Comparative study between dinoprostone gel and vaginal misoprostol in induction of labour

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ABSTRACT
The study compares the efficacy and safety of 25mcg Misoprostol tablet administered vaginally with that of 0.5mg Dinoprostone gel intra vaginally in induction of labour. This is prospective comparative study between dinoprostone gel and vaginal misoprostol in induction of labour carried out between 1st July 2009 to 30 Jun 2010 at department of obstetrics & gynecology, s.s.ghospital ,baroda medical college,baroda. 100 patients are included in this study. 50 cases each in both the groups are taken for induction of labor with 25 mcg misoprostol intravaginal & 0.5 mg dinoprostone gel intravaginally.Requirement of augmentation was only 56% in Misoprostol group compared 84% in Dinoprostone gel group, which was significant (P value <0.05). The Mean induction to vaginal delivery interval was shorter in Misoprostol group, 10‘30”± 4 ’41”hours, as compared to Dinoprostone gel group, which was 12’06” ± 4’41”hours. In Dinoprostone gel group, main indication for LSCS was fetal distress in first stage of labour and in Misoprostol group fetal distress in first stage of labour, hyperstimulation & non progression in first stage of labour were indications. Misoprostol induction is 10-15 times cheaper than induction with Dinoprostone gel. Intravaginal Misoprostol is an efficacious agent in terms of short induction delivery interval, lesser requirement of augmentation ,increase in bishop score and low cost over intravaginal Dinoprostone gel.Due to these advantages Misoprostol has become a preferred option for labour induction of labour and to solve problem of cervical ripening .

Keywords : Bishop score, cervical ripening, uterine contraction.

INTRODUCTION
Induction of labour means deliberate termination of pregnancy beyond 28 weeks of gestation (age of viability) by any method which aims at initiation of labour and a "vaginal delivery". It is many a times done while keeping in mind the well being of mother and fetus in various medical and obstetrical conditions. This is needed when benefits of termination of pregnancy outweigh those of continuing the pregnancy.

A delicate balance between uterine activity, cervical dilatation and response of fetus should be sought to achieve the goal. Timely induction could reduce the maternal mortality and morbidity as well as ensure the delivery of healthy baby. The mechanism involved in the onset of human labour is highly complex. Often ripening of cervix is not completely separated from uterine contractions, and may be either a cause or an effect of those contractions occurring at the onset of labour. The medical history of labour induction began in eighteenth century. George Maculey advocated inducing labour to prevent dystocia due to pelvic contraction. In the past, castor oil, enema and warm bath have all been used as a method of labour induction But there are no conclusive data available for their use in clinical practice, as cervical ripening and induction of labour. In 1810, James Hamilton of England introduced stripping of membranes which is still prevalent in current practice. The neurohormonal mechanism behind the stretching of cervix was proposed by Ferguson in 1941. Various other methods like insertion of lamanaria tents,osmotic dilators,rubber balloon were introduced,which were found hazardous and risky for both mother and baby. In 1953, Du Vigneaud and associates isolated pure oxytocin and its chemical characterization, for which he was awarded Nobel Prize in 1955. Prostaglandins (PGs) of different classes have been widely used as alternatives to oxytocin for induction of labour. Induction of labour with local application of PGs offers the advantage of promoting both cervical ripening and myometrial contractility. Traditionally, PGE2 preparations, containing Dinoprostone, have been used locally (Intravaginal / Intracervical) with a high success rate. More recently, Misoprostol, a synthetic PGE1 analogue, introduced as a gastric cytoprotective agent for the
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prevention of peptic ulcers, has been shown to be highly effective for cervical ripening and labour induction in patients at term. This medication has the advantage of being inexpensive, easy to store, stable at room temperature and convenient to use.

The present study aims at comparing the efficacy and safety of the two above mentioned PGs for cervical ripening and labour induction, and thus helps in finding out an ideal drug that is safer and yields better results.

Our study is undertaken to compare the efficacy and safety of 25mcg Misoprostol tablet administered vaginally with that of 0.5mg Dinoprostone gel intra vaginally in achieving cervical ripening and induction of labour within a reasonable time with minimal contractile problems.

The aim of the study was to achieve safe vaginal delivery of a fetus, without undue prolongation, with minimal aid and without any complications affecting the health of the mother or the baby.

