

# Comparison of the Effectiveness of Sub Lingual Vs Vaginal Misoprostol in Termination of First Trimester Missed Abortion

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Submitted for Publication: 03-11-2024  
Accepted for Publication 11-12-2024

**How to Cite:** Hijaz S, Mubeen N, Khan RI, Ahmad R, Khan SJ, Nasir A. Comparison of the Effectiveness of Sub Lingual Vs Vaginal Misoprostol in Termination of First Trimester Missed Abortion. APMC 2024;18(4):324-330. DOI: 10.29054/APMC/2024.1697

## ABSTRACT

**Background:** The incidence of spontaneous miscarriages increases with age. In the first trimester, the leading cause of spontaneous abortion is embryonic abnormalities, responsible for 80-90% of all miscarriages. Miscarriage affects 10-20% of clinically recognized pregnancies. **Objective:** To compare the effectiveness of sublingual versus vaginal routes of misoprostol in termination of first trimester missed abortion. **Study Design:** Quasi-experimental trial. **Settings:** Department of Obstetrics and Gynecology, Khyber Teaching Hospital, Peshawar Pakistan. **Duration:** March, 2022 to March, 2023. **Methods:** The study enrolled 78 participants, equally divided into two groups, Group-A receiving misoprostol sublingually while Group-B receiving vaginal misoprostol. Data collected was analyzed using SPSS version 20, with a p-value <0.05 considered significant. **Results:** The mean age of participants in the sublingual group was 30 years (SD±4.24), while in the vaginal group, it was 26 years (SD±5.22). The mean gestational age was similar in both groups, about 10 weeks. Women aged 31-45 years experienced significantly higher failure rates in the vaginal group (15.38%) compared to the sublingual group (2.56%) with a p-value of 0.027. Additionally, a shorter induction-to-abortion interval of less than 12 hours was associated with a higher failure rate in the vaginal group (5.12%) vs the sublingual group (20.51%), with a p-value of 0.027. **Conclusion:** Our study found that misoprostol administration through sublingual route is effective than vaginal route for the medical management of missed miscarriage but the results obtained were not significant statistically.

**Keywords:** Sublingual misoprostol, Vaginal misoprostol, First trimester missed abortion.

## INTRODUCTION

Early pregnancy loss, commonly referred to as miscarriage, occurs before 20 weeks of gestation. The leading cause of spontaneous abortion in the first trimester is embryonic abnormalities, responsible for 80-90% of all miscarriages.<sup>1</sup> Miscarriage affects 10-20% of clinically recognized pregnancies. A missed miscarriage, also known as a silent miscarriage, occurs when a nonviable embryo or fetus remains within the gestational sac before 22 weeks of gestation, without any clinical signs of expulsion.<sup>1</sup> In this condition, known as missed abortion, the non-viable pregnancy remains in the uterus without the onset of spontaneous abortion. Typically, the only sign is amenorrhea, with the patient often unaware

that the pregnancy has ceased to develop until the detection of a fetal heartbeat at a preferable time. The diagnosis is usually confirmed via ultrasound, and there are no accompanying symptoms such as cervical changes, passage of tissue, abdominal pain, or vaginal bleeding.<sup>1,2</sup>

Approximately 15-20% of miscarriages occur during pregnancies which mostly happen in the first trimester, particularly in old gestational age women. Recurrent early pregnancy loss, characterized by the loss of 2-3 consecutive clinical pregnancies, affects approximately 1% of couples.<sup>3</sup> Early pregnancy loss occurs across all racial groups without discrimination. However, the incidence of spontaneous miscarriages rises with advancing maternal age. The typical miscarriage rates by

age group are approximately 15% for women under 35, 20-25% for those between 35 and 39, about 35% for women aged 40-42, and around 50% for those over 42 years old.<sup>4</sup> Literature shows that the risk of death in a year for women who were not pregnant was 57 out of 100,000. After an abortion, it increased to 83 out of 100,000. After a miscarriage, it was 52 out of 100,000, and for women who gave birth, it was 28 out of 100,000.<sup>5</sup>

