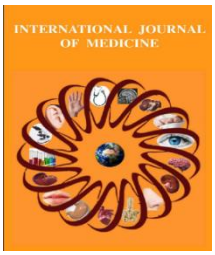
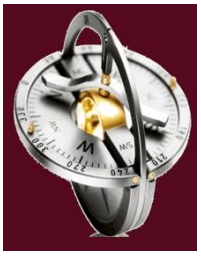


International Journal of Medicine
ISSN (P): 1468-3814; ISSN (e): 2667-7008

https://www.theinternationalmedicine.com

Volume: 4(1) 2022



Original Research

PROSPECTIVE RANDOMISED CONTROLLED TRIAL TO COMPARE SAFETY AND EFFICACY OF INTRAVAGINAL MISOPROSTOL WITH INTRACERVICAL DINOPROSTONE FOR INDUCTION OF LABOUR.

[1]*Dr. Sushma Shet, [2]Dr. Ritimukta Panda, [3]Dr. Priyanka B Reddy
[1,2]*Assistant Professor, Dept of Obstetrics and Gynaecology, Dr Chandramma Dayananda Sagar Institute of Medical Education and Research CDSIMER*
[3]*Senior Resident, Dept of Obstetrics and Gynaecology, Dr Chandramma Dayananda Sagar Institute of Medical Education and Research CDSIMER*

Received: 12 Nov 2022 / Accepted: 01 Dec 2022

Abstract

Background: Induction of labour is one of the most commonly performed obstetric interventions for achieving vaginal delivery when continuation of pregnancy poses greater risk to the mother or fetus. Prostaglandins such as Misoprostol and Dinoprostone are widely used for cervical ripening and induction of labour. However, there is ongoing debate regarding their comparative efficacy and safety. *Aim:* To compare the safety and efficacy of intravaginal Misoprostol with intracervical Dinoprostone for induction of labour. Materials and Methods: This prospective randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology among 100 term pregnant women requiring induction of labour. Participants were randomly divided into two groups: Group A: Intravaginal Misoprostol (n=50), Group B: Intracervical Dinoprostone (n=50). Outcome measures assessed included number of doses required, induction-delivery interval, uterine hyperstimulation, mode of delivery, meconium-stained liquor and NICU admission. Statistical analysis was performed using Chi-square test, Fisher exact test and Independent Student t-test. P value <0.05 was considered statistically significant. *Results:* The majority of women in both groups belonged to the 21-25 years age group. A significantly higher proportion of women in the Misoprostol group required only a single dose for successful induction compared to the Dinoprostone group (40% vs 22%; p=0.041). The mean induction-delivery interval was significantly shorter in the Misoprostol group (10.8 ± 3.1 hours) compared to the Dinoprostone group (14.6 ± 4.2 hours) with p<0.001. Vaginal delivery rate was higher in the Misoprostol group (82%) compared to the Dinoprostone group (68%), though the difference was statistically insignificant. Hyperstimulation, meconium-stained liquor and NICU admission were slightly higher in the Misoprostol group, but the differences were not statistically significant. *Conclusion:* Intravaginal Misoprostol is more efficacious than intracervical Dinoprostone for induction of labour due to fewer doses required and shorter induction-delivery interval, while maintaining comparable maternal and neonatal safety outcomes. Misoprostol can therefore be considered an effective and economical alternative induction agent in term pregnancies.

