Original Article

Comparison of Vaginal Versus Sublingual Misoprostol in The Treatment First Trimester Missed Miscarriage

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Abstract

Objective: To assess the efficiency of misoprostol administered sublingually versus vaginally in the treatment of missed miscarriages in the first trimester.

Methodology: This Randomized Controlled Trial study was conducted gynecology and obstetrics department of Akbar Niazi Teaching Hospital, Islamabad from June 2021 to June 2022. In accordance with the FIGO protocol, patients were randomly divided into two groups based on whether misoprostol was administered orally or vaginally. Both the sublingual 600 microgram 3 hourly and the vaginal 800 microgram 3 hourly dosages were used. After 24 hours, patients were checked for vaginal bleeding and expulsion; if neither occurred, the dose was repeated. If significant vaginal bleeding persisted after a maximum of two cycles, surgical evacuation was used to treat the failure of the treatment as determined by the USG. To confirm, an ejection pelvic USG was performed.

Results: The mean age (26.76 ± 5.83 vs. 25.85 ± 5.61), parity (3.21 ± 0.58 vs. 3.42 ± 0.64), gestational age (8.95 ± 1.73 vs. 9.27 ± 1.58) and duration of induction to abortion interval (13.86 ± 3.54 vs. 12.92 ± 3.12) were comparable in both groups, with no statistically significant (P-value > 0.05) difference between groups. Higher no. of doses (4.18 ± 0.95 vs. 3.36 ± 1.13, P-value < 0.05) was required for complete miscarriage in vaginal misoprostol group. A higher level of comfort (P-value < 0.05) during the administration of drug was observed in sublingual group (88.33%) as compared to vaginal misoprostol group (55%). The rate of success was significantly (P-value < 0.05) higher in sublingual misoprostol group (76.67%) in contrast to (58.33%) in vaginal misoprostol group. The side effects like vaginal bleeding (68.33% vs. 93.33%), bleeding > menstruation (31.67% vs. 83.33%), diarrhea (31.67% vs. 60.00%) were found to be significantly (P-value < 0.05) associated with sublingual use of misoprostol.

Conclusions: Sublingual misoprostol is more effective than vaginal misoprostol. Patients respond more favorably to the sublingual route and are more satisfied with it.

Key words: Misoprostol, Sublingual Misoprostol, Vaginal Misoprostol, Miscarriage, First Trimester

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Introduction

The most frequent early pregnancy issue is miscarriage, which is the natural demise of an embryo or foetus before the age of viability or independent survival. Miscarriages happen in about 10-15% of clinical pregnancies, and 80% of them do so in the first trimester. When there is an empty gestational sac measuring 25mm or more, or a foetal pole measuring 7mm or more, without foetal cardiac activity, an ultrasound diagnosis of missed miscarriage is made. To confirm the diagnosis, a follow-up scan should be performed at least seven days (for transvaginal ultrasound) and fourteen days (for transabdominal ultrasound).[1,2]

Miscarriages can occur naturally or be brought on. A spontaneous miscarriage may be complete and not require medical attention, or it may be overlooked or require uterine evacuation. Around 10% of pregnancies

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are complicated by miscarriage, which also causes the pair severe psychological suffering. WHO estimates that 47,000 women die each year due to unsafe abortions, almost majority of which occur in underdeveloped nations where access to safe abortion services is scarce.[3] One of the types of miscarriage where the patient is largely asymptomatic, yet USG demonstrates nonexistent foetal cardiac activity is missed miscarriage, also known as early foetal demise.[4]

Expectant management (waiting for spontaneous ejection), pharmacological management (delivery of misoprostol), and surgical management are available treatments for missed miscarriages (evacuation of the uterus under anaesthesia). The closed cervical os and potential for adhesion of sperm to the uterine wall have raised concerns regarding the modality of treatment. The mental burden of bearing a nonviable foetus is linked to expectant management's high failure rate. Surgical evacuation is a popular and effective treatment for missed miscarriages, although it can cause complications such as uterine perforation, heavy bleeding, infection, cervical damage, and Asherman's syndrome as a late complication.[5,6]

The preferred miscarriage treatment in the past was surgical uterine evacuation, however, in recent years, this approach has undergone significant change. Misoprostol medical management is the most recent treatment available.[7,8] Misoprostol, a prostaglandin E analogue made synthetically, is frequently used for medical miscarriages. It can be administered sublingually, vaginally, or orally.[9]

In addition to the fact that women find vaginal administration uncomfortable, there are a number of issues with vaginal misoprostol, including uneven absorption, which may be improved by dissolving the tablets in water, and incomplete absorption of the tablet even after several hours of administration. Due to its maximum absorption, misoprostol may be most effective when administered sublingually, according to more recent research.[10,11] In this study, the effectiveness of sublingual misoprostol and vaginal misoprostol for the medical management of missed miscarriage was compared.

