

OBSTETRICS

Vaginal assessment and expedited amniotomy in oral misoprostol labor induction in nulliparas: a randomized trial



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BACKGROUND: Labor is induced in 20–30% of maternities, with an increasing trend of use. Labor induction with oral misoprostol is associated with reduced risk of cesarean deliveries and has a safety and effectiveness profile comparable to those of mechanical methods such as Foley catheter use. Labor induction in nulliparous women continues to be challenging, with the process often quite protracted. The eventual cesarean delivery rate is high, particularly when the cervix is unfavorable and ripening is required. Vaginal examination can cause discomfort and emotional distress particularly to nulliparous women, and plausibly can affect patient satisfaction with the induction and birth process.

OBJECTIVE: The aim of this study was to evaluate regular (4-hourly prior to each oral misoprostol dose with amniotomy when feasible) compared with restricted (only if indicated) vaginal assessments during labor induction with oral misoprostol in term nulliparous women.

MATERIALS AND METHODS: We performed a randomized trial between November 2016 and September 2017 in a university hospital in Malaysia. Our oral misoprostol labor induction regimen comprised 50 µg of misoprostol administered 4 hourly for up to 3 doses in the first 24 hours. Participants assigned to regular assessment had vaginal examinations before each 4-hourly misoprostol dose with a view to amniotomy as soon as it was feasible. Participants in the restricted arm had vaginal examinations only if indicated. Primary outcomes were patient satisfaction with the birth process (using an 11-point visual

numerical rating scale), induction to vaginal delivery interval, and vaginal delivery rate at 24 hours.

RESULTS: Data from 204 participants (101 regular, 103 restricted) were analyzed. The patient satisfaction score with the birth process was as follows (median [interquartile range]): 7 [6–9] vs 8 [6–10], $P = .15$. The interval of induction to vaginal delivery (mean \pm standard deviation) was 24.3 ± 12.8 vs 31.1 ± 15.0 hours ($P = .013$). The vaginal delivery rate at 24 hours was 27.7% vs 20.4%; (relative risk [RR], 1.4; 95% confidence interval [CI], 0.8–2.3; $P = .14$) for the regular vs restricted arms, respectively. The cesarean delivery rate was 50% vs 43% (RR, 1.1; 95% CI, 0.9–1.5; $P = .36$). When assessed after delivery, participants' fidelity to their assigned vaginal examination schedule in a future labor induction was 45% vs 88% (RR, 0.5; 95% CI, 0.4–0.7; $P < .001$), and they would recommend their assigned schedule to a friend (47% vs 87%; RR, 0.6; 95% CI, 0.5–0.7; $P < .001$) in the regular compared with the restricted arms, respectively.

CONCLUSION: Despite a shorter induction to vaginal delivery interval with regular vaginal examination and a similar vaginal delivery rate at 24 hours and birth process satisfaction score, women expressed a higher preference for the restricted examination schedule and were more likely to recommend such a schedule to a friend.

Key words: cesarean delivery, early amniotomy, induction to delivery interval, labor induction, nulliparas, oral misoprostol, patient satisfaction, vaginal examination

Induction of labor (IOL) is a common obstetric intervention;¹ in the United States, the national rate in 2014 was 23.2%.² The World Health Organization (WHO) strongly recommends oral misoprostol for induction of labor.¹ The PROBAAT II trial, which premised safety as a primary outcome, finds that IOL with oral misoprostol in women with unfavorable cervixes at term has a safety profile similar to that using a Foley catheter.³

Regular vaginal examination is unavoidable with a bolus-dose vaginal prostaglandin labor induction regimen, but can be optional with an oral regimen. Regular vaginal examinations in labor care are thought to permit earlier detection to ripen cervix, expedite amniotomy, and titrate oxytocin infusion, resulting in more rapid vaginal delivery.^{4,5}

Vaginal examinations can cause discomfort and emotional distress, particularly to nulliparous women; the WHO recommends that vaginal examinations during first-stage labor care be limited to every 4 hours unless there are signs of decreasing uterine contractility or the urge to push, or before administration of analgesia.⁴ Interestingly, a meta-analysis of randomized trials of sustained-release prostaglandin vaginal

inserts, in which such inserts are typically left in situ for 12 hours (minimizing vaginal examinations) show that the induction-to-delivery interval and mode of delivery are similar when compared to bolus-dose vaginal prostaglandin arms with regular vaginal examinations.⁶

Elective induction of nulliparas at term with an unripe cervix who used prostaglandins has been reported to result in vaginal delivery rates of 56.8–58% in nulliparas compared with a 97% vaginal delivery rate for elective labor induction in multiparas.⁷ In our center, in multiparas who had their labor induced by amniotomy followed by immediate titrated oxytocin infusion, the mean time from amniotomy to vaginal delivery is only 5.3 ± 3.1 hours, with 91 of 96 infants (94.8%) delivered vaginally within 12

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AJOG at a Glance

Why was this study conducted?

The study compared the effect of a regular (4-hourly prior to each oral misoprostol dose with amniotomy when feasible) to that of a restricted (only if indicated) vaginal examination regimen in nulliparas labor induction on the interval to vaginal delivery and women's satisfaction with their births.

Key findings

A regular vaginal examination regimen shortens the interval to vaginal birth by a significant 7 hours but the point estimate of women's satisfaction score (7 vs 8, $P = .15$) favors the restricted regimen (nonsignificant). Women assigned to the restricted vaginal examination arm expressed significantly higher fidelity to, and were more likely to recommend their allocated regimen to, a friend by large margins of 87–88% to 45–47%.

What does this add to what is known?

