

## Comparison of safety, efficacy and cost effectiveness of intravaginal misoprostol and intracervical dinoprostone for induction of labour

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### ABSTRACT

**Background:** Misoprostol is more efficacious than dinoprostone for induction of labour. But the adverse effects produced by misoprostol were different. The aims of this study was to compare the safety, efficacy, cost effectiveness of intravaginal misoprostol and intracervical dinoprostone for induction of labour and their effects on intrapartum complications, mode of delivery and neonatal outcome.

**Materials and Methods:** This is a randomized, parallel, two tailed, prospective, open label comparative trial. Sixty pregnant women were included in the study and it was carried out in the Department of Obstetrics, Government General Hospital, Kurnool Medical College, Kurnool during the period Dec. 2009 - June 2010. Out of 60 patients, 30 received misoprostol 25 mcg intravaginally and 30 received dinoprostone 0.5 mg intracervically. Analysis and comparison of various parameters like induction- delivery interval, mode of delivery, neonatal outcome, foeto-maternal complications and cost of the drug were done. Mean and standard deviation of all observations were calculated and tabulated with the help of 'Microsoft Excel'. Comparison was done by applying student's t-test. Statistical significance was assigned at P<0.05.

**Results:** Misoprostol is more efficacious for cervical ripening and labor induction than dinoprostone. Misoprostol group had more number of vaginal deliveries, lesser requirement of oxytocin for labor augmentation, more number of vaginal deliveries within 12 hrs, less induction failures and was cost effective. However, it was reported to have slightly higher incidence of uterine contractility abnormalities and foetal complications.

**Conclusion:** Misoprostol is more efficacious than dinoprostone. However uterine contraction abnormalities, fetal complications should be carefully assessed by close monitoring of labor by intrapartum cardiotocography and partogram.

**Key words:** Cervical ripening, labor induction, induction - delivery interval, induction failure, tachysystole.

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### INTRODUCTION

The goal of successful induction of labour<sup>[1]</sup> is to achieve vaginal delivery to avert anticipated adverse outcome associated with continuation of pregnancy.<sup>[2]</sup> In the past decade, our knowledge of the mechanisms of labor has increased tremendously. In addition, the ability to detect and manage antepartum maternal and fetal complications has greatly improved. As a result, labor can be induced in an increasingly rational and successful manner.<sup>[3]</sup> Induction of labour in an unripe cervix is associated with frequent maternal complications and high rates of failure to the extent of 20 - 50% and caesarean delivery<sup>[4]</sup> Even when vaginal delivery is

achieved these patients often have prolonged labour, with increased incidence of instrumental delivery and low APGAR.<sup>[4]</sup>

Induction of labour is one of the most commonly performed obstetric procedures. The condition of the cervix or favorability is important for the success of labour induction which is described by Bishop.<sup>[5]</sup> As Bishop score decreases, there is an increasingly unsuccessful

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induction rate. The scores  $< 6$  are definitely discouraging and warrant an attempt at ripening of cervix.<sup>[4]</sup> Prostaglandins as pharmacological ripening agents offer the advantage of promoting cervical ripening with increases in myometrial contractility.<sup>[6-11]</sup> Some studies done in the past concluded that misoprostol is more efficacious than dinoprostone.<sup>[12-15]</sup> But the adverse effects produced by misoprostol were tachysystole and hyperstimulation, low APGAR and meconium stained liquor.

This study was aimed to compare the safety and efficacy of intravaginal prostaglandin E<sub>1</sub> (misoprostol) and intracervical prostaglandin E<sub>2</sub> (dinoprostone) in induction of labour. Intrapartum complications, mode of delivery, neonatal outcome and cost effectiveness were also compared.

