Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Obstetrics and Gynecology Research

Journal homepage: www.ijogr.org

Original Research Article

The study of low dose oral misoprostol solution and its comparison with intracervical dinoprostone gel for induction of labour

Neelam Singh[1], Urvashi Verma[1]*, Mohita Agarwal[1]

[1]Dept. of Obstetrics and Gynecology, Sarojini Naidu Medical College, Agra, Uttar Pradesh, India

Abstract

Background: Induction of labour is defined as iatrogenic stimulation of uterine contractions to accomplish delivery prior to the onset of spontaneous labour aimed at delivery by vaginal route. Dinoprostone has been used successfully for years as an agent for induction of labour. Misoprostol as an agent for induction of labour agent has rapidly gained popularity because it is inexpensive, stable at ambient temperatures, and easier to administer in comparison to dinoprostone and oxytocin.

Materials and Methods: During the study period 220 antenatal cases were randomly allocated into two groups consisted of 110 cases each group. One group received low dose oral misoprostol solution and other group received intracervical dinoprostone gel for induction of labour. All cases were analyzed and outcomes were evaluated.

Results: Successful induction was obtained in majority of cases in both the groups. However, misoprostol was more effective in inducing labour, improving the bishop score and less need for oxytocin augmentation then dinoprostone. Mean induction delivery rate was less in misoprostol group in both nulliparous and multiparous women. Cases with age less than equal to 30 years had a better induction delivery in misoprostol group. Induction done for the reason of post term pregnancy and pre-mature rupture of membrane had better delivery results in misoprostol group. Similarly, irrespective of period of gestation misoprostol had a significantly lower induction delivery duration.

Conclusion: Misoprost as a drug for induction of labour in low dose oral solution is as effective as the standard dinoprostone.

Keywords: Misoprostol, Induction of labour, Cerviprime gel, Intracervical balloon.

Received: 27-05-2024; **Accepted:** 17-01-2025; **Available Online**: 14-08-2025

1. Introduction

Induction of labour is defined as iatrogenic stimulation of uterine contractions to accomplish delivery prior to the onset of spontaneous labour aimed at delivery by vaginal route. In recent years, the rate of induction of labour has gradually gained momentum and the incidence for labour induction dramatically varies from 8-44%.[1]

Induction of labour is indicated when the benefits of induction to either mother or fetus outweigh those of pregnancy continuation.[2]

It could be done by pharmacological or mechanical method. Pharmacological methods are mainly using either dinoprostone (prostaglandin E2) or misoprostol (prostaglandin E1 analogue). The use of prostaglandins, in different varieties and forms of administration, has become a common method of labour induction.[3]

Pharmacological methods are mainly using either dinoprostone (prostaglandin E2) or misoprostol (prostaglandin E1 analogue).

Dinoprostone, prostaglandin E2, is one the prostaglandins, most commonly used to achieve cervical ripening and induction of labour. It has been approved by the Food and Drug Administration, U.S., for cervical ripening in women at or near term by intracervical administration. The

*Corresponding author: Urvashi Verma
Email: drurvashibijnor@gmail.com

https://doi.org/10.18231/j.ijogr.v.12.i.3.33

gel needs to be kept refrigerated and brought to room temperature immediately before its use.

Misoprostol, as a drug is approved by FDA for reducing the risk of non-steroidal anti- inflammatory drugs-induced gastric ulcers. It is also used to prevent and treat post partum bleeding. American college of Obstetrics and Gynaecology has recommended misoprostol for cervical ripening for induction of labour and dose should be 25mcg.[4]

Misoprostol is safe, reliable, inexpensive and easily available drug that can be given by various routes for induction of labour. It can be stored at room temperature and is easy to handle. It not only causes cervical ripening but induces uterine contractions as well. Dinoprostone on the other hand only causes cervical ripening. It is expensive, needs storage, and is tedious to handle. Many a times it needs augmentation and repetitive dose.

The objective of this study was to study the efficacy and safety of low dose oral misoprostrol (PGE1) solution and compare it with intracervical dinoprostone (PGE2) gel for induction of labour, in women scheduled for induction.

2. Materials and Methods

It was a prospective study carried out in the Department of Obstetrics and Gynaecology, S.N. Medical College, Agra over a period of one year. 220 antenatal women of 35 to 41 weeks with singleton live pregnancies with vertex presentation, clinically adequate pelvis, modified Bishop Score less than six were selected for the study. Women with hypertension, gestational diabetes, foetal growth restricted requiring induction of labour were included. Exclusion criteria were multiple pregnancy, fetal distress, non-reassuring cardiotocography (CTG) on admission, obstetric contraindications, scarred uterus and contraindication to misoprostol.

