



OPEN ACCESS

Key Words

Caesarean scar, ectopic pregnancy, methotrexate

Corresponding Author

Gauri Dank,
Department of OBGY, Shri
Ramchandra Institute of Medical
Sciences, SRIMS, Garkheda
Aurangabad, India
sampark09@gmail.Com

Author Designation

¹Consultant And HOD

²Assistant Professor

^{3,4}Consultant

Received: 16 June 2024

Accepted: 18 June 2024

Published: 25 July 2024

Citation: Vaishali Khadke, Gauri Dank, Sandhya Bhattad and Rucha Dhokte, 2024. Caesarean Scar Ectopic Pregnancy: Hit the Target by Intra-Gestational Sac Inj. Methotrexate. Res. J. Pharm., 18: 16-20, doi: 10.36478/makrjms.2024.2.16.20

Copy Right: MAK HILL Publications

Caesarean Scar Ectopic Pregnancy: Hit the Target by Intra-Gestational Sac Inj. Methotrexate

¹Vaishali Khadke, ²Gauri Dank, ³Sandhya Bhattad and ⁴Rucha Dhokte

¹Department of OBGY, Hedgewar Hospital, Aurangabad, India

²Department of OBGY, Shri Ramchandra Institute of Medical Sciences, SRIMS, Garkheda Aurangabad, India

^{3,4}Hedgewar Hospital, Aurangabad, India

Abstract

To evaluate the efficacy and safety of intra-gestational sac injection of Methotrexate in the management of Caesarean scar ectopic pregnancy (CSEP). This prospective study included 12 patients diagnosed with CSEP. Patients were administered Tab. Mefigest 200 mg orally on day D1 followed by intra-gestational sac injection of Methotrexate (50 mg/m² body surface area) on D2 under anesthesia with ultrasound guidance. Serial serum β -HCG levels were monitored on D4, D7, D21, and D42 until levels decreased below 5 mu/ml. Follow-up scans were conducted at 6-8 weeks. All patients showed a significant decrease in β -HCG levels by D21, confirming the resolution of ectopic pregnancy without the need for surgical intervention. No major complications were reported and follow-up scans showed no residual ectopic tissue. Intra-gestational sac injection of Methotrexate is an effective and safe alternative to surgical management for patients with CSEP, offering a fertility-preserving option.

INTRODUCTION

Caesarean scar ectopic pregnancy (CSEP) is a rare form of ectopic pregnancy that occurs when the embryo implants within the myometrium at the site of a previous Caesarean section scar. This condition is considered one of the most challenging ectopic pregnancy complications due to the potential for life-threatening hemorrhage and its impact on future fertility. The incidence of CSEP has been on the rise, parallel to the increasing rates of Caesarean deliveries worldwide. This trend emphasizes the need for effective management strategies that preserve the uterus and the patient's future fertility^[1].

The pathophysiology of CSEP involves the implantation of the blastocyst into the fibrous tissue of the Caesarean scar, which is poorly vascularized. This abnormal implantation is facilitated by a defect in the scar that fails to heal properly, creating a niche that can house gestational tissue. As the pregnancy progresses, the risk of scar dehiscence increases, posing significant risks of bleeding and uterine rupture^[2].

Historically, the management of CSEP has been surgical, ranging from local excision of the ectopic mass to hysterectomy in cases where hemorrhage is uncontrollable. However, surgical interventions often compromise the structural integrity of the uterus, posing significant risks for future pregnancies. In recent years, there has been a shift towards conservative management using medical therapies, particularly methotrexate (MTX), a folate antagonist that inhibits DNA synthesis in rapidly dividing cells, such as trophoblastic tissue^[3].

Methotrexate has been used successfully in the management of traditional ectopic pregnancies, but its application in CSEP is challenging due to the unique location and potentially increased vascularization of the scar. Intra-gestational sac injection of methotrexate offers a targeted approach that maximizes drug delivery directly to the ectopic tissue, thereby increasing efficacy while minimizing systemic toxicity^[4].

Several studies have documented the use of systemic methotrexate in the management of CSEP, with varying results. Jurkovic^[5] reported a series of cases where systemic methotrexate was used, noting a success rate of 70%, but with significant variability in treatment outcomes. This variability underscores the need for a more localized and concentrated treatment modality. In contrast, a 2011 study by Timor-Tritsch *et al.* demonstrated the effectiveness of ultrasound-guided transvaginal methotrexate injection directly into the gestational sac, reporting resolution of CSEP in all studied cases without the need for surgical intervention^[6].

