

Efficacy and Safety of Sublingual Versus Vaginal Misoprostol for Pre-induction Cervical Ripening Among Primigravida

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ABSTRACT

Background: Induction of labor is an intervention intended to artificially initiate uterine contractions resulting in progressive effacement and dilatation of the cervix. This is a common intervention during pregnancy in both industrialized and non-industrialized countries. Misoprostol is the commonly used induction agent. The objective of this study was to compare the efficacy of sublingual route of misoprostol with that of vaginal for pre-induction cervical ripening at term among Primigravida.

Methods: This study was a hospital based cross sectional comparative study, conducted at a tertiary maternal care center, Kathmandu over a period of 6 months extending from July 2010 to December 2010. Primigravida at 40-42 weeks of gestation who met the inclusion criteria were enrolled in this study and were randomly enrolled for sublingual misoprostol and vaginal misoprostol.

Results: More women in the vaginal misoprostol group had Bishop score more than six after 8 hours of insertion of first dose (80%) compared to those who received sublingual misoprostol (48%). The mean induction to delivery interval was shorter in the vaginal misoprostol group (12.12 hours) compared to (12.96) in sublingual group. Use of oxytocin for augmentation of labour was required more in the sublingual group but the difference was not significant statistically

Conclusions: Both sublingual and vaginal routes of misoprostol administration were equally effective and appeared safe for pre-induction cervical ripening at term.

Key words: sublingual misoprostol, vaginal misoprostol, vaginal delivery

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INTRODUCTION

Introduction of labour can be defined as an intervention intended to artificially initiate uterine contractions resulting in the progressive effacement and dilatation of the cervix.¹ It is a common intervention in obstetrics, both in industrialized and non-industrialized countries.^{2,3} Success of induction leading to vaginal delivery depends largely on the state of cervix; induction in an unripe cervix often results in failure. Induction is associated with increased risk of prolonged labour, febrile morbidity and caesarean delivery rate if cervix is not favorable.⁴ Numerous physical and hormonal methods have been tried in past and recently, prostaglandins have been tried.^{4,5}

Prostaglandins are the current drug of choice and have been tried for cervical ripening and labour induction in pregnant women with an unfavourable cervix.⁶ Misoprostol has been extensively and successfully used for labour induction due to its efficacy, low cost and stability at room temperature.⁷ Oral, vaginal or sublingual are possible routes, and client acceptability of misoprostol for cervical ripening and labour induction is increasing.⁸ Vaginal misoprostol has been studied extensively and has been shown to be an effective method of pre induction cervical ripening.⁹ Sublingual route of misoprostol has been less extensively studied for induction of labour, though this route is appealing for several reasons, including the convenience, lack of invasiveness and a higher patient's acceptability.¹⁰ Preliminary reports showed that misoprostol could be used sublingually for induction, and was found to be effective and well tolerated.^{11,12}

Intravaginal misoprostol is being extensively used for induction of labour in our institute and till date no study has been conducted with sublingual misoprostol. This study was done to explore whether sublingual misoprostol may be tried as a

new option for induction of labour comparing the efficacy of administration of sublingual misoprostol with vaginal misoprostol for pre-induction cervical ripening at term among Primigravida.

METHODS

This was a cross sectional comparative study, comparing efficacy and safety of sublingual and vaginal routes of administration of misoprostol conducted at tertiary level maternity hospital, Kathmandu, Nepal for a duration of 6 months from July 2010 to December 2010. During this period, 100 Primigravidas at 40-42 weeks of gestation with singleton pregnancy having Bishop score <6 and who expressed willingness to participate and gave informed written consent were enrolled for this study. While, pregnant lady with known allergy to prostaglandin, cephalo-pelvic disproportion, antepartum hemorrhage, previous uterine surgery, cardiac disease, asthma, hypertension, fetal distress, fetal anomaly, premature rupture of membrane, intrauterine growth restriction (IUGR), and any contraindication to vaginal delivery were excluded from study cohort. Pre-tested verified questionnaire was used for data collection. Collected data were entered analysis was done using SPSS version 17. Chi-square test was used for statistical association. Study was conducted after approval from local institutional ethical review committee.

The enrolled cases were randomly allocated in two groups; one received 50 mcg of sublingual misoprostol and next received 50 mcg of vaginal misoprostol. Both groups received two doses of misoprostol (each dose containing 50 mcg of misoprostol) 4 hours apart and the drug was administered sublingually or vaginally according to allocated group. Second dose of misoprostol was withheld if there was sign of uterine contraction or fetal distress, spontaneous rupture of membrane.

