

A Comparative Study of Dinoprostone Gel and Dinoprostone Insert for Induction of Labor at Term Pregnancy

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Abstract: ***Aim:** The study was done to compare the efficacy of dinoprostone gel and dinoprostone insert for induction of labor. **Material and Methods:** A hospital-based prospective comparative study was conducted in the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur from April 2018 to November 2018. 100 pregnant women at term attending antenatal clinic were enrolled and were divided into two groups, Group-A (intracervical gel) and B (vaginal insert) comprising 50 women in each group. The primary outcomes measured were the number of women progressing to active labor i.e. cervical dilation >4 cm, time taken to achieve active labor and need for oxytocin augmentation. **Results:** In our study, 86.00% women in the gel group and 90.00% in insert group achieved active labor within 24 hours but there was no statistically significant difference between the two groups (P-value >0.05). In Group-A, mean time of induction to active phase was 11.8 ± 2.34 hours in primiparas and 10.8 ± 2.51 hours in multipara. In Group-B, mean time of induction to active phase was 11.42 ± 2.18 hours in primipara and 8.6 ± 2.39 hours in multipara, which was statistically insignificant in gel group but significant in insert group. The need for oxytocin administration was greater in gel group, but the difference was statistically insignificant (p-value= 0.509). A higher number of women failed to achieve a successful induction of labor in gel group as compared to insert group. But the difference was not statistically significant (p = 0.486). **Conclusions:** In terms of successful induction of labor, dinoprostone vaginal insert is similar to intracervical gel in efficacy. **Clinical Significance:** Dinoprostone vaginal insert has been introduced only recently in India. Therefore it needs evaluation of efficacy as well as comparison with the conventional intracervical gel preparation for use in the Indian population.*

Keywords: labor, dinoprostone, induction

1. Introduction

Induction of labor (IOL) is one of the commonest interventions performed in modern obstetrics. Over the past decades, more and more pregnant women around the world have undergone induction of labor to deliver their babies. In India, the rate of elective induction of labor is 32.1%.¹

Induction of labor is defined as the process of artificially stimulating the uterus to start labor.² WHO recommends induction to be performed with a clear medical indication which generally includes gestational age of 41 completed weeks or more, prelabour rupture of amniotic membranes, hypertensive disorders, maternal medical complications, and other complications.²

According to WHO guidelines, prostaglandins should be the first-line drugs for IOL.² Common prostaglandins used are dinoprostone (PGE₂) and misoprostol (PGE₁). Dinoprostone comes in two formulations which are-

1. Dinoprostone gel (3 g gel/0.5 mg Dinoprostone) - intracervical, but not above the internal os. The application can be repeated after 6-8 hrs, not to exceed 3 doses in 24 hrs.
2. Dinoprostone vaginal pessary (10 mg embedded in a mesh) - placed transversely in the posterior fornix of the vagina for 24 hrs.

Dinoprostone insert was introduced in 1995 worldwide.³ Since then, numerous studies have been done at various international levels and this novel Dinoprostone preparation has been put to judicial use in many countries for more than 2 decades. However, in India, it was licensed for use in June 2016.⁴ It has been utilized since then at many health care facilities. Still a lot of institutes favor use of traditional Dinoprostone gel for induction of labor.

Rationale for Development

The dinoprostone vaginal pessary was developed to provide a continuous, controlled release of a low-dose dinoprostone in an easy-to-use formulation. It eliminates the risk of 'dose dumping', which has been associated with an increased likelihood of adverse events. The presence of a retrieval system also means that the pessary can be rapidly and easily removed, immediately eliminating the source of dinoprostone.

2. Material and Methods

A hospital based prospective comparative study was conducted in the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur from April 2018 to November 2018. 100 pregnant women were enrolled and divided into two groups, Group-A and B, each comprising of 50 women. Group-A was intracervical gel and Group-B was vaginal pessary. All singleton pregnancies, at term, with cephalic presentation and giving consent were included. Women with

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a scarred uterus, allergy to the drug or an inadequate pelvis were excluded from study. Informed written consent was taken.

