management of this entity has been mainly based on experiences reported in case studies. In this study, we aimed to evaluate the clinical outcomes and the safety of treating CSP with suction curettage followed by Foley tamponade with or without prior methotrexate (MTX) therapy.

MATERIALS AND METHODS

In this retrospective study we analysed pre- and post-operative records of CSP patients treated between August 2008 and April 2012 in either the Department of Obstetrics and Gynaecology of the Suleymaniye Maternity Hospital for Research and Training or that of Bezmialem Vakif University, both in Istanbul. The study was approved by Bezmialem Vakif University's Ethics Committee. Informed consent had been obtained from each patient prior to initiating MTX and/or suction curettage treatment.

Inclusion criteria were: the absence of uncontrolled vaginal bleeding, an unruptured CSP, a CSP gestational age of ≤ 11 weeks, haemodynamic stability, and no other gynaecological disorder. Gestational age was calculated based on the last menstrual period. Where necessary, an adjusted date of confinement was determined using a 7 MHz covered ultrasound vaginal probe (Voluson 730 expert; GE Medical Systems, Zipf, Austria). Exclusion criteria were: contraindications for use of MTX such as neutropenia, elevated liver

enzymes, and abnormal renal function tests. A diagnosis of CSP was made in the presence of (i) an empty uterine cavity and cervical canal with endometrium clearly visible, (ii) a gestational sac located anteriorly in the isthmus of the uterus with absence of any defect in the myometrial layer between the uterine bladder and the sac, and (iii) the gestational sac, with or without identifiable cardiac activity, embedded in and surrounded by the myometrium and the fibrous caesarean scar⁷. All cases complied with the aforementioned criteria (Figure 1).

Associated risks of therapy were discussed with each subject, including the side effects of MTX, blood transfusion, life-threatening haemorrhage, uterine scar rupture, and the possible need for hysterectomy. After obtaining informed consent, the following primary treatments were applied: for Group A ($n = 11$) managed by the first medical team, systemic MTX followed by suction curettage; for Group B ($n = 14$) cared for by the second team of doctors, suction curettage only.

The suction curettage was performed under trans-abdominal ultrasound (TAS) guidance, using a No. 6 Karman canulla. Each of the 11 patients in Group A received prior to that a single intramuscular injection of MTX (50 mg/m² body surface area). If any patient's β -human chorionic gonadotrophin (hCG) level decreased by less than 50% of the pretreatment value and the ultrasound revealed fetal cardiac activity seven days after treatment, the same dosing regimen was repeated. On day 8 after the last MTX administration, the uterocervical canal was dilated to 7 mm by a cervical dilator, then suction curettage under transabdominal ultrasound (TAS) guidance was performed to remove the retained products of conception as well as any blood clots. To reduce the risk of uterine rupture and bladder injury, sharp curettage was not performed. The 14 patients in Group B received suction curettage under guided TAS.

Foley catheter tamponade (with a conventional rubber catheter, 16 French) was an optional, additional treatment used if, in either group, uncontrolled vaginal bleeding occurred during or after operation. The balloon, filled with 10–15 ml physiological saline, was positioned under real time TAS guidance into the isthmus portion of the uterus to apply pressure on the caesarean section scar. The Foley catheter was left in place for 48 hours. If this treatment was not effective, a laparotomy was performed.

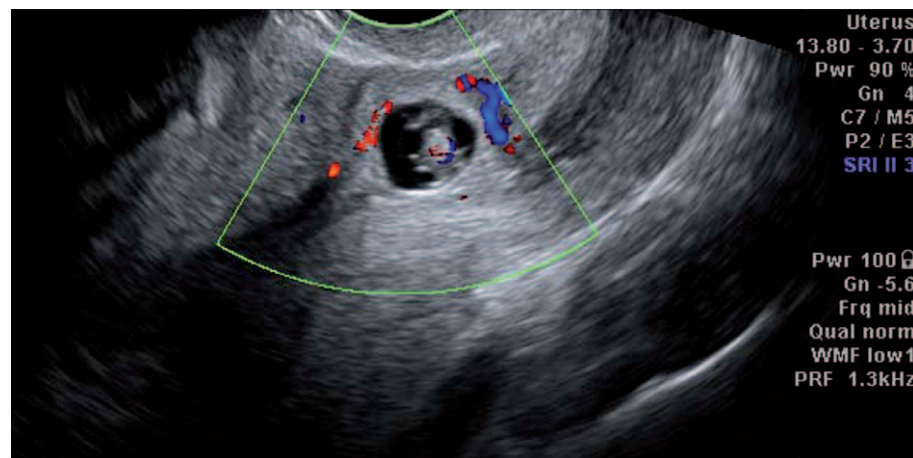


Figure 1 Transvaginal sonogram of the caesarean scar pregnancy, showing the empty uterine cavity and the empty cervical canal. The gestational sac is located in the thin lower anterior wall of the uterus behind a caesarean section scar and protrudes toward the urinary bladder. A rich vasculature surrounds the gestational sac.

