Original Article

Outcome of induction of labor with prostaglandin E1 25 mg vaginal tablet – A retrospective study

Puliyath G, Balakrishnan A, Vinod L, Hameed H

Department of Obstetrics and Gynaecology, SUT Academy of Medical Sciences, Vencode, Vattapara, Trivandrum, Kerala, India

ABSTRACT

Context: Labor induction with prostaglandin E1 (PGE1) vaginal tablet results in shorter induction delivery interval and decreased rate of failed induction of labor and reduced caesarean section rate. However, higher doses may be associated with uterine hyper stimulation. It is therefore necessary to determine the safe dose of PGE1 for labor induction.

Aims: To assess the maternal and neonatal outcome with use of 25 mg vaginal misoprostol for induction of labor.

Settings and Design: A retrospective analysis conducted in an obstetric department of a tertiary care teaching institute.

Materials and Methods: The sample consists of women with singleton term pregnancy, with Bishop's score <6 compared with women with spontaneous onset of labor.

Statistical Analysis Used: Statistical significance was assessed at 5% level of significance. Chi-square test, with correction for continuity where applicable, was carried out to compare proportions across subgroups or between induction and spontaneous onset groups.

Results: The rate of vaginal delivery was higher among spontaneous onset group compared with induction group (χ^2 (1) = 30.3, P < 0.001). The induction delivery interval of vaginal delivery was less than 24 h in 91.85% of women. Neonatal intensive care unit admission frequency was similar among both groups (χ^2 (1) = 0.14, P = 0.704). The induction group was with less frequency of meconium staining than the control group (χ^2 (1) = 8.05, P = 0.0046).

Conclusion: Our study showed a higher rate of vaginal delivery with induction delivery interval less than 24 h in a majority of women with better neonatal and maternal outcomes.

Key words: Induction of labor; labor; prostaglandin E1; prostaglandins in labor; vaginal misoprostol.

Introduction

Being one of the most common obstetric interventions, labor induction is done in 1 of 5 pregnancies in developed countries and 1 in 10 in developing and underdeveloped countries.[1] Induction of labor is done when the benefit of delivery outweighs the potential risks of continuing the pregnancy, like gestational hypertension, intrauterine growth retardation, postdated pregnancy, premature rupture of membranes, and gestational diabetes.[2] However, induction of labor in women with unfavorable cervix may often lead to prolonged labor, increased risk of instrumental deliveries and caesarean section, increased risk of postpartum hemorrhage, prolonged hospital stay, and admission to neonatal intensive care unit (NICU).[3] Various prostaglandin (PG) preparations were tried for labor induction and shown to reduce the risk of failed induction of labor.[4] Misoprostol, a synthetic structural analog of PGE1 widely used for treatment of peptic

Address for correspondence: Dr. Puliyath G,
Department of Obstetrics and Gynaecology, SUT Academy of Medical Sciences, Vencode, Vattapara, Trivandrum, Kerala, India.
E-mail: pgeetha98@yahoo.co.in

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ulcer, is found to be effective in labor induction.[5] Compared with other PGs, misoprostol is cheap, better available, can be stored at room temperature, and has only few side effects such as diarrhea, nausea, vomiting, and fever. Uterine hyperstimulation and rupture uterus are rare.[6-8] Vaginal misoprostol, being long-lasting at low serum levels, is more effective than oral or sublingual routes.[9,10] At present, there is no definite opinion regarding the dose and frequency of administration of misoprostol in labor induction.[11,12] Other recommended methods of induction of labor are oxytocin, oral misoprostol, PGE2, and mechanical method like balloon catheter.[13,14] Compared with oxytocin, misoprostol administration results in shorter induction delivery interval and decreased rate of failed induction of labor, resulting in a reduced rate of caesarean section.[15,16] However, higher doses may be associated with uterine hyper stimulation.[8,11,15] It is therefore necessary to determine the safe dose of misoprostol for labor induction.

