A Comparison of the Efficacy and Safety Profile of Sub-lingual and Vaginal Misoprostol for Induction of Labour: A Randomized Controlled Trial

[1]Atemie Gordon, [2]Harry T. Clement, [1]Porbeni-Fumudoh B. Offiong, [1]Ozori E. Stanley [1]Warisuo S. Ariwelo, [1]Nwanze C Nnamdi, [3]Akanatei I Daniel

[1]Department of Obstetrics and Gynaecology,
Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria.

[2]Department of Obstetrics and Gynaecology,
Bayelsa Medical University, Yenagoa, Bayelsa State, Nigeria.

[3]Department of Obstetrics and Gynecology,
Niger Delta University Teaching Hospital, Bayelsa State, Nigeria

Correspondence:
Dr. Atemie Gordon,
Department of Obstetrics and Gynaecology,
Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria;
+2347060643152; atemieg@yahoo.com

How to cite this article:
Atemie G, Harry T.C, Porbeni-Fumudoh B.O, Ozori E. S, Warisuo S.A, Nwanze C.N, Akanatei I.D: **A Comparison of the Efficacy and Safety Profile of Sub-lingual and Vaginal Misoprostol for Induction of Labour: A Randomized Controlled Trial**
NDJMS 2025; 5(1): 9-23

Received: 13th December, 2025 | **Accepted**: 25th March, 2025 | **Published** 24th April, 2026

ABSTRACT

Background*: To prevent adverse obstetric outcomes during pregnancy, induction of labour may become necessary to. Either sublingual or vaginal misoprostol can be used however the optimal dosage and route of administration for induction of labour remain unclear in our clinical setting. This study therefore sought to compare the efficacy and safety of sublingual versus vaginal misoprostol for induction of labour in term pregnancies.*

Aim*: To compare the outcome of events of labour and delivery using the sub-lingual and vaginal routes for induction of labour.*

Methodology*: One hundred and forty (140) pregnant women at term who fulfilled the inclusion criteria were equally randomized into the two arms of the study to receive either 25 µg of misoprostol sublingually or 25µg vaginally and the efficacy and safety profile of the different routes were compared. Data was entered into SPSS spread sheet and analyzed using IBM SPSS version 25 (IBM SPSS Inc., Illinois, USA). A p-value < 0.05 will be considered significant statistically. Results will be reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.*

Results*: The efficacy of sublingual and vaginal misoprostol for induction of labour was comparable. Though a higher proportion of women in the vaginal group achieved delivery within 24 hours compared with the sublingual group (84.3% vs. 74.3%), this difference was not statistically significant ($\chi^2 = 2.13$, $P = 0.14$), meeting the predefined non-inferiority margin (difference = 0.14). The mode of delivery was similar between the two groups, with spontaneous vaginal delivery being the most common outcome (84.3% vs. 80.0%), followed by assisted vaginal delivery (2.8% vs. 4.3%) and Caesarean section (12.9% vs. 15.7%), with no significant difference (p = 0.84). The study found no statistically significant difference in the induction delivery interval between the sublingual misoprostol group and the vaginal misoprostol group*

Safety outcomes were also comparable across both routes. There were no statistically significant differences in the rates of antepartum haemorrhage (1.4% vs. 2.9%, p = 0.55), postpartum haemorrhage (5.7% vs. 7.1%, p = 0.73), blood loss ≥ 500 ml (5.7% vs. 7.1%, p = 0.73), or need for blood transfusion (5.7% vs. 7.1%, p = 0.73). No cases of uterine rupture occurred in either group. Cervical (5.7% vs. 11.4%) and vaginal lacerations (15.7% vs. 47.1%) were more frequent in the vaginal group but without statistical significance (p > 0.05). The study identified a statistically significant difference in the time required to reach the active phase of labour between the sublingual misoprostol group and the vaginal misoprostol group. Mean number of misoprostol doses required was significantly lower in the sublingual group Need for augmentation was lower in the sublingual group, but this difference was not statistically significant.

Conclusion: *The sublingual and vaginal routes for administration of misoprostol at the same dose showed comparable safety and efficacy for induction of labour and delivery.*

KEYWORDS*:* Efficacy, Safety, Misoprostol, Vaginal, Sublingual, Induction of labour.

