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Vaginal Misoprostol Safety and Efficacy in Second Trimester Pregnancy Termination in Women with a Previous Cesarean Section

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ABSTRACT
Background: In patients who have already undergone a cesarean section, there is increasing use of medications to terminate the pregnancy due to fetal death or fetal anomalies.
Objectives: To study the safety and efficacy of pregnancy termination using vaginal misoprostol in women undergone a single lower segment cesarean section.
Patients and methods: This clinical trial study included 100 women (attending the Department of Gynecology and Obstetrics, Benha University hospitals) with one previous lower segment cesarean section who were advised to terminate their pregnancy (after 13-26 weeks) due to intrauterine fetal death or fetal structural anomalies. They were divided into two equal groups Group I (cases) who had uterine scars, while Group II (control) without scars. History, clinical examination, and ultrasound imaging were performed on all patients. There were 72 hours in which the patient was given misoprostol every four hours via the vaginal route.
Results: It was found that the induction-to-abortion period was much shorter in the control group than in the cases group despite no significant differences in age, parity, gestational age, or doses required to induce abortion between the two groups. There were non-significant differences between patient group I with uterine scar and control group II without uterine scar regarding doses needed, except for 1-4 doses and 9-12 doses which exhibited significant differences.
Conclusion: In women who have had a previous cesarean section, the vaginal route of misoprostol in a dose of 50 µg /4 hours is safe and successful for inducing a second-trimester abortion.
Keywords: Second-trimester pregnancy termination, Vaginal misoprostol, Previous one cesarean section.

INTRODUCTION

Fetal abnormalities are easier to detect using prenatal ultrasonography and serum screening tests. [(1)]. When it comes to congenital abnormalities, prenatal ultrasonography and strategies for treatment vary greatly from country to country[(2)]. Unlike their American counterparts[(3)], France, where three prenatal ultrasounds are covered by the national health insurance program [(4)], is seeing an increase in the number of women seeking an abortion after 15 weeks of pregnancy[(5)].

As a result, about 12 percent of all pregnancies are clinically missed abortions[(6)]. Historically, the treatment for missed abortion has been dilation and curettage, which is often performed in a hospital setting, increasing costs greatly[(7)]. Second-trimester missed abortions treated medically rather than surgically save a great deal of money[(8)].

Expectant management comes with a certain amount of uncertainty, and the psychological pain of carrying a nonviable pregnancy for an extended time can be overwhelming for some women[(9)].

In light of the increasing prevalence of cesarean sections[(10)], Among women who have previously undergone a cesarean section, the likelihood of a medical reason to terminate the pregnancy is rising. Second-trimester pregnancy termination in the case of a past cesarean delivery is becoming more common among obstetricians due to the growing number of women who have given birth by cesarean section[(11)].

In the context of previous uterine surgery, there is little data on how safe any termination approach is, and no treatment is risk-free. Physician opinion and skill are likely to play a greater role in deciding on a second-trimester termination method than objective outcomes data[(12)].

When Misoprostol was first developed, it was meant to prevent NSAID-induced stomach ulcers by mimicking the effects of prostaglandin E1. Because of its cervical ripening and uterotonic properties, misoprostol has become one of the most important medications in obstetrics and gynecology. Taking Misoprostol via the mouth, rectally, vaginally, and sublingually has shown to be a very convenient and flexible method of administering the medicine. With unsupervised use, significant problems and teratogenicity can occur, despite the considerable amount of medical evidence supporting its efficacy and relative safety[(13)].

Misoprostol can be used even if a patient has had a cesarean section in the past [(14).] Regardless of gestational age, uterine rupture is a greater concern, so extreme care must be used[(15)].

The purpose of this research is to find out if vaginal misoprostol may safely and effectively terminate second-trimester pregnancies in women who have had a previous single lower segment cesarean surgery.

PATIENTS AND METHODS

The Benha University Hospital's Department of Gynecology and Obstetrics conducted this clinical trial investigation. All women aged 19 to 41 who had had a previous lower segment cesarean section and who were being evaluated for termination of pregnancy due to either intrauterine fetal death or fetal structural

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anomalies were included in the study. Gestational ages ranged from 13 to 26 weeks based on dates of LMP or first-trimester ultrasonography.

A total of 100 women were analyzed and divided into two equal groups, one for those who had uterine scarring (group I) and the other for those who did not (group II).

Exclusion criteria:

1. Cases with more than one lower segment cesarean section or other previous uterine surgeries.
2. Cervical cerclage or past cervix injuries; failed therapy for the present pregnancy; placenta previa (placenta in front of the mother) and contraindications to prostaglandin usage; chorioamnionitis; incomplete abortion; severe polyhydramnios; diabetes mellitus or hypertension (cardiovascular diseases or hypersensitivity).
3. Cases with a history of blood transfusion during the previous lower segment cesarean section.
4. Cases with a bleeding tendency (inherited bleeding disorder, chronic liver disease, valve replacement).

