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Research Article

A COMPARITIVE STUDY OF INTRAVAGINAL MISOPROSTOL WITH INTRA CERVICAL DINOPROSTONE GEL FOR INDUCTION OF LABOUR IN PREGNANCY

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ABSTRACT

Induction of labour is one of the most common procedures in the Obstetrics. Forty pregnant women requiring induction of labour were randomized to receive either 25 µg vaginal misoprostol 4-hourly or 0.5 mg of intracervical dinoprostone gel 12 hourly. The maternal and foetal outcome were measured i.e., Bishop's score, time intervals from induction to active phase, induction to delivery, need for oxytocin, mode of delivery, maternal and foetal side effects. The results of the present study show that the time intervals from induction-Active phase, induction-Delivery intervals were significantly shorter and the requirement of oxytocin was less for augmentation of the labour in the misoprostol group than dinoprostone gel group. Intra vaginal misoprostol is an effective agent for induction of labour than intra cervical gel. The drug is easy to use, effective and safe to mother and the foetus. Misoprostol is cheaper and is stable at room temperature and can be routinely used for induction of labour than dinoprostone gel.

Keywords: Bishop's score, Dinoprostone, Labour Induction, Misoprostol, Oxytocin

INTRODUCTION

Induction of labour implies the artificial initiation of uterine contractions after the period of viability by medical and / or surgical method for the purpose of vaginal delivery. It is indicated when there is risk of continuation of pregnancy is more either to the mother (or) the foetus. Augmentation is the process of stimulation of uterine contractions that are already present but found to be inadequate [1]. It is a common procedure; and about 20% of pregnant women will have labour induced for a variety of reasons[2]. Induction primarily refers to attempt to produce regular uterine contraction along with cervical changes to begin the active phase of labour [3].

To be successful, induction of labour must fulfill three aims. First it should result in labour namely adequate uterine contractions and progressive dilatation of cervix. Second this labour should result in vaginal delivery, as there is little purpose in bringing about labour as a mere preparation for caesarean section. Third, in viable pregnancies, these aims must be achieved with minimum discomfort and risk to both mother and foetus. The drugs commonly available for the purpose of induction are misoprostol, dinoprostone and oxytocin [4].

Cervical ripening is an essential prerequisite for induction and is assessed with Bishops scoring system. A favorable cervix is with a modified Bishop score of more than 8 and unfavorable cervix with a Bishop score of < 4.2 [2]. In order to improve cervical score and induce myometrial contractility, prostaglandins in various forms and preparations have been used [5]. Misoprostol, a prostaglandin E_1 analogue is an effective synthetic PGE1 analogue which has become an important drug in obstetric and gynaecological practice because of its uterotonic and cervical priming actions. Risk benefit analysis is necessary before any induction of labour [6].

Prostaglandins were first used intravenously in the late 1960s but this route of administration was associated with significant side effects [7]. Intravaginal or intracervical administration of exogenous PGE1 (misoprostol) and PGE2 (dinoprostone) are the most widely used pharmacological method to promote cervical ripening and labour induction. For induction misoprostol is used as tablet form and dinoprostone as gel [8, 9].

In this perspective, the study was undertaken to evaluate the safety and efficacy of intra vaginal Misoprostol and intra cervical Dinoprostone gel for the induction of labour.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Narayana tertiary care Hospital, Nellore. The study was approved by the Institutional Ethics Committee, Narayana Medical College with protocol number 46 / NMCH – 10. Forty (40) pregnant women undergoing delivery were enrolled in the study. Informed consent form was prepared in both Telugu and English, signed by the pregnant women after proper explanation in their mother language. They were randomly allocated to either intravaginal misoprostol tablet or intracervical dinoprostone gel with 20 pregnant women in each group.

Inclusion criteria

- Medical indication for labour induction.
- Gestation age greater than 36 weeks.
- Vertex presentation, intact membranes; Bishop Index less than 6.
- Normal foetal heart rate.
- Primigravida and Multigravida women were included.

