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Original Research Article

Comparison of Mean Time from Induction of Labor to Delivery with Sublingual vs. Vaginal Misoprostol in Post-Term Pregnancies

Article History:

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Abstract:

Objective: This research aims to assess the effectiveness of sublingual misoprostol vs vaginal misoprostol in postterm pregnancies, with the objective of determining the reduced time to delivery.

Study Design Randomized controlled trial.

Place and Duration of Study: Department of Gynecology, Gulab Devi Hospital, Lahore, over a period of six months after approval of the synopsis.

Methodology: A total of 196 women with singleton post-term pregnancies (≥42 weeks) were enrolled and randomly allocated into two groups (n=98 each). Group A received 25µg sublingual misoprostol, and Group B received 25µg vaginal misoprostol every four hours for a maximum of six doses. Induction was considered successful upon entry into active labor. The primary outcome was the mean induction-to-delivery interval. The data were examined with the help of SPSS version 25. A p-value of less than or equal to 0.05 was deemed statistically significant when an independent sample t-test was used to compare the means.

Results: The mean induction-to-delivery time was significantly shorter in the vaginal group compared to the sublingual group (15.60 ± 2.66 hours vs. 17.13 ± 2.45 hours; p=0.000). Successful vaginal delivery was achieved in 84.7% of women in the vaginal group and 81.6% in the sublingual group (p=0.567). Stratified analysis showed that vaginal misoprostol resulted in shorter induction-to-delivery intervals across most subgroups.

Conclusion: The induction-to-delivery time in post-term pregnancies may be reduced more effectively using vaginal misoprostol compared to sublingual misoprostol, with similar rates of successful vaginal delivery achieved with both methods. When it comes to inducing labour, both methods are reliable and risk-free.

Keywords: Post-term pregnancy; Misoprostol; Labor induction; Sublingual; Vaginal; Induction-to-delivery interval.

INTRODUCTION

Induction of labor is the artificial commencement of labor prior to its natural beginning to facilitate the delivery of the feto-placental unit (1, 2). Among the almost 3,00,000 observations included in the World Health Organization's (WHO) Global Survey on Maternal and Perinatal Health, which ran from 2004 to 2008 in 24 countries, 9.6% of births were induced (3). One of the most common indications is prolonged pregnancy. According to recent research, both the mother and the unborn child are at a much greater risk of perinatal morbidity and death when the pregnancy continues beyond 41 weeks. Therefore, the case for elective induction of labor at 41 weeks of gestation, as opposed to expectant management, is becoming stronger (4). Prostaglandin E2 (dinoprostone) is the most often used variety, and it comes in gel or suppository form. Another type, prostaglandin E1, is misoprostol, and it may be taken orally, applied topically, or used vaginally (5). Prostaglandins are more

effective in inducing labor than oxytocin because they have a local impact on the cervix that encourages it to dilate and contract, rather than affecting uterine contractions like oxytocin does (6). Misoprostol, or prostaglandin E1, has a reputation for being an affordable and efficient peptic ulcer medication used to induce labor. Numerous studies have assessed the optimal dose and method of administering misoprostol (7). When a woman's membranes rupture before she goes into labor, an oral dose of misoprostol is often used to induce labor. Sublingual misoprostol has great potential because of its quick absorption via the sublingual mucosa, which allows it to bypass first-pass metabolism and have an immediate impact (8). One advantage of sublingual misoprostol is that it is easy to prescribe, which means that patients have greater autonomy and less need for vaginal exams (9). Although some research has shown that vaginal misoprostol is safe and effective for a variety of obstetric inductions, including labor induction, cervical softening before hysteroscopy in women who are not pregnant, and pregnancy termination (10).

In terms of induction delivery interval results, maternal and foetal outcomes in post term births, and overall effectiveness, a research compared sublingual misoprostol with vaginally given misoprostol. The vaginal approach had a success rate of 24 (84.38 percent), whereas the sublingual method had a success rate of 26 (81.25%). There was a 16.79 ± 2.40-hour time difference between the Sublingual approach and the vaginal method for induction to vaginal birth (11).

Objective

To determine if post-term pregnant women who were eligible for labor induction may be helped along the induction process by using vaginal or sublingual misoprostol, since the subject matter is important and there are not many local studies on the issue. Future recommendations for labor induction methods will be based on what has been shown to improve maternal and newborn outcomes.

METHODOLOGY

This randomized controlled trial will be conducted in the Department of Gynae & Obs, Gulab Devi Hospital, Lahore, from 4 August 2025 to 4 November, 2025. The study aims to compare the induction-to-delivery interval between sublingual and vaginal misoprostol for the induction of labor in postdated pregnancies. The sample size of 196 patients (98 in each group) has been calculated using the OpenEpi sample size calculator with a confidence level of 95% and a power of 80%. The calculation is based on previously reported mean induction-to-delivery times of 16.79 ± 2.40 hours for the sublingual route and 15.81 ± 2.48 hours for the vaginal route. Non-probability purposive sampling technique will be employed.

