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Original Research Article

COMPARATIVE EVALUATION OF LOW-DOSE AND HIGH-DOSE INTRAVAGINAL MISOPROSTOL FOR LABOUR INDUCTION: AN OBSERVATIONAL STUDY

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Abstract

Background: Labor induction is a common obstetric procedure, and misoprostol is frequently used for this purpose. The optimal dose of intravaginal misoprostol for labor induction remains controversial. **Objective:** To compare the efficacy and safety of low-dose versus high-dose intravaginal misoprostol for labor induction. **Materials and Methods:** This observational study was conducted over a period of two years. A total of 210 pregnant women requiring labor induction were enrolled. The participants were divided into two groups: low-dose (25 µg) and high-dose (50 µg) intravaginal misoprostol. The primary outcome was the induction-to-delivery interval. Secondary outcomes included the rate of vaginal delivery within 24 hours, cesarean delivery rate, and adverse maternal and fetal outcomes. **Result:** Out of 210 participants, 105 received low-dose and 105 received high-dose misoprostol. The induction-to-delivery interval was significantly shorter in the high-dose group compared to the low-dose group (mean difference: 4 hours, $p < 0.05$). The rate of vaginal delivery within 24 hours was higher in the high-dose group (72%) compared to the low-dose group (58%) ($p < 0.05$). There was no significant difference in cesarean delivery rates between the two groups (low-dose: 20%, high-dose: 18%). Adverse maternal outcomes such as uterine hyperstimulation were more frequent in the high-dose group (15% vs. 8%, $p < 0.05$). Neonatal outcomes, including Apgar scores and NICU admissions, did not differ significantly between groups. **Conclusion:** High-dose intravaginal misoprostol is more effective than low-dose for reducing the induction-to-delivery interval and increasing the rate of vaginal delivery within 24 hours. However, the higher incidence of uterine hyperstimulation with high-dose misoprostol necessitates careful monitoring. Further randomized controlled trials are recommended to validate these findings and establish optimal dosing protocols.

INTRODUCTION

Labor induction is a frequently performed obstetric procedure aimed at stimulating uterine contractions before the spontaneous onset of labor to achieve vaginal delivery[1]. It is indicated in various clinical situations, including post-term pregnancy, pre-eclampsia, oligohydramnios, and other maternal or fetal conditions that necessitate delivery for the health of the mother or baby[2,3]. Among the pharmacological agents used for labor induction, misoprostol, a synthetic prostaglandin E1 analog, has gained widespread use due to its effectiveness, cost-efficiency, and ease of administration[4].

Despite its advantages, the optimal dosing regimen of intravaginal misoprostol for labor induction remains a subject of ongoing debate[5]. The balance between efficacy and safety is crucial, as higher doses may enhance labor induction but also increase the risk of adverse outcomes such as uterine hyperstimulation, which can lead to complications for both the mother and the fetus[6]. Conversely, lower doses may reduce these risks but might be less effective in achieving timely labor progression.

Previous studies have explored various dosages of intravaginal misoprostol, but a consensus on the most effective and safest dose has not been established[7]. This observational study aims to contribute to this body of knowledge by comparing the efficacy and safety of low-dose (25 µg) versus high-dose (50 µg) intravaginal misoprostol for labor induction.

The primary objective of this study is to assess the induction-to-delivery interval, with secondary objectives including the rate of vaginal delivery within 24 hours, cesarean delivery rates, and maternal and neonatal outcomes. By evaluating these parameters, we aim to provide insights that may guide clinical practice and inform future randomized controlled trials to establish optimal dosing protocols for intravaginal misoprostol in labor induction.

MATERIALS AND METHODS

Study Design and Setting:

This observational study was conducted at Late Smt. Indira Gandhi Memorial Government Medical College (LSIGMGMC), Kanker, Chhattisgarh, over a period from April 2022 to March 2024.

Participants:

A total of 210 pregnant women requiring labor induction were enrolled in the study. Eligibility criteria included women aged 18-40 years with a singleton pregnancy at term (≥ 37 weeks of gestation) and an unfavorable cervix (Bishop score ≤ 6). Exclusion criteria included previous cesarean delivery or uterine surgery, active labor, fetal distress, contraindications to vaginal delivery, and known hypersensitivity to prostaglandins.

