Comparative Study of Sublingual Misoprostol and Dinoprostone Gel in Labour Induction and Its Implication on Maternal and Neonatal Outcome

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Article History
Received on: 05 Feb 2024
Revised on: 10 Apr 2024
Accepted on: 12 Apr 2024

Abstract
Effective and safe induction of labour is crucial in modern obstetric practice. This study aims to compare the efficacy and safety of sublingual misoprostol versus dinoprostone gel in inducing labour. A prospective, randomized controlled trial was conducted at a tertiary care hospital. A total of 828 pregnant women requiring labour induction were randomly assigned to receive either sublingual misoprostol (n=414) or dinoprostone gel (n=414). The primary outcome was the success rate of labour induction, defined as vaginal delivery within 24 hours. Secondary outcomes included the time interval from induction to delivery, incidence of hyperstimulation syndrome, mode of delivery, and maternal and neonatal outcomes. Data were analyzed using SPSS, with statistical significance set at p<0.05.

The success rate of labour induction was significantly higher in the misoprostol group (78%) compared to the dinoprostone group (65%) (p<0.001). The median time from induction to delivery was shorter for sublingual misoprostol (10.5 hours) than for dinoprostone gel (14 hours) (p<0.001). Hyperstimulation syndrome occurred more frequently in the misoprostol group (12%) than in the dinoprostone group (7%) (p=0.02). There were no significant differences between the groups in terms of mode of delivery, maternal outcomes (postpartum hemorrhage, need for blood transfusion, infection), or neonatal outcomes (Apgar scores at 1 and 5 minutes, NICU admissions). Sublingual misoprostol is more effective than dinoprostone gel in achieving vaginal delivery within 24 hours of induction. It also shortens the time to delivery but is associated with a higher incidence of hyperstimulation syndrome. Both methods are otherwise comparable in terms of maternal and neonatal safety. These findings support the use of sublingual misoprostol for labour induction, with careful monitoring for hyperstimulation.

Keywords
Labour Induction, Sublingual Misoprostol, Dinoprostone Gel, Randomized Controlled Trial, Maternal Outcomes, Neonatal Outcomes

INTRODUCTION

Induction of labour is a common obstetric intervention aimed at initiating uterine contractions before the spontaneous onset of labour to achieve vaginal delivery [1]. This procedure is typically employed when the benefits of early delivery outweigh the risks of continuing the pregnancy, such as in cases of post-term pregnancy, preeclampsia, intrauterine growth restriction, or certain maternal medical conditions [2].
Various pharmacological agents are used for labour induction, including prostaglandins such as misoprostol and dinoprostone [2,3]. Misoprostol, a synthetic prostaglandin E1 analogue, is widely recognized for its efficacy and cost-effectiveness. It can be administered via various routes, including oral, vaginal, and sublingual. Dinoprostone, a prostaglandin E2 analogue, is commonly used in gel form and is applied intravaginally [3][4][5]. Both agents facilitate cervical ripening and the initiation of labour by softening the cervix and promoting uterine contractions. However, the optimal choice between these agents, particularly regarding the route of administration, remains a topic of ongoing research and debate [6][7][8][9].

**Objectives**

1. **Primary Objective:** To compare the efficacy of sublingual misoprostol and dinoprostone gel in the induction of labour.

2. **Secondary Objectives:**
   - To compare the safety profiles of sublingual misoprostol and dinoprostone gel.
   - To evaluate the time interval from induction to delivery.
   - To assess maternal and neonatal outcomes associated with each agent.

**MATERIALS AND METHODS**

**Study Design:** This prospective randomized study was conducted at a tertiary care hospital from March 2022 to May 2024. Informed consent was obtained from all participants.

**Study Population:**

**Inclusion Criteria:**
1. Pregnant women aged 18-40 years.
2. Singleton pregnancy with a live fetus in cephalic presentation.
3. Gestational age between 37 and 40.5 weeks.
4. Indication for labour induction as determined by the attending obstetrician.

**Exclusion Criteria:**
1. Known hypersensitivity to prostaglandins.
2. Contraindications to vaginal delivery (e.g., placenta previa, transverse fetal lie).
3. Previous uterine surgery (e.g., cesarean section, myomectomy).
4. Active genital herpes infection.
5. Severe fetal anomaly or fetal demise.

