Original Article

Sequential Foley Catheter and Misoprostol Versus Misoprostol Alone for Induction of Labor in Postdated Pregnancy: a Randomized Controlled Trial

Baburam Dixit (Thapa), Tara Manandhar, Sarita Sitaula, Tulasa Basnet
Department of Obstetrics and Gynecology, BP Koirala Institute of Health Sciences, Dharan, Nepal

Abstract

Introduction: Induction of labor is done with the aim of normal vaginal delivery. There are different methods; mechanical like intra-cervical Foley's or pharmacological agents like misoprostol or dinoprostone.

Objectives: To compare sequential use of Foley's catheter and vaginal misoprostol in comparison with vaginal misoprostol only.

Methods: Patients with period of gestation more than or equal to 41 weeks without any complications were assigned randomly according to computer generated randomization into sequential use of intracervical Foley followed by vaginal misoprostol after 24 hours (sequential group) or vaginal misoprostol only. Primary outcome was rate of normal vaginal delivery. Secondary outcomes were induction to delivery interval, maternal and fetal morbidity.

Results: Rate of normal vaginal delivery in sequential group (n= 353) and misoprostol alone group (n= 356) was 71.6% and 53.3% ($p < 0.001$) but the time to delivery from induction is statistically more in sequential group (30.3 vs. 11.2 hours, $p< 0.001$). Maternal outcomes like postpartum hemorrhage, hyper-stimulation syndrome, chorioamnitis and neonatal outcomes like low Apgar score, meconium stained baby and stillbirth are similar in both the groups.

Conclusions: The priming of cervix using intracervical Foley catheter before giving vaginal misoprostol was beneficial in increasing the rate of normal vaginal delivery but it increased the induction to delivery interval.

Keywords: cesarean section; induction; non-stress test

Introduction

Different methods are used for labor induction with the aim of normal vaginal delivery. Intra-cervical Foley's catheter acts by either direct distension or release of endogenous prostaglandins.[1] It is as effective as prostaglandins with less adverse effects[2] but with potential risk of infections not seen in randomized trials.[3-5] Misoprostol either vaginal or oral[6,7] helps in both cervix ripening and uterine contractions by increasing collagenases and proteinases with in the cervix.[8]

Different studies comparing safety and effectiveness of different methods are not consistent.[1] So, the optimal method is unclear.[9] Some have shown that they have synergistic effect when used in combination[10,11] while some show they have similar effects.[12,13]

Different methods of induction are used in different centers. In BPKIHS, either misoprostol alone or Foleys catheter alone is being used for induction of labor.

This study was designed to compare the efficacy of the sequential use of Foley catheter and

Address for correspondence
Dr. Baburam Dixit (Thapa), Assistant Professor
Department of Obstetrics & Gynecology,
BP Koirala Institute of Health Sciences, Dharan
Email: baburamdixit@yahoo.com

vaginal misoprostol; with vaginal misoprostol alone for normal vaginal delivery so that there will be option for induction of labor.

Methods

This is an open-label randomized controlled trial, which was conducted in B. P Koirala Institute of Health Sciences (BPKIHS). Women with period of gestation (POG) ≥ 41 weeks without exclusion criteria requiring induction of labor were recruited. Period of gestation was calculated by last menstrual period and confirmed with early ultrasound. Postdated patients with hypertension, diabetes, ruptured membranes, intrauterine death and any other conditions like multiple pregnancy, previous cesarean section and non-cephalic presentations were excluded. Patients who had irregular menstrual cycles and didn't have 1st trimester ultrasound were also excluded. Study was conducted after ethical clearance from Institutional Review Committee of BPKIHS. The participants were given written information about the trial, and for those who agreed to participate, informed written consent was obtained prior to recruitment. Computer generated randomization sequence was used. They were allocated to either sequential induction group or misoprostol alone group with 1:1 allocation. To decrease the information bias patient were recruited only after patients were counseled regarding risk and benefits of both the methods of induction and they gave informed consent. After random allocation, Bishop Score was assessed by resident doctor and proceeded for induction, if score < 6. In sequential induction group, Foley's catheter 16 FG was inserted with aseptic precautions and balloon inflated intra-cervically with 40-60 ml of distilled water. External end of catheter was fixed on thigh without traction. Foleys catheter was removed after 24 hours if it did not expel itself. If it expelled out, it was not reinserted and the woman was observed for 24 hours from Foleys insertion. It was removed if woman requested to and excluded from the study. If patient went to labor she was shifted to labor room and managed accordingly. If patient didn't go to labor, after 24 hours of Foleys insertion, 25 µg of misoprostol was inserted per vaginally in posterior fornix and repeated in 4 and 8 hours with maximum 3 doses. If patient didn't go to labor even after 4 hours of third dose, she was termed as failed induction and patient was taken for lower segment caesarean section (LSCS). If she went to labor, she was taken to labor room and managed accordingly.

