

Lessons Learnt from Cases of Misoprostol-Based Pregnancy Termination Followed by Uterine Rupture: Report of 3 Cases

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ABSTRACT

With increase in the second-trimester pregnancy termination, debates continue on the most suitable mode of termination. Misoprostol is used as an agent for the medical abortion. Some authors believe that uterine rupture risk as a complication of medical termination is higher in the patients with positive cesarean section history while some others have no report of such effect. This complication cannot be predicted and can occur under various circumstances with different misoprostol regimens. Hereby, we reported three cases with positive cesarean section history undergoing second-trimester pregnancy termination due to preterm premature rupture of the membranes (PPROM) who developed uterine rupture with similar misoprostol dosages. Finally, we conclude that more cautions should be undertaken in the setting of PPRM with previous history of cesarean section or gestational age >20 weeks about uterine rupture risk and full recommended misoprostol dose must not be administered to prevent life-threatening events.

Keywords: Misoprostol, Second trimester pregnancy termination, Uterine rupture, Vaginal birth after cesarean (VBAC)



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Introduction

Raise in the rates of cesarean delivery during recent decades have been reported in all regions of the world. Thus, many women carry uterine scars in their next pregnancies which may put them at higher risk for occurrence of complications such as uterine rupture (1-3). The advances in timely detection of abnormalities and conditions needing termination have led to increase in the second trimester termination of pregnancy (4). Due to high number of patients with previous history of cesarean section (C-section) who may need second trimester termination, it is essential to choose an appropriate method to avoid the risk of uterine rupture in at-risk patients. Growing trends toward the medical abortion approach has made surgical methods a choice only for the specific cases.

Medical abortion in the second trimester has gained more and more popularity over years with misoprostol being one of the most common agents used for this indication. Misoprostol as a synthetic prostaglandin E1 analogue was primarily used for the treatment of gastric ulcers but then it was approved for the induction of abortion with favorable safety and efficacy (5). Several complications including coagulation disturbances, vaginal bleeding and uterine rupture have

been reported in the literature after misoprostol use for abortion (3, 6). Although uterine rupture is rare after using misoprostol, its higher rates in patients with scarred uterus and remarkable morbidity and mortality have turned misoprostol into a relative contraindication in this sub-group of patients (1, 3). While misoprostol in the patients with previous history of C-section must be used cautiously, its use is still so common in daily practice around the world. Hereby, we report three cases of uterine rupture subsequent to misoprostol use for the second-trimester pregnancy termination due to PPRM which have occurred over the past 5 years in our center (Yas Hospital, Tehran University of Medical Sciences, Iran) as a referral teaching hospital. Our center has a rate of up to 100-120 cases of misoprostol-based second-trimester pregnancy terminations monthly which makes it one of the most experienced hospitals in this field. Our hospital protocol for the pregnancy termination is based on FIGO misoprostol-only recommended regimens 2017. Another point to keep in mind is that mifepristone is not available for use in our country. Also due to controversy in using mechanical methods for cervical ripening in PPRM cases regarding increased risk of chorioamnionitis, insertion of cervical foley catheters or osmotic cervical

dilators are prohibited for such patients in our hospital. In all cases presented here only misoprostol was used for the termination and oxytocin was not used due to low initial BISHOP score.

Case Presentation

The 1st case- The patient was a 32 year-old woman, gravida3 in 21st week of pregnancy. She was referred for pregnancy termination due to PPRM. She had a history of two terms cesarean deliveries. The first C-section was due to prolonged fetal heart rate (FHR) deceleration and the second was due to repeat in C-section 3 years before current pregnancy (both with low-transverse incisions). Her BISHOP score was 2 at admission. Anterior placental position was observed. To terminate the pregnancy, sublingual misoprostol was initiated for the patient with 100 ug followed by 200 ug doses with 4-hour intervals. At 4 hours after the last dose with a total dose of 900 ug misoprostol, the patient became agitated and painful with tachycardia of 100 bpm and temperature of 39.5°C. Contractions were not sensed with tocotransducers exactly. Along with these changes, the uterine fundus was palpated as floating in the abdomen suggestive of possible uterine rupture which was further confirmed by bedside emergent ultrasonography. The patient was transferred to the operating room just after initiating intravenous antibiotic with suspicion of chorioamnionitis, before she becomes hemodynamically unstable. In the operating room, the abdominal and pelvic cavity was cleared out from hemorrhage and clots with an estimated volume of 500ml. After extraction of dead fetus and placenta which was bulged out from previous hysterotomy scar, no active bleeding from hysterotomy scar margins was identified. The rupture was repaired as with a simple hysterotomy and uterus could be preserved successfully. After operation, no extraordinary bleeding was observed and the patient was discharged after 4 days without any complication.