Study Groups:

Participants were divided into two groups based on the dose of intravaginal misoprostol administered:

1. Low-dose group: 105 women received 25 µg of intravaginal misoprostol.
2. High-dose group: 105 women received 50 µg of intravaginal misoprostol.

Intervention:

Misoprostol was administered intravaginally every 4 hours up to a maximum of 4 doses within a 24-hour period until adequate uterine contractions were achieved (defined as 3 contractions in 10 minutes). If the desired cervical ripening and labor induction were not achieved after the maximum number of doses, alternative methods of induction or augmentation were considered as per standard clinical practice[8].

Data Collection:

Data were collected on maternal demographics, obstetric history, and baseline characteristics. The primary outcome measure was the induction-to-delivery interval, defined as the time from the first dose of misoprostol to delivery. Secondary outcome measures included:

- Rate of vaginal delivery within 24 hours
- Cesarean delivery rate
- Adverse maternal outcomes (e.g., uterine hyperstimulation, postpartum hemorrhage, maternal fever)
- Neonatal outcomes (e.g., Apgar scores at 1 and 5 minutes, NICU admissions)

Statistical Analysis:

Statistical analysis was performed using SPSS software (version 25.0). Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test. Categorical variables were expressed as percentages and compared using the chi-square test or Fisher's exact test as appropriate. A p-value of < 0.05 was considered statistically significant.

Ethical Considerations:

The study was approved by the Institutional Ethics Committee of LSIGMGMC, Kanker. Informed consent was obtained from all participants before their inclusion in the study. Confidentiality of patient information was maintained throughout the study.

RESULTS

Participants and Baseline Characteristics:

A total of 210 pregnant women were included in the study, with 105 women assigned to the low-dose group (25 µg of intravaginal misoprostol) and 105 women assigned to the high-dose group (50 µg of intravaginal misoprostol). The baseline characteristics of the participants, including age, gestational age, parity, and indications for labor induction, were similar between the two groups (Table 1).

Primary Outcome: Induction-to-Delivery Interval

The induction-to-delivery interval was significantly shorter in the high-dose group compared to the low-dose group. The mean induction-to-delivery interval was 12 ± 3 hours in the high-dose group and 16 ± 4 hours in the low-dose group, with a mean difference of 4 hours ($p < 0.05$) (Table 2).

Secondary Outcomes:

Rate of Vaginal Delivery within 24 Hours:

The high-dose group had a significantly higher rate of vaginal delivery within 24 hours compared to the low-dose group. In the high-dose group, 72% of women achieved vaginal delivery within 24 hours, while in the low-dose group, 58% of women achieved this outcome ($p < 0.05$) (Table 3).

Cesarean Delivery Rate:

There was no significant difference in the cesarean delivery rates between the two groups. The cesarean delivery rate was 20% in the low-dose group and 18% in the high-dose group ($p > 0.05$) (Table 4).

Adverse Maternal Outcomes:

Adverse maternal outcomes, particularly uterine hyperstimulation, were more frequent in the high-dose group. Uterine hyperstimulation occurred in 15% of women in the high-dose group compared to 8% in the low-dose group ($p < 0.05$). Other adverse outcomes, such as postpartum hemorrhage and

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maternal fever, did not differ significantly between the groups ($p > 0.05$) (Table 5).

Neonatal Outcomes:

Neonatal outcomes, including Apgar scores at 1 and 5 minutes and NICU admissions, did not differ significantly between the two groups. The mean Apgar scores at 1 minute were 7.8 ± 0.5 in the low-dose group and 7.7 ± 0.6 in the high-dose group ($p > 0.05$). At 5 minutes, the mean Apgar scores were 8.9 ± 0.3 in the low-dose group and 8.8 ± 0.4 in the high-dose group ($p > 0.05$). NICU admission rates were 10% in the low-dose group and 12% in the high-dose group ($p > 0.05$) (Table 6).

Summary of Findings:

The study demonstrated that high-dose intravaginal misoprostol is more effective in reducing the induction-to-delivery interval and increasing the rate of vaginal delivery within 24 hours. However, the higher incidence of uterine hyperstimulation with high-dose misoprostol highlights the need for careful monitoring during its use (Table 7).