The objectives were:
To determine the efficacy, safety and reliability of intravaginal PGE1 and intravaginal PGE2 for induction of labour.
To compare the results of PGE1 with those of PGE2 induction.
To analyze results with reference to the following points:
- Need of augmentation.
- Induction to delivery interval.
- Success and failure rates.
- Associated side effects and complications

MATERIALS AND METHODS

This is prospective comparative study between dinoprostone gel and vaginal misoprostol in induction of labour carried out between 1st July 2009 to 30 Jun 2010 at department of obstetrics & gynecology, s.s.g.hospital, baroda medical college, baroda.

This study includes 100 patients, 50 cases each in both the groups including induction of labor with 25 mcg misoprostol intravaginally & 0.5 mg dinoprostone gel intravaginally

Indications:
1. Pregnancy induced hypertension.
2. Ecclampsia
3. Intrauterine fetal death
4. Intrauterine growth restriction
5. Rupture of membranes
6. Oligohydroamnios
7. Postdatisim

Inclusion Criteria:
1. More than 37 wks of gestational age
2. Fetus alive or dead 3. Singleton pregnancy

Exclusion Criteria:
1. Previous uterine surgeries
2. Placenta previa
3. Malpresentations other than cephalic
4. Cephalopelvic disproportion
5. Previous/s or rupture uterus or hyperstimulation
6. Pelvic mass
7. H/o asthama 8. Well compromised fetus

Prerequisites before induction
1. Gestational age confirmation
2. Parity confirmation
3. Lie
4. Bishop’s score
5. Fetal well being
6. Pelvic assessment
7. Informed consent

a) Group of patients with Dinoprostone (PGE2) gel

Dosage Primi 0.5 mg or 1 mg, max 3mg. Multi 0.5 mg, max 1.5 mg place in post fornix of vagina.

Note the induction time and patient should be in bed for 30 minutes.

Continuous hourly monitoring of progress by bishop’s score, vitals of patient and of fetal heart rate.

Repeat if needed only after 6 hrs.

Maximum 2 repetition.

Do amniotomy and or start oxytocin infusion after more than 3cms dilatation of cervix.

Don’t jump to any other method until, 1. Max dose has been used 2. Max induction delivery interval 24hrs have passed. 3. Any adverse reaction to induction has surfaced.

(2) Group of patients with Misoprostol (PGE1) tablet;

Dose: 25 mcg 4hrly. Max 5 times repetition place in post fornix after making wet and patient should be in same position for 30 minutes.

Further protocols are same as pgE2 gel except repetition after 4 hrs and max 5 doses allowed.

In 2004, N Van Gemund and colleagues suggested that low dose Misoprostol (25 mcg) instead of 50 mcg intravaginally is more effective and quite safer drug for cervical ripening and induction of labour

Failed induction;

PGE2: failure to progress to 3 cms cervical dilatation even after max 3 doses and or max 24 hrs has been passed from induction. PGE1: failure to progress to 3 cms cervical dilatation after max 5 doses or max 24 hrs have passed from induction.

Adverse reactions;

1. Intolerable nausea, vomiting, high grade fever with rigors, severe local abdominal pain
2. Fetal tachycardia
3. Hyper stimulation of uterus or rupture uterus.

Results and Discussions

This prospective study was carried out from 1st July 2009 to 30th June 2010. In present study, 100 patients were included, who required cervical ripening and induction of labour for either fetal or maternal indications and fulfilling the inclusion criteria.

Of these 100 patients, 50 patients were selected for induction with 25 mcg intravaginal Misoprostol (PGE1 methyl analogue) kept in posterior vaginal fornix and other 50 patients were induced with 0.5mg intravaginal dinoprostone gel(PGE2) randomly.
Table 1 : Patient’s requiring reinsertion according to initial Bishop’s score

<table>
<thead>
<tr>
<th>Initial Bishop’s score</th>
<th>Misoprostol (n=50)</th>
<th>Dinoprostone (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>28 (87%)</td>
<td>17 (63%)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>8 (44%)</td>
<td>10 (43.4%)</td>
</tr>
</tbody>
</table>

Above table shows that when initial bishop’s score <4, in PGE1 group 87% patients and in PGE2 group 63% patients require reinsertion. P value < 0.05 for this table which is significant. Lesser bishop’s score at initiation leads to higher no of reinsertions for same patient.