After selection, cases were randomly divided into two groups consisted of 110 cases each. Group 1 cases received low dose oral misoprostol solution and group 2 cases received intracervical dinoprostone gel for induction of labour.

Oral misoprostol solution was prepared by dissolving 200mcg tablet in 10 ml of distilled water. 1ml of this solution was administered orally by insulin syringe every two hourly. The doses were repeated till effective uterine contractions were achieved to a maximum of 80mcg i.e. misoprostol solution of 20mcg strength was repeated to a maximum of four times.

Dinoprostone (prostaglandin E2) used in the study comes as a gel in a prefilled syringe containing 0.5mg/3gm that was inserted intracervical. The progress of labour was monitored carefully by obstetrician through partogram and continuous electronic fetal monitoring.

The administration of the drug was stopped after failure to achieve effective uterine contractions after 4 doses or earlier if any adverse events appeared like hyper stimulation, tachysystole, hyper systole, non- reassuring CTG trace, fetal distress, or appearance of meconium. Induction was terminated and the case was labelled as failed induction.

Primary outcome was success of induction, induction delivery interval. Secondary outcome was vaginal delivery rate, need for augmentation with oxytocin, Apgar score at 1min and 5 min, NICU admission and perinatal morbidity and mortality. Data was collected and statistical analysis was performed using "student t test" and "chi square test".

3. Results

During the study period 220 antenatal cases were randomly allocated into two groups consisted of 110 cases each group. One group received low dose oral misoprostol solution and other group received intracervical dinoprostone gel for induction of labour.

Majority of the women were primiparous at 38 weeks of gestation with a mean age of 24.9yrs and 24.14yrs with an admission Bishops score of 2.99 and 2.79 in both the groups respectively. (**Table 1**) 38 cases required 40mcg of dose, 23 cases required 60mcg of dose, and the rest 28 cases required 80mcg of dose. Mean dose required in misoprostol group was 40mcg (2 doses). In Dinoprostone group 48 cases required twice instillation of gel, 33 cases required one-time instillation and 12 cases required the dinoprostone gel to be instilled thrice.

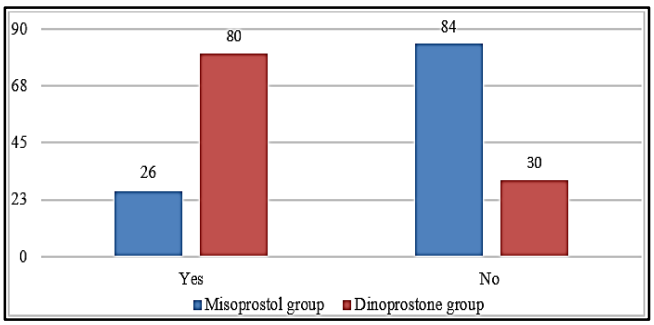

Figure 1: Need for augmentation with oxytocin

The observations obtained were tabulated as below:

The improvement in bishop score after 6 hours of induction was 8.11±2.01 in misoprostol group and 7.69±1.83 in dinoprostone group. The difference was clinically significant.(**Table 2**)

Figure 1, Only 26 cases (23.63%) in Misoprostol group and 80 cases (72.73%) in dinoprostone group had to be augmented with oxytocin. The p value was <0.0001 which was statistically significant. Oxytocin was given in the recommended doses started at 8drops/min and doubled every 30mins till effective uterine contractions were initiated upto a maximum of 60drops/min.(**Table 3**)

Table 1: Distribution of cases according to demographic characteristics

	Misoprostol Group	Dinoprostone Group	p-value
Mean Age	23.90 ± 3.49	24.14 ± 3.77	0.568
Period of Gestation (Mean)	38.72±1.33	38.85±1.36	0.546
Modified Bishop Score at the time of Admission	2.99±1.91	2.79±1.74	0.541
Parity			
Primi	72	78	0.4692
Multi	38	32	
Socio Economic Status			
Upper	1	0	0.5831
Middle	9	8	
Lower	100	102	

Table 2: Distribution of cases according to bishop score after 6 hours of induction

Bishop score	Misoprostol group		Dinoprostone Group	
	No.	%	No.	%
<6	19	17.27	18	16.36
6-8	61	55.45	76	69.09
>8	30	27.27	16	14.55
Total	110	100.00	110	100.00
Mean score	8.11±2.01		7.69±1.83	
p-value	0.05			

Table 3: Induction delivery interval and its correlation with demographic characteristics

