

**A COMPARATIVE STUDY OF THE SAFETY AND EFFICACY OF INTRA VAGINAL MISOPROSTOL TABLET VERSUS INTRA CERVICAL DINOPROSTONE GEL FOR CERVICAL RIPENING AND INDUCTION OF LABOUR**K. N. Madhavi<sup>1</sup>, K. P. Polaiah<sup>2</sup>, Thokala Sivaiah<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: BACK GROUND:** To study and compare the efficacy and safety of intra vaginal misoprostol versus intra cervical dinoprostone gel for cervical ripening and induction of labour.

**Objectives:** 1. To study and compare efficacy and safety of misoprostol and dinoprostone gel. 2. To study the success rate and outcome of induction 3. To Study the average induction –delivery interval 4. To study the side effects during induction with these drugs. **DESIGN:** It is a prospective study.

**STUDY AREA:** Department of Obstetrics & Gynecology, Government General Hospital, Guntur, affiliated to Guntur Medical College. **STUDY SUBJECT:** Antenatal Women. **SAMPLE SIZE:** 100 Antenatal women who were admitted in Antenatal ward in Department of Obstetrics.

**STUDY PERIOD:** September 2013 to September 2014. **RESULTS:** 100 antenatal women requiring induction of labour were followed 50 received 25 µg misoprostol 4<sup>th</sup> hourly, 0.5 mg of intracervical dinoprostol gel 12 hourly. The result of the study shows induction delivery interval was significantly shorter in misoprostol group than dinoprostone group. Caesarean section rate is low in misprostol group compared to dinoprostone group. With the lower dosage of misoprostol, no maternal complications were observed and foetal complication i.e., meconium stained liquor was seen in 8% of misoprostol group, but Apgar score was good in both group. **CONCLUSION:** On basis of our study misoprostol is an effective and safe drug to mother and foetus, easy to administer, and stable at room temperature, and misoprostol is a cheaper drug better and effective alternate to dinoprostone gel in a women belonging to resource constrained developing countries.

**KEYWORDS:** Misoprostol, Dinoprostone gel, Bishop Score, Induction delivery interval.

**INTRODUCTION:** Day to day challenge to an obstetrician is induction of labour for obstetric indications and to achieve successful induction. The indications for induction have been steadily widened in recent year. Induction of labour is the non-spontaneous initiation of uterine contractions prior to their spontaneous onset leading to progressive effacement and dilation of cervix and delivery of the baby. Induction primarily refers to attempt to produce regular uterine contraction along with cervical changes to begin the active phase of labour.<sup>[1]</sup> It is a common procedure and about 20% of pregnant women will have labour induced for a variety of reason.<sup>[2]</sup>

The aim of successful induction is to achieve vaginal delivery and to reduce caesarean section. The neonate should be delivered in a good condition with an acceptable time, and a minimum of maternal side effects.

It has become clear that prostaglandins have the advantage over oxytocin, both by acting locally or secondarily by including endogenous oxytocin release. PGE<sub>2</sub> has been used for more than a

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decade for cervical ripening and labour induction and has been approved by food and drug administration. Recently a prostaglandin E<sub>1</sub> analogue misoprostol has received increased attention as a high effective cervical ripening agent. This medication has the advantage of being inexpensive, easy to store and stable at room temperature.

Initial studies by Fletcher et al, 1995, Chuck and Haftaker 1995,<sup>[3]</sup> Varaklij and colleagues 1995, Win et al 1995a, 1995b, Herabutya Y et al 1997<sup>[4]</sup>, suggested that Misoprostol tablets placed into vagina were either superior to or equivalent in efficacy compared with intra cervical PGE<sub>2</sub> gel.

Intra vaginal or intra cervical administration of exogenous PGE<sub>1</sub> (Misoprostol) and PGE<sub>2</sub> (Dinoprostone) are the most widely used pharmacological method to promote cervical ripening and labour induction.<sup>[5,6]</sup>

There is increasing evidence in the literature that Misoprostol, a synthetic analogue of PGE<sub>1</sub> plays an essential role in initiation and maintain of parturition in humans. Successful induction of labour has been achieved by PGE<sub>1</sub> analogue misoprostol administered orally and intra vaginally.

Successful outcome of spontaneous or induced labour is the result of well co-ordinated interplay between upper segments dominant and contracting, lower segment passive and delaying. Prostaglandins are found to achieve this goal.

**MATERIAL AND METHODOLOGY:** After taking informed consent, 100 patients who have completed 37 weeks of gestation are selected from antenatal ward of OBG department of Government General Hospital, Guntur, during the period September 2013 to September 2014. Indications for induction of labour were varied. Among the 100 patients half of them were induced with intra vaginal misoprostol of 25 µg kept in the posterior fornix of the vagina every 4 hourly for a maximum of 6 does. In 50 cases induction was carried out by single application of 0.5 µg dinoprostone gel. In some dinoprostone gel instilled cases supplementation was done with oxytocin or misoprostol and results were compared.