Materials and Methods

A retrospective study was carried out in a tertiary care teaching hospital from January 2012 to January 2017. Data were collected from hospital records. The selected women included those who completed 37 weeks of gestation, with Bishop's score of less than 6, and who had undergone elective induction for various reasons. Women who were excluded were those with multiple pregnancy, preterm induction of labor for conditions such as severe intrauterine growth retardation, preterm premature rupture of membranes, previous caesarean section, uterine scarring as from previous myomectomy, Bishop's score of more than 6 at the time of misoprostol application, presentations other than cephalic, unsure gestational age or who did not have a first trimester dating scan, and having a history of intrauterine death or baby with congenital malformations. The induction group was compared with women who had spontaneous onset of labor after 37 completed weeks of gestation. The hospital protocol for labor induction was PGE1, 25 mg tablets to be introduced into posterior vaginal fornix under aseptic precautions, after wetting the tablet with sterile water. Repeated doses were introduced after 6 h for a maximum of three doses. The decision for repeated doses was determined by assessing uterine contraction and fetal heart rate. Women were kept in the antenatal ward near the labor room and monitored for contractions and fetal heart every hourly. Once contractions were started, they were shifted to the labor room and close monitoring was done. Further doses of PGE1 were withheld at the onset of labor. Labor onset was determined by palpable appreciation of one or more contractions in 10 min. Progress of labor was monitored using partogram which was started when the cervical dilatation was 4 cm. Artificial rupture of membrane was done when the cervical dilatation was 4 cm or more after the head engaged. If uterine contractions were inadequate (adequate contractions mean there should be three contractions in 10 min and each should last for 45 s), five units of oxytocin was started to accelerate labor. The mode of deliveries, indications for caesarean sections, induction delivery interval, need for oxytocin acceleration, fetal or neonatal morbidities (such as admission in NICU unit due to poor APGAR scores, meconium aspiration, hyper bilirubinemia, encephalopathy), meconium-stained liquor, postpartum hemorrhage, blood transfusion, uterine hyper stimulation, and rupture uterus were documented and studied. As per World Health Organization guidelines, uterine hyperstimulation is defined as occurrence of a single uterine contraction lasting for more than 60 s or occurrence of more than four contractions within 10 min.[13] Uterine hypertonicity was defined as occurrence of single contraction lasting for more than 2 min.[13] Uterine rupture is defined as an intraoperative finding of fetal parts within the abdominal cavity and dehiscence is a window in the lower segment with either membranes bulging or parts of the baby visible through it.[16-19] Those with APGAR score of 7 or less than that at 1 min were considered as poor score or birth asphyxia.[13] Statistical significance was assessed at 5% level of significance. Chi-square test, with correction for continuity where applicable, was carried out to compare proportions across subgroups or between induction and spontaneous onset groups. Odds ratio (OR) analysis was also carried to assess association between variables, and the statistical significance at 5% level was ascertained from the 95% confidence interval (CI) of OR – OR was judged to be statistically significant if its 95% CI does not contain the null value of 1. Independent *t*-test was used to compare means between two groups. Though several statistical tests were conducted for comparison of the major end-point, the type of delivery, and other maternal and newborn characteristics across subcategories in the induction group and between induction and spontaneous onset groups, correction for multiple comparisons was not used. The study had been approved by the ethics committee of the Academic Division of SUT Academy of Medical Sciences (date of approval 4 the January 2012) and the director of the Department of Obstetrics and Gynaecology and Department of Neonatology of the hospital.

Results

A total of 700 term pregnant women were included in the study group of induction of labor. However, one woman who requested an elective caesarean section after single dose of misoprostol was excluded from data analysis. Therefore, a total of 699 women were included in the

