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Comparison of Sublingual Misoprostol and Per Vaginal Dinoprostone for Induction of Labour

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ABSTRACT

Introduction: Misoprostol and dinoprostone are two widely used induction agents. Our study was designed to compare both these drugs in terms of induction to labour time, ceserean section rate and meconium staining. **Objective:** To compare the outcome of sublingual misoprostol and per-vaginal dinoprostone for induction of labour. **Methods:** A total of 110 patients were enrolled using blocked randomization sampling, with 55 patients in each group. The primary outcome was the mode of delivery. The need for an emergency cesarean section was recorded in cases of reduced labor pains, failed induction, pathological cardiotocography, or thick meconium-stained liquor. Additional outcome variables were determined for all enrolled subjects which were the success of induction (induction was considered successful if delivery occurred within 12 hours of induction), induction-to-delivery interval (the time from induction to fetal delivery was recorded in minutes), meconium passage and the total number of doses administered from the first dose until delivery. **Results:** Both groups exhibited comparable baseline characteristics, including age, BMI, gestational age, and parity. Dinoprostone was shown to be better than misoprostol in all study outcomes. **Conclusions:** Our study suggests that dinoprostone was associated with a significantly shorter induction-to-delivery interval and a higher proportion of deliveries within 12 hours compared to misoprostol. The increased incidence of meconium-stained amniotic fluid in the misoprostol group highlights a potential risk factor that needs further investigation.

INTRODUCTION

Induction of labour is the process of initiating contractions in pregnant women who are currently not in labour, to help them achieve vaginal delivery within 24 to 48 hours.[1, 2] Induction of labor is a common obstetric intervention that stimulates the onset of labor using artificial methods.[3] Cervical ripening is one of the methods used for labour induction; it is "the use of pharmacological or other means to soften, efface, or dilate the cervix to increase the likelihood of a vaginal delivery."[4] In the past 20 years prostaglandins have been used in a variety of formulations for labor induction and cervical ripening. Prostaglandins were used intravenously but the route of administration was associated with significant side effects.[5]

Literature supports the use of two prostaglandin preparation for induction of labor, which includes Dinoprostone (prostaglandin E2), and misoprostol (prostaglandin E1). Misoprostol and Dinoprostone are equally efficacious in achieving spontaneous vaginal delivery, reduction in induction-delivery interval and in reducing the need for oxytocin.[5] Sublingual misoprostol is an effective way for induction of labor at term, it has the advantage of easy administration and may be more suitable than other routes.[6] But also has some side effects including tachysystole, uterine hypertonicity and abnormal fetal heart during tachysystole or uterine hypertonicity.[7] Side effects of Dinoprostone include hypertonic uterine contractions, impact on gastrointestinal smooth muscle, leading to vomiting, diarrhea, nausea, headache, shivering, pyrexia, chance of fetal distress without uterine hyper-stimulation, and increased fetal heart rate.[8, 9]

One trial reported that the induction to delivery interval was 4 hrs 2min with misoprostol while 10 hrs 45 min with Dinoprostone, this lower interval in misoprostol group was statistically significant (p= < .002); cesarean section rate was 6% with misoprostol while 26% with Dinoprostone and meconium was passed in 4% cases with misoprostol while in 6% cases with Dinoprostone ($p<0.05$).[10] Another trial compared efficacy and side effects of induction with Misoprostol and Dinoprostone, as the induction to delivery interval was 14.42±7.182 hours with misoprostol while 14.73±7.022 hours with Dinoprostone, cesarean section rate was 26.3% with misoprostol while 35.1% with Dinoprostone, successful

induction within 12-24 hours in 88.8% vs. 90.2% and meconium was passed in 9.3% cases versus 8.8% cases, respectively (p>0.05).[11]

One more trial found that the induction to delivery interval was 1356±1033 min with misoprostol while 1208±613 min with Dinoprostone, cesarean section rate was 32.9% with misoprostol while 27.3% with Dinoprostone, delivery within 12 hours in 13.8% vs. 15.1% and meconium was passed in 22.2% cases versus 26.2% cases respectively. The difference was insignificant (p>0.05).[12] A randomized prospective study comparing Misoprostol and Dinoprostone for elective induction of labor in nulliparous women at full term found that fewer additional doses were required in the misoprostol group compared to the Dinoprostone group (7.5% vs. 22% p < 0.05 [13].