The inclusion criteria of patients for induction are, women not in active labour with intact membranes and should be

### INCLUSION CRITERIA:

1. singleton pregnancy,
2. cephalic presentation,
3. completed 37 wks gestation,
4. bishop score less than or equal to 4,
5. contraindications for vaginal delivery like CPD, contracted pelvis and abnormal lie, no contraindications for usage of prostaglandins and no lower genital tract infection.

### EXCLUSION CRITERIA FOR INDUCTION:

1. Non reassuring foetal heart pattern.
2. Malpresentations.
3. Multiple pregnancy.
4. Cephalo pelvic disproportion.
5. History of previous caesarean section or scar on the uterus.
6. Antepartum haemorrhage.

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7. Grand Multi paras.
8. Allergy to prostaglandins.

The indications for induction taken in this study are (1) Past dates (2) Preeclampsia (3) Oligohydromnios (4) Polyhydromnios.

**METHODS:** Misoprostol after taking informed consent the 100 µg or 200 µg tablets were divided into 25µg bits and under aspects precautions, 25µg misoprostol kept in the posterior fornix of vagina, the drug was repeated every 4<sup>th</sup> hourly until delivery occurs or within 24 hours (up to 6 doses) after starting of induction or method was terminated when the foetal distress or uncontrolled PIH warranted immediate termination by abdominal delivery. PGE<sub>2</sub> (Dinoprostone) Gel: dinoprostone gel, in a special syringe with a catheter containing 0.5mg of dinoprostone per 2 gms of gel is instilled into the cervical canal. Following application patient should remain supine position for at least 15-30 minutes to prevent leakage of gel.

**MONITORING:** The treatment was considered successful if the patient delivered spontaneously within 24 hours. In failed cases the cervical scores were recorded at the end of the study and compared with initial scores. The type of delivery and induction – delivery interval were recorded. The weight of baby Apgar score at 1 min and 5 min were recorded and neonatal complications were noted.

**RESULTS:** 100 antenatal women were followed in this study among them 50 were induced with 25 µg misoprostol intra vaginal tablets and rest of the 50 we induces with dinoprostone intra cervical gel.

**STATISTICAL ANALYSIS:** The collected data was entered into Microsoft Office Excel - 2007 and date analysis was performed by using the statistical software Graph pad prism - 6. The analyzed data was presented as Mean, Standard deviation (SD) and percentages. Data between misoprostol group and dinoprostone gel group was analyzed by using unpaired t test to find out the differences between the two means and by Chi square t test.

The demographic features of women, i.e., age, gravidity and parity were similar.

	Misoprostol		Dinoprostone	
	No of Cases	Percentage	No of Cases	Percentage
Pre Eclampsia	16	32%	12	24%
Oligo & Polyhydromnios	8	16%	8	16%
Post Dated Pregnancy	26	52%	30	60%

**Table 1: Indications for Induction**

\* P value is <0.9999 (by chi square test) statistically not significant.

The major percentage 52% in misoprostol group, 60% in dinoprostone group had 41-42 weeks of gestational age needed induction for post-dates, 16% in both groups needed induction for oligo and polyhydromnios. 32% in misoprostol group, 24% in Dinoprostone group had need induction for preeclampsia. The prior Bishop Score in both groups were almost similar.

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Time in Hours	Misoprostol		Dinoprostone	
	No of Cases	Percentage	No of Cases	Percentage
<0-6	06	12	00	00
7-12	22	44	12	24
13-18	14	28	22	44
19-24	08	16	10	20
>24	00	00	06	12

**Table 2: Induction delivery Interval**

\*P value is 0.0020 (by chi square test) statistically significant.

In this study maximum no of women i.e., (84% in misoprostol group, 68% in dinoprostone group) delivered within 18 hours of induction. No women in misoprostol group >24 hours, where as in dinoprostone group 12% patients took >24 hours for delivery after induction. It is a statically significant, p value: 0.0020.

Time (hours)	Average Induction delivery interval (Hours)		
	Misoprostol Group Mean + SD	Dinoprostone Group Mean + SD	Statistical Analysis (P value)
All Patients	(No =50) 11.64 + 4.869	(N=50) 16.98 + 5.212	<0.0001 Significant
Primi Gravida	(No = 34) 13 + 4.997	(N=32) 18.53 + 5.511	<0.0001 Significant
Multi Gravida	(N=16) 8.750 + 3.066	(N=18) 14.22 + 3.021	<0.0001 Significant

**Table 3: Average induction delivery interval in relation with parity**

\*P value is 0.0001 (by chi square test) statistically significant.