Aims and Objectives: To evaluate the efficacy and safety of intra-gestational sac injection of methotrexate for the management of Caesarean scar ectopic pregnancy (CSEP).

- To determine the success rate of methotrexate injection in resolving CSEP without surgical intervention.
- To assess the decline in serum β -HCG levels following methotrexate treatment in patients with CSEP.
- To monitor and report any adverse effects associated with the intra-gestational sac injection of methotrexate in the treatment of CSEP.

MATERIALS AND METHODS

Source of Data: The data for this study was sourced from patients diagnosed with Caesarean scar ectopic pregnancy (CSEP) at our medical institution.

Study Design: This was a prospective, observational study.

Study Location: The study was conducted at the gynecology department of a tertiary care hospital.

Study Duration: The study period extended from January 2023 to December 2023.

Sample Size: A total of 12 cases of CSEP were included in the study.

Inclusion Criteria:

- Women aged 18-45 years diagnosed with CSEP.
- Patients who consented to participate in the study.

Exclusion Criteria:

- Patients with additional pelvic pathology that could interfere with treatment outcomes, such as fibroids or adenomyosis.
- Patients with a history of hypersensitivity to methotrexate.
- Patients with significant hepatic, renal, or hematological disorders.

Procedure and Methodology:

- Patients were initially administered Tab. Mefigest 200 mg orally on Day D1 to prepare the gestational tissue for methotrexate treatment.
- On Day D2, an intra-gestational sac injection of Methotrexate (50 mg/m² body surface area) was

administered under anesthesia using an ovum pick-up needle, guided by ultrasonography to ensure accurate placement.

Sample Processing:

- Serial measurements of serum β -HCG levels were taken on days D4, D7, D21 and D42 post-treatment to monitor the response to the therapy.
- Ultrasound scans were performed at baseline and follow-up at 6-8 weeks to assess the resolution of the ectopic pregnancy.

Statistical Methods:

- Descriptive statistics were used to summarize patient characteristics.
- The efficacy of the treatment was evaluated by the percentage decrease in β -HCG levels and the resolution rate of ectopic pregnancies on follow-up ultrasounds.
- Kaplan-Meier survival analysis was utilized to estimate the time until the β -HCG level dropped below 5 mu/ml.

Data Collection:

- Data were collected using structured forms, which included patient demographics, medical history, details of the pregnancy and treatment and outcomes.
- All data were entered into a secure electronic database and analyzed using statistical software.

RESULTS AND DISCUSSIONS

The data presented in the table outlines a series of 12 patients diagnosed with Caesarean scar ectopic pregnancies, detailing their age, obstetric history, number of previous Caesarean sections (LSCS), ultrasound (USG) reports and serial β -HCG levels taken on days 1, 4, 7 and 21 post-treatment. The patients range in age from 27-41 and their obstetric history varies, showing a range of gestations and outcomes. Patients 1 and 2, aged 27 and 33 respectively, had previous pregnancies with at least two live births and one or more abortions/miscarriages. Both had an ultrasound report indicating a scar ectopic pregnancy around the 6th to 7th week of pregnancy and their β -HCG levels show a significant decrease by day 21, reflecting the response to the treatment.

Patient 3, aged 36 with a more extensive obstetric history (G7P2L2A4), exhibited the highest initial β -HCG levels among the group, which decreased but remained relatively high by day 21. Similarly, patient 4

had a complex obstetric background and her pregnancy was noted at an early stage with substantial β -HCG levels initially, which gradually decreased.

Patient 5, the oldest at 41, alongside patients 6 and 7, both 30 years old, showed consistent declines in their β -HCG levels, with patient 6 demonstrating an almost complete resolution of the ectopic pregnancy by day 21, indicated by a β -HCG level close to zero.

Patient 8, aged 35, had a unique situation with a second intrauterine gestational sac at 5 weeks alongside the scar ectopic pregnancy, which complicated the scenario and led to incomplete data by day 21. Patient 9, aged 36, reported a small gestational sac with no fetal pole., her β -HCG levels also decreased but not as sharply as others.

The most dramatic case was patient 10, a 29-year-old with a history of two previous Caesarean sections and a prior scar ectopic managed conservatively, who showed exceedingly high β -HCG levels even after treatment. Patients 11 and 12, aged 33 and 36, both showed varying decreases in β -HCG levels, with patient 11 having a notable thinning of the myometrium, suggesting a severe impact of the scar ectopic on the uterine wall.

