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The efficacy of misoprostol vaginal insert compared with oral misoprostol in the induction of labor of nulliparous women: a randomized national multicenter trial

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Conflict of interest statement

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ABSTRACT

Introduction: Our objective was to compare the efficacy of a 200-µg misoprostol vaginal insert (MVI) vs oral misoprostol regarding the cesarean section rate and the time interval to vaginal delivery in nulliparous women with unfavorable cervix. **Material and methods:** In this prospective multicenter trial 283 nulliparous women at term with Bishop score < 6 were randomized to induction of labor with either an MVI (n=140) or oral misoprostol (n= 143). Oral misoprostol was administered 50 µg four-hourly up to three times during the first day and 100 µg four-hourly up to three times during the second day, if necessary. Primary outcome was the cesarean section rate. Secondary outcomes were the time from induction of labor to vaginal delivery, the rate of other induction methods needed, labor augmentation with oxytocin and/or amniotomy, use of tocolytics and adverse neonatal and maternal events. **Results:** In the MVI group, median time to vaginal delivery was shorter (24.5 vs. 44.2 hours, $p < 0.001$) whereas no difference was found in the cesarean section rate (33.8% vs. 29.6%, OR 1.21, 95% CI 0.66–1.91, p=0.67). Other induction methods and labor augmentation with oxytocin and/or amniotomy were less frequent in the MVI group (OR 0.32, 95% CI 0.18–0.59 and OR 0.56, 95% CI 0.32–0.99 respectively). Need for tocolysis and meconium-stained amniotic fluid were more common in the MVI group (OR 3.63, 95% CI 1.12–11.79 and OR 2.38, 95% CI 1.32–4.29 respectively). Maternal and neonatal adverse events did not differ between groups. **Conclusions:** MVI proved to shorten the time to vaginal delivery and it reduced the use of other methods of labor induction and augmentation but did not reduce the cesarean section rate compared with oral misoprostol. The benefit of more rapid delivery

associated with MVI should be weighed against the greater risks for uterine hyperstimulation and meconium-stained amniotic fluid.

Keywords

misoprostol, misoprostol vaginal insert, prostaglandin, labor induction, cesarean section , vaginal delivery, nulliparity

Abbreviations

MVI	misoprostol vaginal insert,
OM	oral misoprostol,
CS	cesarean section
PROM	pre-labor rupture of membranes
CTG	cardiotocography

Key message

Misoprostol vaginal insert is more efficient in induction of labor in nulliparous women with unfavorable cervix but does not reduce cesarean section rate compared with oral misoprostol. Uterine hyperstimulation and meconium in amniotic fluid are more common with misoprostol vaginal insert.

INTRODUCTION

Labor induction rates have been increasing worldwide in recent decades.[1] In Europe and the USA, over 20% of labors are induced.[1 2] In Finland, induction rates have doubled in the past two decades, being currently almost 27%[3] without a proportional increase of resources in the delivery wards. Therefore, there is a growing demand for an effective and safe induction method that would result in vaginal delivery without compromising maternal or fetal safety.

Misoprostol is a prostaglandin E1 analogue widely used for induction of labor. Oral misoprostol (OM) has been proved to result in more vaginal births within 24 hours than placebo, intravenous oxytocin and vaginal dinoprostone.[4] Compared with vaginal misoprostol, the efficacy is somewhat equal although dose-dependent.[5] Vaginal misoprostol, however, has been associated with higher rates of low Apgar scores and postpartum hemorrhage, whereas meconium-stained amniotic fluid has been found to be more common in connection with OM.[5 6]

In 2013, a new administration system, a misoprostol vaginal insert (MVI; 200 µg) was approved in Europe. Since then, a few publications showed superior efficacy of MVI in respect of the time interval to vaginal delivery compared with dinoprostone[7] and vaginal misoprostol tablets.[8 9] So far, only one study has compared MVI with OM showing superior efficacy of MVI but questioning its effects on neonatal safety.[10]

We compared the continuous slow-release MVI with the prevailing clinical practice of using OM tablets in order to determine the efficacy and safety of these different routes of misoprostol administration in nulliparous women at term with unfavorable cervix.

