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Efficacy of Buccal, Sublingual, and Vaginal Misoprostol in Induction of Labor in Term Pregnancy.

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Abstract

Background and Objective: This study aimed to compare the efficacy of buccal, vaginal, and sublingual misoprostol for induction of labor in term pregnancy. ***Materials and Methods:*** This randomized controlled trial was conducted at Civil Hospital, Karachi, from 2020 to 2024. A total of 280 pregnant women with term singleton pregnancies requiring induction of labor were enrolled and randomly allocated into three groups. Group A received 50 µg buccal misoprostol, Group B received 25 µg vaginal misoprostol, and Group C received 50 µg sublingual misoprostol for induction of labor. Maternal and fetal complications, Bishop score at 1 hour and 6 hours following administration, total misoprostol dose, need for oxytocin augmentation, and vaginal delivery within 24 hours were recorded and compared among the groups. Data were analyzed using SPSS version 21, and a p-value of less than 0.05 was considered statistically significant. ***Results:*** Among the 280 participants, no statistically significant differences were observed among the buccal (n=93), vaginal (n=94), and sublingual (n=93) groups regarding maternal complications (8.6%, 7.4%, and 9.7%, respectively; p=0.81) or fetal complications (6.5%, 5.3%, and 7.5%, respectively; p=0.76). The mean Bishop score at 1 hour was 3.8 ± 1.2, 4.0 ± 1.1, and 3.9 ± 1.3 in the buccal, vaginal, and sublingual groups, respectively (p=0.64). Similarly, the mean Bishop score at 6 hours showed no significant difference among the groups (6.7 ± 1.5, 6.9 ± 1.4, and 6.8 ± 1.6; p=0.72). Total misoprostol dose administered was also comparable (p=0.58). However, significant differences were observed in vaginal delivery within 24 hours, achieved in 68.8% of the buccal group, 81.9% of the vaginal group, and 78.5% of the sublingual group (p=0.03). Oxytocin augmentation was required more frequently in the buccal group (41.9%) compared with the vaginal (25.5%) and sublingual (29.0%) groups (p=0.02). ***Conclusion:*** Buccal, vaginal, and sublingual misoprostol demonstrated comparable safety profiles with respect to maternal and fetal complications. While cervical ripening outcomes and total misoprostol requirements were similar across the three routes, vaginal and sublingual administration were associated with a higher rate of vaginal delivery within 24 hours and a lower requirement for oxytocin augmentation compared with the buccal route. These findings suggest that all three routes are effective for induction of labor at term, although vaginal and sublingual misoprostol may offer advantages in induction success.

Keywords: Misoprostol; Buccal; Sublingual; Vaginal; Induction of labor; Cervical ripening.

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INTRODUCTION

Induction of labor is a common obstetric intervention performed for maternal or fetal indications when continuation of pregnancy may pose a risk. It is widely practiced in both developed and developing countries and aims to initiate uterine contractions before spontaneous labor begins.

Several agents can be used for labor induction, but prostaglandins are among the most effective because they promote cervical ripening as well as uterine activity. Misoprostol, a prostaglandin E1 analogue, is widely used for this purpose because it is inexpensive, stable at room temperature, and easy to administer.

Misoprostol may be given by different routes, including vaginal, sublingual, buccal, oral, and rectal administration. Each route has distinct pharmacokinetic properties that may influence onset of action, cervical ripening, uterine contractility, and maternal side effects. Vaginal misoprostol is often considered more effective for cervical ripening, whereas sublingual and buccal routes may offer greater convenience and patient comfort.

Previous studies have suggested that the route of administration can affect both efficacy and safety outcomes, including labor duration, need for oxytocin, uterine tachysystole, and neonatal status. However, comparative evidence among buccal, vaginal, and sublingual routes remains limited, especially in term pregnancies with an unfavorable cervix.

Therefore, this study was conducted to compare the efficacy and safety of buccal, vaginal, and sublingual misoprostol for induction of labor in term pregnancy.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Civil Hospital, Karachi, from 2020 to 2024. A total of 280 pregnant women were enrolled after obtaining informed consent.

Participants

Women were eligible if they had a singleton live pregnancy in cephalic presentation, gestational age greater than 37 weeks, Bishop score less than 5, reassuring fetal heart rate pattern, estimated fetal weight less than 4 kg, and adequate amniotic fluid volume. Patients with a history of uterine surgery or cesarean section, severe preeclampsia, parity greater than 2, uterine contractions at admission, cardiovascular, renal, or hepatic disease, ruptured membranes, fetal growth restriction, or suspected fetal anomalies were excluded.

