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ORIGINAL ARTICLE

Exclusive use of intrasac potassium chloride and methotrexate for treating cesarean scar pregnancy: effectiveness and subsequent fecundity

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STUDY QUESTION: **Is exclusive use of intragestational sac potassium chloride (KCl) and methotrexate (MTX) effective in the management of viable cesarean scar pregnancy (CSP)?**

SUMMARY ANSWER: **Exclusive use of intragestational sac KCl and MTX was effective in the management of viable CSP.**

WHAT IS KNOWN ALREADY: **Owing to a paucity of randomized studies on management of CSP, evidence-based management remains unclear. Intragestational sac KCl or MTX along with either systemic MTX or surgical intervention, such as uterine artery embolization or dilation and curettage, has proved to be effective in the management of CSP. Furthermore, there are limited data in the literature on the use of exclusive intragestational sac KCl and MTX for management of CSP and subsequent fecundity.**

STUDY DESIGN, SIZE, DURATION: **A prospective cohort study was conducted from June 2017 to September 2019. We recruited nine CSP patients referred to our unit. There was no lost to follow-up noted.**

PARTICIPANTS/MATERIALS, SETTING, METHODS: **Patients with an ultrasound diagnosis of CSP who fulfilled the inclusion criteria were recruited. The study was conducted in a tertiary care center. Clinical symptoms, pregnancy viability, gestational age and human chorionic gonadotrophin (HCG) values determined the management in each individual case. Accordingly, patients were grouped into the expectant management (Group I, n = 3) and intragestational sac KCl with MTX (Group II, n = 6) groups. Demographic details, clinical characteristics, ultrasound details at diagnosis, post-treatment HCG normalization time, menses resumption, mass resolution and subsequent fecundity were noted. Descriptive statistics were used for analyses.**

MAIN RESULTS AND THE ROLE OF CHANCE: **Of the nine patients with CSP, six patients had viable CSP and required intervention. Out of these, four patients expressed a desire for future fertility. Mean gestational age at treatment among patients in Group II was 54.33 ± 7.51 days (range 46–65). Mean HCG value at the time of diagnosis was 84 110 ± 38 679.39 IU/l in Group II patients as compared with 2512 ± 709.36 in Group I. HCG had decreased by 92.7 ± 3.78% 2 weeks after intervention and normalized (<5 IU/l) by 53.5 ± 14.97 days. No major complications occurred and additional treatment was not required in these patients. Menstruation had resumed by 26 ± 6.6 days after treatment in Group II. On follow up, a small unresolved mass was present in two patients and the cesarean scar niche was visible in the remaining four patients. Out of the four patients**

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desirous of future conception, three conceived naturally and one delivered a term baby via repeat lower segment cesarean section.

LIMITATIONS, REASONS FOR CAUTION: The main limitation of our study was small sample size. All the patients were asymptomatic at presentation and hence we cannot comment on use of this method in those presenting with active vaginal bleeding.

WIDER IMPLICATIONS OF THE FINDINGS: Intragestational sac KCl plus MTX may be a highly effective approach for the management of viable CSP despite high initial HCG values. There seems to be no need for any further intervention. It can be considered as the first line minimally invasive treatment option in patients desirous of future fertility. Nevertheless, accumulation of further cases is required to validate this treatment modality.

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TRIAL REGISTRATION NUMBER: N/A

Key words: cesarean scar pregnancy / transvaginal intrasac potassium chloride plus methotrexate / minimally invasive technique / reproductive counseling / subsequent fecundity / reproductive outcomes

WHAT DOES THIS MEAN FOR PATIENTS?

