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Comparison of Induction of Labour with Sublingual Versus Vaginal Misoprostol 25 UG in a Primigravida with Post-Date Pregnancy

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ABSTRACT

In obstetrics, the induction of labour has been widely used in clinical practice for a decade. Misoprostol is effective for the induction of labour. It can be administered either sublingually or via the vaginal route. **Objective:** To compare the induction of labour with sublingual versus vaginal Misoprostol 25 ug in primigravida with postdate pregnancy. **Methods:** Our Study Prospective Comparative Study with consecutive sampling, conducted at the department of Gynecology, and Obstetrics at Saidu Group of Teaching Hospitals Swat, from March 2025 to September 2025 (6 months duration). **Results:** 160 participants were analyzed, with 80 in Group A (sublingual) and 80 in Group B per-vaginal route). Vaginal delivery within 24 hours occurred in 84.4% of the sublingual group and 80.8% of the vaginal group (p=0.612), while the mean induction-to-delivery time was significantly shorter in the sublingual group (9.1 ± 2.9 hrs vs. 10.4 ± 3.2 hrs; p=0.04). Maternal side effects and neonatal outcomes, including Apgar scores and birth weights, were comparable between the two groups. **Conclusions:** Both sublingual and vaginal misoprostol (25 µg) were effective for labour induction in post-date primigravida. The sublingual route demonstrated a significantly shorter induction-to-delivery interval with comparable safety outcomes, offering a practical alternative for routine clinical use.

INTRODUCTION

Induction of labour was first described by Thomas Denman, who explained amniotomy in his textbook in the 1780s [1]. In obstetrics, induction of labour has been widely used in clinical practice for decades. This trend has significantly increased, especially in the last few years, during which around 9.6% of worldwide deliveries have been medically induced. These statistics are particularly high in the United States and Europe, where around 27% and 33% of overall deliveries are induced through medical therapy [2, 3]. There are several indications for the Induction of labour (IoL); the most common ones are when maternal or fetal life is at risk with an ongoing pregnancy and gestational age above 41 weeks. According to the literature, in a high-risk pregnancy, one can induce labour preterm (<37 weeks), and, whenever possible, IoL should be delayed until 39 weeks of pregnancy. Most international guidelines recommend induction of labour at or after 41 weeks of gestation [4, 5]. In obstetrics, induction of labour is one of the most significant practices, and over the past decade, the number of women undergoing induction of labour has increased substantially [6]. The mechanical methods were previously used for labour induction, but these conventional methods have largely been replaced by medical therapy, including Prostaglandins and synthetic

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oxytocin. Misoprostol is currently a topic of interest among scholars as it is a more convenient and much safer alternative for the induction of labour [7]. It promotes cervical ripening and enhances cervical dilatation, resulting in shorter duration of labour and facilitates vaginal delivery [8]. Misoprostol is effective for the induction of labour. It can be administered either sublingually or via the vaginal route. Current international guidelines support dose-adjusted misoprostol, which should not exceed 25mg to prevent maternal and neonatal adverse outcomes [9]. Women often prefer to take misoprostol orally due to various concerns, one of which is that oral administration is more convenient and provides privacy compared to the vaginal route. However, the literature does not provide strong evidence regarding the best route for misoprostol administration in induction of labour[10].

Although multiple studies in the literature described different administration routes, the existing literature lacks research studies evaluating how sublingual misoprostol compares to vaginal administration in terms of safety and efficacy. Therefore, our study aimed to address the literature gap by answering the question: Is sub-lingual misoprostol (25mg) as effective and safe as vaginal misoprostol (25mg) for the induction of labor in primigravida women with post-dated pregnancy in our set-up? our study aims to compare the induction of labour with sublingual versus vaginal Misoprostol 25 ug in primigravida with postdate pregnancy at the tertiary care hospital of the northern region of Pakistan. Finding the optimal route of misoprostol administration would help the clinician to improve maternal comfort, effective labor induction, and minimize adverse effects.