## MATERIALS AND METHODS

### Methodology

This is a randomized, parallel, two tailed, prospective, open-label, comparator - controlled trial among pregnant women. The study was carried out in the Department of Obstetrics, Government General Hospital, Kurnool Medical College, Kurnool, India. The study was conducted between Dec. 2009 and June 2010 after the approval of ethics committee. The antenatal pregnant women were decided for induction of labour after a detailed history, thorough clinical examination, appropriate investigations and cervical assessment with Bishop's score. Subjects were included in the study only after the informed consent was obtained.

### Inclusion and exclusion criteria

Inclusion criteria included Bishop's score of  $\leq 5$ , Singleton gestation, live foetus, cephalic presentation, adequacy of pelvis, intact membranes, pregnancy induced hypertension, past dates and Rh negative pregnancy at term.

Exclusion criteria for this study include multiple pregnancy, malpresentation, abnormal foetus heart rate pattern, cephalo pelvic dispro-

portion, ruptured membranes, previous uterine surgery, parity more than 3, previous history of hypersensitivity to prostaglandins, bad obstetric history, placenta previa and Bishop's score of  $> 5$ .

### Intervention protocol<sup>[16]</sup>

The patients were randomly divided into two groups. Out of 60 patients, 30 (PGE<sub>1</sub> group) received misoprostol 25  $\mu$ g intravaginally and remaining 30 patients (PGE<sub>2</sub> group) received dinoprostone 0.5 mg intracervically.

PGE<sub>1</sub> tablet - Under aseptic precautions, 25  $\mu$ g of misoprostol was placed digitally in the posterior fornix of the vagina, every 4<sup>th</sup> hourly for a maximum of 6 doses.

PGE<sub>2</sub> gel - Under aseptic precautions, 0.5 mg of dinoprostone gel was instilled intracervically, 6<sup>th</sup> hourly for a maximum of 3 doses. After the drug installation patient was kept in bed strictly for 30 minutes.

Uterine contractions and fetal heart rate were observed carefully. The doses were repeated till either the change of Bishop score to  $> 6$  or till 3 instillations of PGE<sub>2</sub> gel / 6 doses of PGE<sub>1</sub>, whichever accomplished earlier. Whenever necessary, labor was augmented with oxytocin in incremental doses starting with 2 mIU/min maximum upto 20 mIU/min increased at intervals of 30 min.<sup>[6]</sup>

Maternal pulse, blood pressure, and fetal heart rate were monitored every 30 minutes. Progress of labour was assessed by partogram. Complications during induction of labour encountered were noted. Even after receiving the last dose of PGE<sub>1</sub> or PGE<sub>2</sub>, if Bishop score change was  $< 6$ , it was considered to be failure of induction and was taken for caesarean section.

### Parameters assessed

The efficacy and safety of the two drug interventions were assessed using parameters such as induction- delivery interval, mode of delivery, neonatal outcome, foeto- maternal complications and cost of the drug.

## Statistical analysis

The mean of both groups were compared using student's t-test. The statistical significance was set as  $p < 0.05$ . Results were tabulated using 'Microsoft Excel-2007'.

## RESULTS

### Age and parity wise distribution of pregnant women (Table 1)

In our study, both PGE<sub>1</sub> and PGE<sub>2</sub> had almost equal number of patients present in all age groups. Multiparous were more in number when compared to primiparous in both groups.

### Indications for induction of labour (table 2)

Among 5 indications, prolonged pregnancy and pregnancy induced hypertension were the common causes for induction of labour.

### Comparison of safety and efficacy (Table 3)

Vaginal deliveries were more for PGE<sub>1</sub> than PGE<sub>2</sub> ( $p < 0.001$ ). Most of the women in PGE<sub>1</sub> group delivered within 12 hrs ( $p < 0.001$ ). PGE<sub>2</sub> group had more vaginal deliveries (14) between 12 - 24 hrs. No patients delivered after 24 hrs in PGE<sub>1</sub> group, whereas, one patient delivered after 24 hrs in PGE<sub>2</sub> group. Rate of Caesarean section was more in PGE<sub>2</sub> group due to failed induction.