Exclusion criteria

- Pelvic dystocia
- Evidence of cephalopelvic disproportion
- Placenta previa or any unexplained vaginal bleeding; parity > 5
- Foetal malformation
- Previous uterine scar

Any situation where the vaginal delivery is not indicated
The demographic details such as the age, gravidity, parity, gestation age were noted. Primary outcome measures assessed were time taken for induction to active phase and induction to vaginal delivery intervals and requirement of oxytocin for augmentation. Secondary outcome measures assessed were number of vaginal deliveries, incidence of caesarean section with failed induction, side effects of mother and foetus especially uterine hyper stimulation, meconium staining and neonatal outcome with reference to apgar at 1min and 5 minutes and body weight.

During a vaginal examination, cervical effacement, cervical dilatation in centimeters, consistency, head station, position of the cervix, whether the membranes are intact or not were evaluated by using Bishop scoring system initially and after six hours. The cervix was graded as a favorable cervix when the Bishop score was equal to or greater than five points. These patients either went into spontaneous labour or the labour was augmented by Oxytocin. All the patients were monitored clinically under close supervision. Progress of labour was charted on a partogram. Afterward the patient was also evaluated every one hour for vital signs (Temperature, pulse, blood pressure), every 10 minutes for foetal heart rate and every 15 minutes for uterine contractions in the labour ward. In most cases, monitoring was done by auscultation; Cardiotocography was reserved for cases with foetal distress. Success of induction was declared when effective uterine contractions were started along with improvement in Bishop Score.

In the misoprostol group, 20 pregnant women of primigravida and multigravida were included with 10 in each group. Each woman was administered 25 µg tablet in the posterior fornix of the vagina. Depending on the response, the patients received upto 4 doses and the maximum dosage given was 100 µg, after that bishop score was evaluated. Dose was repeated every 4th hourly until an adequate uterine contraction pattern was set or till the cervical dilatation reached 3cm and uterine contraction reached a frequency of 3 in 10 minutes lasting for 30 to 45 seconds. The dose was withheld in the presence of active labour, (>3 cm cervical dilatation and regular uterine contractions). If labour did not ensure even after 4 hours following last dose or cervix was not favorable enough for artificial rupture of membranes, it was considered as failed induction and other methods like oxytocin was tried for augmentation or referred for surgical interventions.

In the dinoprostone gel group, 20 pregnant women of primigravida and multigravida were included with 10 in each group. By using sterile technique a prefilled syringe containing 0.5mg of dinoprostone gel was instilled endocervically. After that Bishop's score was assessed. If the Bishop's score remained less than 5 after 6-12 hours, reapplication was done. When the score remained below 5 after 6 hours of second application and if there was failure to induce labour in 24 hours, or evidence of maternal or foetal compromise then it was taken as failure.

STATISTICAL ANALYSIS

The collected data was entered into Microsoft office excel – 2007 and data analysis was performed by using the statistical software Graph pad prism- 4 USA. The analyzed data was presented as Mean, Standard deviation (SD) and percentages. Data between misoprostol group and dinoprostone gel group was analyzed by using unpaired t test to find out the differences between the two means and by Chi-square t test. The two tailed probability value ($P < 0.01$) was considered as statistically significant. The difference in the Induction to active phase and Induction to delivery time intervals in primigravida and multigravida were determined by ONE-WAY ANOVA test.

RESULTS

The demographic characteristics of the women in the two groups including age, gravidity, parity and gestational age were similar. In misoprostol group, 40% were post term pregnant, 20% had Oligohydromnios, and 30% had Pre-eclampsia. Whereas, this was 45%, 25% and 20% respectively in the dinoprostone gel group. The other indications for induction were diabetes and foetal distress in both the groups. The indication of labour induction was similar in both the groups (Table 1).

The induction - active phase interval was significantly shorter in all pregnant women in misoprostol group than in dinoprostone gel group and it was statistically significant. In primigravida, the observed time interval difference between the two groups were statistically significant, whereas in multigravida the time interval was not statistically significant, indicating dinoprostone gel was effective in multigravida compared to primigravida. The Bishop's score in both the groups for misoprostol group 9.25±1.29 Vs 9.05±1.50 for dinoprostone gel group, it was statistically non significant. (Table 2).