METHODS

This was a prospective comparative study employing consecutive sampling conducted at the Department of Gynecology and Obstetrics of Saidu Group of Teaching Hospitals, Swat from July 2025 to December 2025 (6 months duration). Ethical approval was obtained from the Institutional Review Board of Saidu Medical College (IRB-SMC number = 90-ERB/024; dated 3rd June 2024). The required sample size was calculated using a WHO sample size calculator based on the following specifications: level of significance = 5%, statistical power of 80%, an expected prevalence of 91.0% for population group A and 89.0% for population Group B [11]. For the given population, the optimal sample size for the study was 160 patients. Data were collected using a preformed questionnaire through the consecutive sampling technique. To control cofounders and minimize bias, patients were recruited after obtaining written informed consent using a predefine inclusion and exclusion criteria. Inclusion criteria include: maternal age ranging from 15 to 45 years, Primigravida with singleton pregnancy, single gestation with viable fetus in cephalic position, live fetus with cephalic presentations, and gestational age exceeding ≥ 40 weeks. While exclusion criteria include those having history of uterine surgery, major fetal malformation, patients having premature rupture of membrane, antepartum hemorrhage, Patients with documented known medical comorbidities, or any other contraindication to vaginal delivery. For this study, labor induction was defined as the initiation of uterine contraction before the spontaneous onset of labor for vaginal delivery, using either pharmacological or mechanical methods [12]. Uterine tachysystole was defined as excessively frequent uterine contractions during pregnancy, typically more than 5 uterine contractions per 10 min in consecutive. Failed induction was defined as the necessity for cesarean delivery due to failure to establish active labor (cervical dilation ≥4 cm with adequate contractions) after completion of the maximum six doses of misoprostol (25 µg every 4 hours for 24 hours). Intervals [13]. Fetal distress was defined as compromised fetal well-being indicated by pathological pattern of fetal heart rate including late decelerations, and persistent bradycardia (<110 bpm), or loss of variability on continuous CTG interpreted by an obstetrician. [14]. Uterine hypertonus, as a single contraction lasting >2 minutes or baseline intrauterine pressure >25 mmHg, whereas hyperstimulation involves hypertonic activities associated with non-reassuring fetal heart rate patterns, both are well-recognized complications of labor induction with prostaglandins. After obtaining approval of Ethical Committee of Saidu Medical College, Swat, all 160 patients were stratified into two groups i.e. Group A, and Group B. The group-A received vaginal misoprostol (25 µg) and Group B sublingual misoprostol (25 µg), administered 4-hourly up to six doses. Continuous electronic fetal monitoring (cardiotocography) was performed for 20–30 minutes prior to administering each repeat dose to confirm fetal well-being and absence of uterine tachysystole. Detailed history, physical, and obstetric examinations, and Bishop scoring were performed at admission. Bishop scoring was performed by a single trained obstetrician at admission to ensure consistency. Labor progress and fetal heart rate were monitored; subsequent doses were administered until effective uterine contractions (3 contractions every 10 mins), cervical dilation > 3cm, Bishop score > 8, or complications (tachysystole, hypertonus, or hyperstimulation) occurred. In the event of such complications, patients were managed with left lateral positioning, oxygen (8 L/min) via face mask, and subcutaneous terbutaline (250 µg). The principal outcome assessed was the frequency of vaginal birth. The study also identified total drug administration, duration from drug

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administration to birth completion, failure of induction within 24 hours, pathological uterine contractions, undesired maternal response, fetal compromise, newborn Apgar scores, and requirement for NICU admissions.

