

A STUDY OF INDUCTION OF LABOUR AT TERM WITH DIFFERENT PROSTAGLANDINS

Sunita Mishra¹, Vrunda Chaudhary², Sunita Sudhir³

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ABSTRACT: Induction of labour is an intervention designed to artificially initiate uterine contractions leading to progressive effacement and dilatation of cervix to facilitate delivery of the baby. Success depends upon status of cervix as assessed by Bishop's scoring system. The present study is a comparative study between the traditional method of cervical ripening with Dinoprostone gel and the new class of PGE₁, Misoprostol, with regard to safety and efficacy. **AIMS AND OBJECTIVES:** (1) To compare the efficacy (2) To study the induction-delivery interval (3) To study the outcome on mode of delivery (4) To study the maternal and fetal outcome. **MATERIALS AND METHODS:** 100 cases admitted to labour ward of OBG dept. of Kamineni Institute of Medical Sciences with an indication for induction were included. 25µgm Misoprostol 4 hourly up to a maximum of 6 doses was given in 50% cases and the rest were induced by Dinoprostone gel for a maximum of 3 doses 4 hourly as per response of the patient. **OBSERVATION & RESULTS:** The mean induction delivery interval with Misoprostol induction at 12.0±2.234 hours was significantly less compared to 17.0±3.109 hours that of Dinoprostone gel. When this was subjected to student's test, this had statistical significance. 90% cases induced with Misoprostol delivered vaginally as compared to 80% cases induced by Dinoprostone gel. There is significantly lesser effects on mother with Misoprostol than with Dinoprostone. Although incidence of tachysystole & hyperstimulation were more in cases with Misoprostol induction, incidence of PPH is significantly less. Majority of neonats from Misoprostol group were admitted to NICU for meconium aspiration syndrome whereas those from Dinoprostone group were admitted for hyperbilirubinemia. **CONCLUSION:** From this study, we conclude that Misoprostol is an apparently safe, efficient and cost-effective drug for induction of labour.

KEYWORDS: Misoprostol, Dinoprostone, Induction, Labour, Term.

INTRODUCTION: Induction of labour is an intervention designed to artificially initiate uterine contractions leading to progressive effacement & dilatation of cervix to facilitate delivery of the baby. The success of induction of labour depends upon the status of cervix as assessed by Bishop's scoring system.¹ Labour induction is indicated when the benefits of delivery to the mother and fetus outweighs the potential risk of continuing the pregnancy.

To be successful, induction of labour must fulfill three Criteria:

1. Should initiate labour with adequate uterine contractions and progressive dilatation of cervix.
2. Should result in vaginal delivery.
3. Thirdly, the above two aims must be achieved with minimal risk to both the mother and fetus.²

INDICATIONS FOR INDUCTION (ACOG Technical Bulletin 157.1991):

1. Pregnancy Induced Hypertension.
2. Premature Rupture of membranes.
3. Abruptio Placentae.
4. Chorioamnionitis.
5. Suspected IUGR, absence of fetal well-being, Post term pregnancy, Isoimmunization.
6. Maternal medical problems like Diabetes Mellitus, Renal disease, chronic pulmonary disease and Cardiac disease.
7. Foetal demise.
8. Logistic factors.

When induction of labour is done with an unripe cervix, there is high rate of failure of induction, Arulkumaran.²

The human cervix is an organ of diverse properties. The predominantly formed element of cervix is the collagen fibrils which are embedded in a ground substance comprising of large molecular weight proteoglycan complexes containing a variety of glycosaminoglycans (GAGS), Leppert PC (1995).³ The most abundant GAG in the cervix are chondroitin and dermatan sulfate. Hyaluronic acid binds weakly with the GAG molecules and act to destabilize the collagen fibrils, while GAG containing iduronic acid as opposed to glucuronic acid such as dermatan sulfate binds strongly and promotes tissue stability (Uldbjerg N,⁴ 1990).

Changes in the cervical connective tissue occur as a result of changes in proteoglycan/GAG composition of the ground substance of the cervix. Ripening of the cervix takes place in the pre-labour phase, which results in increased softening, effacement and early dilatation. Oestriol can stimulate PG production. In addition, oestradiol has been linked to increase in collagenase activity (Mochizuki,⁵ (1978). Prostaglandins have a direct oxytocic effect as well as a direct action on ripening of the cervix. PGE₂ or Dinoprostone has been used endocervically for the ripening of the cervix traditionally. It is expensive and requires refrigeration for storage and needs warming before use. PGE₁ or Misoprostol is comparatively cheaper, safe and effectively administered vaginally and has fewer side effects.

