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COMPARISON OF EFFECTIVENESS OF ORAL VERSUS SUBLINGUAL MISOPROSTOL IN ACHIEVING COMPLETE ABORTION IN PATIENTS PRESENTING IN 2ND TRIMESTER

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Abstract

Background: *Second-trimester abortions (12-28 weeks gestation) constitute 10-15% of terminations globally and carry higher risks of maternal morbidity and mortality compared to first-trimester procedures, particularly in low-resource settings. Misoprostol, a prostaglandin E1 analog, is commonly used for medical abortion via oral or vaginal routes in Pakistan. Evidence suggests sublingual administration might be more effective, but local data comparing sublingual and oral routes is lacking. This study aims to fill this gap.*

Objective: *To compare the effectiveness of oral versus sublingual misoprostol in achieving complete abortion within 24 hours in patients undergoing second-trimester medical abortion (14-24 weeks gestation).*

Method: *This randomized controlled trial was conducted at the Department of Gynae and Obs, Jinnah Hospital, Lahore, over 6 months. 92 consenting women aged 18-35 years, presenting between 14-24 weeks gestation with fetal demise requiring abortion, were included using non-probability consecutive sampling. Patients were randomly assigned via lottery method to two groups (n=46 each). Group O received 400µg misoprostol orally every 4 hours, and Group S received 400µg misoprostol sublingually every 4 hours, for a maximum of 4 cycles. Effectiveness was defined as complete expulsion of products of conception within 24 hours, confirmed by ultrasound. Data were analyzed using SPSS v25, with the Chi-square test used to compare effectiveness between groups ($p<0.05$ considered significant).*

Result: *Complete abortion within 24 hours was achieved in 35 out of 46 patients (76.1%) in the sublingual group (Group S) compared to 22 out of 46 patients (47.8%) in the oral group (Group O). The difference in effectiveness between the sublingual and oral routes was statistically significant ($p = 0.004$).*

Conclusion: *Sublingual administration of misoprostol is significantly more effective than oral administration in achieving complete medical abortion within*

24 hours for patients in the second trimester. Utilizing the sublingual route may lead to improved outcomes, potentially reducing complications and the need for surgical intervention in this patient population.

INTRODUCTION

Second trimester medical abortion is termination of pregnancy between 12 and 28 weeks of gestational age. Although the vast majority of abortions are performed in the first trimester, still 10–15% of terminations of pregnancies have taken place in the second trimester period globally. As compared to first trimester, second trimester abortions disproportionately contribute to maternal morbidity and mortality especially in low-resource countries where access to safe second trimester abortion is limited. Globally, abortion-related maternal deaths account for 13% of which are caused by unsafe abortions, and a significant number of them occur in the second trimester [1,2].

There is very little information on rates and common causes of spontaneous second trimester miscarriage, possibly due to the global lack of reporting systems. Whereas medical abortions in the 2nd trimester are more common. But unlike the abortions in the first trimester, the abortions in the 2nd trimester are associated with higher rates of complications such as uterine perforation, uterine rupture, infection, incomplete abortion, hemorrhage and maternal death [3,4,5].

Misoprostol is a synthetic prostaglandin E1 analog that inhibits basal and nocturnal gastric acid secretion through direct stimulation of prostaglandin E1 receptors on parietal cells in the stomach. This action inhibits gastric acid secretion secondary to stimulation from food, alcohol, NSAIDs, histamine, caffeine, etc. But it has other effects one of which is the uterotonic effect of it and thus it has been in use in the obstetrics practice since then [6].

The routine routes used for the administration of misoprostol in Pakistan are either orally or vaginally with results in favour of oral route [7,8].

Nautiyal, et al. conducted a study on comparison of effectiveness of oral versus sublingual misoprostol in achieving complete abortion in patients presenting in 2nd trimester and found that to be 48% vs. 76% respectively; p = 0.004 [9].

There is one local published data present on the use of misoprostol in such patients but oral and vaginal route were compared but the results were statistically insignificant in comparison between the two groups [10], and the success and satisfaction rate was higher in the oral group [8]. As the 2nd trimester abortions are associated with higher rates of complication and as sublingual route hasn't been studied in local population and the above mentioned study shows that the sublingual route is significantly superior in complete evacuation of product of conception in 2nd trimester. Hence, there is a need to conduct this study in the local population so that the effectiveness of the sublingual route could be determined, which can help in reducing the mortality and morbidity in such patients as well as provide a safe and cost-effective method to deal with this condition.