In gel group, we originally enrolled a total of 128 pregnant women. Out of 128, 78 women (60.90 %) went into active labor after first gel insertion and all those women were excluded from study. The remaining 50 women who were eligible for second gel insertion were studied thereafter. After second gel, reassessment was done after 6 hrs. In the insert group, insert removal was done when women achieved active labor or after 12 hours of induction, whichever was earlier.

In both groups, after 12 hours, if the cervical dilatation was less than 4 cm, we waited for another 12 hours along with monitoring of the fetal heart. Augmentation with oxytocin was given if uterine contractions were present but inadequate for the progression of labor. Labor monitoring was done as per WHO guidelines. Data collection and statistical analysis were done. Continuous variables were summarized as mean and standard deviation and were analyzed by using unpaired T-test. Nominal/ categorical variables were summarized as proportions and were analyzed by using chi-square/Fischer exact test. A P-value of less than 0.05 was taken as significant.

3. Results

In our study, the mean age in Group-A was 23.78 ± 2.17 years and in Group-B it was 23.20 ± 2.67 years.

In our study, percentage of primipara was 68.00% in Group-A and 66.00% in Group-B. The difference was statistically insignificant ($p = 0.99$).

In our study, postdatism was the most common indication for the induction of labor in both groups (gel=24%, insert=26%) followed by hypertensive disorder in pregnancy.

Obstetric History Wise Distribution

Obstetric history	Group-A (Gel Group)		Group-B (Insert Group)	
	No.	%	No.	%
Primipara	34	68.00	33	66.00
Multipara	16	32.00	17	34.00

$p = 0.99$

Induction to Active Phase Interval

Duration (in hrs)	Group-A {n=50} (Gel Group)		Group-B {n=50} (Insert Group)	
	No.	%	No.	%
<12	26	52.00	27	54.00
12 to 24	17	34.00	18	36.00

$p = 0.520$

There was no statistically significant difference between the two groups (p -value >0.05)

In Group-A 52% and Group-B, 54% of patients achieved active labor in less than 12 hours. The difference was not statistically significant ($p = 0.520$). In our study, we found that in Group-A, 38.24% primiparas and 81.25% multiparas reached an active phase of labor within 12 hrs as compared to Group-B, where there were 39.40% primiparas and 82.35% multiparas.

In Group-A, 47.11% primiparas and 12.50% multiparas & in Group-B, 45.45% primiparas and 17.65% multiparas took 12-24 hrs to achieve active labor. In relation to parity, the difference was found to be statistically insignificant ($p = 0.99$).

In Group-A, the average duration of induction to active phase was 11.8 ± 2.34 hrs in primiparas and 10.8 ± 2.51 hrs in multipara. In Group-B, it was 11.42 ± 2.18 hrs in primipara and 8.6 ± 2.39 hrs in multipara. The relation between parity and induction to active phase interval was found to be statistically insignificant in gel group (p -value = 0.116) and significant in insert group (p -value = 0.001).

In Group-A, 12.00% and in Group-B, 6.00% women failed to achieve successful induction of labor. All cases of failure were seen in primiparas. But the difference was not statistically significant ($p = 0.486$).

In our study, we found that a higher number of primiparas (20.50% vs 10.00%) required oxytocin administration in gel group, but the difference was insignificant ($p = 0.509$).

In our study, fetal distress was more common with gel insertion as compared to insert (16% vs 10%). The incidence of tachysystole was higher with gel as compared to insert (12% vs 2%). The difference was statistically insignificant (P value >0.05).

Induction to Active Phase Interval In Relation to Parity

Duration (in hrs)	Group-A {n=50} (Gel Group)				Group-B {n=50} (Insert Group)				p-value
	Primipara {n=34}		Multipara {n=16}		Primipara {n=33}		Multipara {n=17}		
	No.	%	No.	%	No.	%	No.	%	
<12	13	38.24	13	81.25	13	39.40	14	82.35	0.99
12 to 24	15	47.11	2	12.50	15	45.45	3	17.65	0.99

p = 0.99

Induction to Active Phase Interval (in hours) in Relation to Parity

Parity	Group-A (Gel Group)		Group-B (Insert Group)	
	Average Duration (in hours)			
	Mean	SD	Mean	SD
Primipara	11.8	2.34	11.42	2.18
Multipara	10.8	2.51	8.6	2.39
p-value	0.116		0.001	

