

Oral misoprostol for 48 hours versus a supra cervical foley catheter for 48 hours for induction of labour in post dated pregnancies: a randomized control trial

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(Index words: induction of labour, oral misoprostol, foley catheter)

Abstract

Aims: To assess the feasibility of administration of three doses of oral misoprostol (OM) 50 µg four hourly per day for 48 hours versus the insertion of a supra cervical Foley catheter for 48 hours, in women at 40 weeks + 5 days gestation, and compare the effectiveness of the two methods for induction of labour (IOL).

Method: An investigator blinded, randomized controlled trial was conducted at the academic obstetric unit, Teaching Hospital Mahamodara, Galle from 13.10.2016 to 30.04.2017. Consecutive women (n=144) with singleton uncomplicated pregnancies having Modified Bishop Score (MBS) <5 at 40 weeks + 5 days gestation were allocated by stratified (primigravidae/ multigravidae) block randomization to receive three doses of OM 50µg four hourly per day for 48 hours or a supra cervical Foley catheter for 48 hours.

Results: Compared to the Foley, OM resulted in higher rates of successful IOL (67% vs 47%, RR 1.4, 95% CI 1.1-2.0, p=0.029), more vaginal deliveries within 24 hours and 48 hours, shorter mean induction delivery intervals and greater mean increase in MBS in those not in labour after 48 hours. There was non-significant increased frequency of excessive uterine activity, cardiotocograph abnormalities and meconium stained liquor after OM but no differences in the rates of caesarean deliveries and maternal or neonatal morbidity or mortality between the two groups.

Conclusion: The administration of three doses oral misoprostol (OM) 50 µg four hourly per day for 48 hours as well as the insertion of a supra cervical Foley catheter for 48 hours were feasible for women at 40 weeks + 5 days gestation, but OM was more effective than the Foley catheter for IOL.

Introduction

Oral misoprostol (OM) is becoming increasingly popular as a method of induction of labour (IOL) worldwide, mainly because of its ease of administration and convenience to the patient, in contrast to intravenous and per vaginal interventions [1]. It has been shown that in women at gestations of > 37 weeks, IOL with three doses of OM 50µg per day for four days and a supracervical Foley catheter for four days are equally effective and safe with approximately 75% in the OM group and 80% in the Foley catheter group being delivered within 48 hours respectively [2]. In a previous study carried out in the academic obstetrics and gynaecology unit of the Teaching Hospital Mahamodera, Galle (THMG), it was shown that compared to a supracervical Foley catheter for 24 hours, three doses of OM 50µg four hourly was more effective for cervical ripening and even resulted in IOL in approximately 38% of women in the OM group compared to approximately 12% in the Foley catheter group [3]. OM is currently not used in clinical practice in Sri Lanka, and further research in to its use is needed [1,4]. The current practice in most obstetric units in Sri Lanka is to remove the supracervical Foley catheter after 24 hours, on account of concerns regarding the risks, especially ascending infection, if the Foley catheter is kept *in situ* longer. It has been shown that keeping the supracervical Foley catheter for up to four days is safe, and that it is not associated with increased risks including ascending infection [2, 5-9]. However, many clinicians in Sri Lanka are reluctant to keep the supracervical Foley catheter *in situ* for more than 24 hours. Although OM is not used as a primary method of IOL in Sri Lanka, it is used for this purpose internationally. Therefore, the current study was designed, to determine the feasibility and the effectiveness of these two methods

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as primary methods of IOL, by doubling the duration of both interventions up to 48 hours, in contrast to the previous study in 2017 where both interventions were only for 24 hours with objective of achieving the pre induction cervical ripening, prior to IOL with other methods.

Method

An investigator blinded, randomized controlled trial was conducted in the academic obstetric unit, THMG from 13 October 2016 to 30 April 2017. Based on the results of the previous study carried out in the unit [3], the sample size was calculated with the objective of achieving an IOL rate of at least 55% in the OM group expecting an IOL rate of up to 30% in the Foley catheter group. The minimum sample size (having a power of 80% and a significance level of 95%) to detect this difference was calculated to be 120, using the standard formula [10]. Allowing provision

