High-dose Misoprostol as an Alternative Therapy After Failed Medical Abortion

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SUMMARY

Objective: The aim of this study was to determine the complete abortion rate for the vaginal administration of high-dose misoprostol after a failed medical abortion.

Materials and Methods: When their medical abortions failed after the conventional oral administration of mifepristone and misoprostol, participants then received 1,000 μg of misoprostol vaginally. The efficacy and side effects of this treatment were evaluated.

Results: Twenty-seven women who failed to abort after the conventional administration of mifepristone and misoprostol were enrolled in this trial. Fourteen days after the vaginal administration of 1,000 μg misoprostol, the overall complete expulsion rate had reached 88.8% (24/27). Most adverse effects were mild to moderate and did not require treatment.

Conclusion: The vaginal administration of 1,000 μg misoprostol as a salvage therapy after a failed medical abortion appears to be a safe and highly effective alternative to surgical intervention. [*Taiwan J Obstet Gynecol* 2008;47(4):408–411]

Key Words: medical abortion, mifepristone, misoprostol

Introduction

In Taiwan, the mifepristone–misoprostol method of medical abortion is now growing in popularity as an alternative to surgical abortion [1]. The regimen approved by the United States' Food and Drug Administration consists of 600 mg oral mifepristone, followed by 400 μg oral misoprostol 48 hours later, when the gestational age is less than 49 days [2]. However, a total of 200 mg mifepristone has been shown to be as effective as the 600 mg dose [3–5]. Hence, many early medical abortion regimens use a dose of 200 mg mifepristone. Usually, the standard management of medical abortion failure has been a dilatation and curettage (D&C). In recent years, the medical community has begun to question whether immediate evacuation using surgical intervention is truly necessary in most cases of medical abortion failure. In addition, few trials have described the salvage therapy after failed medical abortion [6]. Thus, we studied the efficacy of the vaginal administration of 1,000 μg misoprostol as a salvage therapy rather than surgical abortion.

Materials and Methods

Initially, 592 women seeking an elective termination of pregnancy were progressively enrolled. Before undergoing a medical abortion, a patient had to meet the following criteria: (1) the patient requested a medical abortion; (2) an intrauterine pregnancy with a gestational age ≤ 49 days was confirmed using vaginal ultrasonography; (3) the patient had signed an agreement of consent, had been informed of the advantages/risks

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of medical abortion, and understood the necessity of receiving a surgical abortion if the medical abortion failed; and (4) the patient promised to attend follow-up appointments.

No medical abortions were performed on pregnant women with any of the following exclusion criteria: (1) allergy to mifepristone or prostaglandins; (2) the presence of symptoms of threatened abortion; (3) medical history of heart, respiratory system, kidney, liver or adrenal disease; (4) medical history of thromboembolism, hypertension, coagulopathy, glaucoma or diabetes mellitus; (5) medical history of uterine pathology; (6) a hemoglobin level of less than 10 g/dL; (7) pregnancy with intrauterine device *in utero*; or (8) active pelvic infection.

To induce abortion, the women received 200 mg of oral mifepristone and 400 μg of oral misoprostol 48 hours after administration of the mifepristone. If no expulsion had occurred within 4 hours of taking the misoprostol, another 200 μg of misoprostol was administered orally. Individuals were scheduled to return for follow-up examinations 7±2 days after the second misoprostol administration, during which transvaginal ultrasonography was performed. At that time, if the presence of intrauterine gestational sac was detected, the subjects were diagnosed with a failed medical abortion. Those women who had expelled the product of conception then visited the clinic again 14 days later.

The women who failed to achieve a medical abortion according to the above protocol were offered the choice of a surgical abortion or another attempt at medical abortion. If the patient elected to take the latter course, she then received 1,000 μg of misoprostol vaginally. The participants were given three 500 mg tablets of acetaminophen that could be taken every 6 hours if they had lower abdominal pain. The subjects returned 2 days after the vaginal administration for a follow-up examination. Participants who had not aborted by this follow-up and still had a gestational sac were offered a surgical intervention. If the gestational sac had been expelled, they were scheduled to return for their follow-up examination 14 days after the expulsion, at which transvaginal ultrasonography was performed. Suction curettage was also performed at any time if it was clinically necessary because of uterine hemorrhage, incomplete abortion or at the subject's request.

At each of the participant's final follow-up visit, she completed a visual analog scale measuring the amount of pain experienced during the abortion process [7]. On a 100-mm line, "0" equaled no pain and "100" represented severe pain.

The primary aim of this trial was to estimate the complete uterine evacuation rate in women who received the 1,000 μg vaginal misoprostol regimen. The secondary aim included evaluation of the adverse effects of using such a high-dose misoprostol protocol. This study received approval from the institutional review board and written informed consent was obtained from all participants. A successful abortion was defined as complete medical abortion without surgical intervention.

Results

From October 2001 through November 2007, 592 subjects were enrolled for medical abortions. The mean age of the 592 women was 25.8 years (range, 16–44 years) and the mean gestational age was 43.7 days (range, 36–49 days). Of these women, 305 (51.5%) were nulliparous, 92 (15.5%) were primiparous, and 195 (32.9%) were multiparous. Seven days after the second misoprostol administration, the clinical results of the medical abortions were determined based on a complete expulsion rate of 93.1% (551/592). Thus, there was abortion failure in 41 cases (6.9%) of the recruited women. Of these 41 women with failed abortions, 10 women were diagnosed as having incomplete abortions and 31 women had viable pregnancies.