The induction - delivery interval was significantly shorter in all pregnant women in misoprostol group than in dinoprostone group. In both primigravida and multigravida the observed difference in the induction - delivery interval was statistically significant.

Para Meters	Misoprostol		Dinoprostone	
	No of Cases	Percentage	No of Cases	Percentage
Success Rate Vaginal Delivery	46	92%	42	84%
Failure Rate (Caesarean Section)	4	8%	8	16%

**Table 4: Success and Failure Rates**

\*P value is 0.2184 (by chi square test) statistically not significant.

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The percentage of women who had vaginal delivery taken as a criteria for success rate, and who had caesarean section taken as a criteria for failure rate, the percentage of success rate is 92% in misoprostol group, 84% were dinoprostone group, caesarean section rate 8% in misoprostol group, 16% in dinoprostone group. But the difference was not statically significant. The indication for caesarean section in both groups was for failed induction, for foetal distress, and for failure to progress.

The foetal complications like meconium stained liquor has occurred in misoprostol group was 8% in dinoprostone group was 4%, but they were not significant.

Apgar		Misoprostol		Dinoprostone	
		No of Cases	Percentage	No of Cases	Percentage
1 Min	<8	0	0	0	0
	>8	50	100%	50	100%
5 min	<8	0	0	0	0
	>8	50	100%	50	100%

**Table 5: Foetal Outcome**

Apgar scoring in both the groups was same. Even though meconium stained liquor noticed little high in misoprostol group, but APGAR score was same. It is not significant.

**DISCUSSION:** Induction of labour with prostaglandins offers the advantage of promoting both cervical ripening and myometrial contractility. The use of prostaglandins for this purpose had been extensively reported. Prostaglandin E<sub>1</sub> i.e., misoprostol in this group is compared with the PGE<sub>2</sub> Gel.

The present study was undertaken to compare the efficacy of intra vaginal misoprostol tablet with intra cervical dinoprostone gel for cervical ripening and induction of labour. 100 Antenatal women who were having indications for induction, divided into two groups. 50 cases were induced with 25 µg of misoprostol kept in the vagina repeated every 4<sup>th</sup> hourly for a maximum of 6 doses.

In 50 cases induction was carried out by single application of dinoprostone gel. The dose was repeated only if the patient could afford another dose, otherwise she was supplemented with oxytocin or misoprostol and results were compared.

The study group consists of primi gravid to multi gravid. In majority of cases the indication was done past dates. The Bishop Score was almost same in the both groups. 84% in misoprostol group and 68% in dinoprostone group delivered within 18 hours of induction, no women are seen in misoprostol group >24 hours. Where as in dinoprostone group 12% of patients, took >24 hours for delivered of induction.

In the present study the average induction delivery interval was 13± 4.997. in primi's, 8.75±3.06 in multi's in misoprostol group, where as it was 16.98 ± 5.511 in primi's, 14.22 ± 3.02 in multi's in dinoprostone group respectively. It was statistically significant and was in accordance with the study by Nanda et al.<sup>[7]</sup>

The no of vaginal deliveries are 92% in misoprostol and 84% in dinopostone group. Gupta N et al <sup>[8]</sup> have also reported that vaginal deliveries were 86% in misoprostol, 68% in dinoprostone group.

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Foetal complications were less in dinoprostone gel group but there was no significant difference (8% vs 4%). Chuck et al also reported that no significant difference was noted in maternal and foetal effects. Rates of caesarean section were less in misoprostol group (8% vs 16%) but statistically insignificant. Jouatte et al<sup>[9]</sup> stated that, there was no significant difference in the rates of caesarean section.

In this study there was no significant statistically difference apgar score at 1 min and min between both group similar to the study by Daniel et al <sup>[10]</sup> and Herabutya et al Van Gemund et al <sup>[11]</sup>. In this study with this lower dosage 25 µg of misoprostol lesser neonatal complications and maternal complication were noted.

**CONCLUSIONS AND RECOMMENDATIONS:** For induction of labour in obstetrics indications, prostaglandins are effective agents to achieve successful outcome on the basis of our study misoprostol appears effective agent for indication of labour as compared to dinoprostone.

The result shows that successful outcome was more and caesarean section rate was less in misoprostol group. Induction deliver interval was shorter compare to Dinoprostone group. Coming to cost wise misoprostol is cheaper than dinoprostone, easy to administer by intra vaginal route and does not require refrigeration.

Hence the intra vaginal misoprostol for induction of labour is a better, effective and safe alternative drug for induction of labour, in a women belonging to resource constrained developing countries.

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