A successful outcome was defined as normalisation of serum β -hCG levels, disappearance of the CSP mass confirmed by ultrasound examination, avoidance of major complications (uterine scar rupture, laparotomy, and hysterectomy). The success rate, peri- and post-treatment complications, mean estimated blood loss, number of patients in whom Foley catheter balloons were used for tamponade, mean duration of treatment, length of stay in the hospital, and laparotomies or hysterectomies were recorded.

Statistical analysis

The Mann-Whitney U test was used to analyse differences in all quantitative data. Analysis of categorical data was performed using Fisher's Exact Test with $p < 0.05$ considered as significant. For data analyses SPSS software 11.5 was used.

RESULTS

Twenty-five women with CSP were included in this retrospective study. On admission, four of them were experiencing abdominal pain and vaginal bleeding, four more complained of painless vaginal bleeding, and the other 17 were asymptomatic with incidental identification having occurred through comprehensive prenatal screenings. In the study population, 12 women had had one previous caesarean delivery, 11 had had two, and two had had three. Eleven

women received systemic MTX followed by suction curettage whereas the 14 others had a suction curettage only. As shown in Table 1, the groups were comparable with regard to maternal age, gravidity, number of prior caesarean sections, time interval between previous caesarean sections, estimated gestational age, gestational sac/mass diameter (mm), β -hCG levels before treatment, cardiac activity discerned within the gestational sac, abdominal pain, vaginal bleeding, and haemoglobin levels before treatment. Table 2 also shows no differences between groups as to post-treatment major complications (i.e., uterine scar rupture, laparotomy, and hysterectomy), number of patients in whom Foley catheter balloons were used for tamponade, or success rates. The mean hospital stay and mean estimated blood loss were lower in Group B than in Group A, but not markedly so. On the other hand, Group B (2.36 ± 0.49 days) needed far less time for completion of treatment than Group A (14.45 ± 4.9 days, $p < 0.001$). After the MTX injection, the CSP mass did not disappear in any patient. Thirteen patients required Foley tamponade; overall, 23 subjects were successfully treated. Treatment was considered to have failed in two women who each needed a laparotomy to stop haemorrhage. Hysterotomy was performed in the patient belonging to Group A, whereas manual compression was applied for 20 minutes to the lower segment of the uterus of the patient in Group B.

Table 1 Clinical information on the 25 women with caesarean section scar pregnancy.

Characteristic	Group A (n = 11)	Group B (n = 14)	p-value
Maternal age, years	33.0 (33.4 ± 5.2) [IQR: 31.0–37.0]	33.5 (32.5 ± 4.8) [IQR: 27.8–37.3]	0.763
Gravidity	4.0 (3.9 ± 1.0) [IQR: 3.0–5.0]	3.0 (3.2 ± 1.3) [IQR: 2.0–3.5]	0.070
Number of prior caesarean sections (CSs)	1.0 (1.6 ± 0.7) [IQR: 1.0–2.0]	2.0 (1.6 ± 0.6) [IQR: 1.0–2.0]	0.647
Estimated gestational age, days	48.0 (50.1 ± 13.7) [IQR: 38.0–63.0]	55.5 (52.6 ± 7.9) [IQR: 44.8–59.3]	0.411
Diameter of gestational sac or mass, mm	10.0 (13.9 ± 7.8) [IQR: 8.0–23.0]	15.5 (15.1 ± 6.4) [IQR: 12.3–20.3]	0.510
β-hCG level before treatment, mIU/ml	32486 (42431 ± 38834) [IQR: 9705–68558]	19011 (38526 ± 41961) [IQR: 8475–62671]	0.743
Haemoglobin level before treatment, g/l	13.0 (12.5 ± 1.3) [IQR: 11.4–13.1]	12.4 (12.3 ± 1.3) [IQR: 11.2–13.2]	0.545
Cases with cardiac activity, n (%)	3 (27%)	2 (14%)	0.623
Abdominal pain before treatment, n (%)	1 (9%)	3 (21%)	0.604
Vaginal bleeding before treatment, n (%)	3 (27%)	5 (36%)	1.000

Data presented as median (mean ± SD) [IQR]. IQR, interquartile range.

DISCUSSION

Findings and interpretation

Suction curettage, followed when required by Foley catheter tamponade, is an effective way to treat women who have an unruptured CSP. Systemic administration of MTX before the aforementioned surgical approach, does not seem to augment the efficacy of treatment.