Keywords: *Induction of labour; Misoprostol; Dinoprostone; Hyperstimulation; Vaginal delivery; NICU admission.*

Introduction

Induction of labour (IOL) is defined as the artificial initiation of uterine contractions before the spontaneous onset of labour with the purpose of achieving vaginal delivery when the benefits of delivery outweigh the risks of continuing pregnancy. It is one of the most frequently performed obstetric interventions worldwide and plays a major role in reducing maternal and perinatal morbidity and mortality.[1] Globally, approximately 20-25% of pregnancies undergo induction of labour, with rising rates observed in both developed and developing countries due to increasing institutional deliveries, better fetal surveillance and improved obstetric care.[2] Induction is commonly indicated in postdated pregnancy, hypertensive disorders of pregnancy, premature rupture of membranes, fetal growth restriction, oligohydramnios, diabetes mellitus and intrauterine fetal demise.[3]

India contributes nearly one-fifth of the global births annually, making safe labour management a major public health priority. Despite substantial improvement in institutional deliveries and maternal healthcare services, maternal and neonatal complications such as birth asphyxia, meconium aspiration syndrome, neonatal sepsis and rising caesarean section rates continue to contribute significantly to healthcare burden in India.[4] Studies from India have shown wide variations in labour induction rates ranging from 3% to 84%, with increasing use of prostaglandins and uterotonics in tertiary care hospitals.[4] At the same time, increasing rates of caesarean section have become an important concern. According to the World Health Organization, caesarean section rates above 10-15% do not significantly improve maternal or neonatal mortality outcomes, emphasizing the importance of safe and effective induction methods that can promote vaginal delivery while minimizing complications. [5]

Address for Correspondence Dr. Sushma Shet, Assistant Professor, Dept of Obstetrics and Gynaecology, Dr Chandramma Dayananda Sagar Institute of Medical Education and Research CDSIMER.

DOI: 10.61336/im/22-1-12

unfavourable cervix often experience prolonged labour, failed induction and increased operative delivery rates. Prostaglandins are therefore widely used for cervical ripening and induction because they enhance cervical softening and stimulate effective uterine contractions. [6] Dinoprostone, a synthetic prostaglandin E_2 analogue, has been extensively used as an intracervical gel for cervical ripening and labour induction. It has a well-established safety profile and predictable pharmacological action, but its disadvantages include higher cost, need for refrigeration and repeated dosing in many patients.[7]

Misoprostol, a synthetic prostaglandin E_1 analogue, has emerged as an effective alternative agent for induction of labour because of its low cost, easy storage at room temperature, long shelf life and potent uterotonic activity. The World Health Organization recommends low-dose vaginal misoprostol for induction of labour in suitable clinical situations.[8] Several randomized trials and systematic reviews have demonstrated that vaginal misoprostol may reduce the number of doses required and shorten the induction-delivery interval compared to dinoprostone.[9] However, concerns remain regarding adverse effects such as uterine tachysystole, hyperstimulation syndrome, fetal distress and meconium-stained liquor, particularly with higher doses of misoprostol.[10]

The ideal induction agent should provide effective cervical ripening, shorter induction-delivery interval, higher vaginal delivery rate and minimal maternal or neonatal complications. Neonatal outcomes such as NICU admission, fetal distress and meconium-stained liquor are important indicators of the safety of induction methods. Although both misoprostol and dinoprostone are widely used for labour induction, there remains ongoing debate regarding their comparative efficacy and safety, especially in Indian obstetric settings where resource availability, patient load and affordability significantly influence clinical practice. Therefore, the present prospective randomized controlled trial is undertaken to compare the safety and efficacy of intravaginal misoprostol with intracervical dinoprostone for induction of labour with respect to number of doses required, induction-delivery interval, side effects including hyperstimulation, mode of delivery, NICU admission and meconium-stained liquor.

Aim
The aim of this study is to compare the safety and efficacy of intravaginal Misoprostol with intracervical Dinoprostone for induction of labour in term pregnant women.

Objectives
The primary objectives of this study are twofold. First, to compare the efficacy of intravaginal Misoprostol and intracervical Dinoprostone in terms of the number of doses required for successful induction, the induction-delivery interval, and the mode of delivery, whether vaginal delivery or lower segment caesarean section. Second, to compare the safety profile of both agents with respect to uterine hyperstimulation or tachysystole, meconium-stained liquor, and neonatal intensive care unit (NICU) admission. [10]

Materials and Methods
This is a prospective randomized controlled trial conducted in the Department of Obstetrics and Gynaecology. The study population comprises pregnant women admitted for induction of labour in the antenatal ward or labour room who fulfil the specified inclusion criteria.

