Indian J Physiol Pharmacol 2007; 51 (1): 55–61

# COMPARATIVE STUDY OF MISOPROSTOL VS DINOPROSTONE FOR INDUCTION OF LABOUR

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**( Received on June 22, 2006 )**

**Abstract :** Various methods of induction of labour may be associated with risk and complications. Therefore, this study has been undertaken to compare the safety and efficacy of intra-vaginal misoprostol ($PGE_1$ analogue) with intra-cervical dinoprostone ($PGE_2$) in progress and induction of labour, the maternal side effects and the foetal outcome. 40 pregnant women aged between 16–35 years with indication of induction of labour participated in the study. Twenty patients (control) were administered 0.5 mg dinoprostone intra-cervically, 12 hourly while 20 patients (study group) were given misoprostol 100 µg, 4 hourly, intravaginally. The mean induction of labour initiation interval was $2.08 \pm 1.46$ hours in study group and $2.21 \pm 1.20$ hours in dinoprostone group. The Induction delivery interval was $6.92 \pm 4.01$ hours in misoprostol group and $12.54 \pm 7.73$ in dinoprostone group, whereas vaginal route of delivery was 95% in misoprostol group and 85% in dinoprostone group. Average dosages required were $1.55 \pm 1.02$ in misoprostol group and $1.30 \pm 0.46$ in dinoprostone group. All these result were statistically significant. Very few maternal side effects were reported in study group. There was no significant difference in foetal out come in either group. Therefore, it can be concluded that misoprostol is easy to administer and is cheap, effective, safe and convenient drug for induction of labour.

**Key words :** misoprostol, dinoprostone, induction of labour, prostaglandins

## INTRODUCTION

Induction of labour is an integral part of obstetric practice. In modern obstetrics, it is mainly attempted when continuation of pregnancy may harm either mother or foetus or both (1). Induction of labour traditionally has been done by oxytocin infusion but numerous studies (2) have shown that it is unable to achieve equally gratifying results in un-favourable cervix. Various methods of induction and augmentation of labour were associated with a number of risks and complications.

Karim (3) introduced the use of

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prostaglandins (PG's) to induce labour. $PGE_2$ and $PGE_{2V}$ have been commonly used for induction of labour, but they are expensive and have some limitations. Dinoprostone is being used intracervically which is inconvenient method for induction (4). Recently an alternative prostaglandin $PGE_1$ analogue misoprostol has been used for cervical ripening and to induce labour (5).

Misoprostol, a synthetic $PGE_1$ analogue, was commercialized in 1987 for antiulcer, antisecretory and cytoprotective effects. Misoprostol was also effective as cervical priming agent (6). It is now being tried orally, intravaginally and intracervically for induction of labour (7, 8).

The present study was undertaken to assess the efficacy and safety of intravaginal misoprostol as compared to intracervical dinoprostone for induction and progress of labour and to assess maternal and foetal outcome.

## MATERIAL AND METHODS

The present study was conducted in the Department of Obstetrics & Gynaecology and Pharmacology of S. N. Medical College and Hospital, Agra. Study protocol was approved by the Institutional Ethics Committee and written informed consent was obtained from all the women or their attendant.

A complete history was taken. General, per abdominal and per vaginal examination with routine investigations of each woman, was done.

**Inclusion criteria :**

Both primigravida and multigravida, antenatal women with 34 or more weeks of singleton gestation, with cephalic presentation, having indication of vaginal delivery were included in the study.

**Indication for induction :**

Post maturity (more than 41 wks), premature rupture of membrane, absence of contraction, pre-eclamptic toxaemia (BP more than 140/90 mm of Hg, albuminuria), intrauterine death, congenital anomalies, intrauterine growth retardation and anencephaly.

**Exclusion criteria**

Abnormal foetal heart rate, multigravida (more than 3), cephalopelvic disproportion, multiple pregnancy, unexplained vaginal bleeding, previous uterine surgery, women with glaucoma/bronchial asthma and mal-presentation.

