

# Comparison of Misoprostol with Dinoprostone for Induction of Labor in Postdated Pregnancy

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## ABSTRACT

**Objective** To compare the efficacy of misoprostol with dinoprostone in induction of labor in nulliparous women at and beyond 41 weeks of gestation.

**Study design** Experimental comparative study.

**Place & Duration of study** Department of Obstetrics & Gynecology Unit-II, Jinnah Post Graduate Medical Center, Karachi, from September 2007 to October 2010.

**Methodology** A total of 105 women with more than 287 days (41 weeks) gestation with unfavorable cervix and intact membranes were selected for induction of labor. Dinoprostone was inserted in 41 patients while 64 patients were induced with intravaginal misoprostol.

The primary outcome measures were induction-delivery interval, number of doses required for induction, rate of spontaneous vaginal delivery, C-section and instrumental delivery. Secondary outcomes were the incidence of meconium stained amniotic fluid, fetal weight at the time of delivery, fetal distress and need for admission to NICU.

**Results** Out of 63 patients in the misoprostol group, 43 (67.1%) women had spontaneous vaginal delivery (SVD) while 26 (63.4%) patients out of 41 in dinoprostone group had SVD. The induction to delivery interval was 13.03±3.52 hours in misoprostol group while it was 14.12±3.31 hours in dinoprostone group. With misoprostol, induction of labor started in 18, 33 and 13 women with 1, 2 and 3 doses respectively within 24 hours but in dinoprostone group 16 women were successfully induced with 1 tablet only, while 21 patients required 2 doses for induction. The need for oxytocin infusion was the same in both the groups. The neonatal weight was 3.54±3.38 kg in misoprostol group as compared to 3.10±0.26 kg in dinoprostone group ( $p=0.41$ ,  $t=1.57$ ).

Four neonatal deaths were reported in the misoprostol group as compared to two with dinoprostone. Sixteen neonates were admitted to NICU in misoprostol group as compared to five patients in dinoprostone group. Twenty-eight (44.4%) patients in misoprostol group had meconium stained liquor as compared to 14 (34%) patients in dinoprostone group.

**Conclusions** Dinoprostone was most effective in comparison with misoprostol in gravida with 41 weeks and above gestation. Misoprostol though showed comparable results, but is not the drug of first choice.

**Key words** Misoprostol, Induction, Post dated pregnancy, Dinoprostone.

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## INTRODUCTION:

Induction of labor is carried out for maternal and fetal reasons. One of the commonest indications is the postterm pregnancy. Its incidence is 3-14%.<sup>1</sup> There is higher incidence of prenatal morbidity and mortality with increasing gestation, after 40 weeks. Elective induction is usually preferred at 41 weeks

rather than expectant management.<sup>2,3</sup> Strict fetal surveillance is needed once the patient has been induced. The overall rate of induction is as high as 44 %.<sup>4</sup>

Induction of labor with prostaglandins results in efficient cervical ripening and dilation, resulting in an increased rate of spontaneous vaginal delivery.<sup>5,6</sup> However problems like ineffective labor resulting in failed induction and uterine hyperstimulation are associated risks.

Dinoprostone, a prostaglandin E2, is FDA approved drug and has been the standard agent used for induction of labor. It is effective in patients with unripe cervix. However they are expensive and require refrigeration. Misoprostol, a synthetic prostaglandin E1 analogue is an oral drug manufactured for the prevention and treatment of peptic ulcer disease. Although not currently approved for induction of labor by FDA, it is increasingly used for this purpose as it is inexpensive, stable at room temperature, and may be given as an oral medication.<sup>7,8,9</sup> The aim of this trial was to compare safety, efficacy and neonatal outcome in vaginally administered misoprostol and dinoprostone in postdated pregnancy.

#### **METHODOLOGY:**

One hundred and five nulliparous pregnant women with more than 287 days of gestation with unfavorable cervix and intact membrane were selected for induction of labor. The allocation of drugs was decided after taking informed consent from the women. Most patients decided for misoprostol as it was less expensive. Forty-one patients were included in the dinoprostone group while 64 patients were induced with vaginal misoprostol. Non-probability convenient sampling was carried out to allocate the patients to the groups. This experimental study was carried out from September 2007 to October 2010 in unit II, Department of Obstetrics & Gynaecology, Jinnah Postgraduate Medical Center Karachi.