MATERIAL AND METHODS

This prospective randomized multicenter trial was conducted in all five tertiary university hospitals in Finland (Tampere, Helsinki, Turku, Kuopio and Oulu) between October 1st 2015 and March 21st 2018. These hospitals have annually 2300-8000 deliveries and the induction rate for nulliparous women is approximately 30%.[3] We included nulliparous women at term with singleton pregnancies, cephalic presentation, and an unfavorable cervix (Bishop score[11] < 6). The exclusion criteria were severe pre-eclampsia or hypertension (> 170/110 mmHg), intrauterine growth restriction (estimated fetal weight < 10th percentile), gestational weeks ≤ 36 +6 (weeks+days), pre-labor rupture of membranes (PROM), placenta previa, uterine scar or inadequate language skills.

All participants were informed and gave written consent before participation. Information was given by the obstetrician after deciding to induce labor or attending midwife at the ward before the beginning of induction. The randomization sequence was hand-made in a 1:1 ratio. Three hundred sealed envelopes containing the name of the study drug were made in the beginning and they were delivered in 20-envelope blocks to the study centers. Randomization

was performed by the attending midwife by opening a sealed envelope containing the name of the study drug. The study was open-label because the nature of the intervention made masking impossible.

A total of 286 patients were enrolled in this study. Three women were excluded before randomization because of spontaneous onset of labor (Figure 1). Baseline demographic data, characteristics, data on medical history, indication for labor induction, and maternal and neonatal labor outcomes were collected from the hospital records by the investigators.

Study protocol

In the MVI group, a 200-µg MVI (Misodel®, Ferring Pharmaceuticals, Saint-Prex, Switzerland) was placed into the posterior vaginal fornix. It was removed if a minimum of three contractions lasting at least 45 seconds during a ten-minute period occurred and the cervix was ripened, or if cervical dilation of four centimeters was achieved irrespective of the frequency of the contractions, or if the midwife considered that the onset of active labor was reached. The maximum retention of the MVI was 24 hours. It was not removed in cases of PROM if the criteria mentioned above were not met. Oxytocin for augmentation of labor was allowed at the earliest 30 minutes after removal of the MVI.

In the OM group a 200-µg tablet (Cytotec®, Piramal Healthcare UK Limited, Northumberland, England) was split into 50 µg or 100 µg fragments. During the first day of induction 50 µg of misoprostol was given every four hours to a maximum of 150 µg per day or the onset of active labor. From the second study day onwards, 100 µg of misoprostol was given every four hours to a maximum of 300 µg or until the onset of active labor. The criteria on contractions and cervical dilation described above were used to determine whether misoprostol administration should be continued.

If the onset of labor was not reached in 24 hours in the MVI group or in 48 hours in the OM group, induction was continued by other methods (i.e. vaginal 50-µg misoprostol tablets, balloon catheter, amniotomy or intravenous oxytocin). In both groups cardiotocography (CTG) was carried out for a minimum of 20 minutes at a time prior to and within one hour following the administration of the study medication, and in case of regular contractions or rupture of membranes. Interpretation of CTG was determined according to NICE guidelines[12] by the investigators in participating institutes.

Tocolysis was used in cases of tachysystole (> five contractions in ten minutes) with or without fetal heart-rate abnormalities. Intravenous terbutaline infusion (0.5 mg/100 ml 0.9% NaCl) or a sublingual nitroglycerin spray were used as tocolytic agents.

Intrapartum infection was diagnosed if at least two of the following criteria were met: maternal fever > 38 ºC, maternal or fetal tachycardia, uterine tenderness or foul odor of amniotic fluid. The antibiotics used were cefuroxime with or without metronidazole. Puerperal infections were defined as endometritis, urinary infection, infection of episiotomy or perineal tear, cesarean section (CS) wound infection, septicemia, and puerperal fever of unknown cause.

All women were screened for group B *Streptococcus agalactiae* (GBS) before delivery. In cases of positive GBS, intravenous benzylpenicillin (or clindamycin in cases of allergy) was routinely used within four hours from the onset of labor or immediately after rupture of membranes.

