EXPERT VIEW/REVIEW PAPER

Comparing SL and VAG Misoprostol for Labor Induction in Full-term Pregnant Women: A Comprehensive Review

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Abstract

The induction of labor in full-term pregnant females is a critical aspect of obstetric care aimed at mitigating important maternal and fetal risks correlated with prolonged pregnancies or medical conditions necessitating expedited delivery. Misoprostol [Miso], a synthetic prostaglandin E1 analog, has been promoted as a pharmacological agent for labor induction due to its effectiveness and ease of administration. Nonetheless, the optimal route of misoprostol administration remains a subject of ongoing debate.

This comprehensive review systematically examines clinical trials, cohort trials, and randomized controlled trials (RCTs) to understand the comparative effectiveness of sublingual (SL) and vaginal (VAG) misoprostol for inducing labor in full-term pregnant females. Key findings reveal that both routes are adequate, with the choice dependent on patient-specific factors and preferences. Sublingual administration offers advantages regarding the faster onset of labor and reduced maternal fever risk but is associated with a higher incidence of shivering. Standardized dosing protocols, tailored to individual patient characteristics, are vital for safe and effective induction.

Incorporating shared decision-making is integral for patient satisfaction and positive outcomes. Ultimately, the choice between SL and VAG misoprostol for labor induction should be guided by a comprehensive patient assessment in consultation with healthcare providers. Further research and clinical trials are needed to refine our understanding of these methods' comparative efficacy and safety.

Keywords: Induction, Induction of labor, Intravaginal misoprostol, Misoprostol.

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Introduction

The induction of labor in full-term pregnant females is a clinical practice employed to mitigate potential maternal and fetal risks associated with prolonged pregnancies or medical conditions warranting expedited delivery.[1,2] Misoprostol, a synthetic prostaglandin E1 analog, has emerged as a prominent pharmacological agent for labor induction due to its efficacy and ease of use. However, the perfect route of administration remains a subject of ongoing debate within obstetric care. This comprehensive review article critically assesses and synthesizes the evidence comparing the efficacy of sublingual (SL) and vaginal (VAG) misoprostol administration in achieving successful labor induction while maintaining maternal and fetal safety.[3–5]

The article will delve into the pharmacokinetics, safety profiles, and clinical outcomes associated with each administration route, ultimately shedding light on the most efficacious and safest approach for labor induction in full-term pregnant women. In doing so, this review aspires to contribute valuable insights to the obstetric community, aiding healthcare professionals in making informed decisions regarding the misoprostol administration route for labor induction in this population (Tables 1 and 2).

Methodology

Study Selection Criteria

Inclusion Criteria

- Studies that were published in the English language were included.
- Clinical trials, cohort studies, and RCTs that compared SL and VAG misoprostol for labor induction in full-term pregnant women were included.
- Studies conducted on human subjects were considered.
- Studies involving full-term pregnancies (≥37 weeks of gestation) were included.
- Studies that reported relevant outcomes such as induction success rate, time to delivery, maternal outcomes (eg, uterine hyperstimulation, postpartum hemorrhage), fetal outcomes (eg, APGAR scores, Neonatal intensive care unit admission), and adverse events were included.

Exclusion Criteria

- Studies not published in English were excluded.
- Studies involving preterm pregnancies (<37 weeks of gestation) were not considered.
- Studies with inadequate or incomplete data were excluded.

Literature Search

- Comprehensive electronic searches were conducted using PubMed, Embase, Scopus, and the Cochrane Library databases.
- Keywords and MeSH terms, including "misoprostol," "labor induction," "SL," "VAG," and related variations, were used.

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Table 1: Studies included in the present review

Author	*Year*	*Country*	*Sample size*	*Study design*	*Objectives*
Ayati et al.[6]	2014	Iran	140 in each group	Randomized controlled trial	To evaluate and compare the safety and efficacy of utilizing SL vs VAG misoprostol for cervix softening and labor induction.
Jahromi et al.[7]	2016	Iran	200 in each group	Randomized controlled trial	To evaluate and compare the effectiveness and safety of SL vs VAG misoprostol in terminating a live, full-term pregnancy.
Dorr et al.[8]	2019	United States of America	207 total	Retrospective cohort study	To assess and compare the effectiveness of equivalent doses of buccal and VAG misoprostol for inducing labor.
Amini et al.[9]	2022	Sweden	2404 total	Retrospective cross-sectional study	To assess and contrast the safety and efficacy of an oral misoprostol regimen with an SL misoprostol regimen, with the occurrence of cesarean birth as the primary outcome.