For data analysis SPSS software version 22.0 was employed. For descriptive variables, mean ± standard deviation was computed for continuous variables (age, mean birth weight, and Apgar score), and frequencies and percentages for categorical variables (mode of delivery, uterine activity abnormalities, side effects, fetal distress, and NICU admissions). Comparative analysis between the two groups was performed for all key outcomes. Effect modifiers such as age, uterine tachysystole, hypertonus, hyperstimulation, side effects, and fetal outcomes were stratified, and post-stratification comparisons were made using the Chi-square test. The primary outcome (vaginal birth rate within 24 hours) was analyzed using the Chi-square test (or Fisher's exact test, as appropriate for cell counts) to compare proportions between Group A (sublingual) and Group B (vaginal). independent t-test or Mann-Whitney U test were used for continuous variables e. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 160 primigravida with post-date pregnancy were recruited into two groups for the study over six months of duration. In Group A, three patients and 2 in group B underwent cesarean section and were excluded from final data analysis 77 patients in group A received sublingual misoprostol 25 mg, and 78 patients in group B received vaginal misoprostol. Mean age of participants in group A was 25.9 ± 3.4 years and 26.3 ± 3.9 years in group B. In group A, the mean gestational age was 41.1 ±0.6 weeks, while in group B it was 41.3 ± 0.8 weeks. The mean Bishop score at admission in group A was 3.1 ± 0.9, while in group B it was 3.0 ± 1.1. The comparison shows that there were no statistically significant differences between the two groups regarding mean age, gestational age, and Bishop score (Table 1).

Table 1: Baseline Characteristics among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Mean Age (Years)	25.9 ± 3.4	26.3 ± 3.9	0.61
Mean Gestational Age (Weeks)	41.1 ± 0.6	41.3 ± 0.8	0.46
Mean Bishop Score (at Admission)	3.1 ± 0.9	3.0 ± 1.1	0.71

Among group A, 65 out of 77 participants (84.41%) achieved vaginal delivery within 24 hours, while in group B, 63 participants achieved that (p=0.612). Moreover, the mean induction to delivery interval was calculated and compared between the two groups. This interval was significantly shorter in the sublingual group (9.1 ± 2.9 hours) compared to the vaginal misoprostol group (10.4 ±3.2 hours) (p=0.04). Additionally, the average misoprostol dose required in the sublingual group was relatively lower (i.e., 3.1 ±0.7) compared to the vaginal misoprostol group (3.5 ± 1.1) (p = 0.735). The labor and delivery outcomes in Group A (sublingual) and Group B (per-vaginal route). While the two cohorts showed similar success rates for vaginal delivery within a 24-hour window (p>0.05), Group A exhibited a statistically significant reduction in the mean induction-to-delivery time compared with Group B (p<0.05). Additionally, the mean dose requirement did not differ significantly between the groups (Table 2).

Table 2: Labor and Delivery Outcomes among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Vaginal Delivery within 24 hours	n=65 (84.41%)	n=63 (80.76%)	0.61
Mean induction delivery interval (Hours)	9.1 ± 2.9 hours	10.4 ± 3.2 hours	0.04
Mean number of doses required	3.1 ± 0.7	3.5 ± 1.1	0.73

Maternal side effects and uterine activity were assessed in both groups. In Group A (Sublingual), 10 participants developed tachysystole, 4 developed hypertonus, 3 developed hyperstimulation syndrome, 3 developed fever, and 08 patients experienced nausea and vomiting. In Group B (Vaginal misoprostol), 6 developed tachysystole, 3 developed hypertonus, 2 developed hyperstimulation syndrome, 5 developed fever, and 6 experienced nausea and vomiting. The incidence of tachysystole, hypertonus, hyperstimulation syndrome, fever, and nausea/vomiting was comparable between the sublingual and per-vaginal groups. There were no statistically significant differences between any parameter (p > 0.05) (Table 3).