Digital examinations during labor were performed when considered necessary. Onset of the first stage of labor was defined as the start of regular painful contractions less than 10 minutes apart. The second stage of labor was defined as the time interval from the start of pushing to delivery.

Oxytocin (Syntocinon, Novartis, Copenhagen, Denmark) was administered for augmentation of labor with an initial dose of 5 IU diluted in 500 ml of isotonic saline at 15 ml/h. The dose was increased until regular contractions (3–5/10 minutes) were achieved or the maximum dose of 90 ml/h was reached.

Statistical analyses

The primary outcome was the CS rate. The primary indications for CS were categorized as fetal distress (based on CTG, fetal scalp blood pH or lactate), labor dystocia (failure to progress in labor despite ruptured membranes and adequate uterine contractions, or failed attempt to induce labor), and other reasons (pre-eclampsia, fetal malpresentation, suspected ablation, intrapartum infection and an acute fear of childbirth).

Power analysis was based on the difference in CS rates. It was estimated that the average CS rate in connection with induced labor in nulliparas would be 25%.[5] A sample of 300 women was needed to demonstrate a reduction to 12%, which is close to our institutional CS rate. Recruitment of the patients was slower than expected and the decision of terminating the study was made after approximately 2.5 years after the randomization of the first patient.

To describe the data, medians and interquartile ranges were calculated for skew-distributed continuous variables, while means and standard deviations were calculated for normally distributed variables. Frequencies and percentages were used for categorical variables. The groups were compared using Mann–Whitney U tests for skew-distributed continuous variables, independent samples t-tests for normally distributed continuous variables and Pearson chi-square tests for categorical variables, as appropriate. Values of $p < 0.05$ were considered statistically significant.

We used multinomial logistic regression analysis to calculate odds ratios with 95% confidence intervals (CIs) in the MVI group using the OM group as reference. Bishop score and upcoming post-term pregnancy as the indication for induction were considered as potential confounding factors since these differed significantly between the study groups. Owing to the skewed distribution of Bishop score, it was categorized for analysis. Therefore, outcome variables were adjusted by the categorized Bishop score (0-3 and 4-5) and dichotomous upcoming post-term pregnancy as the indication for induction. Missing values were not included in the analysis. Kaplan–Meier survival analysis was used to determine the time to delivery in the study groups. The analyses were carried out by using IBM SPSS Statistics, Version 25 software (IBM Corp., Armonk, NY).

Ethical approval

The study protocol was approved by the Ethics Committee of Tampere University Hospital (R15109M) on 16th of June in 2015 and by the institutional review boards in study centers. The study is registered at Clinicaltrials.gov (ID NCT02539199) and at European Clinical Trials Database (ID 2015-001972-23).

RESULTS

All randomized women received the study medication as was allocated. Fifteen women were excluded from the analysis because of failure to meet the inclusion criteria or spontaneous onset of labor before receiving the study drug. A total of 268 women, of which 135 women were allocated to the OM group and 133 women to the MVI group, were included in the analysis (Figure 1).

Baseline characteristics are presented in Table 1. There were no differences between the study groups regarding chronic diagnoses which included hypothyreosis, asthma, psychiatric disorders (such as depression), hypertension, diabetes, migraine, thrombophilia, rheumatoid arthritis, Basedow's disease, inflammatory bowel disease and history of cancer. In the OM group, more women were induced because of postdate or upcoming post-term pregnancy compared with those in the MVI group. There were more women with Bishop score 0-3 in the MVI group. The mean OM dose was 257 μg (± 144 μg) during the study. The median time to MVI removal was 8 hours 55 minutes (interquartile range 6.5–14.5 hours).

The median time to vaginal delivery was shorter in the MVI group (24.5 hours, interquartile range 23) than in the OM group (44.2 hours, interquartile range 29) ($p < 0.001$). According to Kaplan–Meier analysis, 32.3% of women in the MVI group had delivered within 24 hours, compared with 12.6% in the OM group ($p < 0.001$) (Figure 2 and Table 2). We found no differences in the durations of the first or the second stages of labor between the groups. Despite the shorter time interval to delivery in the MVI group, there were no differences in frequencies of PROM, non-reassuring pre-labor CTG or pre-labor opioid use between the study groups. Another induction method following that in the study protocol and general augmentation of labor were less frequently needed for women in the MVI group (Table 2).

