ABSTRACT

Purpose: In this work, we tried to evaluate the effects of systemic methotrexate (MTX) in caesarean scar pregnancy (CSP) in patients treated with ultrasound-guided manual vacuum aspiration (MVA).

Patients and Methods: A prospective non randomized comparative study that was initially conducted on 50 cases diagnosed with caesarean scar pregnancy at Mansoura University hospital in one year from August 2021 till August 2022. In the assessment of treatment outcome, we included patients who met the following criteria: (1) they were diagnosed with undisturbed caesarean scar pregnancy. (2) The residual myometrial thickness was more than 3mm and (3) No contraindication for systemic MTX. Twenty four cases therefore were excluded as they didn’t meet the inclusion criteria, the other 26 cases were divided into two groups, (group 1) included 16 cases who underwent suction using MVA and (group 2) included 10 cases who received intramuscular (MTX) injection (dose of 50 mg/m2) followed by MVA. The clinical characteristics and the outcomes were analysed. Treatments were regarded as successful if there were complete resolution of the CSP mass, no complications, and no requirement to re-treat.

Results: Among (group 1), two cases were complicated with scar hematoma which resolved spontaneously and one case was complicated with severe bleeding and needed urgent laparotomy and hysterectomy was done. While in (group 2) all of the cases were successful without any detected complications or need for additional treatment. There were no significant differences among the two groups in demographic and clinical characteristics, such as maternal age, gravidity, parity, fetal cardiac activity, gestational age at diagnosis, thickness of anterior lower uterine wall on US, type of CSP, initial human chorionic gonadotropin (HCG) levels and number of previous caesarean sections.

Conclusion: By grouping CSP patients who shared similar demographic and clinical characteristics we found that when suction by MVA is preceded by MTX injection, it tends to give better results with less complications detected and without further needed intervention.

Key Words: B-HCG, bleeding, CSP, MTX, MVA, suction curettage, ultrasound guided.

INTRODUCTION

Caesarean scar pregnancy (CSP) is a rare but serious complication of caesarean section[1]. The reported incidence of CSP ranges from 1:1,800 to 1:2,226, occurring in 0.15% of women with previous caesarean deliveries[2]. The incidence of CSP is increasing rapidly because of the increased rate of caesarean section[3].

There are two types of CSP; endogenous where the gestational sac is implanted at the site of previous caesarean scar and develops towards the uterine cavity and exogenous where the sac is implanted into the CS defect and grows towards the uterine serosa and urinary bladder[4].

The exact pathogenesis is not clearly understood but the endometrial and myometrial disruption could be the predisposing factors in abnormal uterine implantation[5].

Clinical presentations of CSP vary from vaginal bleeding, abdominal pain or even asymptomatic in cases which were diagnosed during the routine first trimester sonographic screening[6].
This pregnancy can cause serious complications, such as placenta previa uterine rupture, haemorrhage, infertility or even death⁷).

The main lines of treatment are suction curettage, MTX injection either systematically or local injection, laparoscopy and laparotomy⁸ but there is no consensus on the treatment and management, and individualized therapy should be performed⁹. Some complicated cases may require application of different methods of treatment⁹.

The aim of this study was to evaluate the effects of systemic methotrexate in caesarean scar pregnancy (CSP) in patients treated with ultrasound-guided manual vacuum aspiration (MVA).

**PATIENTS AND METHODS**

This study is a prospective non randomized comparative study, it was totally conducted on fifty cases diagnosed with caesarean scar pregnancy in one year from August 2021 till August 2022 at Obstetrics and Gynecology department, Mansoura university hospitals (tertiary hospital), Mansoura University, Egypt. The patients included in this study were who met the following criteria: (1) they were diagnosed with undisturbed caesarean scar pregnancy. (2) The residual myometrial thickness was more than 3mm (endogenic type) and (3) No contraindication for systemic MTX. Excluded from the study cases with residual myometrial thickness less than 3mm or cases with disturbed caesarean scar ectopic.

A full detailed history of each patient was taken with explanation of the study protocol, the expected complications of the management procedures were explained to the patients then informed consent was obtained.