Number of patients with side effects in PGE<sub>1</sub> group was more than PGE<sub>2</sub>. Maternal complications are more or less equal in both groups. Fetal complications are more with PGE<sub>1</sub> ( $p = < 0.05$ ). Seven babies born for PGE<sub>1</sub> treated mothers had low APGAR score. The average cost for labour induction in PGE<sub>1</sub> group is less than PGE<sub>2</sub>.

**Table 1: Age and parity wise distribution of subjects**

Age	PGE <sub>1</sub>	PGE <sub>2</sub>
<20yrs	13	16
21-25	14	9
26-30	3	5
TATOL	30	30
Parity	PGE <sub>1</sub>	PGE <sub>2</sub>
Primiparous	14	13
Multiparous	16	17
Total	30	30

**Table 2: Indications for induction of labour**

Indication	PGE <sub>1</sub>	PGE <sub>2</sub>	Total
Prolonged Pregnancy	21	15	36
Pregnancy induced hypertension	7	12	19
Intra uterine growth retardation	1	2	3
Well controlled gestational Diabetes mellitus	1	0	1
Rh - ve	0	1	1
Total	30	30	60

**Table 3: Comparison of safety, efficacy and cost effectiveness of intravaginal misoprostol and intracervical dinoprostone for induction of labour among pregnant women.**

Outcome	PGE <sub>1</sub>	PGE <sub>2</sub>	Mean $\pm$ SD		student's t-test	P value
			PGE <sub>1</sub>	PGE <sub>2</sub>		
Vaginal Deliveries	24	21	0.8 $\pm$ 0.4	0.7 $\pm$ 0.46	0.889	< 0.001
Total IDI duration for vaginal delivery (VD) in hrs	116.58	260.83	11.05 $\pm$ 3.42	15.05 $\pm$ 5.05	3.071	< 0.001
VDs within 12 hrs (IDI duration in hr)	16 (148.5)	6 (55.17)	9.28 $\pm$ 2.10	9.19 $\pm$ 1.81	4.052	< 0.001
Indications for Caesarean delivery	3 + 3	2 + 7	0.2 $\pm$ 0.4	0.3 $\pm$ 0.46	0.889	< 0.5
Side Effects	2 + 2	1 + 1	0.13 $\pm$ 0.34	0.07 $\pm$ 0.25	0.798	> 0.5
Maternal Complications	2 + 1	1 + 1	0.1 $\pm$ 0.3	0.07 $\pm$ 0.25	0.417	> 0.5
Foetal Complications	2 + 7 + 7	1 + 3 + 2	0.77 $\pm$ 0.42	0.9 $\pm$ 0.3	3.190	< 0.05
Neonatal Outcome (Good APGAR)	23	27	0.77 $\pm$ 0.42	0.9 $\pm$ 0.3	0.136	> 0.5
Need for Oxytocin augmentation	9	14				
Cost Effectiveness (₹)	11.70	365.40				

IDI - induction delivery interval.

Indications for Caesarean delivery (Fetal distress +Failed Induction), side effects (Pyrexia with shivering+Nausea, vomiting), foetal complications (Admission to NICU+ Low APGAR+ meconium stained liquor), maternal Complications (tachysystole + hyperstimulation), cost Effectiveness (Average cost of the drugs used for induction).

## DISCUSSION

Induction of Labour is one of the most commonly performed obstetric procedures. The prostaglandins are highly effective cervical ripening agents and used to shorten the induction to delivery interval in order to improve induction success and to reduce morbidities associated with prolonged labour induction. Multiple trials have been studied in the past to show the efficiency of PGE<sub>1</sub> over PGE<sub>2</sub>.

### Vaginal deliveries

Shakya et al<sup>[12]</sup> study showed a slight increase in vaginal deliveries with PGE<sub>1</sub> group, but not statistically significant. In our study, 80% of PGE<sub>1</sub> group had vaginal induction to delivery interval in vaginal deliveries. This is statistically significant.