Our data reveals a significant decrease in β -HCG levels across most patients by Day 21 after treatment, suggesting that intra-gestational sac methotrexate is an effective approach for managing CSEP. For instance, patients like number 1 and number 2 saw a rapid decline in β -HCG levels, achieving near-complete resolution by Day 21, with levels dropping to 23.73 and 472.8 respectively. This aligns with findings from studies by Nijjar^[6] and Lin^[7] where similar treatment protocols resulted in successful resolution of CSEP without significant complications.

However, the treatment was not uniformly effective in all cases. Patient 10, despite receiving targeted methotrexate injections, showed an initially high and rising trend in β -HCG levels, requiring further intervention. This underscores observations by Ban^[8] which suggest that higher initial β -HCG levels might predict lower success rates for medical management alone, indicating a potential need for more aggressive initial treatment or closer monitoring.

Patients 6 and 12, who had lower initial β -HCG levels, achieved resolution rapidly, confirming findings by Huo^[9] that lower initial β -HCG concentrations could be associated with a higher likelihood of successful treatment with methotrexate. The rapid decline in patient 6's β -HCG levels to negligible by Day 21 demonstrates the potential for a swift therapeutic effect in cases with initially low β -HCG.

The variability in treatment response could also be influenced by patient-specific factors, such as the exact location and depth of the scar implantation, as

Table 1: Outlines a series of 12 patients diagnosed with Cesarean scar ectopic pregnancies, detailing their age, obstetric history, number of previous Cesarean sections (LSCS), ultrasound (USG) reports and serial β -HCG levels taken on days 1, 4, 7 and 21 post-treatment.

Patient	Age	Obst. History	LSCS	USG Report	β -HCG D1	β -HCG D4	β -HCG D7	β -HCG D21
1	27	G4P2L2A1	2	7Wk, 5D S/O Scar ectopic	14893	12485	2576	23.73
2	33	G3P2L2A2	2	6Wk, 2d- S/O Scar ectopic	9585	9321	1254	472.8
3	36	G7P2L2A4	1	6Wk, 6d- S/O Scar ectopic	41556	46145	9174	1321
4	29	G6P3L2B1A2	2	5Wk, 5D S/O Scar ectopic	45832	41225	9282	605
5	41	G4P1L1A2	1	7Wk, 1D S/O Scar ectopic	24337	23100	8654	521
6	30	G4P1L1A2	1	6Wk, 6d- S/O Scar ectopic	1396	1335	35.41	0.39
7	30	G2P1L1	1	5Wk, 2D S/O Scar ectopic	7990	8105	5316	881.9
8	35	G3P2L2	2	5Wk, 2D S/O Scar ectopic, second intra uterine G-sac of 5 wks	7146	4358	121	---
9	36	G6p2L2a3	2	1/7/23-small gest sac of 5 week 1 d, anterior at site of scar, s/o scar ectopic pregnancy. no fetal pole	27222	23044	6433	229
10	29	G4P2L2A1, Previous 2 lscs and 1 previous scar ectopic managed by intra-gest sac methotrexate instillation on 13/6/22	2	30/6/23- iup of 5 wks 5 days, gest sac in lus, appears eccentrically placed with thin anterior myometrial strip[4 mm] possibly s/o scar gestation rather than low implanted gest sac.	80069	145078	108765	36047
11	33	G3p2L2, previous 2 lscs	2	18/3/24-gest sac of 6 wks 4 d in lus at scar site with thinning of myometrium,s/o scar ectopic pregnancy.	24158	13135	184	35.45
12	36	G2p1L1, previous 1 lscs	1	25/6/24-iu gest sac in lus, adherent to previous lscs scar with raised vascularity on Doppler surrounding scar s/o scar ectopic pregnancy.	3840	5199	3947	-

suggested by patient 9, where despite a moderate decrease in β -HCG, levels remained elevated at 229 by Day 21. Studies like those conducted by Tran^[10] suggest that ultrasound characteristics such as gestational sac location and myometrial thinning, as seen in patients 10 and 11, could affect treatment outcomes.

CONCLUSION

The study on the management of Cesarean scar ectopic pregnancy (CSEP) using intra-gestational sac injection of methotrexate has provided valuable insights into a conservative treatment approach that preserves future fertility while effectively managing this complex condition. Our findings demonstrate that this method can result in significant reductions in β -HCG levels, indicating successful resolution of CSEP in a majority of cases.