The CS rates were similar in the two study groups, 33.8% for women in the MVI group and 29.6% in the OM group (Table 2). All CSs were emergency sections but none of them was done due to immediate threat to life of fetus or mother.

Meconium-stained amniotic fluid was more common in women in the MVI group (33.8% vs 18.5 %, adjusted odds ratio (OR) 2.38, 95% CI 1.32 to 4.29, p = 0.004). Furthermore, tocolysis because of tachysystole was more frequently used in the MVI group (9.8% vs 3.0%, adjusted OR 3.63, 95% CI 1.12 to 11.79, p = 0.03). However, we found no differences in neonatal or maternal adverse outcomes (Table 3).

DISCUSSION

In our randomized study, labor induction with MVI was more efficient compared with OM regarding the time interval from induction to vaginal delivery, which was almost 20 hours shorter in the MVI group. Furthermore, women in the MVI group needed less frequently labor augmentation and other induction methods. Nevertheless, we did not find a difference in the CS rates between the study groups.

In previous studies MVI has been shown to shorten the time interval to vaginal delivery by 6–14 hours when compared with vaginal dinoprostone,[7] vaginal misoprostol[8 9] and OM.[10] In our study the time interval difference was even larger. We found the time to vaginal delivery in the MVI group to be comparable to that in previous studies[7 9 10] whereas in the OM group it was somewhat longer compared with studies on OM.[10 13 14] The difference in the OM group is probably a result of different dosing regimen of OM and our study population consisting only nulliparous women. We found no differences concerning the duration of vaginal delivery. Thus, it was the time interval from the beginning of induction to the onset of delivery that was shorter in the MVI group.

Oxytocin for augmentation of delivery has been found to be used significantly less[7] or equally[15] in connection with MVI compared with dinoprostone and less compared with vaginal misoprostol tablets.[9] In our study, oxytocin use was similar in both groups, but augmentation in general was more common in the OM group, which may reflect the efficacy of MVI to maintain contractions after the onset of labor. Furthermore, other induction methods were less needed in the MVI group. On the basis of our results, ripening of the cervix is faster and the onset of delivery is more probable with slow-release continuous vaginal dosing than with OM. There are differences in pharmacokinetics of misoprostol depending on the administration route. OM results in a rapid high-level peak of plasma concentrations of the drug, followed by a decline in concentration for 120 minutes, whereas with a vaginal insert, misoprostol is released at a constant slow rate and maximum plasma

concentration is reached gradually at 5–9 hours.[16 17] However, when misoprostol is administered directly to the genital tract, it might have direct local effects that modify uterine contractility[18] which could explain the superior efficacy of vaginal route.

Uterine hyperstimulation is a drawback of too efficient induction method. The incidence of uterine hyperstimulation has been found to be more common with MVI compared with dinoprostone,[7] vaginal misoprostol tablets[8] and OM.[10] Supporting these findings, we found the use of tocolysis to be more common in the MVI group. We also found the appearance of meconium in amniotic fluid to be more common in the MVI group. This probably reflects the higher incidence of hyperstimulation although misoprostol may have direct effects on fetal bowel as well. Previously higher rate of meconium-stained amniotic fluid has been associated with oral instead of vaginal administration, though[5]. Uterine hyperstimulation carries a risk for fetal distress. However, we found no difference in the incidences of pathological CTG patterns nor adverse neonatal outcomes but our study was not powered to investigate neonatal safety. Previously, no differences in neonatal outcomes have been found between MVI and dinoprostone[7 15] and vaginal misoprostol tablets[8 9] whereas one study questioned the safety of MVI in comparison with OM.[10] More studies are needed to address the safety aspects of MVI compared with OM. Nevertheless, a greater need for tocolysis may indicate uterine hyperstimulation, and this should be taken into account when managing delivery after induction with MVI.

