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Original Research Article

Comparative study of intravaginal misoprostol versus dinoprostone gel for induction of labour in primigravida

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ABSTRACT

Background: Labour is an inevitable consequence of pregnancy. The aim of the present research was to study the safety, efficacy and effect of intravaginal misoprostol and dinoprostone gel for induction of labour.
Methods: 300 patients who required induction of labour in a tertiary care centre were included in this prospective randomized controlled study from August 2019 to August 2021 with a study duration of 12 months. 50% of cases received 25 µg of intravaginal misoprostol and repeated for a maximum of 6 doses every 4 hours as needed. 50% cases received 0.5 mg dinoprostone gel and repeated for maximum of 2 doses every 6 hours as needed. The patients selected were evaluated initially by modified Bishop's score and admission test for fetal wellbeing. After drug insertion, patients were monitored for fetal heart rate, vital signs, progress of labour. A partogram was strictly maintained in all patients.
Results: The highest number in both groups being below 40 weeks which were 74% and 76% in dinoprostone and misoprostol groups respectively. Rest were between 40.1-41.6 weeks. The mean induction delivery interval in dinoprostone was more (16.15±3.1) than in misoprostol (12.26±2.21). Requirement of oxytocin augmentation was less in misoprostol group than dinoprostone group. Caesarean section rate was less in misoprostol group. Maternal side effects were minimal in either groups and neonatal outcome was good in both the groups.
Conclusions: Both misoprostol and dinoprostone gel are safe, effective for cervical ripening and induction but misoprostol is more cost effective and stable at room temperature.

Keywords: Dinoprostone, Induction of labour, Misoprostol

INTRODUCTION

Labour is an inevitable consequence of pregnancy. Induction of labour is an obstetric procedure, designed to pre-attempt the natural process of labour by initiating its onset artificially, before this occurs spontaneously. The aim of successful induction is to achieve safe vaginal delivery when continuation of pregnancy is a threat to the life or wellbeing of the mother or her unborn child. The infant should be delivered in a good condition, in an acceptable time frame and with minimum material discomfort or side effects.

In order to be successful, induction of labour must fulfil three criteria. First, it should result in labour with adequate uterine contractions and progressive dilation of the cervix and descent. Second, this labour should result in vaginal delivery and reduce number of caesarean sections. Thirdly, these aims must be achieved with minimal risk to both mother and foetus.

The human cervix has diverse properties.[1] Ripening of the cervix result in increased softening, effacement and early dilatation. Prostaglandins have two direct actions associated with labour ripening of the cervix and a direct oxytocic effect.[2]

The method of administration that has been explored thoroughly is dinoprostone or prostaglandin E_2. Though this is widely used, it is expensive and required refrigeration for storage where as another agent which is comparably cheap, safe and effective vaginally administered prostaglandin with limited side effects would be available and misoprostol or PGE_1 tablet fitted those criteria exactly.[3,4]

A number of recently published clinical trials all over the world and in India have shown that intravaginal misoprostol is an effective agent for induction of labour and cervical ripening at term, when compared to other methods of labour induction.

In this study, our traditional methods of cervical ripening with prostaglandin E_2 gel, and intravaginal prostaglandin E_1 tablet are compared with regard to efficacy safety and fetomaternal outcome in primigravida with poor Bishops score.

METHODS

After obtaining permission from institutional ethical committee, all the patients coming to labour room after fulfilling the inclusion and exclusion criteria, and those who were willing to give informed written consent were included in the study. It was a single blinded study.

Study design

It was a randomized controlled study.

Study setting

The study took place at a tertiary care hospital.

Sample size

300 of all the cases were included in the study by census enumeration method. Data was collected for duration of 12 months.

Inclusion criteria

Singleton foetus with cephalic presentation, patients requiring induction of labour, appropriate maternal and fetal indication, reactive fetal pattern, no contradiction to vaginal delivery, >37 weeks completed gestation confirmed by ultrasonography, primigravida.