The rationale of this study was to compare the outcome of Sublingual Misoprostol and per vaginal Dinoprostone for induction of labour. Literature reported that the outcome of misoprostol was good as compared to dinoprostone. So we want to conduct this study to find the more appropriate drug in order to prevent complications of induction of labor. Moreover, we may implement the results of this study in local settings to implement more effective drug with less side effects or without compromising the health of mother and her neonate.

MATERIALS AND METHODS

This randomized controlled trial was conducted at the Department of Obstetrics and Gynecology, Shifa International Hospital, Islamabad, over a period of 6 months from September, 2024 to February, 2025. The study's aim was to compare the outcome of sublingual misoprostol and per-vaginal dinoprostone for induction of labour. The null hypothesis being tested was that “there is no difference in the outcome of sublingual misoprostol and per vaginal dinoprostone for induction of labour”. Induction of labor was defined as the application of pharmacological agents to stimulate uterine contractions during pregnancy before the spontaneous onset of labor to achieve vaginal delivery. The primary outcome was the mode of delivery. The need for an emergency cesarean section was recorded in cases of reduced labor pains, failed induction, pathological cardiotocography, or thick meconium-stained liquor. Additional outcome variables were determined for all enrolled subjects which were the success of induction (induction was considered successful if delivery occurred within 12 hours of induction), induction-to-delivery interval (the time from induction to fetal delivery was recorded in minutes), meconium passage and the total number of doses administered from the first dose until delivery.

A total of 110 patients were enrolled using non-probability consecutive sampling technique using the inclusion criteria. Sample size was calculated using the WHO sample size calculator with a significance level of 5%, power of 80%, proportion of the population for group 1 (misoprostol) was taken as 6%[10] and population for group 2 (Dinoprostone) was taken as 26%[10]. Inclusion criteria included female patients aged 18-40 years, parity <5, presenting at gestational age >37 weeks (on LMP) undergoing induction of labor (as per operational definition). Exclusion criteria were females with preeclampsia (BP≥140/90mmHg with proteinuria >+1 on dipstick method), thyroid disorder (TSH>5mIU), liver disease (ALT & AST >40 IU), chronic or gestational diabetes (BSR>200mg/dl), previous cesarean section(s), abnormal placenta (previa, accreta, increta, abruption), amniotic fluid index <5cm or >21 cm (detected on ultrasound), multiple fetus, intrauterine growth restriction, congenital anomaly or macrosomia (fetal weight >4kg) (detected on ultrasound) and ruptured membranes (on clinical examination).

After obtaining informed consent, demographic information, including name, age, parity, BMI, and gestational age, was recorded. Participants were then randomly assigned to two groups using the lottery method. In Group A, all participants received 50 mcg of misoprostol sublingually, while in Group B, all participants received 3 mg of dinoprostone intravaginally. Participants were then followed in the labor room until delivery. The induction-to-delivery interval was recorded in minutes. Participants were assessed every six hours for the need for an additional dose. If delivery occurred within 12 hours, successful induction was documented. Continuous monitoring was conducted for meconium-stained liquor. The mode of delivery was recorded according to the operational definition. All data were documented on a specially designed proforma.