When a woman becomes pregnant following a cesarean section and the new baby implants at the scar site, this is known as cesarean scar pregnancy (CSP). This condition can be treated in a number of ways, but there is no agreement among doctors as to what is the best treatment. Surgery has the highest success rates but many patients may not want surgery and want a less invasive treatment. There is a higher chance of success with less invasive treatment if the patient has lower human chorionic gonadotrophin (HCG) (pregnancy hormone) levels. Injection of a drug named methotrexate (MTX) into the protective covering of the growing baby (also called the gestational sac) has been tried before, with some success although these patients had lower HCG levels. In this study, we injected two drugs, potassium chloride (KCl) and MTX, into the gestational sac despite patients having high HCG values. This combined treatment had a good success rate and it did not appear to affect a subsequent pregnancy in those patients who conceived after treatment in our study. However, this treatment needs to be tested further, especially in patients with a CSP who go to the doctor with vaginal bleeding.

Introduction

Implantation in a cesarean section scar is known as a cesarean scar ectopic. The incidence of cesarean scar pregnancy (CSP) has been estimated to range from 1/531 to 1/2000 of all cesarean deliveries (Fylstra, 2002; Rotas et al., 2006). Impaired healing of a cesarean section incision predisposes to CSP (Rotas et al., 2006) and it is now commonly believed that CSP and abnormal invasion of placenta represent the same histopathological entity presenting at different gestational ages (Timor-Tritsch et al., 2014). Diagnosis is predominantly dependent on ultrasonographic visualization of a gestational sac at the site of the previous scar, with empty uterine cavity (Seow et al., 2001; Timor-Tritsch et al., 2019). More than 30 different treatment regimens have been mentioned in the literature, but there is a lack of consensus on which one is most appropriate, since the majority of recommendations are based on case series rather than randomized controlled trials (RCTs). Conservative approaches for CSP have been reported previously, with opposing results (Wang et al., 2015a; Glenn et al., 2018; Levin et al., 2019; Tahaoglu et al., 2019). Among the conservative approaches, exclusive local treatment has not been used previously. The aim of this prospective study was to evaluate the role of exclusive local treatment in management of CSP and delineate the subsequent reproductive outcomes.

Materials and Methods

Study design

A prospective cohort study was conducted from June 2017 to September 2019 at the Department of Reproductive Medicine & Surgery, Sri Ramachandra Medical College & Research Institute (SRMC & RI), Chennai, India.

Methodology

We recruited nine patients with CSP who were referred to our unit by primary physicians.

The inclusion criteria were as follows: diagnosed cases of CSP (by the criteria mentioned below); and hemodynamically stable cases of CSP without vaginal bleeding.

All CSP cases were numbered in a serial order. A detailed medical history was taken and noted in the case sheets. Clinical examination was carried out by the attending physician, which included a sterile speculum vaginal examination. A transvaginal

ultrasound (TVS) was then performed by two consultant gynecologists (fully trained in gynecological ultrasound) independently, to examine the viability and location of the pregnancy. Endocavity transducer 4–10 MHz bandwidth (RIC 5-9A-RS, GE Voluson S8 BT 16, GE Healthcare, Chicago, IL, USA) was used. A CSP was diagnosed when the following criteria were met: empty uterine cavity (Godin et al., 1997); gestational sac or solid mass of trophoblast located anteriorly at the level of the internal os, embedded at the site of the previous lower uterine segment cesarean section scar (Jurkovic et al., 2003); thin or absent layer of myometrium between the gestational sac and the bladder (Godin et al., 1997; Timor-Tritsch et al., 2012); evidence of prominent trophoblastic/placental circulation on Doppler examination (Seow et al., 2001); empty endocervical canal (Godin et al., 1997); and negative 'sliding organ sign', which was defined as the inability to displace the gestational sac from its position at the level of the internal os using gentle pressure applied by the transvaginal probe.