The induction - delivery interval was significantly shorter in all pregnant women in misoprostol group than in dinoprostone gel group. In both primigravida and multigravida, the observed difference in the induction-delivery interval was statistically significant (Table 3).

The percentage of women who had vaginal delivery was 15 (75%) in the misoprostol group as compared to that 12 (60%) in the dinoprostone gel group and the percentage of women who underwent caesarean section was lower 5 (25%) in the misoprostol group as compared to that 8 (40%) in the dinoprostone gel group, but this difference was not statistically significant. The indications for caesarean section in both the groups were for failed induction, for foetal distress and for failure to progress. Oxytocin requirement for augmentation in the misoprostol group was 2(10%) and in the dinoprostone gel group it was 9 (45%) which were statistically significant (Table 4).

The maternal complications mainly constituting uterine hyper stimulation was 6 (30%) and 2 (10%) in misoprostol group and dinoprostone gel group respectively, were not statistically significant. The foetal complications like meconium staining 6 (30%) and 1(5%) has occurred in misoprostol group and dinoprostone gel group respectively, were not statistically significant (Table 5). The comparison of Apgar scoring in both the groups was not significant at both 1 minute and 5 minute. Mean birth weight of babies (2.59±0.44) kg in misoprostol group and dinoprostone gel group (2.75±0.31) kg were similar (Table 6).

DISCUSSION

Induction of labour is an increasingly common obstetrical procedure done to ensure benefits or minimize risks to mother and or foetus. Previously oxytocin was the commonest inducing agent but with introduction of prostaglandins it was found that prostaglandins are better agents when cervix is unripe [10]. Dinoprostone is the preferred method of pharmacologic method of induction of labour but due to its high cost and storage difficulties, it was less favoured. The search for an effective, easily stored, affordable labour inducing agent has led to the use of misoprostol. Unlike dinoprostone, it is very stable at room temperature and is extremely inexpensive. The general concern in the use of intravaginal misoprostol for induction of labour was significant incidence of uterine tachysystole, hyperstimulation and potential of foetal threat. At lower doses of 25 µg, misoprostol was found to be effective with less frequent incidence of hyperstimulation and meconium passage [11].

The purpose of the study was to compare the efficacy and safety of intra vaginal misoprostol and intracervical dinoprostone gel application for induction of labour. The present study showed that the average time interval from induction to active phase and induction to delivery was significantly shorter in misoprostol group and lesser number required oxytocin for augmentation than dinoprostone gel group. Both the groups did not differ significantly with age, parity, gravidity, gestational age and indications for induction.

In the present study of 40 women, the mean induction delivery was shorter i.e 10.7 and 16.4 hrs (Table 3) and the average interval ranged from 3 - 10.7 and 4.9 - 16.4 hrs in misoprostol and dinoprostone group respectively, it was statistically significant (Table 2 & 3) and was in accordance with the study by Nanda et al[12]. The no. of vaginal deliveries were 75% in misoprostol group compared to 60% in dinoprostone gel group (Table.3). Thus, misoprostol is more efficacious for cervical ripening and labour induction than dinoprostone gel as seen by shorter induction delivery interval and greater number of vaginal deliveries. Gupta N et al[13], have also reported that spontaneous vaginal deliveries were 86% in misoprostol group compared to 68% in dinoprostone gel.

The interval from the application of the initial dose to the beginning of active phase of the labour, induction – delivery intervals were shorter in misoprostol group with no change in Bishop's score (Table 2 and Table 3). These results were quiet consistent with the study conducted by Nunes et al[14], Belfrage et al[15], Neiger et al[16], Buser et al[17] and Rozenberg et al[18]. Oxytocin requirement for augmentation was 10% in misoprostol group compared to 45% of

cases in the dinoprostone gel group, indicating that the misoprostol group required less oxytocin augmentation. This was similar to the study by Danielian et al[19], which mentioned 21% in the misoprostol group and 47% in the dinoprostone gel group (Table 4).