A complete abortion generally does not require additional medical or surgical intervention. In cases of suspected early pregnancy loss, pelvic ultrasonography and examination with a vaginal probe examination are done to find the hematometra, retained products of conception, ectopic pregnancy, or other potential causes.<sup>6</sup> Usually, diagnosis is confirmed by the absence of a fetal heartbeat on ultrasound. In such situations, the mother may report persistent, light vaginal bleeding.<sup>2,6</sup> Genetic abnormalities, particularly chromosomal anomalies are one of the leading causes of spontaneous abortion with 50-65% miscarriages. Among all chromosomal abnormalities, 45X karyotype is most common followed by trisomy and triploidies account for around 15% of these genetic issues. Teratogenic and mutagenic factors, along with maternal age, polycystic ovary syndrome (PCOS), corpus luteum deficiency, and infections like rubella, CMV, toxoplasmosis, and bacterial vaginosis, are additional risk factors for spontaneous abortion.<sup>7-10</sup> For the past five decades, dilation and curettage (D&C) has been the standard treatment for missed abortion.<sup>11</sup> While dilation and curettage (D&C) is generally regarded as a safe procedure, it can result in complications such as infection, bleeding, uterine perforation, and decreased fertility in approximately 10% of cases. Recent research has sparked debate about the routine use of D&C, suggesting that expectant management or medical intervention may be more appropriate alternatives in select cases.<sup>12</sup> Stable patients who are not in pain may opt for observation with monitoring of hCG levels every few days. If hCG levels plateau and then decline, it indicates a likely spontaneous miscarriage or tubal abortion.<sup>13</sup>

Misoprostol is a synthetic analogue of prostaglandin E1 which is stable at room temperature and enhances uterine tone. It has been widely used for various medical purposes, including medical abortion.<sup>14</sup> However, the protocols for its use in early pregnancy failure vary and are not yet fully standardized. Earlier clinical trials suggested that vaginal misoprostol was more effective, despite having a slower onset and lower peak concentration than oral misoprostol. Nevertheless, vaginal administration required smaller doses due to its more prolonged effect after 60 minutes. Recent pharmacokinetic studies show that sublingual misoprostol offers the fastest onset of action, the highest peak concentration, and the greatest bioavailability

compared to other routes of administration.<sup>14,15</sup> A study conducted by Latif S. et al. in Bahawalpur, Pakistan, revealed that the efficacy of misoprostol-induced abortion varied by administration route. Specifically, the study found that complete abortion rates were 66.7% for vaginal administration and 73.3% for sublingual administration.<sup>12</sup> Another study by Nasir SK. et al. in 2011 showed that all women in the study passed the products of conception after the first course of treatment, with a significantly higher complete abortion rate in the sublingual group (50%) compared to the vaginal group (13.63%).<sup>2</sup> Previous randomized controlled trials (RCT) performed which show misoprostol is an effective medical management in these patients.<sup>12</sup>

Medical termination of missed abortion is less commonly practiced in our region, with many people prefer surgical methods due to concerns about the efficacy of medical alternatives. Although a variety of misoprostol regimens have been utilized for this purpose, the vaginal route remains the preferred method. This study aims to evaluate the effectiveness of medical termination of the first trimester missed abortion using sublingual versus vaginal misoprostol. By comparing these two routes, the study seeks to address the limited research on this topic in our region and potentially increase confidence in medical termination as a viable alternative to invasive procedures. The objective of the study was to compare the effectiveness of misoprostol administered sublingually vs vaginal route in terminating first-trimester missed abortion.

## METHODS

This quasi-experimental trial was conducted at the Department of Obstetrics and Gynecology, Khyber Teaching Hospital, Peshawar, from March 2022 to March 2023. The study included a total of 78 participants, divided into two distinct groups of 39 each, while the calculated sample size was 68 using OpenEpi, based on a success rate of 96.3% for complete abortion induced by vaginal misoprostol, with a confidence interval of 97% and a 5% margin of error.<sup>16</sup>

Non-probability consecutive sampling technique was used. The study inclusion criteria comprised women of reproductive age (15-45 years) presenting with first-trimester missed abortion, confirmed by pelvic and ultrasound examinations. Exclusion criteria included known hypersensitivity to misoprostol, threatened, or incomplete abortion, suspected ectopic pregnancy, and high-risk conditions such as asthma or chronic heart disease.