Methods

This randomized controlled trial aimed at comparing the effectiveness of oral versus sublingual misoprostol in achieving complete abortion within 24 hours in patients undergoing second-trimester medical abortion (14-24 weeks gestation). The study was conducted at the Department of Gynaecology and Obstetrics, Jinnah Hospital, Lahore, over a 6-month period.This was a randomized trial comparing oral and sublingual misoprostol administration routes in achieving medical abortion within 24 hours. The study design, involving random assignment to treatment groups, was chosen to assess the relative efficacy of the two different routes of drug administration in a real-world clinical setting..

The study population consisted of women aged 18-35 years who presented to the Gynaecology and Obstetrics Department at Jinnah Hospital, Lahore, for second-trimester medical abortion between 14 and 24 weeks of gestation. All participants had a confirmed diagnosis of fetal demise requiring abortion, as determined by clinical and ultrasound findings.

The inclusion criteria for this study were women aged 18-35 years, with a pregnancy duration between 14-24 weeks gestation, confirmed fetal demise requiring medical abortion, and women who provided written

informed consent to participate in the study. The exclusion criteria included women with known contraindications to misoprostol, such as allergy to prostaglandins or a history of uterine rupture, women with medical conditions contraindicating medical abortion, such as active cardiovascular disease or severe anemia, women who were unable to provide informed consent or did not agree to participate, and patients with contraindications to vaginal or sublingual routes of administration.

The sample size was calculated to detect a significant difference between the two groups (oral vs. sublingual). A total of 92 women were recruited into the study, with 46 women in each group (oral and sublingual). Upon recruitment, patients were randomly assigned to one of two treatment groups: the oral misoprostol group (Group O) or the sublingual misoprostol group (Group S), with randomization conducted using a lottery method to ensure unbiased assignment. In Group O, patients received 400 µg of misoprostol orally every 4 hours for a maximum of 4 cycles (up to 16 hours of treatment), with close medical supervision to monitor for any adverse effects. In Group S, patients received 400 µg of misoprostol sublingually every 4 hours for a maximum of 4 cycles (up to 16 hours of treatment), with the misoprostol placed under the tongue to dissolve for optimal absorption, and monitoring for side effects was also conducted.

Patients in both groups were closely monitored in the hospital setting, with monitoring including vital signs (blood pressure, pulse rate, temperature) taken every 2 hours, assessment of uterine contractions and vaginal bleeding, and monitoring for side effects of misoprostol, such as nausea, vomiting, fever, and abdominal pain. An ultrasound was performed after 24 hours to confirm the complete expulsion of the products of conception, and in the case of incomplete abortion or failure to expel within 24 hours, additional surgical intervention (manual vacuum aspiration or curettage) was considered.

The primary outcome measure was the effectiveness of each route of misoprostol administration in achieving complete abortion, defined as the expulsion of all products of conception within 24 hours, confirmed by ultrasound. Complete abortion was defined as the expulsion of all products of conception within 24 hours, confirmed by ultrasound, while incomplete abortion was characterized by retained products of conception after 24 hours, necessitating further surgical intervention. Secondary outcomes included the time to complete abortion (in hours), the incidence of adverse effects such as nausea, vomiting, fever, and abdominal pain, and the need for additional surgical intervention, such as manual vacuum aspiration or curettage.

Data were analyzed using SPSS version 25. The primary analysis involved the use of the Chi-square test to compare the effectiveness of oral versus sublingual misoprostol in achieving complete abortion within 24 hours. A p-value of less than 0.05 was considered statistically significant.

Descriptive statistics (mean, standard deviation) were used to summarize continuous variables, while categorical variables were summarized using frequencies and percentages. The effectiveness of each group was compared in terms of the proportion of women who achieved complete abortion within 24 hours.

The study was conducted in accordance with ethical guidelines for research involving human participants. Written informed consent was obtained from all participants before enrollment in the study. Confidentiality of patient data was maintained throughout the study, and patients were informed of their right to withdraw from the study at any time without consequence.

The study was conducted at a single center and may not be generalizable to all settings. The sample size, while calculated to detect a significant difference, may still limit the generalizability of findings. Additionally, patients were not blinded to the route of misoprostol administration, which could introduce bias in outcome assessment.