for a dropout rate of 20% after randomization, due to subjects who had consented for the trial subsequently withdrawing consent or due to pre labour rupture of membranes, increased uterine activity, fetal distress or suspected vaginal infections, a total of 200 eligible women who had singleton uncomplicated pregnancies, with a vertex presentation and no contra indication for IOL, were selected at the gestational age (GA) 40 weeks + 3 days and informed written consent obtained the following day. Any woman with a previous caesarean delivery (CD), history of myomectomy, hypersensitivity to misoprostol, or currently having pregnancy induced hypertension, gestational diabetes mellitus or pre labour rupture of membranes, was excluded from the trial. Of those eligible for inclusion, 144 consecutive women with Modified Bishop Scores (MBS) ≤ 5 at a GA of 40 weeks + 5 days were allocated to receive three doses of OM 50 μ g four hourly per day for 48 hours or a supra cervical Foley catheter for 48 hours (Figure 1).

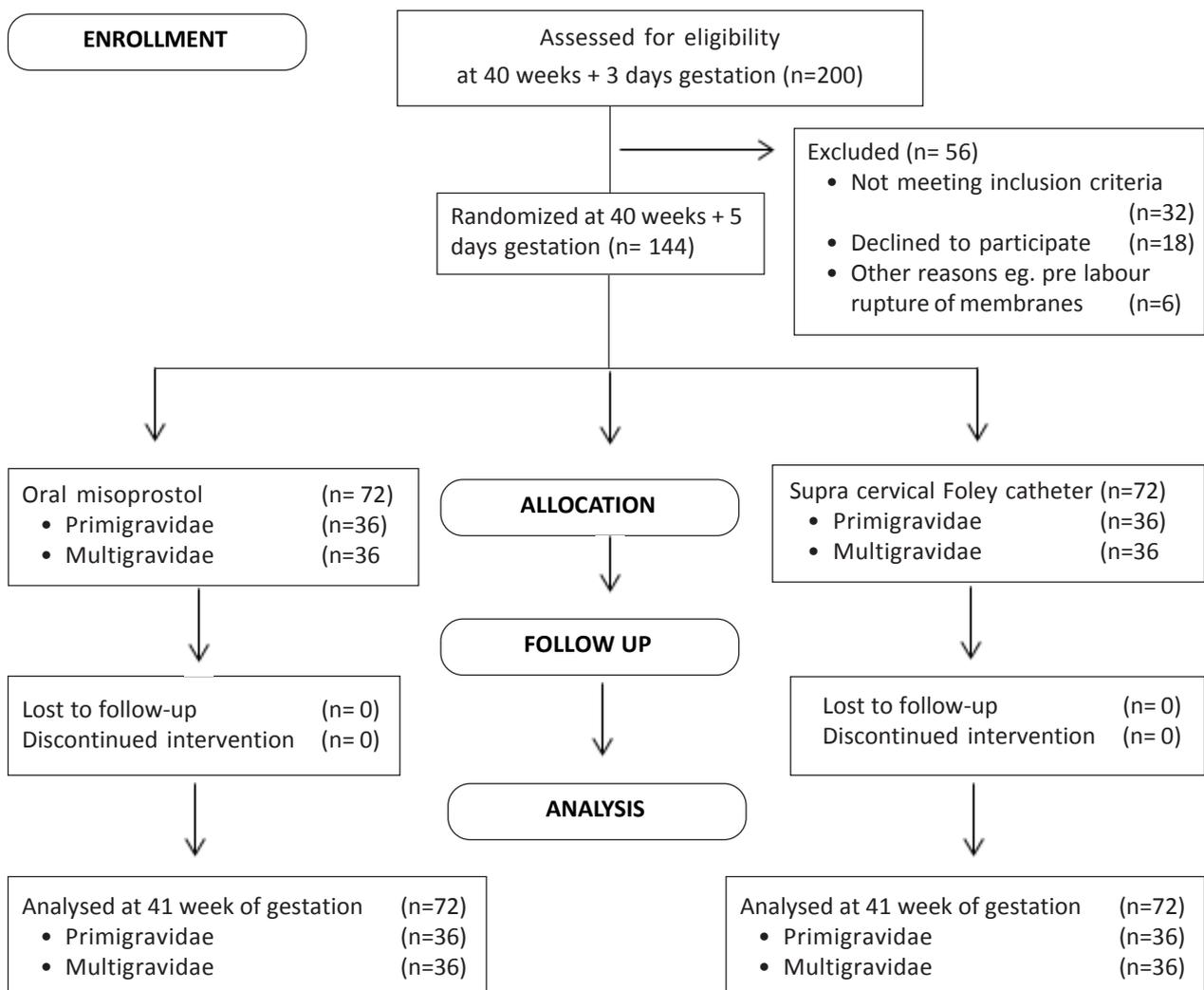


Figure 1. Flow Diagram of Method.

