COMPARISON OF VAGINAL VERSUS SUBLINGUAL MISOPROSTOL IN THE TREATMENT OF FIRST-TRIMESTER MISSED MISCARRIAGES

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ABSTRACT

OBJECTIVES

To evaluate the efficacy of sublingual versus vaginal misoprostol for the treatment of missed miscarriages in the first trimester of pregnancy.

METHODOLOGY

The gynecology and obstetrics department of Khyber Teaching Hospital in Peshawar conducted this Randomized Controlled Trial investigation from January 2021 to December 2023. Two groups of patients were formed, according to the FIGO procedure, based on whether misoprostol was given vaginally or orally. The dosages of 800 micrograms were administered vaginally to the first group and sublingually to the second group every three hours. Patients were observed for vaginal bleeding and evacuation after 24 hours; if neither happened, the dose was repeated.

RESULTS

The groups did not differ statistically (P-value > 0.05). The mean age of the patients (26.56 ± 5.73 versus 25.45 ± 5.63), parity of the patients (3.31 ± 0.56 versus 3.22 ± 0.54), period of gestation (8.85 ± 1.63 versus 9.37 ± 1.48), and time from initiation of induction till expulsion (13.68 ± 3.52 versus 12.94 ± 3.45) were similar in both groups. For a complete miscarriage in the vaginal misoprostol group, more doses (4.28 ± 0.65 vs 3.26 ± 1.23, P-value < 0.05) were needed. In comparison to the vaginal misoprostol group (56%), the sublingual group (91.6%) reported feeling more comfortable (P-value < 0.05) throughout the drug's administration. The sublingual misoprostol group had a considerably (P-value < 0.05) better success rate (77.66%) compared to the vaginal misoprostol group (56.32%). Such adverse effects as bleeding during menstruation (68.33% versus 93.33%), vaginal bleeding (31.66% versus 84%), and diarrhoea (30.57% vs 59%) had significant (P-value < 0.05) association with sublingual misoprostol.

CONCLUSION

The efficacy of sublingual misoprostol surpasses vaginal misoprostol. Patients are more satisfied and respond more favourably to the sublingual approach.

KEYWORDS: *Miscarriage, Misoprostol, Mifepristone, Uterine Evacuation, Manual Vacuum Aspiration, Gestational Age*

INTRODUCTION

A missed abortion occurs when an embryo or fetus dies within the uterus.[1] Any therapy, including induced abortion, should meet the highest criteria of accessibility, affordability, safety, and patient acceptance. A synthetic prostaglandin E1 analogue called misoprostol encourages the ripening of the cervix and the contraction of the uterine smooth muscle. There are three routes of administration available: sublingual, vaginal, and oral.[2] Previous studies have looked at the consequences of giving misoprostol and have identified advantages and disadvantages related to each approach.[3] While no appreciable difference in the results of oral and vaginal methods was noted, other studies showed that the vaginal route was more successful.[4] The vaginal and sublingual methods were almost equivalent in treatment success rates; nevertheless, sublingual delivery is linked to a greater prevalence of adverse drug reactions, such as fatigue and diarrhea.[5] Miscarriages may happen on their own or be induced. Miscarriage complicates around 10% of pregnancies and creates severe psychological distress for the couple. According to WHO estimates, unsafe abortions are responsible for significant maternal mortality, the vast majority of which take place in developing countries where access to safe abortion services is limited Missed miscarriage, sometimes called early foetal demise, is a type when the fetus is seen on USG but shows no fetal heart activity.[6,7] Missed miscarriages may be treated surgically, which

involves removing the products of conception from the uterus while under anaesthesia, with the administration of misoprostol, and expectantly, which consists in waiting for spontaneous ejection.[8] The psychological effect of having a dead fetus is associated with the unsuccessful expectant management.[10] Although surgical evacuation is a popular and effective therapy, there is an association with postprocedure heavy bleeding, infection, damage to the cervical region, and Asherman‟s syndrome.[9] The recommended course of treatment for miscarriages used to be surgical uterine evacuation. However, things have evolved dramatically in the last several years. Misoprostol is the most current treatment modality. Misoprostol is a prostaglandin E that is often administered for termination of miscarriages. This is used sublingually, via the vaginal route, and orally.[8,9] Although misoprostol can be used with different roots, including oral, sublingual and vaginal, however, a few evidences are available on drug effectiveness as well as its related side effects when used in different roots. Hence, the present study aimed to compare the efficacy of misoprostol in first -trimester abortion through two sublingual and vaginal routes of administration.

