Intra Cervical Foley Catheter vs Oral Misoprostol for Pre Induction Cervical Ripening of Postdated Pregnancies

Goonewardene M, Kumara DMA, Ziard MH, Bhabu B

Abstract

Introduction: An intracervical Foley catheter is a common method used for pre-induction cervical ripening in Sri Lanka. Low dose oral Misoprostol (25 µg 2 hrly) has been recently recommended as a method for ripening of cervix and induction of labour (IOL)

Objectives: To compare the effectiveness of the insertion of an intra-cervical Foley catheter for 24 hrs versus two doses of oral Misoprostol - 25µg four hours apart, in ripening the cervix prior to IOL, in postdated pregnancies.

Methods: A Randomized controlled trial. Women with uncomplicated singleton pregnancies, having a cephalic presentation and a cervix unfavorable for IOL [modified Bishop Score (MBS) < 6] at 40 weeks and 6 days of gestation, were allocated to receive either two doses of oral Misoprostol - 25 µg, four hours apart (n=74) or intracervical Foley Catheter for 24 hrs (n=78), by stratified (primip / multip) block randomization. The following morning all were assessed and their MBS recorded by one of the last three authors, all of whom were blind to the interventions, as other doctors supervised and carried out the interventions. If the cervix was favourable, IOL was carried out with amniotomy and intravenous oxytocin infusion. The method of delivery and induction delivery interval (IDI) were recorded. If spontaneous labour (SOL) was established prior to this assessment, it was recorded.

Results: There were no significant differences in the distribution of parity, and the mean ages and the mean pre intervention MBS in the primigravidae and multigravidae, between the two study groups. There were significant increases in mean MBS (ranging from 2.6 – 3.3 and 95% CIs 1.7- 4.1, p <0.001) after the interventions in both groups. However there was no significant difference between the mean increases of MBS between the groups. In the primigravidae, the mean MBS after 24 hours was greater in the Foley catheter group compared to the misoprostol group (6.9, 95%CI 6.3 – 7.5 vs 5.7, 95% CI 4.8 – 6.7, p < 0.05). There were no significant differences in the proportions of primips and multips establishing SOL. More primips and multips had cervices favourable for IOL in the Foley catheter group compared to the misoprostol group (p < 0.05). There were no significant differences in the mean IDI after IOL; successful vaginal delivery after IOL; and the caesarean section rates between the groups. In the Misoprostol group there were no cases of uterine hyperstimulation, but two women complained of dyspepsia.

Conclusions: Intracervical Foley catheter for 24 hours was better than two doses of 25 µg misoprostol administered orally four hours apart, for pre induction cervical ripening in postdated pregnancies.

INTRODUCTION

A postdated pregnancy is one of the commonest indications for Induction of Labour (IOL). The success of IOL will depend on the favourability of the cervix for IOL, which is assessed by the Bishop score[1] and its modified versions[2]. Cervical ripening is the process that culminates in softening and stretchability of the cervix, making it favourable for IOL or facilitating spontaneous onset of labour (SOL). The ideal method of artificial cervical ripening should soften the unripe cervix without stimulating uterine contractions. Mechanical methods and pharmacological methods are used for cervical ripening.

In the mid-19th century a balloon catheter was used for the first time, as a cervical ripening agent[3]. The intra cervical insertion of a Foley catheter has been practiced as a method of cervical ripening for many years[4], and is commonly used in Sri Lanka. It causes mechanical separation of fetal membranes from the cervix and stimulates the release of local cytokines and prostaglandins. This leads to a breakdown of cross links between the glycosaminoglycans of the ground substance of the cervix and results in cervical ripening. There is evidence that the use of an intra-cervical Foley catheter carries an increased risk of infection (OR 2.05, 95 % CI 1.22 – 3.44)[5]. Therefore it is contraindicated in women with overt infections. Although it is associated with mild bleeding, maternal anxiety, some maternal discomfort and even pain sometimes, it is generally well tolerated by women, and with appropriate antiseptic and sterile techniques it is a safe and effective method for cervical ripening prior to IOL.