Maternal and foetal complications were less in dinoprostone gel group but there was no significant statistical difference (30% vs 5%) for uterine hyper stimulation and (30% vs 5%) for meconium staining of liquour in misoprostol group and dinoprostone gel group respectively (Table 5). Chuck et al[20], also reported that no significant differences were noted in maternal and foetal effects. Rates of caesarean sections were less in misoprostol group (25% vs 40%) than dinoprostone gel group but statistically insignificant. Jouatte et al[21] stated that, there was no significant difference in the rates of caesarean section (21% vs 23%) and in the rates of uterine hyper stimulation (30% vs 27%) in misoprostol and dinoprostone gel groups, which was supportive to our study.

In this study, there was no significant statistically difference in apgar score at 1 min and 5 min between both the groups, similar to the study by Daniel et al[22] and Herabutya Y et al[23]. Van Gemund et al[24], compared 25 µg vaginal misoprostol with dinoprostone 1mg with adverse neonatal outcome as the primary outcome measures concluded that lower dose of misoprostol is safer with lesser neonatal complications. But in the present study, less neonatal complications occurred in both the groups and there was no significant statistical difference (Table 6).

TABLE 1 : INDICATIONS FOR INDUCTION

Indications	Misoprostol Group		Dinoprostone gel Group		P value
	Number	Percentage	Number	Percentage	Chi Square Test
Post-dated pregnancy	8	40%	9	45%	0.7491
Oligohydromnios	4	20%	5	25%	0.7050
Pre-eclampsia	6	30%	4	20%	0.7150
Others	2	10%	2	10%	0.5483

TABLE 2 : INDUCTION – ACTIVE PHASE INTERVAL

Time (Hrs)	Misoprostol Group	Dinoprostone gel Group	Statistical analysis
	Mean ±SD	Mean ±SD	P value
All patients N=40 (20 in each)	3.03±0.96	4.87±2.16	0.0013
Primigravida N=20 (10 in each)	3.47±0.94	6.22±1.95	0.0008
Multigravida N=20(10 in each)	2.60±0.81	3.53±1.42	0.0902
Bishop's Score	9.25±1.29	9.05±1.50	0.6545

TABLE 3: INDUCTION – DELIVERY INTERVAL

Time (Hrs)	Misoprostol Group	Dinoprostone gel Group	Statistical analysis
	Mean ±SD	Mean ±SD	P value
All patients N=40 (20 in each)	10.6±2.83	16.3±4.86	< 0.0001
Primigravida N=20 (10 in each)	12.5 ±2.16	19.2±4.09	0.0002
Multigravida N=20 (10 in each)	8.76±2.08	13.5±3.87	0.0030

TABLE 4: MODE OF DELIVERY

	Misoprostol group		Dinoprostone gel group		P value
Parameters	Number	Percentage	Number	Percentage	Chi Square test
Vaginal deliveries	15	75%	12	60%	0.4996
Caesarean section	5	25%	8	40%	0.4996
Oxytocin for augumentation	2	10%	9	45%	0.03

TABLE 5: MATERNAL AND FOETAL COMPLICATIONS

Parameters	Misoprostol group		Dinoprostone gel group		P value
	Number	Percentage	Number	Percentage	ChiSquare test
Uterine hyperstimulation	6	30 %	2	10%	0.2357
Meconium staining of liquor	6	30%	1	5%	0.0960

TABLE 6: FOETAL OUTCOME

Apgar Score		Mi soprostol		Dinoprostone gel		P value
		Number	Percentage	Number	Percentage	Chi Square test
1 min	>7	16	80%	18	90 %	
	<7	4	20%	2	10%	0.6579
5 min	>7	18	90%	19	95%	0.5483
	<7	2	10%	1	5%	
Body weight (kg)		2.59±0.44		2.75±0.31		0.2074