Sample Size
The sample size was calculated based on previous studies comparing induction-delivery interval and successful vaginal delivery rates between the Misoprostol and Dinoprostone groups. Using the standard formula for comparison of two proportions — $n = (Z\alpha/2 + Z\beta)^2 [p_1(1-p_1) + p_2(1-p_2)] / (p_1-p_2)^2$ — with a 95% confidence interval ($Z\alpha/2 = 1.96$), 80% power ($Z\beta = 0.84$), and based on previous literature reporting successful vaginal delivery rates of approximately 85% with Misoprostol and 65% with Dinoprostone, the minimum calculated sample size is 50 patients per group. Accordingly, Group A (Intravaginal Misoprostol) will comprise 50 patients and Group B (Intracervical Dinoprostone) will comprise 50 patients, giving a total sample size of 100 patients.

Sampling Method and Randomization
Simple random sampling will be employed. Eligible participants will be randomly allocated into one of the two groups using computer-generated random numbers or the sealed opaque envelope method. Group A will receive intravaginal Misoprostol and Group B will receive intracervical Dinoprostone.

Inclusion and Exclusion Criteria
Women eligible for enrolment must have a singleton pregnancy with cephalic presentation, a gestational age of 37 completed weeks or more, a reactive non-stress test, a Bishop score of less than 6, and a valid indication for induction of labour. Participants must be between 18 and 35 years of age and must provide written informed consent. Women will be excluded if they have a previous caesarean section or any uterine scar, cephalopelvic disproportion, malpresentation, placenta previa or unexplained vaginal bleeding, multifetal pregnancy, fetal distress at admission, hypersensitivity to prostaglandins, maternal medical disorders contraindicating vaginal delivery, severe oligohydramnios with fetal compromise, cord prolapse, or obstructed labour.

Study Procedure
Following Institutional Ethics Committee approval and written informed consent, all eligible participants will be enrolled. A detailed history including maternal age, parity, gestational age, and indication for induction will be documented. General physical and obstetric examination along with Bishop score assessment will be performed at admission. Baseline investigations including haemoglobin, blood grouping and Rh typing, urine albumin and sugar, random blood sugar, obstetric ultrasonography, and non-stress test or fetal heart rate monitoring will be reviewed prior to initiation of induction.

Participants in Group A will receive Misoprostol 25 µg placed in the posterior vaginal fornix under aseptic precautions. The dose may be repeated every 4-6 hours depending on cervical response and uterine contractions, to a maximum of 4 doses. Participants in Group B will receive Dinoprostone gel 0.5 mg administered intracervically under aseptic precautions, with repeat dosing permissible after 6 hours if adequate cervical ripening or labour has not been achieved, in accordance with institutional protocol.

All patients will be closely monitored throughout the induction process for uterine contractions, fetal heart rate pattern, maternal pulse and blood pressure, cervical dilatation and effacement, and overall progress of labour. Continuous or intermittent cardiotocography will be employed as clinically required. Artificial rupture of membranes and oxytocin augmentation will be carried out when indicated. Uterine hyperstimulation is defined as more than 5 contractions in 10 minutes, or contractions lasting more than 2 minutes associated with fetal heart rate abnormalities.

Statistical Analysis
Data will be entered in Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) software version 25. Continuous variables will be expressed as mean ± standard deviation. Categorical variables will be expressed as frequency and percentage. Independent Student t-test will be used for comparison of continuous variables. Chi-square test or Fisher exact test will be used for categorical variables. P value <0.05 will be considered statistically significant.