This original study shows that regular vaginal examination during oral misoprostol labor induction can be acceptably avoided, and that women's views should be sought and respected regarding their preferred regimen.

hours of amniotomy; this suggests that in appropriately selected cases, such a regimen is rapid and effective,⁸ whereas in nulliparas who required bolus-regimen vaginal dinoprostone labor induction, only 8.7% had vaginal delivery at 12 hours and 35.9% at 24 hours.⁹ These findings indicate a wide disparity in induction outcomes between nulliparas and multiparas, highlighting the prolonged induction process and frequent failure to achieve vaginal delivery in the induction of nulliparas.

The use of IOL with an oral misoprostol bolus regimen provides a unique opportunity for vaginal examinations to be minimized plausibly without affecting the efficiency of the labor induction regimen while improving patient satisfaction. We therefore sought to evaluate whether regular vaginal examinations (with amniotomy as soon as it is deemed clinically feasible, followed by expeditious titrated oxytocin infusion) compared to a regimen in which vaginal examinations are restricted, expedite the induction process and influence patient satisfaction in nulliparas undergoing IOL with oral misoprostol.

Materials and Methods**Trial design**

This is a randomized, controlled, clinical interventions trial with an open-label design comparing vaginal examinations

prior to each 4-hourly oral dose of misoprostol with a view to expedited amniotomy to a restricted regimen whereby vaginal examinations are performed only clinically indicated. The trial was approved by the Medical Ethics Committee of University Malaya Medical Center (date of approval: September 20, 2016; reference number: 2016728-4061) and registered in the International Standard Randomised Controlled Trials Number registry (<http://www.isrctn.com/ISRCTN68476694>) prior to enrollment of trial participants. The study was conducted in University Malaya Medical Center, with the first participant recruited on November 28, 2016, and the last participant discharged following delivery on September 25, 2017.

Participants

Upon admission for their planned labor induction (any indication), nulliparous women (no prior pregnancy beyond 20 weeks) with a singleton fetus, ≥ 37 weeks gestation, cephalic presentation and reassuring fetal heart rate tracing, were identified for participation. Women having regular contractions (≥ 2 in 10 minutes), ruptured membranes, previous uterine surgery (eg, myomectomy or hysterotomy), known prostaglandin allergy, or contraindication to vaginal delivery were excluded. Eligible women were approached, provided with the patient

information sheet, and verbally counseled with regard to trial participation by a co-author (S.T.W.). Written informed consent was obtained from all participants.

All participants' relevant demographic and clinical data were transcribed onto the Case Report Form. Pre-induction assessment included transvaginal ultrasound for cervical length¹⁰ (3 measurements taken, shortest considered as representative length), fetal heart tracing, and maternal blood pressure, pulse, and temperature.

Randomization

Participants were randomized to either regular (4-hourly) vaginal examination or restricted (as indicated) vaginal examination by the opening of the lowest-numbered, sealed and opaque envelope available. Envelopes were prepared based on a computer-generated (using random.org) random sequence in blocks of 4 or 8 by an investigator (P.C.T.) who was not involved in the trial recruitment. The recruitment ratio was 1 to 1.

Interventions

Women assigned to the regular vaginal examination arm had a vaginal examination prior to the first dose of oral misoprostol. Amniotomy can be performed at the initial vaginal examination if the cervix is found to be favorable (cervical dilatation of at least 2–3 cm and station of not higher than 2 cm above the ischial spine), in which case oral misoprostol will not be given. Women in the restricted arm had their first oral misoprostol dose without a vaginal examination.

In our center, the standard oral misoprostol labor induction regimen comprises 50 μg of oral misoprostol to be given every 4 hours to a maximum of 3 doses in the first 24 hours.³ Routine labor induction typically commenced at 8 AM. Fetal heart tracing¹¹ monitoring was performed for half an hour before each dose and for up to 1 hour after. A misoprostol dose was withheld if the woman was distressed with regular uterine contractions (≥ 3 in 10 minutes), fetal heart tracing demonstrated uterine tachysystole (>5 contraction in 10 minutes even if painless) or hypertonus (a contraction lasting ≥ 2 minutes), fetal

heart rate pattern was non-reassuring, or a membrane rupture occurred.

In the regular vaginal examination arm, vaginal examinations were performed to assess the cervix for suitability to perform amniotomy prior to each scheduled 4-hourly dose of oral misoprostol. After an amniotomy, no further prostaglandin was used for induction, and titrated oxytocin infusion may be started as deemed appropriate by the care provider. In the restricted vaginal examination arm, vaginal examination was avoided and oral misoprostol administered 4-hourly if there was no clinical indication to withhold the dose.

Unscheduled vaginal examination was performed in either trial arm if a clinical indication arose (eg, membrane rupture, excessive bleeding, suspected uterine overstimulation, maternal and/or fetal concerns, suspected second stage of labor, or suspected established labor with request for strong analgesia).

At 12 hours after the start of the oral misoprostol induction regimen (the primary study period), a vaginal examination was performed if the patient had not already delivered or was previously found to be in established labor, to allow forward care planning in both trial arms.

Also at the 12-hour mark, all participants were asked about their satisfaction with their induction regimen, using an 11-point visual numerical rating scale (VNRS; scored from 0 to 10, with higher scores indicating greater satisfaction), and a Likert scale questionnaire response on their preference for vaginal examination schedule in a future similar labor induction and recommendation of their vaginal examination schedule to a friend ([Supplemental Material](#)).

After this 12-hour primary study period had lapsed, and if delivery still had not occurred, standard labor induction and delivery care were provided to all participants. In cases in which the cervix remained unfavorable and maternal–fetal conditions were both reassuring, expectant management applied and active induction commencement was planned for the next day.

