A COMPARISON OF TWO DOSING REGIMENS OF MISOPROSTOL IN LABOUR INDUCTION: A RANDOMISED CONTROLLED TRIAL

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Abstract

Objective: To compare the effectiveness and safety of 50µg of sublingual misoprostol administered six (6) hourly to that of 50µg of vaginal misoprostol administered four (4) hourly.

Methodology: A non-blinded, randomized controlled trial conducted from Sept 1, 2014, to Nov 31, 2014, at a tertiary hospital in Ghana. Hundred and sixty women with medical or obstetric indications for labour induction were randomized into two groups.

Results: The rate of vaginal delivery, caesarean section, uterine tachysystole and uterine hyperstimulation were similar in both groups. Sixty-three (78.8%) and 66 (82.5%) mothers in the vaginal and sublingual groups delivered vaginally. More (10.0%) mothers in the vagina group required emergency caesarean for foetal distress. Six (vaginal group) and 8 (sublingual group) of the mothers required emergency caesarean for cephalopelvic disproportion. Three mothers from each group had an emergency caesarean section due to failed labour induction. Almost the same number of mothers had uterine tachysystole in both groups. More (3.8%) mothers in the vaginal group had uterine hyperstimulation. Differences in the mean induction delivery interval and the need for oxytocin augmentation were not significant. No differences were found in the intrapartum passage of meconium, blood loss in the third stage of labour, 5-minute Apgar score <7, and neonatal intensive care unit admissions.

Conclusion: The sublingual regimen was as effective and safe as the vaginal regimen in achieving vaginal delivery.

Key words: *Ghana, Labour Induction, Sublingual misoprostol, Premature rupture of membranes*

Introduction

Induction of labour (IOL) is a frequently performed obstetric procedure, utilized in 9.5 – 33.7% of all pregnancies.[1,2] IOL is defined as the initiation of uterine contractions at or after 28 weeks of gestation, and before the onset of spontaneous labour, by medical or surgical means for the purpose of vaginal delivery.[3] IOL is indicated for a wide range of maternal and foetal conditions, including postdates, premature rupture of membranes (PROM), and hypertensive disorders of pregnancy, when the anticipated outcomes for the foetus, the mother or both, are better than waiting for spontaneous onset of labour.[4,5] Despite its widespread practice, there is a lack of agreement in the literature on medication type, dosing, route, and dosing interval. Misoprostol, a prostaglandin E1 analogue, is a commonly used medication for IOL.[6] Misoprostol is typically available as a 200µg scored tablet, which often is broken into pieces to approximate 25, 50 and 100µg doses.[7–9] Misoprostol is inexpensive and widely available, and thus is frequently used in Sub-Saharan Africa and other low-resource settings. The most common protocol in Sub-Saharan Africa is 50µg of misoprostol administered vaginally every four hours.[9,10]

As an alternate route of administration, sublingual misoprostol is easy to administer, more acceptable to women[7] and may reduce ascending infection risk associated with vaginal exams in certain clinical contexts such as PROM. Despite these advantages of sublingual administration, there is concern about potential associations with foetal distress, meconium-stained amniotic fluid, low Apgar scores, and NICU admission.[11] Poor neonatal outcomes associated with induction agents like misoprostol may be secondary to uterine tachysystole.[12] Since the rate of uterine tachysystole appears to decrease with increasing dosing interval,[13] increasing the dosing interval of sublingual misoprostol may increase its safety profile while maintaining the other advantages of a sublingual route.

It is unknown how an extended-interval dose of sublingual misoprostol compares to the commonly used vaginal misoprostol regimen regarding efficacy and safety. This study fills this gap by comparing the effectiveness and safety of the standard 50µg of vaginal

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misoprostol administered every four hours to 50µg of sublingual misoprostol administered every six hours.