Results

A total of 100 antenatal women undergoing induction of labour were included in the present prospective randomized controlled trial. Among them, 50 women received intravaginal Misoprostol (Group A) and 50 women received intracervical Dinoprostone (Group B). The following tables summarize the comparison of efficacy and safety outcomes between the two groups.

Table 1. Age-wise Distribution of Study Participants

Age Group (years)	Misoprostol Group n (%)	Dinoprostone Group n (%)	Total n (%)
18-20	6 (12.0%)	5 (10.0%)	11 (11.0%)
21-25	22 (44.0%)	24 (48.0%)	46 (46.0%)
26-30	15 (30.0%)	14 (28.0%)	29 (29.0%)
31-35	7 (14.0%)	7 (14.0%)	14 (14.0%)
Total	50 (100%)	50 (100%)	100 (100%)

The majority of study participants in both groups belonged to the 21-25 years age group. The age distribution between the Misoprostol and Dinoprostone groups was comparable, indicating adequate baseline matching between the study groups.

Table 2. Comparison of Number of Doses Required for Successful Induction

Number of doses required	Misoprostol Group n (%)	Dinoprostone Group n (%)	Total	P value
1 dose	20 (40.0%)	11 (22.0%)	31	**0.041**
2 doses	19 (38.0%)	18 (36.0%)	37	
3 doses	9 (18.0%)	15 (30.0%)	24	
4 doses	2 (4.0%)	6 (12.0%)	8	
Total	50 (100%)	50 (100%)	100	

A higher proportion of women in the Misoprostol group required only one dose for successful induction compared to the Dinoprostone group. More women in the Dinoprostone group required three or more doses. The difference in number of doses required between the two groups was statistically significant (p=0.041), suggesting better induction efficacy with Misoprostol.

Table 3. Comparison of Induction-Delivery Interval Between Study Groups

Variable	Misoprostol Group	Dinoprostone Group	P value
Mean induction-delivery interval (hours)	10.8 ± 3.1	14.6 ± 4.2	**<0.001**

The mean induction-delivery interval was significantly shorter in the Misoprostol group (10.8 ± 3.1 hours) compared to the Dinoprostone group (14.6 ± 4.2 hours). The difference was statistically highly significant (p<0.001), indicating faster labour induction with intravaginal Misoprostol.

Table 4. Comparison of Mode of Delivery Between Study Groups

Mode of delivery	Misoprostol Group n (%)	Dinoprostone Group n (%)	Total	P value
Vaginal delivery	41 (82.0%)	34 (68.0%)	75	0.104
LSCS	9 (18.0%)	16 (32.0%)	25	
Total	50 (100%)	50 (100%)	100	

Vaginal delivery rate was higher in the Misoprostol group compared to the Dinoprostone group, whereas LSCS rate was higher in the Dinoprostone group. However, the difference in mode of delivery between the groups was not statistically significant (p=0.104).

Table 5. Comparison of Maternal and Neonatal Safety Outcomes

Outcome	Misoprostol Group n (%)	Dinoprostone Group n (%)	P value
Hyperstimulation	6 (12.0%)	2 (4.0%)	0.269
Meconium-stained liquor	8 (16.0%)	5 (10.0%)	0.372
NICU admission	7 (14.0%)	6 (12.0%)	0.766

The incidence of hyperstimulation, meconium-stained liquor and NICU admission was slightly higher in the Misoprostol group compared to the Dinoprostone group. However, these differences were not statistically significant (p>0.05). Both induction agents demonstrated comparable neonatal safety profiles.

Discussion

The present prospective randomized controlled trial compared the safety and efficacy of intravaginal Misoprostol with intracervical Dinoprostone for induction of labour among term pregnant women. The study evaluated important maternal and neonatal outcomes including number of doses required, induction-delivery interval, hyperstimulation, mode of delivery, meconium-stained liquor and NICU admission.

