Misoprostol for termination of second trimester pregnancy in a scarred uterus

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ABSTRACT

Objective: To investigate whether Misoprostol for mid-trimester pregnancy interruption in women with a scarred uterus has any adverse effects compared with those without a scar.

Methods: During 5-year period from 2000-2004 at Queen Alia Military Hospital, Royal Medical Services, Amman, Jordan, a consecutive series of 520 women of 15-28 weeks of gestation who underwent termination of pregnancy were studied. Sixty-three patients had undergone at least previous one cesarean section and 457 served as control. Termination was undertaken using Misoprostol 400 μg vaginally as a starting dose followed by 200 μg vaginally every 6 hours, complications for each group were recorded.

Results: The induction to abortion time was not significantly different in both groups (p=0.16); the median dosage was almost the same (p=0.31). The rate of incomplete abortion was significantly higher in the study group than control 82% versus 60% and 11.5% versus 6.1% for bleeding of more than 500 cc, while the rate of other complications was almost the same.

Conclusion: In the second trimester termination of pregnancy, the use of Misoprostol in women with previous single or multiple cesarean sections was not associated with excess complications.

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During the last 2 decades, the cesarean section (C/S) rate increased worldwide. During the same period, termination has become a more common procedure, so a specific group emerged, those with an uterine scar who needed termination. The principle concerns in providing second trimester termination include safety, efficacy, simplicity, low-cost, and fast acting with minimal side effects. The usual agents employed to induce a medical termination of pregnancy were prostaglandin preparations.[1,2] The synthetic prostaglandin Misoprostol is commonly used to induce abortion in this situation. Misoprostol (Cytotec) is a synthetic prostaglandin E1 analogue that can cause cervical changes and uterine contractions. There are limited informations on the safety profile of Misoprostol in women with prior C/S. There are some case reports on uterine rupture, which have been published with the use of Misoprostol in a scarred,[3,4] and unscarred uterus,[5] while other studies[6] reported no complications.

Methods. During 5-year period from 2000-2004 a total number of 520 patients underwent second trimester (15-28 weeks) termination on pregnancy at obstetrical department. Sixty-three patients (12.1%) had previous one or more uterine scars and these constitute the study group while the remaining 457 (87.9%) served as control. All data were recorded from the hospital charts, and these include maternal age, gestational age, parity, duration of termination, total dose of Misoprostol used and presence of complications which include: fever, excessive bleeding of more than

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500 cc, need of blood transfusion, nausea, vomiting, and diarrhea, analgesia, retained placenta, incomplete abortion, failure of induction and rupture of the uterus. Gestational age was calculated from the time of the last menstrual period, and in those with irregular menstruation it was calculated according to ultrasound findings. Duration of termination was defined as the time from introduction of first Misoprostol tablet until the expulsion of the fetus. The method employed was as follows: after preparing one unit of cross-matched blood we started introducing Misoprostol in a loading dose of 400 μg vaginally followed by 200 μg every 6 hours until the fetus is expelled. Meanwhile, vital signs and side effects were recorded. Pethidine was given as analgesia. A total period of 48 hours was allowed after which failure of procedure was considered. Spontaneous expulsion of the placenta within 60 minutes of delivery was awaited, after which removal of the placenta under general anesthesia was considered. Indications of termination were only dead fetus, rupture of membrane, and maternal diseases.

Statistical analysis was performed for continuous variables such as age, length of pregnancy; descriptive statistics were calculated and are reported as mean ± SD. The Mann-Whitney U-Test was used to compare the total dose of Misoprostol used for each group. Chi-Square was used to detect differences in categorical variables. All tests were considered significant at $p<0.05$.

Results. Five hundred twenty women underwent termination of pregnancy, for either missed abortion; rupture of membrane or for maternal diseases that contraindicate continuation of pregnancy. Sixty-three women of the study group had undergone at least one previous C/S (12.1%). Thirty-eight women (60.3%) had one lower transverse C/S, 15 (23.8%) had 2 lower segment C/S and 10 (15.9%) had more than 2 lower segments C/S. The time interval from the last C/S ranged from 7 months to 11 years. **Table 1** shows the details of both study groups. No statistical difference was found between the 2 groups regarding maternal age, gestational age, the Misoprostol dose and induction to abortion time, while parity was higher in the C/S group. Delivery in ≤24 and >48 hours was not significant in the study and control group (82.5%, n=52 versus 75%, n=343) and (4.7%, n=3 versus [3.0%, n=14). Curettage was higher in the study group (82% versus 60%) compared with the control group. **Table 2** shows the complications of induction. The most frequent not significant complication was the need of analgesia, while the least were diarrhea and the need of blood transfusion. Only the bleeding of more than 500 cc was significant in the study group comparing to the control (11.5% versus 6.1%).