After delivery, patient satisfaction with the birth process and the labor induction were separately scored using an 11-point

VNRS (scored 0 to 10, with a higher score indicating greater satisfaction, and a Likert scale questionnaire on their preference for vaginal examination schedule in a future labor induction and recommendation of vaginal examination schedule to a friend, which was identical to the questionnaire filled out at 12 hours, was used.

Outcomes measures

Primary outcomes were patient satisfaction with birth process using an 11-point VNRS (scored from 0 to 10, with higher score indicating greater satisfaction) taken as soon as possible after delivery, induction to vaginal delivery interval and vaginal delivery rate at 24 hours.

Secondary outcomes include patient satisfaction with conduct of labor induction using an 11-point VNRS (scored from 0 to 10, with a higher score indicating greater satisfaction) at the 12-hour study period, and Likert scale questionnaire response on their preference for vaginal examination schedule in a future labor induction and recommendation of vaginal examination schedule to a friend, total number of oral misoprostol doses and vaginal examination in the 12-hour study period, other prostaglandins given during labor induction, oxytocin infusion in labor, intrapartum epidural analgesia, mode of delivery, delivery blood loss, induction to maternal hospital discharge interval and neonatal outcomes such as Apgar score at 5 minutes, umbilical arterial cord blood pH, and neonatal admission.

Sample size

Sample size calculations were based on a study¹² that showed a 64% 24-hour vaginal delivery rate in nulliparas with oral misoprostol labor induction, then assuming a one-third reduction (to 42.7%) in the 24-hour vaginal delivery rate with a policy of restricted vaginal examinations. Applying the χ^2 test, setting α at 0.05 and power at 80%, 85 participants were needed in each arm. Taking into consideration a 15% dropout rate, a total of 100 women would need to be recruited in each arm. To detect a 6-hour difference in induction

to vaginal delivery interval with a standard deviation of 14 hours,⁹ applying the Student *t* test with α set at 0.05 and power at 80%, 86 participants were needed in each arm. To detect a 1-point difference in the satisfaction VNRS score (11-point), assuming that the VNRS score has a standard distribution of 2, applying the Student *t* test with α set at 0.05 and power at 80%, 64 participants were needed in each arm. Thus, we planned to recruit 100 women in each arm for an adequately powered study covering our prespecified primary outcomes.

Data were entered into a statistical software package SPSS (Version 23, IBM SPSS Statistics; IBM Corp., Armonk, NY). The *t* test was used to analyze means and distributions, the Mann–Whitney *U* test for nonnormal data or ordinal data, and χ^2 test for categorical. Two-sided *P* values were reported, and a *P* value of $<.05$ was regarded as significant. Analysis was on intention-to-treat basis.

Results

Recruitment

[Figure 1](#) depicts the recruitment flow of participants into and through the study. Of the 209 eligible women approached, 205 agreed to participate, with 101 and 104 women randomized to regular and restricted arms, respectively. We stopped recruitment on exceeding target sample size. One woman assigned to the restricted vaginal examination arm who had an emergent cesarean delivery due to her pre-induction fetal heart rate tracing turning non-reassuring (prior to commencing her oral misoprostol labor induction) was excluded from the analysis. All participants received their first oral dose of misoprostol.

Participants

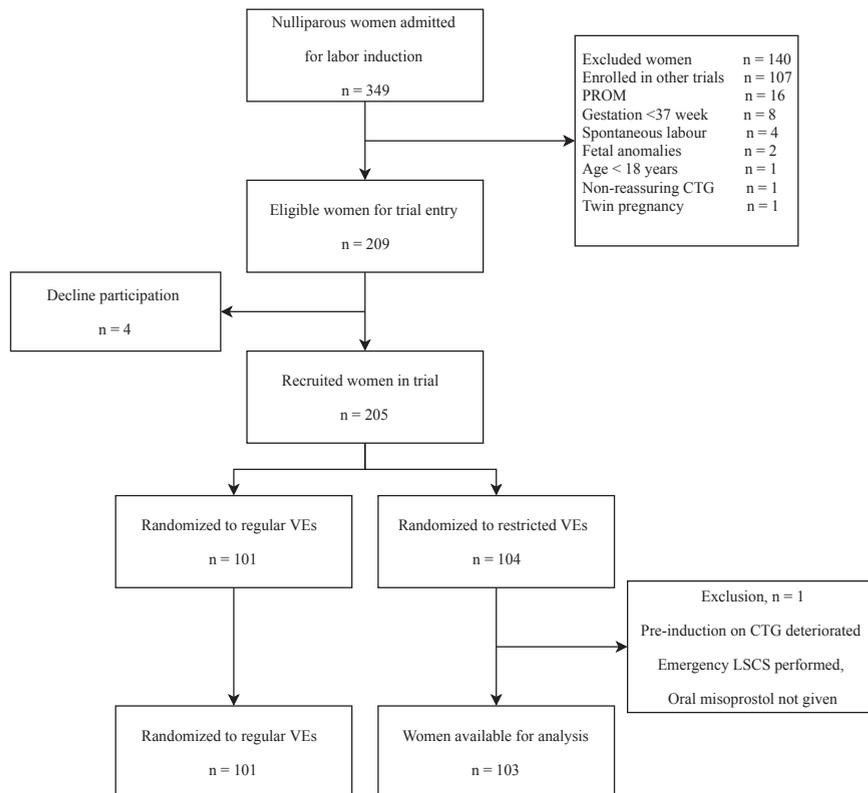
[Table 1](#) shows the characteristics of the trial participants dichotomized according to assignment to the intervention arms. The shortest cervical length in our trial population was 15 mm.

Outcomes

[Table 2](#) reports the primary outcomes for 101 and 103 participants in the regular and restricted vaginal examination arms, respectively. Of the 3 primary outcomes,

FIGURE 1

Recruitment flow chart into a randomized trial Vaginal Assessment and Expedited Amniotomy in Oral Misoprostol Labor Induction in Nulliparas



CTG, cardiotocography; PROM, premature rupture of membranes.