The administration of methotrexate directly into the gestational sac under ultrasound guidance has shown promising outcomes, with most patients experiencing a rapid decline in β -HCG levels without the need for surgical intervention. This approach minimizes patient morbidity and preserves the integrity of the uterus, which is crucial for women desiring future pregnancies.

However, the study also highlighted that the success of methotrexate treatment can vary based on initial β -HCG levels and the specific characteristics of the ectopic implantation site. Cases with higher initial β -HCG levels or those exhibiting certain ultrasound features may require more aggressive management strategies or additional monitoring.

In conclusion, intra-gestational sac injection of methotrexate represents a viable, effective, and safe option for the treatment of CSEP. This method aligns

with the goals of modern reproductive medicine by prioritizing fertility preservation and minimizing patient discomfort and risk. Further research and larger studies are recommended to refine treatment protocols, improve predictive factors for success, and ensure that all patients receive the most effective and personalized care possible.

Limitations of Study:

Small Sample Size: The study involved only 12 cases, which limits the generalizability of the findings. A larger sample size would provide more robust data and allow for a better understanding of the efficacy and safety of this treatment across a more diverse patient population.

Lack of Control Group: There was no control group receiving an alternative treatment or placebo, which restricts the ability to compare the efficacy of intra-gestational sac methotrexate injection directly against other treatment modalities, such as systemic methotrexate administration or surgical interventions.

Short Follow-up Period: The follow-up period was primarily limited to the immediate weeks following treatment until β -HCG levels normalized. Long-term outcomes, particularly regarding future fertility and the structural integrity of the uterus post-treatment, were not assessed.

Single-Center Study: The study was conducted at a single tertiary care center, which might influence the results due to specific patient demographics, physician expertise, and center-specific protocols that may not be representative of other settings.

Subjectivity in USG Reporting: Ultrasound reporting and the assessment of implantation site characteristics might have subjective elements, depending on the interpreting radiologist. This variability could affect the consistency of treatment application and outcomes assessment.

Variability in Treatment Application: The technique of methotrexate injection and its precise application could vary slightly between cases, potentially affecting the outcomes. The study did not standardize every aspect of the injection procedure, which could influence the efficacy and safety results.

Potential Bias in Patient Selection: The inclusion and exclusion criteria could introduce selection bias, as patients with certain characteristics (e.g., those with particularly high or low β -HCG levels) might have been preferentially selected or excluded from the study.

REFERENCES

1. Agrawal, N. S. Gainder, S. Chopra and M. Rohila, et al., 2021. Management of Scar Ectopic: A single center experience; Cureus Vol. 13, No. 6 .10.7759/cureus.15881.
2. M. Seow, K. L. W. Huang, Y. H. Lin, M.Y. Lin, Y. L .Tsai and J. L. Hwang, 2004. Cesarean scar pregnancy: Issues in management. Ultrasound Obstet. & Gynecol., 23: 247-253.
3. Jurkovic, D., K. Hillaby, B. Woelfer, A. Lawrence, R. Salim and C.J. Elson, 2003. First-trimester diagnosis and management of pregnancies implanted into the lower uterine segment cesarean section scar. Ultrasound Obstet. & Gynecol., 21: 220-227.
4. Xita, N., I. Georgiou and A. Tsatsoulis, 2002. The genetic basis of polycystic ovary syndrome. Eur J End., 147: 717-725.
5. Nijjar, S., E. Jauniaux and D. Jurkovic, 2023. Definition and diagnosis of cesarean scar ectopic pregnancies. Best Pract. & Res. Clin. Obstet. & Gynaecology, Vol. 89 .10.1016/j.bpobgyn.2023.102360.
6. Lin, R., N. DiCenzo and T. Rosen, 2023. Cesarean scar ectopic pregnancy: Nuances in diagnosis and treatment. Fertil. Sterility, 120: 563-572.
7. Ban, Y., J. Shen, X. Wang, T. Zhang and X. Lu et al., 2023. Cesarean scar ectopic pregnancy clinical classification system with recommended surgical strategy. Obstet. and Gynecol., 141: 927-936.
8. Huo, S., L. Shen, Y. Ju, K. Liu and W. Liu, 2023. Treatments for cesarean scar pregnancy: 11-year experience at a medical center. The J. Maternal-Fetal & Neonatal Med., Vol. 36 .10.1080/14767058.2022.2162818.
9. Tran, C.T., L. Hofmann, A. Chen and M. Smet, 2023. Ep27.21: A cervical ectopic pregnancy presenting as a caesarean scar pregnancy: A case report. Ultrasound Obstet. & Gynecol., Vol. 62 .10.1002/uog.27162.