

Treatment of caesarean section scar pregnancy with systemic administration of methotrexate

Huili Yang¹, Fuli Li¹, Ping Zhang², Jie Dong^{1*}, Jiaoling Wang¹ and Yongqian Wang³

¹Obstetrics and Gynecology Department, Jinan Central Hospital Affiliated to Shandong University, Jinan, China

²Obstetrics and Gynecology Department, Zhangqiu People's Hospital of Jinan, Jinan, China

³Rehabilitation Department, Zhangqiu People's Hospital of Jinan, Jinan, China

Abstract: To observe and analyze the therapeutic effect of systemic administration of methotrexate on caesarean section scar pregnancy. The 160 patients who had been confirmed with caesarean section scar pregnancy in our hospital were selected research objects. They were randomly divided into two groups (research group and control group), each containing 80 patients. The research group was subjected to systemic administration of methotrexate, while control group was applied with local administration of methotrexate. The total treatment effective rates of two groups were observed and compared. The total treatment effective rate of research group was higher than that of control group, $p < 0.05$; in terms of time required for β -HCG restoring to normal state, the research group was significantly shorter than control group, $p < 0.05$; the time required for disappearing of scar lump for research group was shorter than that of control group, $p < 0.05$. No complications were observed for both groups. Systemic administration of methotrexate can significantly improve the curative effect for patients with caesarean section scar pregnancy.

Keywords: Methotrexate, systemic administration, caesarean section scar pregnancy, therapeutic effect.

INTRODUCTION

Caesarean section scar pregnancy is a major postoperative complication of caesarean section, which may cause serious impact on daily life or even life safety of patient. For patients with caesarean section scar pregnancy, transvaginal color doppler sonography should be conducted as soon as possible to obtain clear diagnosis. Furthermore, a targeted treatment scheme is a key factor to improve patients' prognosis (Yi, Shi, 2014; Sun, Yin, 2015; Ke, 2014). With the change of life mode, the global caesarean section rate is now continuously rising, which leads to increased rate of caesarean section scar pregnancy and attracts extensive attention of medical sphere.

At present, there has been no agreement on pathogenesis of caesarean section scar pregnancy (fig. 1), but it is well recognized to be associated with the gestational sac implantation (fig. 2) caused by the formation of small tube in the scar. Caesarean section scar pregnancy is an unusual type of ectopic gestation. According to relevant statistics, the caesarean section scar pregnancy accounts for about 6% of all types of ectopic gestation (Tsai, *et al.*, 2017). However, caesarean section scar pregnancy is of higher hazardness, which may lead to uterine rupture, hemorrhage, hysterectomy, and thus causing loss of fertility. Methotrexate therapy has been extensively used to treat caesarean section scar pregnancy, with sound results being achieved. This study analyzes the curative effect of with systemic administration of methotrexate in treatment of caesarean section scar pregnancy, which provides valuable basis for practical treatment.

*Corresponding author: e-mail: 1979932392@qq.com

MATERIALS AND METHODS

General data

160 patients who had been confirmed and treated for caesarean section scar pregnancy in our hospital from June 2013 to March 2018 were selected as research objects. All of selected patients enjoyed the right to know and signed informed consent form. This study was approved by the ethics committee. The inclusion criteria: Patients with positive result in determination of β -HCG and urine pregnancy test; enlargement of the uterus, thickening of the endometrium, enlargement of incision site at lower uterus, attachment of mixed mass or pregnancy cystic adhesion were observed when determining pregnant bursa parts and gestational weeks by ultrasonic testing and vaginal ultrasonography (Domrse, *et al.*, 2016; Yi, *et al.*, 2018); Then thinnest part of mesometrium between the uterine wall and gestation sac was 0.09cm. Exclusion criteria: patients without good compliance or who will not join this study; patients with contraindication to methotrexate, or with severe liver, heart, kidney dysfunction.

The patients were grouped according to the sequence of admission, with the singular as the research group and the dual as the control group, each having 80. The age of patients in research group varied from 25 to 35 years old, averaging at 28.6 ± 3.2 , with gravidity ranging from 1 to 3 (averaging at 2.3 ± 0.9), at an interval of 2-8 years (averaging at 5.7 ± 2.1), menopause period ranging from 42 to 60 d (averaging at 50.4 ± 10.2). In contrast, the age of patients in control group varied from 26 to 34 years old, averaging at 29.8 ± 3.5 , with gravidity ranging from 1 to 3 (averaging at 2.8 ± 1.0), at an interval of 2-10 years

(averaging at 6.4 ± 2.3), menopause period ranging from 42 to 58 d (averaging at 48.8 ± 11.9). The comparison of basic data between two groups before treatment showed no statistical significance, $p > 0.05$.

