Archives of Razi Institute, Vol. 77, No. 1 (2022) 199-204

DOI: 10.22092/ARI.2021.356535.1862

Original Article

Safety of Vaginal Misoprostol for the Termination of Second Trimester Miscarriage in Women with Previous Uterine Scar in Iraq

Mahmood Shakir, H[1 *]

1. Ibn Sina University of Medical and Pharmaceutical Sciences, Baghdad, Iraq

Received 22 October 2021; Accepted 9 November 2021
Corresponding Author: hudaalfatal2010@gmail.com

Abstract

Pregnancy termination for a variety of fetal or maternal conditions has been defined as one of the common obstetrical procedures. The presence of an earlier uterine scar has been found as a highly significant risk factor, which needs to be considered before the election of the misoprostol for the termination of pregnancy (TOP) uses. This study aimed to evaluate the safety of vaginal misoprostol in patients who had an earlier uterine scar, and whether its utilization might result in increasing the risks of uterine ruptures. In total, 250 participants were included in the experimental model and divided into two groups including 95 patients in their 2nd trimester of pregnancy with confirmed non-viable fetus and scarred uterus (study group) and 155 pregnant women with no scar in their uterus and missed miscarriage (control group). They received misoprostol tablets in accordance with the Security Hospital Protocol for the TOP. The safety has been specified according to the number of women that had full abortions with no complications. The study group with uterine scar included 95 cases that comprised 38% of the total participants in the study (n=250). Out of 95 cases, 64 (67.3%) patients had successful abortions completely, compared to the control group (the patients with no scar), 111 (71.6%) of whom had complete abortions (P<0.001). However, 44 (28.4%) and 31 (32.6%) patients in the control and study groups, respectively, were in need of surgical evacuations either for the incomplete conception product expulsion or as a result of the excessive per-vaginal bleeding. The use of the misoprostol for the TOP has not been contra-indicated in the females who had Caesarean scars. Moreover, it is efficient in females who do not have scarred uterus.

Keywords: Caesarean, Pregnant, Termination of pregnancy

1. Introduction

Miscarriage and abortion terms are synonyms, and they represent the fetus expulsion prior to the viability age or prior to the end of the 24th week (1). Pregnancy termination for various fetal and maternal conditions has been considered one of the common obstetrical procedures. The induction of abortion requires effective and meticulous care. There are surgical and medical ways that are used to terminate the pregnancy. The surgical interventions include more morbidity and mortality risks, compared to the medical interventions (2). Concerning the medical interventions for the termination of pregnancy (TOP), there are numerous choices for the 1st and 2nd trimesters' cervical ripening (2). At first, the prostaglandin F2α has been utilized to induce the abortion (3).

In the current practices, the misoprostol, which is an orally active and stable analog of the prostaglandin E-1 had entered clinical utilization in gynecology and obstetrics on wide scales. It is a gastric cytoprotective agent which was marketed first in the US in 1988 to prevent peptic ulcers (2).

The misoprostol (i.e., the Cytotec) has been utilized for the first-time labor induction in obstetrics in 1993. After that, it became widely used for a variety of indications, such as cervix ripening and postpartum hemorrhage control. In one study, it has been found that the missed miscarriage's medical management with vaginal or oral misoprostol has been of high effectiveness and considerably approved, with higher acceptability and a shorter interval between the induction and miscarriage (4).

As a result, misoprostol became one of the significant medications in obstetrical practice (5). It is important for cervical priming prior to the surgical abortion, elective medical abortion, and evacuation of the uterus in embryonic fetal death cases (6-8). Caesarean (C-section) rates have been in an increase all over the world. Therefore, the rates of females that have a previous C-section keep increasing, and uterine rupture risks are getting higher. Even though the uterine rupture incidence rates in the females who have previous-scar uteri is still quite low (i.e., less than 1%), it remains to be viewed as a threat for the obstetricians.

Numerous risk factors have significant impacts on the increase of the rates of morbidity and mortality associated with TOP. The presence of an earlier scar in the uterus has been considered a very significant risk factor, which is why an abortion induction approach has to be chosen quite carefully. There is not sufficient research on using the misoprostol in patients who had an earlier uterine scar (9). The morbidity and mortality which are associated with abortions are significantly increased with the advancement of the pregnancy and a sudden increase in severe complication rates in induced abortion 14 weeks after pregnancy (8).