In the group assigned for misoprostol alone; 25 µg of misoprostol was inserted per vaginally in posterior fornix and repeated in 4 and 8 hours with maximum 3 doses. If patient didn't go to labor even after 4 hours of third dose, she was termed as failed induction and patient was taken for lower segment caesarean section (LSCS). If she went to labor, she was taken to labor room and managed accordingly.

The primary outcome was taken as rate of normal vaginal delivery (NVD) and secondary outcome were induction to delivery interval, and maternal complications like maternal infection, postpartum hemorrhage (PPH) and neonatal outcomes meconium stained liquor (MSL), Apgar score at 5 minutes and stillbirth. For intrapartum infection, any two of the criteria should be present: maternal fever (≥ 38 °C) during labor, fetal tachycardia (≥ 160 bpm),

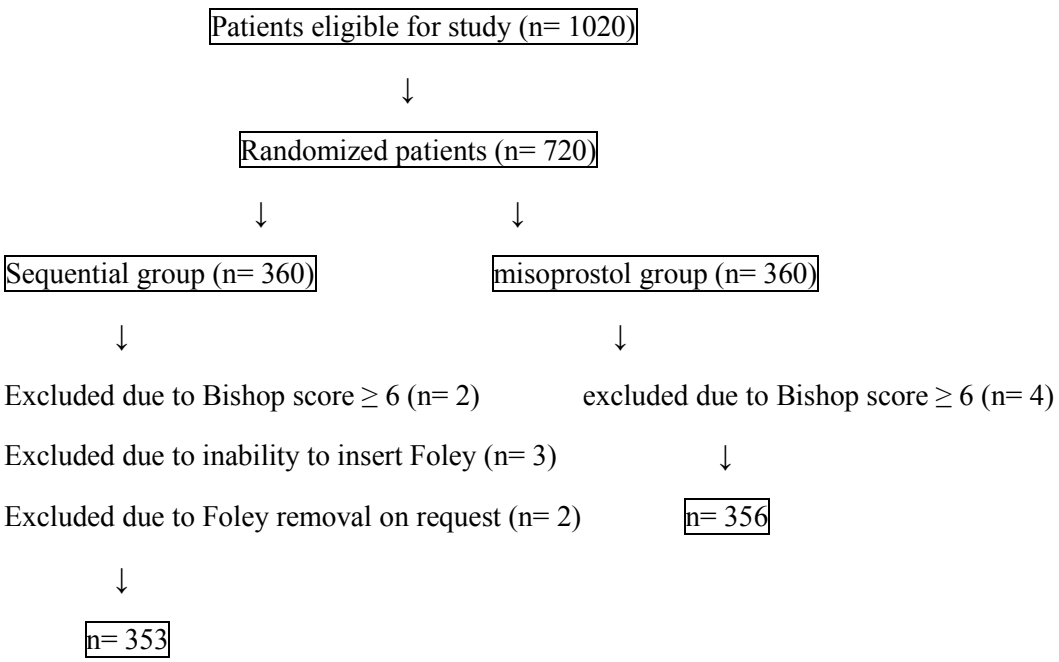
uterine tenderness, purulent amniotic fluid or vaginal discharge and total white cell count > 20,000/mm.[3] Antibiotics were prescribed for them.