Exclusion criteria

Previous LSCS or any uterine surgery, malpresentation and malposition, multiparty, abnormal fetal heart rate pattern, allergy to prostaglandins, contracted pelvis or cephalo-pelvic disproportion, antepartum haemorrhage.

Method of induction

150 cases getting admitted in a tertiary care centre with an indication for labour induction received 25 µg of intravaginal misoprostol and repeated for a maximum of 6 doses every 4 hours as needed. 150 cases with indication for induction of labour received 0.5 mg dinoprostone gel and repeated for maximum of 2 doses every 6 hours as needed. The patients selected were evaluated initially by modified Bishop's score and admission test for fetal wellbeing. After drug insertion, patients were monitored for fetal heart rate, vital signs, progress of labour. A partogram was strictly maintained in all patients.

Oxytocin was started depending on the modified Bishop's score and in the absence of adequate uterine contractions after 6 hours of the last dose, and or for augmentation of the labour in the arrest of labour. Oxytocin was started the dose of 2.5 units in 500 ml RL in primigravida.

The data on categorical variables presented as n (% of cases) and the values on continuous variables was presented as mean±standard deviation (SD). The significance of difference of distribution is tested using Chi square test and Students' 't' test were used for analysis at 95% confidence interval. P value less than 0.05 was considered to be statistically significant. All the hypotheses were formulated using one tailed alternative against each null hypothesis (hypothesis of no difference). The entire data was statistically analysed using Statistical Package for Social Sciences (SPSS ver. 21.0,) and Microsoft Excel 2010 was used for most analysis and graphical representation respectively.

RESULTS

Total number of patients studied was 300. 150 patients were induced with 25 µg intravaginal misoprostol tablets and the other 150 patients induced with 0.5 mg intracervical dinoprostone gel.

The result observed were subjected to statistical analysis by student's 't' test and Chi-square test. The following observations were made:

Table 1: Distribution of cases by gestational age.

Gestational age	Dinoprostone		Misoprostol	
	N (n=150)	%	N (n=150)	%
≤40 weeks	111	74	114	76
40 weeks 1 day-41 weeks 6 days	39	26	36	24
Total	150	100	150	100

Test: Pearson's Chi square value =0.16, p value =0.6892

From the Table 1, when gestational age was compared it was seen that there was almost equal number of patients in both groups with similar gestational age who underwent induction. This had no statistical non significance

(p>0.05). The highest number in both groups being below 40 weeks which were 74% and 76% in dinoprostone and misoprostol groups respectively.

Table 2: Mean induction delivery interval.

Drug's mean induction delivery interval	Dinoprostone	Misoprostol
	Mean±SD	Mean±SD
	16.15±3.19	12.26±2.21

Test: Unpaired T value= 12.27, p value <0.001

The mean induction delivery interval in dinoprostone was 16.15±3.19. The mean induction delivery interval in misoprostol was 12.26±2.21. Mean induction delivery interval subjected to student's t test. This had highly statistical significance (p value <0.001).

Table 3: Indications for induction.

Indications for induction	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
Mild preeclampsia	30	20.0	26	17.3
Severe preeclampsia	28	18.7	31	20.7
Post-dated pregnancy	40	26.7	32	21.3
Mild polyhydramnios	12	8.0	18	12.0
Mild oligohydramnios	22	14.7	28	18.7
Gestational diabetes mellitus	12	8.0	9	6.0
Chronic hypertension	3	2.0	3	2.0
Rh –ve pregnancy	3	2.0	3	2.0
Total	150	100	150	100

The largest group for induction in dinoprostone group were post-dated pregnancy, mild preeclampsia and severe preeclampsia, which were of 26.7%, 20% and 18.7% respectively. In misoprostol group, post-dated pregnancy, severe preeclampsia and mild oligohydramnios which were of 21.3%, 20.7% and 18.7 respectively.

Table 4: No. of doses required.