Ultrasound details of the CSP and myometrial wall thickness at the implantation site were noted. Gestational age was assigned according to last menstrual period. Sac dimensions and crown rump length (CRL) was used to determine gestational age when patients did not remember the last menstrual period. After diagnosis, patients' baseline complete blood count, blood grouping and total human chorionic gonadotrophin (HCG) (5th IS). Serum total HCG estimation was performed using a chemiluminiscent immunoassay technique, with the UniCel DxI 800 Access Immunoassay System (Beckman Coulter, Inc. Brea, CA, USA). Women were informed about the poor understanding of the natural history and clinical significance of first-trimester CSP. Patients were counseled about the risks of the condition and management options, including potential benefits and risks. Reproductive counseling was provided. The fertility goal of each patient was noted. Clinical symptoms, pregnancy viability, gestational age and HCG values determined the management in each individual case. Women with minimal clinical symptoms, small pregnancies with uncertain viability and low HCG values were considered suitable for expectant management (Group I) and they were followed up by weekly scans. A nonviable pregnancy was declared if there was no fetal pole 3 weeks after the baseline diagnosis scan. Women with a viable pregnancy (cardiac activity noted on baseline scan) were offered TVS-guided intrasac instillation of KCl plus MTX after appropriate counseling (Group II). Baseline liver and renal function tests were performed in patients in Group II. Women in both groups were informed about the need for further surgical intervention if there was a continuation of pregnancy or in case of excessive bleeding. Out of the nine patients, three patients were managed expectantly while six patients underwent intervention. Written, informed and signed consent was obtained from every patient.

Details of the procedure

The procedure was performed in a minor operation theater. An injection of 1 ml of Ketorolac (30 mg/ml Ketanov, Sun Pharmaceutical Industries Limited, Mumbai, India) was given (i.m.) 30 min prior to the procedure. Antibiotic prophylaxis with a single dose of 1 gm Cefotaxime (Taxim 1 gm, Alkem Laboratories, Mumbai, India) was given (i.v.) to all patients. The patient was placed in the lithotomy position and an injection of 2 mg midazolam (Midaz 1 mg/ml, Abott Healthcare Pvt Ltd, Mumbai, India) was given (i.v.). A needle guide was attached to the TVS probe, and a 17 gauge, 35 cm, single lumen, ovum aspiration needle (Cook Medical, Bloomington, IN, USA) was used. The vulva and vagina were disinfected with 10% povidone iodine. Under TVS guidance, the needle was introduced into the gestational sac and 1.5 ml KCl (150 mg/ml Potcl, Neon Laboratories LTD, Mumbai, India) was injected in the embryo. Disappearance of cardiac activity was confirmed and embryo scratching was performed. The gestational sac contents were aspirated using a 20-cc syringe followed by injection of 2-ml MTX (25 mg/ml: Folitrax—50, IPCA Laboratories, Mumbai, India) into the sac.

Postprocedure follow up

A day after the procedure, a transvaginal scan was performed to confirm the absence of cardiac activity and then the patient was discharged. All patients attended follow-up sessions for HCG level examinations every week until HCG was <5 IU/l, and for an ultrasound scan once every 4 weeks until the mass resolved sonographically. Patients were advised to avoid pregnancy for a minimum of 3 months after the intervention. During the follow up, the success rate of treatment, complications, mean time for HCG normalization, menses resumption and subsequent fecundity in patients desiring a future pregnancy were noted.

Outcome measures and statistical analysis

The primary outcome measure was treatment success. Treatment success was defined as disappearance of cardiac activity and resolution of HCG by sole use of intrasac KCl plus MTX, without additional surgical intervention. Complete sonographic resolution of the CSP was defined as the absence of the gestational sac, hyperechogenic chorionic rim and any other echo densities under the cesarean section scar, along with a regular endometrial line in the lower uterine segment on TVS. The secondary outcome measure was subsequent fecundity following treatment with intrasac KCl plus MTX. Major complications were defined as uterine perforation, hemorrhage >1000 ml and hysterectomy. Uncomplicated miscarriage was defined as a spontaneous miscarriage that did not require further surgical intervention. Descriptive statistics were presented as mean ± SD or percentages.

Ethics

The study was approved by the Institutional ethics committee of Sri Ramachandra Medical College & Research Institute (CSP-MED/17/APR/35/39).

Results

Nine patients were diagnosed with CSP at our department during the study period. Three patients were managed expectantly

Table I Baseline characteristics of patients diagnosed with CSP.