Table 1. Change in Bishop Score

Bishop score after 8 hrs of first dose of misoprostol	Sublingual (n = 50)	Vaginal (n=50)	p value
Unchanged	26 (52%)	10 (20%)	0.002
6-8	14 (28%)	29 (58%)	
>8	10 (20%)	11 (22%)	
Total	50 (100%)	50 (100%)	

Second dose of misoprostol was not given if Bishop score was six or more. Privacy and confidentiality were maintained properly. Per vaginal examination was done to assess Bishop score. Fetal heart sound (FHS) and uterine contraction were monitored regularly by attending staff. Women were advised to lie on left lateral position, record fetal movement count and inform staff on duty in case of P/V leaking, decreased fetal movement and frequent uterine contractions with increasing intensity.

Partograph was maintained in active phase of labour. Labour was augmented with oxytocin in the coming morning if she did not deliver by next morning. Decision regarding analgesia and oxytocin augmentation was made by on duty registrar. Patients, who developed irregular FHS, were hydrated and given oxygen inhalation. Close monitoring of the fetal heart sound was done for half an hour. If FHS became regular, patients were given second dose of misoprostol. If FHS remained irregular or there was presence of meconium stained liquor in case of SROM, further dose of misoprostol was withheld and patient was prepared for emergency caesarean section.

RESULTS

Majority of women were between the age of 20-24 years in both groups (27 in sublingual and 32 in vaginal), followed by 25-29 years (16 and 14

Table 2. Need of oxytocin for augmentation of labour

Oxytocin	Sublingual misoprostol 50mcg (n=50)	Vaginal Misoprostol 50mcg (n=50)	p value
Yes	25(50%)	17 (34%)	0.09
No	25(50%)	33 (66%)	
Total	50 (100%)	50 (100%)	

respectively). In the sublingual group, 10 had Bishop score > eight after eight hours of the drug insertion compared to 11 cases in the vaginal group. Only ten women had Bishop score unchanged after eight hours in the vaginal group compared to 26 in the sublingual group ($p = 0.002$) (Table 1).

Bishop score prior to induction was 4.14 ± 0.85 in sublingual and vaginal group, which was non-significant ($p = 0.51$). However, after eight hours of first dose of misoprostol it was significantly more in vaginal group (6.42 ± 1.33) compared to sublingual group (5.48 ± 1.18) ($p = 0.001$). Oxytocin was needed for augmentation of labour in 17 cases in vaginal group compared with the 25 cases in sublingual group. Overall, 43% of women needed oxytocin for augmentation where as rest did not (Table 2).

Among sublingual group three delivered within six hours of induction; seven in 6-12 hours, 14 within 24 hours and 26 after 24 hours of induction. Whereas ten women delivered within 6-12 hours, 16 within 24 hours and 24 after 24 hours of induction. Mean time interval between administration of first dose of misoprostol was lower in vaginal group (23.06 ± 10.93) compared to sublingual group (24.77 ± 12.81) but this finding was statistically non-significant ($p=0.47$). In most cases pregnancy terminated by spontaneous vaginal delivery while in some cases from both groups

Table 3. Mode of delivery

Mode of delivery	Sublingual group (n=50)	Vaginal group (n=50)	Total	P value
SVD	37 (74%)	42 (84%)	79	0.21
Vacuum	5 (10%)	3 (6%)	8	0.46
LSCS	8 (16%)	5 (10%)	13	0.37
Total	50 (100%)	50(100%)	100	

needed LSCS or vacuum assisted delivery. There were eight cases of caesarean delivery in the sublingual group and five cases in the vaginal group (Table 3). The indication of caesarean delivery was almost similar and included fetal distress, failed induction, and non-progress of labour.

Mean Apgar score after five minutes of delivery was more in the sublingual group (8.04 ± 0.92) in comparison to vaginal group (7.62 ± 1.17) ($p=0.05$). Nine babies (18%) in the vaginal group needed admission to special care baby unit (SCBU) compared to five babies (10%) in the sublingual group. In vaginal group, in 12 cases (24%) there was thin meconium and thick meconium in seven (14%) while only in nine cases (18%) there was thin meconium in sublingual group and neither had thick meconium ($p=0.006$). There were three neonatal deaths in the vaginal group and one in the sublingual group. In the sublingual group, nausea was significantly higher in comparison with vaginal group ($p=0.004$). Other adverse events were vomiting and fever in some cases (Table 4).