**Study design**

A total of 40 women were randomly selected for the prospective study and were divided into two groups of 20 each.

*Group I :* Control group- Dinoprostone gel was administered intracervically (0.5 mg) and repeated after 12 hours, if required.

*Group II :* Study group-Misoprostol tablet was administered intravaginally (100 µg). The tablet was repeated every 4 hours for a

maximum of 6 doses or until active labour starts, that is 3 or more contractions in first 10 minutes and cervical ripening, dilatation of at least 3 cm.

During drug therapy, maternal status, foetal status and progress of labour were observed carefully. To assess the efficacy of drug, the induction-initiation interval, induction- delivery interval, duration of 1st, 2nd and 3rd stage of labour and mode of delivery were recorded.

Efficacy and safety of misoprostol as a method of cervical priming and labour induction as compared to dinoprostone was assessed.

Therapy was discontinued if woman developed severe diarrhoea, vomiting, signs of foetal or maternal distress, uterine hyper-contractility, tachycardia, fever or rigors.

Foetal outcome was evaluated by Apgar score at 1 min and 5 min of life and their birth weights according to the gestational age. Maternal outcome was evaluated by any complication and side effects.

Statistical analysis was performed by Student ‘t’ test.

## RESULTS

On the basis of the above study , it was observed that majority of women were in age group of 21 to 30 years , gravida 1 to 3 , period of gestation between 37 to 41 weeks and Bishop’s score between 0 to 10 (Table I). The distribution of cases according to indication of induction of labour has been shown in Table II.

TABLE I: Patient’s profile in both groups.

| | *Misoprostol* | *Dinoprostone* |
|---|---|---|
| Age (years) | 20±3.75 | 25.35±3.31 |
| Parity | 2.1±1.82 | 2.4±1.54 |
| Gestational age (weeks) | 38.90±1.58 | 38.15±2.03 |
| Bishop’s score | 4.45±1.77 | 4.25±1.89 |

Values expressed, as Mean±SD.

TABLE II: Distribution of cases according to indication of induction of labour.

| *S.No.* | *Indication* | *Misoprostol Group* | | *Dinoprostone Group* | |
|---|---|---|---|---|---|
| | | *n=20* | *%* | *n=20* | *%* |
| 1. | Post dated pregnancy | 6 | 30 | 8 | 40 |
| 2. | IUD (Intra-uterine death) | 6 | 30 | 4 | 20 |
| 3. | PIH (Pregnancy induced hypertension) | 1 | 5 | 2 | 10 |
| 4. | Eclampsia | 1 | 5 | – | – |
| 5. | Premature rupture of membranes | 6 | 30 | 5 | 25 |
| 6. | Cogenital anomalies (Anencephaly) | – | – | 1 | 5 |
| | Total | 20 | 100 | 20 | 100 |

Indication for induction of labour did not differ significantly.

The mean time period between application of drug and establishment of satisfactory and regular uterine contractions in misoprostol group was 2.08 ± 1.46 and dinoprostone group was 2.21 ± 1.20 hours which was statistically insignificant (Table III). In this study the time from insertion of vaginal delivery was significantly shorter in misoprostol group 6.92 ± 4.01 hours as compared to 12.54 ± 7.73 hours in dinoprostone group Table IV.

TABLE III : Distribution of patient's according to induction initiation labour interval.

| *Time (hours)* | *Misoprostol Group (n=20)* | | *Dinoprostone Group (n=20)* | |
|---|---|---|---|---|
| | *Number of patient's* | *%* | *Number of patient's* | *%* |
| 0–2.00 | 12 | 60 | 09 | 45 |
| 2.01–4.00 | 06 | 30 | 09 | 45 |
| 4.01–6.00 | 02 | 10 | 02 | 10 |
| Mean±SD* | 2.08±1.46 | | 2.21±1.20 | |
| P** | >0.05 | | | |

*Values are expressed as Mean±S.D.
**P>0.05 Misoprostol vs Dinoprostone (paired 't' test)