Case	I	II	III	IV	V	VI	VII	VIII	IX
Age (years)	26	24	20	30	29	27	36	37	22
Obstetric history	G2P1L1	G3P1D1A1	G3P2L2	G3P1L1A1	G3P1L1A1	G4P1D1A2	G3P2L2	G3P2L2	G3P2L2
Previous D&C	No	1	No	No	1	2	No	No	No
Number of previous LSCS	1	1	2	1	1	1	2	2	2
Type of LSCS	El	Em	Both El	El	Em	Em	El	El and Em	Em and El
Indication of LSCS	Placenta praevia	Pre-eclampsia and Abruption	1st—Placenta praevia 2nd—Previous scar not willing for VBAC	Breech	Failure of descent	Deep transverse arrest	1st—Breech 2nd—Previous scar not willing for VBAC	1st—PROM with failure to progress 2nd—Previous LSCS not willing for VBAC	1st—Fetal distress 2nd—Previous cesarean scar with CPD
Time interval between LSCS and CSP (months)	24	28	36	40	14	25	48	108	56
Clinical presentation	Asy	Asy	Asy	Asy	Asy	Asy	Asy	Asy	Asy

Asy, asymptomatic; El, elective; Em, emergency; G, gravida; P, parity; A, abortion; L, live; D, dead; D&C, dilation and curettage; CSP, cesarean scar pregnancy; LSCS, lower segment cesarean section; PROM, premature rupture of membranes; VBAC, vaginal birth after cesarean section; CPD, cephalopelvic disproportion.

Table II CSP details for women in Group I (expectant management group).

Sr. no.		Case III	Case V	Case VI
1	Mode of conception	Natural	Natural	Natural
2	GA at diagnosis (days)	43	45	48
3	GA at treatment (days)	NA	NA	NA
4	HCG at diagnosis (IU/l)	2348	1899	3289
5	Maximum HCG (IU/l)	2348	1899	3289
6	Percentage fall in HCG at 2 weeks	68	64.6	62.7
7	Time for HCG to normalize (days)	42	36	45
8	Major complications			
a	Uterine perforation	Nil	Nil	Nil
b	Hemorrhage >1000 ml	Nil	Nil	Nil
c	Hysterectomy	Nil	Nil	Nil
10	Genital infection	No	No	No
11	Menses resumption (days)	15	21	25

GA, gestational age; NA, not applicable.

(Group I) whereas six patients underwent intervention (Group II). The case characteristics are summarized in Table I. The mean age of patients at the time of diagnosis was 26.87 ± 5.30 years (range 20–37). Only three patients had a history of prior curettage, one of whom had two previous curettage procedures. Four patients had two previous cesarean deliveries whereas the remainder had one prior cesarean delivery. The mean interval from previous cesarean section to CSP was 40.37 ± 29.28 months (range 14–108 months) and all patients were asymptomatic at the time of presentation.

All patients had a natural conception. The mean gestational age at diagnosis was 50.11 ± 6.71 days (range 43–63). Mean gestational age at treatment among patients in Group II was 54.33 ± 7.51 days (range 46–65). The mean HCG value at the time of diagnosis was 84 110 ± 38 679.39 IU/l (range 36 199–137 695 IU/l) in Group II compared with 2512 ± 709.36 in Group I. All patients had a declining trend of HCG after treatment. HCG decreased by 92.7 ± 3.78% by 2 weeks after intervention and normalized (<5 IU/l) by 53.5 ± 14.97 days. In all the patients, no major complications occurred and no further treatment was required. It took 26 ± 6.6 days for menstruation to resume in Group II patients. The details are summarized in Tables II and III.