The MBS was assessed at 40 weeks +5 days of gestation, every Monday to Friday, at 7.00am by the first author (BA) until the required sample was achieved. Pregnant women who withdrew their consent, and women with ruptured membranes, spontaneous onset of labour, or having MBS >5, were excluded before randomization. Using computer generated random numbers and stratified (primigravidae and multigravidae) block randomization, 144 sealed opaque envelopes containing the parallel allocation sequences for the two strata (76 primigravidae and 76 multigravidae) in blocks of four in a 1:1 ratio, were prepared by the second author (MG) and kept securely in the antenatal ward. Using these, the third author (RP) allocated the participants to receive the appropriate intervention at 7.30 am Monday to Friday in the ward. Before the intervention a 10 minute cardiotocograph (CTG) was carried out in all the randomized women and if there was any suspicion of abnormality, a fetal acoustic stimulation test (FAST) was carried out and the CTG reassessed for normality. If any woman did not have a normal CTG she was not included in the trial. In the Foley catheter group, after cleaning the vagina and ecto cervix with povidone iodine, a 16 gauge Foley catheter was inserted through the cervical canal and placed supra cervically under sterile conditions, and its bulb inflated with 60 ml of distilled water. This was done by the third author (RP). All the authors were skilled and had adequate experience in assessing the MBS and inserting a supra cervical Foley catheter. In the OM group, three doses per day of OM 50µg were given four hourly at 7.30 am, 11.30am and 3.30 pm on each day for 48 hours, by the staff nurses. Tablet containing 200µg misoprostol (Misoprost 200, Cipla, India) were used for the study. Each 200µg tablet of misoprostol was inserted into a separate small polythene bag and crushed. Thereafter, the entire content in the polythene bag was dissolved in 200 ml of water and then it was carefully divided into four 50 ml samples using sterile pipettes, burettes and beakers by the first author. OM solutions were kept in refrigerated and the 50 ml remaining after the third dose was discarded. Routine monitoring was carried out according to the guidelines in the unit. If any of the women established labour, or if increased uterine activity and or fetal distress was detected, appropriate measures were adopted according to the guidelines in the unit, and no further doses of OM were given. MBS was re-assessed, 48 hours after the commencement of the trial, by BA. Prior to this, the women were assessed as per the routine in the unit by RP or a skilled, experienced senior house officer (SHO). At the completion of 47 hours, if the Foley catheter was still *in situ*, it was removed (at 6.30 am) by a skilled, experienced house officer. Prior to 47 hours if the patient established labour or the Foley catheter fell out, appropriate measures were adopted according to the guidelines in the unit. Women who were unfavorable for IOL after 48 hours, with MBS ≤ 7, were considered for cross over therapy with either Foley catheter (OM group) or vaginal dinoprostone (PGE₂) for Foley catheter group by MG and the fourth

author (FR) who were not involved in any MBS assessments. Either RP or a skilled, experienced SHO carried out the appropriate intervention and they were managed according to the guidelines in the unit. BA continued to be blind to this intervention too.

Successful IOL (defined as painful uterine contractions occurring with a frequency of ≥ 2 per 10 minutes with a MBS ≥ 7), vaginal delivery within 24 hours (VD 24), vaginal delivery within 48hours (VD 48), the induction delivery interval (IDI) following IOL, instrumental vaginal delivery (IVD), CD, reasons for operative delivery, and the number of women becoming suitable for IOL with MBS ≥7 after 48 hours of the interventions were recorded. Any excessive uterine activity [11], fetal cardiotocograph (CTG) abnormalities [12], occurrence of meconium stained liquor, maternal vomiting or diarrhea or pyrexia of >38°, a clinical diagnosis of a post-partum haemorrhage, need for post-partum blood transfusion, maternal admission for special care, uterine rupture, peripartum hysterectomy, perinatal outcome, 1 minute Apgar scores, admission to the special care baby unit (SCBU) and the reasons for such admission, were also recorded. The data were stored confidentially in a password protected, ongoing computer database by BA. The randomized allocation sequence was kept confidentially by MG and FR and BA was blinded to it, until all the data were entered in to the database. Means and 95% confidence intervals (CI) were calculated for the continuous variables and t-test was used for comparison of means. The medians and inter quartile ranges were calculated for the parity distributions and the Mann-Whitney U test was used to compare medians. The Chi Square test and Fisher's Exact test were used to compare proportions, the relative risks (RR) and their 95% CI were calculated, and a *p* value of < 0.05 was considered to be statistically significant. The Statistical Package for Social Sciences (SPSS version 20) and Epi Info version 7 were used for data analysis.