The 2nd case- The patient was a 27 year-old woman, gravida2 patient who was referred for pregnancy termination at 23rd week of pregnancy due to PPRM and non-viable gestational age. The patient had positive history of one prior C-section with low-transverse incision at 5 years before the current pregnancy. Her BISHOP score was 0. The placenta was located in fundal anterior position. For pregnancy termination, sublingual misoprostol was started for the patient. Four doses of 200 ug were administered for the patient with 4- to 6-hour intervals. After reaching a total dose of 800 ug, the patient complained of severe abdominal pain without vaginal bleeding. Due to hemodynamic instability of the patient reflected with tachycardia of 130 bpm and hypotension, she was

immediately sent to the operating room. During the operation, 500 ml of hemorrhage and clots were suctioned from abdominopelvic cavity. The rupture site was exactly on the previous C-section scar on uterus which was extended to the left lateral side of the uterus. The fetus and placenta were removed and uterus was preserved successfully. The patient was admitted at ICU after operation. She received combined parenteral antibiotic therapy due to possible antepartum chorioamnionitis. Post-operative ultrasonographic assessment showed no free fluid in the abdominal and pelvic cavities. The patient was discharged after 5 days with good general condition.

The 3rd case- The patient was a 27 year-old woman, gravida3 patient with a history of one previous C-section with low-transverse incision at 29 weeks due to late deceleration of FHR 18 months before. In this admission, she was referred for pregnancy termination at 20-week gestation due to PPRM but she refused termination. After 3 days of observation in the ward she was sent to labor ward for the termination due to development of fever and mild tachycardia with prompted diagnosis of chorioamnionitis. Her BISHOP score was 3. The placenta was in anterolateral position. Besides starting intravenous antibiotic for her, pregnancy termination began with routine sublingual misoprostol dose for her gestational age as 400 ug every 5 hours. After total dose of 1200 ug the patient became tachycardic with 140 bpm and her hemoglobin level declined by 2 units. The patient was urgently sent to the operating room. After abdominal exploration and clearing out the abdominopelvic cavity of 1 liter of blood, clot, fetus and placenta, the rupture site which was exactly at the previous hysterotomy scar, was repaired as usual and uterine was preserved. Due to blood loss of more than 75% of mother's estimated blood volume, blood transfusion was started for her during surgery. She was then sent to ICU for close hemodynamic monitoring and after receiving 2 units of packed cells and rise of hemoglobin level up to 9.5 mg/dL, the patient was sent to the general ward and dismissed from hospital 2 days later with good general conditions ([Figure 1](#)).

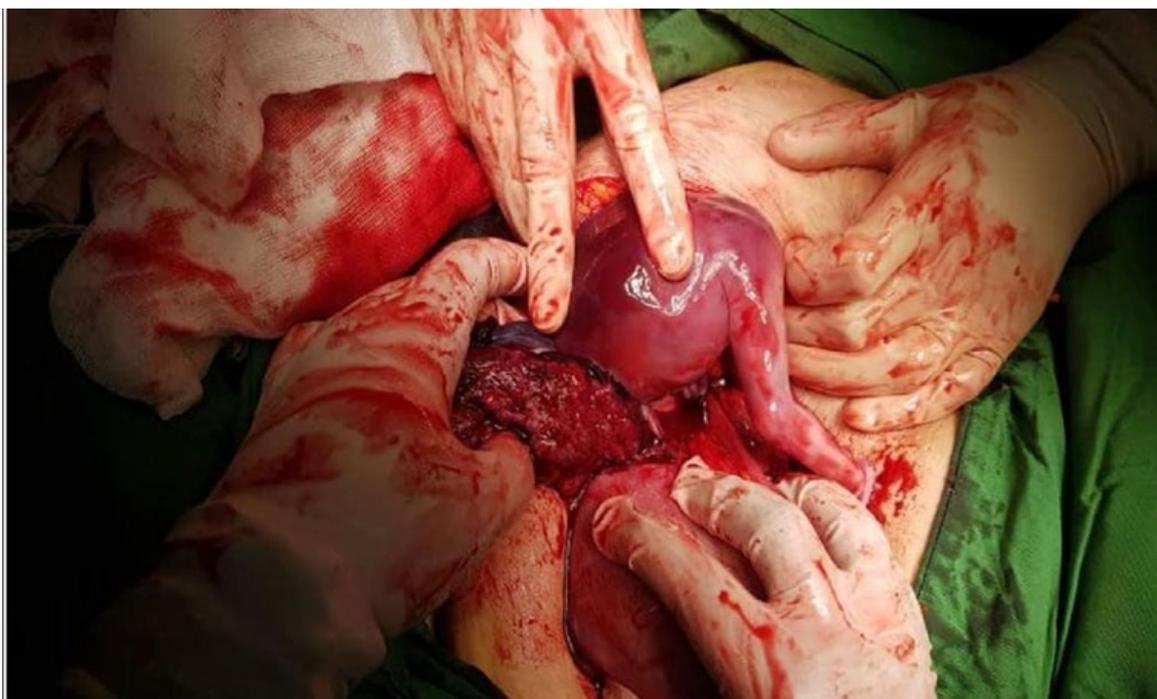


Figure 1. This picture refers to first case, in which fetus and placenta bulging out of uterine rupture site could be seen

Discussion

Uterine rupture as a serious and life-threatening complication can endanger mothers' lives. During the past decades, efforts have been made on determining the optimal pregnancy termination paths to reduce termination complications but there has not been any consensus on the recommended drug type, administration route and dosage (7). This lack of conclusive information is more pronounced in the patients with history of multiple cesarean deliveries.

