



Review Article

Systematic review: What is the best first-line approach for cesarean section ectopic pregnancy?

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ABSTRACT

This systematic review aims to analyze the case reports, case series, or clinical studies describing the women with cesarean scar ectopic pregnancy (CSEP), and thus, to determine the efficacy and safety of different primary treatment modalities in the management of CSEP.

A thorough search of electronic databases showed that 274 articles on CSEP were published between January 1978 and April 2014.

Systemic methotrexate, uterine artery embolization, dilatation and curettage (D&C), hysterotomy, and hysteroscopy were the most frequently adopted first-line approaches. The success rates of systemic methotrexate, uterine artery embolization, hysteroscopy, D&C, and hysterotomy were 8.7%, 18.3%, 39.1%, 61.6%, and 92.1%, respectively. The hysterectomy rates were 3.6%, 1.1%, 0.0%, 7.3%, and 1.7% in CSEP cases that were treated by systemic methotrexate, uterine artery embolization, hysteroscopy, D&C, and hysterotomy, respectively. The ability to achieve a subsequent term pregnancy is related to successful systemic methotrexate treatment ($p = 0.001$) or hysterotomy ($p = 0.009$). Future term pregnancy was significantly more frequent in the hysterotomy group ($p = 0.001$).

Hysteroscopy and laparoscopic hysterotomy are safe and efficient surgical procedures that can be adopted as primary treatment modalities for CSEP. Uterine artery embolization should be reserved for cases with significant bleeding and/or a high suspicion index for arteriovenous malformation. Systemic methotrexate and D&C are not recommended as first-line approaches for CSEP, as these procedures are associated with high complication and hysterectomy rates.

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Introduction

Cesarean scar ectopic pregnancy (CSEP) refers to implantation of pregnancy within the myometrial tissue that corresponds to the site of prior hysterotomy. However, CSEP usually occurs as a late complication of a previously performed cesarean section [1].

Up to date, caesarean scar pregnancy (CSEP) is considered as the rarest form of the ectopic pregnancies. Although its exact incidence is unknown, the incidence of CSEP has been estimated to be 1/3000 for the general obstetric population, 1/1800–1/2500 for all

cesarean deliveries, and 1/531 for women who had at least one cesarean delivery [2].

The diagnosis of CSEP is often difficult, and a false-negative diagnosis may result in major complications such as severe hemorrhage, uterine rupture, and emergency hysterectomy. The following criteria are required for the diagnosis of CSEP: (1) empty uterus and empty cervical canal; (2) development of gestational sac or placental tissue in the anterior wall of the cervical isthmus; (3) discontinuity on the anterior uterine wall as demonstrated on a sagittal plane of the uterus running through the amniotic sac; (4) absent or diminished healthy myometrium between the bladder and gestational sac/placental tissue; and (5) high velocity with low impedance peritrophoblastic vascular flow clearly surrounding the sac in Doppler examination [2,3].

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Up to date, there is no standard treatment modality for CSEP. Therapeutic options can be medical, surgical, or a combination of both. Since there is a dramatic rise in the prevalence of cesarean delivery, it is obvious that more women will be diagnosed with CSEP in the near future. Therefore, a set of criteria should be developed for the therapeutic options [3].

This systematic review aims to analyze the case reports, case series, or clinical studies describing the women with CSEP, and thus, to determine the efficacy and safety of different primary treatment modalities in the management of CSEP. To the best of our knowledge, the present review is the most extensive and comprehensive account of first-line approaches that have been adopted for the treatment of CSEP cases.

Materials and methods

Literature search

In order to conduct the present meta-analysis, a detailed search was conducted within the following electronic databases: CENTRAL (in the Cochrane Library, current issue), PUBMED/MEDLINE (Silver Platter, from January 1978 to April 2014), and EMBASE (from January 1978 to April 2014). A search was initiated to acquire all the related publications using the keyword “cesarean section ectopic pregnancy”. After that, all free text MH exact subject headings and MH exact subject heading terms were explored. Any new terms found were fed into the search strategy so that new searches could be run. After the relevant articles were identified and scanned, reference lists of the relevant papers were scrutinized for further studies. Besides, relevant articles were re-entered into PubMed (up to April 2014), and using the “related articles” feature, a further search was carried out. There was no language restriction so that the papers in all languages were sought and translated. Full texts of the identified articles were selected with final inclusion or exclusion decisions made after independent and duplicate examination of the papers. This systematic review included the case reports, case series, and clinical studies that reported on the diagnosis and treatment of CSEP. The year 1978 was chosen as a starting point for literature search because it was the year of the first published report on CSEP [4].