Inclusion criteria were single viable gestation, with more than 287 days, nulliparity, approximate fetal weight less than 3.5 kg, cephalic presentation, Bishop score < 4.7, intact membranes and reactive non-stress test. The criteria for exclusion were previous uterine surgery and any known contraindication to prostaglandin insertion or vaginal delivery.

A baseline CTG was performed before induction. The women allocated to misoprostol group received initially 50 microgram of tablet in the posterior fornix. Cervical findings were assessed after 4 hours. If

cervix was found unfavorable, subsequent doses of misoprostol (50 microgram) were inserted every 4 hours, to a maximum of 48 hours. The women allocated to the dinoprostone group received 3 mg tablet every six hours to a maximum of 48 hours depending on the Bishop score on vaginal examination. Intravenous oxytocin augmentation was used after spontaneous or artificial rupture of membranes in case with inadequate uterine contraction or failure to progress in active phase of labor. Oxytocin was started at a rate of 4 mu/min and was increased stepwise every 30 minutes by doubling the dose. Partograms were maintained to assess the progress of labor.

Vigilant fetal heart rate monitoring was performed along with evaluation of uterine activity. Tachysystole was defined as contraction frequency of more than five within ten minutes for two consecutive ten minutes periods. Hyperstimulation was defined as exaggerated uterine response with late fetal heart deceleration or fetal tachycardia greater than 160 beats per minutes or other worrisome fetal heart rate changes. Cesarean section was decided in case of fetal compromise, failed induction or failure to progress.

Primary outcome measures were induction-delivery interval, frequency of vaginal delivery and number of doses required for induction. The secondary outcomes were meconium stained amniotic fluid, incidence of uterine hyperstimulation and admission to neonatal intensive care unit in first 24 hours. A proforma was filled for each woman that included demographic data (age, parity and gestational period), number of doses and primary and secondary outcomes.

Data were analyzed by using SPSS version 15. Age and gestational age were presented by using mean-standard deviation. Frequency and percentage were calculated for parity, indication of induction, cervical ripening, mode of delivery and induction to delivery interval. Chi-square test was computed to compare the variables.

#### **RESULTS:**

A total of 105 pregnant women were enrolled in the study. Maternal satisfaction was evaluated after delivery. Table I shows the difference of mean age between the two groups as statistically significant ( $p=0.017, t=2.43$ ), while mean gestational age was found statistically non-significant ( $t=1.12, p=0.26$ ). The mean Bishop score in both groups was found statistically non-significant ( $t=0.32, p=0.57$ ).

Table II compares findings of the primary and

secondary outcome measures between the two groups. Regarding mode of delivery, the majority of the women had a successful vaginal delivery in both the groups. Forty three (67.1%) women in misoprostol group and 26 (63.4%) women in dinoprostone group had spontaneous vaginal delivery. There was no statistically significant difference between the two groups regarding the cesarean section rate.

The induction-delivery interval between the two groups was insignificant ( $t=1.57$ ,  $p=0.12$ ). In dinoprostone group, induction of labor started with one or two doses in most of the patients while in misoprostol group more dosage was required for the labor to start. The requirement of oxytocin was independent of groups (Chi-square=2.58,  $p$ -value=0.108).

The neonatal weight was  $3.54+3.38$  kg in misoprostol group as compared to  $3.10+0.26$  kg in dinoprostone group ( $p=0.41$ ,  $t=1.57$ ). Four neonatal deaths were reported in misoprostol group (6.2%) whereas 2 were reported in dinoprostone group (4.87%). The difference is statistically significant with Yate's corrected Chi-square. The difference in neonatal admission to NICU in both the groups was statistically significant with Chi-square=7.12,  $p=0.01$ . Meconium staining of amniotic fluid was found statistically non significant (Chi-square=1.09,  $P$ -value=0.29) in both the groups. None of these cases had complications like uterine rupture or genital infection after the use of prostaglandins. Only four patients in misoprostol group had uterine hyperstimulation which led to emergency cesarean section.

**DISCUSSION:**

Postdated pregnancy is the commonest indication for induction of labor. Gestational age in our study was calculated according to last menstrual date or first trimester scan only. Continuing pregnancy beyond term is associated with significant fetal morbidity. Intervention at 41 weeks has a decreased incidence of intrapartum fetal distress as compared to induction after 42 weeks.