Sample size was calculated using previous studies. Previous study[14] shows success rate of normal vaginal delivery in sequential group of about 67% and with misoprostol alone was about 59%. Taking this into account sample size of 344 in each group would be required with α= 0.05 and β = 0.20**.** OpenEpi data software was used to calculate the sample size. All data were collected prospectively with the use of structured Proforma and were recorded. The data were entered in MS excel and were analyzed using SPSS version 11.5. P value of ≤ 0.05 was considered statistically significant.

Results

During the study period, 1020 patients were eligible for the study. Among them, 720 patients gave informed consent for the trial. The flow diagram of the study is given in Figure 1. 360 patients were randomized in each group. Of 360 who were randomly assigned to the sequential group, four patients were excluded because of high Bishop score ≥ 6; three were excluded because of inability to insert the Foley catheter and two were excluded due to removal of Foley on request by the woman. In misoprostol only group, four patients were excluded because of high Bishop score ≥ 6. In the end, 353 patients in the sequential group and 356 patients in the misoprostol only group were included.

Figure 1: Flow diagram of the study



The baseline characteristics of both the group were similar (Table 1). Among the total patients, 253 (71.7%) patients had normal vaginal delivery in the sequential group whereas 190 (53.3%) patients had normal delivery in misoprostol alone group. This difference was statistically significant (p = 0.001, Table 2) and is significant even when considered differentiating with parity.

Table 1: Baseline characteristics

Characteristics	Sequential group (n= 353)	Misoprostol group (n= 356)
Age	24.87	24.92
Nullipara	319	327
Period of gestation	41+3 wks	41+5 wks
Bishop score	3	3

Table 2: Primary outcome

Outcome variables	Sequential group (n= 353)	Misoprostol group (n= 356)	P value	Rate difference (CI)
Normal vaginal delivery	253 (71.7%)	190 (53.3%)	0.001	1.38 (1.03- 1.73)
Cesarean section	96 (27.2%)	156 (43.9%)	0.017	4.06 (2.6- 5.5)
Instrumental delivery	4 (1.1%)	10 (2.8%)	0.109	2.21 (1.83- 2.66)

Induction to delivery interval in sequential group was 30.3 hours and 11.2 hours in misoprostol only group, which was statistically significant (p= 0.001). The most common cause of cesarean in both the cases were non-reassuring non-stress test but there was significantly higher number of failed induction in vaginal misoprostol group than in sequential group (p= 0.017). Other maternal and neonatal outcomes are shown in Table 3 and 4. Only three patients had intrapartum infection with maternal fever and fetal tachycardia in sequential group. There were no cases of maternal fever in misoprostol only group. There were two still births in the sequential group and only one still birth in misoprostol only group.

Table 3: Secondary outcome (maternal)

Outcome variables	Sequential group (n= 353)	Misoprostol group (n= 356)	P value
Induction to delivery interval (hrs)	30.3	11.2	**< 0.001**
Indications of cesarean section			
Failed induction	22	58	**0.017**
Failure to progress	20	7	**< 0.001**
in 1st stage	2	6	0.435
Failure to progress	35	64	0.457

in 2nd stage	17	20	0.293
Non reassuring NST	0	01	0.453
Meconium stained liquor			
Cord prolapse			
Hyperstimulation syndrome	01	00	0.315
Postpartum hemorrhage	12	18	0.273

Table 4: Secondary outcome (Fetal)

Outcome variables	Sequential group (n= 353)	Misoprostol group (n= 356)	P value
MSL	54	66	0.250
Apgar score at 5 minutes (<7)	12	16	0.788
Still birth	2	1	0.558

The rate of normal vaginal delivery was significant even when the patients were compared according to parity but the rate of cesarean section was statistically significant in nulliparas but not in parous women (Table 5).

Table 5: Outcome in nulliparous and parous women

Outcome variables	Nulliparous			Parous		
	Study group (n= 224)	Control group (n= 240)	**P value**	Study group (n= 129)	Control group (n= 116)	**P value**
NVD	147	107	**0.001**	105	82	**0.04**
LSCS	73	125	**0.001**	24	32	0.09
Instrumental delivery	4	8	0.294	0	2	0.13
Induction to delivery interval	31.4	11.75	**0.03**	30.9	10.2	**0.04**
PPH	5	12	0.113	7	6	0.92
MSL	45	48	0.981	9	18	0.54
Apgar score at 5 min (<7)	21	26	0.683	3	8	0.08
Still birth	2	1	0.52	0	0	-

Discussion

This study assessed the use of Foley catheter before vaginal misoprostol for induction of labor in postdated pregnancy. Our analyses showed that the sequential induction with Foley followed by vaginal misoprostol have higher success vaginal delivery rate than with vaginal misoprostol only (71.6% vs. 53.3%) but they have longer induction to delivery interval (30.3 hours vs. 11.2 hours) than vaginal misoprostol only group. When assessed according to parity, this finding did not differ. Other maternal and neonatal outcomes were comparable.