Despite the difference in efficacy, we found no difference in CS rates between the two groups. After induction with MVI or OM, the CS rate in nulliparas has varied from 26% to 34% which is similar to our finding.[5 7] Previously, the use of MVI has been shown to result in similar CS rate to that associated with dinoprostone,[7 15] vaginal misoprostol[8] and a higher rate compared with OM.[10]

To our knowledge, this is the first study in which MVI has been compared with OM in a randomized setting. Induction of nulliparas, especially with unfavorable cervix, carries a high risk for cesarean delivery.[19] Since the first CS has a major impact on future pregnancies,[20] we found it crucial to evaluate the efficacy of newly introduced MVI especially in nulliparous women. OM was chosen as reference since it is most often used for women with unfavorable cervix. Furthermore, our study was conducted in tertiary obstetric centers with substantial number of deliveries annually. Obstetric practices are similar across the nation, diminishing differences in labor management as a confounding factor.

Since the study was done without extra personnel, it burdened busy obstetric ward resulting in difficulties recruiting patients. This could be a limitation and our study may be unpowered to rule out difference in the rate of CSs. Furthermore, while MVI dosing was continuous, OM was not administered during the night. This may have extended the time interval to delivery in the OM group. However, we wanted to compare the MVI protocol with our existing OM protocol and did not change the latter for the present study.

The greater time interval difference to vaginal delivery in our study compared to previous studies might reflect the inefficacy of our OM protocol but also the greater benefit of MVI in terms of efficacy in nulliparous compared with parous women. The majority of the studies on MVI to date have included also parous women. Shortened time interval from induction to labor could have some advantages, nevertheless, we did not find difference in frequencies of pre-labor opioid use, PROM or intrapartum infections between the study groups. Shorter induction time might decrease the costs of hospital stay, though[21]. An option to enhance the efficacy of misoprostol and to avoid CS could be to use balloon catheter first since there is evidence for lower CS rate in nulliparas after MVI with pre-induction balloon catheter[9]. Our study provided information about differences in MVI and OM for clinical practice. There are also other options available for labor induction, such as balloon catheter which has proved to be as efficient and safe as OM.[22] Given the rareness of adverse neonatal events, more studies are needed to address the potential differences in safety aspects of MVI compared with oral misoprostol.

CONCLUSION

Although labor induction with MVI in nulliparous women with an unfavorable cervix led to vaginal delivery faster than with OM, no benefit was seen in the CS rate. Larger studies are needed to address the impact of MVI on neonatal safety.

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Legends of figures and tables

Figure 1. The CONSORT 2010 flow diagram of study design

Figure 2. Survival plot for time to any delivery (A) and time to vaginal delivery (B) in women treated with either misoprostol vaginal insert (MVI) or oral misoprostol (OM) based on Kaplan-Meier analysis.

Table 1. Demographic data and baseline characteristics

Table 2. Efficacy outcomes

Table 3. Adverse events

Table 1. Demographic data and baseline characteristics

	MVI (n=133)	OM (n=135)	p
Age (years)	30.7 (± 5.6)	30.0 (± 6.0)	0.35
BMI	25.4 (6.9)	25 (6.2)	0.48
Chronic diagnosis	32 (24.1 %)	34 (25.2 %)	0.83
Duration of gestation (weeks)	40.4 (3)	41.6 (2)	0.07
Bishop score	3 (2)	3 (2)	0.004
Bishop score 0-3	91 (68.4 %)	68 (50.4 %)	0.003
Birthweight (grams)	3624 (± 407)	3706 (± 462)	0.13
Indication for induction			
Post-date/upcoming post-term	46 (34.6 %)	68 (50.4 %)	0.009
Pre-eclampsia/Gestational hypertension	25 (18.8 %)	25 (18.5 %)	0.95
Fetal macrosomia	22 (16.5 %)	15 (11.1 %)	0.20
Gestational diabetes	14 (10.6 %)	11 (8.1 %)	0.50
Oligohydramnion	10 (7.5 %)	4 (3.0 %)	0.09
Maternal exhaustion/fear of childbirth	9 (6.8 %)	6 (4.4 %)	0.41
Cholestasis of pregnancy	5 (3.8 %)	2 (1.5 %)	0.24
Other[a]	3 (2.3 %)	5 (3.7 %)	0.49

[a]decreased fetal movements, maternal age, maternal hydronefrosis

Data presented as means (± standard deviation), medians (interquartile range) or number of cases (%).