DISCUSSION

Misoprostol has been proved to highly effective for pre-labor cervical ripening in many studies but ideal dose and route of administration for efficacy as well as safety is still being explored. There is plenty of evidence supported by studies about

Table 4. Maternal side effects and fetal complications

Events	Sublingual group (n=50)	Vaginal group (n=50)	P value
SCBU Admission	5 (10%)	9 (18%)	0.240
Thin MSL	9 (18%)	12 (24%)	0.460
Thick MSL	0 (0%)	7 (14%)	0.006
Neonatal death	1 (2%)	3 (6%)	0.610
Nausea	10 (20%)	1 (2%)	0.004
Vomiting	5 (10%)	1 (2%)	0.200
Fever	1 (2%)	1 (2%)	1.000

efficacy of vaginal route, this study was done to explore comparison of vaginal with sublingual route. In this study, we enrolled only postdated pregnancy which is most common indication for induction worldwide.¹³⁻¹⁶ In our study, majority of women who were induced belonged to age group of 20 to 24 years in both groups being we included only primigravidas. Mean age of participants in a similar study reported was 27 ± 5.2 in sublingual group and 29 ± 5.3 in vaginal group.¹⁷ Effect of misoprostol on cervical ripening in terms of change in Bishop score showed that vaginal route was more effective compared to sublingual. Augmentation with oxytocin was needed in 34% of women in vaginal group ($n = 17$) compared to 66 % of women in sublingual group ($n = 25$) ($p = 0.09$). As in our study no significant difference was seen in need for oxytocin in two routes in other studies.^{16,17}

In this study, mean time interval between administration of first dose of misoprostol and delivery was shorter in vaginal group (23.06 ± 10.93) compared to sublingual group (24.77 ± 12.81) ($p = 0.47$). On the other hand, induction-delivery interval was much shorter compared to our study and shorter with mean induction- vaginal

delivery interval was 15.0 ± 3.7 in sublingual group and 16.7 ± 4.1 in vaginal group.¹⁷ Comparable findings were shown in other studies.^{16,18}

Caesarean section rate in other studies were much higher than in our study.^{18,19} Instrumental delivery rate was reported as 5.9% in sublingual and 14.1% in vaginal group by Nassar et al., 7.1% in sublingual group and 2.9% in vaginal group by Bartusevicius et al.^{16,17} There were three cases of neonatal deaths in the vaginal group (6%) and one in the sublingual group (2%). Similarly, mean Apgar score at five minutes was better in sublingual group (8.04 ± 0.92) compared to 7.62 ± 1.17 in the vaginal group ($p = 0.05$). Also, thick meconium stain liquor is lower in sublingual route in our study and previous other studies as well. These findings suggest that sublingual route is better for neonatal perspective than vaginal route but large sample size is required to see any statistical significance. In our study, maternal side effects profile was more in favour of use of vaginal misoprostol as side effects were more in sublingual group. Ten women complained of nausea in sublingual group (20%) compared to one in vaginal group (2%) [$p = 0.004$]. Similarly, five women had vomiting in sublingual group and one case in vaginal group (2%). Similar side effect profiles were reported by other studies.^{16,18} It has been speculated that direct effect of vaginal misoprostol on the cervix might contribute to excessive uterine activity, FHR abnormalities and higher rate of meconium stained liquor.²⁰ Our study showed that vaginal route was comparatively more effective in cervical ripening compared to sublingual route.

The induction of labor remains a major challenge in modern obstetrics. One systemic review on efficacy and safety of sublingual administration of misoprostol compared to vaginal route showed no

statistically significant difference with respect to the rate of vaginal delivery not achieved within 24 hours, uterine hyperstimulation syndrome or caesarean section.¹⁹ In our study, however, vaginal route appears to be significantly better than sublingual group in terms of improvement in Bishop score and mean induction to delivery interval. However, incidence of meconium stained liquor was seen more in vaginal route. There was no significant difference in need for oxytocin augmentation, caesarean delivery rate and neonatal outcome and maternal side effect and complication in two routes of administration of misoprostol. Our study was limited to two doses of misoprostol for pre-induction cervical ripening among primigravidas.

CONCLUSIONS

This study showed that vaginal route of misoprostol administration had better effect on cervical ripening as reflected by change in mean Bishop score, mean induction to delivery interval was shorter in the compared to sublingual group. However, women who received misoprostol via vaginal route had significantly higher rate of meconium stained liquor compared to sublingual group. Mean Apgar score after five minutes of delivery was better in the sublingual group than in vaginal. There was no significant difference in neonatal outcome in two groups. Intrapartum maternal side effects were observed more in the sublingual group than vaginal group but was statistically not significant. Hence both sublingual and vaginal routes of misoprostol administration were equally effective for pre-induction cervical ripening at term. Both routes appeared safe in this study with fewer maternal and neonatal adverse effects. However, more study in strict setting of randomized controlled clinical trials will be helpful to derive any firm conclusion.

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