The strength of this study was that it is a randomized controlled trial and the patients involved were homogenous as only postdated patients with no other co-morbidities were included. The limitation was that it didn't involve all the patients that need cervical priming before induction and the result may not be relevant to all the patients who need induction.

There are different studies, which show that sequential use of Foley followed by vaginal misoprostol has higher vaginal delivery or lower cesarean section as compared to the vaginal misoprostol only but have longer induction to delivery interval[14,15] which was similar to our study. Study done by Kehl et al[14] showed normal vaginal delivery in sequential induction was about 67.9% and induction to delivery interval was 32.4 hours which was similar to our study where we had normal vaginal delivery rate of 71.6% and induction to delivery interval was 30.3 hours but different to the study done by OA Rust et al[13] where rate of Cesarean was similar in both the misoprostol induction and combined group.

Induction with Foley catheter has been reported to be a method that is well accepted by women[16] but this study showed that cervical priming with Foleys still results in unfavorable cervix. The common sequential use was with oxytocin rather than misoprostol.[17] Different studies have shown the beneficial effect of misoprostol in comparison to oxytocin.[6]

There are very few studies that compared sequential Foley followed by vaginal misoprostol but there are numerous studies that have concurrent use of Foley and vaginal misoprostol which has beneficial effects on normal vaginal delivery and decreased cesarean section rate.[18,19]

Although there has been concern about increased risk of infection associated with use of Foleys catheter;[12] this has not been demonstrated in randomized controlled trials[13-15] which is also consistent with our study. Study by Barrilleaux PS et al[12] showed infection rate with Foley's catheter insertion was about 3% which was higher than in our study which had intra-partum infection rate of about 0.84% only. Neonatal outcomes like meconium stained liquor, low Apgar score and stillbirth were comparable in both the groups; which are also similar in other studies.[14,15]

Future investigations about mechanical methods for induction should also focus on the possibility of out-patient priming of cervix with these methods and also the immediate use of vaginal misoprostol after Foley expulsion to decrease

the induction to delivery interval in sequential group.

Conclusions

The use of intra-cervical Foley catheter for priming of cervix before inducing the patient with vaginal misoprostol was beneficial to increase the chance of normal vaginal delivery although it caused prolonged induction to delivery interval.