INTRODUCTION

Induction of labour is common in obstetric practice and refers to the process whereby uterine contractions are initiated by medical or surgical means before the onset of spontaneous labour.[1,2] Induction of labour implies artificial initiation of regular uterine contraction before their spontaneous onset, resulting in progressive effacement and dilatation of cervix, with an aim to secure safe vaginal delivery.[3,4] When the continuation of pregnancy represents a risk to the mother and/or the fetus that is greater than the risk of interrupting the pregnancy, labour induction is an option to allow vaginal delivery to occur.[5]

Induction of labour has been a longstanding practice in obstetrics, and in recent years, the proportion of medically induced deliveries has risen sharply, with anecdotal reports suggesting it now accounts for approximately 9.6% of all deliveries worldwide.[6] In the United States these rates are considerably higher, reaching approximately 27%, while in Europe they seem to range between 6.8 and 33%.[7,8] In Nigeria, the incidence of induction of labour at the Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, was 6.5 % in 2011, [9] a figure comparable to 4.5% at Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, Nigeria. [10] Whereas several methods have been used to induce cervical ripening as well as onset of labour, including the use of oxytocin, prostaglandins, laminaria tents and foley's

balloon catheter, prostaglandins and oxytocin are the most widely accepted. [11] The exact mechanisms responsible for this process are currently not well understood. What is clear is that cervical ripening occurs before the onset of labour; and in the absence of a ripe or favourable cervix, a successful vaginal birth is less likely[12-14]. The duration of labour is also inversely correlated with the Bishop score, a clinical tool used to assess cervical readiness for labour, evaluating dilation, effacement, consistency, position, and fetal station, with higher scores indicating a more favourable cervix and a greater likelihood of successful induction. [15-17]A major factor that influences successful induction of labour is the cervical status. If the cervix is closed, firm and uneffaced, with Bishop score less than 6, the conventional method of induction of labour by surgical amniotomy becomes technically difficult and intravenous infusion of oxytocin results in prolonged labour with risks of maternal and fetal complications, unsuccessful inductions and unnecessarily increased rate of Caesarean section.[3,4,15-17]

To increase the success of labour induction it is essential to achieve cervical ripening in women with an unfavourable cervix. Induction of labour with an unfavourable cervix is associated with prolonged labour compared to spontaneous onset of labour or induction of labour with a favourable cervix. It is also associated with, an increase in instrumental deliveries and a higher rate of Caesarean sections. [14,15] Various methods have been used in the past to achieve cervical ripening and labour induction. Non pharmacologic approaches included the use of castor oil, hot baths, enemas, sexual intercourse, breast stimulation, acupuncture, acupressure, transcutaneous nerve stimulation, and membrane stripping.[11,12,15] Pharmacologic agents available for cervical ripening and labour induction include prostaglandins, mifepristone and relaxin.[11,12-15]

The American College of Obstetricians and Gynecologists suggest the use of prostaglandins for cervical ripening and labor induction at intervals that should be at least 3–6 hours apart to avoid the risk of uterine tachysystole, although the minimum interval that is considered safe has not been standardized yet. [18] Regarding misoprostol, the World Health Organization recommends either oral (25 µg, 2-hourly) or vaginal route (25 µg, 6-hourly) for induction of labour. [6] In a previous meta-analysis that was conducted by Alfirevic et al [19], misoprostol combined with oxytocin and amniotomy has been proven to be the best method for achieving vaginal delivery within 24 h.

Misoprostol, a synthetic prostaglandin E1 (PGE1) analogue has been studied and widely accepted as a labour inducing agent in different doses and routes.[3] Originally, misoprostol was licensed as an oral treatment for gastric ulcers while it is used off label worldwide in obstetrics. [3, 20] Several studies have found that misoprostol is effective as an agent for cervical ripening and induction of labour.[12-15]Misoprostol has several advantages such as its stability in ambient temperature, long shelf-life and low cost, which have made it a central focus of research in Obstetrics and Gynaecology for over 25 years.[3,14,15] Misoprostol is rapidly absorbed via the oral route and, although not formulated for parenteral use, can also be administered sublingually (buccally), rectally and vaginally. [17-19] Pharmacological studies suggest that sublingual misoprostol

might be the optimal route of administration.[20] Despite many widely reported trials on misoprostol, several practical aspects of its administration were still not well established in the past and these include; the appropriate dosage, the dosing interval, and route of administration, with doses ranging from 25 µg to 100 µg.[12-16]

Higher doses or shorter dosing intervals are associated with a higher incidence of side effects, especially hyper-stimulation syndrome, defined as contractions lasting longer than 90 seconds or more than five contractions in 10 minutes. Risks also include tachysystole, defined as six or more uterine contractions in 10 minutes for two consecutive 10-minute periods, and hyper systole, a single contraction of at least two minutes' duration.[14,15] Other complications associated with misoprostol use include hyperpyrexia, nausea, vomiting, diarrhea, uterine rupture, fetal distress and fetal demise.[12-16]

Several articles have addressed the efficacy of the various routes of misoprostol in achieving a successful vaginal delivery and a previous meta-analysis that was published in 2008 suggested that both sublingual and vaginal routes seem to be comparable in terms of achieving vaginal delivery. [3,21] More recently, Alfrevic et al [22] published a systematic review comparing oral misoprostol to other methods of induction of labour (including oxytocin) and observed that it was associated with fewer Caesarean sections. Since then, several randomized trials have been published and an update is indicated to review current knowledge as, to date, there is no consensus on the optimal route of misoprostol intake for induction of labour.