Statistical Methods

Data were entered and analyzed using SPSS version 25. Quantitative variables, including age, BMI, gestational age, induction-to-delivery interval, and the number of doses required, were presented as mean ± standard deviation (SD). Qualitative variables, such as parity, delivery within 12 hours, meconium passage, and mode of delivery, were presented as frequencies and percentages. Both groups were compared for the mean induction-to-delivery interval and the number of doses using an independent samples t-test, while successful induction, meconium passage, and mode of delivery were compared using the chi-square test. A p-value of ≤ 0.05 was considered statistically significant. Data were stratified for age, BMI, parity, and gestational age. Post-stratification, both groups were compared for the mean induction-to-delivery interval and the number of doses using an independent samples t-test, while successful induction, meconium passage, and mode of delivery were analyzed using the chi-square test within each stratum. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 110 pregnant women were included in the study, with 55 participants in each group: one receiving misoprostol and one receiving dinoprostone. The baseline characteristics, stratified results, and comparisons are detailed below.

Baseline Characteristics

The baseline demographic and clinical variables for both groups were comparable, with no statistically significant differences observed (Table I).

Table 1

Demographic and Clinical Variables of Study Groups

Variable	Sublingual Misoprostol (n=55)	Intravaginal Dinoprostone (n=55)
Mean Age (Years)	31.00 ± 4.63	30.64 ± 5.64
Mean Parity	3.47 ± 1.69	3.45 ± 1.69
Gestational Age (Weeks)	39.67 ± 1.14	39.27 ± 1.16
BMI (kg/ m^2)	29.09 ± 7.19	30.33 ± 6.73

These findings confirm that the two groups were well matched regarding demographic and clinical variables.

Study Outcomes

The results demonstrated a significant difference in the proportion of women who delivered within 12 hours of induction between the two groups. In the dinoprostone group, 50 out of 55 patients (90.9%) achieved delivery within 12 hours, whereas in the misoprostol group, only 30 out of 55 patients (54.5%) delivered within the same timeframe. This difference was found to be statistically significant ($p < 0.001$), indicating a faster onset of labor and progression to delivery with dinoprostone compared to misoprostol.

Table 2

Comparison of Labour Induction Outcomes between Intravaginal Dinoprostone and Sublingual Misoprostol

Variable	Intravaginal Dinoprostone (n=55)	Sublingual Misoprostol (n=55)	p-value
Delivered within 12 hours	50 (90.9%)	30 (54.5%)	<0.001
Had passage of meconium	4 (7.3%)	13 (23.6%)	0.018
Mode of Delivery: a. C-Section b. Instrumental Delivery c. Normal Vaginal Delivery	 10 (18.2%) 5 (9.1%) 40 (72.7%)	 16 (29.1%) 8 (14.5%) 31 (56.4%)	0.200
Induction to delivery interval (hours, mean ±SD)	8.11 *(±2.6)*	12.25 *(±3.4)*	<0.001
Number of doses received (mean ±SD)	1.47 *(±0.5)*	1.95 *(±0.8)*	<0.001

* Mean values are reported with standard deviation (±SD). Mode of delivery categories are mutually exclusive. p-values derived from chi-square test for categorical variables and independent samples t-test for continuous variables.

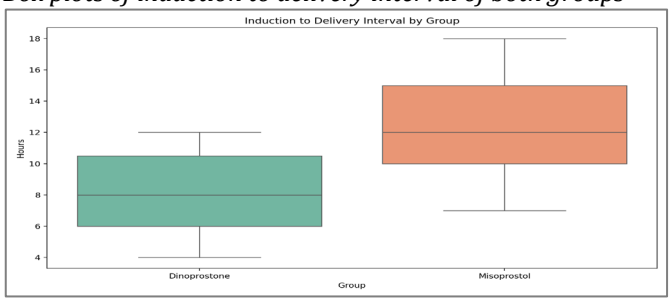
A higher incidence of passage of meconium was observed in the misoprostol group than in the dinoprostone group. Among the patients who received dinoprostone, there were only 4 patients (7.3%) who had meconium-stained amniotic fluid during labor. However in the misoprostol group, 13 patients (23.6%) had meconium passage. This difference was statistically significant ($p = 0.018$) which suggests a potential increase in fetal distress associated with misoprostol usage.