Discussion. With the expanding population of women with prior C/S, second trimester pregnancy termination in women with a previous scar became a common practice. The problem emerged with the limited information on the safety method of termination in the presence of a previous scar. Prostaglandins are commonly used to induce second trimester termination of pregnancy (TOP). Misoprostol has been shown to be an effective agent for TOP, and several studies have shown the vaginal administration to be more effective than oral.[7-9] Studies involving the use of vaginal Misoprostol in mid-trimester termination have used doses of 100-800 μg with dosing intervals of every 3-12 hours. Successful termination was considered to be delivered within 48 hours, which ranged from 71-100%.[10-14] Our study shows successful induction in 95.3% of study group versus 97% of the control. Increasing dosages (200 μg, 400 μg, 600 μg vaginally every 12 hours) of Misoprostol obtained increase rate of successful termination within 48 hours, but side effects also increased.[12] Misoprostol has numbers of advantages over other drugs including its low cost, and stability at room temperature. It might be given vaginally or orally, and it is effective in a variety of doses.[15] Despite its safety for use in women with prior scar remains in question.

This study showed that the mean maternal age, gestational age, induction to abortion time, and mean dose of Misoprostol were the same in both study groups, but there was a significant difference between the 2 groups in the rate of incomplete abortion which could be due to scarred area in the uterine cavity which can lead to abnormal implantation.[16] The incidence of side effects such as nausea, vomiting and diarrhea was the same in both groups and this was reported also in other studies.[17] The same study confirms blood loss of more than 500 cc to be present more in the scarred uterus and reported this complication to be present in 11.3% of cases. Tejuja et al[18] reported it in 17.6% by using intra and extra-amniotic prostaglandins for the termination of pregnancies, while in our study using Misoprostol bleeding was present in 11.5% of the study group and 6.1% in the control. The important complications that has to be considered is rupture of uterus. There have been few case reports published on uterine rupture associated with Misoprostol.[3-5] Chapman et al[17] reported rupture of uterus in 3.8% cases of scarred uterus versus 0.2% of the control group, but all these patients received Oxytocin with Misoprostol. Other study reported a rupture of uterus in 1.3% of scarred uterus by using hyperosmolar urea and prostaglandin F2 alpha.[19] Uterine rupture is a recognized complication of TOP despite the technique

Table 1 - Characteristic of patient groups.

Characteristics	Previous C/S (n = 63)	Control (n = 457)	*P*-value
Age (years)	31.52 ± 4.28	3.46 ± 3.92	NS
Gestational age (weeks)	18.70 ± 2.50	19.65 ± 2.62	NS
Parity	3.00 ± 1.0	2.30 ± 1.40	0.02
Induction to abortion time (hours)	17.3 ± 7.2	20.6 ± 6.2	NS
* Total dose Misoprostol (μg)	1200 (800,1600)	1200 (600,1600)	NS
Results are expressed as median (25, 75) percentile C/S - cesarian section, NS - not significant.			

Table 2 - Complications of induction with Misoprostol.

Complication	Study group (N = 63) n (%)	Control (N = 457) n (%)	*P*- value
Fever	4 (6.5)	21 (4.5)	NS
Bleeding >500 cc	7 (11.5)	28 (6.1)	<0.05
Nausea and vomiting	3 (4.7)	30 (6.5)	NS
Diarrhea	1 (2)	13 (2.8)	NS
Chills	5 (7.7)	29 (6.4)	NS
Treatment failure	3 (4.7)	14 (3)	NS
Analgesia	25 (40)	174 (38.1)	NS
Retained placenta	18 (28)	149 (32.5)	NS
Blood transfusion	1 (2)	15 (3.2)	NS
Rupture of uterus	0 (0)	0 (0)	-
NS - not significant			

used and it is not unexpected that this event occurred with Misoprostol although a recently published report[20] claimed the absence of a single case of rupture, but the study number remains small to draw a firm conclusion of safety of Misoprostol. Large series have demonstrated the safety of prostaglandin in TOP in second trimester[21] and our data are in accordance with these.

In conclusion, although Misoprostol has low rate of minor adverse outcomes, no major side effects including rupture of uterus was found. However, we do not conclude that Misoprostol is safe, but may be an alternative if close attention is paid.

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