Methodology

This Randomized Controlled Trial study was conducted gynecology and obstetrics department of Akbar Niazi Teaching Hospital, Islamabad from June 2021 to June 2022. After receiving written consent for medical care, patients who arrived at the gynaecology OPD with a pelvic ultrasound showing a confirmed diagnosis of missed miscarriage in the first trimester were included. The study excluded patients who chose surgical or expectant treatment, had gestational age greater than 13 weeks, and had any co-morbidities.

For the study, a non-probability consecutive sample of 120 women was used, divided into two equal groups of 60 women each. The sample size was determined using the WHO sample size calculator with the following parameters: 5% level of significance, 90% test power, and a total complication rate of 48% vs. 20% in the sub inguinal and vaginal misoprostol groups.[12]

In accordance with the FIGO protocol, patients were randomly divided into two groups based on whether misoprostol was administered orally or vaginally. Both the sublingual 600 microgram 3 hourly and the vaginal 800 microgram 3 hourly dosages were used. After 24 hours, patients were checked for vaginal bleeding and expulsion; if neither occurred, the dose was repeated. If significant vaginal bleeding persisted after a maximum of two cycles, surgical evacuation was used to treat the failure of the treatment as determined by the USG. To confirm, an ejection pelvic USG was performed. Following admission, coagulation testing and a baseline investigation were carried out. Information about demographics was logged. Patients were evaluated based on how long it took for the conceptus to completely expel. Patient satisfaction, the number of dosages needed, the need for surgical evacuation, the need for blood transfusion, and side effects of misoprostol such shivering, fever, diarrhoea, and oral ulcers etc, were noted.

For analysis, all the gathered data was entered into SPSS v. 21. The mean and standard deviation of quantitative data were shown. To compare the quantitative factors [such age and gestational age] between the two groups, an independent sample t-test was used. For qualitative data, frequency with percentages was determined, and the chi-square test was performed to compare the qualitative variables (such complications and abortion) between the two groups. P-values under 0.05 were considered significant.

Results

In this randomized controlled trial study, a total of 120 patients were included, 60 patients in vaginal misoprostol group and Sublingual misoprostol group. The mean age of both groups was comparable (26.76 ±

5.83 vs. 25.85 ± 5.61) without any statistically significant (P-value > 0.05) difference. The mean parity was also similar in both groups (3.21 ± 0.58 vs. 3.42 ± 0.64, P-value > 0.05) without any significant difference. Similarly, the mean gestational age was also equal in both groups (8.95 ± 1.73 vs. 9.27 ± 1.58) having no statistically significant (P-value > 0.05) difference in both groups as shown in table I.

Table I: Demographic Characteristics of the women.

Characteristics	Vaginal Misoprostol	Sublingual Misoprostol	P-value
Age of the women			
Mean ± SD	26.76 ± 5.83	25.85 ± 5.61	0.385
Parity			
Mean ± SD	3.21 ± 0.58	3.42 ± 0.64	0.058
Gestational Age			
Mean ± SD	8.95 ± 1.73	9.27 ± 1.58	0.284

There was no any statistically significant (P-value > 0.05) difference in the duration of the induction to abortion interval (13.86 ± 3.54) of vaginal misoprostol when compare with (12.92 ± 3.12) sublingual misoprostol group. The mean value of the doses required for complete miscarriage was significantly (P-value < 0.05) higher in vaginal misoprostol group (4.18 ± 0.95) as compared to sublingual misoprostol group having mean value of (3.36 ± 1.13). The comparison of level of comfort during the administration of drug in both groups showed that the comfort level was significantly (P-value > 0.05) higher in sublingual group (88.33%) as compared to vaginal misoprostol group (55%) as shown in table II.

Table II: Comparison of induction to abortion interval, doses required and level of comfort between both groups

Characteristics	Vaginal Misoprostol	Sublingual Misoprostol	P-value
Induction to Abortion interval			
Mean ± SD	13.86 ± 3.54	12.92 ± 3.12	0.125
Doses required for complete miscarriage			
Mean ± SD	4.18 ± 0.95	3.36 ± 1.13	0.000*
Level of comfort during administration of the drug			
Comfortable	33 (55%)	53 (88.33%)	0.000*
Uncomfortable	27 (45%)	7 (11.67%)	

* Significant at 5% level of significance

The main comparison of efficacy of the drug in both groups was made on the basis of complete abortion of all the residuals of pregnancy from the uterus and it was found that the rate of success was significantly (P-value < 0.05) higher in sublingual misoprostol group (76.67%) in contrast to (58.33%) in vaginal misoprostol group as elaborated in table III.