Misoprostol is a synthetic prostaglandin E_1 (PGE_1) analogue which was initially used as a gastric protective agent for prevention and treatment of peptic ulcers. Subsequently, when its action on the uterine myometrium was identified, it also entered the field of obstetrics and gynecology, where it is being used for many indications, of which IOL is one. Oral misoprostol has been shown to be rapidly absorbed after oral administration, reaching peak serum levels at 30 mins, having a half-life of approx. 20 – 40 mins, and declining rapidly after 120 mins, to remain low thereafter. (Product information: Misogyn tablets, Acme Formulation (P) Limited, Himachi Pradesh, India). Misoprostol has several potential advantages – stable at room temperature, relatively inexpensive and can be given via several routes (oral, buccal, sublingual and vaginal). It has also been shown that misoprostol is a safer and more effective method of IOL compared to the other

Academic Unit of Obstetrics & Gynaecology, Teaching Hospital Mahamodara, Galle, Sri Lanka.

Correspondence: Prof. Malik Goonewardene

E-mail: malikg@eureka.lk

Competing interests: None

conventional methods currently used and significantly reduced caesarean section (CS) rates has been reported following IOL with misoprostol[6-15]. On studying the evidence available, the WHO has graded the evidence as being of moderate quality and has made a strong recommendation to use oral misoprostol for IOL[6,7]. The recommended dose is 25µg administered orally at two hourly intervals up to a maximum of six doses per day.

Uterine hyper stimulation remains as a potential risk but is considered to be less than with vaginal prostaglandin E_2[11,15]. It has been shown that oral misoprostol carries a lower risk of hyperstimulation and neonatal asphyxia compared to vaginal misoprostol[6,9-,11]. The administration of a medication at two hourly intervals is logistically difficult in an antenatal ward with a heavy patient load. Furthermore the objective of the current study was to assess the effectiveness and feasibility of oral misoprostol in achieving only pre induction ripening of the cervix in postdated pregnancies, and not achieving IOL itself. Therefore it was decided to use only two doses of oral misoprostol 25µg given at four hourly intervals.

The cost of Foley catheters and misoprostol tablets are much less compared to PGE_2 which is also not freely available in Sri Lanka. Therefore if oral misoprostol gives similar or better results than the Foley catheter for cervical ripening, it could become a very acceptable method of pre induction cervical ripening in Sri Lanka.

METHOD

A randomized controlled trial was conducted at the Academic Obstetric Unit, Teaching Hospital, Mahamodara, Galle (THMG) from 02.01.2011 up to 15.03.2012.

A previous study carried out at the same unit showed that 47% of women with unfavourable cervices at a period of gestation (POG) of 40 weeks and 5 days established SOL or their cervices became favourable for IOL within the next 48 hours, without any intervention16. With the aim of achieving an increase of this percentage by a further 25% in the misoprostol group, the minimum sample size (having a power of 80% and a confidence interval of 95%) was calculated to be 120 using the standard formula[17]. When inflated by 25% to accommodate any dropouts or crossover between groups, the total sample size required, became 150. Ethical approval was obtained from the Ethical Review Committee of the Faculty of Medicine, Galle and the trial was registered in the Sri Lanka Clinical Trials Registry (SLCTR / 2011 / 002). Informed written consent was obtained from all the women who participated in the study. Women with uncomplicated singleton pregnancies having a cephalic presentation and a cervix unfavourable for induction of labour (MBS < 6) at a POG of 40 weeks and 6 days, were recruited consecutively from Monday to Friday excluding the weekends until the required sample was obtained.

Women with multiple pregnancies, malpresentations, pregnancies with previous CS or any contraindication for normal delivery or for the use of misoprostol, or had received any prior intervention for ripening of the cervix, were excluded.

All the women who consented to participate in the study had a 10 minute cardiotocograph (CTG) followed by a fetal acoustic stimulation test (FAST) if needed, to assess the fetal wellbeing. Women with a non-reactive CTG in spite of the FAST were excluded from the study.