TABLE IV : Induction to delivery interval.

| | *Misoprostol Group (n=20)* | | *Dinoprostone Group (n=20)* | | *P*** |
|---|---|---|---|---|---|
| | *Number of patient's* | *%* | *Number of patient's* | *%* | |
| Vaginal delivery in 12 hours | 17 | 85 | 13 | 65 | <0.05# |
| Vaginal delivery in 24 hours | 19 | 95 | 17 | 85 | <0.05# |
| Failure | 1 | 5 | 3 | 15 | <0.05# |
| Insertion to vaginal delivery (Mean hours±SD) | 6.92±4.01 | | 12.54±7.73 | | <0.05^ |

**P>0.05 Misoprostol vs Dinoprostone (paired 't' test, #'z' test)

In misoprostol group 85% women required two doses of drug whereas in dinoprostone group 71% women required only one dose. The mode of delivery was observed and it was found that in misoprostol group 95% women delivered spontaneously vaginally and 5% underwent Caesarean section whereas, in dinoprostone group 80% delivered spontaneously vaginally, only 5% women delivered by forceps application and 15% underwent Caesarean section, because induction failed in 10% women and there was foetal distress in 5% women. Number of caesarean sections performed in dinoprostone group was significantly higher than in misoprostol group (Table V). As observed ,the occurrence of maternal side effects were

TABLE V : Mode of delivery.

| | *Misoprostol Group (n=20)* | | *Dinoprostone Group (n=20)* | | *P*** |
|---|---|---|---|---|---|
| | *Number of patient's* | *%* | *Number of patient's* | *%* | |
| Vaginal | 19 | 95 | 17 | 85 | <.05 |
| -Spontaneous | 19 | 95 | 61 | 80 | |
| -forcep | 0 | 0 | 01 | 5 | |
| Caesarean indication | 01 | 05 | 03 | 15 | <.05 |
| -Failed induction | 01 | 05 | 02 | 10 | |
| -Foetal distress | 0 | – | 01 | 05 | |
| Total | 20 | 100 | 20 | 100 | |

**P>0.05 Misoprostol vs Dinoprostone (paired 't' test, #'z' test)

TABLE VI : Neonatal outcome (Apgar score at 1 minute.

| *Apgar score* | *Misoprostol Group (n=20)* | | *Dinoprostone Group (n=20)* | |
|---|---|---|---|---|
| | *Number of patient's* | *%* | *Number of patient's* | *%* |
| 0–5 | 12 | 60 | 12 | 65 |
| 6–8 | 7 | 35 | 06 | 30 |
| 9–10 | 1 | 5 | 01 | 05 |
| Total | 20 | 100 | 20 | 100 |
| Mean | 3.39±0.32 | | 3.36±0.41 | |

**P>0.05 Misoprostol vs Dinoprostone (paired 't' test)

lesser in misoprostol group than in dinoprostone group. Common side effects were vomiting, diarrhea, fever with, cervical tear, hypotonus and tachysystole.

The mean Apgar score at one minute (neonatal-outcome) was approximately same in both groups. There was no statistically significant difference in the mean one minute Apgar score in both the groups (Table VI).

## DISCUSSION

Labour induction with prostaglandins is an emerging technology (9). The usual agent, dinoprostone is now well established. The importance of misoprostol as a cervical ripening agent, in its own, is clear (4). Unlike dinoprostone, misoprostol is cheap, and does not require refrigeration for its storage, as it is stable at room temperature.

Women in the present study had similar age distribution. In the misoprostol group 45% cases and in dinoprostone group 50% were primigravida. Mean gravidity in misoprostol and dinoprostone group was $2.1 \pm 1.82$ and $2.4 \pm 1.54$ respectively. The mean period of gestation in misoprostol group and dinoprostone group were $38.90 \pm 1.58$ weeks and $38.2 \pm 2.03$ weeks respectively. However, the mean Bishops score in the misoprostol and dinoprostone group was $4.45 \pm 1.77$ and $4.25 \pm 1.89$ respectively (Table II). These values are consistent with the studies of other workers (1, 10).