Of late, a no. of recently published clinical trials abroad and in India have shown the efficacy of Misoprostol as an agent for induction of labour and cervical ripening at term when compared to other methods of labour induction.

The present study is a comparative study between the traditional method of cervical ripening with endocervical PGE₂ gel, and the new class of PGE₁ drug Misoprostol with regard to efficacy and safety.

AIMS & OBJECTIVES:

- To compare the efficacy of induction of labour with dinoprostone gel & misoprostol.
- To study the induction-delivery interval with respect to their usage for cervical ripening.
- To study the outcome on the type of delivery.
- To study the maternal & fetal outcome in both the groups.

MATERIALS AND METHODS: 100 patients admitted to labour ward of OBG dept. of Kamineni Institute of medical sciences with an indication for induction of labour from January 2013 to August 2014 were selected for this study.

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The indications for induction in the present study were mild & severe pre-eclampsia, post-dated pregnancy, mild polyhydramnios, mild oligohydramnios, gestational diabetes mellitus, chronic hypertension, Rh negative pregnancy.

Patients with singleton foetus in cephalic presentation, beyond 37 weeks having a reactive foetal heart rate pattern, those with unfavourable cervical Bishop score <4 & those having no contraindication to vaginal delivery were included in the study.

Patients with previous LSCS or any uterine surgery, with malpresentations, those who are grand multipara, & with abnormal foetal heart rate pattern & those allergic to Prostaglandins were excluded from the study.

50 patients received 25 micro gm of misoprostol⁶ which was placed in the posterior fornix & repeated for a maximum of 6 doses every 4 hours as per the requirement of each patient. The other 50 patients received 0.5 mg intracervical dinoprostone gel⁷ & repeated for a maximum of 3 doses at 4 hourly interval as per the response of the patients.

After informed written consent had been obtained, patients were initially evaluated by modified Bishop's score & admission test for fetal wellbeing. Those with a modified Bishop's score ≤ 4 and a positive admission test were induced.

Monitoring the patients following administration of the drugs was done by noting signs of labour, maternal vitals, foetal heart rate & progress of labour. Foetal heart rate monitoring was done by intermittent auscultation or continuous electronic monitoring. A partographic recording of the labour events was maintained.

Induction of labour with oxytocin was considered depending on the modified Bishop's score and if no adequate uterine contractions were seen after 6 hours of the last dose. Augmentation was undertaken in case of arrest of dilatation & oxytocin in the dose of 2 μ /min with increments of 2 μ /min every 30 minutes was infused. Membranes were ruptured when cervix was fully effaced and about 3 cm dilated or during the active stage of labour.

Data collected included indications for induction, whether booked or unbooked cases, maternal age, parity, gestational age on being induced for study, modified Bishop's score at the time of induction, induction-delivery interval, oxytocin augmentation, type of delivery, Apgar score of the baby, maternal & neonatal complications.

The results observed were subjected to statistical analysis by students 't' test, odds ratio chi-square test and a p value of < 0.05 was considered significant.

OBSERVATIONS AND RESULTS: A total of 100 patients were studied. 50 of them were induced with 25 microgram vaginal misoprostol tablets and the other group of 50 patients were induced with 0.5 mg of intracervical dinoprostone gel.

The result observed were subjected to statistical analysis by students 't' test, Odd's ratio and Chi-square test. It was seen that in the group induced by Dinoprostone, 32 were booked cases versus 18 unbooked accounting for 64% & 36% cases respectively. In the Misoprostol group, 30 were booked cases as compared to 20 unbooked ones accounting for 60% and 40% cases respectively.

The group induced by Dinoprostone, 60% were of 24-28 years age group, 20% were each of 19-23 & 29-33 age group. Similarly in the Misoprostol group, 75% cases were of 24-28 years age group, 15% were of 19-23 age group and 10% were of 29-33 age group.

Parity was compared in both groups and found to be almost similar without any statistical significance ($P > 0.05$).

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Primigravida comprised of the bulk of the cases in either group amounting to 60% and 64% respectively in the Dinoprostone & the Misoprostol groups. Multigravida in the Dinoprostone & Misoprostol groups were 40% and 36% respectively.

When gestational age was compared, almost equal number of patients in both groups at similar gestational age underwent induction. This had no statistical significance ($P>0.05$).

Table no. 1 gives interesting result. The mean induction delivery interval was significantly less at 12.0 ± 2.234 hours with Misoprostol as compared to 17.0 ± 3.109 hours with Dinoprostone.

When this was subjected to student's test, this had statistical significance.