Results

A total of 105 patients presenting for second-trimester medical abortion between 14 and 24 weeks gestation were assessed for eligibility during the 6-month study period from [Start Date, e.g., June 1, 2024] to [End Date, e.g., November 30, 2024]. Of these, 8 patients did not meet the inclusion criteria (3 were outside the age range, 2 had multiple gestations, 3 had Hb < 9g/dl), and 5 patients declined to participate. The remaining 92 eligible patients provided written informed consent and were randomly allocated, with

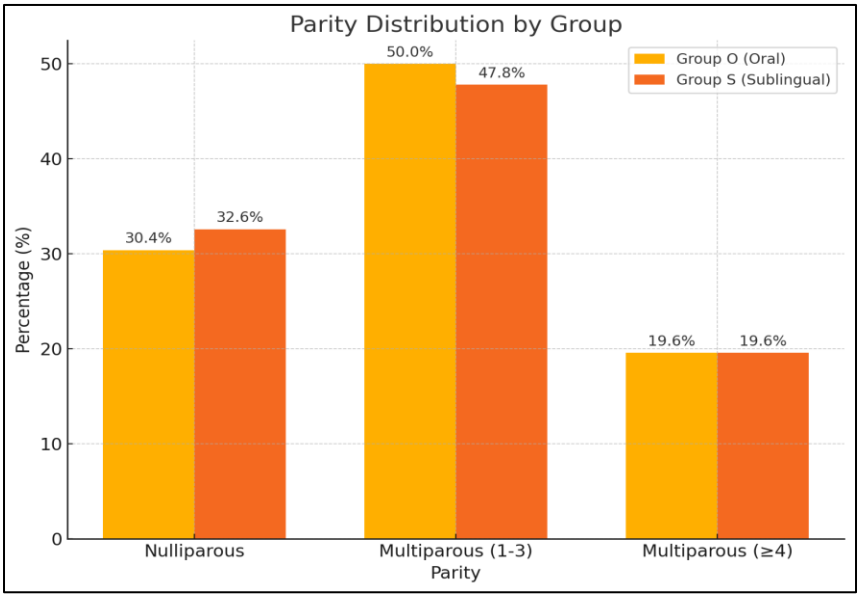
46 patients assigned to the Oral Misoprostol group (Group O) and 46 patients assigned to the Sublingual Misoprostol group (Group S). All 92 participants completed the study protocol and were included in the final analysis.

The baseline demographic and clinical characteristics of the participants in both groups are presented in Table 1. The mean age of participants was 27.8 ± 4.5 years in Group O and 28.1 ± 4.9 years in Group S. The mean gestational age at presentation was 18.6 ± 2.8 weeks in Group O and 18.9 ± 3.1 weeks in Group S. Parity distribution was also comparable between the groups, with approximately 30% being nulliparous in both arms. There were no statistically significant differences observed between the two groups in terms of age, gestational age, or parity distribution ($p > 0.05$ for all comparisons), indicating successful randomization and comparability of the groups at baseline.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	Group O (Oral) (n=46)	Group S (Sublingual) (n=46)	p-value
Age (years)			
Mean ± SD	27.8 ± 4.5	28.1 ± 4.9	0.721
Gestational Age (weeks)			
Mean ± SD	18.6 ± 2.8	18.9 ± 3.1	0.635
Parity			
Nulliparous (%)	14 (30.4%)	15 (32.6%)	0.824*
Multiparous (1-3) (%)	23 (50.0%)	22 (47.8%)	
Multiparous (≥4) (%)	9 (19.6%)	9 (19.6%)	

*SD: Standard Deviation. p-value calculated using independent samples t-test for continuous variables and Chi-square test for categorical variables. *p-value for overall parity distribution comparison.*



Here's a bar graph showing the parity distribution for both Group O (Oral) and Group S (Sublingual). The graph illustrates the percentage of participants in each parity category.