Materials and Methods

Study design and participants

This was a non-blinded, randomized controlled trial conducted from Sept 1 to Nov 30, 2014, at the Komfo Anokye Teaching Hospital (KATH), located in Kumasi, Ghana. KATH is a tertiary hospital for the northern half of Ghana. Participants were adult pregnant women presenting for planned IOL at KATH. Inclusion criteria included age greater than or equal to 18 years, gestational age of 28 weeks or greater, single live foetus in cephalic presentation, and amniotic fluid index of more than 5. Exclusion criteria were abnormal cardiotocograph (CTG) on admission, known hypersensitivity to prostaglandins, previous caesarean delivery or myomectomy, and any other contraindications to vaginal delivery. Eligible women were enrolled in the study after obtaining written informed consent. The study was approved by the Committee on Human Research, Publication and Ethics (CHRPE) of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology, and KATH, Kumasi **(CHRPE/AP334/14**). This clinical trial was registered with the Pan African Clinical Trial Registry (**PACTR202101825071744).**

Randomization

Participants were randomly allocated, in a 1:1 ratio, to receive misoprostol either sublingually or vaginally. The randomization sequence was computer-generated, using block sizes of 8, with each containing twenty random numbers. The allocation sequence was given to an independent pharmacist who prepared 160 consecutively numbered, opaque, sealed envelopes, each containing four 200-µg tablets of misoprostol and a regimen assignment. The treatment allocation was broken to the research assistant and the participant at the time of treatment application.

Procedures

Decisions regarding indication and timing of IOL were determined by KATH's obstetricians according to standard practice. On admission, routine clinical assessment included a history and physical exam, assessment of foetal presentation, sterile cervical exam, placement of intravenous access, obstetric ultrasound, and biophysical profile. A cardiotocograph (CTG) was performed prior to starting the IOL to rule out frequent uterine contractions or abnormal foetal heart tracing. 200µg tablets of Misoprostol (Cytotec®, Piramal Healthcare UK Limited, Northumberland, United Kingdom) were used in both study arms. Each tablet was split into approximate 50 µg portions using a pill cutter, a 50 µg portion was administered, and the other portions were discarded. In the vaginal route arm, 50µg of misoprostol was administered vaginally every 4 hours for a maximum of 4 doses.

In the sublingual arm, 50µg of misoprostol was administered sublingually every 6 hours for a maximum of 4 doses. Intravenous normal saline was started at a maintenance rate after the onset of contractions. The administration of misoprostol was stopped after the maximum of 4 doses was reached or if active labour was achieved. Active labour was defined as at least three regular painful contractions in a 10-minute period, each lasting 40 to 60 seconds. After active labour was achieved, artificial rupture of membranes or augmentation with oxytocin infusion was carried out as clinically indicated, according to department protocol. Augmentation was not started earlier than 4 hours after the last dose of misoprostol. If labour did not start within 4 hours of giving the fourth dose of misoprostol, the induction was considered to have failed, and the attending obstetricians determined subsequent management. Per routine clinical practice, uterine contractions were monitored every 30 minutes using palpation, and foetal heart rate was auscultated every 30 minutes after the start of the induction and every 15 minutes during the second stage of labour using a hand-held Doppler. Vaginal examinations were performed every 4 hours to assess cervical dilation and Bishop score. In addition, CTG was performed every 4 hours to evaluate uterine activity and foetal heart rate patterns. Relevant clinical data were extracted from participants' paper charts, including demographics, medical history, and obstetric history. Data on misoprostol given, IOL course, mode of delivery, and maternal and perinatal outcomes were prospectively collected.

Outcomes

The primary outcomes were 1) the rate of vaginal delivery and 2) the presence of uterine tachysystole/hyperstimulation. Secondary outcomes were induction-delivery interval (IDI), need for oxytocin augmentation, meconium-stained amniotic fluid, blood loss at vaginal delivery, 5-minute Apgar score less than 7, and neonatal intensive care unit (NICU) admission. Uterine tachysystole was defined as more than 5 contractions in 10 minutes, averaged over a 30-minute window.[14] Uterine hyperstimulation was defined as uterine tachysystole together with foetal tachycardia, late decelerations or absence of beat-to-beat variability on CTG.[15] Failed IOL was defined as the inability to achieve active labour at least four hours after the fourth dose of Misoprostol.[16]

Sample size and power

We assumed that the proportion of women achieving vaginal delivery and rate of uterine tachysystole were similar to those observed by Caliskan et al. [11] and Zahran et al[13]. for 50µg misoprostol administered 4-hourly vaginally and 6-hourly sublingually respectively. A total sample size of 160 participants (80 per group) has 80% power to detect a difference in the vaginal delivery rate of 22% and tachysystole rate of 13% between the two groups.[17]