Table 2 : Total Dose Required

<table>
<thead>
<tr>
<th>Total dose required</th>
<th>Misoprostol (n = 50)</th>
<th>Dinoprostone (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14 (28%)</td>
<td>34 (68%)</td>
</tr>
<tr>
<td>2</td>
<td>16 (32%)</td>
<td>13 (26%)</td>
</tr>
<tr>
<td>3</td>
<td>13 (26%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>4</td>
<td>5 (10%)</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>2 (4%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Above table shows that maximum number of patients (86%) in PGE1 group required 3 doses Misoprostol to achieve active phase of labour. While most of patients (94%) in PGE2 group achieved this with 2 doses of Dinoprostone

Table 3 : Requirement of Augmentation with Oxytocin

<table>
<thead>
<tr>
<th>Augmentation with Oxytocin</th>
<th>Misoprostol (n=50)</th>
<th>Dinoprostone (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required</td>
<td>28 (56%)</td>
<td>42 (84%)</td>
</tr>
<tr>
<td>Not required</td>
<td>22 (44%)</td>
<td>8 (16%)</td>
</tr>
</tbody>
</table>

Above table suggests that augmentation of labour with oxytocin is more required in Dinoprostone group (84%) than in Misoprostol group (56%). P value <0.05 significant for this table. Which means lesser no of patients in PGE1 induced group requires oxytocin augmentation than PGE2 group.

Study of Meyer M, Pfum J, Howard D in march 2005 suggested that single dose of Misoprostol (25 mcg intravaginally) administered in the outpatient setting significantly decreased Oxytocin use as compared to Dinoprostone (0.5 mg intracervically).1,6,17

Table 4 : Comparison of need for Oxytocin Augmentation

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>E1</th>
<th>E2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>2010</td>
<td>56%</td>
<td>84%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>D.A. Wing</td>
<td>1995</td>
<td>45.7%</td>
<td>72.6%</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Table 5 : Induction to Vaginal Delivery Interval

<table>
<thead>
<tr>
<th>IVD. Interval</th>
<th>Misoprostol (n=46)</th>
<th>Dinoprostone (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 hrs.</td>
<td>5 (10.8%)</td>
<td>3 (6.6%)</td>
</tr>
<tr>
<td>6-12 hrs</td>
<td>2.5 (54.2%)</td>
<td>20 (44.4%)</td>
</tr>
<tr>
<td>13-24 hrs</td>
<td>15 (32.8%)</td>
<td>20 (44.4%)</td>
</tr>
<tr>
<td>&gt; 24</td>
<td>12.2%</td>
<td>2 (4.6%)</td>
</tr>
</tbody>
</table>

Mean ± SD (hours) 
| 10'30" ± 4' | 12'06" ± 4 41" |

Above table mentions that in present study, lesser number of patients in Misoprostol group required augmentation with Oxytocin as compared to Dinoprostone group and this result was comparable with other study.18

Above table depicts that after application of intravaginal Misoprostol of 25 mcg tablet, 65% of patients delivered within 12 hours, and number increase to 97.8% within 24 hours. A single patient had induction delivery interval beyond 24 hours. The Mean induction-vaginal delivery interval was 10'30" ± 4' hours (mean ±SD) in PGE1 group.

In PGE2 group, only 51% of patients delivered within 12 hours period. More number of patients (90%) delivered within 24 hours. 46% of patients had induction to delivery interval greater than 24 hours. The Mean induction-vaginal delivery interval was 12’06" ± 4’41’’ hours.

The Mean induction to vaginal delivery interval was shorter in Misoprostol group, 10’30" ± 4 hours, as compared to Dinoprostone group, which was 12’06" ± 4’41’’hours. T test value is significant for this study.

Our study shows that Misoprostol is more effective in inducing labour as well as shortening the total duration of the labour. (T test-value < 0.05, significant).

In 2004, Rozenberg P and his collagues studied intravaginal Misoprostol and Dinoprostone vaginal insert for the induction of labor in patients with postdate pregnancy and intrauterine growth restriction.19 They showed that Misoprostol and Dinoprostone are equally safe for the induction of labor in pregnancies that are at high risk of fetal distress; however, Misoprostol allowed the earlier induction of labor than did Dinoprostone.

PGE1 group, 92%(n=46) patients had vaginal delivery. In PGE2 group, 90%(n=45) patients had vaginal delivery and 2% (n=1) patients had instrumental vaginal delivery by Low Outlet Forceps.

In both group, the incidence of LSCS was 8%(n=4).

Table 6 : Success Rate

<table>
<thead>
<tr>
<th>RATES</th>
<th>PGE1</th>
<th>PGE2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success Rates</td>
<td>96%</td>
<td>98%</td>
</tr>
<tr>
<td>Failure Rates</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Success rate = (no. Of paties achieving 3 cms cervical dilatation x 100) / no. Of total patients induced.