METHODOLOGY

This randomized controlled trial was conducted in the Gynae department of Khyber Teaching Hospital in Peshawar between January 2021 and December 2023. Written informed consent for medical intervention was taken. Patients attending the Outpatient Department with a final diagnosis of missed miscarriage presenting in the first trimester of pregnancy were the inclusion criteria. The research did not include any patients with co-morbidities, a gestational age higher than 13 weeks, or who chose surgical or expectant therapy. Because of the small sample size, block randomization was performed according to the time of admission. Single blind allocation and intervention were conducted by a medical officer working in the gynae A unit. A non-probability consecutive sampling technique was used, and a sample of 120 women was taken, further classified into two groups of 60 women each. The sample size was calculated, taking a total complication rate of 48% as compared to 20% in the sublingual and vaginal misoprostol groups. 90% confidence interval and a 5% margin of error were observed. Depending on whether misoprostol was given sublingually or vaginally, patients were randomly divided into two groups per the FIGO technique. The dosages of 800 micrograms 3 hours vaginally and 800 micrograms 3 hours sublingually were used. After 24 hours, all the women were evaluated for bleeding per vaginum and, therefore, evacuation. In case none of these occurred, the dosage was administered again. When after completion of two cycles of misoprostol, the bleeding continued to appear, evacuation was performed. For confirmation, a pelvic sonogram was performed. After admitting the patient, baseline evaluation and coagulation tests were conducted. Demographic information was recorded. The patients were evaluated from the time of initiation of administration of misoprostol till complete evacuation of the uterus was done, which was confirmed by doing pelvic ultrasound for retained products. Total misoprostol doses, bleeding per vaginum in excess or less than menses, evacuation of the uterus, and misoprostol side effects - such as chills, pain, fever and diarrhoea were recorded. The mean and standard deviation were calculated for the quantitative data. The age and gestation period were compared between the two groups, and an independent sample t-test was performed. Percentages were used to determine the frequency of qualitative data, and the chi-square test was performed to compare the qualitative variables among the two groups. P-values were significant if < 0.05.

RESULTS

Table 1: Demographic Characteristics

Characteristics	Vaginal Misoprostol	Sublingual Misoprostol	P- Value
Age of the women			
Mean ± SD	26.56 ± 5.73	25.45 ± 5.63	0.384
Parity			
Mean ± SD	3.31 ± 0.56	3.22 ± 0.54	0.057
Period of Gestation			
Mean ± SD	8.85 ± 1.63	9.37 ± 1.48	0.283

Table 2: Comparison of Initiation of Termination to Miscarriage Duration, Doses Needed and Satisfaction Level among both Groups

Characteristics	Vaginal Misoprostol	Sublingual Misoprostol	P- Value
Initiation of termination to miscarriage duration			
Mean ± SD	13.68 ± 3.52	12.94 ± 3.45	0.124
Doses needed for complete abortion			
Mean ± SD	4.28 ± 0.65	3.26 ± 1.23	0.000*
Level of satisfaction regarding the route of administration			
Comfortable	34 (56%)	55 (91.6%)	0.000*
Uncomfortable	26(44%)	05(8.3%)	

* Significant at a 5% level of significance

Table 3: Comparison of Efficacy of both Groups

Complete Miscarriage	Vaginal Misoprostol	Sublingual Misoprostol	Total	P-Value
Successful	34 (56.32%)	47 (77.66%)	81 (67.5%)	0.032*
Unsuccessful	26 (42%)	13 (22.33%)	39 (32.5%)	
Total	60 (100%)	60 (100%)	120	

Table 4: Comparison of Adverse Effects in Both Groups

Adverse effects	Vaginal Misoprostol	Sublingual Misoprostol	P-Value
Vaginal bleeding	42 (68.33%)	56 (93.33%)	0.000*
P/v bleeding more than menses	19 (31.66%)	50 (84%)	0.000*
P/v bleeding less than menses	42 (68.32%)	10 (15.66%)	
Abdominal Cramping	37 (63.32%)	44 (72.67%)	0.949
Intolerable pain	09 (15.40%)	16 (25.00%)	0.171
Vomiting	07 (13.33%)	14 (21.67%)	0.230
Diarrhea	18 (30.67%)	37 (59%)	0.002*
Pyrexia	12 (21.67%)	22 (35.00%)	0.105