Table 1: Sociodemographic and reproductive characteristics of the patients

Variable	Number	Percentage
Age	28.2(5.5)	
<25	43	26.9
26 to 30	65	40.6
31 to 35	36	22.5
> 35	16	10.0
BMI	26.5(4.6)	
Underweight	3	1.9
Normal	57	35.6
Overweight	67	41.9
Obese	33	20.6
Educational Level		
No formal education	23	14.4
Primary education	75	46.8
Secondary education and higher	62	38.8
Occupation		
Unemployed	35	21.9
Self-employed	84	52.5
Civil servants	41	25.6
Marital status		
Never married/separated	19	11.9
Married/cohabiting	141	88.2
Parity		
Nulliparous	62	38.7
Primiparous	39	24.4
Multip-of- 2-4	55	34.4
Grandmultip	4	2.5
EGA, completed weeks	40.6 (2.3)	
31-36	12	7.5
37-41	88	55.0
42+	60	37.5
Initial Bishop's score	8.2 (1.6)	
<6	14	8.7
6-8	63	39.4
>8	83	51.9
Indication for induction of labour		
Postdate pregnancy	121	75.6
Premature rupture of membranes	19	11.9
Medical condition in pregnancy/IUGR	20	12.5

Statistical analysis

Stata 13.0 (Stata Corporation, Texas USA) was used for analysis. The sociodemographic and obstetric characteristics, maternal and foetal outcomes were compared using Pearson's Chi-square (χ^2) or Fisher's exact tests (as appropriate) for categorical variables, while continuous variables were compared using student t-tests for mean differences, and Mann-Whitney U tests for median differences. All tests were two-tailed, and a p-value ≤ 0.05 was considered statistically significant.

Results

A total of 160 participants were included in the study, with 80 participants randomly assigned to the vaginal group and 80 to the sublingual group. Of all participants, the mean age was 28.2 (5.5) years, and the mean body mass index (BMI) was 26.5 (4.6). (**Table 1**). Most women had completed at least primary education (46.8 %), were employed (78.1%), and were married or cohabitating (88.2%). Most women (61.3%) were multiparous, and 92.5% were at least 37 weeks gestation or later. Prolonged pregnancies (≥ 42 weeks gestation) were common at 75.0% of the vaginal group and 76.3% in the sublingual group. (Table 2). The sociodemographic and reproductive characteristics were similar between the groups, with no significant difference in demographic variables, reproductive history, initial Bishop score, or indication for IOL. (**Table 2**).

Most participants (80.6%) delivered vaginally (**Table 3**). Of the 129 participants with vaginal delivery, oxytocin augmentation was needed by 19.4%, and 48.1% had an induction to vaginal delivery interval of less than 24 hours. Close to half of the participants delivered with a single dose of misoprostol. Of the 31 participants with a caesarean section, cephalopelvic disproportion was the most common indication (45.2%). The rates of vaginal delivery (78.8% vs. 82.5%) and caesarean section (21.2% vs. 17.5%) were similar in the two groups (**Table 4**). The groups did not differ significantly with regards to the proportion of women who delivered vaginally after a single dose of misoprostol, the mean total dose of misoprostol required to achieve delivery or the need for oxytocin augmentation.

The mean induction-to-vaginal delivery interval was similar, at 10.5 hours in the vaginal group compared to 11.9 hours in the sublingual group (p=0.10). The groups did not differ in the proportion of caesarean section for failed IOL, at 17.6% (n=3) in the vaginal group and 21.4% (n=3) in the sublingual group. Rates of uterine tachysystole (6.3% vs. 5.0%; p=0.73) and hyperstimulation (3.8% vs 1.3%; p= 0.64) were low and comparable in the two groups, (Table 5). Two (2.5%) women in the vaginal group compared to 1 (1.3%) in the sublingual group had uterine tachysystole accompanied by late FHR decelerations. One (1.3%) woman in the vaginal group had uterine tachysystole accompanied by foetal tachycardia, compared to 0 (0%) in the sublingual group. The incidence of meconium-stained amniotic fluid, mean blood loss at vaginal delivery, and rate of postpartum haemorrhage (defined as blood loss >500cc) after vaginal delivery did not differ significantly between groups. Regarding neonatal outcomes, the mean birth weight was 3.2 (0.6) kg, 14.4 % has an APGAR score less than 7 at 5 minutes of life, and

20 % were admitted to the NICU. Although mean birth weight did not differ between groups, there was a significant difference in birth weight ≥4.0kg, with 6.2% (n=5) in the vaginal group compared with 15.0% (n=12) in the sublingual group. The proportion of low Apgar scores at 1 and 5 minutes and NICU admission were similar between groups.