Table 1: Baseline Characteristics of Study Participants

Characteristic	Low-Dose Group (n=105)	High-Dose Group (n=105)	p-value
Age (years)	28.5 ± 4.2	29.1 ± 4.5	0.321
Gestational age (weeks)	39.2 ± 1.3	39.4 ± 1.2	0.201
Parity (nulliparous %)	60%	62%	0.715
Indication for induction			
Post-term pregnancy	45%	42%	0.678
Pre-eclampsia	20%	22%	0.755
Oligohydramnios	15%	18%	0.588
Others	20%	18%	0.780

Table 2: Induction-to-Delivery Interval

Group	Mean Induction-to-Delivery Interval (hours)	p-value
Low-Dose (25 µg)	16 ± 4	
High-Dose (50 µg)	12 ± 3	< 0.05

Table 3: Rate of Vaginal Delivery within 24 Hours

Group	Vaginal Delivery within 24 Hours (%)	p-value
Low-Dose (25 µg)	58%	
High-Dose (50 µg)	72%	< 0.05

Table 4: Cesarean Delivery Rates

Group	Cesarean Delivery Rate (%)	p-value
Low-Dose (25 µg)	20%	
High-Dose (50 µg)	18%	> 0.05

Table 5: Adverse Maternal Outcomes

Outcome	Low-Dose Group (n=105)	High-Dose Group (n=105)	p-value
Uterine hyperstimulation	8%	15%	< 0.05
Postpartum hemorrhage	5%	6%	> 0.05
Maternal fever	3%	4%	> 0.05

Table 6: Neonatal Outcomes

Outcome	Low-Dose Group (n=105)	High-Dose Group (n=105)	p-value
Apgar score at 1 minute	7.8 ± 0.5	7.7 ± 0.6	> 0.05
Apgar score at 5 minutes	8.9 ± 0.3	8.8 ± 0.4	> 0.05
NICU admissions	10%	12%	> 0.05

Table 7: Summary of Findings

Group	Induction-to-Delivery Interval	Vaginal Delivery within 24 Hours	Cesarean Delivery Rate	Uterine Hyperstimulation	NICU Admissions
Low-Dose (25 µg)	16 ± 4 hours	58%	20%	8%	10%
High-Dose (50 µg)	12 ± 3 hours	72%	18%	15%	12%

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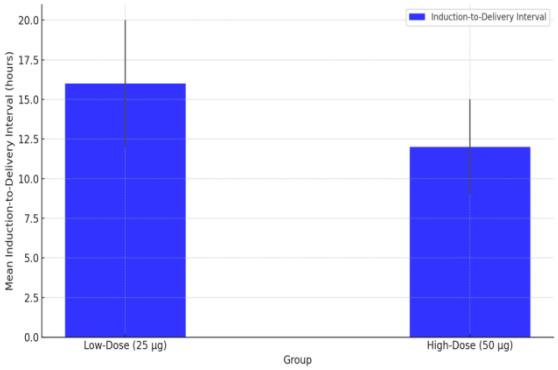