Table 2: Comparison of SL and VAG misoprostol in terms of effects and adverse effects in various studies

Author	*Adverse effects*	*Assessment*	*Overall inference*
Ayati et al.[6]	This study compared two groups: One receiving SL misoprostol and the other receiving VAG misoprostol. The results indicated that 0.87% of the SL group experienced placental residue, while 2.2% in the VAG group had the same issue. Tachysystole occurred in 0.65% of the SL and 2.2% of the VAG groups. Vomiting was reported in 0.34% of the SL group and 12% of the VAG group. Atony was observed in 0.09% of the SL group and 3.3% of the VAG group. Additionally, 0.23% of the SL group experienced abdominal pain, while 5.5% of the VAG group had this symptom.	Frequency of successful induction Additional measures encompassed the occurrences of cesarean sections resulting from fetal distress, the time between the initial dose and the onset of active labor, the time between induction and delivery, the length of the labor process, the total number of misoprostol doses given, and the requirement for oxytocin to augment labor. As for neonatal outcomes, these encompassed variations in fetal HR during labor, the passage of meconium during labor, fetal demise during labor, and admission to the neonatal intensive care unit.	Fetal distress was the main factor in both groups that led to a cesarean section, followed by a lack of progress in active labor. The examination of cesarean section indications, which included FD, the absence of active labor, uterine overactivity, and failure to advance. These had no significant difference between the two groups. Remaining placenta (2%), tachysystole (2%), vomiting (12%), atony (3.3%), and abdominal pain (5.5%) were all maternal problems in the SL group.
Jahromi et al.[7]	Nausea was reported by 4% in one group and 5% in the other ($p = 0.50$). Vomiting occurred in 2% of one group and 5% of the other ($p = 0.44$).	Average time between starting the drug and delivery Type of delivery Meconium-stained liquor Nausea and vomiting Fetal parameters	The average amount of time between beginning misoprostol treatment and delivery was 511.67 minutes for VAG administration and 497.10 minutes for SL. While 14 females in the VAG group had Cesarean deliveries, 22 females in the SL group got the procedure. 12 females in the SL group and 4 in the VAG group were found to have amniotic fluid that was meconium-stained ($p = 0.03$). 8 females in the SL group and 4 in the VAG group experienced late fetal heart rate deceleration ($p = 0.22$). The average neonatal birth weight, blood gas readings at birth, APGAR ratings, and length of stay in the neonatal intensive care unit were not significantly different between the two groups.
Dorr et al.[8]	Non-reproductive fetal heart tracing was the primary cause of cesarean delivery in 40% of VAG and 54.5% of buccal groups. Failing induction resulted in 5 cesarean births in each group. All VAG cesarean deliveries for maternal indications included misoprostol via the VAG route.	Time between induction to delivery Mode of delivery Failed induction Tachysystole Chorioamnionitis	No significant differences were observed in the time taken for females to give birth when compared between buccal and VAG patients (18.2 hours) compared to those receiving buccal (mean 18.3 hours). This finding was maintained when other factors were taken into account ($p = 0.381$). Females with early rupture of membranes were significantly more likely to receive buccal (92.7%) vs VAG (7.3%) misoprostol.

(Contd...)

Table 2: *(Contd...)*

Author	*Adverse effects*	*Assessment*	*Overall inference*
			The proportion of females who delivered vaginal was similar in both groups (88.2%). There were no significant differences in the incidence of uterine tachysystole or chorionic gonaditis based on misoprostol route.
Amini et al.[9]		The primary outcome was the proportion of patients who achieved VAG delivery, expressed as the inverse of the cesarean section rate. Secondary outcomes included: • The interval from induction to delivery, • Achieving VAG delivery within 24 hours, • Postpartum hemorrhage, • APGAR scores below seven at 5 minutes after birth, and • Umbilical artery pH levels below 7.10.	Cesarean birth rates were lower in women who were first-time moms (first-time mothers) compared to those who had previously given birth. There was no difference in rates among women who had already given birth (Parous women), with 4.9 and 7.5% cesareans respectively (not statistically significant). The increased risk for cesareans persisted even after adjustment for factors such as weight, height, and gender. The SL vs SL groups had a median VAG delivery time that was shorter than that of women who were induced with the oral solution. The VAG delivery time was also shorter than that of those who received the oral solution. The VAG delivery time was longer for women who received SL vs non-SL groups. The median VAG delivery time was 9.9 hours vs 13 hours (median). The SL delivery time was longer than the VAG delivery time (median 16.7 hours vs 21 hours). The overall VAG delivery rate was longer than the preterm delivery rate (median 9.3 hours).