Fetal pole and cardiac activity were not present in all Group I patients, whereas in contrast it was present in all Group II patients. At diagnosis, mean gestational sac diameter was 9.4 ± 0.87 mm in Group I patients. The mean gestational sac diameter and CRL were 21.05 ± 6.14 mm and 12.21 ± 7.47 mm, respectively, at diagnosis among Group II patients. Myometrial wall thickness at the site of implantation was 3.56 ± 1.70 and 2.93 ± 0.85 mm in patients from Group I and II, respectively. On follow up, a small unresolved mass was present in two patients at 5 months, whereas it had disappeared in the remaining patients. Cesarean scar niche/defect aka Isthmocele was visible in four patients after resolution of the mass. These are triangular anechoic areas in the anterior abdominal wall at the site of previous cesarean scar, as visualized by ultrasound. The ultrasound details at diagnosis and follow up are summarized in Tables IV and V.

Table III CSP details for women in Group II (intervention group: intragestational sac KCl and methotrexate).

Sr. no.		Case I	Case II	Case IV	Case VII	Case VIII	Case IX
1	Mode of conception	Natural	Natural	Natural	Natural	Natural	Natural
2	GA at diagnosis (days)	52	53	44	57	46	63
3	GA at treatment (days)	53	58	46	58	46	65
4	HCG at diagnosis (IU/l)	74 238	112 752	36 199	95 309	48 467	137 695
5	Maximum HCG (IU/l)	74 238	141 304	39 323	95 309	63 034	137 695
6	Percentage fall in HCG at 2 weeks	88.57	91.8	98	89	92	95.5
7	Time for HCG to normalize (days)	65	55	26	48	63	64
8	Major complications						
a	Uterine perforation	Nil	Nil	Nil	Nil	Nil	Nil
b	Hemorrhage >1000 ml	Nil	Nil	Nil	Nil	Nil	Nil
c	Hysterectomy	Nil	Nil	Nil	Nil	Nil	Nil
9	Additional treatment	Nil	Nil	Nil	Nil	Nil	Nil
10	Genital infection	Nil	Nil	Nil	Nil	Nil	Nil
11	Menses resumption (days)	32	22	17	26	24	35

Table IV Ultrasound details for Group I at diagnosis and follow up.

	Case III	Case V	Case VI
Mean gestational sac diameter (mm)	9	10.4	8.8
Fetal pole	No	No	No
Cardiac activity	No	No	No
Endometrial thickness (mm)	9.2	10.1	8.9
Residual myometrial wall thickness (mm)	1.8	3.7	5.2
Follow up when mass has resolved (weeks)	4	4	4
Cesarean scar niche when mass resolved	Present	Present	Present

Among Group II patients, four patients were desirous of future conception. Three of them conceived naturally by 6 months after the CSP, whereas one patient is attempting conception. At time of writing this article, one patient each was in the second and third trimester, respectively, and one patient had delivered a term baby weighing 3.2 kg by elective lower segment cesarean section. There were no intraoperative complications noted in this patient, such as morbidly adherent placenta or adhesions. The details of subsequent fecundity are summarized in Table VI.

Discussion

Patients with a CSP have a wide spectrum of clinical presentation ranging from no symptoms to vaginal bleeding with or without abdominal pain and, rarely, hypovolemic shock (Vial et al., 2000; Einenkel et al., 2005). In a review of 57 patients with CSP, 36.8% of the women were asymptomatic (Rotas et al., 2006). In two different studies most patients were asymptomatic at presentation (Grechukhina et al., 2018; Levin et al., 2019). These findings are in line with our study, where all the patients were asymptomatic and were referred to our unit by primary physicians.

Diagnosis of CSP is most often obtained by TVS (Glenn et al., 2018), with a sensitivity of 86.4% (Vial et al., 2000; McKenna et al., 2008). Magnetic resonance imaging can be used as a second-line investigation if the diagnosis is equivocal on TVS (Peng et al., 2014). Hysteroscopy can be used for further evaluation of pregnancy location but this is not compulsory (Maymon et al., 2004). Our patients did not require any additional assessment other than TVS. The mean residual myometrial wall thickness in Group II patients was 2.93 ± 0.85 mm, which was comparable to the local treatment group (2.9 ± 1.6 mm) in an RCT conducted by Peng et al. (2015).