Results

Prior to the interventions (at GA 40weeks + 5 days), there were no significant differences in the distributions of parity, age and pre interventional MBS between the two intervention groups (Table1). At GA 41 weeks (48 hours after the interventions), successful IOL was significantly higher in the OM group compared to the Foley catheter group, (67% vs 47%, RR 1.4, 95% CI 1.0 - 2.0, *p*=0.029). The VD 24 and the VD 48 were also significantly greater in the OM group compared to the Foley catheter group (35% vs 8%, RR 4.2, 95% CI 1.8 - 9.5, *p* < 0.001 and 67% vs 44%, RR 1.5, 95% CI 1.1 - 2.0, *p*=0.012). The mean IDI was significantly less in the OM group compared to the Foley catheter group (24.2 hours 95% CI 21.7-26.7 vs 31.9 hours 95% CI 29.3 - 34.5, *p*=0.003). Of the 80 cases of VD 24, three had instrumental vaginal delivery (IVD) between 24-48 hours of the intervention for delay of the second stage of labour

following successful IOL. There were two intra partum CD for fetal distress diagnosed by pathological CTGs at 32 hours and 36 hours in the Foley catheter group, one participant having intact membranes and the other having spontaneous rupture of membranes. The mean increase in MBS in those not in labour was also greater in the OM group compared to the Foley catheter group (4.8, 95% CI 4.4 -5.2 vs 4.1 95% CI 3.7 -4.4, $p=0.017$) (Table 2). There were significantly less VD 24 in primigravidae compared to multigravidae in the OM group (19% vs 50%, RR 0.4, 95% CI 0.2 - 0.8, $p=0.013$). However, no such difference was seen in the VD 48. The mean IDI was significantly more in primigravidae compared to multigravidae in the OM group (30.0 hours 95% CI 26.6-33.4 vs 19.2 hours 95% CI 15.0-23.3, $p=0.003$). There were no significant differences in the primary outcomes at 48 hours between the primigravidae and the multigravidae in the Foley Catheter group (Table 3).

There were relatively more cases of excessive uterine activity with suspicious CTGs and meconium stained liquor in the OM group compared to the Foley catheter group among the primigravidae (3/36 vs 1/36, $p=0.614$ for each complication) However, there was no significant difference in the other maternal or neonatal complications. One primigravida who had a prolonged stage 2 of labour (> 2 hours), approximately 44 hours after the insertion of a Foley catheter, had a vacuum delivery of a neonate with APGAR < 7. The baby was resuscitated with the use of an

Ambu bag with oxygen and managed with air and oxygen in the SCBU and discharged home, well, after two days. There were two cases of excessive uterine activity with normal CTGs after three doses of OM. They did not require tocolytics and resulted in normal deliveries within 24 hours. There were five cases of excessive uterine activity with suspicious CTGs who were also managed conservatively with no tocolytics: two primigravidae and one multigravida were after three doses of OM and they resulted in normal deliveries within 24 hours; one primigravida was after the fourth dose of OM, no further doses were given, and she delivered normally in approximately 30 hours; one was a primigravida with a Foley catheter for approx. 36 hours, which was therefore removed, and she delivered within 48hrs. Of the cases who had a successful IOL with a Foley catheter and delivered between 24-48 hours, there were three cases of baseline fetal tachycardia without excessive uterine activity and one only required increased intravenous hydration, and delivered a healthy non asphyxiated baby. Two had additional single spikes of maternal pyrexia $\geq 38^{\circ}\text{C}$ and tachycardia, occurring approximately 44 and 35 hours after the insertion of a Foley catheter. Intravenous broad spectrum antibiotics and paracetamol was commenced and two healthy non asphyxiated babies were delivered at approx. 46 hours and 37 hours respectively. The neonatologists managed the neonates conservatively without antibiotics and both babies were discharged home after two days (Table 4).