Table 2: Sociodemographic and reproductive characteristics of the patients

Misoprostol administration route			
Variable	**Vaginal (n=80)**	**Sublingual (n=80)**	**P-value**
	n (%)[a]	**n (%)[a]**	
Mean age (SD), years	28.6(5.8)	27.8(5.2)	0.37
Mean BMI (SD), kg/m^2	26.6(4.8)	26.4(4.4)	0.83
Educational Level			0.42
No formal education	11(13.8)	12(15.0)	
Primary education	34(42.5)	41(51.3)	
Secondary education and higher	35(43.7)	27(33.7)	
Occupation			0.37
Unemployed	18 (22.5)	17 (21.3)	
Self-employed	38 (47.5)	46 (57.5)	
Civil servants	24 (30.0)	17 (21.2)	
Marital status			0.46
Never married/separated	8 (10.0)	11 (13.8)	
Married/cohabiting	72 (90.0)	69 (86.2)	
Parity			0.33
0	28(35.0)	34(42.5)	
1+	52(65.0)	46(57.5)	
EGA, completed weeks			0.95
31-36	6 (7.5)	6 (7.5)	
37-41	43 (53.8)	45 (56.3)	
42+	31 (38.7)	29 (36.2)	
Initial Bishop's score			0.20
<6	4 (5.0)	10 (12.5)	
6-8	31 (38.8)	32 (40.0)	
>8	45 (56.2)	38 (47.5)	
Median (IQR)	9 (8-10)	8 (7-9)	0.08
Indication for induction of labour			
Postdate pregnancy	60 (75.0)	61 (76.3)	
Premature rupture of membranes	10 (12.5)	9 (11.3)	
Medical condition in pregnancy/IUGR	10 (12.5)	10 (12.5)	0.97

[a]Values are given as number (percentage) unless otherwise indicated. SD, standard deviation; BMI, body mass index; EGA, estimated gestational age; IQR, interquartile range; IUGR, intrauterine growth restriction.

Table 3: Maternal Outcomes

Variable	**N=160**	**N (%)**
Mode of delivery		
Caesarean section	31	19.38
Vaginal delivery	129	80.63
Vaginal delivery , N=129		
Vaginal delivery with 50	61	47.3
Vaginal delivery with 100	48	37.2
Vaginal delivery with 150	20	15.5
Need for oxytocin augmentation		
Yes	31	19.4
No	129	80.6
IDI, N=129		
less 12	15	11.6
12 to 24	64	49.6
more 24 hours	37	28.7
Indication for CS, N=31		
foetal distress	10	19.4
Failed IOL	6	32.3
CPD	14	45.2
Cord prolapse	1	3.23

[a]N=160 unless otherwise specified; bValues are given as number (percentage) unless otherwise indicated; SD, standard deviation; NICU, neonatal intensive care unit.

Tables 4: Clinical outcomes of induction in both groups

Variable	**Vaginal group n (%)[a]**	**Sublingual group n (%)[a]**	**P-value**
Mode of delivery, n=160			0.55
Vaginal	63 (78.8)	66 (82.5)	
Caesarean section	17 (21.2)	14 (17.5)	
NMD[b], vaginal delivery, n=129			0.40
1	31 (49.2)	30 (45.5)	
2	25 (39.7)	23 (34.9)	
3 or 4	7 (11.1)	13 (19.7)	
Mean total misoprostol dose (SD), mcg	86.3 (41.3)	93.1 (43.4)	0.31
Need for oxytocin use	15 (18.8)	15 (18.8)	1.00
Induction-vaginal delivery interval, n=129			0.11
<12 hours	42 (66.7)	35 (53.0)	
12-24 hours	21 (33.3)	31 (47.0)	
Mean (SD)	10.5 (4.6)	11.9 (5.1)	0.10
Indication for caesarean section, n=31			0.32
Failed IOL	3 (17.6)	3 (21.4)	
Foetal distress	8 (47.1)	3 (21.4)	
CPD	6 (35.3)	8 (57.2)	

[a]Values are given as number (percentage) unless otherwise indicated. [b]NMD number of misoprostol doses. SD, standard deviation; IOL, induction of labour; CPD, cephalopelvic disproportion.