The purpose of this study is to compare sublingual and vaginal misoprostol administration in terms of inducing labour and leading to a vaginal delivery, taking into cognizance the efficacy and safety concerns.

MATERIAL AND METHODS

This was a single-center, non-inferiority, parallel, open labelled, randomized controlled trial (RCT). Randomization was into two equal arms and the participants were parturients undergoing induction of labour at the Federal Medical Center Yenagoa, Bayelsa State, Nigeria. Pregnant women at term carrying a live singleton fetus in cephalic presentation, with a reassuring biophysical profile and a documented obstetric indication for induction of labour were included into the study. Exclusion criteria included women who refused to give consent, immunosuppression, previous uterine scar, antepartum hemorrhage, hypersensitivity to misoprostol and oxytocin, intrauterine fetal death and macrosomia. All procedures followed the 2013 Helsinki Declaration. Ethical approval was obtained from the ethical committee of the Federal Medical Centre, Yenagoa, Bayelsa State with application number; 2023/Dec/967 and Protocol number 984. Each participant gave written informed consent to participate.

Intervention

All pregnant women at term who met the inclusion criteria were randomized into two groups: Group A and B respectively. An astute vaginal examination was done to assess the bishop score. Then participants in Group A had twenty-five micrograms of misoprostol placed sublingually every six

hours for a maximum of four doses before onset of labour. Fetal heart rate and uterine activity were monitored continuously for at least half an hour after misoprostol application. Then participants in Group B were placed in dorsal position, vulva cleaned with diluted chlorhexidine solution and aseptic procedure ensured. Twenty-five micrograms of misoprostol was placed intravaginally at the posterior vaginal fornix every six hours for a maximum of four doses before onset of labour. Fetal heart rate and uterine activity was monitored continuously for at least half an hour after misoprostol application before the patient was allowed to ambulate.
Both Group A and B participants had a vaginal examination done every 6 hours until the onset of labour.

When the active phase parameters were achieved, oxytocin (Pitocin) augmentation was commenced following amniotomy if required. A minimum interval of six hours was maintained after the last misoprostol dose before initiating augmentation.

Primary Outcome Measures
The primary outcome was vaginal delivery within 24 hours from the start of induction.

Secondary Outcome Measures
Secondary outcomes included the number of misoprostol doses administered, time from first dose to active labour and induction-to-delivery interval in hours, antepartum hemorrhage, postpartum hemorrhage, need for transfusion, uterine rupture, cervical, and vaginal lacerations

Sample Size Determination
Sample size was determined using the formula for sample size determination for non-inferiority clinical trials with a continuous outcome.

$$n = \frac{2(Z_{1-a} + Z_{1-\beta})^2 \text{ X } SD^2}{d^2}$$

[2]Where n = minimum sample size.
$Z_{1-\alpha =}$ is the standard normal deviate giving a confidence level of 95% and a level of significance (α) of 5% = 1.96.
$Z_{1-\beta}$ = the standard normal deviate at a power of 80%, = 0.842
SD = the standard deviation of successful induction of labour (primary outcome measure) in a study done in Nigeria and reported as 3.97 [24]
d (non-inferiority limit) = 2 from a previous study. [25]
A minimum sample size of 62 was calculated and after using an attrition rate of 10%, approximately 70 women were selected into each arm of this study, giving a total sample size of 140.

Recruitment
A convenient sampling method was used to enroll patients into the study based on their eligibility and willingness to participate in the study. All women being prepared for induction of labour were met by the researcher or trained assistant in the antenatal ward or labour ward. To obtain informed consent, the researcher or a trained assistant explained the aim and processes of the study and its benefits to eligible women in simple and clear terms, and an assurance of safety was given. Eligible participants signed the consent form for the study only after they have expressed an understanding of the study and showed willingness to participate.

Randomization and Allocation Concealment Mechanism
Allocation sequence generation: Using the WINPEPI software for randomization, a random and balanced allocation of

numbers 1 to 140 to Group A and B conducted. The women were allocated to receive either Twenty-five microgram of misoprostol sublingually (Group A) or intravaginally (Group B).

Allocation concealment mechanism: Identical, sealed, sequentially arranged and opaque envelopes with cards inscribed with letter A or B concealed within them according to the randomly assigned letter to each number from 1 to 140. These envelopes were also labelled outwardly using serial numbers from 1 to 140.

Implementation: As each eligible woman was received into the antenatal ward or labour ward for induction of labour, a research assistant picked an envelope according to the sequence. The letter inscribed on the card in the envelope was announced and shown to the researcher and nurse. The serial number / identification number on the envelope selected was attached to the case folder and other documents for the study.