Table 1. Characteristics of the participants at 40 weeks + 5 days' gestation (n=144)

	<i>Misoprostol (n=72)</i>	<i>Foley (n= 72)</i>	<i>p</i>
Parity: Range 2-4	2-4		
Median (Inter Quartile Range)	2 (2-3)	2 (2-3)	0.854*
Primigravidae			
Age in years: Range	22-34	19-33	
Mean (95%CI)	26.6 (25.6-27.6)	26.6 (25.5-27.7)	0.969**
Mean pre interventional Modified Bishop Score (95%CI)	3.1 (2.7-3.3)	3.1 (2.9-3.3)	1.00**
Multigravidae			
Age in years: Range	22-38	22-38	
Mean (95%CI)	30.5 (29.3-31.6)	30.1 (28.9-31.2)	0.625**
Mean pre interventional Modified Bishop Score (95%CI)	3.2 (3.1-3.5)	3.2 (3.1-3.5)	1.00**

95% CI = 95 % Confidence Interval, *by comparison of medians using Mann Whitney U test **by comparison of means using t-test

There were no significant differences in the rates of VD, CD or the mean IDIs after subsequent IOL with amniotomy and intravenous oxytocin infusion in the participants who had not delivered within 48 hours of the primary intervention between the two groups (Tables 5). There were

no cases of maternal diarrhoea, vomiting or uterine rupture following OM in this study. There were no cases of severe maternal or neonatal morbidity or mortality. Overall, there were no significant differences in the frequency of complications between the two groups in the trial (Table 6).

Table 2. Primary outcomes at 41 weeks of gestation (n=144)

	<i>Misoprostol</i> <i>n = 72</i>	<i>Foley</i> <i>n = 72</i>	<i>RR</i> <i>(95%CI)</i>
Successful IOL prior to 41 weeks gestation	48 (67%)	34 (47%)	1.4 (1.0-2.0)
VD within 24 hours	25 (35%)	6 (8%)	4.2 (1.8-9.5)
VD within 48 hours	48 (67%)	32 (44%)	1.5 (1.1- 2.0)
IVD within 48 hours (for prolonged stage II of labour)	2	1	2.0 (0.9-21.6)
IDI in hours	4.2-36.1	8.4-39.5	
Range			
Mean (95% CI)	24.2 (21.7-26.7)	31.9 (29.3-34.5)	-
Emergency CD after successful IOL prior to 41 weeks gestation	0	2	-
Number undelivered at 41 weeks gestation	24	38	0.4 (0.2-0.9)
If undelivered, MBS.			
Rang	7-9	6-9	
Mean (95% CI)	7.4 (7-7.9)	7.3 (7.0-7.7)	-
If undelivered, increase in MBS			
Range	3-7 4.8 (4.4 -5.2)	3-7 4.1 (3.7-4.4)	
Mean (95% CI)			-
If undelivered, MBS \geq 7	24 (31%)	37 (50%)	0.5 (0.2-0.9)
Cross over therapy for further ripening of cervix	0	1	-

IOL = Induction of Labor, MBS = Modified Bishops Score, CD = Caesarean Delivery, VD = Vaginal Delivery, IVD = Instrumental Vaginal delivery, IDI = Induction to Delivery Interval, 95% CI = 95% Confidence Interval, RR = Relative Risk

Table 3. Comparison of primary outcomes between primigravidae and multigravidae at 41 weeks of gestation (n=144)