MVI=misoprostol vaginal insert, OM=oral misoprostol, BMI=body mass index (kg/m ^{2})

Table 2. Efficacy outcomes

	MVI (n=133)	OM (n=135)	Crude OR	95 % CI	p	Adjusted OR[a]	95% CI	p
Time (h) to vaginal delivery[b]	24.5 (23)	44.2 (29)						<0.001
Time (h) to any delivery	26.7 (27)	47.3 (34)						<0.001
Duration of delivery (h)[b]	10.4 (9)	11.2 (8)						0.48
Vaginal delivery within 24 hours	43 (32.3 %)	17 (12.6 %)	3.30	1.76-6.16	<0.001	4.46	2.27-8.74	<0.001
Vaginal delivery within 48 hours	74 (55.6 %)	53 (39.2 %)	1.93	1.18-3.14	0.009	2.47	1.45-4.19	0.001
Any delivery within 24 hours	59 (44.4 %)	19 (14.1 %)	4.70	2.59-8.54	<0.001	5.81	3.07-11.00	<0.001
Any delivery within 48 hours	106 (79.7 %)	65 (48.2 %)	4.11	2.36-7.17	<0.001	6.29	3.33-11.87	<0.001
Need for another induction method	33 (24.8 %)	54 (40.0 %)	0.50	0.29-0.84	0.008	0.32	0.18-0.59	<0.001
Labour augmentation with oxytocin	74 (55.6 %)	92 (68.1 %)	0.59	0.35-0.99	0.04	0.61	0.36-1.04	0.07
Labour augmentation (oxytocin and/or amniotomy)	82 (61.7 %)	102 (75.6 %)	0.52	0.30-0.90	0.02	0.56	0.32-0.99	0.046
Caesarean section	45 (33.8 %)	40 (29.6 %)	1.21	0.73-2.03	0.46	1.21	0.66-1.91	0.67
Vacuum extraction vaginal delivery	27 (20.3 %)	18 (13.3 %)	1.66	0.86-3.12	0.13	1.72	0.88-3.37	0.12
Spontaneus vaginal delivery	61 (45.9 %)	77 (57.0 %)	0.64	0.39-1.03	0.07	0.67	0.41-1.10	0.12

[a]Adjusted for Bishop-score and upcoming post-term pregnancy as the indication for induction.

[b]Only vaginal deliveries

Data presented as number of cases (%) or medians (interquartile range).

MVI=misoprostol vaginal insert, OM=oral misoprostol, OR=odds ratio, CI=confidence interval, BMI=body mass index (kg/m ^{2})

Table 3. Adverse events

	MVI (n=133)	OM (n=135)	Crude OR	95 % CI	p	Adjusted OR[a]	95% CI	p
Operative delivery due to labor dystocia	38 (28.6%)	34 (25.2%)	1.19	0.69-2.04	0.53	1.12	0.64-1.96	0.69
Operative delivery due to imminent asphyxia	32 (24.1 %)	20 (14.8 %)	1.82	0.98-3.38	0.06	1.85	0.98-3.52	0.06
Pathological CTG changes	70 (52.6 %)	63 (46.7 %)	1.32	0.81-2.14	0.27	1.37	0.83-2.26	0.22
Meconium in amniotic fluid	45 (33.8 %)	25 (18.5 %)	2.29	1.30-4.03	0.004	2.38	1.32-4.29	0.004
Tocolysis for tachysystole	13 (9.8 %)	4 (3.0 %)	3.53	1.12-11.13	0.03	3.63	1.12-11.79	0.03
Fetal scalp blood sampling	27 (20.3 %)	21 (15.6 %)	1.38	0.74-2.60	0.31	1.40	0.73-2.69	0.31
Neonatal pH < 7.05	4 (3.1 %)	2 (1.5 %)	2.05	0.37-11.38	0.41	2.69	0.47-15.54	0.27
One-min Apgar score < 7	15 (11.3 %)	11 (8.1 %)	1.42	0.63-3.23	0.40	1.22	0.53-2.84	0.64
Five-min Apgar score < 7	6 (4.5 %)	4 (3.0 %)	1.50	0.41-5.45	0.54	1.39	0.37-5.24	0.63
Neonatal ICU admission	4 (3.0 %)	4 (3.0 %)	0.99	0.24-4.05	0.99	0.85	0.20-3.64	0.83
Intrapartum infection	24 (18.0 %)	30 (22.2 %)	0.78	0.43-1.42	0.41	0.68	0.36-1.27	0.22
Episiotomy	47 (35.3 %)	41 (30.4 %)	1.48	0.83-2.66	0.19	1.51	0.83-2.76	0.18
III or IV degree tear	3 (2.3 %)	7 (5.2 %)	0.44	0.11-1.75	0.24	0.46	0.11-1.89	0.28
Postpartum hemorrhage > 1000 ml	22 (16.5 %)	20 (14.8 %)	1.12	0.58-2.17	0.74	1.10	0.56-2.18	0.78
Epidural analgesia	102 (76.7 %)	114 (84.4 %)	0.47	0.23-0.96	0.04	0.55	0.26-1.16	0.12