Early accurate diagnosis and effective management of CSP are essential for avoiding catastrophic complications such as uterine rupture and life-threatening

haemorrhage, as well as for preserving the uterus and future fertility⁸. Despite the greatly increased incidence of CSP in the recent past, universal treatment guidelines that are based on solid research are lacking. Suction curettage, followed if needed by Foley catheter tamponade, is easy, fast, and effective, and it causes fewer complications and is less costly than other treatment modalities. Side effects due to use of systemic MTX (such as serum transaminase elevation, leukopenia) and prolonged treatment are avoided.

Table 2 Clinical outcomes of the 25 patients with caesarean section scar pregnancy.

Therapeutic outcomes	Group A (n = 11)	Group B (n = 14)	p-value
Estimated blood loss, ml	468 (555 ± 310) [IQR: 371–858]	360 (422 ± 200) [IQR: 286–554]	0.171
Major complication rate (uterine scar rupture, laparotomy, and hysterectomy), n (%)	1 (9%)	1 (7%)	1.000
Mean duration treatment, days	17.0 (14.5 ± 5.0) [IQR: 9.0–17.0]	2.0 (2.4 ± 0.5) [IQR: 2.0–3.0]	<0.001
Mean hospital length of stay, days	3.0 (2.9 ± 0.8) [IQR: 2.0–4.0]	2.0 (2.4 ± 0.5) [IQR: 2.0–3.0]	0.078
Number of patients requiring Foley catheter balloon tamponade, n (%)	6 (55%)	7 (50%)	0.821
Success rate, %	91%	93%	1.000

Data presented as median (mean ± SD) [IQR]. IQR, interquartile range.

Differences in results and conclusions in relation to other studies

Expectant management and medical and surgical approaches for the treatment of CSP are reported in the literature. Expectant management is not routinely recommended because of its high failure rate⁵. MTX is another treatment option; it is not recommended because it takes a long time for the CSP mass to disappear, and it has a high failure rate^{9,10}. Despite it leading to a rapid resolution of the CSP, sharp curettage should not be resorted to, even at an early gestational age. In the review of Rotas *et al.* encompassing 21 cases, 76% of patients undergoing this procedure experienced severe haemorrhage, while in 14% of other reported cases, hysterectomy was performed because of a complication that arose from the curettage¹¹.

In recent years, a medical approach has been combined with suction curettage of the sac^{12–15}. For instance, Jiang *et al.*, who treated 45 women with CSP, reported that systemic MTX administration followed by suction curettage and Foley catheter tamponade was very effective¹². Seow *et al.* had tested a new and very different approach: under transvaginal ultrasound guidance they inserted a double-lumen ovum aspiration needle into the gestational sac; after aspiration of the liquid content they slowly injected 50 mg of MTX into the sac¹³. This combined approach was highly effective and allowed preservation of the uterus, but required the intervention of a physician with the necessary expertise. Conversely, Jurkovic *et al.* used suction curettage under ultrasound guidance, without prior administration of MTX, but followed by Foley tamponade in case of heavy intraoperative bleeding⁴. Like in our study, suction curettage followed if needed by Foley catheter tamponade, without MTX therapy, was an effective treatment of CSP.

Bilateral uterine artery embolisation (BUAE) as an invasive radiological procedure has recently gained acceptance for treating CSP. This procedure usually consists of a bilateral uterine artery chemoembolisation with MTX or a BUAE combined with local MTX^{16–21}. In these studies, most patients underwent suction curettage 24–72 hours after BUAE. In our opinion, however, vacuum aspiration, followed if indicated by Foley catheter tamponade, should be considered as the primary treatment in CSP cases because of its simplicity and lower cost. Additionally, BUAE may affect ovarian function and future fertility. In recent years, various authors have

reported surgical evacuation under transrectal ultrasound guidance, hysteroscopic evacuation, and laparoscopic removal of the ectopic mass, but these approaches are more expensive and the patients need to undergo endotracheal intubation for general anaesthesia^{7,22–26}.

Relevance of the findings, unanswered questions, and future research

Although no consensus yet exists as to the most effective method to treat CSP, based on the results of this study, suction curettage, followed if needed by Foley tamponade, should be encouraged since it is safe, fast, and cost effective, especially when compared to other CSP management options. Further prospective randomised studies with adequate case numbers are necessary to gain sufficient statistically valid evidence to support universal application of this surgical treatment for CSP.

Strengths and weaknesses of the study

The main limitation of this study is its retrospective design, the lack of randomisation not allowing a reliable statistical comparison of the two groups, and the relatively small sample size. Another limitation is that patients were operated upon by different obstetricians. On the other hand, the lack of follow-up with serial β -hCG measurements is a strength of this study.

CONCLUSION

The results of our study demonstrate the efficacy of guided suction curettage as the primary treatment modality for unruptured CSP and the use of Foley catheter tamponade, if needed, in case of haemorrhage. Systemic administration of MTX does not appear to add to the success of this surgical approach; moreover patients who did not receive MTX recovered faster and had shorter hospital stays.

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