The subjects were allocated to receive either two doses of oral Misoprostol - 25 µg, (Misogyn tablets, Acme Formulation (P) Limited, Himachi Pradesh, India) four hours apart or intracervical Foley catheter for 24 hrs, by stratified (primip / multip) block randomization. Sequentially numbered and sealed opaque envelopes coded with the appropriate treatment regimen were prepared by the first author. Each mother randomized to misoprotol or Foley group had the intervention administered in the ward by other doctors in the unit, who were not involved in the study, according to the pre-determined randomized allocation sequence.

The insertion of a Foley catheter was carried out as sterile, aseptic procedure, after cleaning the cervix and vagina with betadine. Routine fetal monitoring was carried out according to the unit protocol after insertion of intracervical Foley catheter or the administration of oral misoprostol.

Each mother in the misoprostol group had 25 µg of misoprostol administered orally four hours apart. These mothers were monitored with abdominal palpation and intermittent auscultation half hourly. A 10 minute CTG followed by FAST if needed was carried out at one hour after the intervention. If hyperstimulation and or evidence of fetal compromise were detected, appropriate measures were adopted according to the unit policies. If no such abnormality was detected 25 µg of oral misoprostol was repeated after four hours and the patient monitored for a further four hours as above.

The following morning all were assessed and their MBS was recorded by one of the last three authors, all of whom were blind to the interventions. If SOL was established or any woman underwent CS before the next morning (ie at 41 weeks gestation) the details were documented. If the cervix was favourable (MBS > 6), IOL was carried out with amniotomy and intravenous oxytocin infusion. The method of delivery and induction delivery interval (IDI) were recorded. If the cervix was not favourable for IOL, a CS was carried out, according to the unit policies.

The data were stored confidentially in a password protected, ongoing computer database, by the last three authors. The randomized allocation sequence was kept confidentially by the first author until all the data were entered in to the database. Means and 95% confidence intervals were calculated for the continuous variables and Student's t-test was used for comparison of means. The medians and inter quartile ranges were calculated for the parity distributions

Table 1. The basic characteristics of subjects (n = 152)			
	Foley catheter (n=78)	Misoprostol (n=74)	p
Parity: Range	1 to 7	1 to 6	NS
Median (IQR)	1(1-3)	1(1-2)	
Primigravidae	n=36	n=40	
Age in years: Range	17 - 34	18 - 37	NS
Mean (95% CI)	25.6 (24.1-27.1)	25.2 (24-26.4)	
Mean pre intervention MBS (95% CI)	3.4 (3-3.9)	2.9 (2.6-3.3)	NS
Multigravidae	n=42	n=34	
Age in years: Range	20 - 41	23 - 40	NS
Mean (95% CI)	30.1 (28.6-32.2)	30.7 (29.1-32.2)	
Mean pre intervention MBS (95% CI)	3.3 (3-3.6)	3.4 (3-3.8)	NS

MBS = Modified Bishop Score
IQR = Inter Quartile Range
NS = Not significant (p > 0.05)

Table 2. Outcomes after 24 hrs of the interventions (n = 152)			
	Foley catheter	Misoprostol	p
Primigravidae	n=36	n=40	
Spontaneous onset of labour (%)	1 (2.8)	4 (10.0)	0.20
Cervix favourable for induction of labour (%)	28 (77.8)	21 (52)	0.02
Emergency Caesarean Section (%)	1 (2.8)	2 (5)	0.62
Multigravidae	n=42	n=34	
Spontaneous onset of labour (%)	7 (16.7)	11 (32.4)	0.11
Cervix favourable for induction of labour (%)	28 (66.7)	14 (41.2)	0.03
Emergency Caesarean Section (%)	0	1 (3)	0.34

and the Mann-Whitney test was used to compare medians. The Chi Square test was used to compare proportions. A p value of < 0.05 was considered as being statistically significant.