The mode of delivery was also compared between both the induction agents. In the dinoprostone group the majority of patients (40 out of 55, or 72.7%) had a vaginal delivery, 5 patients (9.1%) had instrumental delivery whereas 10 patients (18.2%) underwent a cesarean section. Similarly, in the misoprostol group, 31 patients (56.4%) delivered vaginally, while 8 (14.5%) required instrumental delivery, and 16 (29.1%) underwent a cesarean section. Although a trend was observed towards a higher rate of vaginal deliveries in the dinoprostone group and a higher cesarean section rate in the misoprostol group, the difference in the mode of delivery between the two groups did not reach statistical significance ($p = 0.200$).

The Misoprostol group had significantly longer induction to delivery intervals (12.25 ± *3.41* hours) as compared to Dinoprostone (8.11 ± 2.61 hours), $p < 0.001$ as shown in Figure 1. The Misoprostol group required significantly more doses (1.95 ± 0.76) compared to Dinoprostone (1.47 ± 0.5), $p < 0.001$. These distributions show a clear separation between the groups for both measures, suggesting consistent differences in effectiveness.

Figure 1

Box plots of induction to delivery interval of both groups



Data Stratification

Data were stratified for effect modifiers and it was seen that dinoprostone showed higher success rates across all strata. The stratification is shown in Figures 5-12. The difference was particularly pronounced in the age 25-35 group ($p=0.005$), obese BMI group ($p=0.002$), higher parity group ($p=0.001$) and the 37-40 weeks gestational age group ($p=0.001$). This showed that the advantage of Dinoprostone persists even after controlling for these potential confounding variables