analysis. They were compared with 644 women who had spontaneous onset of labor (control group). The mean age of women in both groups was 24.1 years [standard deviation (SD): 3.70; range 18–40). A majority of the women were of primigravida in both spontaneous and induction groups (54.8% and 60.7%, respectively). Though primigravida mothers appear to be slightly higher among induction group, the difference in the distribution of gravida in the two groups was comparable ($\chi^2_{(3)} = 4.97$, $P = 0.174$). For all further analyses, gravida status was considered as either primigravida or multigravida (gravida ≥2).The overall rate of vaginal delivery was higher among spontaneous onset group compared with induction group (79.7% vs 66.1%, $\chi^2_{(1)} = 30.3$, $P < 0.001$). The difference was more striking among primigravida mothers (72.5% vs 56.4% in spontaneous and induction groups, respectively, $\chi^2_{(1)} = 21.0$, $P < 0.001$) than multigravida mothers (88.3% vs 81.1%, $\chi^2_{(1)} = 5.2$, $P = 0.017$). The overall proportion of vaginal delivery was 56.4% among primigravida women compared with 81.1% among multigravida ($\chi^2_{(1)} = 44.4$, $P < 0.001$) in the induction group. Of the 424 primigravida women, as many as 310 (73.1%) had to be given a second dose of PGE1 and 94 of 310 (30.3%) were given a third dose of PGE1. The corresponding figures for multigravida were 57.4% (158/275) and 22.8% (35/158), respectively. The rate of vaginal delivery after giving a single dose of PGE1 was 36.4% (100/275) among multigravida compared with 17.5% (74/424) among primigravida. The odds for vaginal delivery were 2.70 times higher among multigravida compared with primigravida (95% CI: 1.90–3.84). Similar findings were seen among those who were given two (63.3% vs 42.3%, OR = 2.36; 95% CI: 1.59–3.49) and three (65.7% vs 36.2%, OR = 3.38; 95% CI: 1.50–7.64) doses of PGE1. Therefore, overall there was more number of vaginal deliveries among multigravida than primigravida in the induction group. Oxytocin acceleration was given for 339 of 699 (48.5%) induction group, whereas it was given for 179 of 644 (27.8%) spontaneous group of women ($\chi^2_{(1)} = 59.8$, $P < 0.001$). The mean induction delivery interval among primigravida was 7.1 ± 2.2 with single dose, 12.4 ± 2.6 in those with two doses, and 25.4 ± 4.6 among those with three doses of PGE1. Among 114 primigravida, 74 (17.5%) delivered vaginally with single dose of PGE1 and 40 (9.4%) delivered by caesarean section. Among primigravida, 216 women received two doses of PGE1. Among them, 131 (42.31%) delivered vaginally and 85 (27.41%) had caesarean section. The remaining 94 primi women had three doses of PGE1. Out of them, 34 (36.2%) delivered vaginally and 60 (63.8%) had caesarean section. Therefore, induction delivery interval was more than 24 h only in those who received three doses of PGE1. Among 94 primigravida, who had three doses of PGE1, only 34 women delivered vaginally with an induction delivery interval of more than 24 h (8.01%). Only 35 women among 275 multigravida received three doses of PGE1 and 23 women had vaginal delivery with an induction delivery interval of more than 24 h (8.36%). Therefore, among 699 women who were induced with PGE1, a total of 129 women had an induction delivery interval of more than 24 h. If we take induction delivery interval of vaginal delivery, only 57 women among 699 (8.15%) had vaginal delivery with an induction delivery interval of more than 24 h. Therefore, a majority of women delivered within 24 h of induction of labor [Tables 1 and 2]. The majority of caesarean sections were done for failed progress of labor in both groups (96 and 55, respectively). The second indication in both groups was fetal distress. Postnatal complications such as cervical lacerations, paraurethral tear, and traumatic postpartum hemorrhage were slightly more in the spontaneous delivery group even though they were not statistically significant. However, there were four cases of vaginal hematomas and one of uterine dehiscence in the induction group. Among the spontaneous group, there was only one case of vaginal hematoma and no cases of uterine rupture or dehiscence. The woman who

Table 1:Characteristics of primi women who had vaginal delivery and emergency caesarean following induction of labor with one, two, and three doses of PGE

Characteristics	Primigravida			
	Women undelivered	Vaginal delivery	Emergency CS	Total
One PGE1 dose				
No. of women (%)	310 (73.1%)	74 (17.5%)	40 (9.4%)	424
Mean induction delivery interval (h) ± SD		7.1±2.2	6.2±2.0	
Oxytocin required		39 (52.70%)	11 (27.50%)	
Two PGE1 dose				
No. of women (%)	94 (30.3%)	131 (42.3%)	85 (27.40%)	310
Mean induction delivery interval (h) ± SD		12.4±2.6	11.7±2.8	
Oxytocin required		65 (49.61%)	41 (48.23%)	
Three PGE1 dose				
No. of women (%)	-	34 (36.2%)	60 (63.8%)	94
Mean induction delivery interval (h) ± SD		25.4±4.6	25.9±5.7	
Oxytocin required		21 (61.76%)	24 (40%)	