RESULTS

A total of 152 subjects (Foley catheter group =78 and misoprostol group = 74) were recruited for the study. There were no significant differences in the distribution of parity, and the mean ages and the mean pre intervention MBS in the primigravidae and multigravidae, between the two study groups. [Table 1]

Although numerically more women in the misoprostol group (15 out of 74) appeared to have established SOL compared to the Foley catheter group (8 out of 78), this difference was not statistically significant (p = 0.1) Greater proportions of women in the Foley catheter group (77.8% in primips and 66.7% in multips) were favourable for IOL after 24 hours of the intervention compared to the misoprostol group (52% primips and 41.2% in multips), (p <0.05). [Table 2].

In the Misoprostol group there were no cases of uterine hyperstimulation, but two women complained of dyspepsia.

As 27 subjects established SOL or underwent emergency CS during the next 24 hours only 125 of the 152 subjects remained for assessment after 24 hours of the interventions. In the primigravidae, the mean MBS after 24 hours was greater in the Foley catheter group compared to the misoprostol group (6.9, 95%CI 6.3 – 7.5 vs 5.7, 95%CI 4.8 – 6.7, p < 0.05). However no significant differences were observed in the MBS in multigravidae or the change in mean MBS in primigravidae and multigravidae [Table 3].

Of the 125 subjects who were assessed after 24 hrs of the intervention, 114 subjects underwent IOL and the remaining 11 had scheduled CS. Of the 114 who underwent IOL, 26 had emergency CS. Of these 114 subjects who underwent IOL, 10 in the Foley catheter group and 13 in the misoprostol group had unfavourable cervices (MBS 3-5). In these 23 women who underwent IOL with unfavourable cervices the mean MBS was 4.26 (95% CI 3.94-4.59). However there were no significant differences in the CS rates after IOL between those who had favourable cervices and those who had unfavourable cervices in both study groups. [Table 4]

In the 114 women who underwent IOL, the mean IDI appeared to be shorter in the multigravidae in the Foley catheter group (223 mins, 95% CI 185.8 – 260.2) compared to the multigravidae in the misoprostol

Table 3. Modified Bishop Score after 24 hrs (n=125)			
	Foley catheter	Misoprostol	p
Primigravidae :	n=34	n=34	
Mean Modified Bishop Score (95 % CI)	6.9 (6.3 -7.5)	5.7 (4.8 – 6.7)	0.049
Change in mean Modified Bishop Score (95% CI)	3.3 (2.8-3.9)	3.3 (2.5-4.1)	0.52
Multigravidae :	n=35	n=22	
Mean Modified Bishop Score (95 % CI)	6.5 (6.0 – 7.1)	6 (5.1 – 6.8)	0.33
Change in mean Modified Bishop Score (95% CI)	3.3 (2.7-3.9)	2.6 (1.7-3.5)	0.19

Table 4. Cervical favourability and outcomes (n=125)			
	MBS > 6	MBS 3-5	p value CS vs ND after IOL
Foley Catheter Group	n=56	n=14	0.87
Induction of Labour (IOL) →Normal delivery (ND)	46 (82.1)	8 (80)	
Induction of Labour →Caesarean Section (CS)	10 (17.8)	2 (20)	
Scheduled Caesarean Section	0	4	
Misoprostol Group	n = 35	n = 20	0.39
Induction of Labour →Normal delivery	26 (74.3)	8 (61.5)	
Induction of Labour →Caesarean Section	9 (25.7)	5 (38.5)	
Scheduled Caesarean Section	0	7	

Table 5. Characteristics and outcomes in subjects who underwent induction of labour (n=114)			
	Foley catheter	Misoprostol	p
Primigravidae	n=34	n=29	
Mean MBS at IOL (95% CI)	6.6 (6.1 – 7.2)	6.2 (5.2 – 7.1)	0.52
Induction delivery interval - mins.	354 (283.4 – 424.6)	355 (266.2 – 443.2)	0.98
Emergency Caesarean Section (%)	8 (24.3)	12 (41.4)	0.15
Mean MBS at IOL (95% CI) in subjects who had successful IOL	7.1 (6.4 – 7.8)	6.6 (5.3 – 7. 9)	0.46
Multigravidae	n=32	n=19	
Mean MBS at IOL (95% CI)	6.7 (6.1 – 7.3)	6.5 (5.7 – 7.3)	0.87
Induction delivery interval – mins.	223 (185.8 -260.2)	289 (220.4 – 357.6)	0.09
Emergency Caesarean Section (%)	4 (12.5)	2 (5.6)	0.88
Mean MBS at IOL (95% CI) in subjects who had successful IOL	6.8 (6.2 – 7.4)	6.7 (5.8 – 7.5)	0.77
MBS = Modified Bishop Score IOL = Induction of Labour			