No. of doses required	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
Dose 1	45	30	27	18
Dose 2	3	2	15	10
Dose ≥3	0	0	9	6

Test: Pearson's Chi square =21.43, p value =0.00002222

The above Table 4 shows that 30% of the patients needed only one dose of the dinoprostone followed by 2% patients who needed second dose also, while 18% of the patients needed only one dose of the misoprostol followed by 10% patients who needed second dose. This was highly statistically significant as p<0.001.

Table 5: Requirement of oxytocin augmentation.

Oxytocin augmentation	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patient	%
Required	126	84	63	42
Not required	24	16	87	58

Test: Pearson's Chi square =56.7,6 p value =0.0000001

Majority (84%) of the patients receiving dinoprostone required the oxytocin augmentation while only 42% of the patients receiving misoprostol required the oxytocin augmentation which shows misoprostol is more effective than the dinoprostone which was highly statistically significant also (p<0.001).

Table 6: Modified Bishop's score at 6 hours.

Drug	Modified Bishop's score at 6 hours					
	01 to 03		04 to 06		07 to 10	
	No. of patients	%	No. of patients	%	No. of patients	%
Dinoprostone	27	18	117	78	6	4
Misoprostol	9	6	105	70	36	24

Test: Pearson's Chi sq. value =31.08, p value =0.000000179

The above Table 6 shows the comparison of the modified Bishop's score prior to induction in both groups. In the dinoprostone group majority of patients were found to have a modified Bishop's score of 4 to 6 being 78% followed by 18% with score of 1 to 3. In the misoprostol group majority of patients were found to have a modified Bishop's score of 4 to 6 being 70% and 24% with score of 7 to 10.

The above table indicates the modified Bishop's score at 6 hours. It was seen in the present study the overall Bishop's score at 6 hours in the misoprostol group was more than the dinoprostone group which was highly statistically significant (p<0.001).

Table 7: Mode of delivery.

Mode of delivery	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
Vaginal delivery	117	78	135	90
Caesarean delivery	33	22	15	10
Total	150	100	150	100

Test: Peason's Chi sq. value =8.036, p value =0.004586

The above Table 7 shows the mode of delivery in both groups. In the dinoprostone group 78% patients delivered vaginally and 22% patients underwent caesarean delivery.

In the misoprostol group 90% patients delivered vaginally and 10% patients underwent caesarean delivery ($p<0.05$).

Table 8 indicates the number and indications for failed inductions in the present study. Failed inductions were those cases which did not fulfil the criteria for the definition of 'induction of labour'. In the words all caesarean deliveries were considered as 'failed inductions'.

Table 8: Indication for failed induction.

Indication for failed induction	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
Fetal distress	6	4	12	8
Deep transverse arrest	6	4	0	0
Secondary arrest of dilation	21	14	3	2
Total	33	22	15	10

Test: Pearson's Chi square =17.16, p value =0.0001875

In the dinoprostone group the total number of failed induction were 33 out of 150 patients giving an incidence of 22%. The majority of failed inductions were due to secondary arrest of dilation- 21 cases. 6 patients had fetal distress and 6 patients had deep transverse arrest.

In the misoprostol group the total numbers of failed inductions were 15 out of 150 patients giving an incidence of 10%. The majority of failed inductions were due to fetal distress- 12 cases. It was seen that fetal distress was associated with uterine hyperstimulation in 8 out of 12 cases. 3 patients had secondary arrest of dilation.

Table 9: Effects on the mother.

Complications	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
Tachystystole	0	0	6	4
Hyperstimulation	3	2	9	6
Fever	3	2	3	2
Vomiting	12	8	6	4
Diarrhoea	6	4	3	2
Postpartum haemorrhage traumatic	18	12	9	6
Postpartum haemorrhage (atonic)	9	6	0	0
Total	51	34	36	24

Test: Pearson's Chi sq. value =22.07, p value =0.001176

Above Table 9 shows the effects on the mother in the dinoprostone and misoprostol group. There was a 34% incidence of side effects in the dinoprostone group and 24% incidence of side effects in the misoprostol group.