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induction to vaginal delivery interval was significantly shorter in the regular vaginal examination arm compared to the restricted vaginal examination arm (mean \pm standard deviation, 24.3 ± 12.8 vs 31.1 ± 15.0 ; $P = .013$) but neither vaginal delivery rate at 24 hours (27.7% vs 20.4%; RR, 1.4; 95% confidence interval [CI], 0.8–2.3; $P = .14$) nor patient satisfaction (VNRS) with birth process (median [interquartile range] score, 7 [6–9] vs 8 [6–10]; $P = .15$) were significantly different across the trial arms. The cesarean delivery rate was similar (50% vs 43%; RR, 1.1; 95% CI, 0.9–1.5; $P = .36$) in the regular compared with restricted arms, respectively.

Patient satisfaction score with conduct of labor induction at 12 hours was 7 (5–8) vs 8 (5–9) ($P = .06$) for the regular vs restricted arms, respectively, and while favoring the restricted arm, did not reach

significance at the 5% level. Nevertheless, women consistently expressed a significantly higher preference for and fidelity to the restricted vaginal examination schedule when responding to questionnaires at induction, 12 hours into their induction, and after their delivery and were also more likely to recommend the restricted vaginal examination schedule to a friend (Table 3).

As to be expected, vaginal examinations in the first 12 hours of labor induction were more frequently performed in the regular arm (4 [4–4] vs 1 [1–1]; $P < .001$), but total oral misoprostol dose used (2.0 ± 0.8 vs 2.2 ± 0.7 ; $P = .13$), oxytocin use in labor (61/101 [60%] vs 75/103 [73%]; RR, 0.8; 95% CI, 0.7–1.0, $P = .07$), frequency of vaginal examinations in active labor (from cervical dilation of 4 cm) was (2 [1–3] vs 2 [1–4]; $P = .88$) were similar.

All other labor outcomes were also similar (Table 4).

Table 5 reports the other secondary maternal and neonatal outcomes that were not statistically significant different in both arms. Maternal blood transfusion (1/101 [1%] vs 1/103 [1%]; RR, 1.0; 95% CI, 0.1–16.1, $P = 1.00$), maternal fever (2/101 [2%] vs 2/103 [2%]; RR, 1.02; 95% CI, 0.14–7.4; $P = .98$), and 1 woman (allocated to the restricted arm) was identified with a specific diagnosis of chorioamnionitis. Neonatal antibiotic treatment was (4/101 [4%] vs 1/103 [1%]; RR, 4.1; 95% CI, 0.5–35.9; $P = 0.17$) in regular and restricted arms, respectively.

We assessed fetal heart rate tracing for all participants in the 12-hour primary study period for uterine overactivity (tachysytote, hypertonus, and hyperstimulation syndrome). There was no significant difference in the occurrence of uterine hyperstimulation syndrome (tachysystole or prolonged contraction with fetal heart rate abnormality) across trial arms, which occurred in 1 woman in each arm. Both women responded to a bolus terbutaline injection. No perinatal or maternal mortality occurred in this study.

Post hoc analyses

Post hoc, we collected and compared the data of participants who had membrane rupture in the 12-hour main study period (Table 3). Overall membrane rupture was (33.7% vs 18.4%; RR, 1.8; 95% CI, 1.1–3.0; $P = .01$) in the regular compared to the restricted vaginal examination arm, respectively. In the regular vaginal examination arm, membranes were more likely to be artificially ruptured within the 12-hour study period (28/34 [82.4%] vs 7/19 [36.8%]; RR, 4.1; 95% CI, 1.9–8.9; $P < .001$), whereas the rate of spontaneous membrane rupture (6/34 [17.6%] vs 12/19 [63.1%]; RR, 0.5; 95% CI, 0.2–1.3; $P = .15$) was not significantly different.

Comment Main findings

We compared a regular (4-hourly) to a restricted (as indicated) vaginal examination schedule during the first 12 hours

TABLE 1
Characteristics of the nulliparous trial participants

Characteristics	Regular vaginal examination (n = 101)	Restricted vaginal examination (n = 104)
Age, y	29.5 ± 3.7	29.9 ± 3.8
Gravidity	1 [1–1]	1 [1–1]
1	81 (80.2)	86 (82.7)
≥2	20 (19.8)	18 (17.3)
Gestational age, wk	39.1 ± 1.3	39.1 ± 1.3
Body mass index	29.3 ± 6.0	29.8 ± 4.9
Ethnicity		
Malay	58 (57.4)	49 (47.6)
Chinese	21 (20.8)	18 (17.5)
Indian	16 (15.8)	25 (23.3)
Others	6 (5.9)	12 (11.7)
Indications for labor induction		
Diabetes in pregnancy	38 (37.6)	35 (33.7)
Non-reassuring fetal status ^a	30 (29.7)	36 (34.6)
Prolonged pregnancy ≥40 wk	16 (15.8)	16 (15.4)
Hypertension	7 (6.9)	9 (8.7)
Others ^b	10 (9.9)	8 (7.7)
Cervical length by transvaginal ultrasound ^c (mm) Full range	25.0 ± 4.4 (15.5–31)	24.8 ± 3.9 (15–35)
Systolic blood pressure	115 ± 12	114 ± 12
Diastolic blood pressure	72 ± 10	70 ± 9
Pulse rate	82 ± 10	81 ± 10
Temperature	36.4 ± 0.2	36.4 ± 0.2
Questionnaire response to vaginal assessment regimen during oral misoprostol labor induction, (pre-induction)		
Prefers regular (4-hourly)	22 (21.8)	9 (8.7)
Prefers restricted (less often)	46 (45.5)	64 (61.5)
No preference	33 (32.7)	31 (29.8)

Data are number (%), mean ± standard deviation, or median [interquartile range]. Analyses were by Student *t* test for comparison of means for continuous data, Mann–Whitney *U* test for ordinal data, and χ^2 test for categorical data sets.