At this point, the 10 women with incomplete abortions and four with viable pregnancies requested D&C. Among the remaining 27 women, all had persistent pregnancies and 16 had embryonic heart beats that could be detected. The demographics of these 27 women who enrolled in the study are listed in Table 1. This group received 1,000 μg of misoprostol vaginally. During the follow-up, expulsion of the products of conception occurred at 2 days after administration of misoprostol in 25 (92.6%) of the women. The remaining two women were recommended to receive D&C because of the presence of intrauterine gestational sacs. When examined after the 2 weeks of follow-up, abortion had been successfully induced in 24 of the 25 women, while one patient requested D&C because of the presence of persistent bleeding. The histopathologic findings revealed the presence of conception products. Overall, 24 (88.9%) participants had complete

Table 1. Demographics of study population (*n* = 27)

Mean age (yr)	25.8 (range, 16–44)
Mean gestational age (d)	45.8 (range, 42–53)
Parity, *n* (%)	
0	14 (51.9)
1	7 (25.9)
2	6 (22.2)

Table 2. Efficacy ($n = 27$)

Success rate (%)	88.9
Failure rate (%)	11.1
Surgical intervention (%)	
Viable pregnancy	7.4
Patient's request	3.7

Table 3. Number and percentage of side effects ($n = 27$)

Side effects	*n* (%)
Pelvic pain	22 (81.8)
Diarrhea	19 (70.3)
Shivering	15 (55.6)
Fever	13 (48.1)
Nausea	12 (44.4)
Vomiting	7 (25.9)
Dizziness	2 (7.4)

abortions after the high-dose misoprostol treatment regimen. The number and percentage of the efficacious abortion and reasons for surgical intervention are listed in Table 2.

With the 1,000 μg vaginal misoprostol abortion regimen, the mean time from drug administration to bleeding was 2.5 hours (range, 1.5–4.5 hours), and the time to expulsion of the products of pregnancy was 4 hours (range, 3–8 hours). The mean duration of bleeding was 12.5 days (range, 8–22 days). The adverse effects of the treatment included pelvic pain (81.8%), diarrhea (70.3%), shivering (55.6%), fever (48.1%), nausea (44.4%), vomiting (25.9%), and dizziness (7.4%). The mean level of pain reported on the post-questionnaire was 60 mm (range, 10–90 mm). The maximum body temperature recorded was 38.2°C and the mean number of episodes of vomiting was 2.5 (range, 1–6 episodes). However, most adverse effects were mild to moderate and did not require treatment except for analgesics. Table 3 provides details of the women's reports of the side effects experienced following vaginal misoprostol administration. During the treatment course involving the administration of 1,000 μg misoprostol as a salvage therapy, no patient became infected, had severe hemorrhaging or had any need for blood transfusion.

Discussion

In regard to medical abortion, since vaginal bioavailability of misoprostol is three times greater than the drug's oral bioavailability, vaginal administration of misoprostol is more efficacious than oral administration. Citing several papers, Kahn et al [3] asserted that the oral administration of misoprostol had an incomplete abortion rate of 6.4%, while that for vaginal administration was 2.1%. Thus, vaginal administration of misoprostol was more efficacious than oral administration.

Generally, the success rate of medical abortion in early pregnancy has been reported to be about 95% [8,9]. If medical abortion fails, surgery is usually performed to terminate the pregnancy. However, in a 2001 study involving 300 women with a pregnancy duration of 6–9 weeks, Carbonell and colleagues [10] reported a success rate of 93% using 1,000 μg of misoprostol administered vaginally, a procedure that could be repeated every 24 hours up to three times. In their report, no patient needed to receive a blood transfusion or be treated for pelvic infection. The authors recommended that 1,000 μg misoprostol administered vaginally could be a valid method for the termination of pregnancies of up to 9 weeks of gestation. Therefore, we adopted vaginal administration of misoprostol and used the high 1,000 μg misoprostol dose as a salvage therapy after medical abortion failure. In our study, the overall successful expulsion rate reached 88.9%, so most women with failed abortions were able to avoid surgical intervention. Furthermore, excessive hemorrhaging and/or pelvic infections did not occur in this trial.

The use of misoprostol as a salvage therapy has undergone studies for failed medical abortion. Li et al [6] reported that 1,000 μg of vaginal misoprostol led to complete abortion in 10 of 11 (90.9%) early pregnant women after medical abortion failure with acceptable side effects. In another report, Li et al [11] described that supplementary use of 1,000 μg misoprostol vaginally may be an alternative when terminating an early pregnancy in association with a myomatous uterus, if the conventional combination of mifepristone and misoprostol failed. These studies suggest a high safety profile for high-dose misoprostol regimen after failed medical abortion. In our present trial, which included the administration of 1,000 μg vaginal misoprostol, we also found that most of the adverse effects were mild to moderate and did not require any treatment except pain killers.

In conclusion, if early medical abortion fails, the vaginal administration of 1,000 μg of misoprostol may be considered instead of surgical abortions, with tolerable side effects. Although few reports exist on medical abortions using high doses of vaginal misoprostol, the surgical risks of anesthesia, hemorrhaging, infection and perforation can be avoided when vaginal misoprostol is used.

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