Method

The research group was applied with systemic administration of methotrexate. The intramuscular injection of $0.4 \text{ mg}/(\text{kg} \cdot \text{d})$ methotrexate was performed for consecutive 5 days. Scientific course of treatment should be determined by strictly according to the decrease of blood $\beta\text{-HCG}$ level. The control group was applied with local administration of methotrexate. First, a flexible plastic conduit (2mm in diameter) was inserted via cervical canal, and then 50mg of methotrexate combined with 2mL of normal saline were injected via plastic conduit. All patients in both groups should be given with oral mifepristone therapy if needed, by dosage of 75mg-50mg per day.

Observation indexes

The total treatment effective rates of both groups were observed and compared, which can be categorized into cured case, effective case, ineffective case. The evaluation criteria for cured case refer to complete removal of clinical symptoms and signs, disappearance of enlarged lump at lower incision of the uterus upon B-ultrasonography and remaining in normal status of $\beta\text{-HCG}$ level (Chen, *et al.*, 2016); the evaluation criteria for effective treatment case refer to certain degree of relief of clinical symptoms and signs after treatment, normal status of $\beta\text{-HCG}$ level and significantly reduced pregnancy sac; the evaluation criteria for ineffective treatment case refer to no improvements of clinical symptoms and signs, occurrence of internal bleeding or increased vaginal bleeding, increasing level of $\beta\text{-HCG}$, primitive heart tube pulsation, and even deterioration of disease. In addition, the time required for $\beta\text{-HCG}$ restoring to normal state as well as the time required for disappearing of scar tissue were recorded.

STATISTICAL ANALYSIS

SPSS21.0 software was used for statistical analysis. The measurement data was expressed in the form of mean \pm average ($\pm s$), and inter group difference was compared by t test. The enumeration data was expressed by natural number (n) and percentage (%) and the intergroup difference was tested by chi-square. The difference was of statistical significance when $P < 0.05$.

RESULTS

Comparison of total treatment effective rate between two groups

As shown in table 1, The overall treatment efficiency of patients in the research group treated with methotrexate was significantly better than that of the control group

treated with local medication, with statistical significance, $p < 0.05$ ($X^2 = 10.28$).

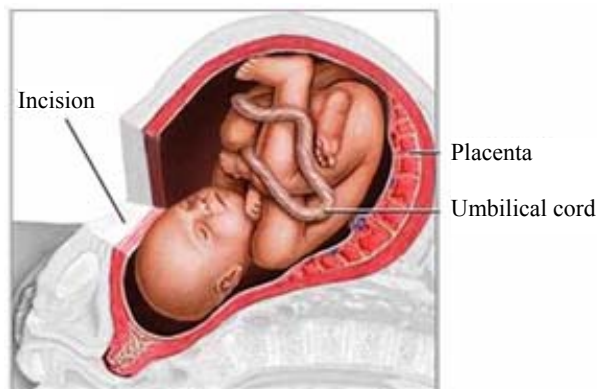


Fig. 1: Cesarean section scar pregnancy



Fig. 2: Gestational sac implantation

Comparison of the time required for $\beta\text{-HCG}$ restoring to normal state for two groups

As shown in table 2, the time required for $\beta\text{-HCG}$ restoring to normal state in research group was 15.29 ± 7.20 days, which was shorter than that (42.18 ± 8.31 days) of control group, $p < 0.05$, the intergroup difference was of statistical significance.

Comparison of the time required for disappearing of scar tissue between two groups

As shown in table 3, the time required for disappearing of scar tissue in research group was 40.29 ± 6.35 days, which was significantly shorter than that (58.09 ± 10.12 days) of control group, $p < 0.05$, the intergroup difference was of statistical significance.

DISCUSSION

Cesarean section scar pregnancy is a type of ectopic gestation of high hazardness. If being clearly diagnosed, immediate termination of pregnancy is needed to kill embryo, discharge gestation sac and thus realize preservation of reproductive function (Moschos, *et al.*,

Table 1: Comparison of overall treatment efficiency between two groups [n(%)]

Group	Case number	Cured case	Effective case	Ineffective case	Overall effective rate
Research group	80	50	27	3	77(96.25)
Control group	80	30	34	16	64(80.00)
χ^2					15.28
p					<0.05

Table 2: Comparison of the time required for β -HCG restoring to normal state for two groups ($\bar{x} \pm s$)

Group	Case number	Time required for β -HCG restoring to normal state (d)
Research group	80	15.29 \pm 7.20
Control group	80	42.18 \pm 8.31
t		9.67
p		<0.05

Table 3: Comparison of the time required for disappearing of scar tissue between two groups ($\bar{x} \pm s$)

Group	Case number	Time required for disappearing of scar tissue (d)
Research group	80	40.29 \pm 6.35
Control group	80	58.09 \pm 10.12
t		8.02
p		<0.05

2016). Currently, China has not reached unified method in terms of diagnosis and treatment of caesarean section scar pregnancy. Surgical approach and conservative drug therapy are still common methods, which should be applied by strictly according to actual disease condition of patients. Methotrexate is a folic acid antagonist which can bind with dihydrofolic acid and thus prevent the resulting dihydrofolic acids. Moreover, methotrexate can effectively inhibit DNA synthesis, thus realize inhibition of trophoblast cell division and proliferation, and finally damage the embryonic tissue (Uysal, 2018; Wang, *et al.*, 2017).