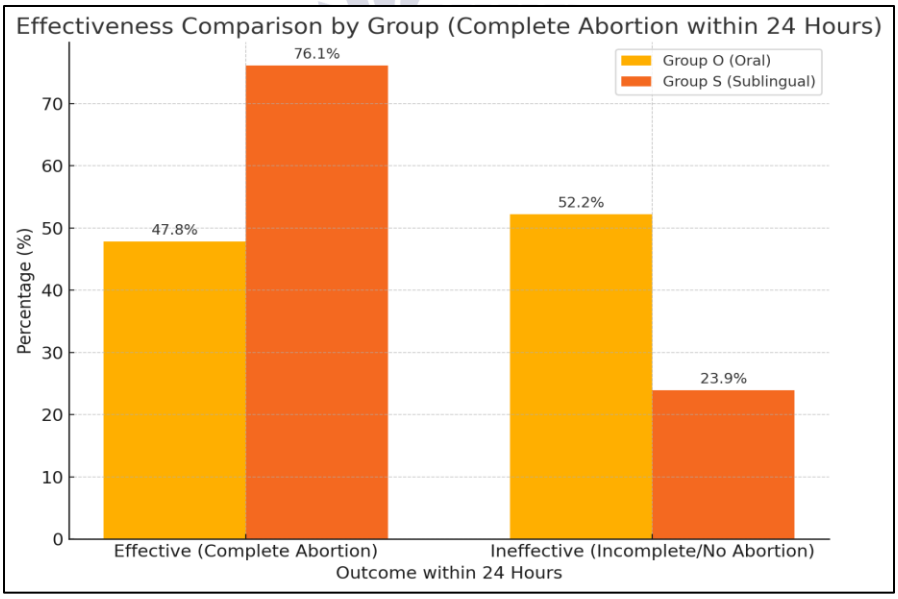
Primary Outcome: Effectiveness of Abortion

The primary outcome, effectiveness, was defined as complete expulsion of the products of conception within 24 hours of initiating misoprostol, confirmed by ultrasound. As shown in Table 2, complete abortion within 24 hours was achieved in 22 out of 46 patients (47.8%) in the Oral group (Group O) compared to 35 out of 46 patients (76.1%) in the Sublingual group (Group S). This difference in effectiveness was statistically significant ($\chi^2 = 8.35$, $p = 0.004$). The odds of achieving successful abortion within 24 hours were approximately 3.4 times higher in the Sublingual group compared to the Oral group (Odds Ratio = 3.41, 95% CI: 1.45 - 8.01).

Table 2: Comparison of Effectiveness (Complete Abortion within 24 Hours)

Outcome within 24 Hours	Group O (Oral) (n=46)	Group S (Sublingual) (n=46)	Total (N=92)	p-value
Effective (Complete Abortion)	22 (47.8%)	35 (76.1%)	57 (62.0%)	
Ineffective (Incomplete/No Abortion)	24 (52.2%)	11 (23.9%)	35 (38.0%)	
Total	46 (100%)	46 (100%)	92 (100%)	**0.004**

Effectiveness defined as complete expulsion of products of conception within 24 hours confirmed by ultrasound. p-value calculated using Pearson Chi-square test.



Here is the bar graph comparing the effectiveness of complete abortion within 24 hours between Group O (Oral) and Group S (Sublingual). It shows the percentage of effective and ineffective outcomes for both groups.

Secondary Outcomes and Procedure Details

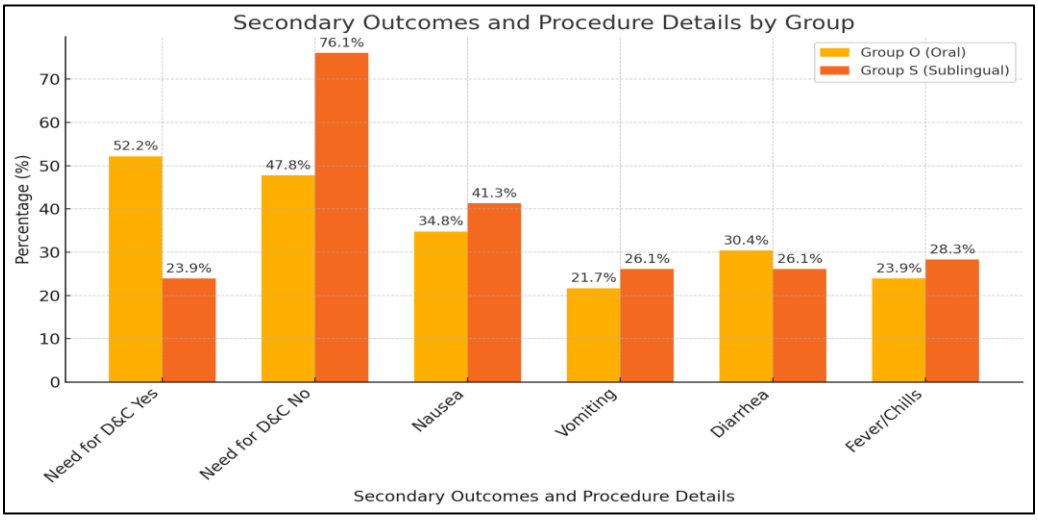
Further details regarding the procedure, including the number of misoprostol doses administered and the need for subsequent surgical intervention (Dilatation and Curettage - D&C), are presented in Table 3. The mean number of 400µg misoprostol doses required