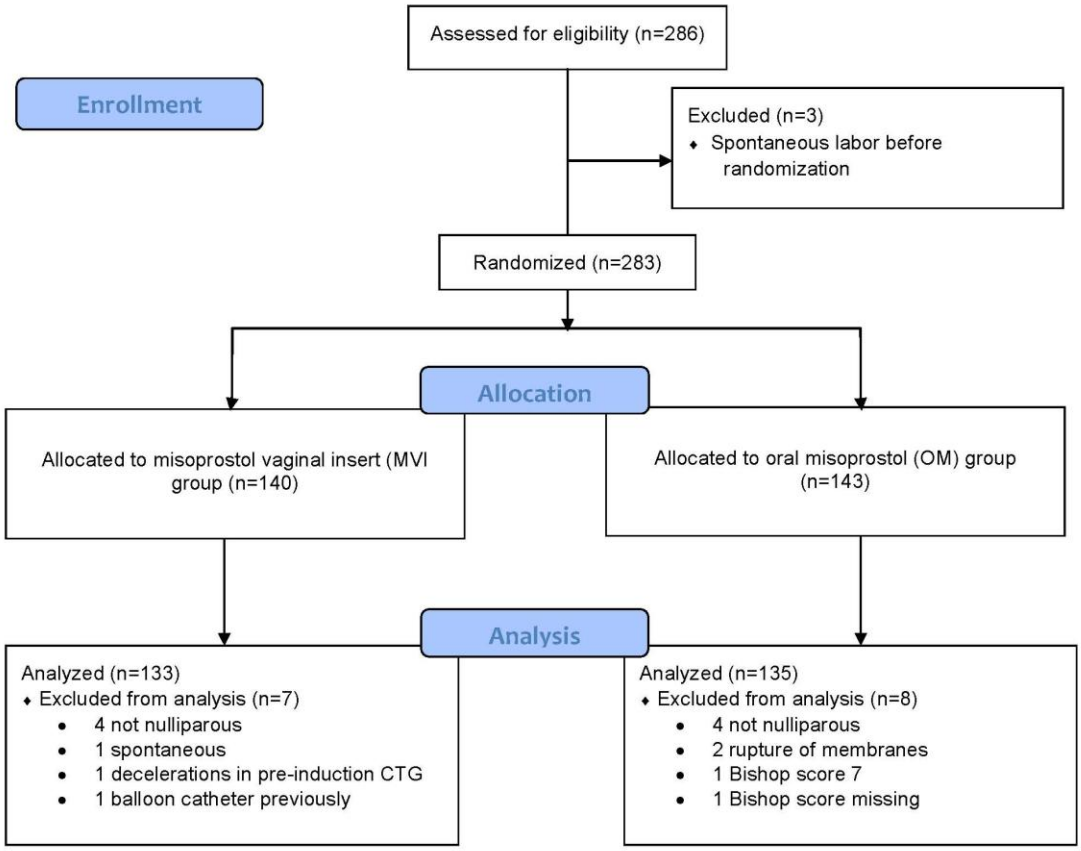
[a]Adjusted for Bishop-score and upcoming post-term pregnancy as the indication for induction.

