

The Complete Evacuation Rate of Two Different Single Dose Misoprostol Regimens for Termination of Missed Abortion

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OBJECTIVE: To compare the complete evacuation rate of two different single dose misoprostol regimens in termination of missed abortion within 24 hours.

STUDY DESIGN: Hundred and one women with a diagnosis of missed abortion were randomized into two groups. Women in Group I received four tablets of misoprostol (800 mg) vaginally. In Group II, two tablets of misoprostol were administered vaginally simultaneously with two tablets taken orally. Women were evaluated by transvaginal sonography after the initiation of vaginal bleeding (primary visit) or in cases with no bleeding within 24 hours after the administration. In cases that had not completed the abortion at the primary visit, a surgical evacuation was performed. Mean expulsion time, clinical outcomes, side-effects, complications and any additional interventions required were analyzed in two groups.

RESULTS: There was no statistically significant difference between the two groups in terms of age, number of previous pregnancies, the complete evacuation rate at the primary visit or mean expulsion time. The complete evacuation rate within 24 hours was 18% in Group I and 14% in Group II ($p=0.38$). The overall complete evacuation rate was 16% ($n=16$). There was a statistically significant difference between the groups for mean hemoglobin values before and after treatment (0.64 vs 0.62 respectively, $p<0.05$).

CONCLUSION: With a single dose misoprostol regimen regardless of the route of administration, overall complete evacuation rate was low at the first follow-up visit.

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Key Words: Complete evacuation rate, Misoprostol, Missed abortion

Introduction

Approximately 10-20% of clinically recognized pregnancies are diagnosed as miscarriage in the first and second trimester.¹ Most widely accepted management of asymptomatic miscarriages is dilatation and curettage but surgical intervention is occasionally associated with serious complications such as perforation of the uterus, postcurettage infection or Asherman's syndrome.² In a study, the overall complication rate with the surgical method was reported as 6,6%³ Expectant management of miscarriages is an also an option, but complete evacuation rate is variable depending on the duration of observation.⁴

Medical termination with prostoglandins or antiprogesterons has recently been explored as an alternative for treatment for miscarriages. Misoprostol, a prostoglandin E1 analogue is the drug of choice as it is cheap and widely used to induce abortion. Various routes of misoprostol administration

including oral, vaginal and sublingual routes have been studied for termination of the first and second trimester pregnancies.^{2,5,6,7,8}

The effectiveness of misoprostol in the treatment of asymptomatic non-viable pregnancies (missed abortion) has been assessed in several clinical studies.^{2,9,10,11,12,13} These studies reported success rates between 80-88% with vaginal misoprostol. Recently, Tang et al. randomized 80 women to receive 600 µg misoprostol either vaginally or sublingually and they found the success rate of 87,5% in both groups.² But the optimal regimen and route of misoprostol in treating missed abortions is still unclear.

The aim of this study was to compare the effectiveness of two different single dose of misoprostol regimen in termination of missed abortions within 24 hours.

Material and Methods

A total of 101 women with an ultrasonographically proven diagnosis of asymptomatic first trimester missed abortion were recruited in the study. Asymptomatic missed abortion was defined as an intact gestational sac, no evidence of fetal cardiac activity and closed cervical os by transvaginal ultrasonography. Local Ethics Committee approval was obtained and all participants were asked to fill in the informed consent form if and when they chose to participate in the study after

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detailed counselling about the study was accomplished.

Women with complete or incomplete miscarriages, hemoglobin value <10 gr/dl, history of inflammatory bowel disease, known intolerance or allergy to misoprostol and contraindication to administration of misoprostol were excluded.

All women were randomized according to computer-generated random numbers into two groups. In Group I, four tablets of 200 mg misoprostol (800 mg) were administered vaginally into the posterior fornix of the vagina. In Group II, two tablets of misoprostol (400 mg) were administered vaginally and additional 2 tablets (400 mg) were given orally at the same time. Transvaginal ultrasonography and vaginal examination were performed in patients with reported heavy vaginal bleeding (primary visit). If, at the primary visit, the abortion was still not completed, a surgical evacuation was performed under general anaesthesia. Cases who had no bleeding or who reported spotting within 24 hours after misoprostol administration were evaluated by transvaginal ultrasonography, the findings were recorded and a surgical evacuation under general anaesthesia was performed. Outcome measures assessed included clinical outcome, the rate of patients who needed to have a surgical evacuation, the overall complication rate in cases where surgical evacuation was required and side effects and mean decrease in serum levels of hemoglobin in cases who had a medical termination.