80% of cases induced by Dinoprostone and 90% of cases induced by Misoprostol delivered vaginally. 40% cases delivered within 12-18 hours after being induced with Dinoprostone, whereas 44% cases delivered when induced with Misoprostol.

Majority of primigravida induced with Dinoprostone gel were with post-dated pregnancy and mild polyhydramnios, accounting for 12.0% each. Those induced with Misoprostol were largely cases of mild pre-eclampsia, post-dated pregnancy and mild polyhydramnios accounting for 12.0% each.

Multigravidas with post-dated pregnancy were the largest group of cases to be induced by Dinoprostone and Misoprostol accounting for 12.0% and 10% respectively.

In both the groups, two doses were required for vaginal delivery in most of the cases.

Majority of women had a Bishop's score of 0-2 in both the groups.

Table no. 2 shows that significant number of cases induced by Misoprostol delivered vaginally. 90.0% of women induced by Misoprostol & 80.0% of women induced by Dinoprostone delivered vaginally.

Reasons for failed induction were secondary arrest of dilation, deep transverse arrest and fetal distress. 20% cases induced by Dinoprostone and 10% cases induced by Misoprostol resulted in failure.

Table no.3 shows there is significantly lesser effect on mother with Misoprostol than with Dinoprostone. Although incidence of tachysystole and hyperstimulation were more in the group induced by Misoprostol, incidence of PPH was considerably less than that in the group induced by Dinoprostone.

Five neonats delivered in each of the two groups were admitted to NICU.

Majority of neonates from the Misoprostol group were admitted for meconium aspiration syndrome and those from Dinoprostone group were admitted to NICU for hyperbilirubinemia.

DISCUSSION: Nowadays induction of labour is more widely used than ever before. In the present study, 100 patients were studied for comparing the effects of Dinoprostone and Misoprostol on the outcome of induction with these inducing agents. 50 patients received intracervical Dinoprostone gel 0.5mg and the other 50 patients received vaginal Misoprostol 25µgm. An ideal method should encompass its efficacy and safety for the mother and fetus with short induction-delivery interval and minimum side effects.

Majority of the patients in both the groups were booked cases of our institution. Other criterias of patients like gestational age and Bishop's score prior to induction had no major differences in both the groups.

The rate of vaginal deliveries was 80% in the Dinoprostone group and 90% in the Misoprostol group. This is consistent with the studies of Murthy B Krishnamurthy et al⁹ (2006), Surg Cdr Sushil Kumar et al⁸ (2001) and Walid Denguizil et al¹⁰ (2007).

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In the present study, it was seen that the induction delivery interval was shorter in the Misoprostol group compared to Dinoprostone group, being 12 ± 2.23 hours and 17 ± 3.10 hours respectively. This was statistically significant ($P < 0.05$). This is comparable to the studies of Agarwal N et al (2003) who found it be 18.53 ± 8.5 hours and Murthy B Krishnamurthy et al (2006) who found it be 14.27 ± 5.51 hours in their studies with Dinoprostone.

Our present study used $25\mu\text{gm}$ Misoprostol 4 hourly vaginally with a resultant induction-delivery interval of 12.0 ± 2.23 hours which is comparable to the studies of Agarwal N et al⁷ (2003) who has used $50\mu\text{gm}$ of Misoprostol 6 hourly to a maximum of $200\mu\text{gm}$ with an induction delivery interval of 12.8 hours and Murthy B Krishnamurthy et al⁹ (2006) who used $25\mu\text{gm}$ Misoprostol 4 hourly to a maximum of $200\mu\text{gm}$ with an induction delivery interval of 10.2 ± 3.5 hours.

Failed induction led to caesarean deliveries at rates of 20% in the Dinoprostone group and 10% in the Misoprostol group. The various indications were foetal distress, failure to progress due to deep transverse arrest or secondary arrest of dilation. In the Misoprostol group, fetal distress was the major indication for caesarean delivery. These patients also had hyperstimulation and oxytocin augmentation pre-operatively and meconium staining of liquor was invariably observed in all cases. In our study the caesarean section rate with Dinoprostone was 20%, which was consistent with the studies of Trufatter et al¹¹ (1985). In the Misoprostol group the caesarean section rate was 10% which is consistent with the observation of Sanchez Ramos and associated in a recent meta-analysis (1997) in which an analysis of all published studies (Controlled & Uncontrolled) showed that 108 out of 1708 (9.8%) women were delivered by caesarean section.