	Misoprostol Group	Dinoprostone Group	p-value
Parity			
Primigravida	11.97± 3.30	17.30 ± 3.59	<0.0001
Multigravida	12.10 ± 2.67	13.77 ± 3.36	0.0431
Age			
< 30	12.10 ± 3.12	16.75 ± 3.48	<0.0001
> 30	11.30 ± 2.91	13.62 ± 5.01	0.2073
Indication of Induction			
Post Term	11.96 ± 2.84	16.12 ± 3.68	<0.0001
PROM	10.62 ± 2.02	17.20 ± 5.12	0.0010
FGR	12.80 ± 3.49	16.71 ± 4.73	0.1114
Others	16.50 ± 5.80	16.25 ± 3.62	0.9036
POG (Weeks)			
< 40	12.12 ± 3.13	16.53 ± 3.87	<0.0001
> 40	10.71 ± 2.29	15.00 ± 3.63	0.0113

Table 4: Distribution of cases according to maternal outcome

	Misoprostol Group	Dinoprostone Group	p-value
Mode of delivery			
Vaginal	86	92	0.444
Caesarean Section	21	17	
Instrumental	3	1	
Induction delivery interval	12.01 ± 3.09	16.31 ± 3.85	<0.0001
Duration of stages of labor			
First Stage	10.66 ± 2.91	14.86 ± 4.16	<0.0001
Second Stage	1.37 ± 0.68	1.43 ± 0.64	0.5405
Third Stage	1.97 ± 1.11	1.88 ± 0.70	0.5119

Table 4 Continued…			
Complications			
Cervical Tear	2	1	0.8425
Perineal Tear	3	3	
PPH	2	1	

Table 5: Neonatal Outcome

	Misoprostol Group	Dinoprostone Group	p-value
Apgar Score			
1 Minute (8-10)	88.18%	89.09%	0.832
5 Minute (8-10)	94.55%	98.18%	0.150
Neonatal Birth Weight	2.68 ± 0.56	2.74 ± 0.69	0.4796
NICU Admission	6	2	0.1546
Neonatal Mortality	0	0	0

The mean induction-delivery interval was 11.97 and 17.30hrs in primigravida. It was 12.10 and 13.77hrs in multigravida cases respectively. It was significantly less in misoprostol group statistically. Women less than 30 years in misoprostol group had a significantly less mean duration of induction delivery interval. Misoprostol is better inducing agent in post term pregnancies and in induction given for pre-mature rupture of membranes than dinoprostone. There was a statistically significant difference in the induction delivery interval in the two groups. Similarly irrespective of period of gestation misoprostol group had a significantly lower induction delivery interval than dinoprostone.(**Table 4**)

The number of caesarean section were more in misoprostol group (21 vs 17) but the difference was statistically insignificant. The mean induction delivery time was 12.01 and 16.31hrs and mean duration of first stage labour was 10.66 and 14.86hrs in the two groups respectively. The difference was statistically significant. However, the two groups were comparable in duration of second and third stage of labour and also in terms of post-partum maternal complications. (**Table 4**)

There was no statistically significant difference seen in neonatal outcome in both the groups. (**Table 5**)

4. Discussion

Labour usually starts as a natural process, but at times it needs to be started artificially. Dinoprostone has been used successfully for years as an agent for induction of labour. However, it is tedious to use, requires refrigeration, is expensive, requires trained staff for proper insertion intracervically. Misoprostol as an agent for induction of labour (IOL) agent has rapidly gained popularity because it is inexpensive, stable at ambient temperatures, and easier to administer in comparison to dinoprostone and oxytocin.

Misoprostol can be administered by vaginal and oral routes. Misoprostol solution, given as low dose allows us to minimise its side effects. Purpose of administering it every 2 hours is supported by pharmacokinetic studies that show that oral misoprostol reaches its peak serum level within 30 minutes. Its half-life is only 90 minutes as it is rapidly metabolized by the liver and excreted by the kidneys. With oral misoprostol sustained uterine activity is achieved in 90 minutes and the duration of action is approximately 2 hours.[2] Here we have made an effort to study to whether or not misoprostol in low dose and as an oral formulation effective enough to induce labour like the standard drug dinoprostone, the only prostaglandin approved for marketing by FDA for induction of labour.