DISCUSSION

In the present research, surgical curettage was not necessary since induction resulted in a complete abortion in most cases during the first 24 hours of therapy. The sublingual group had a greater success rate for abortions than the vaginal group when the treatment results of the two groups were compared. Research has shown that taking drugs under the tongue increases their effectiveness. Similar results regarding the medication‟s effectiveness for two routes are seen, according to research by Kapp N, as long as the dose and interval of drug administration in the sublingual and vaginal procedures are carried out correctly.[11,12] According to Munn Z‟s study, there isn't any valuable data that compares the efficiency of the oral and vaginal procedures between weeks 9 and 12 of pregnancy, yet, the vaginal approach has generally been claimed to have a higher success rate. Furthermore, the sublingual technique reduces the pain that many women experience while taking it vaginally. The results of the study are consistent with those of other local studies, according to Bracken H, who found that the sublingual group had a success rate of 73.3% and the vaginal group had a success rate of 66.7%, and Libei D, who found that sublingual group had a success rate of 72% and the vaginal group had a success rate of 63%.[14,15] Chu JJ's study indicates that sublingual administration has higher success rates than oral and vaginal methods in the first 24 hours after induction. Treatment failure was defined as the residual volume of retained products more than 10 mm at the end of the first induction week. The oral group had the highest failure rate and the highest requirement for surgical curettage. This is pertinent in terms of medicine. Similar findings were reported in this aspect by the same research.[16] The vaginal group had the longest bleeding time, while the sublingual group had the worst haemorrhage. This might have significant clinical implications. Between the three groups, there was no appreciable variance in haemoglobin levels. The sublingual group‟s haemoglobin levels (less than 10 g/dl) decreased most. When we examined the side effects of the two groups the vaginal and sublingual misoprostol groups-we found that several of the adverse effects were notably more common in the former. Bleeding per vaginum (68.33% vs 93.33%), excessive menstrual blood loss (31.67% vs 83.33%), and lose motions (31.66% vs 84%) were among the adverse effects that were shown to be substantially (P-value <0.05) related to the misoprostol used sublingually. These results contrast with previous studies, like one by Stanuloy J, which showed that the sublingual group was more effective than the vaginal group (sublingual 84.5%, vaginal 46.4%, P = 0.000), there was a higher incidence of bleeding, pain intensity, fever, and diarrhoea in the sublingual group.[17] Schiavou JH also reported diarrhoea (10% against 4%), vomiting (20 versus 10%), and changed taste (62% versus 4%). This study suggests that the vaginal method with the lowest rate of complications was safer than the other routes, despite some studies showing the same frequency of problems for both oral and vaginal routes.[18] Numerous studies have reported differing rates of medication-related issues; these differences are probably due to differences in dosage, time between doses, number of doses, and drug pharmacokinetics.[19,20] The study‟s findings suggest that misoprostol is more effective in uterine evacuation during the first trimester of pregnancy when compared to other pharmaceutical administration strategies. Misoprostol is inexpensive, widely accessible, and stable at room temperature. In terms of pharmacokinetic characteristics, misoprostol delivered vaginally has the lowest frequency of issues and the most effective therapeutic efficacy within the first 24 hours after induction. The biggest drawback of the research was that the patient knew the treatment plan, making it impossible to keep the inquiry blind. However, the main advantage of this research was its relatively large sample size, which produced more precise and impactful findings. Another interesting aspect of this research that makes a variety of outcomes in different ways is a comparison of the two methods of misoprostol administration.

LIMITATIONS

This study has several limitations. First, the sample size may not be large enough to generalize the findings to all populations. The study was conducted in a single center, which could introduce institutional biases and limit the external validity of the results. Additionally, the trial only evaluated the immediate effects of misoprostol, without considering long-term outcomes or potential complications. The use of subjective measures, such as patient comfort and satisfaction, may be influenced by individual perceptions, and the study

did not account for potential confounding factors like comorbidities or prior pregnancies.

CONCLUSIONS

Sublingual misoprostol is a more successful medication than vaginal misoprostol for treating missed miscarriages in the first trimester. Patients reported improved outcomes and higher levels of satisfaction with the sublingual method. The sublingual approach has been shown to have a more significant possibility of adverse effects, such as vaginal haemorrhage, blood loss in excess of menses, and loose motions, but patients react more positively and are more happy with it. It offers safe, efficient, and socia lly acceptable abortion treatment in environments with and without resources.

CONFLICT OF INTEREST: None

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CONTRIBUTORS

1. ***Maimoona Qadir*** - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval*

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