Table 3: Maternal Side Effects and Uterine Activity among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Tachysystole	n= 10	n= 06	0.30
Hypertonus	n= 04	n= 03	0.71
Hyperstimulation Syndrome	n= 03	n= 02	0.65
Fever (>38℃)	n= 03	n= 05	0.54
Nausea and Vomiting	n= 08	n= 06	0.62

Neonatal outcomes were also assessed in both groups. In Group A, the mean birth weight was 3.31 ±0.30 kg, while in Group B the mean birth weight was 3.28 ± 0.34 kg (p=0.60). The mean 5-minute Apgar score for neonates delivered in Group A was 8.8 ±0.5, while in Group B, the mean 5-min Apgar score was 8.6 ±0.5 with no statistical significance (p= o.43). Five patients in Group A and four in Group B developed fetal distress (p = 0.73). Mean birth weight and 5-minute Apgar scores were comparable between the

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sublingual and per-vaginal groups, and the incidence of fetal distress was low in both. No statistically significant differences were observed (p > 0.05) (Table 4).

Table 4: Neonatal outcomes among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Mean Birth weight (in Kg)	3.31 ± 0.30	3.28 ± 0.34	0.60
Mean 5-min Apgar score	8.8 ± 0.5	8.6 ± 0.5	0.43
Fetal Distress	n=5	n=4	0.73

DISCUSSION

Initiation of labour is one of the most common obstetrical interventions. A decade or more ago, mechanical techniques such as balloon catheter and amniotomy were used for cervical ripening. However, at present, pharmacological agents, including prostaglandins, are more commonly used in case of an unfavorable cervix, as they act on both the cervix and the uterus to increase contractions [15]. In our study, we compared induction of labour using sublingual versus per-vaginal misoprostol in primitive gravida. Our principal finding indicated that participants receiving sublingual misoprostol exhibited a shorter induction to delivery interval compared to those administered vaginal misoprostol (p= 0.04), our findings do support by multiple studies in literature including the study carried out by Shafqat *et al.* in Peshawar Pakistan (the population with same cultural and demographic profile like our study population) concluded that, the use of misoprostol could reduce mean induction to delivery time [16]. A meta-analysis conducted by Pergialiotis *et al.* [17] concluded that the sublingual misoprostol administration could lead to a decrease in induction to delivery time compared to the per-vaginal route without any accompanying side effects. Although both of them are equally safe in terms of induction of labour. Moreover, aside from comparison with per-vaginal administration, sublingual administration also had reduced induction to delivery time when compared with per-oral administration of misoprostol [18]. All these studies support our study findings. Additionally, in contrast to our study findings, some studies in the literature have found no difference between the two groups. A study conducted by Galidevara *et al.* [19], comparing oral, vaginal, and sublingual routes of misoprostol administration, concluded that all three routes of misoprostol administration are equally effective for labor induction. However, there was no statistical significance difference (p=0.88). Moreover, the maternal and neonatal side effects in both groups were also compared in our study. Maternal side effects included Tachysystole, Hypertension, and Hyperstimulation syndrome. Several studies in the literature have also reported the maternal side effects associated with sublingual and vaginal misoprostol use [20].

Overall, the incidence of side effects varies and depends upon the route, dose, and population. The prospective comparative design represents a notable strength of this study, which helps in minimizing bias. The use of consecutive sampling and adherence to standard protocols ensures consistency in data collection and analysis between groups. However, our study has certain limitations: because the data were collected from only one, the findings may not be readily generalizable to wider populations Future research should consider multicenter studies with larger cohorts to validate these findings. Despite these limitations, our study can assist the clinician in identifying the more effective and safer route of misoprostol administration for the induction of labour, improving overall maternal and neonatal outcomes. Implementation of the results could enhance safe, cost-effective, and standardized labour induction practice.

CONCLUSIONS

In this study, both the sublingual, and vaginal misoprostol (25 µg) were equally effective for labour induction in post-date primigravida women with comparable vaginal delivery rates and safety outcomes. However, the sublingual route shows a significantly shorter induction-to-delivery interval and offers the practical advantage of non-invasive administration. Overall, sublingual misoprostol can be considered an effective and practical alternative to the vaginal route for routine clinical use.

Authors' Contribution

Conceptualization: HG, STK
Methodology: HG, SK, S
Formal analysis: STK, KJ, N
Writing and Drafting: KJ, SK, ZI
Review and Editing: HG, STK, KJ, SK, ZI, S, N

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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