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The Safety of Misoprostol for Medical Termination of Pregnancy in First and Second Trimester in Women with Previous Uterine Scar

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Abstract

Background: Termination of pregnancy for different maternal or fetal conditions is a common obstetrical procedure. Having a previous uterine scar is one of the most important risk factors that need consideration before selecting misoprostol for the use for TOP.

Objective: The main objective of this study is to assess the safety of misoprostol in patients with previous uterine scar, and whether its use will increase the risk of uterine rupture.

Study design: A prospective observational cohort study.

Methods: Five hundred patients in their first and second trimester of pregnancy with a confirmed non-viable foetus were selected for the study. They received misoprostol tablets as per Security Forces Hospital Protocol for TOP Safety was determined by the number of women who had complete abortion without complication.

Conclusion: The use of misoprostol for pregnancy termination is not contraindicated in women with Caesarean scar and is effective and comparable with those in women without scarred uteri.

Keywords: Misoprostol; Prostaglandin E1; Trimester; Pregnancy; Abortion; Miscarriage; Complication; Uterine rupture; Uterine scar

Introduction

Termination of pregnancy for different maternal or fetal conditions is a common obstetrical procedure. Induction of abortion needs meticulous and effective care. There are medical as well as surgical methods for termination of pregnancy. Surgical interventions hold higher risk of mortality and morbidity in comparison to medical interventions.

With respect to medical interventions for termination of pregnancy (TOP), the options for first and second trimester cervical ripening are numerous [1]. Initially, prostaglandin F2α (PGF2α) was used for induction of abortion [2]. In current practice, misoprostol, an orally active, stable prostaglandin E1 (PGE1) analogue has entered its clinical use in obstetrics and gynaecology on a wide scale. It is a gastric cyto-protective agent that has been initially marketed in US since 1988 for the prevention of peptic ulcers. Consequently, misoprostol has become an important drug in obstetrical practice [3]. It is useful for elective medical abortions, cervical priming before surgical abortions, and evacuation of the uterus in the case of embryonic fetal death [4-6].

Many risk factors play substantial roles in increasing the mortality and morbidity related to the termination of pregnancy. For instance, having a previous uterine scar is one of the most important risk factors. Hence, the method of induction of abortion should be carefully selected. To the best of our knowledge, there are limited studies that examined the use of misoprostol in patients with previous uterine scar. This topic is of great importance because epidemiological studies have demonstrated Saudi population tends to have higher rate of caesarean section. We were not able to find any local study of the safety of misoprostol for Medical termination of pregnancy in women with previous uterine scar.

The main objective of this study is to assess the safety of misoprostol in patients with previous uterine scar and whether its use will increase the risk of uterine rupture.

Materials and Methods

Ethical approval

The study was approved by the Institutional Research Committee at Security Forces Hospital.

Design and setting

A prospective observational cohort study was conducted at Department of Obstetrics and Gynaecology, Security Forces Hospital, Riyadh, Saudi Arabia. The study took place from August 2016 to June 2017.

Subjects

A total of 500 patients with medical indications for termination of pregnancy were included in the study. The study's inclusion criteria included: (a) patients in their first or

second trimester of pregnancy with or without previous uterine scars, and (b) patients with medical indications for termination of pregnancy (anembryonic pregnancy, missed miscarriage, anhydramnios, structural fetal anomalies, genetic disorders or chromosomal anomalies). The study's exclusion criteria included: Patients who are not meeting the inclusion criteria such as (a) patients with incomplete miscarriage who were taken directly to the operating room for surgical management, and (b) patients who were admitted from emergency department as a case of incomplete miscarriage and received misoprostol and aborted completely.

Patients fulfilling the inclusion criteria were admitted in the in-patient gynecology ward. For each admitted patient, a complete history was taken and physical examination was performed. Ultrasonographical examination was conducted to identify the gestational age of fetus, placental localization and uterine abnormalities. A panel of laboratory studies was ordered, including: complete blood count (CBC), blood group, urea and electrolytes and coagulation profile. Patients were prospectively analysed for demographics data and misoprostol-related outcomes.

Demographics data included: age, parity, gestational age, number of previous uterine scars and indications for TOP. Misoprostol-related outcomes included: number of doses, number of cases with successful medical abortion, number of cases requiring surgical evacuation, indications for surgical evacuation and misoprostol-related complications.

Successful medical abortion was defined as complete abortion within 24 h of initiation of termination of pregnancy protocol. Surgical evacuation – performed under general anesthesia was needed in patients who had: (a) incomplete expulsion of products of conception, or (b) excessive bleeding with retained products of conception in the uterus. Complete abortion was confirmed on clinical grounds and bedside ultrasonography, and patients were discharged home if clinically stable and no further intervention was undertaken. Patients who had complete abortion and did not exhibit any complications were discharged home after having a post complete abortion haemoglobin results as per hospital policy. Failure of misoprostol protocol was declared if no complete abortion was achieved after completing the misoprostol course of 4 doses. In such case, the patient would be considered for surgical evacuation and then discharged home whenever clinically stable.