Clinical outcome is defined as the complete evacuation rate during the first visit

(defined as no embryonic tissue in the uterine cavity by transvaginal sonography), incomplete evacuation (defined as the requirement for surgical intervention, including all surgical interventions for extracting any retained products of conception) rate. Incomplete evacuation was diagnosed by transvaginal sonography in the presence of thickened endometrial line (≥ 8 mm), with an image of irregular contours with echopositive zones. Two 600 mg tablets of paracetamol were given orally if the woman complained of severe pain.

Statistical analysis was performed by using SPSS 10,0 for Windows. Fisher's exact test or χ^2 test was performed for comparisons of groups as appropriate. Student's t-test was performed for continuous variables. Significance was set at $p < 0,05$.

Results

The mean age of the patients was $28 \pm 5,7$ years (16-41) and mean gestational age was $9,5 \pm 1,1$ (7-11). There were no statistically significant differences between the two groups in terms of age, body mass index, gravity, parity, number of previous dilatation and curettage and gestational age. Characteristics of the patients in both groups are presented in Table 1.

Table 1. Patient characteristics, Mean \pm SD

	Group I (n=50)	Group II (n=51)	P
Age (years)	28 \pm 6(19-41)	28 \pm 5(16-40)	0.75
Body mass index	24 \pm 4(19-33)	24 \pm 5(15-32)	0.4
Gravity	2 \pm 1,4(1-7)	3 \pm 2(0-9)	0.3
Parity	1.1 \pm 1(0-4)	1.1 \pm 1(0-4)	0.9
Number of previous dilatation and curettage	3 \pm 1(0-3)	1 \pm 0,9(0-3)	0.2
Gestation (weeks)	9.6 \pm 1	9.3 \pm 1,1	0.1

A total of 42 (84%) from Group I and 39 (76,5%) from Group II reported heavy vaginal bleeding within the first 24 hours. At the primary visit, there was complete evacuation in 18% (n=9) of Group I cases, and in 14% (n=7) of Group II cases. There was no statistically significant difference in the complete evacuation rate at the primary visit between the two groups ($p=0.38$). A total of 16 cases from both groups (16%) had complete expulsion with the self-reported heavy vaginal bleeding. In cases where complete evacuation is realized, mean expulsion time was $8,7 \pm 4,2$ h in Group I and $10 \pm 4,4$ h in Group II. In 14 cases with no bleeding or spotting within the first 24 hours and 71 cases who were diagnosed to have incomplete evacuation during the primary visit, surgical evacuation under general anaesthesia was performed. Overall 85 cases (84,2%) from both groups required surgical evacuation (82% in Group I, 86,3% in Group II). There was no significant difference in the rates of patients who needed surgical evacuation between the two groups ($p=0.376$). No infection or perforation were observed in cases who had surgical evacuation. The outcomes of treatment are presented in Table 2.

Table 2. Outcomes after single dose misoprostol administration within 24 hours

	Group I (n=50)	Group II (n=51)	P
Complete evacuation	9(18%)	7(14%)	
Incomplete abortion	41(82%)	44(86%)	0.5
Expulsion time (hours)	8.7 \pm 4,2 (2-24)	10 \pm 4,4 (2-22)	0.15

The mean hemoglobin value before treatment was $12,2 \pm 1.09$ gr/dl in Group I and $12,3 \pm 1.04$ gr/dl in Group II and there was no statistically significant difference for the basal hemoglobin values between the groups ($p=0.76$). The difference between the basal Hb levels (Hb1) and day-2 Hb levels was $0.64 \pm 0,5$ in Group I and $0.62 \pm 1,6$ in Group II. The difference in Hb levels was significantly higher in Group I ($p=0.01$).

In both groups, pelvic pain, nausea and vomiting, diarrhea, dizziness and headache were side effects that were encountered (37%, 23%, 25%, 13% and 3%, respectively). Thirty-seven women had a complaint of pelvic pain and 27%

of them (n=10) described the pain as less intense than or same as menstrual pain, 73% of them (n=27) described it as much stronger than menstrual pain. There was no statistically significant difference for incidence of side effects between the two groups (p=0.12). The side effects are presented in Table 3.