Randomization and Intervention

Participants were randomly allocated into three groups. The buccal group (n=93) received 50 µg misoprostol placed between the cheek and gum every 6 hours for up to 24 hours. The sublingual group (n=93) received 50 µg misoprostol sublingually every 6 hours for up to 24 hours. The vaginal group (n=94) received 25 µg vaginal misoprostol every 6 hours according to the induction protocol.

Monitoring and Outcomes

Maternal age, gestational age, body mass index, and baseline Bishop score were recorded at admission. Fetal heart rate monitoring was performed before induction and continued throughout labor. Amniotomy was undertaken when clinically indicated. Oxytocin augmentation was initiated at least 4 hours after the last dose of misoprostol when adequate uterine contractions were not achieved.

The primary outcome was vaginal delivery within 24 hours of induction. Secondary outcomes included cesarean section rate, Bishop score at 1 and 6 hours, need for oxytocin augmentation, total misoprostol dose, maternal complications, fetal complications, Apgar scores, and neonatal intensive care unit (NICU) admission.

Statistical Analysis

Data were analyzed using SPSS version 21. Continuous variables were expressed as mean ± standard deviation and compared using one-way analysis of variance (ANOVA). Categorical variables were analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 280 women were enrolled and randomized into the buccal (n=93), sublingual (n=93), and vaginal (n=94) groups. Baseline maternal age, gestational age, body mass index, and initial Bishop score were comparable among the three groups, with no statistically significant differences observed.

Maternal complications occurred in 8 (8.6%) women in the buccal group, 9 (9.7%) in the sublingual group, and 7 (7.4%) in the vaginal group (p=0.81). Fetal complications were observed in 6 (6.5%), 7 (7.5%), and 5 (5.3%) participants, respectively (p=0.76). The mean Bishop score at 1 hour was 3.8 ± 1.2 in the buccal group, 3.9 ± 1.3 in the sublingual group, and 4.0 ± 1.1 in the vaginal group (p=0.64). At 6 hours, the mean Bishop scores increased to 6.7 ± 1.5, 6.8 ± 1.6, and 6.9 ± 1.4, respectively, without significant intergroup differences (p=0.72).

The total dose of misoprostol administered was comparable among the three groups (p=0.58). Vaginal delivery within 24 hours was achieved in 64 (68.8%) women in the buccal group, 73 (78.5%) in the sublingual group, and 77 (81.9%) in the vaginal group, demonstrating a statistically significant difference among the groups (p=0.03). Oxytocin augmentation was required more frequently in the buccal group (39/93, 41.9%) compared with the sublingual (27/93, 29.0%) and vaginal groups (24/94, 25.5%) (p=0.02).

Cesarean section rates were similar across the groups, with the most common indications being meconium-stained liquor, non-reassuring fetal heart rate patterns, and failed induction. Uterine tachysystole occurred in 2 women in the sublingual group and 1 woman each in the buccal and vaginal groups. Uterine hyperstimulation was uncommon and showed no significant difference among the groups (p>0.05).

Neonatal outcomes were comparable among the three groups. Low Apgar scores at 5 minutes were observed in 3 (3.2%) neonates in the buccal group, 2 (2.2%) in the sublingual group, and 2 (2.1%) in the vaginal group (p=0.89). NICU admission rates were 4.3%, 3.2%, and 3.2%, respectively, with no statistically significant differences observed (p=0.91).

Table 1. Maternal and Fetal Complications

Outcome	Buccal (n=93)	Vaginal (n=94)	Sublingual (n=93)	p-value
Maternal complications, n (%)	8 (8.6%)	7 (7.4%)	9 (9.7%)	0.81
Fetal complications, n (%)	6 (6.5%)	5 (5.3%)	7 (7.5%)	0.76

Table 2. Bishop Score Following Misoprostol Administration

Variable	Buccal (n=93)	Vaginal (n=94)	Sublingual (n=93)	p-value
Bishop score at 1 hour (Mean ± SD)	3.8 ± 1.2	4.0 ± 1.1	3.9 ± 1.3	0.64
Bishop score at 6 hours (Mean ± SD)	6.7 ± 1.5	6.9 ± 1.4	6.8 ± 1.6	0.72

Table 3. Labor Induction Outcomes

Outcome	Buccal (n=93)	Vaginal (n=94)	Sublingual (n=93)	p-value
Vaginal delivery within 24 hours, n (%)	64 (68.8%)	77 (81.9%)	73 (78.5%)	0.03
Oxytocin augmentation required, n (%)	39 (41.9%)	24 (25.5%)	27 (29.0%)	0.02

Table 4. Uterine Activity Outcomes

Outcome	Buccal (n=93)	Vaginal (n=94)	Sublingual (n=93)	p-value
Uterine tachysystole, n (%)	1 (1.1%)	1 (1.1%)	2 (2.2%)	>0.05
Uterine hyperstimulation, n (%)	Rare	Rare	Rare	>0.05