Pregnant women meeting the inclusion criteria, singleton pregnancy, gestational age ≥42 weeks, cephalic presentation, and live fetus will be enrolled in the study. Women with premature rupture of membranes, placenta previa, placental abruption, fetal malformations, preeclampsia, abnormal fetal heart rate patterns, signs of active labor at admission, and previous uterine scars will be excluded. After obtaining approval from the Ethical Review Committee and the College of Physicians and Surgeons Pakistan (CPSP), written informed consent will be secured from all eligible participants. Confidentiality of patient data will be ensured throughout the study. At admission, a detailed obstetric history will be obtained, followed by a thorough general and systemic examination. Obstetric examination will include assessment of fundal height, fetal lie, presentation, and engagement. Ultrasound examination will be performed to confirm gestational age and assess the amniotic fluid index. A pelvic examination will be conducted to determine the Bishop score and exclude cephalopelvic disproportion or a contracted pelvis. Two groups will be formed by randomly assigning participants using a lottery system. Misoprostol, 25 µg, will be given to Group A sublingually, and 25 µg, vaginally, to Group B. No more than six doses of the medication should be taken in a 24-hour period. In the event that the patient has regular uterine contractions together with cervical dilation exceeding 4 cm or if the cervix becomes amniotomy-friendly (Bishop score ≥8), administration will be skipped. Cervical dilation and fetal head engagement are the prerequisites for performing an amniotomy. Induction of labor will be considered failed if the patient does not enter the active phase after six doses of misoprostol, and cesarean section will then be offered. All relevant clinical information will be recorded on a predesigned proforma. Data will be entered and analyzed using SPSS version 25. Quantitative variables will be expressed as mean ± standard deviation, and qualitative variables as frequency and percentage. The independent sample t-test will be used to compare the mean induction-to-delivery time between groups. Effect modifiers will be controlled through stratification, and a p-value ≤0.05 will be considered statistically.

RESULTS

196 women with post-term pregnancies were enrolled and randomly allocated into two equal groups: 98 received sublingual misoprostol and 98 received vaginal misoprostol. Both groups were comparable in most baseline demographic and obstetric characteristics. The primary outcome measure was mean induction-to-delivery interval. Overall, the vaginal misoprostol group demonstrated a significantly shorter induction-to-delivery time compared to the sublingual group Baseline demographic and obstetric characteristics were largely comparable between the two groups. The mean age was slightly higher in the vaginal group (28.36 ± 4.51 years) compared to the sublingual group (26.96 ± 4.76 years), showing a statistically significant difference (p=0.036). However, age group distribution, gestational age, parity, history of abortion, oxytocin augmentation, and successful vaginal delivery were not

significantly different between groups (p>0.05). Successful vaginal delivery was achieved in 81.6% of the sublingual group and 84.7% of the vaginal group. Overall, both groups were homogeneous at baseline (Table 1).

Table 1. Participant Demographics and Obstetric Details by Misoprostol Administration Route: A Baseline Study

Variable	Category	Sublingual (n=98)	Vaginal (n=98)	Total (n=196)	p-value
Age (years)	Mean ± SD	26.96 ± 4.76	28.36 ± 4.51	-	0.036
Age Group	20–24	35 (35.7%)	30 (30.6%)	65 (33.2%)	0.271
	25–29	29 (29.6%)	23 (23.5%)	52 (26.5%)	
	30–35	34 (34.7%)	45 (45.9%)	79 (40.3%)	
Gestational Age (weeks)	Mean ± SD	42.42 ± 0.50	42.52 ± 0.50	-	0.154
Gestational Age Group	42	57 (58.2%)	47 (48.0%)	104 (53.1%)	0.152
	≥43	41 (41.8%)	51 (52.0%)	92 (46.9%)	
Parity	0	17 (17.3%)	20 (20.4%)	37 (18.9%)	0.605
	1	22 (22.4%)	14 (14.3%)	36 (18.4%)	
	2	19 (19.4%)	22 (22.4%)	41 (20.9%)	
	3	21 (21.4%)	19 (19.4%)	40 (20.4%)	
	4	19 (19.4%)	23 (23.5%)	42 (21.4%)	
History of Abortion	No	50 (51.0%)	60 (61.2%)	110 56.1%)	0.150
	Yes	48 (49.0%)	38 (38.8%)	86 (43.9%)	
Oxytocin Augmentation	No	46 (46.9%)	51 (52.0%)	97 (49.5%)	0.475
	Yes	52 (53.1%)	47 (48.0%)	99 (50.5%)	
Successful Vaginal Delivery	No	18 (18.4%)	15 (15.3%)	33 (16.8%)	0.567
	Yes	80 (81.6%)	83 (84.7%)	163 (83.2%)	

