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ORIGINAL RESEARCH

Effects of buccal misoprostol compared with vaginal misoprostol on first-trimester abortions: a randomized clinical trial

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Abstract

Objective: Misoprostol can be used by different routes in the medical management of abortion. This study aimed to compare the efficacy and safety of buccal and vaginal administration of misoprostol for the completion of first-trimester abortions.
Materials and Methods: This study was a randomized clinical trial in which women with first-trimester abortion referred to Imam Hossein Medical Center in 2018 were studied. Women were randomly divided into two groups of buccal or vaginal misoprostol treatment. From the time of drug administration to complete abortion, side effects, duration of drug use until tissue excretion, need for blood transfusion and need for surgical evacuation were recorded and compared in two groups.
Results: One-hundred women (each group, 50 patients) were evaluated in this study. There was a significant difference between the two groups regarding the duration of misoprostol use (p-value = 0.028), and it was longer in the buccal group. Besides, there was a significant difference between the two groups in terms of the dose required until the tissue discharge (p-value = 0.034). In the buccal group, patients received higher doses of misoprostol. The rate of fever had a significant difference between the two groups and was more frequent in the vaginal group (p-value=0.023).
Conclusion: Vaginal misoprostol can be more effective in treating first-trimester abortions compared to buccal misoprostol and may be associated with longer duration of use and lower required doses.

Keywords: Abortion, First-trimester, Misoprostol, Buccal, Vaginal

Introduction

Abortion is considered a spontaneous fetal loss before the age of fetal viability (1). Women diagnosed with first-trimester abortion with the ultrasonography, can be managed expectantly, medically, or surgically (2). Traditionally, uterine evacuation by aspiration curettage was known as the gold-standard technique for the treatment of spontaneous abortion (3). However, medical management with misoprostol is an alternative to surgery for managing first-trimester abortions and is now regarded as being the primary choice for the management of early gestational loss in many centers (4, 5). The treatment of first-trimester abortions with misoprostol has many advantages over surgical treatment. It can be done in an outpatient setting, and hospitalization is not required. So, it appears to be more cost-effective management (6). Misoprostol is a prostaglandin E1 analogue, which is effective, inexpensive, and requires no needles for administration. In addition, it has fewer side effects than prostaglandin E2 analogues (7, 8).

Misoprostol can be used both by oral and vaginal routes; however, some clinical studies in the medical management of abortion found that the vaginal route might be more effective than oral administration because the oral route has extensive and rapid first-pass metabolism (9). Fewer drug doses administered vaginally can slowly induce contraction of the uterus and maintain it for labor induction. Because of the higher peak in oral administration, the side effects are more than the vaginal route (10). However, vaginal administration requires frequent vaginal examinations, which are inconvenient and may not be acceptable for many patients despite its effectiveness (11). Other routes of misoprostol administration, such as buccal and sublingual, have also been tried (12, 13). The buccal route (between the gums and cheek) has easier administration and lesser infection rates compared to the vaginal route (14).

This study aimed to compare the efficacy and safety of buccal and vaginal administration of misoprostol for the completion of first-trimester abortions.

Materials and Methods

This study was a randomized clinical trial in which women with first-trimester abortion referred to Imam Hossein Medical Center affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran, in 2018 were studied. The study protocol was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and was done following the principles of the declaration of Helsinki. Informed consent was obtained from all women to participate in the study. Inclusion criteria were ≥18 years of age, gestational age between 6 weeks to 13 weeks and 6 days and exclusion criteria were cardiovascular or cerebrovascular diseases, severe anemia, hypertension, Severe hepatitis, severe kidney disease, chronic adrenal insufficiency, severe asthma requiring systemic steroids, inflammatory bowel disease, evidence of cervical infection, any allergies and contraindications to the use of misoprostol or women who for any reason were unwilling to participate in the study.

Age, parity, gravidity, and gestational age of all women were recorded, and they subjected to a general and an obstetric examination. In addition, a baseline hemoglobin level of all patients was measured, and transvaginal ultrasonography was done to confirm the diagnosis of abortion.

After confirmation of abortion, the women were randomly divided into two groups of buccal or vaginal misoprostol treatment. The treatment compromised 800 µg misoprostol in the vaginal group and 600 µg in the buccal group, up to two doses every three hours. All doses were administered under the supervision of obstetrics and gynecology residents at the hospital.