Transabdominal ultrasound (TAS) and transvaginal ultrasound (TVS) were carried out by Samsung HS60 ultrasound machine. Diagnosis of CSP was based on the following TVS criteria¹¹:

1. An empty uterine cavity with a clearly demonstrated endometrium and empty cervical canal.

2. The presence of a gestational sac, with or without fetal cardiac activity, embedded and surrounded by the myometrium, in the anterior part of the uterine isthmus.

3. A thin myometrial layer between the gestational sac and the bladder.

4. Peritrophoblastic flow surrounding the CSP appearing on Doppler flow sonography.

5. Negative “sliding sign” (inability to displace the gestational sac from its position using gentle pressure with a transvaginal probe).

Twenty four cases therefore were excluded as they didn’t meet the inclusion criteria, the other 26 cases were divided into two groups, (group 1) included 16 cases who underwent suction using MVA and (group 2) included 10 cases who received intramuscular (MTX) injection (dose of 50 mg/m²) followed by MVA. MVA was done under general anaesthesia using cannula 7 mm. Curettage was done under ultrasound guidance till the sac completely disappeared. Intramuscular (MTX) injection (dose of 50 mg/m²) was followed by MVA within one week. Foley’s catheter insertion for compression at site of ectopic pregnancy to ensure haemostasis was done when needed. The clinical characteristics and the outcomes were analysed.

**Statistical analysis**

Data analysis was performed by SPSS software, version 18 (SPSS Inc., PASW statistics for windows version 18. Chicago: SPSS Inc.). Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for non-normally distributed data and mean± Standard deviation for normally distributed data after testing normality using Kolmogorov-Smirnov test. Significance of the obtained results was judged at the (0.05) level.

**RESULTS**

The clinical characteristics of both groups were summarized in (Table 1) the two groups were similar in age, gravidity, parity, positive fetal heart beat, gestational age at diagnosis, thickness of anterior lower uterine wall on US, type of CSP, initial human chorionic gonadotropin (HCG) levels and number of previous caesarean sections. The table shows no statistically significant difference between the two groups as regards success rate and demographic and clinical characteristics except time since last CS, which was higher in group 2 (Figures 1,2)
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Enrollment

Assessed for Eligibility (n=50)

Excluded for not meeting inclusion criteria (n=24)

Assessed for Eligibility (n=26)

Group (1)
- Allocated to undergo MVA alone (n=13)

Group (2)
- Allocated to receive MTX then MVA (n=13)

Follow-Up

Underwent MVA (n=16)
- 3 cases were added from group 2

Did not undergo MVA (n=0)

- Received MTX (n=10)

- Did not receive MTX (n=3)

- a. Refused to participate (n=2)

- b. Hypersensitive to MTX (n=1)

Analysed (n=16)
- Excluded from analysis (n=0)

Analysed (n=10)
- Excluded from analysis (n=3)

Fig. 1: Consort flow diagram showing the algorithm for enrollment and allocation of subjects.

Table 1: Clinical characteristics of the two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MVA alone (N=16)</th>
<th>MTX then MVA (N=10)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>30.375±3.20</td>
<td>34±6.39</td>
<td>0.065</td>
</tr>
<tr>
<td>Gravidity</td>
<td>4.75±1.65</td>
<td>5.5±2.8</td>
<td>0.396</td>
</tr>
<tr>
<td>Parity</td>
<td>2.625±0.81</td>
<td>3.6±2.01</td>
<td>0.094</td>
</tr>
<tr>
<td>Number of previous CS</td>
<td>2.31±0.79</td>
<td>3.4±2.07</td>
<td>0.067</td>
</tr>
<tr>
<td>Time since last CS (years)</td>
<td>4.41±2.64</td>
<td>7.4±3.54</td>
<td>0.02*</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>7.44±1.37</td>
<td>7±0.94</td>
<td>0.382</td>
</tr>
<tr>
<td>Positive cardiac activity (%)</td>
<td>12.5</td>
<td>20</td>
<td>0.606</td>
</tr>
<tr>
<td>Residual myometrial thickness (mm)</td>
<td>5.875±1.5</td>
<td>4.7±1.49</td>
<td>0.063</td>
</tr>
<tr>
<td>Endogenic Type (%)</td>
<td>93.75</td>
<td>90</td>
<td>1.0</td>
</tr>
<tr>
<td>Basal β-HCG (mIU/mL)</td>
<td>21246.3±2202.73</td>
<td>17382.4±19408.76</td>
<td>0.692</td>
</tr>
</tbody>
</table>