This issue is of great importance due to the fact that epidemiological research in Iraq exhibited a trend of having higher C-section rates in the recent 20 years related to geodemographic changes in society. Since there was no possibility to find any local research on misoprostol safety for the medical TOP in the females who had previous uterine scars, this study aimed to assess the safety of misoprostol in patients who had this complication. Moreover, it attempted to investigate whether or not its uses result in increasing uterine rupture risks.

2. Materials and Methods

A total of 250 patients were included in this study, each of whom had some medical indications for the TOP.

2.1. Inclusion Criteria

The inclusion criteria were: 1) the patients in the 2nd trimester of pregnancy with or without earlier scars in the uterus, and 2) cases who had TOP medical indications, anhydramnios, missed miscarriage, genetic disorders, structural fetal anomalies, or chromosomal abnormalities.

2.2. Exclusion Criteria

On the other hand, the patients who did not meet the inclusion criteria, those who had an incomplete miscarriage and were taken directly to the operating room for the surgical management, and cases who had been admitted in the department of emergency as incomplete miscarriage cases and received misoprostol and aborted completely were excluded from the study.

The patients who fulfilled the inclusion criteria were admitted to an in-patient ward of gynecology. For every one of the admitted patients, a detailed history was obtained, and physical observation was carried out. The ultra-sonographic examinations were carried out for the identification of the fetus's gestational age, uterine anomalies, and placental localization. A lab study panel was ordered, which included the blood group, complete blood count, urea and electrolytes, as well as coagulation profile. The patients were potentially analyzed for the demographic characteristics, as well as the misoprostol-associated results. The age and the number of the earlier uterine scars were the TOP indications. The misoprostol-associated results included the number of the cases that had a successful medical abortion, the number of the cases that required surgical evacuations, indications for the surgical evacuation, and misoprostol-associated difficulties.

The successful medical abortions were characterized as full abortion 24 h after initiating the pregnancy protocol termination. The surgical evacuation, which was carried out under general anesthesia was required in the patients with partial expulsion of the conception products or excessive bleeding with retaining the conception products in the uterus. The complete abortion was confirmed based on the clinical grounds and bedside ultrasonography; moreover, the patients were allowed to go back home in the case they were clinically stable, and no additional interventions were carried out.

Patients that had a full abortion and exhibited no complications were allowed to go back home after they had hemoglobin results post complete abortion according to the policy of the hospital. The failure of the misoprostol protocol was declared in the case there were no complete abortions accomplished after the completion of a 4-dose misoprostol course. In this case, such patients would be taken under consideration for the surgical evacuation, and after that, they were allowed to go home whenever they became clinically stable.

The misoprostol-associated complications included excessive per-vaginal bleeding, pyrexia, and rupture in the uterus. In any case, the TOP was clinically deemed through managing the healthcare team, written informed consent must be obtained from a patient. When informed consent has been signed, hospital-based misoprostol regulations for TOP have been abided by table 1. The misoprostol dosages have been given for each of the medical indications. Vigilant monitoring of the process of abortion was conducted to avoid procedure-related complications.

Table 1. Misoprostol dosages for TOP as per hospital protocol

Indication	Dosage (patients with no scar)	Dosage (patients with uterine scar)
Missed miscarriage by the USS13-17 weeks	200Mg Q-6 hourly,4 doses, P/V	100 Mg Q-6 hourly,4 doses, P/V
Missed miscarriage by USS, 18-24 weeks	100mg Q-6 hourly,4 doses, P/V	50Mg Q-6 hourly,4 doses, P/V

2.3. 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 also utilized for non-normally distributed variables. Categorical variables were compared between groups by the $\chi 2$ test. Results were expressed as mean±SD or number and percentage. All *P*-values were 2-tailed, and $P<0.05$ was considered significant. Statistical analysis was performed using SPSS software (version 11, IBM, Armonk, NY, USA).