Figure 2

Stratification of induction to delivery interval by gestational age

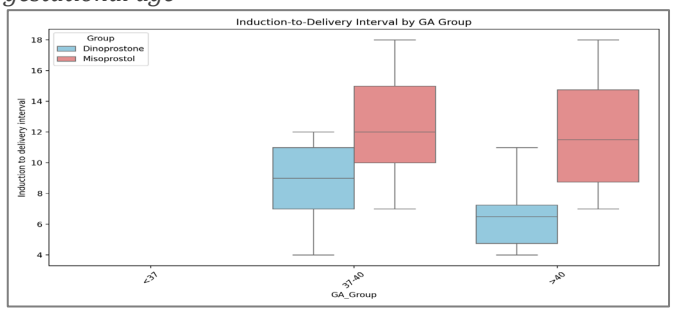


Figure 3

Stratification of induction to delivery interval by parity

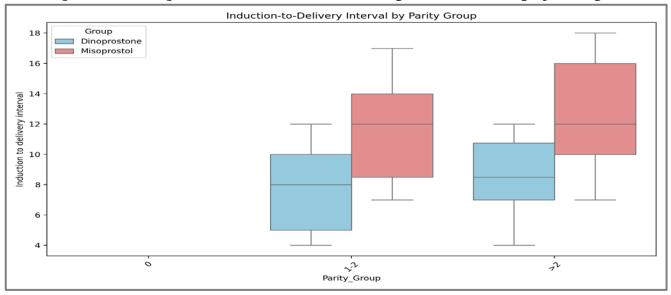


Figure 4

Stratification of induction to delivery interval by BMI

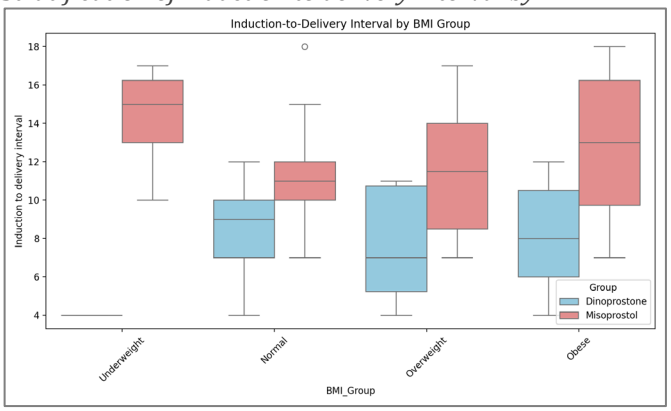


Figure 5

Stratification of induction to delivery interval by age

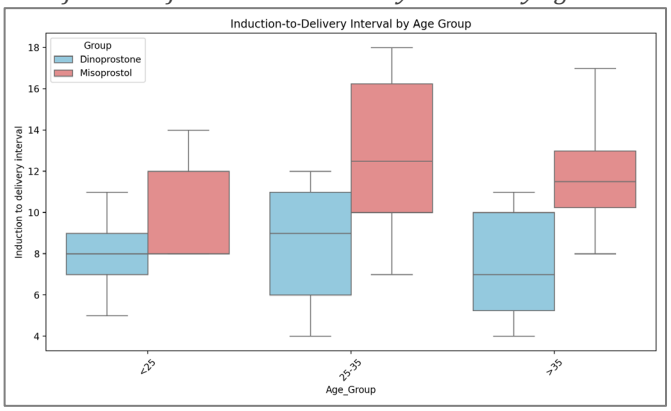


Figure 6

Stratification of success rate by parity

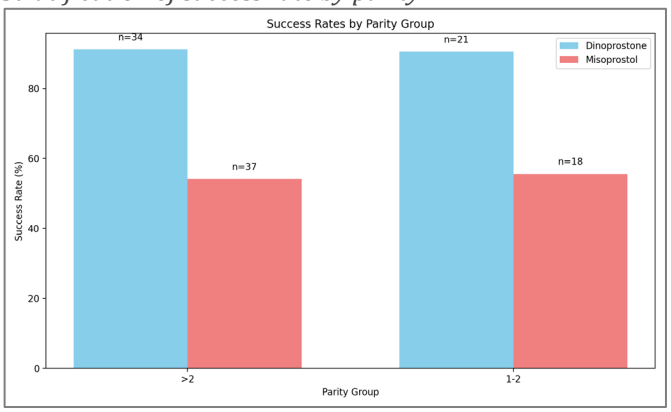


Figure 7

Stratification of success rate by BMI

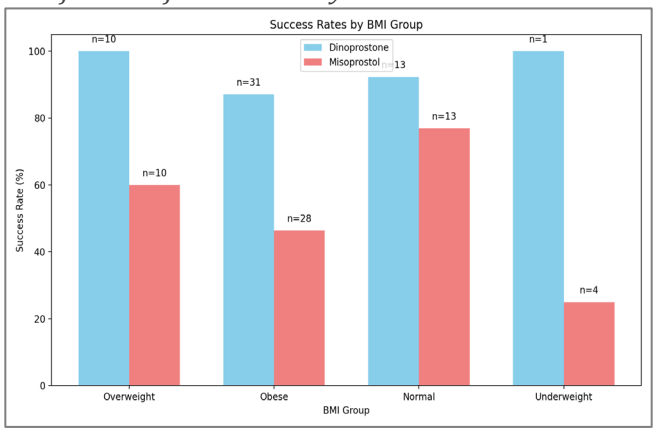


Figure 8

Stratification of success rate by gestational age

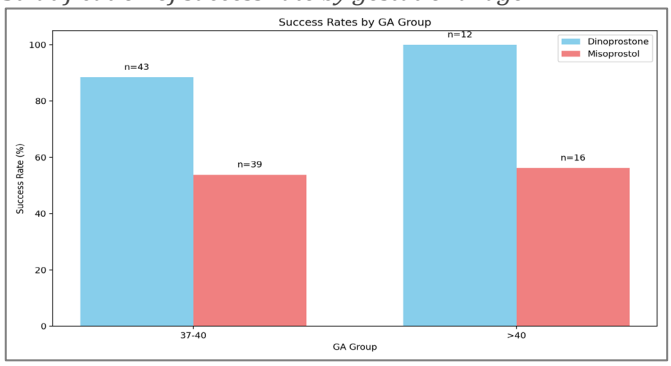
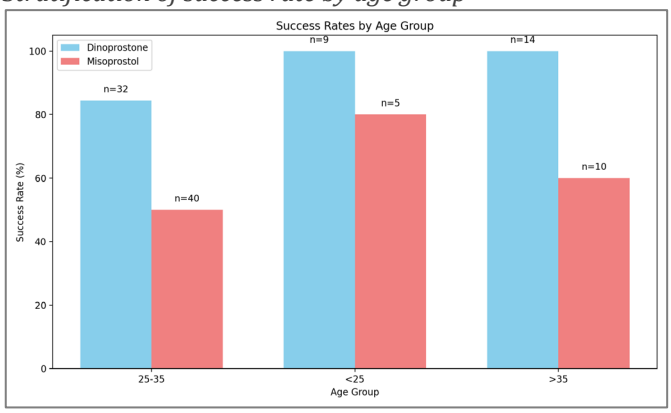


Figure 9

Stratification of success rate by age group



DISCUSSION

The present study compared the efficacy of sublingual misoprostol and intravaginal dinoprostone for labor induction in a cohort of 110 pregnant women. The findings show significant differences in main study outcomes. Our results contrast with much of the existing literature which needs further exploration into the potential reasons for these differences in our population.

Although a higher proportion of patients in the dinoprostone group had vaginal deliveries (72.7%) compared to the misoprostol group (56.4%), this difference did not reach statistical significance (p= 0.200). Similar findings were echoed in another study where it was seen that misoprotstol not only increases the risk of ceserean section but also more non-reassuring cardiotocographs [14]. Other studies report similar vaginal delivery rates for both interventions [15,16]. Our findings may suggest that misoprostol was associated with a higher need for surgical intervention, potentially due to increased uterine hyperstimulation or fetal distress [17].

A key finding of our study is that the induction-to-delivery interval was significantly shorter in the dinoprostone group (8.11 ± 2.61 hours) compared to the misoprostol group (12.25 ± 3.41 hours, p< 0.001). Some studies report similar efficacy in terms of time to labour [18,19]. The divergence from our findings may stem from differences in administration routes (sublingual vs. vaginal), dosing regimens, or variations in labor management protocols, including oxytocin augmentation. We observed that 90.9% of participants in the dinoprostone group delivered within 12 hours, compared