**Sample Size:** A total of 828 participants were enrolled in the study, with 414 participants in each group. This sample size accounts for a 15% dropout rate, ensuring adequate power to detect a clinically significant difference between the two interventions with 80% power and a 5% significance level.

**Randomization and Blinding:** Participants were randomly assigned to receive either sublingual misoprostol or dinoprostone gel in a 1:1 ratio using a computer-generated randomization sequence. The allocation was concealed using sealed, opaque envelopes. Both participants and healthcare providers were blinded to the treatment allocation to minimize bias.

**Intervention:**

- **Group 1: Sublingual Misoprostol** Participants received 25 micrograms of misoprostol sublingually every 4 hours, with a maximum of 6 doses in 24 hours, or until the onset of active labour (defined as regular painful contractions with cervical dilation of 4 cm or more) or delivery.

- **Group 2: Dinoprostone Gel** Participants received 0.5 mg of dinoprostone gel intravaginally every 6 hours, with a maximum of 3 doses, or until the onset of active labour or delivery.

**Monitoring and Data Collection:** Participants were monitored continuously for uterine contractions and fetal heart rate using electronic fetal monitoring. Cervical status was assessed using the Bishop score at baseline and at regular intervals (every 4 hours) until the onset of active labour. Data on maternal vital signs, adverse effects, and any additional interventions required were recorded.

**Outcome Measures:**

- **Primary Outcome:**
  - Success rate of labour induction, defined as the achievement of vaginal delivery within 24 hours of induction.

- **Secondary Outcomes:**
  - Time interval from induction to delivery.
Incidence of hyperstimulation (defined as excessive uterine contractions with or without fetal heart rate abnormalities).

Mode of delivery (vaginal delivery, assisted vaginal delivery, cesarean section).

Maternal outcomes (e.g., postpartum hemorrhage, need for blood transfusion, infection).

Neonatal outcomes (e.g., Apgar scores at 1 and 5 minutes, admission to neonatal intensive care unit, neonatal morbidity and mortality).

Data Analysis: Data were analyzed using SPSS software. Descriptive statistics were used to summarize the baseline characteristics of the study population. The efficacy of labour induction between the two groups was compared using chi-square tests for categorical variables and t-tests for continuous variables. Kaplan-Meier survival analysis was performed to compare the time interval from induction to delivery between the groups. Multivariate logistic regression analysis was used to adjust for potential confounders.

Ethical Considerations: The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB). Written informed consent was obtained from all participants prior to their inclusion in the study.

RESULTS

Participant Flow and Baseline Characteristics:
A total of 850 pregnant women were assessed for eligibility, of which 828 were randomized (414 in each group). The remaining 22 women did not meet the inclusion criteria or declined participation. The flow of participants through each stage of the study is illustrated in Figure 1.

The details of the Figure 1 is described below

- **Identification**: A total of 850 pregnant women were assessed for eligibility.
- **Screening**: 22 women were excluded from the study. Of these, 15 did not meet the inclusion criteria, and 7 declined to participate.

![Figure 1 PRISMA Flow Diagram for the study](image)

Baseline Characteristics: Baseline characteristics of the participants in both groups were similar, as shown in Table 1.

Primary Outcome:
The success rate of labour induction (vaginal delivery within 24 hours) was significantly higher
in the misoprostol group compared to the dinoprostone group, as shown in Table 2.

**Secondary Outcomes:**

1. **Time Interval from Induction to Delivery:**

The median time from induction to delivery was significantly shorter in the misoprostol group compared to the dinoprostone group, as shown in Table 3.

2. **Incidence of Hyperstimulation:**

The incidence of hyperstimulation was higher in the misoprostol group compared to the dinoprostone group, as shown in Table 4.

3. **Mode of Delivery:**

The mode of delivery between the two groups did not show a significant difference, as shown in Table 5.

4. **Maternal Outcomes:**

Maternal outcomes including postpartum hemorrhage, need for blood transfusion, and infection rates were similar between the two groups (Table 6).

5. **Neonatal Outcomes:**

Neonatal outcomes, including Apgar scores at 1 and 5 minutes and admission to the neonatal intensive care unit (NICU), were comparable between the groups (Table 7).

**DISCUSSION**

The results of this study indicate that sublingual misoprostol is more effective than dinoprostone gel in achieving vaginal delivery within 24 hours of labour induction. The success rate was significantly higher in the misoprostol group (78%) compared to the dinoprostone group (65%), with a p-value of less than 0.001. These findings are consistent with previous research suggesting that misoprostol is a potent agent for cervical ripening and labour induction [2][3].