Table 3. Side effects

	Group I (n=50)	Group II (n=51)	Total (n=101)	P
Pelvic pain	8 (16%)	29 (57%)	37 (37%)	0,3
Diarrhea	1 (2%)	24 (47%)	25 (25%)	
Nausea-vomiting	4 (8%)	19 (37%)	23 (23%)	
Dizziness	3 (6%)	10 (20%)	13 (13%)	
Headache	0	3 (6)	3 (3%)	

Discussion

The traditional approach to first trimester miscarriages is surgical evacuation. Surgical evacuation is an effective method with a success rate of up to 98%.¹⁴ However, it may be associated with serious complications. Alternatives for surgical evacuation are expectant management, or medical treatment using misoprostol. The success rate of expectant management ranges from 14 to 47% in different studies.^{12,13,14} In a meta-analysis by Graziosi et al. the effectiveness of expectant management, medical treatment or curettage in the treatment of early pregnancy loss was assessed.¹⁵ Three studies were reported on the comparison of expectant management with curettage. The weighted rate of patients that had a complete evacuation in the expectant management group was found as 71%, whereas this rate was found to be 97,6% in curettage group. In five studies comparing expectant management with misoprostol, the weighted rate of patients that had a complete evacuation in the expectant management group was found 41%, whereas this rate was 79% in those treated with misoprostol. All failures in both groups occurred in women with missed abortion. In five studies comparing misoprostol with curettage, the weighted rate of patients that had a complete evacuation after misoprostol treatment was found to be 68%, whereas this rate was 97% after curettage. Large majority of the failures of misoprostol treatment in these studies also occurred in patients with a diagnosis of missed abortion. The presence of nonviable pregnancy is thus shown to be related with a decrease in the success rate of all three treatment modalities; expectant management, medical treatment or curettage.

Muffley et al. compared complete evacuation rates in women randomized to either repeated doses of vaginally administered misoprostol or curettage in cases of missed abortion below 12 weeks.¹⁶ Success rates were found higher in the curettage group (60% vs 100%). In 2004, Ngoc et al. compared the efficacy of oral and vaginal route of misoprostol for

treatment of missed abortion¹⁰ and reported an efficacy rate of 80% in both arms. In this double-blind study, first follow-up visit was scheduled 2 days after the administration of misoprostol and if substantial debris remained in uterus, women were given the option of either returning 5 days later and then having a surgical intervention at the second visit if the abortion was still not complete, or a curettage was performed. Efficacy was defined as the percent of women discharged from the study without any need for curettage in this study.¹⁰

In the presented study, the success rates were not statistically different in the two groups and overall complete evacuation rate was 16% within 24 hours regardless of the route of administration. In literature, the efficacy of medical abortion in the first trimester missed abortion cases is given with a range of 83 to 87,5%.^{2,12} In a study performed by Wood et al. the outcome was assessed one week after misoprostol administration.¹² Another study performed by Tang et al. final evaluation of success rates was carried out at day-7 and 43.² The lower complete evacuation rates in our study compared to many others is more likely to be associated with the short of time limit used for evaluating the cases. The different misoprostol regimens used might also be another reason for this lower figures. In our study, the evaluation was made when the heavy bleeding started and in cases where complete evacuation was not realized within 24 hours, a surgical evacuation was performed. The patients having little bleeding or spotting were evaluated after the end of 24 hours and surgical evacuation was applied.

In most of the related studies misoprostol administration is made by the patient at home and for the first evaluation the patient is called to hospital few days later (1-7 days). In our study all of the patients are monitored in the hospital. Before starting the study in order not to increase the duration of hospitalization, a maximum period of evaluation was set as 24 hours. The decrease in Hb level was significantly higher in Group I in our study. The basal Hb value of all the patients was 12.25±1,7 and day-2 Hb value was 11,6±1.29 (Hb1-Hb2 = 0.63±1.17) and none of the patients needed a blood transfusion. This finding implies the safety of home use of misoprostol; thus all the patients who are not anaemic can be given misoprostol and requested to come back either when a profuse bleeding starts or if not 24 hours after misoprostol administration.

In all studies women who do not have complete evacuation are treated with varying additional doses of misoprostol after the main doses.^{2,10,12,13,16} In our study, only the main dose of 800 µg misoprostol is administered and no repeat doses were given in order not to extend the hospitalization period of the patients. In spite of the high surgical intervention rates, no complications related with the procedure were observed in any of the patients. It could well be explained by the cervical priming effect of misoprostol allowing easy surgical access to the

uterine cavity.

In conclusion, the administration of misoprostol and evaluating the patient within 24 hours will decrease the need for surgical intervention in cases with missed abortion but in order to avoid surgery a longer observation time and repeated dosages of misoprostol might be required.

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