Tables 5: Adverse Maternal and Foetal Outcomes

Variable	Vaginal group	Sublingual group	P-value
	n (%)[b]	n (%)[b]	
Uterine tachysystole	5 (6.3)	4 (5.0)	0.73
Uterine hyperstimulation	3 (3.8)	1 (1.3)	0.64
UT plus Late FHR deceleration	2 (2.5)	1 (1.3)	
UT plus foetal tachycardia	1 (1.3)	0 (0.0)	
Meconium-stained amniotic fluid	37 (46.3)	30 (37.5)	0.26
Blood loss at vaginal delivery, ml (n=129)			0.80
<200	18 (28.6)	22 (33.3)	
200-499	40 (63.5)	40 (60.6)	
≥500	5 (7.9)	4 (6.1)	
Mean (SD)	240.7 (127.8)	238.6 (106.6)	0.10
Birth weight, kg			0.05
<2.5	11 (13.8)	4 (5.0)	
2.5-3.9	64 (80.0)	64 (80.0)	
≥4.0	5 (6.2)	12 (15.0)	
Mean (SD)	3.1 (0.57)	3.3 (0.56)	0.06
Apgar score <7 at 1 min	30 (37.5)	22 (27.5)	0.18
Apgar score <7 at 5 min	15 (18.8)	8 (10.0)	0.11
NICU admission	18 (22.5)	14 (17.5)	0.63
Reason for NICU admission (n=32)			0.10
Apgar score <7 at 5 min	15 (83.3)	8 (57.1)	
Other reasons	3 (16.7)	6 (42.9)	

[a]N=160 unless otherwise specified; [b]Values are given as number (percentage) unless otherwise indicated; SD, standard deviation; NICU, neonatal intensive care unit

Discussion

We set out to compare the effectiveness and safety of sublingual misoprostol at 6-hourly intervals with the same dose of vaginal misoprostol at 4-hourly intervals for IOL. Except for significantly higher mean birth weights in the sublingual group, the sociodemographic characteristics, general and adverse maternal and perinatal outcomes were comparable between the two groups.

Previous studies comparing sublingual and vaginal misoprostol have reported the effectiveness of the sublingual route.[11,13] The 82.5% vaginal delivery rate in the sublingual arm of our study was higher than the rate of 70.6%, observed in the sublingual arm of a similar study, possibly due to a lower average pre-induction score of 2 in that study.[13] Bishop score correlates closely with the likelihood of successful outcome (i.e., vaginal delivery) at IOL, and the higher the Bishop score, the more likely a vaginal delivery would occur.[18] A far higher vaginal delivery rate of 92.5% was observed in the sublingual arm of another study which used the same dose but a shorter dosing interval of four hours.[11] To the contrary, fewer deliveries (<70%) occurred in the sublingual arms of similar studies that used 25µg of misoprostol in a 6-hourly dosing interval.[19,20] There is some evidence of appreciable increase in effectiveness when the misoprostol dose was increased from 25 to 50 µg at the same dosing interval using the vaginal route.[21]

Based on the acceptability and ease of sublingual administration of misoprostol, it is rewarding to observe more vaginal deliveries within acceptable time limits of induction. Consistent with the results of previous studies,[11,13,16,19,22] more women delivered vaginally in the vaginal arm after a single dose of misoprostol. The patterns of more vaginal delivery after the first misoprostol dose may suggest the possibility of a greater degree of uterine contractility secondary to prolonged plasma misoprostol following vaginal administration.[23]

We also observed that more women in the vaginal group delivered vaginally in less than 12 hours of induction. Similar findings were reported by Caliskan *et al*.[11] This pattern of more vaginal delivery under 12 hours may suggest a greater degree of uterine contractility with the vaginal at a certain critical misoprostol dose, which is likely to be more than 25 µg. The IDI of 11.9 hours in the sublingual arm of this study is much shorter than the 17.2 hours of a similar study by Zahran et al. 2009, using the same dose and dosing interval, but compares favourably with IDIs of 11 hours in a study where 50 µg misoprostol dose was given at 4-hourly intervals.[11,13] These disparities may be attributed to differences in the obstetric characteristics of the mothers. One such difference may be the mean pre-induction Bishop scores reported in the sublingual arms. The mean total misoprostol dose required to achieve vaginal delivery was higher in the sublingual group. This is consistent with the results of other studies.[11,20]

Per the pharmacokinetics of sublingual misoprostol (rapid fall in plasma misoprostol following single sublingual administration), the frequency and amplitude of uterine contractions may fade away quickly after sublingual administration, thus probably necessitating higher misoprostol dose for the same clinical effect.[24] In agreement with the results of one systematic review comparing the effectiveness of sublingual and vaginal misoprostol, we did not find any significant differences in the need for oxytocin augmentation between the two groups.[7] It is worth noting that other studies have reported higher oxytocin augmentation rates of 36-81% following vaginal and sublingual administration of Misoprostol for IOL.[11,13,22] This is probably due to the lower mean dose of misoprostol used in those studies.