Methods:

Prostaglandins contraindications and cervical dilation, effacement, and position were all examined during a thorough clinical history and physical exam, which included a review of the patient's medical history, including her age, parity, and gestational age. Congenital malformations, liquor, placental location, and gestational age were all determined by an ultrasound.

For a maximum of 72 hours, misoprostol (50 µg) (2 vagiprost 25 µg) was administered vaginally every 4 hours. The next dose was delayed if the patient had enough contractions (3 in 10 minutes) or a dilated cervix (more than 4 cm dilated) before the examination. Side effects were recorded. Induction to abortion interval and doses needed were reported. Failure was defined when no expulsion of abortus after 72 hours. After the expulsion, Ultrasonography was done for product remnants that needed either oxytocin or surgical evacuation.

In the labor ward, each patient was constantly observed, and considerable attention was taken to (1) Vital signs (Blood pressure, Pulse, Temperature). (2) Complications of misoprostol (Fever, Diarrhea, Chills, Nausea, Vomiting). (3) Uterine rupture (Persistent acute abdominal pain, maternal tachycardia, hypotension, vaginal bleeding). (4) The need for Oxytocin infusion, which was started at least 6 hours after the last dose of Misoprostol. (5) The need for surgical removal of the placenta or remnants of conception.

If the first dose of misoprostol failed to terminate the pregnancy within 72 hours, it was deemed a failure of termination. In such case, the patient became a candidate for termination either by hysterotomy or continuation of the process of induction using higher doses of misoprostol which was left for the attending consultant to decide.

Ethical consent:

Approval of the study was obtained from Benha University Academic and Ethical Committee. Every patient signed informed written consent for the acceptance of participation in the study. This work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

To analyze the data acquired, Statistical Package of Social Services version 20 was used to execute it on a computer (SPSS). To convey the findings, tables and graphs were employed. The quantitative data were presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t-test (T) is used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X^2) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

Table 1: shows the distribution of women in both groups by age, parity, gestational age, and doses required. Abortion induction dosages had a non-significantly difference between the two groups ($p > 0.05$). Induction-to-abortion interval indicated a significant difference.($p < 0.05$) in the control group than the cases group (17 ±10.4 vs. 22.5± 11.5).

Table (1): Demographic data and doses needed in group I (uterine scar) and group II (no uterine scar)

	Group I (uterine scar)		**Group II (no uterine scar)**		***p*-value**
	Mean	**±S.D**	**Mean**	**±S.D**	
Age	31.5	6	30	7	>0.05 (NS)
Parity	2	0.4	1.5	0.34	>0.05 (NS)
GA	19.5	5	22	5.5	>0.05 (NS)
Dose needed	6	1.34	4.5	0.86	>0.05 (NS)

Table (2), shows that there was a non-significant difference in gestational age between the two groups (p > 0.05).

Table (2): Distribution of women among both group

		Group I (uterine scar)		Group II (no uterine scar)		*p*-value
		No	%	No	%	
Gestational age	13-16	8	16	11	22	>0.05 (NS)
	17-20	21	42	16	32	
	21-24	13	26	15	30	
	25-26	8	16	8	16	

Table (3), shows that patients in groups I and II did not differ significantly in terms of the doses required or the failure rate. (p > 0.05), except for 1-4 doses and 9-12 doses which exhibited significant differences (p < 0.05) being more in group II in 1-4 doses while in 9-12 doses the increase was in group I.

Table (3): Doses needed in both groups

		Group I (uterine scar)		Group II (no uterine scar)		*p*-value
		No	%	No	%	
Doses needed	1-4	13	26	17	34	<0.05 (S)
	5-8	23	46	22	44	>0.05 (NS)
	9-12	9	18	4	8	<0.05 (S)
	13-18	3	6	4	8	>0.05 (NS)
Failure		2	4	3	6	>0.05 (NS)

Table (4) shows that surgical evacuation was needed in 11 women (6 for the placenta and 5 for remnants) (22%) in the case group versus 10 women (5 for the placenta and 5 for remnants) (20%) in the control group. So, there was a non-significant difference between both groups regarding suction evacuation (p > 0.05).

Table (4): Suction evacuation among both groups

		Group I (uterine scar)		Group II (no uterine scar)		*p*-value
		No	%	No	%	
Suction evacuation	For whole placenta	6	12	5	10	>0.05 (NS)
	For parts of placenta	5	10	5	10	>0.05 (NS)
	Total	11	22	10	20	>0.05 (NS)

Table (5) shows that the side effects have non-significant differences between the two groups as fever, chills, nausea, vomiting, and diarrhea (p > 0.05).