^a Non-reassuring fetal status includes oligohydramnios, reduced fetal movements, intrauterine growth restriction, sub-optimal fetal heart rate tracing, and suboptimal umbilical artery Doppler profile; ^b Others include social indication or suspected large gestational age; ^c Performed at recruitment; 3 measurements were made, with the shortest length taken as representative.

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of labor induction, with oral misoprostol administered 4-hourly to a maximum of 3 doses. We found the induction to vaginal delivery interval shortened by 7 hours (mean 24 vs 31 hours, $P = .013$) in the regular vaginal examination arm, but

no significant difference in the vaginal delivery rate at 24 hours and patient satisfaction with the birth process. The cesarean delivery rate (50% vs 43%; RR, 1.1; 95% CI, 0.9–1.5; $P = .36$) was also similar but relatively high, possibly

reflecting the high-risk characteristics of our trial population, which comprised 32% with induction for non-reassuring fetal status and 35% for diabetes in pregnancy. However, women consistently expressed a greater preference and fidelity for the restricted vaginal examination schedule and were more likely to recommend the restricted vaginal examination schedule to a friend.

The regular vaginal examination arm demonstrated a higher incidence of ruptured membranes at the end of first 12-hour main study period (33.7% vs 18.4%; $P < .001$). This difference is the consequence of a higher amniotomy rate (82.4% vs 36.8%; $P < .001$), an anticipated finding, in tandem with our intended practice of performing amniotomy during labor induction as soon as vaginal examination had shown its feasibility. Following amniotomy, our typical practice is to start titrated oxytocin soon thereafter, guided by the presence of uterine contractions; hence, as anticipated, oxytocin use by the end of the first 12-hour main study period was also significantly higher in the regular vaginal examination arm (14.9% vs 5.8%; $P = .03$).

The increase in “early” amniotomy and oxytocin infusion might be expected to result in a decrease in the use of oral misoprostol (2.0 ± 0.8 vs 2.2 ± 0.7 doses; $P = .13$) in the regular vaginal examination arm, but the difference was not statistically significant. Overall oxytocin use in labor was unexpectedly lower in the regular vaginal examination arm (60.4% vs 72.8%; $P = .07$), but the difference was not significant. The induction to vaginal delivery interval was shorter by 7 hours in the regular vaginal examination arm, despite marginally (nonsignificantly) fewer oral misoprostol doses administered and a lower (but nonsignificant) rate of oxytocin use in labor. The inference from the above findings supports the hypothesis that frequent vaginal examinations permitted earlier detection to ripen the cervix, expedited amniotomy, and early titrated oxytocin infusion, resulting in more efficient progression into labor and culminating in a more rapid vaginal delivery.^{4,5}

TABLE 2
Primary outcomes

Outcomes	Regular vaginal examination (n = 101)	Restricted vaginal examination (n = 103)	RR (95%CI)	P value
Satisfaction (VNRS) ^a with birth process	7 [6–9]	8 [6–10]		.15
Induction to vaginal delivery interval (hours)	24.3 ± 12.8	31.1 ± 15.0		.01
	24.4 [13.0–34.5]	29.9 [19.5–40.1]		.03
Vaginal delivery rate at 24 hours	28 (27.7)	21 (20.4)	1.4 (0.8–2.3)	.14

Data are n (%), mean ± standard deviation, or median [interquartile range]. Analyses were by *t* test for means and χ^2 test for categorical data. Mann–Whitney *U* test was also performed for nonparametric data to check for consistency with the *t* test. *P* values are 2-sided.

CI, confidence interval; RR, relative risk.

^a Eleven-point visual numerical rating score (VNRS), with 0 representing most dissatisfied and 10 representing most satisfied.

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In induced labor, early amniotomy shortened the time to delivery interval by 2 hours (19.0 vs 21.3 hours) and increased the proportion of induced nulliparous women who delivered within 24 hours (68% vs 56%) without increased complications.¹³ In our trial, with regular vaginal examinations in the first 12 hours, although the induction to vaginal delivery was significantly shortened by 7 hours (24.3 vs 31.1 hours), the vaginal delivery rate at 24 hours (27.7%

TABLE 3
Questionnaire responses

Outcomes	Regular vaginal examination (n = 101)	Restricted vaginal examination (n = 103)	RR (95% CI)	P value
Satisfaction (VNRS) ^a with conduct of labor induction				
At 12 h ^b	7 [5–8]	8 [5–9]		.06
After delivery ^c	7 [6–8]	7 [5–9]		.15
Prefers allocated vaginal assessment schedule in a future labor induction				
At 12 h ^b			0.5 (0.4–0.7)	<.001
Agree ^d	48 (47.2)	90 (87.4)		
Do not agree ^d	53 (52.5)	13 (12.6)		
After delivery ^c			0.5 (0.4–0.7)	<.001
Agree ^d	45 (44.6)	91 (88.3)		
Do not agree ^d	56 (55.4)	12 (11.7)		
Recommends allocated vaginal assessment schedule to friend having labor induction				
At 12 h ^b			0.6 (0.5–0.7)	<.001
Agree ^d	49 (48.5)	86 (83.5)		
Do not agree ^d	52 (51.5)	17 (16.5)		
After delivery ^c			0.6 (0.5–0.7)	<.001
Agree ^d	47 (46.5)	90 (87.4)		
Do not agree ^d	54 (53.5)	13 (12.6)		

Data are n (%), mean ± standard deviation, or median [interquartile range]. Analyses were by *t* test for means and χ^2 test for categorical data. Mann–Whitney *U* test was also performed for nonparametric data to check for consistency with the *t* test. *P* values are 2-sided.