Following ethical approval by Ethical Review Committee Ref No. ERC/Gyne/22/105 on dated 21/02/2022. Women experiencing a first-trimester missed abortion

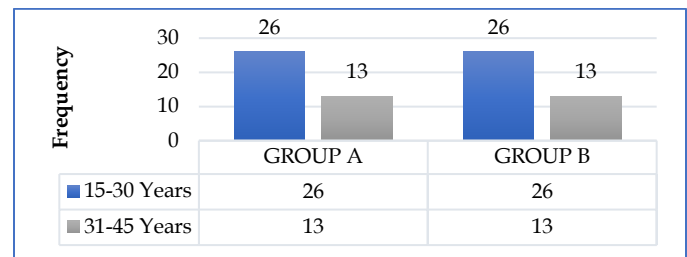
were hospitalized and recruited for the study. A first-trimester missed abortion was defined as a condition where the cervix remains closed, bleeding is minimal or absent, and ultrasound imaging reveals an intrauterine gestational sac with a mean diameter of  $\geq 25$ mm, but no visible embryonic pole. It can also be indicated by an embryonic pole larger than 7mm without detectable cardiac activity or the persistent absence of cardiac activity on a follow-up scan conducted 7-10 days later. Informed written consent was obtained, and personal details, along with hospital registration numbers, were recorded. After taking the history from the participants, blood count and coagulation profile were performed and data was recorded. Randomization was achieved by alternating treatment routes, with the first admitted patient receiving sublingual misoprostol and the second receiving vaginal misoprostol, continuing in this manner. Group A received sublingual misoprostol (three doses of 600 $\mu$ g every 6 hours), while Group B received vaginal misoprostol (three doses of 800 $\mu$ g every 6 hours). Evaluation occurred six hours after the third dose (24 hours). If abortion did not occur within this period, participants were administered another course of misoprostol by the same route and monitored for an additional 24 hours. A pelvic examination was performed for those with vaginal bleeding or passed products of conception, and an ultrasound was used to assess for complete abortion. If significant retained products were found, surgical evacuation was performed. Failure of medical treatment was defined as the lack of passage of products of conception after two courses of misoprostol, leading to surgical intervention. Following the abortion, participants were discharged and scheduled for a follow-up visit after 7 days.

Statistical analysis was conducted using SPSS version 20. Descriptive statistics were used to summarize qualitative variables (frequency and percentage) and quantitative variables (mean  $\pm$  standard deviation). Group comparisons were performed using the Chi-square test, with statistical significance set at  $p \leq 0.05$ . Results were stratified by age, gestational age, presenting complaints, ultrasound findings, and other variables to assess effect modification with a post-stratification chi-square test.

## RESULTS

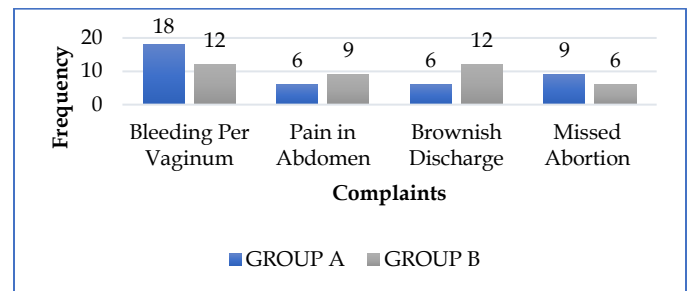
A total of 78 patients were enrolled in the study divided into two groups containing 39 patients each. Group A (sublingual misoprostol) had a mean age of 30 years (SD= $\pm 4.24$ ). The mean gestational age of the participants was 10 weeks, with a standard deviation of 0.94 weeks. In Group A (sublingual misoprostol), 66.66% of participants were aged 15-30 years, while 33.34% were aged 31-45 years. In Group B (vaginal misoprostol), the age distribution was identical, with 66.66% in the 15-30 years range and 33.34% in the 31-45 years range. (Figure 1)

**Figure 1: Age distribution of the participants**



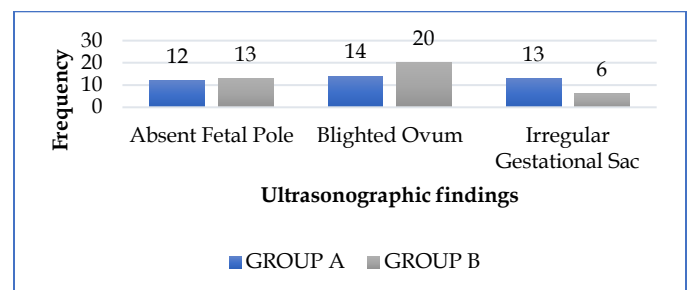
In Group A (sublingual misoprostol), the most common presenting complaint was bleeding per vaginam, reported by 46.15% of participants. Pain in the abdomen was noted by 15.38%, while 15.38% experienced brownish discharge. Missed abortion was reported by 23.07% of participants. In Group B (vaginal misoprostol), 30.76% of participants reported bleeding per vaginam, 23.07% experienced pain in the abdomen, and 30.76% had brownish discharge. Missed abortion was noted in 15.38% of cases, presented in Figure 2.