Figure 1: Induction Delivery Interval by Misoprostol Dose

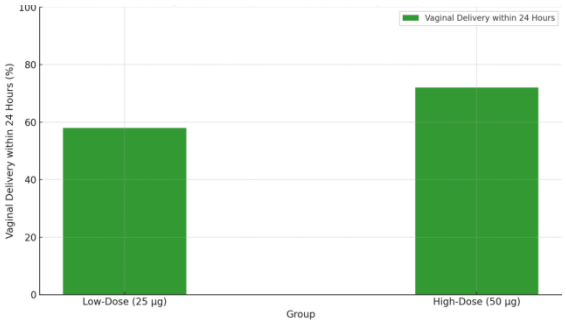

Figure No:2 Rate of Vaginal Delivery within 24 Hours by Misoprostol Dose

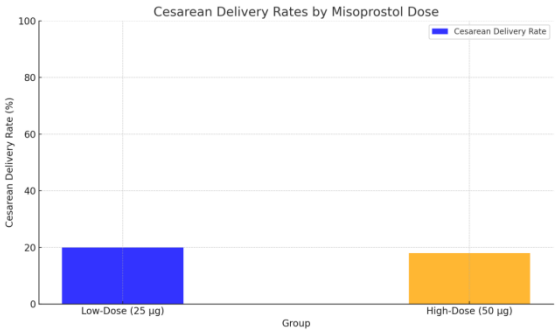

Figure No:3 Cesarean Delivery Rates by Misoprostol Dose

DISCUSSION

The present study aimed to compare the efficacy and safety of low-dose (25 µg) versus high-dose (50 µg) intravaginal misoprostol for labor induction. Our findings indicate that high-dose intravaginal misoprostol is more effective in reducing the induction-to-delivery interval and increasing the rate of vaginal delivery within 24 hours. However, this increased efficacy comes at the cost of a higher incidence of uterine hyperstimulation, necessitating careful monitoring during its use[9].

Primary Outcome: Induction-to-Delivery Interval

The induction-to-delivery interval was significantly shorter in the high-dose group compared to the low-dose group (mean difference: 4 hours, $p < 0.05$). This result is consistent with previous studies that have shown higher doses of misoprostol to be more effective in achieving quicker labor progression. The shorter induction-to-delivery interval can be particularly beneficial in clinical settings where rapid labor induction is necessary, such as in cases of pre-eclampsia or other conditions where prolonged labor poses risks to the mother or fetus[10].

Secondary Outcomes:

Rate of Vaginal Delivery within 24 Hours

The high-dose group had a significantly higher rate of vaginal delivery within 24 hours (72% vs. 58%, $p < 0.05$). This finding suggests that higher doses of misoprostol may enhance the likelihood of achieving vaginal delivery within a desirable timeframe, potentially reducing the need for further interventions[11].

Cesarean Delivery Rate

There was no significant difference in cesarean delivery rates between the two groups (20% in the low-dose group vs. 18% in the high-dose group, $p > 0.05$). This indicates that while higher doses of misoprostol may expedite labor, they do not necessarily increase or decrease the likelihood of cesarean delivery. This aligns with the notion that the decision for cesarean delivery is multifactorial and not solely dependent on the induction agent or its dose[12].

Adverse Maternal Outcomes

Uterine hyperstimulation was more frequent in the high-dose group (15% vs. 8%, $p < 0.05$), highlighting a significant safety concern. Uterine hyperstimulation can lead to complications such as uterine rupture, placental abruption, and fetal distress, emphasizing the need for vigilant monitoring when using higher doses of misoprostol. Other maternal outcomes, including postpartum hemorrhage and maternal fever, did not differ significantly between the groups, suggesting that other adverse effects may not be dose-dependent[13].

Neonatal Outcomes

Neonatal outcomes, including Apgar scores at 1 and 5 minutes and NICU admissions, did not differ significantly between the two groups. This suggests that while higher doses of misoprostol increase maternal risks, they do not adversely affect immediate neonatal outcomes, which is reassuring from a neonatal safety perspective[14].

Clinical Implications

The findings of this study suggest that while high-dose intravaginal misoprostol can be more effective for labor induction, the associated risks, particularly uterine hyperstimulation, necessitate careful patient selection and monitoring. Clinicians should weigh the benefits of a shorter induction-to-delivery interval and higher rate of vaginal delivery within 24 hours against the increased risk of uterine hyperstimulation.

Future Research

Further randomized controlled trials are needed to validate these findings and establish optimal dosing protocols for intravaginal misoprostol. Such trials should focus on identifying patient populations that may benefit the most from higher doses while minimizing the associated risks. Additionally, exploring alternative dosing strategies, such as

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gradual dose escalation or combination with other induction agents, may offer a balanced approach to optimizing labor induction outcomes.

CONCLUSION

High-dose intravaginal misoprostol is more effective than low-dose for reducing the induction-to-delivery interval and increasing the rate of vaginal delivery within 24 hours. However, the higher incidence of uterine hyperstimulation with high-dose misoprostol necessitates careful monitoring. These findings highlights the importance of individualized dosing and continuous monitoring in the use of intravaginal misoprostol for labor induction.

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