From the time of drug administration to complete abortion, side effects (including fever, nausea and vomiting, diarrhea, bleeding, and need for blood transfusion) and duration of drug use until tissue excretion and need for Surgical evacuation were recorded and compared in two groups. The physician who recorded the final outcomes was blinded to the group of patients.

Statistical Analysis

Quantitative variables with normal and abnormal distribution were presented as mean ± standard deviation and median (interquartile range), respectively. Frequency (%) was used to represent qualitative variables. Qualitative variables were analysed using the Chi-squared

test, and quantitative variables with normal distribution were analysed using Student's t-test. Quantitative variables with abnormal distribution were also analysed by the Mann-Whitney test. The normal distribution of variables was evaluated by the Shapiro-Wilk test. The p-value = 0.05 was significant in all analyses. All analyses were performed by SPSS software SPSS 21.

Results

One-hundred women (each group, 50 patients) evaluated in this study. The distribution of age, body mass index and gestational age for these two groups are reported in Table 1. In addition, the parity was similar in the two groups, and the median (interquartile range) was 2 (1-3) in both groups, and there was no significant difference between the two groups (p-value = 0.226). There was no significant difference between the two groups in each variable and they were matching similar with respect to demographic profile and obstetrical parameters.

Table 1 Baseline characteristics of patients

Characteristic	Vaginal misoprostol (n=50)	Buccal misoprostol (n=50)	p-value
Age, years	28.8±6.0	28.8±5.3	0.972
Body mass index, kg.m^{-2}	23.9±3.8	24.3±3.0	0.599
Gestational age, weeks	8.6±1.7	8.3±1.5	0.432

The duration of misoprostol administration until the tissue discharge (Induction–expulsion interval) is shown in table 2. There was a significant difference between the two groups regarding the duration of misoprostol use (p-value = 0.028), and it was longer in the buccal group. The rate of surgical evacuation required in the two groups is also shown in Table 2. There was no significant difference between the two groups in this regard (p-value = 0.461). In addition, as the required doses of misoprostol in the two groups are shown in Table 2, there was a significant difference between the two groups in terms of the dose required until the tissue discharge (p-value = 0.034). In the buccal group, patients received higher doses of misoprostol.

Table 2 Side effects of patients associated with misoprostol

Outcome		Vaginal misoprostol (n=50)	Buccal misoprostol (n=50)	P-value
Induction–expulsion interval	24 hours	30 (60)	19 (38)	0.028
	48 hours	20 (40)	31 (62)	
Required doses of misoprostol	1 dose	10 (20)	3 (6)	0.034
	2 doses	22 (44)	16 (32)	
	3 doses	12 (24)	17 (34)	
	4 doses	6 (12)	14 (28)	
Need for surgical evacuation		9 (18)	12 (24)	0.461

The rate of different possible side effects of misoprostol use is shown in table 3. Among these variables, only the rate of fever had a significant difference between the two groups and was more frequent in the vaginal group (p-value=0.023).

Table 3 Side effects of patients associated with misoprostol

Side effects		Vaginal misoprostol (n=50)	Buccal misoprostol (n=50)	P-value
Amount of bleeding	Spotting	0 (0)	2 (1)	0.275
	Less than menses	14 (28)	16 (32)	
	Equal menses	20 (40)	21 (42)	
	More than menses	8 (16)	10 (20)	
	Clotting	8 (16)	2 (4)	
Hemoglobin level change	≤ 1mg/dl	29 (58)	36 (72)	0.329
	1-2mg/dl	15 (30)	11 (22)	
	≥ 2mg/dl	6 (12)	3 (6)	
Blood transfusion		1 (2)	0 (0)	0.815
Nausea		10 (20)	8 (16)	0.603
Vomiting		5 (10)	2 (4)	0.436
Diarrhea		7 (14)	5 (10)	0.538
Fever		18 (36)	8 (16)	0.023

Discussion

There is ample evidence that misoprostol is a safe, effective, and acceptable method of uterine drainage for women requiring post-abortion care. Misoprostol reduces the cost of post-abortion care services because it does not require immediate access to sterile settings, operating rooms, or skilled personnel (15). It is inexpensive, does not require a refrigerator, and can be administered by several different routes (16).