In the dinoprostone group in the present study there was an 8% incidence of vomiting compared to 4% in the Misoprostol group. There was an 18% incidence of postpartum haemorrhage, out of which 12% were due to traumatic postpartum haemorrhage and 6% atonic postpartum haemorrhage.

In the misoprostol group, the present study says there was an increased incidence of tachysystole 4% and hyperstimulation 6%. Hyperstimulation was associated with fetal distress in three patients for which caesarean delivery was done. 6% patients had postpartum haemorrhage of traumatic type.

Table 10: NICU admission.

No. of days	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
<6 days	12	8	6	4
>6 days	3	2	9	6
Total	15	10	15	10

Test: Pearson's Chi square =5, p value =0.02535

The above Table 10 shows the mean number of days the babies were admitted in NICU. In the dinoprostone group 12 babies were kept in NICU for less than 6 days and 3 babies were admitted for more than 6 days.

In the misoprostol group out of 15 babies, 6 babies were admitted for less than 6 days and 9 babies were admitted for more than 6 days.

Table 11: Indication for NICU admission.

Indication for NICU admission	Dinoprostone		Misoprostol	
	No. of patients	%	No. of patients	%
Meconium aspiration syndrome (MAS)	3	2	12	8
Birth asphyxia	3	2	6	4
Hyperbilirubinemia	12	6	3	2
Total	18	12	15	10

Test: Pearson's Chi square =11.64, p value =0.002970

It was seen in the dinoprostone group the main indication for NICU admission was hyperbilubinemia- 12 babies (6%) and in the misoprostol group, the major indication for NICU admission was meconium aspiration syndrome- 12 babies (6%).

DISCUSSION

In the present study, 300 patients were studied with indications for induction of labour of which 150 patients received dinoprostone gel containing 0.5 mg and 150 patients received intravaginal misoprostol tablet 25µg.

Patients' characteristics

As this study was conducted in government institution in tertiary care hospital, there was no selection of patients according to their booked or unbooked history and all the patients were randomly induced with dinoprostone and misoprostol. Both the inducing agents were available at free of cost at our institution. But infact, a single dose of dinoprostone costs Rs.230 and a single dose of misoprostol cost Rs.8/- Thus, concluding that misoprostol is more cost effective than compared to dinoprostone. The other patients' characteristics like gestational age, and Bishop's score prior to induction had no major differences in both groups.

Response to drug

Vaginal deliveries

The rate of vaginal deliveries was 78% in the dinoprostone group and 90% in the misoprostol group.

Vaginal deliveries rates with misoprostol

In present study, the rate of vaginal delivery in the dinoprostone group was consistent with the studies of Trufatter et al and Nager et al.[5,6] The vaginal delivery rate with misoprostol in present study was consistent with the studies of Ramos et al, Fletcher at al and Bugalho et al.[7-9]

Bishop's score at 6 hours:

In the present study it was shown that the mean modified Bishop's scores at 6 hours were more than in the misoprostol group compared to dinoprostone group. The mean Bishop's score at 6 hours in the misoprostol group was 5.4±1.8 which was consistent with studies of Urale et al who also observed mean Bishop's score at 6 hours was 5.9±2.9.

In the present study it was seen that the induction delivery interval was shorter in the misoprostol group compared to dinoprostone group 12.26±2.21 hours and 16.15±3.19 hours respectively. This was statistically significant ($p<0.05$). Similar results were seen in study Varaklis et al where the induction- delivery interval is 16.0±7.7 (25 µg 2 hours) versus 22.4±10.9 (0.5 mg 6 hours) and in another study Herabutya et al, it was 19.14±10.6 versus 21.36±13.09. Thus misoprostol reduces the mean duration of labour (Table 2) which reduces the duration of suffering of a patient in labour and also provides fast delivery.[10,11]

In present study, indication for induction in misoprostol group were post-dated pregnancy in 21.3%, severe preeclampsia in 20.7%, mild oligohydramnios in 18.7% whereas in dinoprostone group- post-dated pregnancy, mild preeclampsia and severe preeclampsia, which were of 26.7%, 20% and 18.7% respectively (Table 3). Thus, majority of inductions were due to these conditions.