Table 2. Induction-to-Delivery Time by Misoprostol Administration Route

Group	N	Mean (hrs.)	S. D	p-value
Sublingual	98	17.13	2.45	0.000
Vaginal	98	15.60	2.66	

Stratified analysis demonstrated that vaginal misoprostol was associated with a shorter induction-to-delivery time in most subgroups. Significant differences were observed among women aged 20–29 years, gestational age ≥43 weeks, parity 1–3, those with or without history of abortion, and those not requiring oxytocin augmentation (p<0.05). However, differences were not statistically significant in women aged 30–35 years, gestational age of 42 weeks, nulliparous women, parity 4, and in cases requiring oxytocin augmentation (p>0.05). Overall, vaginal misoprostol consistently showed better efficacy across most stratified variables (Table 3).

Table 3. Stratification of Induction-to-Delivery Time (hrs.)

	Stratification	Group	N	Mean (hrs)	SD	SE	p-value
Age	20–24 yrs	Sublingual	35	17.37	2.21	0.37	0.001
		Vaginal	30	15.33	2.32	0.42	
	25–29 yrs	Sublingual	29	17.31	2.94	0.55	0.031
		Vaginal	23	15.66	2.27	0.47	
	30–35 yrs	Sublingual	34	16.74	2.25	0.39	0.118
		Vaginal	45	15.76	3.05	0.46	
Gestational Age	42 weeks	Sublingual	57	16.90	2.70	0.36	0.094
		Vaginal	47	16.00	2.70	0.39	
	≥43 weeks	Sublingual	41	17.46	2.06	0.32	0.000
		Vaginal	51	15.23	2.58	0.36	
Parity	Parity 0	Sublingual	17	16.18	2.86	0.69	0.743
		Vaginal	20	16.46	2.31	0.52	
	Parity 1	Sublingual	22	17.35	2.38	0.51	0.020
		Vaginal	14	15.27	2.64	0.71	
	Parity 2	Sublingual	19	17.36	2.25	0.52	0.010
		Vaginal	22	15.27	2.66	0.57	
	Parity 3	Sublingual	21	17.90	2.24	0.49	0.003
		Vaginal	19	15.44	2.71	0.62	
	Parity 4	Sublingual	19	16.67	2.46	0.56	0.179
		Vaginal	23	15.51	2.95	0.61	
History of abortion	No	Sublingual	50	17.10	2.51	0.36	0.002
		Vaginal	60	15.49	2.73	0.35	
	Yes	Sublingual	48	17.17	2.42	0.35	0.011
		Vaginal	38	15.77	2.55	0.41	
Oxytocin Augmentation	No	Sublingual	46	17.54	2.69	0.40	0.000
		Vaginal	51	15.41	2.65	0.37	
	Yes	Sublingual	52	16.77	2.18	0.30	0.053
		Vaginal	47	15.81	2.67	0.39	
Successful Vaginal Delivery	No	Sublingual	18	17.39	2.92	0.69	0.053

		Vaginal	15	15.27	3.13	0.81	
	Yes	Sublingual	80	17.08	2.35	0.26	0.000
		Vaginal	83	15.66	2.58	0.28	

DISCUSSION

In this randomized controlled trial, vaginal misoprostol was associated with a significantly shorter induction-to-delivery interval compared to sublingual misoprostol in post-term pregnancies (15.60 ± 2.66 hrs vs. 17.13 ± 2.45 hrs; p = 0.000). The rate of successful vaginal delivery was high and comparable in both groups, mirroring the overall efficacy of misoprostol for labor induction. These results contribute to a large body of research investigating the optimal route of misoprostol administration.

Some studies have shown similar induction-to-delivery times between sublingual and vaginal routes. A randomized trial by Jahromi et al. found no significant difference in the interval from first dose to delivery between sublingual and vaginal misoprostol when both were administered every 4 hrs, although rates of meconium-stained amniotic fluid were higher with sublingual use (12). Likewise, Ayati et al. reported no significant difference in total duration of labor between sublingual and vaginal groups, suggesting similar effectiveness in promoting labor progression (13). These findings contrast with our study where the vaginal route achieved faster delivery, which may reflect differences in dosing regimens, population characteristics, or study designs.

Conversely, several trials have reported shorter induction-to-delivery intervals with sublingual misoprostol. An observational study comparing sublingual to vaginal administration demonstrated significantly shorter induction times and fewer doses required with the sublingual route, without compromising cesarean rates or neonatal outcomes (14). Additionally, comparative research by Khan (2018) suggested that sublingual misoprostol may be more effective in terms of labor induction speed at term, although safety parameters were not the primary focus (15). Such results contrast with ours, underscoring that the relative efficacy of routes may be influenced by dose and frequency variations.