**Figure 2: Side effects among the participants of both groups**



In Group A (sublingual misoprostol), the most common ultrasonographic finding was a blighted ovum, observed in 35.89% of participants. An absent fetal pole was noted in 30.76% of cases, while an irregular gestational sac was found in 33.33%. In Group B (vaginal misoprostol), the blighted ovum was the most frequent finding, present in 51.28% of participants. An absent fetal pole was observed in 33.33%, and an irregular gestational sac was identified in 15.38% of cases, as shown in Figure 3.

**Figure 3: Ultrasonographic findings among the participants of both groups**



### Clinical outcome of sublingual and vaginal misoprostol

The mean induction time was 2 hours  $\pm$  0.30, and the mean abortion time was 2 hours  $\pm$  0.50. The mean induction-abortion interval time was 13 hours  $\pm$  0.70. In Group B (vaginal misoprostol), the mean age was 26 years  $\pm$  5.22, with a mean gestational age of 10 weeks  $\pm$  0.80. The mean induction time was 2 hours  $\pm$  0.49, and the mean abortion time was 2 hours  $\pm$  0.46. in Group A (sublingual

misoprostol), 41.02% of participants achieved a complete abortion, while 41.02% experienced an incomplete abortion, and 17.94% had a failure of medical treatment, as shown in Table 1. In Group B (vaginal misoprostol), 17.94% achieved a complete abortion, 48.71% experienced an incomplete abortion, and 33.33% had a failure of medical treatment. The p-value for the difference in complete abortion rates between the two groups was 0.061.

**Table 1: Clinical outcome of intervention among the participants of both groups**

Clinical Outcome	Group-A	Group-B	p-value
Complete Abortion	41.02% (n=16)	17.94% (n=7)	0.061
Incomplete Abortion	41.02% (n=16)	48.71% (n=19)	
Failure of Medical Treatment	17.96% (n=7)	33.33% (n=13)	
Total	100% (n=39)	100% (n=39)	

### Comparison of complete abortion with age, gestational age, and other factors among the study groups

The clinical outcome such as complete abortion is compared among the participants of both groups with the age, gestational age, side effects, and ultrasonographic findings, as illustrated in Table 2. In the sublingual route, 23.07% of women aged 15-30 years achieved a complete abortion, compared to 12.82% in the vaginal route. For women aged 31-45 years, 17.94% in the sublingual route had a complete abortion, while only 5.12% in the vaginal route did, with a significant p-value of 0.039. Among women with gestational ages under 10 weeks, 25.64% in

the sublingual route achieved a complete abortion compared to 12.82% in the vaginal route (p-value 0.128).

For gestational ages over 10 weeks, 15.38% in the sublingual route had a complete abortion versus 5.12% in the vaginal route (p-value 0.083). For abdominal pain, 2.56% in the sublingual route and 7.69% in the vaginal route had complete abortions (p-value 0.474). Brownish discharge led to a 10.25% complete abortion rate in the sublingual route and 15.38% in the vaginal route (p-value 0.502). For missed abortion, 17.94% in the sublingual route and 7.69% in the vaginal route achieved a complete abortion (p-value 0.263).