3. Results

A total of 250 patients participated in this study and were divided into two groups according to whether or not there was an earlier uterine scar. The control group (i.e., without earlier uterine scars) included 155 (62%) patients. On the other hand, the study group (i.e., with uterine scar involved) composed 38% (n=95) of the total, and from these 95 patients in the study group, 64 (67.3%) cases were patients aborted completely and successfully, compared to the control group. Furthermore, 111 (71.6%) cases in the control group (the patients with no scar) had complete abortion ($P<0.001$). However, 44 (28.4%) patients in the control group and 31 (32.6%) cases in the study group were in need of surgical evacuations either for the incomplete conception product expulsion or as a result of the excessive per vaginal bleedings. In the control group, 44 patients required the surgical interventions due to the excessive per vaginal bleeding (n=28; 18%) and incomplete abortion (n=18; 12%). In the study group, 31 patients required the surgical interventions due to excessive per

vaginal bleeding (n=18; 19%) andincomplete abortion (n=13; 13.5%) (P<0.001). It is worth mentioning that the uterine rupture was 0% in the two groups (Table 2).

Table 2. Use of Misoprostol for women and its outcome

Outcome	Control (n=155)		Study (n=95)		*P*-value
Successful medical TOP	111	(71.6%)	64	(67.3%)	<0.001
Required surgical TOP	44	(28.4%)	31	(32.6%)	<0.001
a. Excessive per vaginal bleeding	28	(18%)	18	(19%)	<0.001
b. Incomplete abortion	18	(12%)	13	(13.5%)	<0.001

4. Discussion

As far as it is known, there have not been any published studies that described the results of the low dosage of the misoprostol in the management of the missed miscarriage in the 2nd trimester in females that had earlier C-section scar deliveries. A variety of protocols have been available for medical management of the miscarriage in the 2nd trimester in the females whose uterus has been intact (6, 8). Nonetheless, the options of the management for the scarred uterus cases have been limited, and potential maternal complication risks are quite high which is why it is important to report the management results. The optimum misoprostol dose is widely varied between 20 μg and 600 μg according to indications and the age of the gestation. In the females that have scarred uterus, lower misoprostol dosages are advised as a result of uterine rupture risks (8).

In the present case study, a low dosage misoprostol of 100 μg each 6 h has been viewed to be minimizing uterine rupture risks at the same time as keeping the effectiveness (1). In the literature review, it has been discovered that there is only a limited number of studies that have been carried out prospectively similar to this research for the evaluation of the safety of misoprostol and the TOP in the earlier uterine scar cases. The majority of the research has been retrospective reviews. Accordingly, it is most possibly the first in the area.

Our results were compared with the findings of international studies, and the successful termination of pregnancy in this study group was 67.3% which was consistent with the findings of a study by Chamsi, Morsy (4) in 2018 (67.8%) (9). However, this successful termination rate of pregnancy (67.3%) was lower in a study performed by Munthali and Moodley (10) who have stated an 83.6% success rate with misoprostol inducing the abortion, and possibly, this can be a result of the difference in the followed regimen of the misoprostol. A 74.10% success rate has been presented by Sirimai, Kiriwat (8), who have concluded the fact that the misoprostol on its own may be utilized with caution for inducing the abortion, particularly in the 2nd trimester and the scarred uterus is not a contra-indication for using the misoprostol.

Regarding the safety of misoprostol use in the earlier scarred uterus, the results of this study are in line with the findings of international studies. Güleç, Urunsak (11) have stated the fact that it is safe to utilize the misoprostol to terminate the pregnancy with patients that have a one C-section delivery history. Dickinson (12) induced the abortion with 400 mg vaginally each 6 h, and the existence of an earlier uterine scar had no impacts on the duration of the abortion that is why he had concluded that in the abortions of the 2nd trimester, misoprostol use in the females that have earlier C-section delivery has not been related to an excess in the complications, compared to the females who had no scars in their uteri.

Cuellar Torriente, Steinberg (13) have found that misoprostol use is safe for pregnancy termination in the 2nd-trimester patients with earlier uterine scars; nonetheless, the efficacy has been decreased as a result of the local routine. El Habdel-Hadyand Fawzy (13) utilized the misoprostol 200 mg vaginally with 6 h intervals on the first day and doubled that dosage to

400 mg with an identical interval since the second day in the women with prior three C-sections or more. The results showed a 90.30% rate of success with no negative outcomes.