Majority of the studies available in the literature have discussed the incidence of uterine rupture in the patients with history of single C-section but it is theoretically expected that the risk of rupture increases with higher numbers of uterine scars and cesarean deliveries.

A systematic review by Berghella *et al.*, (8) revealed that the risk of uterine rupture after misoprostol use for the second-trimester pregnancy termination in the patients with history of single low transverse C-section has been 0.4%. Addition of case reports to the analysis of the study had increased the prevalence rate up to 1.1%. Another systematic review by Goyal *et al.*, (9) also reported that risk of uterine rupture was 0.04% and 0.28% in unscarred and scarred uteri, respectively. A recent study on 678 patients who were treated with vaginal misoprostol doses of 100 to 400 ug for the second-trimester pregnancy termination was published (10). In that study, patients were categorized based on the history of C-section: patients without history of C-section, with one C-section and more than one C-sections. Uterine rupture occurred in 0.8% of the patients without C-section history while this rate in patients with history of one and more C-sections was

1.4% and 3.3%, respectively. Although patients with higher numbers of C-sections had relatively higher rates of uterine rupture, the difference was not statistically significant ($P>0.05$).

A study on 19 patients with history of multiple C-sections who underwent termination of pregnancy showed no uterine rupture in these patients. The misoprostol dose did not exceed 800 ug in any of the patients (11). Another study on 15 patients with history of two cesarean surgeries also showed no uterine rupture. In this study, the highest total dose of misoprostol was 1800 ug (12). Another study evaluated 19 patients undergoing pregnancy termination with two or three previous C-sections. The dosage varied in different patients with 400 ug of misoprostol every 6 hours being the most common regimen used. No uterus rupture was observed in this study (13). In a case report, uterine rupture was observed after a single 200 ug dose of misoprostol in a pregnant patient at 23rd week of gestation with chorioamnionitis (14). Another case report revealed silent rupture of uterine after 400 ug of vaginal misoprostol and 400 ug of oral misoprostol which was detected in dilatation and evacuation (15). Nayki *et al.*, reported that in a patient with history of a C-section, uterine rupture occurred after receiving four doses of 200 ug misoprostol with 3-hour intervals (16). A study on 180 patients with positive history of C-section and 216 controls without previous cesarean surgery admitted for the second-trimester pregnancy termination with misoprostol showed no uterine rupture in the case group and one case of uterine rupture among the controls. Misoprostol

maximum dose was totally 800 ug in the patients of both groups (17).

Administration of misoprostol between 13 to 26 weeks of gestation in the patients with history of C-section has been an issue of controversy in the literature due to probability of higher uterine rupture risk. International Federation of Gynecology and Obstetrics (FIGO) concluded that the risk of rupture does not differ between patients with and without scarred uteri. This risk is as low as 0.3% which is acceptable for the patients and medical care providers. FIGO has published recommendation on dosage of misoprostol for the pregnancy termination which is the protocol of reference in daily practice of our center. FIGO recommendation for misoprostol administration in the second trimester is 400 ug every 3 hours in 13 to 24 weeks gestation and 200 ug every 4 hours in 25 and 26 weeks gestation (18). Another points to consider is that chorioamnionitis has been reported to increase the risk of uterine rupture as high as 6-fold (19). Thus, timely diagnosis and management of chorioamnionitis can contribute in prevention of uterine rupture in at-risk patients.

Conclusion

As observed in the studies, there is no conclusive agreement on the role of previous cesarean scars in the occurrence of uterine ruptures during second-trimester pregnancy termination. In addition, it can be concluded that uterine rupture following misoprostol use is not dependent on the dosage and route of misoprostol administration. Thus, this phenomenon cannot be predicted and can occur under various circumstances with different misoprostol regimens.

What all the three cases in this report share in common is being PPROM, having a previous history of at least one C-section and having gestational age

more than 20 weeks for which a FIGO-based misoprostol regimen was used. Besides, in all three cases the uterus was preserved which is a notable achievement.

Thus, we can conclude that in the setting of PPROM which itself has higher risk of chorioamnionitis, addition of features mentioned previously is enough to be more cautious about the risk of uterine rupture and avoid administration of misoprostol in full recommended dose. In this situation, the risk of uterine rupture can be diminished without significant reduction in the efficacy of medication.

Finally, although this complication is rare, close monitoring and careful examination of the patients during pregnancy termination in the second trimester is mandatory to prevent the associated risks, which put patients' lives at danger. Probably, tight monitoring of the patients in the labor ward and early detection of alarm signs can be one of the most critical reasons for preservation of the uterus in all our cases.

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Conflict of Interest

The authors declared no conflict of interest.

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