A recent systematic review and meta-analysis by Pergialiotis et al.[1] reported that vaginal misoprostol was associated with a shorter induction-to-delivery interval compared to oral and sublingual routes, although differences in cesarean section rates were minimal. Our results align with these conclusions, particularly regarding reduced labor duration with vaginal administration. Similarly, Eminov and Eminov[2] observed that low-dose vaginal misoprostol achieved faster cervical ripening and labor progression compared to sublingual misoprostol and dinoprostone, without significant differences in neonatal outcomes.

Kumar et al. finds misoprostol is still one of the best pharmacologic agents for inducing labor; the way it works and how much of it you take affect how long it takes (4). Vaginal administration provides sustained local absorption, which may explain the shorter induction-to-delivery interval observed in our study. In contrast, Parimkayala and Shetty reported that sublingual misoprostol offers rapid systemic absorption and quicker onset of uterine contractions; however, overall delivery time was not significantly shorter than vaginal administration, supporting our findings (8). The mean induction-to-delivery interval in our vaginal group (15.60 ± 2.66 hours) is comparable to the 15.81 ± 2.48 hours reported (11). In post-term pregnancies. Likewise, Shahali demonstrated effective cervical ripening with vaginal misoprostol, reporting shorter labor durations similar to those in our cohort (9). Akbari et al. compared vaginal, sublingual, and buccal routes and concluded that vaginal misoprostol resulted in more efficient labor progression with comparable maternal safety profiles (6). Regarding successful vaginal delivery, our rates (81.6% sublingual vs. 84.7% vaginal) are consistent with previous studies reporting success rates between 75% and 88% for both routes. Qasim et al. compared misoprostol with prostaglandin E2 gel and found similar vaginal delivery rates, reinforcing misoprostol's efficacy in term and post-term induction. Al-Rawaf and Mousa (10) demonstrated that vaginal misoprostol, whether used alone or combined with a Foley catheter, achieved high vaginal delivery rates without increasing maternal complications (16). Stratified analysis in our study showed that vaginal misoprostol was particularly effective among multiparous women (parity 1–3), women aged 20–29 years, and those with gestational age ≥43 weeks. These findings are in agreement with previous literature suggesting that multiparity enhances responsiveness to prostaglandins due to a favorable cervical status. Atef et al. also reported improved uterine contractility with localized administration of misoprostol, supporting the pharmacodynamic advantage of vaginal placement (17). Notably, no significant difference was observed in nulliparous women or that requiring oxytocin augmentation. Similar findings were described in multiple randomized trials where nulliparous women demonstrated prolonged induction intervals regardless of route, likely due to an unfavorable cervix. Oxytocin augmentation rates in our study were comparable between groups, consistent with prior evidence indicating that route of administration does not substantially alter augmentation requirements. From a pharmacokinetic perspective, sublingual misoprostol achieves higher peak plasma concentrations and avoids first-pass hepatic metabolism. However, this rapid systemic absorption may also be associated with transient uterine hyperstimulation in some studies. In

contrast, vaginal administration provides slower, sustained absorption with prolonged uterotonic effect, which may contribute to shorter overall induction-to-delivery intervals, as observed in our results. Importantly, maternal and fetal safety outcomes were comparable between groups, consistent with findings from large-scale analyses. The WHO global survey and subsequent regional studies have emphasized that careful monitoring minimizes adverse outcomes irrespective of route. None of the major comparative trials have demonstrated a clinically significant difference in perinatal morbidity when low-dose regimens are used, supporting the safety profile observed in our study (6).

Overall, the findings of the present study corroborate the majority of published literature indicating that vaginal misoprostol is associated with a shorter induction-to-delivery interval compared to the sublingual route, while maintaining similar rates of vaginal delivery and safety outcomes. Minor variations across studies may be attributed to differences in dosage regimens, parity distribution, Bishop score at baseline, and monitoring protocols. Given the consistency of our findings with previous randomized trials and meta-analyses, vaginal misoprostol appears to be a more efficient route for the induction of labor in post-term pregnancies. However, sublingual misoprostol remains a practical alternative in settings where vaginal administration is less acceptable or feasible. Further multicenter trials with larger populations and standardized dosing protocols would help refine optimal route selection for diverse obstetric populations.

CONCLUSION

Vaginal misoprostol was associated with a significantly shorter induction-to-delivery interval compared to sublingual misoprostol in post-term pregnancies. However, both routes demonstrated comparable rates of successful vaginal delivery and similar obstetric outcomes. Vaginal administration may therefore be considered a more efficient option for reducing labor duration without compromising maternal or fetal safety. Sublingual misoprostol remains an effective alternative, particularly in situations where vaginal administration is less feasible or acceptable. Further large-scale multicenter studies are recommended to establish standardized protocols and optimize route selection for labor induction in post-term pregnancies.

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