PGE: Prostaglandin E; CS: Caesarean section; SD: Standard deviation

Table 2: Characteristics of multigravida women who had vaginal delivery and emergency caesarean following induction of labor with one, two and three doses of PGE

Characteristics	Multigravida			
	Women undelivered	Vaginal delivery	Emergency CS	Total
One PGE1 dose				
No. of women (%)	158 (57.4%)	100 (36.4%)	17 (6.2%)	275
Mean induction delivery interval (h) ± SD		6.7±2.0	6.4±1.8	
Oxytocin required		48 (48%)	7 (41.17%)	
Two PGE1 dose				
No. of women (%)	35 (22.2%)	100 (63.3%)	23 (14.6%)	158
Mean induction delivery interval (h) ± SD		11.6±2.5	12.3±2.9	
Oxytocin required		47 (47%)	13 (56.52%)	
Three PGE1 doses				
No. of women (%)	-	23 (65.7%)	12 (34.3%)	35
Mean Induction delivery interval (IDI) (h) ± SD		27.4±3.8	27.0±3.8	
Oxytocin (Y/N)		18 (78.26%)	5 (41.66%)	

PGE: Prostaglandin E; CS: Caesarean section; SD: Standard deviation

had uterine dehiscence was a fourth gravida with history of surgical evacuation for previous three abortions. She was given a single dose of PGE1 and developed fetal distress within 5 h of induction of labor with mild uterine contractions and an emergency caesarean section was done. Blood transfusion frequency was similar among spontaneous onset and induction groups ($\chi^2_{(1)} = 0.91$, $P = 0.341$) [Table 3]. The mean birth weight of 642 singletons born off induction group of women was 3.01 (SD 0.39) compared with 2.99 (SD 0.41) among spontaneous onset group and there was no statistically significant difference in mean birth weight of the newborns of the two groups, $t_{1312.9} = 0.73$, $P = 0.465$. The babies born off spontaneous onset group of women appeared to have better APGAR score distribution compared with induction group ($\chi^2_{(3)} = 47.3$, $P < 0.001$). NICU admission frequency was similar among both groups ($\chi^2_{(1)} = 0.14$, $P = 0.704$). Meconium stain frequency was higher among spontaneous onset group compared with induction group ($\chi^2_{(1)} = 8.05$, $P = 0.0046$) [Table 3].

Table 3: Postnatal complications and neonatal outcome

Postnatal complications	Spontaneous group	Induction group	Total
Third-degree perineal tear	1	0	1
Abruption placentae	4	2	2
Atonic pph	35 (5.43%)	37 (5.29%)	72
Traumatic pph	6	3	9
Cervical laceration	8	2	10
Incomplete rupture	0	1	1
Paraurethral tear	3	0	3
Manual removal of retained placenta	1	1	2
Shoulder dystocia	12	12	12
Vaginal laceration	2	3	5
Vaginal hematoma	1	4	5
Blood transfusion	10 (1.55%)	17 (2.43%)	27
APGAR score at 5'7 or less	4 (0.6%)	20 (2.9%)	24 (1.8%)
NICU admission	61 (9.47%)	61 (8.72%)	122
Meconeum stain	40 (6.21%)	20 (2.86%)	60

pph: Postpartum hemorrhage; NICU: Neonatal intensive care admission

Discussion

The overall rate of vaginal delivery was higher among spontaneous onset group compared with induction group (79.7% vs 66.1%, $\chi^2_{(1)} = 30.3$, $P < 0.001$). This is similar to a meta-analysis conducted by Caughey *et al*. which included 36 studies with 11 randomized controlled studies showing that women with expectant management had higher OR of caesarean section (OR = 1.22; 95% CI: 1.07–1.39), more vaginal delivery among spontaneous onset group, and more likely to have meconium-stained liquor (OR = 2.04; CI: 1.34–3.09), when compared with elective induction of labor.[20] This is different from the results of a large randomized trial conducted by Hannah *et al*., which showed significantly higher rate of caesarean section among women with expectant management compared with those with induced labor (24.5% and 21.2%, $P = 0.03$).[21]