**Table 2: Association of Complete abortion with Age, Gestational Age, and other factors among the study groups**

Variables	Complete abortion in Group A	Complete abortion in Group B	p-value	
Age	15-30 Years	23.07% (n=9)	12.82% (n=5)	0.211
	31-45 Years	17.94% (n=7)	5.12% (n=2)	0.039
Gestational Age	$\leq$ 10 Weeks	25.64% (n=10)	12.82% (n=5)	0.128
	> 10 Weeks	15.38% (n=6)	5.12% (n=2)	0.083
History	Bleeding Per Vaginum	12.82% (n=5)	10.25% (n=4)	0.744
	Pain Abdomen	2.56% (n=1)	7.69% (n=3)	0.474
	Brownish Discharge	10.25% (n=4)	15.38% (n=6)	0.502
	Missed Abortion	17.94% (n=7)	7.69% (n=3)	0.263
Ultrasonographic findings	Absent Fetal Pole	15.38% (n=6)	7.69% (n=3)	0.264
	Irregular Gestational Sac	5.12% (n=2)	2.56% (n=1)	0.539
	Blighted Ovum	20.51% (n=8)	10.25% (n=4)	0.126
Induction Time	$\leq$ 2 Hours	41.02% (n=16)	12.82% (n=5)	0.015
	> 2 Hours	10.25% (n=4)	5.12% (n=2)	0.017
Abortion Time	$\leq$ 2 Hours	25.64% (n=10)	7.69% (n=3)	0.416
	> 2 Hours	15.38% (n=6)	10.25% (n=4)	0.032
Induction to Abortion Interval	$\leq$ 12 Hours	20.51% (n=8)	5.12% (n=2)	0.027
	> 12 Hours	20.51% (n=8)	12.82% (n=5)	0.311

Regarding specific conditions, 15.38% with an absent fetal pole in the sublingual route achieved a complete abortion, compared to 7.69% in the vaginal route (p-value 0.264). An irregular gestational sac resulted in a 5.12% complete abortion rate in the sublingual route and 2.56% in the vaginal route (p-value 0.539). For blighted ovum, 20.51% in the sublingual route and 10.25% in the vaginal route had a complete abortion (p-value 0.126). For

induction times under 2 hours, 41.02% in the sublingual route achieved a complete abortion compared to 12.82% in the vaginal route (p-value 0.015). For induction times of 2 hours or more, 10.25% in the sublingual route and 5.12% in the vaginal route had complete abortions (p-value 0.017). In the sublingual route, 25.64% of women who aborted within 2 hours achieved a complete abortion, while 7.69% in the vaginal route did (p-value

0.416). For abortions occurring after 2 hours, 15.38% in the sublingual route and 10.25% in the vaginal route had complete abortions (p-value 0.032). For induction-to-abortion intervals of less than 12 hours, 20.51% in the sublingual route and 5.12% in the vaginal route had complete abortions (p-value 0.027). For intervals of 12 hours or more, 20.51% in the sublingual route and 12.82% in the vaginal route had complete abortions (p-value 0.311).

### Comparison of incomplete abortion with age, gestational age and other factors among the study groups

In the sublingual route, 28.20% of women aged 15-30 years experienced incomplete abortion, compared to 35.89% in the vaginal route. For women aged 31-45 years, the rates were 12.82% in both routes, with p-values of 0.405 and 1.00, indicating no significant difference. For gestational ages under 10 weeks, incomplete abortion rates were 35.89% in the sublingual route and 41.02% in the vaginal route (p-value 0.109). For ages over 10 weeks, the rates were 5.12% in the sublingual route and 7.69% in the vaginal route (p-value 0.615). In cases with vaginal bleeding, 23.07% in the sublingual route and 15.38% in the vaginal route had incomplete abortions (p-value 1.00). For missed abortion, the rates were 2.56% in the

sublingual route and 7.69% in the vaginal route (p-value 0.095).

Specific findings showed 12.82% with an absent fetal pole and 17.94% with an irregular gestational sac had incomplete abortions in the sublingual route, compared to 15.38% and 12.82% in the vaginal route, with p-values of 0.821 and 0.215. For blighted ovum, 10.25% in the sublingual route and 20.51% in the vaginal route experienced incomplete abortions (p-value 0.492). For induction times under 2 hours, 35.89% in the sublingual route and 28.20% in the vaginal route had incomplete abortions (p-value 0.954). For times of 2 hours or more, the rates were 7.69% in the sublingual route and 20.51% in the vaginal route (p-value 0.610). In the sublingual route, 28.20% who aborted within 2 hours had incomplete abortions, compared to 12.82% in the vaginal route (p-value 0.970). For abortions over 2 hours, 12.82% in the sublingual route and 35.89% in the vaginal route had incomplete abortions (p-value 0.013). For induction-to-abortion intervals of less than 12 hours, 28.20% in the sublingual route and 23.07% in the vaginal route had incomplete abortions (p-value 0.515). For intervals of 12 hours or more, the rates were 30.76% in the sublingual route and 25.64% in the vaginal route (p-value 0.525).