To date, more than 30 CSP treatment regimens have been published and the majority of recommendations are based on case series rather than RCTs. There have been only five randomized studies on CSP management and evidence-based management remains unclear (Birch Petersen et al., 2016). The goals of treatment are termination of pregnancy, reduction of hemorrhage, avoiding damage to adjacent organs and prevention of uterine rupture. Treatment should be individualized according to clinical presentation, HCG levels, imaging features and the surgeon's expertise. Expectant, medical (local and systemic) and surgical modalities can be used in hemodynamically stable patients.

Expectant management can be used as a first-line treatment for CSP in women without embryonic or fetal cardiac activity who are willing to undergo regular follow up. In a recent systematic review and meta-analysis, 69% of CSP cases without embryonic/fetal cardiac activity experienced an uncomplicated miscarriage, while surgical or medical intervention during or immediately after miscarriage was required in 31% of cases (Cali et al., 2018). In our study, all CSP cases without cardiac activity had an uncomplicated miscarriage.

Medical management can be systemic or local. It is being debated whether systemic MTX can be effective in treatment of

Table V Ultrasound details for Group II at diagnosis and follow up.

	Case I	Case II	Case IV	Case VII	Case VIII	Case IX
Mean gestational Sac diameter (mm)	18.5	24	11.8	25	18	29
Crown rump length (mm)	8.1	17.1	2.6	15	7.5	23
Cardiac activity	+	+	+	+	+	+
Endometrial thickness (mm)	13	9.8	12	8.7	6	8
Residual myometrial wall thickness (mm)	2.6	2.4	1.85	3.6	4.2	2.95
Follow up when mass had resolved (weeks)	1.2 × 1 cm hyper and hypoechoic mass present at 20 weeks	1.1 × 0.95 cm hyper echoic mass present at 20 weeks	8	16	12	16
Cesarean scar niche when mass resolved	Absent	Absent	Present	Present	Present	Present

Table VI Details of subsequent fecundity for Group II.

	Case I	Case II	Case IV	Case VII	Case VIII	Case IX
Mode of conception	Natural	Natural	Natural	Does not want conception	Does not want conception	Attempting conception
Duration between CSP and subsequent conception (months)	6	5.5	6	NA	NA	NA
Status of Subsequent Pregnancy	Delivered girl baby at 38 weeks by LSCS	30 weeks	27 weeks	NA	NA	NA

CSP, as impaired vascularization of fibrous tissue hinders penetration of MTX into the fetal sac (Seow et al., 2004). Numerous adverse effects have been reported with systemic MTX such as alopecia, pneumonitis, bone marrow suppression and stomatitis. In severe cases, cirrhosis and hepatic fibrosis can occur because of accumulation of MTX byproducts in the liver (Chan and Cronstein, 2013). A total of 36% of women experienced side effects in a meta-analysis by Barnhart et al. (2003), with more women in the multidose protocol group showing side effects as compared with single dose. An RCT found 23.9% and 34.8% MTX-associated side effects in single-dose and dual-dose protocol, respectively (Song et al., 2016). For this reason, investigators have advocated local injection as a safer and more effective alternative for CSP patients. Local treatment includes administration of MTX, KCl, hyperosmolar glucose or crystalline trichosanthin under ultrasound guidance. Our main goal was to choose a minimally invasive option, with a high success rate and minimal side effects. Considering the reports of successfully managed cases in ectopic pregnancy, this prospective study was designed to evaluate the efficacy of intragestational sac injection of KCl and MTX in women with CSP.

The successful management of CSP by local KCl and MTX injection was first reported by Godin et al. (1997). Jurkovic et al. (2003) reported 18 cases, of which four were successfully treated with local injections of KCl and MTX. Michaels et al. (2015) successfully treated three cases of CSP with cardiac activity by intrasac KCl alone and four cases with intrasac KCl together with systemic MTX. There is scarcity of literature regarding combined exclusive use of intrasac KCl and MTX in the treatment of CSP. This prospective study, to the best of our knowledge, reports the largest number of CSP cases exclusively treated with this combined method.