In our study, the corresponding values are 20.3% and 33.9% for spontaneous onset group and induction group, respectively. Among vaginal delivery, 8.15% had an induction delivery interval of more than 24 h. The remaining 91.85% were delivered within 24 h of induction of labor. A comparative study of 25 and 50 mg misoprostol, conducted by Azubuike *et al.*, showed an induction delivery interval of more than 24 h in 22.5% among the 25-mg group.[22] Other randomized controlled studies also showed similar results.[23,24] The requirement of oxytocin in our study was comparable to other studies.[22] A meta-analysis of 121 trials done by Hofmeyr *et al*.[12] showed that vaginal misoprostol was associated with higher rate of vaginal delivery within 24 h and lesser use of epidural analgesia. However, higher doses were associated with uterine hyperstimulation without fetal heart changes (Relative risk (RR) = 3.52; 95% CI: 1.78–6.99) and more chance of meconium-stained liquor when compared with placebo, oxytocin, and PGE2. This study also

showed that lower doses of misoprostol were as associated with more need for oxytocin augmentation and less uterine hyperstimulation. A randomized clinical trial (RCT) by Rahman *et al.* showed occurrence of uterine hyperstimulation with intravaginal application of 25 mg PGE1 in their study. However, the interval between two doses was 4 h in their study.[23] There was no case of uterine hyperstimulation or drug side effects such as nausea, vomiting, fever, or diarrhea in our study. This is similar to a study by Wing *et al.* and Farah *et al*.[6,8] In a systematic review conducted by Hannah *et al.* which included one RCT and four observational studies, it was shown that there was no difference between spontaneous onset and induction of labor regarding the rate of postpartum hemorrhage.[21] In a study conducted by Abisowo *et al.*,[3] where induction was done with oxytocin, the rate of postpartum hemorrhage was 4.55% compared with 2.27% with spontaneous onset group (statistically not significant). In our study, the number of cases of atonic and traumatic postpartum hemorrhage was comparable in both study and control groups (5.29% and 5.43%). There was no RCT found during search which examined rates of blood transfusion between elective induction and expectant management. In our study, it was 2.43% and 1.55%, respectively. There were four cases of vaginal hematoma in the study group when compared with one in the control group. Other maternal outcomes such as infection, perineal lacerations, vaginal lacerations, and shoulder dystocia are comparable in both study and control group. Even though statistically not significant, these complications were reported in other studies, even with limited sample size.[21,23] Neonatal outcome is comparable to other studies.[22-25] The babies born off spontaneous onset group of women appeared to have better APGAR score distribution compared with induction group ($\chi^2_{(3)} = 47.3, P < 0.001$). NICU unit admission frequency was similar among both groups ($\chi^2_{(1)} = 0.14, P = 0.704$). Meconium stain frequency was higher among spontaneous onset group compared with induction group ($\chi^2_{(1)} = 8.05, P = 0.0046$). However, there was no case of severe birth asphyxia, neonatal encephalopathy, meconium aspiration syndrome, hyperbilirubinemia, or neonatal death in both and control groups.

Conclusion

The retrospective study showed a significantly higher rate of vaginal delivery with induction delivery interval less than 24 h in a majority of women with better neonatal and maternal outcomes with the usage of PGE1 25 mg vaginal tablet. Being cost-effective, the drug can be recommended for labor induction in developing countries with their higher birth rates.

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Conflicts of interest

There are no conflicts of interest.