Data collection methods: Sociodemographic data and the primary and secondary outcome measures were obtained using a purpose designed proforma.[3]

DATA ANALYSIS

An intention-to-treat (ITT) analysis was employed. Statistical analysis of the data obtained from the study was done using Statistical Package for Social Sciences (SPSS) version 25. Frequencies and percentages of categorical data was determined. Mean and standard deviation of continuous numerical data, median, mode and range of discrete numerical data was determined. Continuous data was assessed for normality using the Shapiro-Wilk test. Comparisons between experimental and control groups was done using Chi-square test of proportions for categorical data, Student 't' test for normally distributed continuous data and Mann-Whitney U test for non-normally distributed continuous data. A non-inferiority margin of 2 was set between experimental group to control group. A p-value < 0.05 was considered significant statistically.

RESULTS

One hundred and forty-nine women were booked for induction of labour at the Obstetrics and Gynaecology Department of the Federal Medical Centre, Yenagoa. However, nine of these women declined to participate in the study. One hundred and forty women were eventually enrolled in the study and randomly assigned to one of two study arms in a 1:1 ratio. The two arms consisted of group A and B respectively. In the group A, 70 women were assigned to receive sublingual misoprostol and were assessed for primary and secondary outcome measures. In the group B, 70 women were assigned to receive vaginal misoprostol and were assessed for primary and secondary outcome measures. Consequently, data from all 140 enrolled women were included in the final analysis.