In the present study, the majority of women in both groups belonged to the age group of 21-25 years, and the age distribution between the two groups was statistically comparable. This finding is similar to the studies conducted by Patel et al.[11] and Sharma et al.[12] where most women undergoing induction belonged to younger reproductive age groups between 20 and 30 years. Comparable baseline demographic characteristics between study groups improve the validity of outcome comparisons in randomized controlled trials.

The present study demonstrated that women in the Misoprostol group required fewer doses for successful induction compared to the Dinoprostone group. About 40% of women in the Misoprostol group achieved adequate induction with a single dose compared to only 22% in the Dinoprostone group, and the difference was statistically significant. Similar findings were reported by Bhat et al.[13] who observed that vaginal Misoprostol resulted in more effective cervical ripening with fewer repeat doses compared to Dinoprostone gel. Likewise, Singh et al.[14] reported that the need for multiple doses was significantly lower with Misoprostol due to its potent uterotonic and cervical ripening action.

The induction-delivery interval was significantly shorter in the Misoprostol group in the present study. The mean induction-delivery interval was 10.8 ± 3.1 hours in the Misoprostol group compared to 14.6 ± 4.2 hours in the Dinoprostone group. This finding is consistent with the observations of Agarwal et al.[15] who reported a significantly shorter induction-to-delivery interval with vaginal Misoprostol compared to intracervical Dinoprostone. Similar findings were also documented by Jindal et al.[16] who concluded that Misoprostol produced faster onset of effective uterine contractions and shorter labour duration. The shorter induction-delivery interval observed with Misoprostol may be attributed to its sustained uterotonic effect and better cervical ripening properties.

In the present study, vaginal delivery rate was higher in the Misoprostol group (82%) compared to the Dinoprostone group (68%), while LSCS rate was comparatively higher in the Dinoprostone group. Although the difference was not statistically significant, the findings suggest better induction success with Misoprostol. Similar results were reported by Khan et al.[17] who observed higher rates of successful vaginal delivery with vaginal Misoprostol. The major indications for LSCS in both groups were fetal distress, failed induction and non-progress of labour, which are consistent with findings from previous induction studies.

Maternal safety outcomes showed that uterine hyperstimulation occurred slightly more frequently in the Misoprostol group compared to the Dinoprostone group, although the difference was not statistically significant. Similar observations were made by Roy et al.[18] who reported increased uterine tachysystole with Misoprostol, particularly with higher or repeated doses. However, in the present study, low-dose vaginal Misoprostol was used, which may have reduced the incidence of severe hyperstimulation and adverse fetal outcomes.
Meconium-stained liquor and NICU admission were slightly higher in the Misoprostol group, but the differences were statistically insignificant. Comparable neonatal outcomes between Misoprostol and Dinoprostone groups have also been reported in several previous randomized trials. These findings indicate that although Misoprostol is associated with stronger uterine activity, careful monitoring can ensure safe neonatal outcomes comparable to Dinoprostone.

Overall, the findings of the present study suggest that intravaginal Misoprostol is more efficacious than intracervical Dinoprostone in terms of fewer doses required and shorter induction-delivery interval, while maintaining comparable maternal and neonatal safety outcomes. Because of its low cost, easy availability, room temperature stability and effectiveness, Misoprostol can be considered a useful alternative induction agent, especially in resource-limited settings with proper intrapartum monitoring.

Conclusion

The present prospective randomized controlled trial demonstrated that intravaginal Misoprostol is more effective than intracervical Dinoprostone for induction of labour in term pregnancies with unfavourable cervix. Women induced with Misoprostol required fewer doses and had significantly shorter induction-delivery interval compared to those induced with Dinoprostone. Vaginal delivery rate was also comparatively higher in the Misoprostol group.

Although maternal side effects such as uterine hyperstimulation and neonatal outcomes including meconium-stained liquor and NICU admission were slightly higher in the Misoprostol group, the differences were not statistically significant. Both agents showed comparable maternal and neonatal safety profiles when used under proper monitoring.

