DOI: 10.7860/JCDR/2019/28209.13287

Original Article

Obstetrics and Gynaecology Section

# Low-dose Misoprostol for Second Trimester Pregnancy Termination in Women with a Prior Caesarean Delivery

EMINE AYDIN[1], OZGUR OZYUNCU[2]

## ABSTRACT

**Introduction:** Termination of Pregnancy (ToP) is an obstetric procedure that can be performed by surgical or medical techniques during the first or second trimester of pregnancy. Medical ToP is recommended in the second trimester owing to its low rate of maternal morbidity. Low-dose misoprostol is an effective option in such cases.

**Aim:** To compare the safety and efficacy of two different vaginal misoprostol regimens for ToP in the second trimester in women with previous Caesarean Deliveries (CDs), against controls.

**Materials and Methods:** This retrospective study was conducted at a university hospital, between January 2005 to December 2014. The study cohort was divided into two groups: history of CD (Group I, n=85) and control (Group II, n=434). The method used for ToP was chosen with respect to history of CD. Four doses of 50 µg misoprostol and 4 doses of 200 µg misoprostol were applied vaginally each day, until regular uterine contractions were observed, to Groups I and II, respectively. Indication of ToP, gestational age at the ToP (weeks), duration from induction to abortion (hours), total misoprostol dose (µg), foetal weight (gram), post-abortion hospitalisation time (day), and any complications were recorded. The Chi-square or Fisher's-Exact test was used for qualitative data, and the Student's t-test or Mann-Whitney U-test was used for quantitative data. The $p<0.05$ was considered significant. Tests were performed using the SPSS statistical package for Windows, version 17 (SPSS, Chicago, Illinois, USA).

**Results:** The success rate of termination was 91.8% (78/85) in Group I and 99.1% (430/434) in Group II ($p<0.001$). The median induction to abortion interval was 54.08±42.85 hours for Group I and 47.19±31.39 hours in Group II ($p=0.371$). One case of uterine rupture was recorded in Group I ($p=0.164$). The incidence of requiring transfusion for haemorrhages was higher in Group I than in Group II (5.9% vs. 1.6%, respectively, $p=0.032$).

**Conclusion:** Low-dose vaginal misoprostol appears to be a safe and effective procedure for second trimester ToP in women with a history of CD.

**Keywords:** Abortion, Caesarean section, Induction, Prostaglandin, Uterine scars

## INTRODUCTION

ToP remains one of the most common procedures in obstetrics and gynaecology. ToP is generally performed by surgical evacuation. Modern induced abortion methods typically include the use of one or a combination of the following: prostaglandin analogues (such as misoprostol, gemeprost, dinoprostone), mifepristone, osmotic cervical dilators, Foley catheters, and oxytocin. In 1994, Jain JK et al., first described the use of the prostaglandins for second trimester ToP [1]. Misoprostol has been widely used, both orally and vaginally, for ToP owing to its low cost and high effectiveness [2]. However, using prostaglandins provides the opportunity to perform a post-mortem autopsy on the foetus, when further information is required. Using prostaglandins also has lower maternal morbidity rates than those using surgical evacuation. Although prostaglandins have shown remarkably good results, serious complications have been reported during ToP procedures in the second trimester. These complications include: blood loss requiring transfusion, infections, uterine rupture, cervical lacerations, obstetric fistulas and major unintended surgery [3,4].

The number of CDs has increased worldwide. CD rates reached 51.9% (42.9% in the public and 87.9% in the private health sector) of all births in Brazil [5]. Due to the increasing rate of CDs, the number of women with a history of CD who is offered ToP has increased. Several guidelines are available on the safety of misoprostol in women with one previous CD [6,7].

The aim of this study was to compare the safety and efficacy of two different vaginal misoprostol regimens in the second trimester ToP in women who had one prior CD against controls.

## MATERIALS AND METHODS

This retrospective study was conducted at the Department of Obstetrics and Hacettepe University Faculty of Medicine from January 2005 to December 2014. The study was approved by the Local Ethical Committee (approval number: GO 14-595), Hacettepe University, Faculty of Medicine, Ankara, Turkey.

The demographic and clinical characteristics of the patients were obtained from patient files and electronic records of the hospital. Patient demographics (age, parity, gravida, etc.,), Body Mass Index (BMI), indication of ToP, gestational age at ToP (weeks), duration between induction to abortion (hours), total misoprostol dose (µg), foetal weight (gram), post-abortion hospitalisation time (days), and complications were recorded. The duration between induction to abortion was defined as the interval between the placement of the first dose of misoprostol and the expulsion of the products of conception.

Patient records with the following characteristics were excluded from the study: first or third trimester ToP, twin pregnancy, history of myomectomy, cervical incompetence, presence of large uterine leiomyoma, or congenital uterine anomaly.

The study cohort comprised 519 women, including 85 with previous CD (Group I) and 434 with no known uterine scar (Group II). The method used for ToP was chosen based on history of CD. Group I included data records of patients with the following procedure done on them as per the hospital protocol; a 50 µg misoprostol tablet (Cytotec®, Ali Raif Pharm. Co, Turkey) inserted vaginally every six hours until regular uterine contraction. Group II consisted data of patients that underwent the following procedure; a 200 µg

misoprostol tablet inserted vaginally every six hours for the first 24 hours; subsequently, 800 µg/day misoprostol applied vaginally until regular uterine contractions.