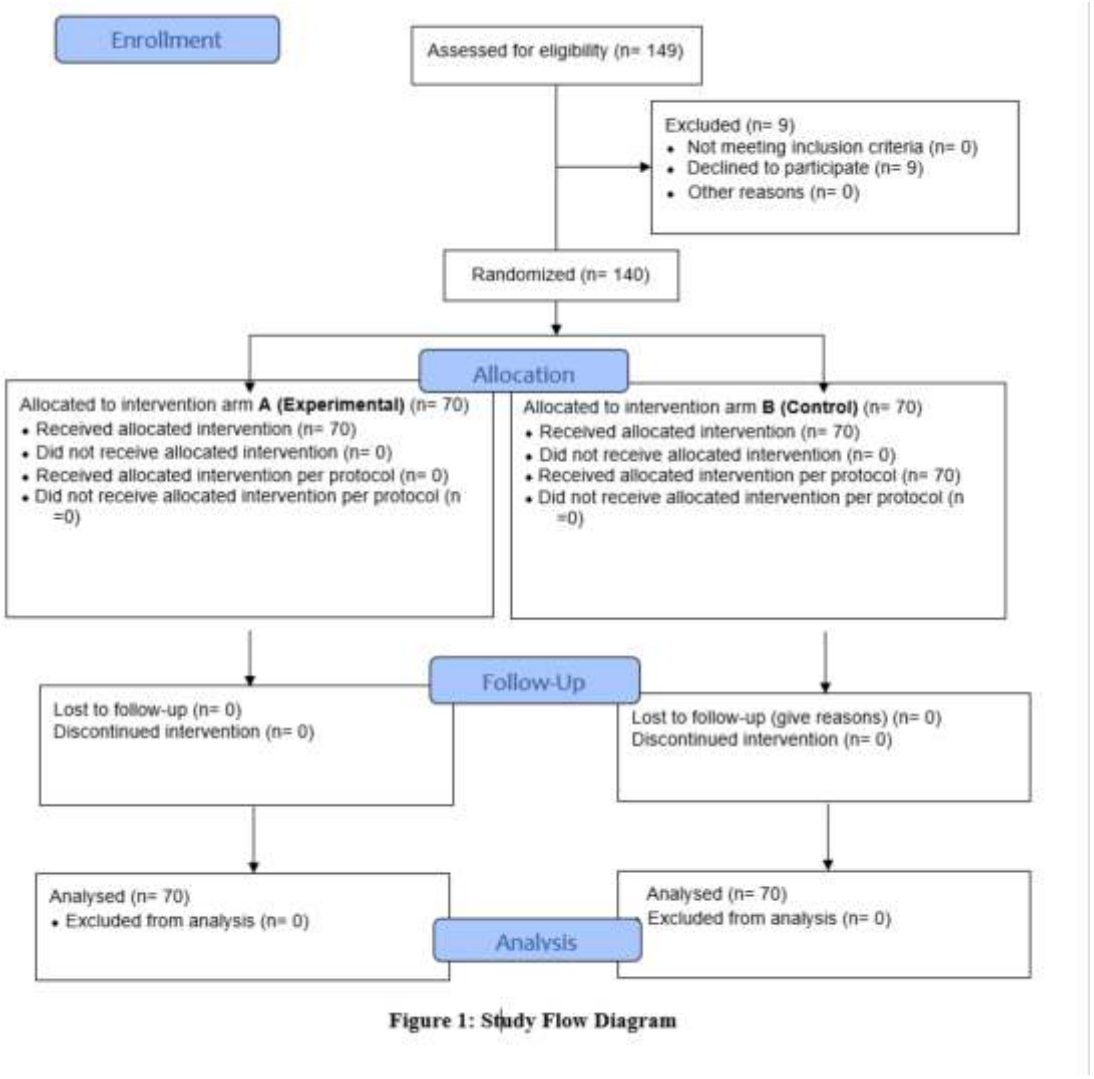

Figure 1: Study Flow Diagram

BACKGROUND

One hundred and forty-nine women were booked for induction of labour at the Obstetrics and Gynaecology department of Federal Medical Centre, Yenagoa. However, nine of these women declined to participate in the study. One hundred and forty women were ultimately enrolled in the study and randomly assigned to one of two study arms in a 1:1 ratio. The two arms consisted of group A and B respectively. In the group A, 70 women were assigned to receive sublingual misoprostol and were assessed for primary and secondary outcome measures. In the group B, 70 women were assigned to receive vaginal misoprostol and were assessed for primary and secondary outcome measures. Consequently, data from all 140 enrolled women were included in the final analysis. The study aimed to establish non-inferiority of the experimental group compared to the control group. With a non-inferiority limit set at 2, the results showed a difference of 0.14 for induction to delivery within 24 hours. This indicates that the experimental group was not inferior to the control group for induction of labour.

Table 1: Sociodemographic data of participants

		Group					
		A		B			
		N	%	n	%	X^2	P-value
Age	<20 years	8	11.6%	8	11.3%		
	21 – 30years	30	43.5%	30	42.3%		
	31 – 40years	23	33.3%	25	35.2%	0.05	.99
	>40years	8	11.6%	8	11.3%		
	Mean Age	30 ± 8		31 ± 7			
Tribe	Ijaw	17	24.6%	21	29.6%		
	Urhobo	17	24.6%	13	18.3%		
	Igbo	14	20.3%	14	19.7%	1.09	.89
	Yoruba	11	15.9%	13	18.3%		
	Others	10	14.5%	10	14.1%		
Educational Status	Primary	23	33.3%	11	15.5%		
	Secondary	11	15.9%	16	22.5%	6.21	.10
	Tertiary	15	21.7%	20	28.2%		
	Post graduate	20	29.0%	24	33.8%		

The demographic characteristics of the participants in the two groups sublingual misoprostol (Group A) and vaginal misoprostol (Group B) were similar and showed no statistically significant differences. The mean age was 30 ± 8 years in Group A and 31 ± 7 years in Group B, with the majority in the 21–30 years age range. The ethnic distribution across Ijaw, Urhobo, Igbo, Yoruba, and other tribes was comparable (P = 0.89). Although there were variations in educational status with Group A having a higher percentage of participants with primary level of education and Group B having more with postgraduate education these differences were not statistically significant (P =0 .10). This suggests that both groups were demographically well-matched at baseline.

Table 2: Obstetrics profile of participants

		Group					
		A		B			
		N	%	N	%	X^2	P-value
Parity	Para 0	8	11.4%	12	17.1%		
	Para 1	15	21.4%	15	21.4%	2.43	.65
	Para 2	15	21.4%	11	15.7%		
	Para 3	16	22.9%	12	17.1%		
	Para 4	16	22.9%	20	28.6%		
	Total	70	100.0%	70	100.0%		
Gestation	37 weeks	10	14.3%	13	18.6%		
	38 weeks	17	24.3%	16	22.9%	2.98	.56
	39 weeks	16	22.9%	9	12.9%		
	40 weeks	12	17.1%	16	22.9%		
	41 weeks	15	21.4%	16	22.9%		
	Total	70	100.0%	70	100.0%		
	Mean GA	39 ±1 weeks		39 ±1 weeks			
Booking parameters	Booked	35	50.0%	40	57.1%		
	Unbooked	35	50.0%	30	42.9%	0.71	.39
	Total	70	100.0%	70	100.0%		

The obstetric characteristics of both groups were similar. Parity and gestational age distributions showed no significant differences (p = 0.65 and p = 0.56, respectively), with most participants between Para 1–4 and at term (mean GA 39 ± 1 weeks). Booking status was also comparable, with 50.0% in Group A and 57.1% in Group B booked for antenatal care (p = .39).

Table 3: Effectiveness of two different routes of misoprostol (sublingual and vaginal) administered for induction of labour

		Group					
		A		B			
		N	%	n	%	X^2	P-value
Induction Delivery Interval	< 24 hours	52	74.3%	59	84.3%		
	> 24 hours	18	25.7%	11	15.7%	2.13	0.14
Mode of Delivery	SVD	59	84.3%	56	80.0%		
	Assisted Vaginal Delivery	2	2.8%	3	4.3%	0.34	0.84
	Caesarean section	9	12.9%	11	15.7%		

The effectiveness of sublingual (Group A) and vaginal (Group B) misoprostol for induction of labour was comparable. Though a higher proportion of women in Group B achieved delivery within 24 hours (84.3%) compared to Group A (74.3%), the difference was not statistically significant (p = 0.14). The mode of delivery was also similar across both groups, with spontaneous vaginal delivery

(SVD) being the most common (84.3% in Group A vs. 80.0% in Group B), followed by assisted vaginal delivery and caesarean section, with no significant differences between the groups (p = .84).