The mean age in our study was 23.90 ±3.49 years in misoprostol group and 24.14±3.77 years in dinoprostone group. In study by Rouzi AA et al[5] the mean age was 28.4 ± 5.4 years. The mean period of gestation in present study group in misoprostol and dinoprostone was 38.72±1.33 weeks and 38.85±1.36 weeks respectively. It is comparable to the mean period of gestation in Rouzi AA et al[4] study that was 39.9 weeks in misoprostol and 39.7 weeks in dinoprostone group. The need for augmentation with oxytocin in present study was in 26 cases (23.63%) in misoprostol group and in 80 cases (72.73%) in dinoprostone group, which was statistically significant p=<0.0001. The difference is because misoprostol not only causes cervical dilatation but also induces uterine contraction. Dinoprostone on the other hand causes only cervical ripening. Therefore, more cases had to be augmented with oxytocin in Dinoprostone group. In a study by Wang X et al, only 17.6% required oxytocin augmentation in misoprostol group and 17.1% in Dinoprostone group which was statistically insignificant in their study. In study by Rouzi AA et al. 39 cases out of 54 (72.2%) required oxytocin augmentation in case group and 39 case out of 52 (75%) in control group.

The mean induction to delivery time was statistically significant less in misoprostol group compared to Dinoprostone group. It was comparable to that reported by several other workers as shown in **Table 6**.

Table 6: Mean induction to delivery time

Workers	Year	Induction delivery interval(hours)	
		Case	Control
Mbaluka CA et al[6]	2014	8.4 ± 2.35	9.45 ± 3.04
Rouzi AA et al[5]	2014	17.6 ± 8.5	20.2±18.0
Wang X et al[1]	2016	21.3±14.5	15.7±9.6
Prameela[7]	2018	13h 43 min	13 h 26 min
Present study	2019	12.01±3.09	16.31±3.85

78.18% cases in misoprostol group and 83.64% cases in Dinoprostone group were able to deliver by vaginal route. In a Kenyan study by Mbaluka CA et al[6] where the caesarean rate was 19% in the misoprostol group and 17% in control group p=0.447, which was not statistically significant. In study by Kafy S[8] 17 cases (20.5%) were taken for caesarean section in misoprostol group.

The mean duration of first stage of labour was 10.66±2.91 hours in misoprostol group. The mean duration of first stage of labour was 14.86±4.16 hours in Dinoprostone group. This difference between the two groups was statistically significant p<0.001. The difference was because misoprostol apart from dilating the cervix induces uterine contractions as well, which leads to early progression of labour. Dinoprostone only cause cervical dilatation and is dependent on maternal oxytocin for stimulating uterine contractions.[9]

Cheng SY et al. in a clinical trial compared the use of vaginal misoprostol (25 µg every 4 h) with a titrated oral misoprostol solution and found increase rate of vaginal delivery with the vaginal route, with no cases of uterine hyperstimulation.[10]

A 2014 Cochrane review found a similar level of efficacy with oral and vaginal routes of administration but reported better perinatal outcomes with the oral route, and therefore recommended oral over vaginal administration.[11]

Titrated doses of misoprostol solution achieves better outcomes than fixed doses, as this produces constant blood levels of the drug.[12] Souza AS et al in their study found that a titrated oral misoprostol solution was as effective and safe for labor induction as vaginal misoprostol tablets.[13] Oral administration of misoprostol in solution is a route that is generally better tolerated by women since it involves fewer vaginal examinations.[14]

Recently two published meta-analyses indicate that although vaginal misoprostol (≥50 µg) is associated with a higher success rate of vaginal delivery within the first 24 h of drug administration, a low dose of titrated oral misoprostol (< 50 µg) is associated with a lower caesarean section rate.[5]

A recently completed UK National Institute of Health Research (NIHR) funded network and cost-effectiveness analysis included 31 induction regimes evaluated in 611 trials with over 100 000 trial participants. Titrated low-dose oral misoprostol was identified as likely to be the most cost-effective method, and also had a favourable safety profile.[15]

These findings suggest that oral misoprostol is as safe and effective for induction of labour as Dinoprostone gel. Also because, low dose is being used the adverse fetal effects were unremarkable.

There was no significant difference in birth weight of new born, Apgar score at 1 and 5 min, neonatal admission to NICU and neonatal mortality in both groups. Majority of neonates in both the groups had an Apgar score ³8. This was similar to study conducted by Pameela where the apgar score was 7.40 and 8.5 at 1 and 5 min respectively to cases subjected to oral misoprostol solution. This further confirms the safety of misoprostol.[7]

5. Conclusion

In our study, we found that misoprostol, as a drug for induction of labour in low dose, and as oral solution is as effective as the standard dinoprostone. It is simple to prepare, easy to administer, does not require trained staff, easily available inexpensive drug that can be stored at room temperature. Does not require titration as well. It can be given in patients with leaking per vaginum or premature rupture of membrane, where vaginal administration of either of the two drugs, vaginal misoprostol or dinoprostone is ineffective.

