Effects of vaginal versus oral misoprostol to terminate second-trimester pregnancy

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Summary

Objectives: Using surgical methods compared to medical methods, such as misoprostol for termination of pregnancy, has several side effects. This study was performed in order to compare the effect of vaginal and oral misoprostol in second-trimester pregnancy termination (14 - 24 weeks). *Materials and Methods:* The authors performed a clinical trial study in 40 pregnant women at 14 to 24 weeks of gestation and candidates for medical interruption of pregnancy. All patients received 600 μg of vaginal misoprostol as primary dosage and then, were placed randomly in two groups consisting of 20 patients that received 400 μg of vaginal or oral misoprostol, every four hours, up to three doses. If the abortion was incomplete, oxytocin was used. Twenty-four hours after the procedure, uterine sonography was performed in all patients and if residue was found, the patients were then candidates for curettage. *Results:* Seventeen patients (85%) in the vaginal group and 17 patients (85%) in the oral group had successful pregnancy interruption. The mean interval until the discharge of pregnancy products in the vaginal group (15 / 42 ± 10 / 84) showed no significant difference compared to the oral group (12 / 65 ± 7 / 8) and no significant differences in side-effects were found between the two groups. *Conclusion*: Oral misoprostol is as effective as vaginal misoprostol in performing second-trimester abortion. It appears that the vaginal misoprostol primary dose together with the continuation of oral dose is not more effective compared to the vaginal misoprostol method alone.

Key words: Second trimester; Pregnancy termination; Misoprostol, Abortion.

Introduction

The termination of pregnancy in second-trimester is performed for various reasons, such as: fetal abnormality, preterm premature rupture of membranes, intrauterine fetal death, and severe maternal disease [1]. Surgical methods to terminate second-trimester pregnancy have been used for many years. During the last decade however, there has been much improvement in treatment without risk, more effective, and non-surgical abortion in second-trimester pregnancy [2, 3]. In medical therapy, different medicines can be used in order to induce an abortion. One of these medicines is misoprostol which is the industrial analogue of prostaglandine E_1 that has effects on labor and abortion induction and is a good alternative to surgical methods performed in second-trimester abortion [4]. Due to fewer side-effects, lower cost, and possibility of storing it at normal room temperature, misoprostol is mostly considered among the variety of prostaglandine choices for second-trimester abortion [5]. There is some debate regarding the ideal dosage and the method of prescription, due to the different pharmacokinetics available [6]. It is prescribable as oral, sublingual, rectal, intramuscular, intravenous, and intraamniotic liquid, but is mainly used in vaginal and oral forms [7]. Many clinical research studies have shown that the vaginal use of misoprostol is more effective than oral [8] and in some studies the success of the oral method is greater [9], while the others also indicated similar effects of these methods in termination of pregnancy in the second trimester [10]. According to contradictory findings of prior studies, for the purpose of examining and comparing the effects of vaginal misoprostol and combination of vaginal and oral forms in second-trimester abortion, one study was designed and performed in Rohany Hospital in Babol (North of Iran) in 2009-2010.

Materials and Methods

This study was performed in a clinical trial method setup and 40 patients referred to therapeutic centers of Babol Medical University for second-trimester (14 to 24 weeks of pregnancy) abortion were enrolled. Interruption of pregnancy was indelated for maternal and fetal reasons. The characteristics of the patients were: nullioparity, parity 1 to 3, absence of pain and uterine infections, Bishop score less than 4, the patients mulltiparity, corioamnionitis in bedridden time in hospital, and uterine incision. Exclusion criteria from the study included complete abortion in clinic, asthma, glaucoma, renal, hepatic, and cardiac diseases. An informed consent to enter the study was received from all patients. Uterine sonography was performed in all patients during the 48 hours before being bed-ridden and the pregnancy age had been calculated according to the sonography. Patients were randomly placed in two groups of 20 persons. Demographic characteristics such as age, height, body mass index (BMI), parity, and gestational age were recorded 600 μg of misoprostol was given as the vaginal primary dose to all patients, and then in one group, 400 μg of misoprostol was prescribed vaginally every four hours in three

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dosages, and oral dosages were prescribed in the other group. If discharge of pregnancy products was incomplete after these dosages, oxytocin was used to complete the process. During treatment, the patients suffering from anaphylaxis, fever, and severe diarrhea were excluded from the study. After 24 hours of pregnancy products discharge, uterine sonography was performed in all patients and if oral residual was more than 2 cm, the patients were then candidates for curettage. Hemoglobin and hematocrit for all patients were previously checked before the initial treatment and 24 hours after abortion and they were recorded. Upon completing the treatment process, the two groups were examined to determine the amount of reaction to misoprostol, duration of the discharge from the initiation of treatment, the frequency of oxytocin used to help pregnancy termination, and the average of amounts of misoprostol taken in both groups, the number of side-effects (fever, diarrhea, and severe bleeding), decrease in Hb level, the need for blood transfusion, and the need of curettage. All parameters were examined and data analysis was then performed by using SPSS software and statistical tests, chi-square and T-test; $p < 0.05$ was considered significant.