In our study, 60% women in misoprostol group and 45% in dinoprostone group, went into labour within 2 hours whereas 30% in misoprostol group and 45% in dinoprostone group within 4 hours. The mean interval from start of induction to initiation of labour was $2.08 \pm 1.46$ hours in misoprostol group and $2.21 \pm 1.2$ hours in dinoprostone group (Table III). These observations are parallel to the reported studies (10, 11, 12).

Women delivered in 12 hours, in misoprostol group were 85% while in dinoprostone group were 65%. This difference was statistically significant ($P<0.05$). The goal of achieving vaginal delivery in 24 hours was 95% in misoprostol group and 85% in dinoprostone group (Table IV).

The present study showed that misoprostol was able to increase the incidence of spontaneous labour and delivery. It was favored by the studies of Wing et al (12) and Nakintu et al (14). Wing et al (12) showed that induction delivery interval, was significantly shorter in misoprostol group. Kandalini (13) and Nakintu et al (14) did a study of vaginal misoprostol for induction of labour, where the success rate within 48 hrs of induction was 100% than with oxytocin. In the similar study done by Wing et al (12), the average interval from initiation to induction of vaginal delivery, was significantly shorter in misoprostol group. Buser et al (15) concluded that induction delivery interval was shorter in misoprostol group than in dinoprostone group. Our results are in agreement with above studies (11, 12, 15).

In our study, caesarian section was significantly less in misoprostol group, one patient (5%) as compared to 3 patients (15%) in dinoprostone group (Table V). These findings are in contrast with the reports of Wing et al, 1998 (16) who could not find any

difference in two groups. However they used 25 µg misoprostol as compared to 100 µg, misoprostol in our study. Even higher doses of misoprostol were used by Chitta Chareon et al., 2003 (17) in their study. They concluded that misoprostol 400 µg orally every 4 hours was more effective than 200 µg of misoprostol, vaginally every 12 hours

Most common side effects observed in our study was tachysystole (30%), in misopropstol group. GIT side effects like nausea, vomiting and diarrhoea were not observed, while vomiting and diarrhoea was observed in 5% cases of dinoprostone group. Fever with rigors occurred in 3 patients (15%) and 1 (5%) patient of misoprostol and dinoprostone group respectively.

Maternal side effects were minimal with misoprostol and were not significantly different from the dinoprostone. The mean Apgar score for neonatal-outcome of babies was almost similar in both groups (Table VI). They were 3.39 in misoprostol and 3.36 in dinoprostone group. In Kandanali et al (13), and Bugalho et al (18) studies, neonatal outcome was similar by both drugs but dosing regimen was different in their studies as compared to our studies.

Oral misoprostol is an effective method for induction of labour in the third trimester. However, the data on optimal regimens and safety are lacking. It is possible that effective oral regimens may have an unacceptably high incidence of complications such as uterine hyper-stimulation and possibly uterine rupture (19, 20). Vaginal misoprostol is also suggested to be more effective than oral regimen, as faster approach is not necessarily, better method for childbirth (20, 21). The cost of dinoprostone gel (cerviprime) is Rs. 170, while of misoprostol 100 µg tablet Rs. 36 as available in Indian market.

**Conclusion**

The use of PG's provide an effective method for achieving the induction of labour. On the basis of our study, misoprostol appears to be an effective agent for the induction and augmentation of labour as compared to the dinoprostone. The results of labour outcome convincingly prove that in the patients treated with misoprostol, induction interval was shorter and the incidence of caesarean section were reduced. There was clearly a superior neonatal outcome in terms of Apgar score and perinatal outcome in misoprostol group.

Therefore, misoprostol is cheaper than dinoprostone, easy to administer by intravaginal route and does not require refrigeration. This indicates that misoprostole is a better, effective and safe alternative drug for induction of labour.

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