- Boolean operators (AND, OR) were used to combine search terms.
- The search was limited to articles published from 2010 to 2023.

Study Selection Process

- Two independent reviewers screened titles and abstracts of identified articles.
- Full texts of potentially relevant articles were retrieved and assessed for eligibility based on inclusion/exclusion criteria.

Data Extraction

- Extracted data included study characteristics, participant characteristics, intervention details, and outcome measures.

Discussion

The comparison of SL and VAG misoprostol for labor induction in full-term pregnant women is of significant clinical importance. Labor induction is a common practice, and selecting the most suitable route of misoprostol administration is essential to ensure maternal and fetal well-being. This comparative analysis reveals that SL and VAG routes have effectively initiated labor. The choice between these methods should be guided by individual patient characteristics and preferences, as well as the expertise of healthcare providers. Sublingual administration exhibits advantages, including a potentially faster onset of labor and a reduced risk of maternal fever. However, it is associated with a higher incidence of shivering, requiring careful management. Dosing considerations are paramount in this context, emphasizing the necessity for standardized protocols to ensure safe and effective labor induction. Personalized dosing adjustments based on gestational age and obstetric history are essential to optimize outcomes.[1,3–5,10]

Ayati et al. conducted an RCT on 140 women who required labor induction due to clinical or obstetric reasons. They were randomly assigned to receive misoprostol either VAGly or SLly. The study found that both methods had similar effectiveness in terms of maternal and neonatal outcomes. The primary reasons for cesarean sections were fetal distress and a lack of progress in active labor. Maternal complications were similar in both groups, with SL misoprostol being as effective as the VAG route and offering the advantage of easier administration.[6]

Jahromi et al. conducted a randomized, triple-blind, placebo-controlled clinical trial with 200 first-time pregnant women. They received SL or VAG misoprostol tablets or a placebo. The study found no significant differences in maternal age, gestational age, or Bishop score at the start of misoprostol administration between the SL and VAG groups. The time from misoprostol administration to delivery was similar in both groups. Still, there were more cases

of meconium-stained amniotic fluid and late fetal heart rate deceleration in the SL group. However, neonatal outcomes, such as birth weight and APGAR scores, did not differ significantly.[7]

In a retrospective study, Amini et al.[9] looked at 2,404 patients who had been admitted to a hospital for induction of labor over a period of several years. They compared SL (buccal) and oral (VAG) misoprostol to see if there was a difference in the number of women who had cesareans when given the SL solution compared to those who were multiparous. They found that there was no difference in the rate of VAG deliveries, and there were no major differences in the rate of tachyarrhythmias or chorionic gonorrhea when administered by the SL route compared to the oral route. In another study, Dorr et al.,[8] looked at the results of a study involving 207 women who had been admitted for induction of labor at a hospital. They found that even after adjustment for certain factors, there were no differences in the amount of time to delivery of the women in the SL or VAG groups.

Conclusion

In conclusion, the comprehensive review of SL and VAG misoprostol for labor induction in full-term pregnant women yields several key findings and insights. First, both SL and VAG misoprostol administration routes have proven effective in initiating labor in full-term pregnant women. The choice between the two methods should be tailored to the patient's specific needs and preferences, considering factors such as prior childbirth experiences, individual medical history, and the expertise of healthcare providers. Second, the review underscores that SL misoprostol may offer advantages over the VAG route, including a potentially faster onset of labor and a reduced risk of maternal fever. Furthermore, the review highlights the importance of dosing considerations, emphasizing the need for standardized protocols to ensure safe and effective labor induction. Dosing adjustments should be made based on the patient's individual characteristics, such as gestational age and prior obstetric history. Overall, the choice between SL and VAG misoprostol for labor induction in full-term pregnant women should be guided by a thorough assessment of the patient's unique circumstances in consultation with healthcare providers. Further research and clinical trials may provide additional insights into the comparative efficacy and safety of these two routes of administration, enhancing our ability to make informed decisions regarding labor induction for full-term pregnancies.

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