Number of Failed Induction

	Group-A {n=50} (Gel Group)		Group-B {n=50} (Insert Group)	
	No.	%	No.	%
Number of Failed Induction	6	12.00	3	6.00

p = 0.486

Oxytocin Administration

Oxytocin Administration	Group-A {n=50} (Gel Group)		Group-B {n=50} (Insert Group)	
	No.	%	No.	%
Primipara	7	20.50	6	10.00
Multipara	1	6.25	1	5.80

p = 0.509

4. Discussion

The process of induction of labor requires a careful assessment of the indication, appropriate choice of the method and skillful procedure to attain the final goal of obstetrics.

In our study, number of primiparas were higher in both gel and insert groups because primipara women commonly require induction of labor as compared to multipara women.

In our study, postdatism was the most common indication for the induction of labor in both groups followed by hypertensive disorder in pregnancy. The WHO Global Survey on Maternal and Perinatal Health (WHOGS-2013) also observed that in the Asian population, the commonest indication for IOL was prolonged pregnancy (19.4%).1

In present study, greater number of patients in the insert group achieved active labor within 12 hours but the difference was not statistically significant ($p > 0.05$). Facchinetti F et al (2007) 5 also found that the vaginal insert was associated with more women going into labor than with the intracervical gel without further stimulation.

The average duration of induction to active phase was shorter for both primiparas and multiparas in the insert group as compared to the gel group. The relationship between parity and induction to active phase interval was found to be statistically insignificant in gel group (p -value = 0.116) but significant in insert group (p -value = 0.001). A possible explanation for this difference can be that gel formulation may get spilled from the cervix during leaking or when the patient is mobile and thus unable to act as was expected. Pessary, however, is immobile and is better able to act on cervix. Also, a primipara cervix is firm, closed and longer as compared to the multipara cervix. This may pose a challenge for intracervical gel instillation.

El-Shawarby SA et al (2006) 6 observed that the time between first insertion and diagnosis of labor was not significantly different between the two groups (19.9 hours in insert group and 18 hours in gel group: $p > 0.05$), and also while comparing primigravidas and multiparous women in each group. Zanconato G et al (2011) 7 and Shirley M (2018) 8 in their respective studies also found similar results. They observed that dinoprostone gel and insert were both efficient and equivalent in achieving cervical ripening and successful labor in both nulliparous and multiparous women. Facchinetti F et al (2007) 5 noted that the time from induction to labor onset was significantly different between

the groups (vaginal insert, 12.4 ± 7.5 ; gel, 16.6 ± 11.1 hours; $p=0.024$). Ashwal E et al (2014) 9 in their study found that vaginal insert was associated with shorter initiation-to-ripening interval (12.4 ± 7.7 versus 18.6 ± 15.2 h, $p<0.001$).

Different literature uses different definitions of failed induction as there is no single consensus or guideline. In our study, we used the term failed induction for those cases in which after 24 hours of two intracervical gel or single vaginal insert, there was no cervical dilation with or without uterine contraction. The gel group had greater number of women who failed to achieve successful induction of labor (12% vs 6%, $p\text{-value}>0.05$). All cases of failure were seen in primiparas. Kumari A et al (2018) 10 and Mazumdar ND et al (2018) 11 also found similar results.

Oxytocin administration was done when uterine contractions were present but were inadequate for the progression of labor. In our study, we found that a higher number of primiparas (20.50% vs 10.00%) required oxytocin administration in gel group, but the difference was insignificant. Zanconato G et al (2011) 7 and Basu A et al (2012) 12 also noticed that the rate of oxytocin augmentation of labor did not differ significantly between the groups.

5. Conclusion

To conclude, in terms of success and failure, vaginal inserts releasing dinoprostone are not different from intracervical gel. However, there are some advantages to insert over conventional gel preparation. These include fewer doses required to achieve ripening and induction, lesser need for oxytocin augmentation, less invasiveness and pain to women along with a decreased number of vaginal examinations. Also, it is easy to administer and remove allowing greater dose control and reduced risk of adverse effects.

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