	Misoprostol (n=72)			Foley (n=72)		
	Primi gravidae (n=36)	Multi gravidae (n=36)	RR (95%CI)	Primi gravidae (n=36)	Multi gravidae (n=36)	RR (95%CI)
IOL = Induction of Labor, MBS = Modified Bishops Score, CD = Caesarean Delivery, VD = Vaginal Delivery, IDI = Induction to Delivery Interval						
Successful IOL prior to 41 weeks gestation	22 (61%)	26 (72%)	0.8 (0.6- 1.2)	15 (42%)	19 (53%)	0.78 (0.5-1.3)
VD within 24 hours	7 (19%)	18 (50%)	0.4 (0.2-0.8)	3 (8%)	3 (8%)	1 (0.2-4.6)
VD within 48 hours	22 (61%)	26 (72%)	0.8 (0.6-1.2)	15 (42%)	17 (47%)	0.8 (0.5- 1.5)
IDI in hours	12.4-36.1	4.2-28.4	-	10.2-37	8.4-39.5	-
Mean (95% CI)	30.0 (26.6-33.4)	19.2 (15.0-23.3)	-	29.12 (24.0-34.2)	33.93 (28.7-39.2)	-
Emergency CD prior to 41 weeks	0	0	-	0	2	-
If undelivered, MBS.						
Range	7-8	7-9	-	6-8	7-9	-
Mean (95% CI)	7.3 (7.0-7.7)	7.8 (7.0-8.6)	-	7.2 (6.9-7.0)	7.3 (7.0-7.6)	-
If undelivered, increase in MBS						
Range	3-6	4-7	-	3-5	3-7	-
Mean (95% CI)	4.8 (4.1-5.4)	5 (3.9-6.0)	-	4.1 (3.8-4.4)	4.2 (3.7-4.8)	-
If undelivered, MBS ≥7	14 (36%)	10 (25%)	1.4 (0.7-2.7)	20 (51%)	17 (47%)	1.2 (0.7-1.8)

95% CI = 95% Confidence Interval, RR = Relative Risk

Table 4. Complications of primary interventions at 41 weeks gestation (n=144)

	Primigravidae		p	Multigravidae	
	Misoprostol (n=36)	Foley (n=36)		Misoprostol (n=36)	Foley (n=36)
Baseline fetal tachycardia without excessive uterine activity	0	1		0	2
Excessive uterine activity with normal cardiotocograph (CTG)	1	0		1	0
Excessive uterine activity with suspicious CTG	0.3	1	0.614*	1	0
Meconium stained liquor	0.3	1	0.614*	1	0
Admission to Special Care Baby Unit with APGAR<7	0	1		0	0
Neonatal Death	0	0		0	0
Maternal pyrexia	0	1		0	1
Maternal vomiting or diarrhoea	0	0		0	0
Uterine rupture	0	0		0	0
Post-partum hemorrhage	0	1		2	0
Blood transfusion	0	1		1	0
Maternal admission for special care	0	0		0	0

* by comparison of proportions using Fisher's exact test

Table 5. Secondary outcomes (n=144)

	Misoprostol (n = 72)	Foley (n = 72)	RR	p
VD after amniotomy + oxytocin infusion at 41 weeks gestation	16 (22%)	26 (38%)	0.6 (0.4-1.0)	0.098*
Mean IDI (95% CI) in hours, after amniotomy + oxytocin infusion at 41 weeks gestation	49.5 (47.9-51.1)	53.7 (52.9-54.6)	-	0.034**
CD after amniotomy + oxytocin infusion at 41 weeks gestation	8 (11%)	11(15%)	0.7 (0.3-1.7)	0.623*

VD = Vaginal Delivery, IDI = Induction to Delivery Interval, 95%CI = 95% Confidence Interval, CD = Caesarean Delivery, RR = Relative Risk, *by comparison of proportions with Chi Square Test, **by comparison of means with t test

Table 6. Frequency of Complications in the trial (n=144)

	Primigravidae			Multigravidae		
	Misoprostol (n=36)	Foley (n=36)	p	Misoprostol (n=36)	Foley (n=36)	p
Baseline fetal tachycardia without excessive uterine activity	0	1		0	2	
Excessive uterine activity with normal cardiotocograph (CTG)	1	2		1	0	
Excessive uterine activity with suspicious CTG	05	1	0.198*	1	0	
Meconium stained liquor	05	03	0.71*	04	2	0.673*
Admission to Special Care Baby Unit with APGAR<7	1	1		1	0	
Maternal pyrexia	0	1		0	1	
Post-partum hemorrhage	0	1		2	0	

*by comparison of proportions using Fisher's exact test

Discussion

Three doses of OM 50µg four hourly per day for 48 hours was feasible, and was more effective for IOL than the insertion of a supra cervical Foley catheter for 48 hours. This is reflected by increased VD24 rates, increased VD48 rates and reduced IDI after OM, compared to the insertion of a supra cervical Foley catheter for 48 hours. Although there were relatively more cases of excessive uterine activity with suspicious CTGs and meconium stained liquor in the OM group compared to the Foley catheter group, especially among the primigravidae, none of these cases required CD. The two cases of CD within 48 hours of the interventions were due to intra partum fetal distress, (after successful IOL), occurring without excessive uterine activity in the Foley catheter group. The two cases with clinical features suggestive of possible chorioamnionitis, occurring approximately 44 and 35 hours after the insertion of a Foley catheter, resulted in normal deliveries of healthy, non-asphyxiated babies who did not require antibiotics.