CI, confidence interval; RR, relative risk.

^a Eleven-point visual numerical rating score (VNRS), with 0 representing most dissatisfied and 10 representing most satisfied; ^b Questionnaire response taken on completion of 12-h study period;

^c Questionnaire response taken as soon as practicable after delivery; ^d Recategorization of Likert scale responses: “agree” includes strongly or somewhat agree; “do not agree” includes neither agree nor disagree, somewhat disagree, and strongly disagree.

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TABLE 4
Labor outcomes

Outcomes	Regular vaginal examination (n = 101)	Restricted vaginal examination (n = 103)	RR (95% CI)	P value
Number of vaginal examinations ^a	4 [4–4]	1 [1–1]		<.001
Number of unscheduled vaginal examinations ^b	0 [0–0]	0 [0–0]		<.001
	0.03 ± 0.2	0.31 ± 0.5		
Unscheduled vaginal examinations ^a	3/101 (3)	30/103 (29)	0.1 (0.03–0.32)	<.001
Number of vaginal examinations in active labor ^c	2 [1–3]	2 [1–4]		.88
	2.27 ± 1.4	2.0 ± 1.5		
Number of oral misoprostol doses given ^a	2 [1–3]	2 [2–3]		.13
	2.0 ± 0.8	2.2 ± 0.7		
1 dose	28 (27.7)	19 (18.4)		
2 doses	43 (42.6)	41 (39.8)		
3 doses	30 (29.7)	43 (41.7)		
Uterine hyperstimulation syndrome	1 (1)	1 (1)	0.9 (0.1–15.9)	.99
Membrane rupture ^a (either spontaneous or amniotomy)	34/101 (33.7)	19/103 (18.4)	1.8 (1.1–3.0)	.01
Spontaneous membrane rupture ^a	6/34 (17.6)	12/19 (63.1)	0.5 (0.2–1.3)	.15
Amniotomy ^a	28/34 (82.4)	7/19 (36.8)	4.1 (1.9–8.9)	<.001
Oxytocin use during 12-h study period	15/101 (14.9)	6/103 (5.8)	2.6 (1.0–6.3)	.03
Induction to amniotomy (h)	20.2 ± 13.5	24.9 ± 12.9		.49
Bishop score at end of 12-h study period	6.5 ± 1.4	6.4 ± 1.4		.51
Oxytocin use in labor ^d	61 (60.4)	73 (72.8)	0.8 (0.7–1.0)	.07
Epidural in labor	23 (22.8)	27 (26.2)	0.9 (0.5–1.4)	.57
Opiate analgesic in labor	27 (26.7)	24 (23.3)	1.1 (0.7–1.8)	.57
Mode of delivery				.25
Spontaneous vaginal	35 (34.7)	33 (32.0)		
Operative vaginal ^e	16 (15.8)	26 (25.2)		
Cesarean delivery	50 (49.5)	43 (42.7)	1.1 (0.9–1.5)	.36
Indications for cesarean delivery				.32
Non-reassuring fetal status	23/50 (46)	16/44 (36)		
Failure to progress during labor	15/50 (30)	14/44 (32)		
Failed induction of labor	4/50 (8)	9/44 (20.5)		
Others ^f	8/50 (16)	5/44 (11.4)		
Undelivered after 24 h, n = 155	(n = 73)	(n = 82)		
Ripening not needed ^g	47/73 (64.6)	49/82 (59.8)		
Oral misoprostol	19/73 (26.0)	22/82 (26.8)		.76
Vaginal prostaglandin	7/73 (9.6)	10/82 (12.2)		
Cervical ripening balloon	0	1/82 (1.2)		

Data are n (%), mean ± standard deviation, or median [interquartile range]. Analyses were by *t* test for means and χ^2 test for categorical data. Mann–Whitney *U* test was also performed for nonparametric data to check for consistency with the *t* test. *P* values are 2-sided.

CI, confidence interval; RR, relative risk.

^a During 12-h study period; ^b Vaginal examination performed outside of original trial protocol of either arm; ^c Vaginal examination performed when cervical dilatation ≥ 4 cm and up to the second stage or the decision for cesarean delivery; ^d Oxytocin use in labor (except third stage of labor); ^e Operative vaginal includes vacuum or forceps delivery; ^f Others include maternal request or abnormal presentation in labor; ^g When participants have membrane ruptured or in labor.

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TABLE 5
Maternal and neonatal outcomes

Outcomes	Regular vaginal examination (n =101)	Restricted vaginal examination (n = 103)	RR (95% CI)	P value
Maternal outcomes				
Delivery blood loss (mL)	300 [200–300]	30 [200–300]		.85
Postpartum hemorrhage \geq 500 mL Blood transfusion	9 (8.9) 1 (1)	10 (9.7) 1 (1)	0.9 (0.4–2.2) 1.0 (0.1–16.1)	.85 1.00
Maternal fever	2/101 (2)	2/103 (2)	1.0 (0.1–7.4)	.98
Maternal readmission ^a	1	0		
Chorioamnionitis	1	0	1.0 (0.9–1.02)	.32
Induction to discharge interval (days)	2.9 \pm 1.2	3.1 \pm 1.2		.29
Neonatal outcomes				
Apgar score at 5 min	9.8 \pm 0.7 10 [10–10]	9.8 \pm 0.4 10 [10–10]		.79
Apgar score \leq 7 at 5 min	4 (4)	2 (1.9)	2.0 (0.3–10.9)	.33
Cord blood pH	7.2 \pm 0.07	7.2 \pm 0.6		.28
pH <7.1	2 (2.0)	2 (1.9)		.98
Neonatal jaundice ^b	5 (5.0)	3 (2.9)	1.3 (0.4–4.7)	.70
Admission to neonatal unit	8 (7.9)	4 (3.8)	2.0 (0.6–6.5)	.23
Indication for neonatal admission				
Neonatal tachypnea	1	1		
Hypoglycemia	4	0		
Observation	0	1		
Others ^c	3	2		
Neonatal antibiotics	4/101(4)	1/103(1)	4.1 (0.5–35.9)	.17