The caesarean section rates in this study are comparable to those of a similar study where 50µg of misoprostol was also given but at shorter dosing intervals of 4 hours in both arms.[11] However, it is

pertinent to note that while rates of foetal distress (ominous FHR alterations) were similar in the vaginal arms of both studies, the rate in their sublingual arm was four-fold higher than the rate in our sublingual arm. This difference may be attributable to the shorter doing interval in their study. Furthermore, the foetal distress rate in their sublingual arm is higher than that in the vaginal arm (15% vs. 8.8%), while the converse was the case in our study (3.8% in the sublingual arm vs. 10% in the vaginal arm). These findings suggest that the 50μg of misoprostol given at six hourly intervals has comparable delivery outcomes with the same dose given vaginally or sublingually at four hourly intervals but with fewer FHR abnormalities.

The incidence of meconium-stained liquor was over one-third in both arms of the study. This is a common finding in labours induced with misoprostol, and it is a direct effect of misoprostol on foetal intestinal smooth muscle.[25] This is of significance in most low-resource settings where electronic foetal monitoring is not readily available and when intermittent foetal heart auscultation with the Pinard stethoscope or foetal doppler is not done meticulously. Meconium-stained liquor becomes an important clinical sign of foetal compromise and consequently an indication for caesarean section during inductions in such settings. In low-risk pregnancies, electronic foetal monitoring tends to be associated with increased operative delivery, while in high-risk pregnancies (such as HDOPs), it could reassure clinicians of foetal condition and avoid unnecessary intervention. Although not a direct cause of foetal hypoxia per se, meconium-stained liquor is associated with increased risks of meconium aspiration and subsequent neonatal morbidity.[25] Despite the high rate of meconium-stained liquor in our study, it is gratifying to note that our caesarean section rate was relatively lower due to meticulous intermittent foetal heart auscultation or use of the CTG.

More babies in the vaginal group had low birth weight, which may have accounted for the relatively higher low Apgar scores at 5 minutes and NICU admission rates in that arm. Despite some inaccurate foetal weight estimations leading to the inclusion of macrosomic babies in the study, our initial clinical assessment suggested that these women could deliver vaginally, and most did. Therefore, the higher rate of foetal macrosomia in the sublingual group was not a major contributor to the CPD rate in that group, which did not differ significantly from the rate in the vaginal group. The study had a couple of limitations. First, breaking off 50 μg from the 200 μg misoprostol tablet may not have been very accurate due to the shattering and crumbling of the tablet. However, trained research assistants, pile cutter, and alignment of the two 50 μg parts from the same 100 μg portion minimised such inaccuracies. Second, the use of intermittent CTG monitoring for a selected group of patients instead of continuous CTG monitoring for every case of induction may have introduced some bias. However, since the department did not have enough CTGs for multiple concurrent inductions and other labour cases, this remained the most practical option. Furthermore, the use of one-on-one care (due to relatively few cases of induction), as well as regular and diligent monitoring of the FHR, contractions, and passage of meconium, ensured that to a large extent, induction of labour-related abnormalities were not missed thus limiting the bias.

Conclusion

Fifty micrograms sublingual misoprostol administered 6-hourly was as effective as the 50 μg vaginal misoprostol administered 4-hourly in achieving vaginal delivery, and the incidence of uterine tachysystole and uterine hyperstimulation were not significantly different. The sublingual regimen had persuasive benefits of less adverse perinatal outcomes. Although the induction-to-vaginal delivery interval was longer, and there was an increased need for oxytocin augmentation in the sublingual arm of the study, the difference was not statistically significant. Therefore, 50 μg sublingual misoprostol given at 6-hourly intervals appears to be a convenient regimen for IOL. Risks of PPH and satisfaction associated with the various routes and dosing regimens of Misoprostol for IOL need to be investigated.

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