## STATISTICAL ANALYSIS

The Chi-square or Fisher's-Exact test was used for qualitative data, and the Student's t-test or Mann-Whitney U-test was used for quantitative data. The p<0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 17 (SPSS, Chicago, Illinois, USA).

## RESULTS

A total of 519 patient's data were enrolled in this study and were divided into two groups. The study group consisted of patients/data with a history of caesarean section (Group I, n: 85). The control group consisted of patients/data with no uterine scar or CD (Group II, n: 434). Forty-six patient records were excluded because of several reasons, such as incomplete data, history of myomectomy, and protocol corruption. Most common indications for ToP in both groups were linked to foetal causes, including chromosomal abnormalities, non-chromosomal malformations, single gene disorders, and congenital infections. There were no statistically significant differences in maternal demographics such as age (years), gravida, parity, BMI (kg/m$^2$) [Table/Fig-1].

| | Group I (n: 85) | Group II (n: 434) | p-value |
|---|---|---|---|
| Maternal age (years) | 32.55±4.50 | 32.17±4.59 | 0.136 |
| Gravida | 3.08±1.29 | 2.98±1.50 | 0.398 |
| Parity | 1.49±0.82 | 1.39±1.37 | 0.076 |
| BMI (kg/m$^2$) | 25.71±3.04 | 25.40±3.59 | 0.192 |

**[Table/Fig-1]:** Demographic and clinical features of the groups.
BMI: Body mass index
Data are given as mean±standard deviation

The mean dose of misoprostol required to induce labour was 579.41±411.90 µg in Group I and 1091.60±515.60 µg in Group II (p<0.001). There were no statistically significant differences detected in foetal weight and the induction to abortion interval (p=0.319 and p=0.371, respectively). [Table/Fig-2] summarises the characteristics of procedures in the two groups.

| | Group I (n:85) | Group II (n: 434) | p-value |
|---|---|---|---|
| Gestational age at time of ToP (weeks) | 19.19±2.63 | 19.6±305 | 0.380 |
| Total doses (µg) | 579.41±411.90 | 1091.60±515.60 | **<0.001** |
| Induction to abortion interval (hours) | 54.08±42.85 | 47.19±31.39 | 0.371 |
| Fetal weight (g) | 280.7±167.9 | 317.2±213.5 | 0.319 |
| Post-abortion hospitalisation (days) | 3.34±2.89 | 2.58±2.27 | **0.003** |

**[Table/Fig-2]:** Clinical characteristics of termination of pregnancy procedures in the both groups.
ToP: Termination of pregnancy

There were no serious adverse effects of misoprostol in this series of patients. However, the procedure was terminated in two patients owing to fever and sepsis, respectively. Three patients (3.6%) in the Group I and 48 (11.1%) patients in the Group II developed fever during labour (p=0.019). There was no statistically significant difference between these two groups in terms of chills and diarrhoea for the period of hospitalisation for termination and for 48 hours post-termination.

Successful rates of procedures were 91.8% and 99.1% in Group I and II, respectively (p<0.001). Cases of haemorrhages requiring transfusion were higher in Group I than in Group II (5.9% vs. 1.6%, p=0.032). Rates of other complications such as placenta retention, uterine rupture, and sepsis were similar in both groups [Table/Fig-3].

| | Group I (n: 85) | Group II (n: 434) | p-value |
|---|---|---|---|
| **Side effects** | | | |
| Fever | 3 (3.6%) | 48 (11.1%) | **0.019** |
| Chills | 3 (3.6%) | 36 (8.3%) | 0.178 |
| Diarrhoea | 1 (1.2%) | 18 (4.1%) | 0.338 |
| **Complications** | | | |
| Procedure failure | 7 (8.2%) | 4 (0.9%) | **<0.001** |
| Haemorrhage | 5 (5.9%) | 7 (1.6%) | **0.032** |
| Placenta retention | 1 (1.2%) | 6 (1.4%) | 1.000 |
| Uterine rupture | 1 (1.2%) | 0 (0%) | 0.164 |
| Sepsis | 0 (0%) | 1 (0.2%) | 1.000 |

**[Table/Fig-3]:** Side effects of misoprostol and complication of both procedures.
Fisher's Exact Test were used for statistical analysis

## DISCUSSION

This study is one of the largest series reported to date in women with one prior CD undergoing ToP using only intravaginal misoprostol. Different ToP protocols were used such as 4 doses of 50 µg misoprostol and 4 doses of 200 µg misoprostol applied vaginally until regular uterine contractions, in the previous CD group and control group, respectively. In our series, unresponsiveness to intravaginal misoprostol was more common in patients with history of CD compared to controls (8.2% vs. 0.9%, p<0.001). The lower success rate in our study may be attributed to the lower dose used in the protocol for Group I. However, the overall success rates in this study (97.88%) are consistent with those reported in the previous literature [4,8,9].