Data are n (%), mean \pm standard deviation, or median [interquartile range]. Analyses were by *t* test for means and χ^2 test for categorical data. Mann–Whitney *U* test was also performed for nonparametric data to check for consistency with the *t* test. *P* values are 2-sided.

CI, confidence interval; RR, relative risk.

^a Readmission due to episiotomy wound breakdown; ^b Neonatal jaundice defined as jaundice requiring phototherapy at maternal bedside; ^c Others include: 1 subarachnoid hemorrhage, 1 imperforate anus, and 3 pneumonia.

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vs 20.4%; *P* = .14) was not significantly increased. The rates of vaginal delivery at 24 hours that we achieved in both trial arms were lower than the numbers that we used in our sample size calculation; however, it should be noted that Faucett et al's oral misoprostol regimen used 50 μ g as a loading dose, followed by 100- μ g doses every 4 hours for a maximum of 4 total doses.¹² Our cesarean delivery rate (50% vs 43%) was also similar.

Unscheduled vaginal examinations (3% vs 29%; RR, 0.1; 95% CI,

0.03–0.32; *P* < .001 in the regular vs restricted arms, respectively) were more commonly performed in the restricted arm, in part reflecting the concern with administering oral misoprostol without the support of cervical findings (especially when there are contractions, so as not to cause uterine hyperstimulation); these concerns are expected, given that our institutional standard practice is early recourse to amniotomy when it is feasible, followed by titrated oxytocin infusion during labor induction.

Clinical implications

Membrane sweeping as an adjunct to formal methods of labor induction (with vaginal prostaglandins or amniotomy) increased the spontaneous vaginal delivery rate, decreased oxytocin drug use, and shortened the induction to vaginal delivery interval.^{14,15} It is plausible that in our regular vaginal examination arm, in which a vaginal examination was routine before the first oral misoprostol dose compared to no initial examination in the restricted vaginal examination arm, the first vaginal examination might

approximate to a “membrane sweeping effect,” which could contribute to a shorter induction to vaginal delivery for the regular vaginal examination arm.

In a contemporary cohort study, elective induction at term that required prostaglandin cervical ripening results in vaginal delivery rates of only 56.8–58% in nulliparas compared with 97% in multiparas,⁷ indicating the still-present challenge with nulliparous labor induction. In our study of exclusively nulliparous women, our vaginal delivery rates were broadly comparable (50% vs 57%) across our trial arms.

Women consistently preferred the restricted schedule (64% vs 46% during pre-induction, 87% vs 47% at 12 hours of labor induction, and 88% vs 45% after delivery) and would recommend a restricted schedule to friend (84% vs 49% at 12 hours of labor induction and 87% vs 47% after delivery) when assessed through their induction of labor to delivery. Also, as could be anticipated with regard to satisfaction score with conduct of labor induction, the earlier assessment made at the end of the 12-hour main study period showed a stronger trend in favor of the restricted vaginal examination arm (8 [5–9] vs 7 [5–8]; $P = .06$, compared to 7 [5–9] vs 7 [6–8]; $P = .15$) after delivery; however, these findings were not significant at the 5% level, which could be the result of a type 2 error due to a lack of statistical power. These findings, namely, that women when assessed after delivery continue to prefer a restricted vaginal examination schedule despite a shorter interval to vaginal birth in the regular vaginal examination arm and similar satisfaction score with conduct of labor induction, probably illustrate the continued negative perception of vaginal examination even during active labor induction in nulliparous women, lending support to the WHO recommendation that vaginal examinations during first-stage labor care be limited to every 4 hours unless there are signs of decreasing uterine contractility, a decreasing urge to push, or before administration of analgesia.⁴

Strengths and limitations

With regard to the strengths of our trial, we performed an original and powered study with few dropouts and replete outcome ascertainment. The recruitment and management of the initial 12 hours was conducted by a single investigator (W.S.T.), allowing a consistent approach, so this trial maybe better construed as an efficacy trial on proof of concept than an effectiveness analysis. We believe our findings to be generalizable, as our oral misoprostol induction regimen and labor care protocol is comparable with practice in a well-resourced setting.³

With regard to limitations, our sample size, albeit powered to our primary outcome assumptions, is fairly small, and we might have overestimated the effect size of the intervention, in particular with regard to vaginal delivery at 24 hours. Our trial is an open design, as the intervention could not be effectively masked. Our trial is also not powered to evaluate the cesarean delivery rate, which is an important clinical outcome in labor induction. A powered trial to evaluate a 50% vs 43% cesarean delivery rate ($\alpha = 0.05$ and 80% power) would require 796 participants in each arm.