to only 54.5% in the misoprostol group (p< 0.001). This was also observed in the study done by Sahu et al [20].

Our study found a significantly higher incidence of meconium-stained amniotic fluid in the misoprostol group (23.6%) compared to the dinoprostone group (7.3%) (p = 0.018), also seen in the study by Ramadan et al [17]. However, other studies found no significant difference in neonatal outcomes between the two drugs [21,22]. The increased passage of meconium in our misoprostol group may indicate a higher rate of fetal distress, possibly linked to stronger uterine contractions and reduced placental perfusion. The pharmacological action of both dinoprostone and misoprostol on the ileum may contribute to the occurrence of meconium passage. Both drugs stimulate ileal contractions, which could lead to increased rates of meconium passage compared to oxytocin, which does not affect the ileum [21].

Our study has several limitations. First, the relatively small sample size may limit the generalizability of our findings. Second, differences in administration routes (sublingual misoprostol vs. intravaginal dinoprostone) may have influenced the results, as prior studies predominantly evaluated vaginal misoprostol. Additionally, variations in labor management protocols, including oxytocin augmentation, may have contributed to the observed discrepancies. Future research should explore these factors in larger, multicenter trials to better understand the relative efficacy and safety of these induction agents.

CONCLUSION

Our study suggests that dinoprostone was associated with a significantly shorter induction-to-delivery interval and a higher proportion of deliveries within 12 hours compared to misoprostol. The increased incidence of meconium-stained amniotic fluid in the misoprostol group highlights a potential risk factor that needs further investigation.

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