Because of its low cost, easy availability, room temperature stability and better efficacy, intravaginal Misoprostol can be considered an effective alternative to intracervical Dinoprostone for induction of labour, particularly in resource-limited healthcare settings.

References

1. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al. Williams Obstetrics. 26th ed. New York: McGraw Hill; 2022. p. 520-538.
2. World Health Organization. WHO recommendations on induction of labour, at or beyond term. Geneva: World Health Organization; 2022.
3. American College of Obstetricians and Gynaecologists. ACOG Practice Bulletin No. 107: Induction of labour. Obstet Gynecol. 2009;114(2 Pt 1):386-397. doi: 10.1097/AOG.0b013e3181b48ef5
4. Population Reference Bureau. Labor induction and augmentation in India. Washington DC: PRB; 2023.
5. World Health Organization. WHO statement on caesarean section rates. Geneva: World Health Organization; 2015.
6. Dutta DC. Textbook of Obstetrics. 10th ed. New Delhi: Jaypee Brothers Medical Publishers; 2022. p. 498-510.
7. Thomas J, Fairclough A, Kavanagh J, Kelly AJ. Vaginal prostaglandin (PGE_2 and $PGF_2\alpha$) for induction of labour at term. Cochrane Database Syst Rev. 2014;(6):CD003101. doi: 10.1002/14651858.CD003101.pub3
8. World Health Organization. WHO recommendations for induction of labour. Geneva: World Health Organization; 2011.
9. Hofmeyr GJ, Gülmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database Syst Rev. 2010;(10):CD000941. doi: 10.1002/14651858.CD000941.pub2
10. van Gemund N, Scherjon S, Le Cessie S, van Leeuwen JH, van Roosmalen J, Kanhai HH. A randomised trial comparing low dose vaginal misoprostol and dinoprostone for labour induction. BJOG. 2004;111(1):42-49. doi:10.1046/j.1471-0528.2003. 00007.x
11. Patel M, Patel S, Desai A. Comparative study of intravaginal misoprostol and intracervical dinoprostone gel for induction of labour. Int J Reprod Contracept Obstet Gynecol. 2019;8(4):1452-1457. doi:10.18203/2320-1770.ijrcog20191345
12. Sharma R, Verma U, Gupta P. Efficacy and safety of misoprostol versus dinoprostone for induction of labour in term pregnancy. J Obstet Gynecol India. 2020;70(2):112-118. doi:10.1007/s13224-019-01275-2
13. Bhat S, Kulkarni V, Giri PA. Comparison of vaginal misoprostol and dinoprostone gel for induction of labour at term. Int J Biomed Adv Res. 2018;9(6):241-245.
14. Singh N, Tripathi R, Mala YM, Dixit R. Comparative evaluation of intravaginal misoprostol and intracervical dinoprostone gel for induction of labour. Indian J Obstet Gynecol Res. 2021;8(1):54-59.
15. Agarwal K, Bhatla N, Mittal S, Kumar S. A randomized comparison of misoprostol and dinoprostone for labour induction. Arch Gynecol Obstet. 2019;300(5):1221-1228. doi:10.1007/s00404-019-05289-5
16. Jindal P, Avasthi K, Kaur M. Comparative study of efficacy of vaginal misoprostol and dinoprostone gel for induction of labour. Int J Clin Obstet Gynaecol. 2022;6(2):35-40.
17. Khan S, Fatima N, Parveen S. Vaginal delivery outcomes following induction with misoprostol versus dinoprostone. J South Asian Feder Obst Gynae. 2021;13(3):152-157.
18. Roy KK, Baruah J, Kumar S, Deorari AK, Sharma JB. Randomized controlled trial of vaginal misoprostol versus intracervical dinoprostone for labour induction. J Obstet Gynaecol Res. 2018;44(7):1268-1275. doi:10.1111/jog.13652.