The increased occurrence of meconium stained liquor, without any associated evidence of neonatal asphyxia is thought to be due to the passage of meconium as a result of stimulation of the fetal gut by OM [13]. However, the maternal and fetal wellbeing need to be closely monitored when administering low dose OM. Low dose OM would be more acceptable to women compared to vaginal or intravenous interventions and would be easier to be administered. Furthermore, OM can be stored at room temperature (unlike vaginal dinoprostone), and is cheaper than vaginal dinoprostone. A systematic review and network meta-analysis which included vaginal and intra cervical dinoprostone, OM and vaginal misoprostol, and

the supracervical insertion of a Foley catheter, has demonstrated that there were no significant differences in VD rates between OM and the supracervical insertion of a Foley catheter, OM had the lowest CD rates, supracervical insertion of a Foley catheter had the lowest rate of excessive uterine activity with fetal CTG abnormalities, and vaginal misoprostol had the least risk of not achieving a VD but had the highest risk of excessive uterine activity with fetal CTG abnormalities [6].

The supracervical insertion of a Foley catheter is suitable for IOL in women with scarred uteri and women at risk of having compromised fetuses (eg pre-eclampsia and fetal growth restriction). Although it has been shown that keeping the supracervical Foley catheter for up to four days is safe, and that it is not associated with increased risks including ascending infection [2,5-9], the Foley catheter should not be inserted in the presence of overt vaginal or cervical infection, and appropriate antiseptic measures and sterile procedures should be adopted during its insertion. The urinary channel of the Foley catheter should be closed off with a sterile cap and the catheter should be taped to the woman's thigh, applying gentle traction. It should be kept *in situ* for at least 48hours. A large, multicenter randomized controlled trial involving 1845 participants has shown that after four days of the interventions, OM was not inferior to the insertion of a supracervical Foley catheter for IOL. The failed IOL rates after four days of the interventions, defined as MBS < 6, were 3.7% and 1.7% respectively (RR 2. 2, 95% CI 1.2 - 4. 0, p=0. 006) and there were no significant differences in maternal and neonatal morbidity and mortality between the two groups in the trial [2]. Therefore, OM should be

considered as an option for IOL in Sri Lanka and a supra cervical Foley catheter should not be removed after 24 hours.

The current trial was not powered to assess complications of the two interventions. Furthermore, as 50µg OM tablets were not available in Sri Lanka during the period of the trial, 200µg OM tablets were dissolved in 200ml of water and 50 ml of this solution was used as a 50µg OM dose. This could have caused small differences in the OM dose regimen. Although the participants and the other care givers could not be blinded to the interventions, the women would have had their early morning tea (but not the breakfast) prior to the first dose of oral misoprostol, and the study was not conducted on Saturdays and Sundays, these factors are unlikely to have had any significant effect on the primary outcomes. The assessment of MBS is subjective and prone to observer variations. However, the pre and post intervention assessments of MBS were carried out by the same skilled and experienced first author (BA) who was kept blind to the interventions until all the data had been collected and documented, and the main primary outcomes of VD, IVD and CD were objective and not liable to any bias.

Conclusion

Three doses of OM 50µg four hourly per day for 48 hours was feasible, and was more effective for IOL than the insertion of a supra cervical Foley catheter for 48 hours. Therefore, OM should be considered as an option for IOL in Sri Lanka. When the insertion of a supra cervical Foley catheter is used for pre induction cervical ripening, it should be kept in situ for at least 48 hours, as it can *per se* lead to IOL, without the need for subsequent amniotomy and intravenous oxytocin infusions.

Author contribution

BA was involved in collection, analysis, interpretation and presentation of data and writing of the manuscript. MG conceptualised and designed the study, and was involved in analysis, interpretation and presentation of data, and writing of the manuscript. RP was involved in data collection. FR was involved in monitoring the conduct of the trial and data collection. All authors read and approved the final manuscript.

Conflicts of interest

The authors have no competing interests.