Table 4: Safety of two different routes of misoprostol (sublingual and vaginal) administered for induction of labour

		Group					
		A		B			
		N	%	N	%	X^2	P-value
Antepartum hemorrhage	No	69	98.6%	68	97.1%		
	Yes	1	1.4%	2	2.9%	0.34	0.55
	Total	70	100.0%	70	100.0%		
Postpartum hemorrhage	No	66	94.3%	65	92.9%		
	Yes	4	5.7%	5	7.1%	0.11	0.73
	Total	70	100.0%	70	100.0%		
Blood loss >500mls	No	66	94.3%	65	92.9%		
	Yes	4	5.7%	5	7.1%	0.11	0.73
	Total	70	100.0%	70	100.0%		
Need for transfusion	No	66	94.3%	65	92.9%		
	Yes	4	5.7%	5	7.1%	0.11	0.73
	Total	70	100.0%	70	100.0%		
Uterine rupture	No	70	100.0%	70	100.0%		
	Yes	0	0.0%	0	0.0%	Not applicable	NA
	Total	70	100.0%	70	100.0%		
Cervical laceration	No	66	94.3%	62	88.6%		
	Yes	4	5.7%	8	11.4%		
	Total	70	100.0%	70	100.0%	0.64	0.42
Vaginal laceration	No	59	84.3%	37	52.9%		
	Yes	11	15.7%	33	47.1%	0.64	0.37
	Total	70	100.0%	70	100.0%		

The safety outcomes for sublingual (Group A) and vaginal (Group B) misoprostol were largely comparable, with no statistically significant differences observed across all parameters. Rates of antepartum hemorrhage (1.4% vs. 2.9%, p = 0.55), postpartum hemorrhage (5.7% vs. 7.1%, p = 0.73), blood loss over 500 ml (5.7% vs 7.1%, p = 0.73), and need for transfusion (5.7% vs 7.1%, p = 0.73), were similar in both groups. Uterine rupture did not occur in either group. Rates of cervical (5.7% vs. 11.4%) and vaginal lacerations (15.7% vs. 47.1%) were also higher in the vaginal group but without statistical significance. Overall, both routes of administration showed a comparable safety profile.

Table 5: Comparison of Labour Progress Parameters Between Sublingual and Vaginal Misoprostol groups

Clinical Outcome	Sublingual Group (n = 70)	Vaginal Group (n = 70)		P-value
Time to Active Phase of Labour (hours)	6.8 ± 2.4	8.1 ± 2.9	2.42	0.018*
Number of Misoprostol Doses Used (Mean ± SD)	2.1 ± 0.9	2.6 ± 1.1	2.12	0.036*
Need for Augmentation (n, %)	18 (25.7%)	24 (34.3%)	1.29	0.26

*Statistically significant

Time to active phase labour was significantly shorter in the sublingual group (P-value <0.001). Mean number of misoprostol doses required was significantly lower in the sublingual group Need for augmentation was lower in the sublingual group, but this difference was not statistically significant.

DISCUSSION

This study found that a greater proportion of women who received vaginal misoprostol delivered within 24 hours compared with those who received sublingual misoprostol, although this difference was not statistically significant, suggesting that both routes have comparable efficacy. This result aligns with findings from Nigeria by Okonkwo *et al* [26] and India by Poonam *et al* [27], likely because those studies used the same misoprostol dose. In contrast, Chhatani *et al* [28] in India reported that more women in the sublingual group achieved vaginal delivery within 24 hours compared to the vaginal group, possibly due to the shorter dosing interval used in that study and the faster time to maximum plasma concentration of sublingual misoprostol compared with vaginal administration. The variation in outcomes across studies may also stem from racial differences among the study populations.

These findings of similar modes or rates of delivery between both groups in the present study are consistent with the results reported by Chhatani *et al* [28] in India. However, they contrast with the findings from the study by Ifarinola *et al* [24], women received misoprostol either sublingually or vaginally at 4-hour intervals. Their results showed that sublingual administration produced a quicker onset of uterine contractions and a shorter time to achieve a favourable Bishop score compared with vaginal misoprostol, although overall delivery outcomes were similar between routes. The discrepancy may be from the greater uterotonic potency of vaginal misoprostol observed in the current study, which can induce changes in fetal heart rate, a primary indication for Caesarean section in this study. However, there is no clear published mention of the specific brand name of misoprostol used in the trial

The current study found that the mean number of misoprostol doses required was significantly lower in the sublingual group compared with the vaginal group. This result is consistent with the findings of Ifariola *et al* [24], who reported a smaller mean number of doses in the sublingual group versus the vaginal group. The lower dose requirement in the sublingual group likely reflects the pharmacokinetics of sublingual

administration, which achieves peak plasma concentration more rapidly and at a higher level, thereby accelerating the onset of uterine contractions and reducing the total number of doses needed. This observation contrasts with the study by Poonam *et al* [27], in which a greater proportion of participants in the sublingual group required two doses (40.6 %) compared with 20.3 % in the vaginal group, and a single dose was more effective in the vaginal group (29.7 % vs. 23.4 %). However, overall dose distribution between the groups in that study showed no significant difference suggesting comparable dosing requirements.