Study selection

A thorough search of electronic databases showed that 274 articles were published between January 1978 and April 2014. All included manuscripts were assessed by at least two reviewers (M.K.P. and O.D.) for study and reporting quality using validated tools. Disagreements were resolved by consensus or arbitration of a third reviewer. By the abstract evaluation of those 274 articles, 243 articles were found to be associated with the diagnosis, presentation, and treatment of CSEP.

Whenever multiple/duplicate publications of the same data set are noticed, only the most recent and/or complete study was included. Multiple/duplicate publications ($n = 6$) and articles presenting insufficient data ($n = 8$) were excluded. Similarly, reviews, letters, comments, and editorials ($n = 35$) were also eliminated. Consequently, data about 1647 women with CSEP were retrieved from 126 individual case reports, 45 case series, and 23 clinical studies, which were included for final analysis. The procedure for study selection is summarized in Figure 1.

Data extraction

Data related to maternal age, gravidity, parity, the number of prior cesarean deliveries, indication for previous cesarean delivery,

interval to prior cesarean delivery, gestational age, crown–rump length measurements, existence of embryonic/fetal cardiac activity, serum concentration of beta-human chorionic gonadotropin (β -HCG) at the time of admission, clinical symptoms, treatment modalities, resolution time, and future fertility were retrieved from the original manuscript.

Limitation and bias

The major limitation of the study was the dependence on nonstandardized knowledge gathered from anecdotal case reports and series. The methods of β -HCG measurement, the methods of crown–rump length measurement, the quality of ultrasonography equipment, and the experience or skillfulness of the sonographers were not uniform and lacked standardization. Moreover, the representation and reportage of data related to CSEP lacked constancy and uniformity.

Statistical analysis

Collected data were analyzed by SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean \pm standard deviation or median, and categorical variables were denoted as numbers or percentages where appropriate. Chi-square test, Mann–Whitney U test, and multiple logistic regression analysis were performed. A p values < 0.05 was considered to be statistically significant.

Results

Systemic methotrexate, uterine artery embolization, dilatation and curettage (D&C), and hysteroscopy were the most frequently adopted first-line approaches for CSEP (Table 1).

Systemic methotrexate was successful in only 8.7% of the cases. Secondary treatment was D&C, uterine artery embolization, hysteroscopy, and transvaginal sonography-guided intragastrational methotrexate injection in, respectively, 40.5%, 24.8%, 12.3%, and 11.6% of CSEP cases that underwent methotrexate treatment. Hysterectomy was indicated in 20 cases, corresponding to a rate of 3.6%. Higher parity, a higher number of prior cesarean deliveries, lower gestational age, absence of bleeding and embryonic cardiac activity, and longer duration of resolution were significantly associated with the success of systemic methotrexate ($p = 0.023$, $p = 0.018$, $p = 0.001$, $p = 0.002$, $p = 0.029$, and $p = 0.001$, respectively; Table 2).

The success rate of uterine artery embolization was only 18.3%. Secondary treatment was D&C, transvaginal sonography-guided intragastrational methotrexate injection, hysteroscopy, and systemic methotrexate in, respectively, 50.2%, 16.9%, 15.9%, and 14.2% of CSEP cases that were primarily treated with uterine artery embolization. Hysterectomy was required in four cases, yielding a rate of 1.1%. Lower maternal age, lower gravidity, lower parity, a higher number of prior cesarean deliveries, and longer duration of resolution were significantly associated with successful uterine artery embolization ($p = 0.007$, $p = 0.001$, $p = 0.001$, $p = 0.001$, and $p = 0.001$, respectively; Table 3).

Hysteroscopic resection of gestational tissue was performed in 60 cases and hysteroscopic hysterotomy was performed in 36 cases. By contrast, intragastrational methotrexate injection was administered in 12 cases, intragastrational ethanol injection was administered in one case, and gestational sac was aspirated following intragastrational methotrexate injection in one case. The success rate of hysteroscopy was 39.1%, and 60.9% of the cases required complementary treatment. Secondary treatment was systemic mifepristone, systemic methotrexate, hysterotomy, and D&C in,

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