References

1. Ten Eikelder M, van Baaren GJ, Oude Rengerink K, Jozwiak M, DeLeeuw JW, Evers I, *et al.* Comparing induction of labour with oral misoprostol or Foley catheter at term: Cost-effectiveness analysis of a randomised controlled multi-centre non-inferiority trial. Br J Obstet Gynaecol 2018;125:375-83.
2. Bako BG, Obed JY, Sanusi I. Methods of induction of labour at the University of Maiduguri Teaching Hospital, Maiduguri: A 4-year review. Niger J Med 2008;17:139-42.
3. Abisowo OY, Oyinyechi AJ, Olusegun FA, Oyedokun OY, Motunrayo AF, Abimbola OT. Feto-maternal outcome of induced versus spontaneous labour in a Nigerian Tertiary Maternity Unit. Trop J Obstet Gynaecol 2017;34:21-7.
4. Thomas J, Fairclough A, Kavanagh J, Kelly AJ. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. Cochrane Database Syst Rev 2014;Issue 6.
5. Collins PW, Pappo R, Dajani EZ. Chemistry and synthetic development of misoprostol. Dig Dis Sci 1985,30(11 Suppl):114S-7S.
6. Wing DA, Park MR, Paul RH. A randomized comparison of oral and intravaginal misoprostol for labor induction. Obstet Gynecol 2000;95 (6 Pt 1):905-8.
7. Bergstrom S, Aronsson A. Misoprostol in resource poor countries. BMJ 2008;336:1032.
8. Farah LA, Sanchez-Ramos L, Rosa C, Del Valle GO, Gaudier FL, Delke I, *et al*. Randomized trial of two doses of the prostaglandin E1 analog misoprostol for labor induction. Am J Obstet Gynecol 1997;177:364-9.
9. Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: Pharmacokinetic profiles, effects on the uterus and side-effects. Int J Gynaecol Obstet 2007;99(Suppl. 2):S160-7.
10. Hapangama D, Neilson JP. Mifepristone for induction of labour. Cochrane Database Syst Rev 2009;3:CD002865.10.1002/14651858.cd002865.pub2.
11. Ekele BA, Nnadi DC, Gana MA, Shehu CE, Ahmed Y, Nwobodo EI. Misoprostol use for cervical ripening and induction of labour in a Nigerian teaching hospital. Niger J Clin Pract 2007;10:234-7.
12. Hofmeyr GJ, Gulmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database Syst Rev 2010;10:CD000941. 10.1002/14651858.cd000941.
13. WHO recommendations for induction of labour 2011 guidelines. ISBN: 9789241501156.
14. National Collaborating Centre for Women and Children's Health. Induction of Labour. Clinical Guideline. London, UK: NICE; 2008.
15. Kramer RL, Gilson GJ, Morrison DS, Martin D, Gonzales JL, Qualls CR. A randomized trial of misoprostol and oxytocin for induction of labor: Safety and efficacy. Obstet Gynecol 1997;89:387e91.
16. Acones GA, Peipert J, Nelson DB, Odibo A, Stevens EJ, Stamilio DM, *et al*. Maternal complications with vaginal birth after cesarean delivery: A multicenter study. Am J Obstet Gynecol 2005;193:1656-62.
17. Greenwald SR, Gonzalez JM, Goldstein RG, Rosenstein MG. Asymptomatic uterine dehiscence in a second-trimester twin pregnancy. Am J Obstet Gynecol 2015;213:590.e1-2.
18. Van Gemund N, Scherjon S, Le Cessie S, Schagen van LeeuwenJ H, Van Roosmalen J. A randomised trial comparing low dose vaginal misoprostol and dinoprostone for labour induction. BJOG 2004;111:42-9.
19. Al-Zirqi, Stray-Pederson B, Forsen L, Vangen S. Uterine rupture after

previous caesarean section. Br J Obstet Gynaecol 2010;117:809-20.
20. Caughey AB, Sundaram V, Kaimal AJ, Cheng YW, Gienger A, Little SE, *et al.* Systematic review: Elective induction of labor versus expectant management of pregnancy. Ann Int Med 151:252-63, W53-63.
21. Hannah ME, Hannah WJ, Hellmann J, Hewson S, Milner R, Willan A. Induction of labor as compared with serial antenatal monitoring in post-term pregnancy. A randomized controlled trial. The Canadian Multicenter Post-term Pregnancy Trial Group. N Engl J Med 1992;326:1587-92.
22. Azubuike IJ, Bassey G, Okpani A. Comparison of 25 and 50 microgram of misoprostol for induction of labour in nulliparous women with postdate pregnancy in Port Harcourt. Niger J Clin Pract 2015;18:263-7.
23. Rahman H, Pradhan A, Kharka L, Renjhen P, Kar S, Dutta S. Comparative evaluation of 50 microgram oral misoprostol and 25 microgram intravaginal misoprostol for induction of labour at term: A randomized trial. J Obstet Gynaecol Can 2013;35:408-16.
24. Girija S, Manjunath AP. Comparison of two dosing regimens of vaginal misoprostol for labour induction: A randomised controlled trial. J Turk Ger Gynecol Assoc 2009;10:220-5.
25. Mundle WR, Young DC. Vaginal misoprostol for induction of labor: A randomized controlled trial. Obstet Gynecol 1996;88:1-525.