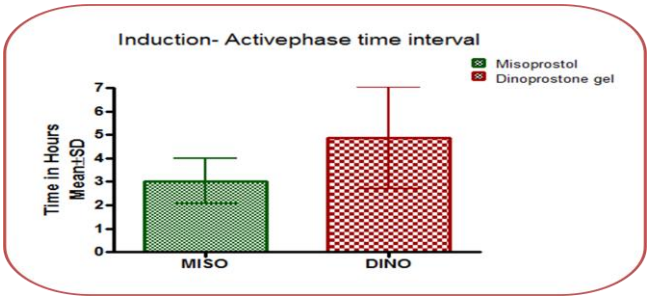

FIGURE 1: THE INDUCTION – ACTIVE PHASE TIME INTERVAL IN ALL PATIENTS

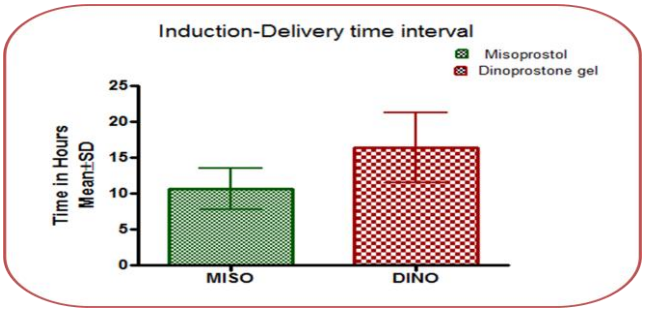

FIGURE 2: THE INDUCTION –DELIVERY TIME INTERVAL IN ALL PATIENTS

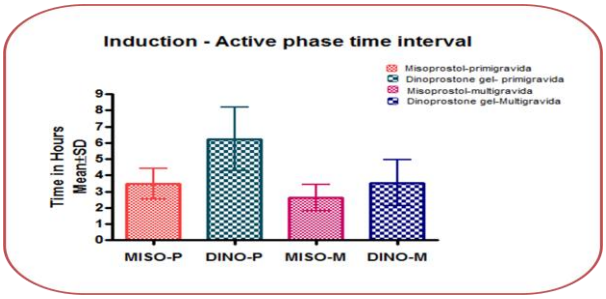

FIGURE 3: INDUCTION – ACTIVE PHASE TIME INTERVAL IN PRIMIGRAVIDA AND MULTIGRAVIDA

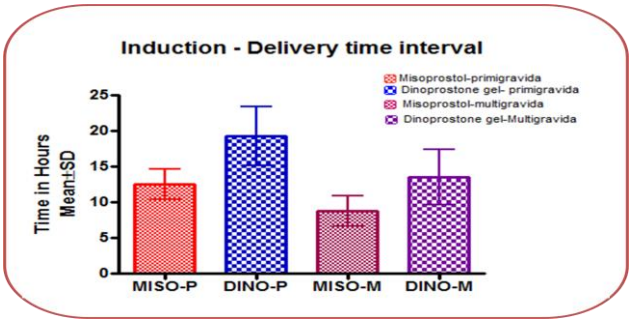

FIGURE 4: IT SHOWS THE INDUCTION –DELIVERY INTERVAL IN PRIMIGRAVIDA AND MULTIGRAVIDA

CONCLUSION

Intra vaginal administration of misoprostol has shorter Induction to active phase, Induction to delivery time intervals and also it requires less oxytocin for augmentation of the labour than the intra cervical dinoprostone gel. It is demonstrated to be a viable alternative technique of labour induction since it is efficacious, easily administered, not expensive, stable at room temperature, needs no refrigeration with a longer shelf-life than dinoprostone gel. It allows the better patient acceptability although uterine hyper stimulation and meconium staining is the main concern with misoprostol use, close maternal-foetal monitorization and timely intervention measures would prevent devastating adverse effects during labour induction and increase tolerability of the drug by both the mother and foetus. So by the present study, it was concluded that intravaginal misoprostol is a more successful, lower-cost agent for induction of labour than intracervical dinoprostone gel.

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