The present study identified a statistically significant difference in the time required to reach the active phase of labour between the sublingual misoprostol group and the vaginal misoprostol group, a finding that mirrors the results of Okonkwo *et al.* [26] This difference likely stems from the shorter time needed for sublingual misoprostol to attain peak plasma concentration compared with the vaginal route. In contrast, a study conducted by Ayati *et al* [1] in Mashhad, Iran observed that the vaginal misoprostol group achieved the active phase of labour more quickly than the sublingual group, though this difference was not statistically significant. The variation in outcomes may be attributable to racial differences among the study populations. Additionally, the current study noted that a smaller proportion of women using sublingual misoprostol required augmentation of labor compared with those using vaginal misoprostol, although this difference was not statistically significant—a result consistent with Okonkwo *et al.* [26] This similarity may be due to the identical misoprostol dosage used in both groups. However, the finding differs from Ifariola *et al* [24], who reported a greater need for augmentation in the sublingual group than in the vaginal group.

The study found no statistically significant difference in the induction delivery interval between the sublingual misoprostol group and the vaginal misoprostol group. The induction delivery interval was slightly shorter in the sublingual group than in the vaginal group. This result contrasts with a study by Kattan *et al* [29] in Egypt, which reported a shorter induction-delivery interval in the sublingual group compared with the vaginal group, though the difference was not statistically significant. The discrepancy may be attributable to the small sample size of 50 participants in the Egyptian study [29], which likely reduced the study's statistical power.

CONCLUSION

The sublingual and vaginal routes for administration of misoprostol showed comparable safety and efficacy for induction of labour.

STRENGTHS AND LIMITATIONS: The study used primary data, which gave precise information. The randomized clinical trial design of this study gives a high level of evidence and also reduces bias. Bias was reduced by randomization.

The study followed an appropriate randomization protocol but could not incorporate blinding of subjects and caregivers in the study. The study did not assess the patient satisfaction rate with the different routes, which could have offered insight into the patient's preference to a particular route.

Additionally, this study's findings may not be generalizable to other populations, as it was conducted exclusively among women undergoing induction of labour at a single hospital, the Federal Medical Centre Yenagoa, Bayelsa State.

RECOMMENDATIONS

Based on the findings of this study, it is recommended that sublingual misoprostol can be used just as the vaginal misoprostol for induction of labour at the Federal Medical Centre Yenagoa, Bayelsa State as the sublingual route appears more convenient for administration and reduces the frequency of digital vaginal examination.

To further validate and generalize these findings, larger, multicenter studies using a similar protocol are suggested which will further increase external validity.

ICONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. Ayati S, Vahidroodsari F, Farshidi F, Shahabian M, Afzal AM. Vaginal Versus Sublingual Misoprostol for Labour Induction at Term and Post Term: a Randomized Prospective Study. Iran J Pharm Res. 2014; 13(1): e125410.
2. Nimbark N, Joshi PM, Joshi MI. A randomized comparative study of induction of labour with sublingual misoprostol 50 µg and oral misoprostol 50 µg in term patients. Int J Basic Clin Pharmacol. 2023; 12:211-5
3. Essam MS, Alaa EH, Amr AE. Randomized controlled trial comparing sublingual and vaginal misoprostol for induction of labour at term. *Evidence Based Women's Health Journal*. 2019;9(2):407–415.
4. Martina K, Franziska K. Maternal and neonatal outcome of labour induction at term comparing two regimens of misoprostol. Journal of perinatal medicine. 2014; 42:603-609.
5. Guerra GV, Cecatti JG, Souza JP, Faúndes A, Morais SS, Gülmezoglu AM *et al*. Factors and outcomes associated with the induction of labour in Latin America. BJOG. 2009; 116:1762–72
6. World Health Organization. *WHO recommendations for induction of labour*. Geneva: World Health Organization; 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK131965/. Accessed November 14, 2023.
7. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK. Births: final data for 2019. Natl Vital Stat Rep. 2021; 70:1–51 3.
8. European Perinatal Health Report 2010. Paris: Euro-Peristat Project; 2013. Available from: www.europeristat.com. Accessed November 14, 2023.
9. Ibrahim IA, Obilahi A, Ekine AA. The Safety of Induction of Labour in the Niger Delta Region. Greener Journal of Medical Sciences. 2012;6(2):173-178
10. Ekele BA, Jaiyeola AO. Induction of labour at Usman Danfodiyo University Teaching Hospital Sokoto. Trop J Obstet Gynaecol.2002; 19:74 -77
11. Vasilios P, Michail P, ·Therapon C, ·Lito VV, Andreas K, Sofoklis S. Efcacy and safety of oral and sublingual versus vaginal misoprostol for induction of labour: a systematic

review and meta-analysis. Archives of Gynecology and Obstetrics. 2023; 308:727–775 https://doi.org/10.1007/s00404-022-06867-9