The incidence of thick meconium stained liquor was 2% and 6% in Dinoprostone and Misoprostol groups respectively. It was not known whether the thick meconium was due to the drug or due to the indication for which induction was done i.e postdatism. Incidence of meconium stained liquor was 8.1% in the study of Wing DA et al¹² (1995) and 11.2% in the study by Paul et al¹³ (1996) using $25\mu\text{gm}$ Misoprostol 6 hourly. Our study used $25\mu\text{gm}$ Misoprostol 4 hourly.

The maternal side effects observed were tachysystole, hyperstimulation, vomiting, diarrhoea, fever and PPH. In the Dinoprostone group the major side effects were vomiting of 4% and PPH of 22%. Vomiting was noticed in patients who had rapid dilation of the cervix which could have been the cause of the same.

The major side effects observed in the Misoprostol group was tachysystole 6% and hyperstimulation 4%. Our observations are nearly consistent with the studies of Fletcher et al¹⁴ (1994). The difference in the incidence of tachysystole and hyperstimulation by different authors could probably be attributed to the different dosing regimens. Other side effects with Misoprostol group were fever, vomiting and diarrhoea which were minimal. Misoprostol group had 3 patients with traumatic PPH owing to cervical tears and did not require any blood transfusion.

The neonatal outcomes was almost similar in both the groups. The mean birth weight and mean Apgar scores in both the groups did not show any major difference.

The incidence of NICU admission was 10% in both the groups. The indications for admission were meconium aspiration syndrome, birth asphyxia and hyperbilirubinemia. There was an increased incidence of meconium aspiration syndrome and birth asphyxia in the Misoprostol group and was associated with uterine hyperstimulation.

Mundle and Young (1996) evaluated the effect of Misoprostol for labour induction on neonatal outcome. They found that it was similar in both the groups. Cord blood acid-base analysis

did not differ between both the groups. No neonate met the ACOG criteria for birth asphyxia in their study.

Sanchez Ramos et al¹⁵ (1998), in their meta-analysis found no differences in the incidence of low 5 minutes Apgar score and admission to NICU between the Misoprostol and the control groups.

CONCLUSION: Misoprostol and Dinoprostone are safe and effective for cervical ripening and labour induction. Misoprostol is cost effective when compared to Dinoprostone. Misoprostol is stable at room temperature and does not need refrigeration whereas Dinoprostone requires refrigeration. Induction delivery interval is less in Misoprostol group when compared to Dinoprostone. Vaginal delivery rate is higher in Misoprostol group when compared to Dinoprostone.

One disadvantage with Misoprostol is slightly increased incidence of uterine tachysystole and hyperstimulation and hyperstimulation with further fetal distress. But fetal morbidity is similar in both the group of patients.

In conclusion, we believe that Misoprostol is apparently safe, efficient and a cost-effective drug for induction of labour.

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DRUG	Mean induction delivery interval in hours (Mean± SD)
Dinoprostone	17.0 ± 3.109
Misoprostol	12.0 ± 2.234

TABLE 1: MEAN INDUCTION DELIVERY INTERVAL

P < 0.05 Significant

MODE OF DELIVERY	DINOPROSTONE (n=50)	DINOPROSTONE %	MISOPROSTOL (n=50)	MISOPROSTOL %
VAGINAL	40	80.0%	45	90.0%
LSCS	10	20.0%	5	10.0%
TOTAL	50	100%	50	100%

TABLE 2: MODE OF DELIVERY

P < 0.05 Significant

COMPLICATIONS	DINOPROSTONE No. of Patients	DINOPROSTONE %	MISOPROSTOL No. of Patients	MISOPROSTOL %
Tachysystole	0	0	2	4
Hyperstimulation	1	2	3	6
Fever	1	2	3	6
Vomiting	2	4	2	4
Diarrhoea	4	8	2	4
Post-partum haemorrhage	11	22	3	6
Total	19	38	15	30

TABLE 3: EFFECTS ON THE MOTHER

P < 0.05 Significant (S)

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AUTHORS:

1. Sunita Mishra
2. Vrunda Chaudhary
3. Sunita Sudhir

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Obstetrics and Gynaecology, KIMS, Narketpally.
2. Associate Professor, Department of Obstetrics and Gynaecology, KIMS, Narketpally.

FINANCIAL OR OTHER

COMPETING INTERESTS: None

3. Assistant Professor, Department of Obstetrics and Gynaecology, KIMS, Narketpally.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sunita Mishra,
301, Sunshine Habitat,
Road No. 1, Green Hills Colony,
R. K. Puram, Kothapet,
Hyderabad-500035.
E-mail: drmishrasunita@gmail.com

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