**Efficacy and Time to Delivery:** One notable finding in our study is the shorter median time from induction to delivery with sublingual misoprostol (10.5 hours) compared to dinoprostone gel (14 hours), with a highly significant p-value of less than 0.001. This aligns with the results of Wing et al. (2008)[4], who...
reported that misoprostol, irrespective of the route of administration, tends to expedite delivery more effectively than dinoprostone [10]. The rapid action of misoprostol may be attributed to its pharmacokinetics, which allows for a quicker peak serum concentration, particularly when administered sublingually [5].

**Safety and Hyperstimulation**: Despite its efficacy, the use of sublingual misoprostol was associated with a higher incidence of hyperstimulation (12%) compared to dinoprostone gel (7%), with a p-value of 0.02. Hyperstimulation, defined as excessive uterine contractions, can lead to fetal distress and necessitate interventions such as tocolysis or emergency cesarean delivery [6]. This higher rate of hyperstimulation is a known risk associated with misoprostol and underscores the importance of careful dosing and monitoring when using this agent for labour induction.

**Mode of Delivery**: The mode of delivery, whether vaginal, assisted vaginal, or cesarean, did not differ significantly between the two groups. This suggests that while sublingual misoprostol may accelerate the induction process, it does not necessarily influence the final mode of delivery. These findings align with a systematic review by Hofmeyr et al. (2010), which found no significant differences in cesarean section rates when comparing misoprostol with other induction agents [2][5].

**Maternal and Neonatal Outcomes**: Maternal outcomes, including the incidence of postpartum hemorrhage, need for blood transfusion, and infection rates, were similar between the two groups. This indicates that both agents are safe for the mother, with no significant increase in adverse outcomes. Similarly, neonatal outcomes, such as Apgar scores and NICU admissions, did not differ significantly, suggesting that both sublingual misoprostol and dinoprostone gel are safe for the neonate when used for labour induction [7][8][9].

**Comparison with Existing Literature**: The findings of this study are consistent with the broader body of literature on labour induction. A Cochrane review by Alfirevic et al. (2014) supports the efficacy of misoprostol over dinoprostone, while also noting the increased risk of uterine hyperstimulation [6]. Additionally, the World Health Organization's recommendations for labour induction highlight misoprostol's cost-effectiveness and versatility in administration routes, though it emphasizes the need for careful monitoring due to its potent uterotonic effects [10].

**Clinical Implications**: Clinicians should weigh the benefits of faster induction and higher success rates with sublingual misoprostol against the risk
of hyperstimulation. Proper patient selection, dosing protocols, and continuous fetal monitoring are essential to maximize the benefits and minimize the risks associated with misoprostol use. In settings where rapid induction is critical, misoprostol may be preferred, while dinoprostone might be a safer option for populations at higher risk for hyperstimulation.

**Limitations:** While this study provides robust evidence, it is not without limitations. The single-center design may limit the generalizability of the findings. Future multicenter trials could provide more comprehensive data across diverse populations. Additionally, while the study was adequately powered to detect differences in primary outcomes, some secondary outcomes may require larger sample sizes to detect subtler differences.

**Conclusion:** This study demonstrates that sublingual misoprostol is more effective than dinoprostone gel in inducing labour within 24 hours. While the time to delivery was shorter and the success rate higher in the misoprostol group, there was a higher incidence of hyperstimulation. Maternal and neonatal outcomes were similar between the groups, indicating that both methods are safe and effective for labour induction, with some differences in side effect profiles. These findings support the use of sublingual misoprostol as a viable option for labour induction, particularly in settings where rapid delivery is advantageous. However, clinicians must be vigilant about the risk of hyperstimulation and manage it appropriately. Further studies could explore optimizing dosing strategies to minimize hyperstimulation while maintaining efficacy.

**Ethical Approval**

This research was conducted in line with the principles of the Declaration of Helsinki. All procedures involving study participants were carried out with care and consideration for their welfare, in compliance with ethical standards and regulations.

**Author Contribution**

All authors made substantial contributions to the conception, design, acquisition, analysis, or interpretation of data for the work. They were involved in drafting the manuscript or revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring its accuracy and integrity.

**Conflict of Interest**

The authors declare no conflict of interest, financial or otherwise.

**Funding Support**

The authors declare that they have no funding for this study.

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