Conclusion

In this study, the interval of induction to vaginal delivery was significantly shorter in the regular examination arm, but the vaginal delivery rate at 24 hours and satisfaction with the birth process were not significantly different across trial arms. Nevertheless, women consistently expressed a higher preference and fidelity toward a restricted examination schedule and were more likely to recommend such a schedule to a friend. In considering patient preference as an outcome, it is important to realize that provision of care should not be homogenized toward majority views, as minority preferences are just as valid. Nulliparous women undergoing labor induction with bolus oral misoprostol regimens should have the option of a regular or a restricted vaginal examination schedule during cervical

ripening, which should be discussed with their care provider to facilitate informed choice. ■

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References

1. World Health Organization. WHO recommendations for induction of labor (2011). Available at: http://apps.who.int/iris/bitstream/10665/44531/1/9789241501156_eng.pdf. Accessed Sept. 25, 2018.
2. Hamilton BE, Martin JA, Osterman MJK, et al. Births: final data for 2014. *Natl Vital Stat Rep* 2015;64(12).
3. Ten Eikelder ML, Rengerink KO, Jozwiak M, et al. Induction of labor at term with oral misoprostol vs a Foley catheter (PROBAAT-II): a multicenter randomised controlled non-inferiority trial. *Lancet* 2016;387:1619–28.
4. World Health Organization. World Health Organization partograph in management of labor. *World Health Organization Maternal Health and Safe Motherhood Programme*. *Lancet* 1996;343:1399–404.
5. Downe S, et al. Routine vaginal examinations for assessing progress of labor to improve outcomes for women and babies at term. *Cochrane Database Syst Rev* 2013;7:CD010088.
6. Hughes EG, Kelly AJ, Kavanagh J. Dinoprostone vaginal insert for cervical ripening and labor induction: a meta-analysis. *Obstet Gynecol* 2001;97:847–55.
7. Laughon SK, et al. Induction of labor in a contemporary obstetric cohort. *Am J Obstet Gynecol* 2012;206:486.
8. Tan PC, et al. Immediate compared with delayed oxytocin after amniotomy labor induction in parous women: a randomized controlled trial. *Obstet Gynecol* 2013;121:253–9.
9. Tan PC, et al. Concurrent oxytocin with dinoprostone pessary versus dinoprostone pessary in labor induction of nulliparas with an unfavourable cervix: a randomised placebo-controlled trial. *Br J Obstet Gynaecol* 2007;114:824–32.
10. Tan PC, et al. Transvaginal sonographic measurement of cervical length vs. Bishop score in labor induction at term: tolerability and prediction of cesarean delivery. *Ultrasound Obstet Gynecol* 2007;29:568–73.
11. Ayres-de-Campos D. Electronic fetal monitoring or cardiotocography, 50 years later: what's in a name? *Am J Obstet Gynecol* 2018;218:545–6.
12. Faucett AM, et al. Oral misoprostol versus vaginal dinoprostone for labor induction in nulliparous women at term. *J Perinatol* 2014;34:95–9.

13. Macones GA, et al. The efficacy of early amniotomy in nulliparous labor induction: a randomized controlled trial. *Am J Obstet Gynecol* 2012;207:403.

14. Foong LC, et al. Membrane sweeping in conjunction with labor induction. *Obstet Gynecol* 2000;96:539–42.

15. Tan PC, Jacob R, Omar SZ. Membrane sweeping at initiation of formal labor induction: a

randomized controlled trial. *Obstet Gynecol* 2006;107:569–77.

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Patient Questionnaires**At 12 hours after commencement of labor induction**

Date & Time:

- A) Please circle a score on the line below to indicate your satisfaction with how your labor induction was conducted to this point

0 1 2 3 4 5 6 7 8 9 10

Most Dissatisfied Most Satisfied

- B) I would like to have the same vaginal examination schedule that I had received if I were to need labor induction in a next pregnancy

- Strongly agree
- Somewhat agree
- Neither agree nor disagree
- Somewhat disagree
- Strongly disagree

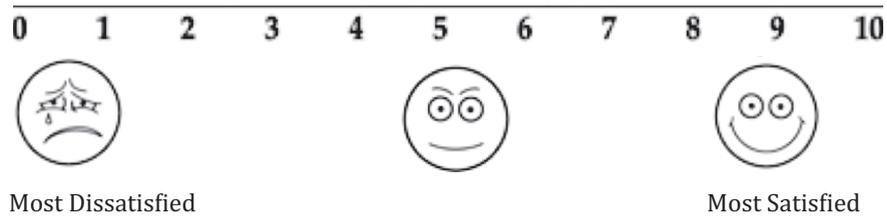
- C) I would recommend the vaginal examination schedule that I had received to a friend who is about to have her labor induced

- Strongly agree
- Somewhat agree
- Neither agree nor disagree
- Somewhat disagree
- Strongly disagree

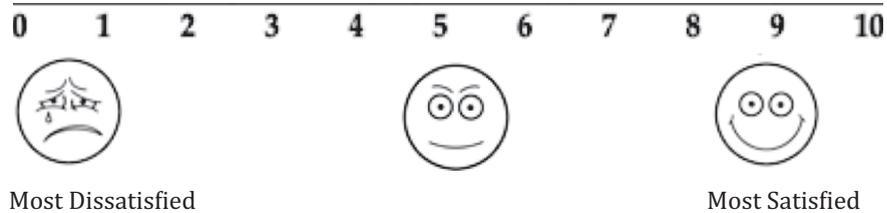
Soon after delivery

Date & Time:

- A) Please circle a score on the line below to indicate your overall satisfaction with your birth process.



- B) Please circle a score on the line below to indicate your satisfaction with how your labor induction was conducted.



- C) I would like to have the same vaginal examination schedule that I had received if I were to need labor induction in a next pregnancy

- Strongly agree
- Somewhat agree
- Neither agree nor disagree
- Somewhat disagree
- Strongly disagree

- D) I would recommend the vaginal examination schedule that I had received to a friend who is about to have her labor induced

- Strongly agree
- Somewhat agree
- Neither agree nor disagree
- Somewhat disagree
- Strongly disagree