The clinical presentation of both groups was presented in (Table 2). In (group 1), 68.75% of the cases presented with vaginal spotting, 12.5% presented with pain and 18.75% were asymptomatic, while in (group 2) 60% of the cases presented with vaginal spotting and 40% of the cases were asymptomatic.

Fig. 2: Imaging of CSP: TVS of 7 weeks CSP

Table 2: Clinical presentations of the two groups

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Treatment</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MVA alone N=16</td>
<td>MVA preceded by MTX N=10</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>3 (18.75)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Rupture uterus</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pain</td>
<td>2 (12.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>11 (68.75)</td>
<td>6 (60)</td>
</tr>
</tbody>
</table>
The outcomes of treatment were shown in (Table 3). Among group 1, MVA alone, two cases were complicated with hematoma which resolved spontaneously and one case was complicated with severe bleeding and needed urgent laparotomy and hysterectomy. While in group 2, all of them were successfully treated without any detected complications or need for additional treatment.

Table 3: Outcomes of the two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MVA alone (N=16)</th>
<th>MTX then MVA (N=10)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe bleeding &amp; urgent laparotomy (hysterectomy) NO &amp; (%)</td>
<td>(1) 6.25</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>Scar hematoma (%)</td>
<td>(2)12.5</td>
<td>0</td>
<td>0.507</td>
</tr>
<tr>
<td>Success rate (%)</td>
<td>81.25</td>
<td>100</td>
<td>0.262</td>
</tr>
</tbody>
</table>

DISCUSSION

There is no universal management option for CSP[12]. It appears that combining different treatment modalities is more beneficial than single therapy[8].

In this study we tried to compare the effect of adding systemic MTX to MVA versus MVA alone for managing CSP. Our findings show that hematoma formation at the site of CSP and severe vaginal bleeding that required hysterectomy were observed in patients treated with MVA alone. Although the difference is not statistically significant, but this may be attributed to the small sample size. It seems that this combined therapy is clinically effective.

The results of our study agree with Özdamar and his associates in a study carried out on 33 cases of CSP that were managed through suction curettage either alone or in combination with systemic or intracavitary administration of methotrexate, the success rate was nearly the same. Fourteen out of 16 cases who were treated with suction curettage alone, and 15 out of 17 patients who received MTX prior to suction curettage revealed successful resolution of the CSP without any complication[13].

The clinical results and safety of suction curettage with or without MTX administration before curettage for treatment of CSP were studied by Sevket and associates[14]. The estimated blood loss and major complication rate were similar. They found that ‘suction curettage only’ group required less treatment time and came to the conclusion that suction curettage is an effective treatment for CSP. The same result was confirmed by Wang and associates[10].

In our study no further therapy was required in MTX-MVA group. This may be related to the effect MTX that reduce size of the mass and decrease vascularity. This finding is consistent with Shao and associates[15]. Datta reported that suction evacuation together with MTX was a successful option with good maternal outcome[16].

The shortcomings of this study include the small number of patients and lack of long term follow up. There are still unanswered concerns about the future fertility, the risk of uterine rupture and recurrence at the location of the scar in subsequent pregnancies. Further randomized controlled trials with longer follow-up duration are required.

Based on this study, both treatment modalities, either MVA alone or MVA preceded by systemic MTX could treat effectively the majority of CSP patients, but the combined therapy resulted in less hematoma formation, haemorrhage and conversion to hysterectomy.

Ethical approval

The study was approved by the Mansoura Faculty of Medicine Institutional Research Board (MFM-IRB).

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

7. Ou J, Peng P, Li C, et al. Assessment of the necessity of uterine artery embolization during suction and