**Table 3: Correlation of incomplete abortion with age, gestational age, and other factors among the study groups**

Variables		Incomplete abortion in Group A	Incomplete abortion in Group B	p-value
Age	15-30 Years	28.20% (n=11)	35.89% (n=14)	0.405
	31-45 Years	12.82% (n=5)	12.82% (n=5)	1.000
Gestational Age	≤ 10 Weeks	35.89 (n=14)	41.02% (n=16)	0.109
	> 10 Weeks	5.12% (n=2)	7.69% (n=3)	0.615
History	Bleeding Per Vaginum	23.07% (n=9)	15.38% (n=6)	1.000
	Pain Abdomen	12.82% (n=5)	7.69% (n=3)	0.314
	Brownish Discharge	2.56% (n=1)	12.82% (n=5)	0.288
	Missed Abortion	2.56% (n=1)	7.69% (n=3)	0.095
Ultrasonographic Findings	Absent Fetal Pole	12.82% (n=5)	15.38% (n=6)	0.821
	Irregular Gestational Sac	17.94% (n=7)	12.82% (n=5)	0.215
	Blighted Ovum	10.25% (n=4)	20.51% (n=8)	0.492
Induction Time	≤ 2 Hours	35.89% (n=14)	28.20% (n=11)	0.954
	> 2 Hours	7.69% (n=3)	20.51% (n=8)	0.610
Abortion Time	≤ 2 Hours	28.20% (n=11)	12.82% (n=5)	0.970
	> 2 Hours	12.82% (n=5)	35.89% (n=14)	0.013
Induction to Abortion Interval	≤ 12 Hours	28.20% (n=11)	23.07% (n=9)	0.515
	> 12 Hours	30.76% (n=12)	25.64% (n=10)	0.525

### Comparison of medical treatment failure with age, gestational age, and other factors in both groups

In the sublingual route group, 15.38% of women aged 15-30 years experienced treatment failure, compared to 17.94% in the vaginal route group, with a p-value of 0.748, indicating no significant difference. However, for women aged 31-45 years, treatment failure was significantly lower in the sublingual route group (2.56%) compared to the vaginal route group (15.38%), with a p-value of 0.027.

For gestational ages under 10 weeks, treatment failure occurred in 25.64% of the sublingual route group and 12.82% of the vaginal route group (p-value 0.128). For gestational ages over 10 weeks, the rates were 15.38% in the sublingual route group and 5.12% in the vaginal route group (p-value 0.083), showing no significant difference, as shown in Table 4.

For specific findings, 15.38% with an absent fetal pole and 5.12% with an irregular gestational sac in the sublingual

route group experienced treatment failure, compared to 7.69% and 2.56% in the vaginal route group (p-values 0.264 and 0.539). For 2 hours or more, the rates were 10.25% in the sublingual route group and 5.12% in the vaginal route group (p-value 0.017). Among those who aborted within 2 hours, treatment failure occurred in 25.64% of the sublingual route group and 7.69% of the vaginal route group (p-value 0.416). For abortions over 2 hours, treatment failure was 15.38% in the sublingual

route group and 35.89% in the vaginal route group (p-value 0.032). For intervals of less than 12 hours, treatment failure was more common in the sublingual route group (20.51%) compared to the vaginal route group (5.12%), with a significant p-value of 0.027. For intervals of 12 hours or more, the rates were 20.51% in the sublingual route group and 12.82% in the vaginal route group (p-value 0.311).

**Table 4: Correlation of age, gestational age, and other factors with the failure of medical treatment**

Variables		Medical Treatment Failure in Group A	Medical Treatment Failure in Group B	p-value
Age	15-30 Years	15.38% (n=6)	17.94% (n=7)	0.748
	31-45 Years	2.56% (n=1)	15.38% (n=6)	0.027
Gestational Age	≤ 10 Weeks	25.64% (n=10)	12.82% (n=5)	0.128
	> 10 Weeks	15.38% (n=6)	5.12% (n=2)	0.083
History	Bleeding Per Vaginum	12.82% (n=5)	10.25% (n=4)	0.744
	Pain Abdomen	2.56% (n=1)	7.69% (n=3)	0.474
	Brownish Discharge	10.25% (n=4)	15.38% (n=6)	0.502
	Missed Abortion	17.94% (n=7)	7.69% (n=3)	0.263
Ultrasonographic Findings	Absent Fetal Pole	15.38% (n=6)	7.69% (n=3)	0.264
	Irregular Gestational Sac	5.12% (n=2)	2.56% (n=1)	0.539
	Blighted Ovum	20.51% (n=8)	10.25% (n=4)	0.126
Induction Time	≤ 2 Hours	41.02% (n=16)	12.82% (n=5)	0.015
	> 2 Hours	10.25% (n=4)	5.12% (n=2)	0.017
Abortion Time	≤ 2 Hours	25.64% (n=10)	7.69% (n=3)	0.416
	> 2 Hours	15.38% (n=6)	10.25% (n=4)	0.032
Induction to Abortion Interval	< 12 Hours	20.51% (n=8)	5.12% (n=2)	0.027
	> 12 Hours	20.51% (n=8)	12.82% (n=5)	0.311