In our study in PGE1 group ,out of 50 induced patients 48 patients had achieved active stage of labour out of these 1 patient had developed fetal distress and one developed hyperstimulation later on in first stage of labour .In both cases cesarean sections were performed. Two patients failed to reach active stage of labour,one had fetal distress in latent phase & one had developed prolonged first stage , in both cases cesarean section had been carried out.

In PGE2 group , 49 patient had reached active phase and out of these 3 patients had developed fetal distress in first stage and cesarean section had been carried out in all cases . One patient had developed fetal distress in latent phase and cesarean section had been carried out.
Study of Sanchez Ramos L, Austin SC, Adir CD in June 2010 showed that intravaginal misoprostol was more effective than intravaginal dinoprostone insert for cervical ripening & induction of labour with similar safety profile.20

Success rates for achieving 3 cms cervical dilatation were almost similar in both groups.

### Table 7: Indication for LSCS

<table>
<thead>
<tr>
<th>Indications of LSCS</th>
<th>Misoprostol (n = 50)</th>
<th>Dinoprostone (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal distress in 1st stage</td>
<td>02 (04%)</td>
<td>04 (08%)</td>
</tr>
<tr>
<td>Non progression in 1st stage</td>
<td>01 (02%)</td>
<td>-</td>
</tr>
<tr>
<td>Hyperstimulation</td>
<td>01 (02%)</td>
<td>-</td>
</tr>
</tbody>
</table>

(4 patients had LSCS in both group, one was operative delivery in PGE2, rest were normal delivery in both the groups)

Above table suggests that fetal distress in first stage of labour was the indication of LSCS in 2 cases in PGE1 group, while in 4 patient in PGE2 group. Hyperstimulation was noted in 1 patient in PGE1 group whereas 1 patients had non progression in 1st stage as an indication for LSCS in PGE1 group.

### Table 8: Side Effects

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Misoprostol (n=50)</th>
<th>Dinoprostone (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIT disturbance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (8%)</td>
<td>2(4%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (4%)</td>
<td>2(4%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2(4%)</td>
<td>-</td>
</tr>
<tr>
<td>Hyper pyrexia</td>
<td>7 (14%)</td>
<td>-</td>
</tr>
<tr>
<td>Headache</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

(2 patients had GIT side effects in PGE1 group)

Above table shows that in PGE1 group, 7 patients had fever after induction. There was a spike of 100° F which responded to oral antipyretic and cold sponging. 8 patients had GIT side effects in PGE1 group. Only 4 patients had GIT side effects were noted in PGE2 group.

### Table 9: Cost Factor

<table>
<thead>
<tr>
<th></th>
<th>Misoprostol (25 mcg)</th>
<th>Dinoprostone gel (0.5 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cost (Rs.)</td>
<td>20.00</td>
<td>207.00</td>
</tr>
</tbody>
</table>

Misoprostol is much cheaper than Dinoprostone gel. In our study majority of patients were from Lower Socio economic area. So cost factor plays an important role.

Requirement of augmentation with Oxytocin was also less in Misoprostol group compared to Dinoprostone group.

In Dinoprostone gel group, patients required its application twice leading to total cost up to 414 Rs. Thus Misoprostol induction is 10-15 times cheaper than induction with Dinoprostone gel.

### CONCLUSION

Cervical ripening is an essential part of successful induction of labour. Recent studies have shown unquestionable role of prostaglandins in this process which promotes both fundal dominance and cervical relaxation.

Our study clearly shows that intravaginal Misoprostol is an efficacious agent, scoring over intravaginal Dinoprostone gel in almost all the measures of adequacy, such as increase in Bishop Score, short induction delivery interval, lesser requirement of augmentation and low cost as an additional advantage.

Fetal distress with or without meconium stained liquor and uterine contractile abnormalities are comparable in both groups.

Misoprostol due to its advantage like stability at room temperature, extremely low cost, and good efficacy, should be consider as a good option for labour induction.

From currently available data, it appears that 25 mcg Misoprostol inserted into the posterior vaginal fornix and repeated every 4 hour as per need, is an clinically effective regimen and confirms the least amount of adverse effects and complications. Because of concern for uterine tachysystole and hyperstimulation syndrome, it is recommended that continuous fetal heart rate and uterine activity should be monitored carefully throughout the induction procedure.

These drugs have become a preferred option among the practicing obstetricians according to their personal experiences and preferences, thus helping to solve the age old problem of cervical ripening and labour induction.

### REFERENCES


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