Misoprostol-related complications were documented. Such complications included: pyrexia, excessive per-vaginal bleeding and uterine rupture. Pyrexia was defined as a sublingual temperature of more than 38.2°C or 100.4°F. Excessive per-vaginal bleeding defined as 500 cc of blood or more per vagina. Uterine rupture was diagnosed based on clinical grounds.

Protocol

Once termination of pregnancy is deemed clinically by the managing healthcare team, a written informed consent was required from the patient. Upon signing the informed consent, the hospital-based guidelines of misoprostol for termination of pregnancy were followed **(Table 1)**. Doses of misoprostol were given per the medical indication. Following the first dose of misoprostol, additional doses were given per cervical softening, vaginal bleeding and abdominal pain. Vigilant monitoring of the process of abortion was done to avoid procedure-related complications.

Misoprostol dosage

Table 1 Guidelines of misoprostol for termination of pregnancy.

Indication	Dosage	Notes
Missed miscarriage by USS <12 weeks	400 µg Q6 hourly, 4 doses PV/PO	In no response for surgical evacuation
Missed miscarriage by USS 13-17 weeks	200 µg Q6 hourly, 4 doses PV/PO	Half dose if previous uterine scar
Missed miscarriage/IUFD by USS 18-26 weeks	100 µg Q6 hourly, 4 doses PV/PO	Half dose if previous uterine scar

Statistical analysis

Comparisons between the two groups were performed using the t test or one-way analysis of variance. The Kruskal-Wallis and the Mann-Whitney U test were used for non-normally distributed variables. Categoric variables were compared between groups by the χ^2 test. Results were expressed as mean and standard deviation or number and percentage. All P values were 2-tailed and $P<0.05$ was considered significant. Statistical analysis was performed using SPSS version 11 (IBM, Armonk, NY, USA).

Results

500 Patients were enrolled in the study, divided into two groups based on the presence of a previous uterine scar or not. Control group (No previous uterine scar) was 295 patients (59%). The study group (with at least 1 previous uterine scar) was 205 patients (41%). Out of the 205 patients, 90 (18%) had previous one lower segment caesarean section (LSCS), 50 (10%) had previous 2 LSCS, 55 (11%) patients had previous 3 LSCS and 10 (2%) patients had previous 4 or more (LSCS). Out of the total number of patients (500) 85 Patients (17%) of our population in the study were primigravid, 255 (51%) were multiparous (P2-P4) and 160 (32%) were grand multiparous (≥ P5).

Table 2 shows the demographics of patients. The mean age for control group was 27 ± 6.1 years old and the mean age for study group was 24 ± 6.2years ($p<0.001$). Whereas the mean gestational age in weeks for control group was 10.2 ± 2.1 and 10.4 ± 1.8 for study group ($p<0.001$).

Demographic and clinical characteristics for the women with and without Prior CD who received misoprostol for TOP

Successful medical termination of pregnancy was accomplished in 218 Patients (74%) of the study group and 139 patients (67.8%) in study group ($p<0.001$).

Table 2 Shows the demographics of patients. Abbreviations: CD: Caesarean Delivery; TOP: Termination of Pregnancy Values are given as mean ± SD or number (Percentage) unless otherwise indicated.

Characteristics	Control Group (n=295)	Study Group (n=205)	P Value
Age (Years)	27 ± 6.1	24 ± 6.2	<0.001
Gravidity	2.4 ± 1.7	2.7 ± 1.0	<0.001
Parity	2.0 ± 1.4	2.1 ± 1.0	<0.001
Gestational age (weeks)	10.2 ± 2.1	10.4 ± 1.8	<0.001

However, 77 Patients (26%) of the control group and 66 patients (32.2%) of the study group needed surgical evacuation either for incomplete expulsion of the product of conception or due to excessive per vaginal bleeding.

Out of the 77 Patients who required surgical intervention in the control group 43 (55.9%) due to excessive PV bleeding and 34 (44.1%) due to incomplete abortion. In the study group, out of the 66 patients who required surgical intervention 35 (53%) due to excessive PV Bleeding and 31 (47%) due to incomplete abortion, both with p value<0.001. Complication rate as of uterine rupture was 0% in both groups (**Table 3**).

Outcome of the use of misoprostol for the women with and without prior CD for TOP

Table 3 Use of misoprostol for the women and its outcomes, CD: Caesarean Delivery; TOP: Termination of Pregnancy Values are given as mean ± SD or number (Percentage) unless otherwise indicated.