Table 1. — *The comparison of demographic variables between the two therapeutic groups of oral and vaginal misoprostol.*

Variables	Vaginal misoprotol	Oral misoprotol	*p* value
Age (yrs)	26/8 ± 6/25	25/10 ± 4/7	0.337
Nulliparity	16 (80%)	14 (70%)	0.715
BMI (kg/m^2)	26/25 ± 3/6	26/21 ± 9/81	0.974
Weight (kg)	66/35 ± 9/59	65/52 ± 49/81	0.79
Gestational age (wks)	17/85 ± 3/54	16/45 ± 2/52	0.158

Table 2. — *The comparison of clinical outcome variables between the two therapeutic groups of oral and vaginal misoprostol.*

Variables	Vaginal misoprotol	Oral misoprotol	*p* value
Successful termination of pregnancy	17 (85%)	17 (85%)	1
Duration of delivery from treatment	15/42 ± 10 / 8	12/65 ± 7/8	0.359
Misoprostol side-effects	5 (25%)	2 (10%)	0.257
Need of emergency curettage after fetal excretion	1 (5%)	5 (25%)	0.1

Results

The patients of these two therapy groups of oral and vaginal misoprostol, had no statistically significant differences with regard to age, nulliparity, weight, BMI, and gestational age ($p > 0.05$) (Table 1). Differences in the number of successful embryo fetal excretions and the mean duration of the process from the initiation of treatment, between the groups was not significant. The side-effects of the oral misoprostol group included diarrhea (5%), and severe bleeding (5%), and in the vaginal misoprostol group, fever (10%) and diarrhea (15%), which showed no significant differences. The difference between the groups regarding the need for curettage to evacuate the residue of pregnancy immediately after excreting the fetus was not significant (Table 2).

Discussion

This study aimed to compare the effect of vaginal and oral misoprostol after the primary dosage in order to terminate second-trimester pregnancy. The results of this study did not shown significant differences with regard to successful termination of pregnancy between these two therapeutic groups of oral and vaginal misoprostol. There was also no significant difference between the two groups with regards to the duration of pregnancy termination, side-effects, and the need for curettage.

In a study by Feldman *et al*., on 43 patients who were candidates for pregnancy termination in the second-trimester, the patients were placed in a vaginal misoprostol group (22 persons) and oral misoprostol group (21 persons). At first, they were all prescribed 800 µg of vaginal misoprostol. They were then divided into two groups and prescribed 400 µg of vaginal or oral misoprostol based on a selective method every eight hours. For mean duration of pregnancy termination from the initiation of treatment in the first 24 hours of the above-mentioned study, there was no significant difference between the oral (15.9 ± 2.3 hours) and vaginal (21.1 ± 3.5 hours) therapeutic groups, and also there was no significant difference with regard to the side-effects between these two groups [10], which is consistent with the results of the current study.

Also in the study by Kurshid *et al*. on 100 patients who were candidates for pregnancy termination in the second trimester, patients were placed in two groups consisting of 30 women. At first all patients received 800 µg of vaginal misoprostol and then 400 µg oral or vaginal misoprostol of four dosages every eight hours for patients of both groups. With regard to termination of pregnancy in the first 24 hours the vaginal group (80%) was significantly more than the oral group (32%). Furthermore, the mean interval of pregnancy termination from initiation of treatment in successful vaginal group (16/12 ± 6/1 hours) was significantly less than the oral group (32/5 ± 6/12 hours) [11], which was not consistent with the results of the current study. Since our case series is smaller than the study of Kurshid, the difference of these studies may be related to this fact or the different effects of the drug in various races. There was no significant difference between the oral groups (18%) and vaginal groups (13%) according to the need for curettage [11], which is consistent with the results of the present study.

Similarly, in the study by Behrashi *et al*., in 60 pregnant women in the second trimester who were candidates for pregnancy termination, the patients were placed in two groups consisting of 30 women that received vaginal or oral misoprostol with the primary dose of 400 µg and it was continued for three doses every six hours. The successful termination of pregnancy in the vaginal group

(86.7%) was significantly higher compared to the oral group (43.3%) [12], which is inconsistent with the results of the current study. Since in the present study in both groups, the first dose had been prescribed vaginally, and vaginal absorption of misoprostol is more effective than oral absorption, this would explain the differences encountered between these studies. With respect to the mean duration of the process between the vaginal group (9.2 ± 4.2 hours) and oral group (12.7 ± 7.3 hours), no significant difference was shown. Also with respect to the side-effects, there was no significant statistical difference [12] between the oral group (46.6%) and the vaginal group [13] which is consistent with the results of the present study.

In another study by Bebbington *et al*. [13] in 114 patients who were the candidates for pregnancy termination in the second trimester, the patients were placed in two groups of oral misoprostol (65 persons) and vaginal misoprostol (49 persons). The oral group of misopraostol, 200 µg of drug was prescribed every hour until three hours, and then 400 µg of drug was prescribed every four hours, and in the vaginal misoprostol group, 400 µg of drug was prescribed every four hours until 24 hours. Successful termination of pregnancy in the first 24 hours in the vaginal group (85.1%) was significantly higher than the oral group (39.5%) and the interval of pregnancy termination from initiation of treatment in the vaginal group (19.6 ± 17.5 hours) was significantly less than the oral group (34.5 ± 28.2 hours) [13] which was inconsistent with the results of the current study. Since, in the present study the first dose had been prescribed vaginally in both groups and the studied cases were also lower than the study of Bebbington, perhaps the difference of these studies is in the number of samples or the method of prescribing misprostol. There was no significant difference between the oral group (7 persons) and vaginal group (4 persons) according to the need for curettage [13], which is consistent with the results of the current study.

Conclusion

It appears that the compound method of vaginal misoprostol in a primary dose with the continuation of the oral dose, is not more effective than the vaginal misoprostol method alone.

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