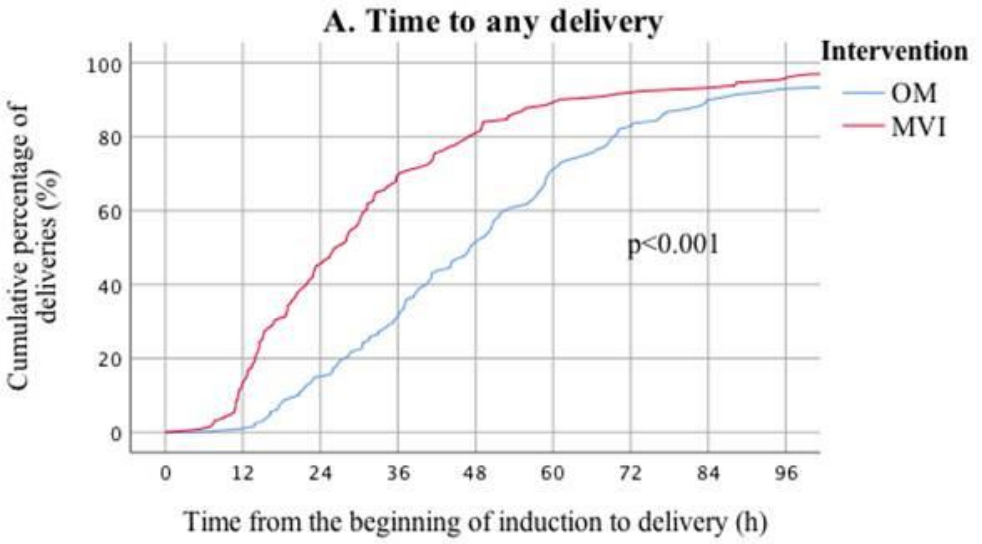
Data presented as number of cases (%).

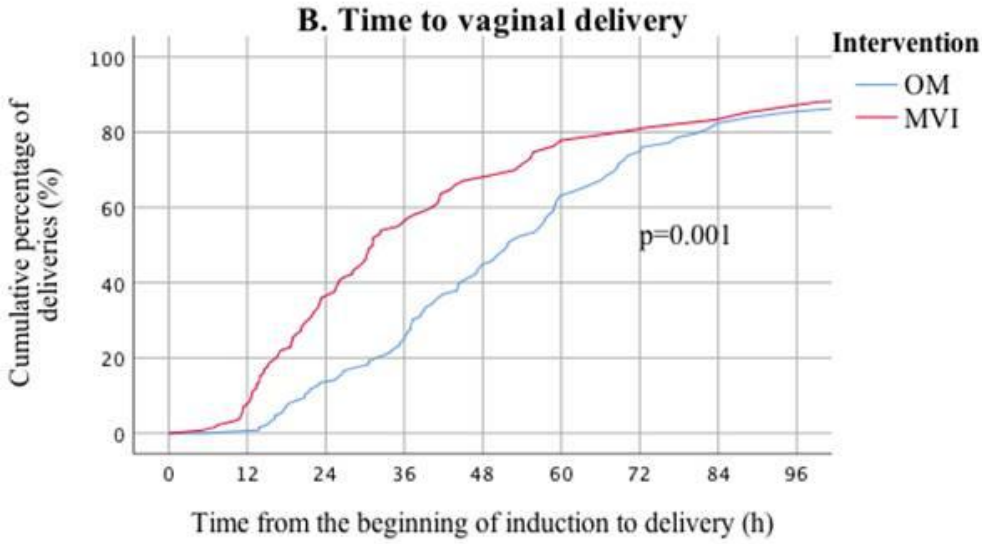
MVI=misoprostol vaginal insert, OM=oral misoprostol, OR=odds ratio, CI=confidence interval, CTG=cardiotocograph, ICU=intensive-care unit, BMI=body mass index (kg/m ^{2})

CONSORT
TRANSPARENT REPORTING of TRIALS

Figure 1. CONSORT 2010 flow diagram of study design.







OM = oral misoprostol
MVI = misoprostol vaginal insert