## DISCUSSION

This study offers significant findings on the comparative efficacy of sublingual and vaginal misoprostol administration for terminating first-trimester missed abortions, informing the ongoing debate on optimal treatment approaches in clinical settings. This study outcome is consistent with the findings of Khan et al. in Lahore, who reported a success rate of 53.1% using an initial dose of 400µg sublingual misoprostol, followed by 200µg every 4 hours for four doses.<sup>17</sup> However, our success rate is notably lower compared to studies by Tang et al. in China (87.5%) and Sharma et al. in India(86%), using 600 µg of sublingual and vaginal misoprostol.<sup>18,19</sup> The higher success rates observed in these studies can likely be attributed to the higher dosages of misoprostol administered.<sup>17,19</sup> In Group A, where the sublingual route was used, 41.02% of patients experienced complete abortion, 41.02% had incomplete abortion, and 17.94% encountered failure of medical treatment. Similarly, in Group B, which followed the vaginal route, 17.94% of patients achieved complete abortion, 48.71% had an incomplete abortion, and 33.33% experienced treatment failure. These findings are consistent with those reported by Tang et al. in a study conducted in China.

Additionally, our findings indicate that sublingual and vaginal misoprostol administration yield comparable complete miscarriage rates for second-trimester missed miscarriages, with no statistically significant difference observed between the two routes. This is consistent with Ngai *et al.*, study, which found higher success rates for vaginal misoprostol than sublingual misoprostol with 85% and 64% respectively at 24 hours, and with no significant difference after 48 hours.<sup>20</sup> Notably, the sublingual route was associated with a significantly shorter induction-to-abortion interval. Specifically, 57% of women in the sublingual group achieved abortion within 12 hours, compared to 41.6% in the vaginal group. This could be due to the early onset and greater peak serum concentrations of sublingual misoprostol.<sup>18</sup>

In our study, the incidence of side effects was significantly higher in the sublingual group compared to the vaginal group, consistent with previous research. The most common side effect reported was an unpleasant taste, happening 3 times frequently in the sublingual group in this study. This finding is in line with a study conducted in the UK, in 63.9% and 37.5% of women in the sublingual group and vaginal group respectively reported an unpleasant taste.<sup>21</sup> Other side effects

including shivering and nausea were also more frequently observed in the sublingual group. This prevalence could be due to the higher bioavailability of sublingual misoprostol, leading to faster absorption and more pronounced adverse effects.<sup>18</sup>

## CONCLUSION

This study on sublingual vs vaginal routes of misoprostol administration for managing first-trimester missed miscarriage found no statistically significant difference in complete abortion rates between the two methods. While sublingual misoprostol resulted in a marginally shorter time to abortion, it was also linked to a higher frequency of adverse effects, most notably an unpleasant taste sensation. The overall success rates were lower than those reported in other studies, which may be attributed to differences in dosage and patient management.

## LIMITATIONS

Our study had limitations in assessing patient satisfaction, as it was an open-label design where patients were aware of the assigned route of administration, and their treatment outcomes may have influenced their preferences. Additionally, the small sample size was a significant limitation.

## SUGGESTIONS / RECOMMENDATIONS

However, a randomized control trial on a large scale is recommended. Despite the limitations of a small sample size and potential biases in an open-label study, our findings suggest that both routes are effective but emphasize the need for further large-scale, randomized controlled trials to determine the optimal route and dosage for achieving complete abortion with minimal side effects.

## CONFLICT OF INTEREST / DISCLOSURE

The authors have no conflict of interest.

## FUNDING SOURCE

Not available.

## ACKNOWLEDGEMENTS

The authors express their sincere gratitude to all the participants and their families for their invaluable contribution to this study.

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