The comparison of side effects showed that many side effects were significantly higher in sublingual misoprostol group as compared to vaginal misoprostol group. The side effects like vaginal bleeding (68.33% vs. 93.33%), bleeding > menstruation (31.67% vs. 83.33%), diarrhea (31.67% vs. 60.00%) were found to be significantly (P-value < 0.05) associated with sublingual use of misoprostol. Some other side effects including cramp pain, severe pain, vomiting, and fever were not significantly (P-value > 0.05) different in both groups as shown in table IV.

Table IV: Comparison of side effect in both groups

Side effects	Vaginal Misoprostol	Sublingual Misoprostol	P-value
Patient with vaginal bleeding	41 (68.33%)	56 (93.33%)	0.000*
Bleeding > menstruation	19 (31.67%)	50 (83.33%)	0.000*
Bleeding ≤ menstruation	41 (68.33%)	10 (16.67%)	
Cramp pain	38 (63.33%)	43 (71.67%)	0.949
Severe pain	9 (15.00%)	15 (25.00%)	0.171
Vomiting	8 (13.33%)	13 (21.67%)	0.230
Diarrhea	19 (31.67%)	36 (60.00%)	0.002*
Fever	13 (21.67%)	21 (35.00%)	0.105

Discussion

An accidental pregnancy termination prior to 20 weeks of gestation occurs because of the pathologic process known as abortion. A missed abortion is a nonviable intrauterine pregnancy with a closed cervix, cramping in the abdomen, or neither. About 15% of all clinically identified pregnancies have this incidence rate.[13] The usual way of treating missed abortions is surgical dilatation and curettage or manual vacuum aspiration (MVA). Despite the fact that MVA and dilatation and curettage are extremely effective techniques, these techniques nevertheless have a high risk of anesthesia-related problems, uterine infections, uterine perforation with or without damage to nearby organs, and Asherman's syndrome.[14]

Patients who are scared of surgery and anaesthesia and wish to avoid any surgical intervention may find that

Table III: Comparison of efficacy of both groups

Complete Miscarriage	Vaginal Misoprostol	Sublingual Misoprostol	Total	P-value
Successful	35 (58.33%)	46 (76.67%)	81 (67.5%)	0.032*
Unsuccessful	25 (41.67%)	14 (23.33%)	39 (32.5%)	
Total	60 (100%)	60 (100%)	120	

vaginal misoprostol in the case of a first trimester miscarriage is a suitable choice. In this investigation, the remaining gestational products were surgically evacuated the following day, however it is also feasible to observe more without surgery. The rate of effective medical treatment would have been higher if the patients in the unsuccessful medical therapy group had taken more misoprostol and held off for a few extra days.[15]

In our study, sublingual misoprostol administration led to a considerably greater success rate (76.67%) compared to the vaginal misoprostol group (58.33%) in the medical management of missed abortion. The sublingual approach also avoids the discomfort that many women experiences while using it vaginally. The study's findings are comparable to those of other local studies, including one by Tang OS from Bahawalpur that found a success rate of 73.3% in the sublingual group and 66.7% in the vaginal group[16] and one by Ehsan N from Quetta that found that 72% of women in the sublingual group and 63% in the vaginal group experienced complete miscarriage.[17]

In our study, the comparison of side effects showed that some adverse effects were significantly higher in sublingual misoprostol group as compared to vaginal misoprostol group. The side effects like vaginal bleeding (68.33% vs. 93.33%), bleeding > menstruation (31.67% vs. 83.33%), diarrhea (31.67% vs. 60.00%) were found to be significantly (P-value < 0.05) associated with sublingual use of misoprostol. These results are in agreement with the previous studies like study by Tanha et al, found that although the effectiveness was high in the sublingual group than in vaginal group (sublingual 84.5 %, vaginal 46.4%, P = 0.000) the sublingual group experienced higher rate of bleeding, pain severity, diarrhea and fever.[18] Similarly, Shirma P, et al also found higher efficacy in sublingual group along with higher rate of complications including altered taste (62% vessus4%) vomiting (20 versus 10%), and diarrhea (10% versus 4%).[19]

Sublingual misoprostol is just as efficient as vaginal misoprostol at resulting in a full miscarriage, although it is linked to more frequent diarrhoea, according to a systematic review of the Cochrane database. 16 Because of its high peak concentration and high absorption, misoprostol causes side effects more frequently when taken sublingually.[20] Misoprostol can be used to control early pregnancy loss since it is non-invasive, reliable, and secure. It can be administered sublingually or vaginally. The sublingual route of administration is just as efficient as the vaginal group, and it offers more comfortable dose, greater privacy, and easily controllable adverse effects.

Conclusion

When treating missed miscarriages in the first trimester, sublingual misoprostol is more effective than vaginal misoprostol. Patients respond more favorably to the sublingual route and are more satisfied with it, but it was found to be associated with an increased risk of side effects especially vaginal bleeding, bleeding > menstruation and diarrhea. It offers abortion care that is acceptable, safe, and efficient in both high- and low-resource environments.

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