In this study, 30% of the patients needed only one dose of the dinoprostone whereas 18% of the patients needed only one dose of the misoprostol. 2% required second dose of dinoprostone compared to 10% in misoprostol group (Table 4).

In present study oxytocin augmentation required in 63 patients in misoprostol group (42%) and in 126 patients in dinoprostone group (84%) (Table 5). In study by Herabutya et al, oxytocin augmentation required in 35% and 34% patients in misoprostol group and dinoprostone group respectively.[11]

It was seen in the present study the overall Bishop's score at 6 hours in the misoprostol group was more than the dinoprostone group which was highly statistically significant (Table 6).

Failed induction

Failed inductions were those cases which did not fulfill the criteria for the definition of 'induction of labour'.[12] Thus, all caesarean deliveries were considered 'failed induction', irrespective of the cause of the same. Caesarean delivery rates in the present study are 22% in the dinoprostone group and 10% in the misoprostol group (Table 7). The various indications were fetal distress, failure to progress due to deep transverse arrest or secondary arrest of dilation. In the dinoprostone group secondary arrest of dilation formed the major indication for caesarean delivery and in the misoprostol group fetal distress formed the major indication for caesarean delivery (Table 8).

In the misoprostol group it was seen that three cases which had fetal distress also had hyperstimulation and in all cases oxytocin augmentation was done and preoperatively it was found the presence of thick meconium-stained liquor, in all cases.

In the present study, the incidence of thick meconium-stained liquor was 2% and 8% in dinoprostone and misoprostol groups respectively. 8 out of 12 patients in the misoprostol group were induced for postdatism and found to have thick meconium-stained liquor. It was not known whether the thick meconium was due to the drug or due to the indication for induction which was postdatism. The incidence of meconium-stained liquors in the present study is consistent with the studies of Wing et al.[13]

The maternal side effects observed were tachysystole, hyperstimulation, vomiting, diarorhea, fever and PPH. In the dinoprostone group the major side effects were vomiting- 8% and PPH of which traumatic- 12% and 6% atonic. Vomiting was noticed in patients who had rapid dilation of the cervix and could have been a cause of the same. 12 patients had traumatic PPH of which 4 cases had uterine atony following vaginal delivery which responded to oxytocin and prostaglandin injections.

The major side effects observed in the misoprostol group was tachysystole 4% and hyperstimulation 6%. A concern with misoprostol induction has been excessive uterine activity namely tachysystole and hyperstimulation, 3 cases of hyperstimulation were seen with fetal distress for which caesarean delivery had to be done.

Our observations are nearly consistent with the studies of Fletcher et al.[8] The difference in the incidence of tachysystole and hyperstimulation by different authors could probably be attributed to the different dosing regimens (Table 9).

Other side effects in the misoprostol group were fever, vomiting and diarrhea which were minimal. Misoprostol had 9 patients with traumatic PPH all were cervical tears and did not require any blood transfusions. In this study, mean birth weight and mean APGAR scores in both groups did not show any major difference. The incidence of NICU admission was 10% in both groups (Table 10).

The indications for NICU 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 (Table 11).

Mundle and Young evaluated the effect of misoprostol for labour induction on neonatal outcome.[14] They found that neonatal outcome was similar in both the groups (PGE_1 and PGE_2 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. Ramos et al in their meta-analysis found no differences in incidence of low 5 minutes APGAR score and admission to NICU between misoprostol and control groups (Table 11).

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, requirement of oxytocin augmentation was less in misoprostol group when compared to dinoprostone.

Vaginal delivery rate was high in misoprostol group when compared to dinoprostone. One disadvantage with misoprostol is hyperstimulation with further fetal distress.

In conclusion, we believe that misoprostol, is apparently safe, efficient and a cost-effective induction agent which may become the drug of choice.

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