Table 6: Caesarean delivery after the interventions (n=152)			
	Foley catheter n=78	Misoprostol n=74	p
Emergency Caesarean Section within 24hrs (%)	1 (1.3)	3 (4.0)	0.29
Emergency Caesarean Section after IOL (%)	12 (15.4)	14 (18.9)	0.56
Scheduled Caesarean Sections after 24 hrs. (%)	4 (5.1)	7 (9.5)	0.30
Total Caesarean Sections (%)	17 (21.8)	24 (32.4)	0.14

group (289 mins, 95% CI 220.4 – 357.6). However this difference was not statistically significant (p = 0.09). [Table 5]

The overall CS rate in the misoprostol group (32.4%) appeared to be greater than the CS rate in the Foley catheter group (21.8%) although this difference was not statistically significant. (p= 0.1) Although the proportion of subjects who had scheduled CS for unfavourable cervices after 24 hrs of the interventions, was greater in the misoprostol group (9.5%) compared to the Foley catheter group (5.1%), this difference was also not statistically significant (p = 0.3). [Table 6]

DISCUSSION

The insertion of an intracervical Foley catheter for 24 hours was better than two doses of 25 µg misoprostol administered orally four hours apart, in causing ripening of the cervix prior to IOL, in both primigravidae as well as multigravidae with postdated pregnancies . This finding is probably due to the fact that only two doses of 25 µg misoprostol were used in the current study. The recommended dose of oral misoprostol is 25 µg administered two hourly, up to a maximum of six doses, with a view to achieving IOL[6,7]. The objective of the current study was not to achieve IOL but only to achieve adequate ripening of the cervix to enable IOL with the currently practiced method of amniotomy and intravenous oxytocin infusion. Therefore since the authors had no prior experience in the use of oral misoprostol for ripening of the cervix, this two dose regimen was decided upon for this preliminary study.

The observation that the change in mean MBS after insertion of an intracervical Foley catheter was not significantly different from the change in mean MBS after two doses of 25 µg misoprostol administered orally four hours apart, indicates that both regimens are effective for pre induction cervical repining although the latter regimen is less effective than the former regimen. As there were no cases of uterine hyperstimulation in the misoprostol group, this method can be considered to be a safe option for pre induction cervical ripening of postdated pregnancies. A large, multicentre randomized controlled trial (PROBATT – II Study) is currently being conducted in the Netherlands to compare the safely and cost effectiveness of intracervical Foley catheter vs oral misoprostol for IOL. In the PROBATT – II Study, 50 µg of misoprostol is being administered every four hours with

a maximum of three times a day for four days and this is being compared with an intracervical Foley catheter for four days[18]. A study to compare the safety and effectiveness of 50 µg of oral misoprostol administered four hourly up to a maximum of three doses for 24 hours vs an intracervical Foley catheter for 24 hours as pre induction cervical ripening methods, has been planned to be conducted in the Academic Unit of Obstetrics and Gynaecology of the THMG.

CONCLUSIONS

The insertion of an intracervical Foley catheter for 24 hours was better than two doses of 25 µg misoprostol administered orally four hours apart, in causing ripening of the cervix prior to IOL, in both primigravidae as well as multigravidae, with postdated pregnancies. Further research is required to identify the optimal dose and frequency of oral misoprostal which should be used for cervical ripening prior to IOL.

CONFLICTS OF INTERESTS

None.