12. Hofmeyr GJ, Gülmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews. In: The Cochrane Library, Issue 06, 2011. Art. No. CD000941.
13. Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews. In: The Cochrane Library, Issue 06, 2011. Art. No. CD004221.
14. Gattás DS, José RJ, Alex SR, Francisco EF, Melania MR. Misoprostol administered sublingually at a dose of 12.5 µg versus vaginally at a dose of 25 µg for the induction of full-term labor: a randomized controlled trial protocol. Reproductive Health. 2018; 15:65
15. Ezebialu IU, Eke boAC, Eleje GU, Nwachukwu CE. Methods for assessing pre-induction cervical ripening. Cochrane Database of Systematic Reviews. In: The Cochrane Library, Issue 6, 2015. Art. No.: CD010762. DOI: 10.1002/14651858.CD010762.pub2.
16. Ugwuoroko HC, Eleje GU, Okafor CG, Okechukwu ZC, Eke AC, Okoro CC, *et al*. Obstetric Outcome of Induction of Labour in a Tertiary Hospital in Nigeria: A Five-Year Retrospective Cross-Sectional Study. Int J Innov Res Med Sci. 2023; 8(7): 235–240
17. Kuba K, Kirby MA, Hughes F, Yellon SM. Reassessing the Bishop score in clinical practice for induction of labor leading to vaginal delivery and for evaluation of cervix ripening. Placenta Reprod Med. 2023; 2:8.
18. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 107: Induction of labour. *Obstet Gynecol.* 2009;114(2 Pt 1):386–397.
19. Alfirevic Z, Keeney E, Dowswell T, Welton NJ, Medley N, Dias S, *et al*. Which method is best for the induction of labour? A systematic review, network meta-analysis and cost-effectiveness analysis. Health Technol Assess (Winch, Engl) 2016;20:1–584.
20. Bartusevicius A, Barcaite E, Krikstolaitis R, Gintautas V, Nadisauskiene R. Sublingual compared with vaginal misoprostol for labour induction at term: a randomized controlled trial. British Journal of Obstetrics and Gynaecology. 2006; 113:1431-1437.
21. Souza AS, Amorim MM, Feitosa FE. Comparison of sublingual versus vaginal misoprostol for the induction of labour: a systematic review. BJOG: Int J Obstet Gynaecol. 2008; 115:1340–1349
22. Alfirevic Z, Aflaifel N, Weeks A. Oral misoprostol for induction of labour. Cochrane Database Syst Rev. 2014:CD001338-CD
23. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med 2013; 35:121-6.
24. Ifariola D, Adeniyi AA, Adewara OE, Okere AR, Adebara IO, Bakare A, *et al*. Randomization of vaginal and sublingual misoprostol for cervical ripening and labor induction. Trop J Obstet Gynaecol 2020; 37:78-84
25. Keulen KJ, Bruinsma A, Kortekaas JC, Dillen VN, Bossuyt PM, Oudijk MA

et al. Induction of labour at 41 weeks versus expectant management until 42 weeks (INDEX): multicenter, randomized non-inferiority trial. BMJ 2019; 364:344

26. Okonkwo RI, Onyeabochukwu AD, Izuka EO, Onyegbule OA, Duke-Onyeabo CP, Obiora-Izuka CE, et al. Effectiveness and safety of vaginal versus sublingual misoprostol for cervical ripening and induction of labor: A randomized controlled trial. Int J Med Health Dev 2023; 28:31-8.
27. Poonam Y, Keerti S, Nazia N, Shikha V, Sonali S. Comparison of Effectiveness of Sublingual Versus Vaginal Misoprostol Use for Labour Induction at Term Pregnancy. Journal of Neonatal Surgery. 2025; 14 (18s): 1089-1094
28. Chhatani PL, Pitre D. Comparison of 25 microgram of sublingual misoprostol with 25 micrograms of vaginal misoprostol for induction of labour at term. IJCOG. 2024;8(1):28-32.
29. Kattan EI, Eman A, Abdel M, Ghada A, Abdel Razek, Abdel Rahman. Sublingual versus vaginal misoprostol for induction of labor in term primigravida's: a randomized study. Evidence Based Women's Health Journal 2013;3(3):111-4.