Several studies revealed that there were no statistically significant differences in induction to abortion time when using same dosage in the two groups [4]. Although we used lower doses in the previous CD group than in the control group, induction to abortion intervals in the two groups were also similar (p=0.371). We found that a lower dose of misoprostol used in the group with previous CD did not impact the delay to abortion significantly. However, when we compared the results of previous studies, the lower induction to abortion time (hours) in present study may be attributed to the lower dose used in the protocols.

Another important finding of this study was that a history of CD appears to increase the frequency of haemorrhage, with the need for a blood transfusion in women who performed a second trimester ToP (5.9% vs. 1.6%, p: 0.032). Present results do not comply with the existing literature. Fawzy M et al., found no significant difference between CD and control groups in the incidence of severe haemorrhage requiring a blood transfusion [3]. Similarly, other studies in the literature reported no evidence that a previous CD affects the incidence of complications including severe haemorrhage [4,9,10].

For labour induction, the risk of uterine rupture is increased with the use of misoprostol in women with CD compared with women without previous CD [11,12]. Recently, a study showed that use of misoprostol for second trimester abortion in women with a history of CD, risk of uterine rupture is similar when compared with the controls [11]. Present data suggest that a CD history cannot be a risk factor for uterine rupture in women scheduled for a second trimester ToP (p=0.164).

## LIMITATION

Limitation of the study is the usage of different doses on the study groups.

## CONCLUSION

History of a CD does not abolish the possibility of using misoprostol for second trimester ToP. However, patients who undergo misoprostol induction must be closely observed for possible side effects and complications.

## REFERENCES


[1] Jain JK, Mishell DR, Jr. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of second-trimester pregnancy. The New England Journal of Medicine. 1994;331(5):290-93.
[2] Pongsatha S, Tongsong T. Misoprostol for second trimester termination of pregnancies with prior low transverse cesarean section. International Journal of Gynaecology and Obstetrics: The Official Organ of the International Federation of Gynaecology and Obstetrics. 2003;80(1):61-62.
[3] Fawzy M, Abdel-Hady el-S. Midtrimester abortion using vaginal misoprostol for women with three or more prior cesarean deliveries. International Journal of Gynaecology and Obstetrics: The Official Organ of the International Federation of Gynaecology and Obstetrics. 2010;110(1):50-52.
[4] Ting WH, Peng FH, Lin HH, Lu HF, Hsiao SM. Factors influencing the abortion interval of second trimester pregnancy termination using misoprostol. Taiwanese Journal of Obstetrics and Gynecology. 2015; 54(4):408-11.
[5] Nakamura-Pereira M, do Carmo Leal M, Esteves-Pereira AP, Domingues RMSM, Torres JA, Dias MAB, et al. Use of Robson classification to assess cesarean section rate in Brazil: The role of source of payment for childbirth. Reproductive Health. 2016;13(3):128.
[6] Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2011. National vital statistics reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2012;61(5):01-18.
[7] Borgatta L, Kapp N, Society of Family P. Clinical guidelines. Labor induction abortion in the second trimester. Contraception. 2011;84(1):04-18.
[8] Berghella V, Airoldi J, O'Neill AM, Einhorn K, Hoffman M. Misoprostol for second trimester pregnancy termination in women with prior caesarean: A systematic review. BJOG: An İnternational Journal of Obstetrics and Gynaecology. 2009;116(9):1151-57.
[9] Dehlendorf CE, Fox EE, Ali RF, Anderson NC, Reed RD, Lichtenberg ES. Medication abortion failure in women with and without previous cesarean delivery. Contraception. 2015;92(5):463-66.
[10] Al RA, Yapca OE. Vaginal misoprostol compared with buccal misoprostol for termination of second-trimester pregnancy: A randomized controlled trial. Obstetrics & Gynecology. 2015;26(3): 593-96.
[11] Rath W, Tsikouras P. Misoprostol for labour induction after previous caesarean section-forever a "no go"? Geburtshilfe und Frauenheilkunde. 2015;75(11):1140-48.
[12] West HM, Jozwiak M, Dodd JM. Methods of term labour induction for women with a previous caesarean section. Cochrane Database of Systematic Reviews. 2017;6.



**PARTICULARS OF CONTRIBUTORS:**
1. Department of Obstetrics and Gynaecology, Istanbul Medipol University, Istanbul, Turkey.
2. Associate Professor, Department of Obstetrics and Gynaecology, Hacettepe University Faculty of Medicine, Ankara, Turkey.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Emine Aydin,
Department of Obstetrics and Gynaecology, Istanbul Medipol University,
Faculty of Medicine, Istanbul, Turkey.
E-mail: eminebaskurtaydin@gmail.com



**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Aug 09, 2019
- Manual Googling: Sep 30, 2019
- iThenticate Software: Oct 19, 2019 (18%)

**ETYMOLOGY:** Author Origin

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: No
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 08, 2019**
Date of Peer Review: **Aug 30, 2019**
Date of Acceptance: **Sep 30, 2019**
Date of Publishing: **Nov 01, 2019**