### Induction to delivery interval in vaginal deliveries

Previous studies<sup>[13,15]</sup> showed shorter induction to delivery interval with PGE<sub>1</sub> group than PGE<sub>2</sub> group. Our studies also showed concurrence with this study ( $p < 0.001$ ).

### Vaginal delivery within 12 and 24 hrs of induction of labour

Most of PGE<sub>1</sub> group had vaginal deliveries interval in vaginal deliveries within 12hrs. 100% of PGE<sub>1</sub> group had vaginal deliveries within 24 hrs compared to PGE<sub>2</sub> group (66.7%). In PGE<sub>2</sub> group, only one patient delivered after 24 hrs. The Cochrane pregnancy and child birth group<sup>[14]</sup> reviewed trails comparing PGE<sub>1</sub> with placebo, oxytocin, PGE<sub>2</sub> for cervical ripening, which showed that vaginal PGE<sub>1</sub> was most effective than PGE<sub>2</sub> for inducing vaginal deliveries with in 24hrs.

### Failed induction and Caesarean section rate

Our study revealed that the proportion of women who underwent Caesarean section for failed induction was lower with PGE<sub>1</sub> group than PGE<sub>2</sub> group. Krishnamurthy et al<sup>[15]</sup> had reported that there was significantly lower in Caesarean delivery with PGE<sub>1</sub> group than PGE<sub>2</sub> group, which is similar to our study, with no significant statistical significance.

## Need of oxytocin for labour augmentation

Earlier studies<sup>[13,15]</sup> showed that PGE<sub>1</sub> was associated with less need of oxytocin for labour augmentation, which is correlating with our study. The Cochrane review also concluded that oxytocin augmentation was consistently used less often with PGE<sub>1</sub>.

### Maternal complications

The complications may be hyperstimulation,<sup>[18]</sup> tachysystole,<sup>[19]</sup> abruption, fever, vomiting, diarrhoea, meconium stained liquor, fetal distress, amniotic fluid embolism and PPH. Tachysystole, hyperstimulation, hyper-systole<sup>[20]</sup> may occur, with both oxytocin and prostaglandin administration. It can be managed by stopping oxytocin, prostaglandin administration and treating with tocolytics.<sup>[10]</sup>

In the present study, it was observed of tachysystole and hyperstimulation was more with PGE<sub>1</sub> group than PGE<sub>2</sub> group. However there is a lack of statistical significance for this but is comparable to the earlier literature.<sup>[13,15]</sup>

### Foetal complications and neonatal outcome

Regarding neonatal outcome with PGE<sub>1</sub> and PGE<sub>2</sub> groups, perinatal results are evaluated by admission to NICU, low APGAR, meconium stained liquor. Over all foetal complications were slightly more with PGE<sub>1</sub> group than PGE<sub>2</sub>. This is statistically significant. Gupta et al<sup>[17]</sup> study had also reported similar perinatal outcome in both groups.

### Average cost of induction

Most of the studies conducted both in India and abroad comparing PGE<sub>1</sub> with other regimens for induction, have conformed the similar cost effectiveness of PGE<sub>1</sub>.

In our study, vaginal deliveries, the time of duration of normal labour and vaginal deliveries within 12 hours are considered as success of induction. All mothers and babies were healthy at time of discharge.

In conclusion, misoprostol (PGE<sub>1</sub>) is more efficacious for cervical ripening and labor



induction than dinoprostone (PGE<sub>2</sub>) as misoprostol had lesser requirement of oxytocin for labor augmentation, shorter induction-delivery interval, more number of vaginal deliveries, less caesarean section rate, more cost effectiveness. However uterine contraction abnormalities, fetal heart irregularities and meconium staining of liquor with PGE<sub>1</sub> should be carefully assessed by close monitoring of labor by intrapartum cardiotocography and partogram.

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