Dinoprostone, is an expensive drug, requires refrigeration and trained staff to instil intracervically. When compared with dinoprostone gel, misoprostol acts as a better cervical ripening agent and requires less need for oxytocin augmentation.

Low dose oral misoprostol is more effective than Dinoprostone gel for labour induction without compromising safety.

Misoprostol can be used in peripheral health centers for induction of labour, where refrigeration is a problem. When compared in two groups in term of maternal and neonatal outcome showed no statistical significance.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Wang X, Yang A, Ma Q, Li X, Qin L, Tongqiang H. Comparative study of titrated oral misoprostol solution and vaginal dinoprostone for labor induction at term pregnancy. *Arch Gynecol Obstet*. 2016;294(3):495–503.
2. Weeks AD, Navaratnam K, Alfirevic Z. Simplifying oral misoprostol protocols for the induction of labour. *BJOG*. 2017;124(11):1642–5.
3. Keirse MJ. Prostaglandins in preinduction cervical ripening. Meta-analysis of worldwide clinical experience. *J Reprod Med*. 1993;38(1 Suppl):89-100.
4. Rouzi AA, Alsahly N, Alamoudi R, Almansouri N, Alsinani N, Alkafy S, et al. Randomized clinical trial between hourly titrated and 2 hourly static oral misoprostol solution for induction of labour. *Am J Obstet Gynecol*. 2017;216(4):405.e1–6.
5. Rouzi AA, Alsibiani S, Mansouri N, Alsinani N, Darhouse K. Randomized clinical trial between hourly titrated oral misoprostol and vaginal Dinoprostone for induction of labour. *Am J Obstet Gynecol*. 2014;210(1):56.e1–6.
6. Mbaluka CM, Kamau K, Karanja JG, Mugo N. Effectiveness and safety of 2-hourly 20 mcg oral misoprostol solution compared to standard intravenous oxytocin in labour induction due to pre-labour rupture of membranes at term: a randomised clinical trial at Kenyatta National Hospital. *East Afr Med J*. 2014;91(9):303–10.
7. Parmeela, Sharma KD. Comparison between use of oral misoprostol versus vaginal misoprostol for induction of labour at term. *J Obstet Gynecol India*. 2018;68(2):88–92.
8. Kafy S. Oral Misoprostol 2 Hourly for Labor Induction. *Open J Obstet Gynecol*. 2018;8(06):553.
9. Papanikolaou EG, Plachouras N, Drougia A, Andronikou S, Vlachou C, Stefos T, et al. Comparison of misoprostol and dinoprostone for elective induction of labour in nulliparous women at full term: a randomized prospective study. *Reprod Biol Endocrinol*. 2004;2:70.
10. Cheng SY, Ming H, Lee JC. Titrated oral compared with vaginal misoprostol for labor induction: a randomized controlled trial. *Obstet Gynecol*. 2008;111(1):119–25.
11. Alfirevic Z, Aflaifel N, Weeks A. Oral misoprostol for induction of labour. *Cochrane Database Syst Rev*. 2014;13;(6):CD001338.
12. O. Lapuente-Ocamica, L. Ugarte, A. Lopez-Picado et al. Efficacy and safety of administering oral misoprostol by titration compared to vaginal misoprostol and dinoprostone for cervical ripening and induction of labour: study protocol for a randomised clinical trial. *BMC Pregnancy Childbirth*. 2019;19:14.
13. Souza AS, Feitosa FE, Costa AA, Pereira AP, Carvalho AS, Paixão RM, Katz L, Amorim MM. Titrated oral misoprostol solution versus vaginal misoprostol for labor induction. *Int J Gynaecol Obstet*. 2013;123(3):207–12.
14. Aceituno Velasco L, Sanchez Barroso MT, Segura García MH, Gonzalez Acosta V, De la Fuente Pedrosa R, Barqueros Ramirez A, et al. Efficacy and safety of oral solution dosed misoprostol versus misoprostol vaginally in labour induction. *Open J Ostet Gynecol*. 2013;3(09):673–9.
15. Alfirevic Z, Keeney E, Dowswell T, Welton NJ, Medley N, Dias S, et al. Methods to induce labour: a systematic review, network meta-analysis and cost-effectiveness analysis. *BJOG.* 2016;123(9):1462–70.

Cite this article: Singh N, Verma U, Agarwal M. The study of low dose oral misoprostol solution and its comparision with intracervical dinoprostone gel for induction of labour. *Indian J Obstet Gynecol Res*. 2025;12(3):570–575.