Ethics approval

Ethics approval was obtained from the Ethical Review Committee, Faculty of Medicine, University of Ruhuna (ERC: Ruhuna 30.08.2016:3.10). Administrative approval was obtained from the Director THMG. The trial was registered in the Sri Lanka Clinical Trials Registry (SLCTR/2016/024) [14].

Patient consent

Informed written consent was obtained from all the participants.

Funding

No external funding was received for this study.

Abbreviations

OM – Oral Misoprostol
 IOL – Induction of Labour
 MBS – Modified Bishop Score
 GA – Gestational Age
 CD – Caesarean Delivery
 VD – Vaginal Delivery
 IVD – Instrumental Vaginal Delivery
 IDI – Induction to Delivery Interval
 CTG – Cardiotocography
 FAST – Fetal Acoustic Stimulation Test

List of figures and tables

Figure 1. Flow Diagram of the Method

Table 1. Characteristics of the participants at 40 weeks + 5 days' gestation (n=144)

Table 2. Primary outcomes at 41 weeks of gestation (n=144)

Table 3. Comparison of primary outcomes between primigravidae and multigravidae at 41 weeks of gestation (n=144)

Table 4. Complications of the Primary Interventions at 41 weeks' gestation (n=144)

Table 5. Secondary outcomes (n=144)

Table 6. Frequency of Complications in the trial (n=144)

References

1. Malik Goonewardene. Cervical ripening and induction of labour: Inpatient or outpatient, oral misoprostol or Foley catheter? *Ceylon Medical Journal* 2017; **62**: 117-20.
2. Ten Eikelder ML, Oude Rengerink K, Jozwiak M, *et al*. Induction of labor at term with oral misoprostol versus a Foley catheter (PROBAAT-II): a multicenter randomized controlled non-inferiority trial. *Lancet* 2016; **387**: 1619-28.
3. Somirathna D, Goonewardene M. Intra cervical Foley catheter for 24 hours vs three doses of oral Misoprostol for pre-induction cervical ripening in postdated pregnancies: a randomized controlled trial. *Ceylon Medical Journal* 2017; **62**(2): 77-82.

4. The Ministry of Health Sri Lanka. Guidelines for use of misoprostol in gynecology and obstetrics. *Circular Number P-49/66/2015* of 04.11.2015.
5. Diederens M, Gommers JSM, Wilkinson C, Turnbull D, Mol BWJ. Safety of the balloon catheter for cervical ripening in outpatient care: complications during the period from insertion to expulsion of a balloon catheter in the process of labour induction: a systematic review. *BJOG* 2018; **125** (9): 1086-95.
6. Chen W, Xue J, Peprah MK, *et al.* A systematic review and network meta-analysis comparing the use of Foley catheters, misoprostol and dinoprostone for cervical ripening in the induction of labour. *BJOG* 2016; **123**: 346-54.
7. McMaster K, Sanchez-Ramos L, Kaunitz AM. Evaluation of a Transcervical Foley Catheter as a Source of Infection: A Systematic Review and Meta-analysis. *Obstet Gynecol* 2015; **126**(3): 539-51.
8. Leopold B, Sciscione A. Is there a place for outpatient preinduction cervical ripening? *Obstet Gynecol Clin N Am* 2017; **44**: 583-91.
9. Ekele BA, Isah AY. Cervical ripening: how long can the Foley catheter safely remain in the cervical canal? *African J of Reprod Health* 2002; **6**(3): 98-102.
10. Kasiulevicius V, Apoka R, Filipaviciute. Sample size calculation in epidemiological studies, *Gerontologija* 2006; **7**(4): 225-31.
11. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Intrapartum Fetal Surveillance. Clinical Guideline 3rd Ed 2014, RANZCOG, Victoria, Australia, p19.
12. Diogo Ayres-de-Campos, Catherine Y. Spong, Edwin Chandraran, for the FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. FIGO consensus guideline on intrapartum fetal monitoring. *Int J Gynecol Obstet* 2015; **131**: 13-24.
13. Z, Weeks A. Oral misoprostol for induction of labour. *Cochrane Database Syst Rev* 2014. Issue 6. Art. No.: CD001338. DOI: 10.1002/14651858.CD001338.pub3. [Accessed 02.02.2018]
14. Sri Lanka Clinical Trials Registry. Available at <http://trials.slctr.lk/trials/551>