Table (5): Side effects among both group

Side effects	Group I (uterine scar)		Group II (no uterine scar)		*p*-value
	No	%	No	%	
Fever	10	20	8	16	>0.05 (NS)
Chills	24	48	23	46	>0.05 (NS)
Nausea	23	46	22	44	>0.05 (NS)
Vomiting	7	14	7	14	>0.05 (NS)
Diarrhea	11	22	7	14	>0.05 (NS)

DISCUSSION

C-section is presently the most common major surgical procedure in obstetrics and gynecology, a trend that has been steadily increasing over the last decade. Misoprostol, a medication used to end pregnancies medically, is widely used all over the world. No type of abortion can be guaranteed to be risk-free after a prior uterine operation, and the safety profile of any such procedure is unknown [(16)].

Misoprostol (PGE1 analog), a synthetic prostaglandin, has largely supplanted all traditional methods of terminating pregnancies, especially in the

second trimester, because of its effectiveness, safety, low cost, and ease of use and storage[17].

The use of misoprostol in patients who have had previous cesarean deliveries and are having a second-trimester abortion is a unique characteristic of our study. Pregnancy termination in the second trimester is safe for women with a history of preeclampsia, according to our findings. Second-trimester induction of labor does not appear to increase the risk of problems among women who have previously undergone a cesarean section, according to our study. Uterine rupture risk can only be accurately assessed through a larger study.

In this study, failure of termination was considered if abortion has not been established within 72 hours of the first dose of misoprostol. In such case, the patient became a candidate for termination by either hysterotomy or continuation of the process by induction using higher doses of misoprostol, in which decision was left to the attending consultant of the casualty. It was found that the induction-to-abortion period was much shorter in the control group than in the cases group (17 ±10.4 vs. 22.5± 11.5).despite no significant differences in age, parity, gestational age, or doses required to induce abortion between the two groups.

In the present study, there were non-significant differences between patient group I with uterine scar and control group II without uterine scar regarding induction-to-abortion intervals ($p > 0.05$), the majority of women delivered within 24 hours, and this was agreed with **Bhattacharjee *et al.*[17],** who studied 80 women with scarred uteri, A median induction-abortion period of 16.4 hours separated the start of the trial from the end of it. (range: 10-21 hours) and the median time between induction and abortion was 15.6 hours for the control group.

In our study, there were non-significant differences between patient group I with uterine scar and control group II without uterine scar regarding doses needed, except for 1-4 doses and 9-12 doses which exhibited significant differences.

In a published study by **Geels *et al.*[18]** misoprostol effects on uterine contractility were studied via various administration methods. For uterine contractility, sublingual application of misoprostol is at least as quick and comparable to oral delivery, and it is also equivalent to the effects of vaginal administration. Certain findings could explain why sublingual misoprostol has a faster time to delivery in these investigations.

During this study, side effects showed non-significant differences between the two groups as fever, chills, nausea, vomiting, and diarrhea as reported by **Geels *et al.*[18],** in their patient records, side effects such as nausea or vomiting were not detected, which indicated that they either did not occur or were not documented. There were no documented side effects among the patients in this study's prospectively evaluated cases.

Von Hertzen *et al.*[19] evaluated the effectiveness of 400 g of sublingual misoprostol every three hours against 400 g of vaginal misoprostol every three hours, finding that the sublingual route was less likely to cause fever.

Naguib *et al.*[20] women who had a single previous cesarean delivery were given misoprostol vaginally for second-trimester abortions and were found to be safe and effective. According to the researchers, women who have had a cesarean section once before tend to be safe and effective during the second trimester of pregnancy when using lower doses of misoprostol.

van Bogaert and Misra[21] The researchers investigated probable correlations between misoprostol efficacy and factors such as age, parity, gestational age (GA), weight, BMI, body surface (BS), and the Ponderal Index (PI). For these women undergoing misoprostol-only medical abortions, they found that the vaginal route of administration was more effective than the oral medical route. When misoprostol was administered without abortion, the rate of surgical evacuation rose. This conclusion may not be clinically meaningful because only 29 percent of the cases had the link between greater GA and the need for repeated doses.

Zangeneh *et al.*[22] compared two strategies utilizing misoprostol alone and in conjunction with concentrated oxytocin and discovered a more successful way to perform a clinical abortion in the second trimester. Misoprostol and oxytocin appear to be effective and appropriate methods of terminating the pregnancy in the second trimester, according to the researchers. Both procedures can be suggested because of their fast induction and termination times and their comparatively minor side effects.

The possibility of an increased risk of problems following a misoprostol-assisted pregnancy termination is still an open subject in these situations. Until then, we believe that cautious selection and monitoring of these patients during labor is necessary. We used misoprostol in a dose that is considered to be low in comparison to other studies; however, we can conclude that this dose (50 µg / 4 h.) is a safe and effective dose for patients undergoing second-trimester pregnancy termination with the presence of a previous single cesarean section.

CONCLUSION

In women who have had a previous cesarean section, the vaginal route of misoprostol in a dose of 50 µg /4 hours is safe and successful for inducing a second-trimester abortion.

Misoprostol can be advised because of its fast induction and termination times and its very minor side effects.

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