Outcome	Control Group (n=295)	Study Group (n=205)	P Value
Successful Medical TOP	218 (74%)	139 (67.8%)	<0.001
Required Surgical TOP	77 (26%)	66 (32.2%)	<0.001
a. Excessive PV Bleeding	43 (55.9%)	35 (53%)	<0.001
b. Incomplete Abortion	34 (44.1%)	31 (47%)	<0.001
Number of Doses			
1 Dose	86 (29%)	51 (25%)	<0.001
2 Doses	56 (19%)	41 (20%)	<0.001
3 Doses	85 (28.8%)	57 (28%)	<0.001
4 Doses	68 (23%)	56 (27 %)	<0.001
Minor complications			
Fever	9 (3%)	4 (2%)	<0.001
Vomiting	18 (6%)	10 (5%)	<0.001
Discomfort	109 (37%)	78 (39%)	<0.001
Uterine Rupture	0	0	

Discussion

Induction of abortion presents a significant problem, especially in mid-trimester as well as in patients with a previous uterine scar. The development of standardized commercially available prostaglandins has improved management. Misoprostol used in this study was found to be safe and efficacious. Moreover, it is stable at room temperature and cheaper than other expensive conventional prostaglandins.

After reviewing the literature, we have found only limited number of studies conducted prospectively, like our study, to evaluate the safety of misoprostol for termination of pregnancy in cases of previous uterine scar. Most of the studies were retrospective review papers. This is most probably the first prospective observational study done on Saudi population studying the safety of misoprostol for TOP in previous uterine.

In this study we have compared the control group (No Previous Uterine Scar) with the Study Group and we had a similar successful the successful medical abortion rate was 74% and 67.8% in the study group with a p value<0.001. The number of patients who required 1, 2, 3 or 4 doses is comparable between the two groups (**Table 3**). Both groups had 0% of uterine rupture. We did not focus on the mean interval time because studying the efficacy of the use of misoprostol for TOP was not our objective.

We have compared our result in the study group with international studies. And our successful medical TOP in the study group of 67.8% is found to be lower as reported earlier on

by Munthali and Moodley [6] who reported a success rate of 83.6% with misoprostol for induction of abortion and maybe this is due to the difference in the misoprostol regimen followed.

A success rate of 74.1% was reported by Sirimai et al. [7] who concluded that misoprostol alone could be used with caution, for induction of abortion especially in 2nd trimester and scarred uterus is not a contraindication for the use of misoprostol.

Regarding the Safety of the use of misoprostol in previously scarred uterus, our result is matching international studies. Gulec et al. [8] reported that it is safe to use misoprostol for termination of pregnancy with patient with a history of 1 cesarean delivery. Dickinson [9] published his results about scarred uterus. Misoprostol was used to induce abortion with 400 mg vaginally every 6 h and the presence of a prior uterine scar did not impact on abortion duration. Thus he concluded that, in second-trimester abortion, the use of misoprostol in women with prior caesarean delivery was not associated with an excess of complications compared with women with unscarred uteri. Torriente et al. [10] concluded that the use is misoprostol is safe for TOP in second trimester patients with previous uterine scar however the efficacy was reduced due to local regimen.

Berghella et al. [11] published their data about women with one prior low-transverse caesarean birth who underwent termination of pregnancy with misoprostol, the incidences of uterine rupture is 0.4%, the incidence of hysterectomy is 0%, and the incidence of transfusion is 0.2%. Fawzy and El Habdel-Hady [12] used misoprostol 200 mg vaginally with 6 h intervals on the 1st day and double the dose to 400 mg with the same intervals since the 2nd day in the women with three or more prior cesarean sections. Their study had a 90.3% successful rate without any adverse outcome. However, for safety, they recommended that women with a scarred uterus should receive lower doses of misoprostol and do not double the dose if there is no initial response [12].

Bhattacharjee et al. [13] concluded that the use of misoprostol for mid trimester pregnancy termination is not contraindicated in women with Caesarean scar and is effective and comparable with those in women without scarred uteri. Shammas et al. [14] reached a conclusion that the use of Misoprostol in women with previous single or multiple caesarean sections was not associated with excess complications [14]. Daponte et al. [15] evaluated the safety and efficacy of misoprostol regimen in women with previous multiple caesarean sections. This was a retrospective cohort study of women with more than one caesarean section who underwent termination of pregnancy (TOP) with 400 mµg of vaginal misoprostol followed by 200 mµg/6 h (max 800 mµg). They did not report any major complication and considered the use of misoprostol effective and safe for termination of pregnancy in women with previous multiple caesarean sections [15].

We recommend more studies with larger population to study the safety and efficacy of misoprostol in patients with missed miscarriage and previous uterine scars. Security Forces Hospital is planning to conduct such study.

Conclusion

We found no evidence that a previous caesarean delivery affects the incidence of complications when women with such a history undergo a pregnancy termination with misoprostol. Therefore, the use of misoprostol for pregnancy termination is not contraindicated in women with Caesarean scar and is effective and comparable with those in women without scarred uteri.

Conflict of Interest

The authors have no conflict of interest.

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