Maternal anxiety increases as pregnancy prolongs. Counseling of the patient is done regarding the risks

and benefits of intervention with prostaglandins as compared to the prolongation of pregnancy. This study differs from another study conducted on women beyond 40 weeks, in which misoprostol (50mcg) had a significantly shorter induction-delivery interval as compared to dinoprostone (11.9h vs.15.5h  $p<0.001$ ).<sup>10</sup>

There was no significant difference between the rate of cesarean section in the both the groups. The higher rate of cesarean section in our study was observed due to abnormal fetal heart rate recordings obtained as a result of elective induction on nulliparous postdated pregnancies. This has been supported by Cochrane meta-analysis as well.<sup>11</sup> Fetal distress starts due to uterine hyperactivity which occurs when the PGE2 receptors respond in addition to PGE1 receptors resulting in uterine hypercontractility and asynchronous contractions with misoprostol.<sup>12</sup>

We observed a higher rate of meconium staining and admission to neonatal unit in first 24 hours in misoprostol group as compared to dinoprostone. These findings were dose-related. We used 50 mcg misoprostol as compared to 25 mcg in other studies that showed no difference in fetal or maternal events such as tachysystole and APGAR score.<sup>13,14</sup> A recent study compared 25 mcg misoprostol with 3 mg dinoprostone administered vaginally every four hours. The admission rate to neonatal intensive care unit was significantly lower in the misoprostol group but the median induction delivery interval was longer (25 vs. 19 hours).<sup>15</sup>

Another study conducted in Nepal found misoprostol an effective drug for induction of labor. Misoprostol group achieved cervical ripening after one dose, induction delivery interval was significantly shorter and 76.92% delivered within 24 hours. More vaginal deliveries were achieved in misoprostol group. This has also been proven from our study.<sup>16</sup>

A systemic review and meta-analysis have shown that misoprostol had a higher incidence of vaginal delivery rate within 24 hours. There was an increased need for oxytocin augmentation in the dinoprostone group.<sup>17</sup> Finally, from the result tabulations, it is seen

Variables	Misoprostol	Dinoprostone	p-value
Age (year)	26.41+ 3.87, n=63	28.93+ 6.67, n=41	P=0.017, t=2.43
Gestational age (weeks)	40.24+ 3.97, n=63	40.90+ 9.02, n=41	P=0.26, t=1.12
Bishop score	2.36+ 0.23, n=63	2.40+0.24, n=41	p-0.57, t=0.32

<b>Table II: Comparison of Primary and Secondary Outcome</b>			
<b>Mode of Delivery</b>	<b>Misoprostol</b>	<b>Dinoprostone</b>	
SVD	43	26	Chi-square=0.98
LSCS	19	12	P-value=0.61
Instrumental delivery	02	03	
<b>Induction to delivery interval (hours)</b>	13.03+3.54, n=41	14.12+3.32, n=41	P=0.1, t=1.57
<b>No. of Doses for Induction</b>			
1	18	16	Chi-square=2.64
2	33	21	P=value= 0.26
3	13	04	
<b>Oxytocin</b>			
Oxytocin required	46	35	Chi-square= 2.58
Oxytocin not required	18	06	P-value=0.108
<b>Fetal outcome</b>			
Alive	59	39	Chi-square=8.91 P=0.002
Neonatal death	04	02	Chi-square=8.91 P=0.002
Weight (Kg)	3.54+3.38, n= 63	3.10+0.26, n=41	P=0.41, t=1.57
NICU Admission	16	05	Chi-square=0.33 P=0.56
<b>Meconium stained amniotic fluid</b>	28 (44.4%)	14 (34%)	Chi-square=1.09 P -value= 0.29

that the rate of cesarean section and induction-delivery interval are almost the same for both the groups. The difference was of meconium staining and admission to neonatal unit. Keeping in view the cost-effectiveness of misoprostol, it is increasingly been used for induction of labor. However, not licensed for this purpose as compared to dinoprostone, the safety and efficacy of misoprostol has been studied with different dosage and modes of administration. More studies are still needed to establish a final protocol of misoprostol.

**CONCLUSIONS:**

Intravaginal misoprostol was less expensive, safe and effective alternative for induction of labor against the standard inducing agent, dinoprostone. However, vigilant fetal monitoring and prompt intervention were required with misoprostol insertion.

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