References

1. Jozwiak M, Bloemenkamp KW, Kelly AJ, Mol BW, Irion O, Boulvain M. Mechanical methods for induction of labor. Cochrane Database Syst Rev. 2012; 3: CD001233. PMid: 22419277.
2. Shechter-Maor G, Haran G, Sadeh-Mestechkin D, Ganor-Paz Y, Fejgin MD, Biron-Shental T. Intra-vaginal prostaglandin E2 versus double balloon catheter for labor induction in term oligohydramnios. J Perinatol. 2015; 35: 95-8. DOI: 10.1038/JP.2014.173.
3. Jozwiak M, Oude RK, Benthem M, van Beek E, Dijksterhuis MG, de Graaf IM. Foley catheter versus vaginal prostaglandin E2 gel for induction of labor at term (PROBAAT trial): an open- label randomized controlled trial. Lancet. 2011; 378: 2095-103. DOI: 10.1016/S0140-6736(11)61484-0.
4. Pennell CE, Henderson JJ, O'Neill MJ, McCleery S, Doherty DA, Dickinson JE. Induction of labor in nulliparous women with an unfavorable cervix: a randomised controlled trial comparing double and single balloon catheters and PGE2 gel. BJOG. 2009; 116: 1443-52. PMid: 19656148
5. Prager M, Eneroth-Grimfors E, Edlund M, Marions L. A randomised controlled trial of intravaginal dinoprostone, intravaginal misoprostol and transcervical balloon catheter for labor induction. BJOG. 2008; 115 (11): 1443-50. PMid: 18715244
6. Alfirevic Z, Weeks A. Oral misoprostol for induction of labor. Cochrane Database Syst Rev. 2006; CD001338. PMid: 16625542
7. Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labor. Cochrane Database Syst Rev. 2004; (4): Cd004221. PMid: 15495088
8. Kelly AJ, Kavanagh J, Thomas J. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labor at term. Cochrane Database Syst Rev. 2003; 4: CD003101. PMid: 14583960
9. Chen W, Xue J, Peprah MK, Wen SW, Walker M, Gao Y, Tang Y. A systematic review and network meta-analysis comparing the use of Foley catheters, misoprostol, and dinoprostone for cervical ripening in the induction of labor. BJOG. 2016; 123: 346-54. DOI: 10.1111/1471-0528.13456.
10. Carbone JF, Tuuli MG, Fogertey PJ, Roehl KA, Macones GA. Combination of Foley bulb and vaginal misoprostol compared with vaginal misoprostol alone for cervical ripening and labor induction: a randomized controlled trial. Obstet Gynecol. 2013; 121: 247-52. PMid: 23303106
11. Hill JB, Thigpen BD, Bofill JA, Magann E, Moore LE, Martin JN Jr. A randomized clinical trial comparing vaginal misoprostol versus cervical Foley plus oral misoprostol

for cervical ripening and labor induction. Am J Perinatol. 2009; 26(1): 33-8. PMid: 18850516

12. Barrilleaux PS, Bofill JA, Terrone DA, Magann EF, May WL, Morrison JC. Cervical ripening and induction of labor with misoprostol, dinoprostone gel, and a Foley catheter: a randomized trial. Am J Obstet Gynecol. 2002; 186 (6): 1124-9. PMid: 12066084
13. Rust OA, Greybush M, Atlas RO, Jones KJ, Balducci J. Preinduction cervical ripening. A randomized trial of intravaginal misoprostol alone vs. a combination of transcervical Foley balloon and intravaginal misoprostol. J Reprod Med. 2001; 46(10): 899-904. PMid: 11725734
14. Kehl S, Ziegler J, Schleussner E, Tuschy B, Berlit S, Kirscht J et al. Sequential use of double-balloon catheter and oral misoprostol versus oral misoprostol alone for induction of labor at term (CRBplus trial): a multicentre, open-label randomised controlled trial. BJOG. 2015; 122: 129-36. DOI 10.1111/1471-0528.13116.
15. Ande AB, Ezeanochie CM, Olagbuji NB. Induction of labor in prolonged pregnancy with unfavorable cervix: comparison of sequential intra-cervical Foley catheter-intravaginal misoprostol and intravaginal misoprostol alone. Arch Gynecol Obstet. 2012; 285: 967-77. DOI: 10.1007/s00404-011-2094-4.
16. Kehl S, Welzel G, Ehard A, Berlit S, Spaich S. Women's acceptance of a double-balloon device as an additional method for inducing labor. Euro J Obstet Gynecol Reprod Biol. 2013; 168: 30-5. DOI: 10.1016/j.ejogrb.2012.12.018
17. Vaknin Z, Kurzweil Y, Sherman D. Foley catheter balloon vs. locally applied prostaglandins for cervical ripening and labor induction: a systematic review and metaanalysis. Am J Obstet Gynecol. 2010; 203: 418-29. DOI: 10.1016/j.ajog.2010.04.038.
18. Lisa D, Katheryne L., Michal A, Mary D. Sindhu K. Mechanical and Pharmacologic Methods of Labor Induction: A Randomized Controlled Trial. Obstet Gynecol. 2016; 128(6): 1357-64. DOI: 10.1097/AOG.0000000000001778.
19. Rust O, Greybush M, Atlas R, Jones K, Balducci J. Preinduction cervical ripening: A randomized trial of intravaginal misoprostol alone versus a combination of transcervical Foley balloon and intravaginal misoprostol. J Reprod Med. 2001; 46: 899-904. PMid: 11725734