However, for safety, they have advised that the females who have scarred uteri must get smaller misoprostol dosages and do not double it in the case where there are no initial responses (14). Daponte, Nzewenga (15) have evaluated the safety and efficacy of the regimen of misoprostol in women that had previously several C-sections. This retrospective cohort study was conducted on females who had two C-sections or more and had undergone TOP with 400 μg of vaginal misoprostol succeeded by 200 μg/6h (maximum 800μg). They reported no major complications and regarded using the misoprostol as one of the safe and effective ways for TOP in the females that had previously multiple C-sections. In the aforementioned study, it has been concluded that the misoprostol was safe in the patients who had several scars, and there were no complications in the control, as well as the study groups.

Authors' Contribution

Study concept and design: H. M. S.
Acquisition of data: H. M. S.
Analysis and interpretation of data: H. M. S.
Drafting of the manuscript: H. M. S.
Critical revision of the manuscript for important intellectual content: H. M. S.
Statistical analysis: H. M. S.
Administrative, technical, and material support: H. M. S.

Ethics

The present study was approved by the Ethics Committee of the Ibn Sina University of Medical and Pharmaceutical Sciences, Baghdad, Iraq.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Organization WH. Safe abortion: technical and policy guidance for health systems: World Health Organization; 2012.
2. Keder LM. Best practices in surgical abortion. Am J Obstet Gynecol. 2003;189(2):418-22.
3. KIRTON KT. Prostaglandins and reproduction. The Prostaglandins: Progress in Research. 2012:47.
4. Chamsi A, Morsy E, El Rifaei R, Al Bahyan R. The Safety of Misoprostol for Medical Termination of Pregnancy in First and Second Trimester in Women with Previous Uterine Scar. Insights Reprod Med. 2018;2(1):3.
5. Goldberg AB, Greenberg MB, Darney PD. Misoprostol and pregnancy. N Engl J Med. 2001;344(1):38-47.
6. Ashok P, Penney G, Flett G, Templeton A. An effective regimen for early medical abortion: a report of 2000 consecutive cases. Hum Reprod (Oxford, England). 1998;13(10):2962-5.
7. Mazouni C, Provensal M, Porcu G, Guidicelli B, Heckenroth H, Gamerre M, et al. Termination of pregnancy in patients with previous cesarean section. Contraception. 2006;73(3):244-8.
8. Sirimai K, Kiriwat O, Neungton S, Suvanichchati S. Misoprostal use for therapeutic abortion in Siriraj Hospital: the year 2000. J Med Assoc Thail=Chotmaihet Thangphaet. 2002;85(4):416-23.
9. Ngoc NTN, Blum J, Westheimer E, Quan TTV, Winikoff B. Medical treatment of missed abortion using misoprostol. Int J Gynaecol Obstet. 2004;87(2):138-42.
10. Munthali J, Moodley J. The use of misoprostol for mid-trimester therapeutic termination of pregnancy. Tropical doctor. 2001;31(3):157-61.
11. Güleç ÜK, Urunsak IF, Eser E, Guzel AB, Ozgunen FT, Evruke IC, et al. Misoprostol for midtrimester termination of pregnancy in women with 1 or more prior cesarean deliveries. Int J Gynaecol Obstet. 2013;120(1):85-7.

12. Dickinson JE. Misoprostol for second-trimester pregnancy termination in women with a prior cesarean delivery. Obstet Gynecol. 2005;105(2):352-6.
13. Cuellar Torriente M, Steinberg WJ, Joubert G. Misoprostol use for second-trimester termination of pregnancy among women with one or more previous cesarean deliveries. Int J Gynaecol Obstet. 2017;138(1):23-7.
14. Fawzy M, Abdel-Hady E-S. Midtrimester abortion using vaginal misoprostol for women with three or more prior cesarean deliveries. Int J Gynaecol Obstet. 2010;110(1):50-2.
15. Daponte A, Nzewenga G, Dimopoulos K, Guidozzi F. Pregnancy termination using vaginal misoprostol in women with more than one caesarean section. J Obstet Gynaecol. 2007;27(6):597-600.