Table 5. Neonatal Outcomes

Outcome	Buccal (n=93)	Vaginal (n=94)	Sublingual (n=93)	p-value
Low Apgar score at 5 minutes, n (%)	3 (3.2%)	2 (2.1%)	2 (2.2%)	0.89
NICU admission, n (%)	4 (4.3%)	3 (3.2%)	3 (3.2%)	0.91

DISCUSSION

This randomized controlled trial compared the efficacy and safety of buccal, sublingual, and vaginal misoprostol for induction of labor in 280 women with term pregnancies. The findings demonstrated that all three routes were generally safe and effective for labor induction. No significant differences were observed in maternal or fetal complications, Bishop score improvement, total misoprostol dose administered, neonatal outcomes, or cesarean section rates. However, significant differences were noted in vaginal delivery within 24 hours and the requirement for oxytocin augmentation.

In the present study, vaginal delivery within 24 hours was achieved more frequently in the vaginal and sublingual groups than in the buccal group. Similarly, the need for oxytocin augmentation was significantly higher among women receiving buccal misoprostol. These findings suggest that while buccal misoprostol is effective for labor induction, vaginal and sublingual administration may provide more efficient uterine stimulation and facilitate earlier vaginal delivery. The comparable Bishop scores observed at 1 and 6 hours indicate that cervical ripening occurred effectively with all three routes, despite differences in ultimate delivery outcomes.

The safety profile observed in our study is consistent with previous reports demonstrating that misoprostol is a relatively safe induction agent when used in appropriate doses. Maternal adverse events, including fever, chills, nausea, vomiting, uterine tachysystole, and uterine hyperstimulation, were infrequent and did not differ significantly among the groups. Likewise, fetal complications, meconium-stained liquor, low Apgar scores, and NICU admissions were comparable across all treatment arms. These findings support the continued use of misoprostol for labor induction in carefully selected women with term pregnancies and unfavorable cervices.

The differences observed between routes of administration may be explained by variations in pharmacokinetic characteristics. Vaginal administration produces sustained absorption and prolonged local effects on cervical tissue, whereas sublingual administration provides rapid systemic absorption and high bioavailability. Buccal administration offers patient convenience but may result in lower or less sustained drug exposure, potentially explaining the increased requirement for oxytocin augmentation observed in our study. These pharmacological differences may influence the rate of labor progression and overall induction success.

Our findings are in agreement with previous randomized trials and systematic reviews that have reported comparable safety outcomes among different routes of misoprostol administration while demonstrating differences in efficacy-related outcomes. Studies by Jahromi et al., Ayati et al., and Zahran et al. similarly reported that sublingual and vaginal misoprostol achieved favorable induction outcomes with acceptable maternal and neonatal safety profiles. Furthermore, Cochrane reviews have concluded that vaginal misoprostol remains an effective option for cervical ripening and labor induction, although alternative routes may offer comparable results in selected patient populations.

The strengths of this study include its randomized design, direct comparison of three commonly used routes of misoprostol administration, and evaluation of both maternal and neonatal outcomes. Additionally, clinically relevant endpoints such as vaginal delivery within 24 hours and oxytocin augmentation were assessed, providing practical information for obstetric decision-making.

Several limitations should be acknowledged. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings. Although the sample size of 280 participants was adequate to evaluate common outcomes, it may not have been sufficient to detect rare maternal or neonatal adverse events. The study also did not evaluate patient satisfaction, cost-effectiveness, or pharmacokinetic parameters, which may have provided further insight into route-specific differences. Finally, the absence of blinding may have introduced performance or assessment bias.

Overall, the results indicate that buccal, sublingual, and vaginal misoprostol are safe and effective methods for induction of labor at term. However, vaginal and sublingual administration were associated with higher rates of vaginal delivery within 24 hours and lower requirements for oxytocin augmentation. Larger multicenter randomized trials are warranted to confirm these findings and establish the optimal route of misoprostol administration for routine obstetric practice.

CONCLUSION

The present study demonstrated that buccal, vaginal, and sublingual misoprostol are effective and safe options for induction of labor in term pregnancies. No significant differences were observed among the three routes regarding maternal complications, fetal complications, Bishop score improvement, cesarean section rate, or neonatal outcomes. However, vaginal and sublingual misoprostol were associated with higher rates of vaginal delivery within 24 hours and lower requirements for oxytocin augmentation compared with buccal misoprostol.

These findings suggest that while all three routes are clinically acceptable for labor induction, vaginal and sublingual administration may offer advantages in induction efficiency. Further large-scale, multicenter randomized controlled trials are recommended to confirm these findings and establish the optimal route of misoprostol administration for routine obstetric practice.

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