In a report of 18 cases by Cok et al. (2015), 11 of 18 cases (61.1%) were managed solely with TVS-guided local MTX administration as a first-line treatment. The remaining seven cases required some form of additional treatment. In an RCT, the success rate in the MTX local treatment group was 69.2% (Peng et al., 2015). In our study, all the patients were successfully treated without additional intervention despite the fact that mean HCG values were considerably higher as compared with these previous two studies [84 110 ± 38 679.39 versus 35 472 ± 28 263 (Peng et al., 2015) versus 36 183 ± 28 870.22 (Cok et al., 2015)]. This finding probably suggests that combined treatment is more effective than only local MTX treatment, although this needs to be confirmed in well-designed adequately powered studies. Median time for HCG remission in our study was 59 days, which was close to that observed by Peng et al. (2015) (56 days) despite having considerably higher pretreatment HCG values.

There are only a few reports on pregnancy outcomes after medical treatment for CSP. In a series of 13 cases treated with systemic multidose MTX, four patients desired pregnancy, three conceived naturally and gave birth to term healthy infants and

one woman was planning to attempt conception a year after completion of treatment (Kutuk et al., 2014). Yamaguchi et al. (2014) reported four uneventful parturitions and one recurrence in CSP patients treated with local MTX only. In a study reported by Levin et al. (2019), out of 34 patients managed conservatively, data on reproductive outcomes were available in 13 patients, of which 69.2% had term deliveries. In our study, four patients desired conception. Three conceived naturally and one patient delivered a baby girl weighing 3.2 kg by cesarean section. There were no complications during the cesarean section. At time of writing, one patient each was in second and third trimester, respectively, and one patient was attempting conception.

Wang et al. (2015b) reported a recurrence rate of 15.6% in CSP patients treated with a variety of methods ranging from dilation and curettage to local resection via various routes. Levin et al. (2019) noted a recurrence in 15.4% cases. None of our patients who conceived after treatment had a recurrence. Uneventful intrauterine term gestations have been reported following all modalities of CSP management. Repair of the uterine scar defect does not always result in live births and recurrence has been reported despite correction (Holland and Bienstock, 2008). Thus, the impact of an unrepaired scar defect on future pregnancies is unclear and further studies are required in this area (Gao et al., 2016).

Based on our experience, it seems less likely that serum levels of HCG influence the response to treatment. In our opinion, intragestational sac KCl and MTX therapy is probably an effective method for treatment of CSP. As a day care or outpatient procedure, a few of the advantages of this technique are that it is a relatively easier technique as compared with the laparoscopic approach, it avoids the risk of surgery and anesthesia-related complications as well as the adverse effects of systemic MTX. The disadvantage of this method is the prolonged follow up and risk of incomplete resolution of mass.

In conclusion, we have shown the possibility of treating CSP with exclusive use of intragestational sac KCl plus MTX injection, even in patients with high HCG levels at diagnosis, and have reported its effect on subsequent fecundity. The rare nature and individual progress of this condition limits the setting of an RCT to compare the treatment modalities. Our aim in reporting this study was to demonstrate that exclusive local treatment can be used for treating CSP effectively with minimal side effects and good post-intervention fecundity rates. Nonetheless, accumulation of further cases is necessary to validate this treatment modality.

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Authors' roles

N.S.R. came up with the idea of exclusive use of local treatment for management of CSP. N.S.R, M.P, R.V. and T.G. finalized the methodology and clinical protocol. M.P., R.V. and C.A. performed the procedure. T.G., V.K. and A.S. were involved in data collection. T.G. drafted the manuscript. M.P., N.S.R., R.V., N.S., A.S. and V.K. have revised the manuscript critically for important intellectual content. All authors approved the final version of the article.

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Conflict of interest

None of the authors had any conflict of interest.

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