Treating caesarean section scar pregnancy with methotrexate is a conservative and effective approach, and the treatment results have been demonstrated by a large number of clinical practices. In this study, the research group was subjected to systemic administration of methotrexate, with ideal effective rate being achieved. Results showed that intramuscular injection of methotrexate has good effect for patients with caesarean section scar pregnancy, especially for those with over concentration of β -HCG over 5000mIU/mL. Even though multiple applications of drug were applied, adverse reactions such as hair loss, gastrointestinal reactions, and pneumonia were not observed, indicating the safety of such therapy. In addition, systemic administration of methotrexate can improve and stabilize the clinical symptoms and signs. For patients of which caesarean section scar pregnancy was less than 8 weeks and the myometrium between caesarean scar and bladder was less than 2mm in thickness, the success rate of such treatment approach can reach 80%.

Through this study, it can be known that the treatment effective rate of research group accepting systemic administration of methotrexate was higher than that of control group accepting local administration of methotrexate, $p < 0.05$; the time required for β -HCG restoring to normal state for research group was significantly shorter than that for control group, $p < 0.05$; the time required for disappearing of scar tissue was significantly shorter than that for control group, $p < 0.05$.

CONCLUSION

In conclusion, systemic administration of methotrexate is a reliable and safe treatment approach for caesarean section scar pregnancy, which can significantly improve curative effect. Therefore, it is worth of being promoted in clinics. To summarize, treatment of postmenopausal atrophic vaginitis with combination of conjugated estrogen cream and metronidazole suppositories can achieve good results, lower incidence of adverse reactions and realize higher safety and reliability. Therefore, it is worth promoting.

REFERENCES

- Yi BN and Shi HR (2014). Analysis of clinical effect of different treatment methods on caesarean section scar pregnancy. *Chinese Journal of Family Planning & Gynecotokology*, 6(02): 35-38.
- Sun HY and Yin SS (2015). Comparison of curative effects of cervical injection of methotrexate and systemic administration of methotrexate in treatment of ectopic gestation. *Studies of Trace Elements and*

- Health*, **32**(01): 17-18.
- Ke L (2014). Comparison of therapeutic effects of different methods in treatment of cesarean section scar pregnancy. *Journal of Guangdong Medical College*, **32**(05): 651-652.
- Tsai SW, Huang KH and Ou YC (2017). Low-lying-implantation ectopic pregnancy: A cluster of cesarean scar, cervico-isthmus and cervical ectopic pregnancies in the first trimester. *Taiwanese Journal of Obstetrics and Gynecology*, **52**(4): 505-511.
- Domrse CM, Geipel A and Berg C (2016). Second- and third-trimester termination of pregnancy in women with uterine scar - A retrospective analysis of 111 gemeprost-induced terminations of pregnancy after previous cesarean delivery. *Contraception*, **85**(6): 589-594.
- Yi L, Hu QL, Cui YP, Huang WJ and Liu YH (2018). Effect of administration frequency on ovarian reserve function in treatment of fallopian pregnancy with systemic administration of methotrexate. *Chinese Medical Innovations*, **15**(05): 98-101.
- Chen X, Li YF and Huang Y (2016). Observation of clinical effect of conservative treatment for early cesarean scar pregnancy. *Shanxi Medical Journal*, **45**(05): 514-518.
- Moschos E, Wells CE and Twickler DM (2016). Biometric sonographic findings of abnormally adherent trophoblastic implantations on cesarean delivery scars. *Journal of Ultrasound in Medicine* (Official Journal of the American Institute of Ultrasound in Medicine), **33**(3): 475-481.
- Uysal F and Uysal A (2018). Spontaneous heterotopic cesarean scar pregnancy: Conservative management by transvaginal sonographic guidance and successful pregnancy outcome. *Journal of Ultrasound in Medicine* (Official Journal of the American Institute of Ultrasound in Medicine), **32**(3): 547-548.
- Wang G, Liu X and Bi F (2017). Evaluation of the efficacy of laparoscopic resection for the management of exogenous cesarean scar pregnancy. *Fertility and Sterility* (Official Journal of the American Fertility Society, Pacific Coast Fertility Society, and the Canadian Fertility and Andrology Society), **101**(5): 1501-1507.