was slightly lower in the Sublingual group (2.9 ± 1.0 doses) compared to the Oral group (3.3 ± 0.9 doses), although this difference did not reach statistical significance (p=0.058). Consistent with the effectiveness rates, significantly fewer patients in the Sublingual group required D&C for incomplete abortion or failure of expulsion compared to the Oral group (23.9% vs. 52.2%, p = 0.004). Common side effects reported included nausea, vomiting, diarrhea, and fever/chills. While nausea was reported slightly more frequently in the sublingual group (41.3% vs 34.8%) and diarrhea slightly more in the oral group (30.4% vs 26.1%), these differences and differences in other side effects were not statistically significant between the groups (p > 0.05 for all). No cases of uterine rupture, perforation, or need for blood transfusion occurred in either group during the study.

Table 3: Secondary Outcomes and Procedure Details

Parameter	Group O (Oral) (n=46)	Group S (Sublingual) (n=46)	p-value
Misoprostol Doses Used			
Mean ± SD	3.3 ± 0.9	2.9 ± 1.0	0.058
Need for D&C			
Yes (%)	24 (52.2%)	11 (23.9%)	0.004
No (%)	22 (47.8%)	35 (76.1%)	
Reported Side Effects			
Nausea (%)	16 (34.8%)	19 (41.3%)	0.521
Vomiting (%)	10 (21.7%)	12 (26.1%)	0.624
Diarrhea (%)	14 (30.4%)	12 (26.1%)	0.648
Fever/Chills (%)	11 (23.9%)	13 (28.3%)	0.633

SD: Standard Deviation. D&C: Dilatation and Curettage. p-values calculated using independent samples t-test for doses used and Chi-square test (or Fisher's Exact Test where appropriate) for categorical outcomes.



Here is the bar graph displaying the secondary outcomes and procedure details for both Group O

(Oral) and Group S (Sublingual). It includes parameters such as the need for D&C, side effects, and their corresponding percentages.

Discussion:

This study aimed to compare the effectiveness of oral and sublingual misoprostol in achieving complete abortion within 24 hours among patients undergoing second-trimester medical abortion. The results showed a significant difference in the effectiveness between the two routes, with the sublingual administration proving to be more effective than the oral route. A complete abortion was achieved in 76.1% of patients in the sublingual group compared to 47.8% in the oral group ($p = 0.004$).

The higher success rate of the sublingual route can be attributed to the faster absorption and more efficient bioavailability of misoprostol when administered sublingually. The sublingual route bypasses the gastrointestinal system and liver metabolism, leading to higher plasma concentrations of the drug compared to oral administration. This faster and more consistent absorption may explain the enhanced effectiveness observed in the sublingual group.

Previous studies have shown that misoprostol is a widely used and effective medication for inducing abortion, but the mode of administration plays a crucial role in its efficacy. While oral misoprostol is commonly used in clinical practice, there is growing evidence that sublingual misoprostol may offer superior outcomes in terms of both the speed and completeness of abortion. The findings of this study align with those of similar studies conducted in other settings, which reported better results with the sublingual route.

In terms of side effects, both groups experienced similar adverse effects, such as nausea, vomiting, diarrhea, and fever/chills. However, these side effects were generally mild and self-limiting, which is consistent with the known safety profile of misoprostol. Notably, the need for Dilatation and Curettage (D&C) was significantly lower in the sublingual group (23.9%) compared to the oral group (52.2%), suggesting that sublingual misoprostol may reduce the need for surgical intervention, thus offering a more efficient and less invasive treatment option.

The study's strengths include its randomized controlled design, which minimized selection bias and allowed for a direct comparison of the two treatment modalities. However, the study's limitations include the small sample size and the lack of long-term follow-up to assess potential complications or the need for subsequent interventions. Additionally, as the study was conducted in a single center, the results may not be generalizable to other settings or populations.

Conclusion:

In conclusion, this study provides compelling evidence that sublingual misoprostol is significantly more effective than oral misoprostol in achieving complete abortion within 24 hours in second-trimester pregnancies. The sublingual route offers a promising alternative to oral misoprostol, with higher success rates and a reduced need for surgical interventions such as D&C. These findings suggest that healthcare providers in similar settings may consider sublingual misoprostol as the preferred method for medical abortion in the second trimester. Future research with larger sample sizes and multicenter trials is needed to confirm these findings and to explore long-term outcomes associated with different routes of misoprostol administration.

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