In this study, the effects of buccal and vaginal misoprostol on first-trimester abortions were investigated and showed that the amount of bleeding, need for surgical evacuation, hemoglobin level changes, need for blood transfusion, nausea, vomiting, and diarrhea did not significantly differ after using buccal or vaginal misoprostol. However, the induction–expulsion interval was significantly longer in the buccal group. Also, the required dose was significantly higher in the buccal group. However, fever was significantly more frequent in patients of the vaginal group.

The study by Khan et al. showed efficacy (complete abortion) of 88% in the vaginal group and 94% in the buccal group in first-trimester abortions. This difference was not statistically significant (P-value >0.05) (12). Middleton et al. also reported the 95% efficacy of 800 µg mifepristone in the buccal group and 93% in the vaginal group (P-value=0.51) (17). Geetika Garg et al., in a randomized controlled trial, reported that the success rate in the buccal group was 96% and in the vaginal

group was 88% (P-value >0.05) (18). Fjerstad et al. reported a 98.3% success rate in medical abortion with 200 mg mifepristone plus 200 µg of buccal misoprostol over 24 to 48 hours (P-value >0.05) (19).

Our results showed that the induction–expulsion interval and dose of drug required for tissue discharge were significantly higher in the buccal group than in the vaginal group and might indicate a higher efficacy of vaginal misoprostol. However, these studies that showed no significant difference in efficacy of vaginal and buccal misoprostol evaluated the first-trimester induced abortions.

Wiebe et al. used misoprostol 600 µg by buccal or vaginal routes 3 to 6 days after 50 mg/m^2 methotrexate and reported that complete abortion on day 8 was 14% greater in the vaginal group and that vaginal misoprostol is more effective than the buccal, which can be similar to the results of our study. In their study, the vaginal route was more acceptable than buccal for patients, which may be due to the burning sensation and the need to keep tablets in the mouth.

The controversial point of many published clinical trials on the treatment of premature abortion is the definition of success rate. Some studies have used the endometrial thickness of 15 mm assessed by transvaginal ultrasound as a cut-off for complete abortion (15). However, evidence from studies of medical termination of missed abortions indicates that this value is too stringent (20, 21). Studies that usually report success rates above 95% do not use endometrial thickness to define the success rate (22).

Unusual differences in success rates in different studies may be due to various factors such as patient selection, concomitant use of mifepristone, and differences in dose, route, and time interval of misoprostol administration. While some studies included patients with incomplete abortion, others included missed abortions or a combination of both (7, 23).

There was no significant difference in vaginal bleeding between the two groups, with most patients reporting amount similar to menses.

There was no significant difference in hemoglobin level changes between the two groups. Also, there was no significant difference in blood transfusion between the two groups, and only one patient in the vaginal group needed a blood transfusion. In our study, except for the fever, there were no statistically significant differences in drug-related side effects similar to those of Middleton et al. (17), Geetika Garg et al. (18), and Khan et al. (12). The incidence of fever was significantly higher in the vaginal group patients. Also, the nausea rate following misoprostol use in the vaginal group was 20%, and in the buccal group was 16%. Vomiting rate was 10% in the vaginal group and 4% in the buccal group. In the study of Khan et al. (12), nausea was 14% in buccal, and 10% in vaginal groups and taste change (12%) was an additional negative side effect in the buccal route. They also reported a satisfaction rate of 90% in the vaginal group and 94% in the buccal group.

The main strengths of our study were that it was randomized and included a relatively large sample size in which the effect of buccal misoprostol was compared with the vaginal route. Also, all patients were given misoprostol under obstetrics and gynecology resident instruction in a timely manner. However, this study also has some limitations. We did not evaluate patient satisfaction because participants could not be blinded to the route of treatment, and the outcome of treatment might affect their preference and satisfaction with a particular route. The success rate in our study was also measured by the duration of misoprostol use and the dose required to discharge tissue, while many other studies have considered the success rate as complete abortion without required surgical intervention. Vaginal misoprostol can be more effective in treating first-trimester abortions compared to buccal misoprostol and may be associated with longer duration of use and lower required doses. Further clinical trials with larger sample sizes are recommended to confirm the results of our study.

Conflict of interest

Authors declare no conflict of interest.

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