ACKNOWLEDGEMENT

The misoprostol 25 µg tablets (Misogyn tablets, Acme Formulation (P) Limited, Himachi Pradesh, India) were supplied by Dr. Kurian Joseph, Joseph's Nursing Home, Chennai, India. ■

REFERENCES

1. Bishop EH. Pelvic scoring for elective induction. *Obstetrics and Gynecology* 1964; 24(2): 266 – 268.
2. Biswas A, Arulkumaran S. Induction of labour. In: Arulkumaran S, Ratnam SS, Bhasker Rao K (eds). *The Management of Labour,* Vol. 14. Madras: Orient Longman Ltd, 1996; 213-227.
3. Woodman WB. Induction of labor at eight month and delivery of a living child in less than four hours by Dr. Barnes method. *Lancet* 1863; 1: 10
4. Bishop EH. Elective induction of labor. *Obstetrics and Gynaecology* 1955; 5: 519-527.
5. Heinemann J, Gillen G, Sanchez-Ramos L, Kaunitz AM. Do mechanical methods of cervical ripening increase infectious morbidity? A systematic review. *American Journal of Obstetrics and Gynecology* 2008; 199 (2):177-88.
6. World Health Organization. WHO Recommendations for induction of labour. 2011. WQ440, World Health Organization, Geneva, Switzerland.
7. Abdel-Aleem H. Misoprostol for cervical ripening and induction of labour: RHL Commentary. 2011. The WHO Reproductive Health Library, World Health Organization, Geneva, Switzerland.
8. Sanchez-Ramos L, Kaunitz AM, Wears RL et al. Misoprostol for cervical ripening and labor induction: a meta-analysis. *Obstetrics and Gynaecology* 1997; 89: 633-642.
9. Rahman H, ,Pradhan A, ,Kharka L et al, Comparative evaluation of 50 microgram oral misoprostol and 25 microgram intravaginal misoprostol for induction of labour at term: a randomized trial. *Journal of Obstetrics and Gynaecology Canada* 2013; 35(5): 408-416.
10. Alfirevic Z, Weeks A. Oral misoprostol for induction of labour, Cochrane database of systematic reviews 2006; Issue 2. ART. No. CD 001338; doi /10.1002/ 14651858. CD001338. pub2 (Accessed on 02.06.2014)
11. Kundodyiwa TW, Alfirevic Z, Weeks AD. Low-dose oral misoprostol for induction of labor: a systematic review. *Obstetrics and Gynecology* 2009; 113 (2 Pt 1): 374-383.
12. Tan T-C, Yan S, Chua T, Biswas A, Chong Y-S. A randomized controlled trial of low-dose misoprostol and dinoprostone vaginal pressaries for cervical priming. *British Journal of Obstetrics and Gynaecology* 2010; 117: 1270 – 1277.
13. Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systemic Reviews* 2004, Issue 4. Art. No.: CD004221. DOI: 10.1002/14651858.CD004221. pub2 (Accessed on 02.06. 2014).
14. Hofmeyr GJ, Gulmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database of Systemic Reviews 2003, Issue 1. Art. No.: CD000941. DOI: 10.1002/14651858.CD00941 (Accessed on 02.06.2014).
15. Wing, Deborah A. MD; Ortiz-Omphroy, Gabriela MDetal, A comparison of intermittent vaginal administration of misoprostol with continuous dinoprostone for cervical ripening and labor induction. *American Journal of Obstetrics & Gynecology* 1997; 177(3):612-618.
16. Rameez MFM, Goonewardene IMR. Nitric oxide donor isosorbide mononitrate for pre-induction cervical ripening at 41 weeks' gestation: a randomized controlled trial. *Journal of Obstetrics and Gynaecology Research* 2007 August; 33(4): 452-456.
17. Armitage P, Berry G (eds). Statistical Methods in Medical Research, 3rd edn. London: Blackwell Science Ltd, 1994; 200.
18. Ten Eikelder MLG, Neervoort F, Rengerink KO, et al. Induction of labour with a Foley catheter or oral misoprostol at term: the PROBAAT-II study, a multicentre randomised controlled trial; *BMC Pregnancy and Childbirth* 2013; 13: 183.