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Original Research Article

Comparison of Efficacy & Safety of Intravaginal Misoprostol Tablet and Intracervical Dinoprostone Gel for Induction of Labour in Unfavourable Cervix in Term Pregnancy: A Randomised Control Trial

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Abstract:

Background: Induction of labour is a commonly performed obstetrical procedure for which numerous methods are adapted and intracervical dinoprostone and intravaginal misoprostol are the most frequently used techniques. This study aimed to compare the safety and efficacy intravaginal misoprostol tablet and intracervical dinoprostone gel for induction of labour at term.

Methods: The present study was conducted in a tertiary care hospital in New Delhi among pregnant females with singleton pregnancy at term requiring induction of labour for various indications. The study subjects were enrolled in group A (misoprostol group) were administered 25 mcg of misoprostol every 4th hourly to a maximum of 5 doses and in group B (dinoprostone) study subjects were administered 0.5 mg of dinoprostone every 6th hourly to a maximum of 4 doses.

Results: A total of 50 cases were enrolled in both the study groups. The baseline parameters among both the study groups were comparable. Nearly two-third of study subjects in misoprostol group delivered within first 12 hours and only 12% had delivered in first 12 hours in dinoprostone group. Requirement of oxytocin augmentation of labour was nearly similar in both the study with 18% of cases in misoprostol group and 16% cases in dinoprostone group requiring it.

Conclusion: Low dose vaginal misoprostol is associated with a lower incidence of uterine tachysystole and a lower caesarean delivery rate.

Keywords: Labour Induction, Term Pregnancy, Intravaginal Misoprostol, Intracervical Dinoprostone.

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Introduction

Induction of labour is a commonly performed obstetrical procedure that involves initiating labour artificially for specific reasons, considering the potential benefits to the mother or foetus that outweigh continuing the pregnancy. Induction can be prompted by either clinical factors, such as post-term pregnancy, premature rupture of membranes, hypertensive disorders of pregnancy, gestational diabetes mellitus, intrauterine growth restriction, and others, or occasionally by social factors, based on the convenience and preferences of both the patient and clinician[1]. Numerous methods are adapted for induction of labour such as intravenous prostaglandins, oxytocin, mechanical methods using Foley's catheter, castor oil bath/ enema, use of buccal/ sublingual/vaginal misoprostol, acupuncture, vaginal prostaglandins, intracervical dinoprostone, breast stimulation, corticosteroids etc [2-13].

Dinoprostone has been the preferred agent for pre-induction cervical ripening for several years and is known to reduce incidence of caesarean deliveries and decreased need for oxytocin. Despite its extensive use, dinoprostone has the disadvantage of being relatively costly and requires specific cold chain maintenance [14]. Thus, there was always a need to find a less costly and less temperature sensitive alternative. Misoprostol is an analogue of prostaglandin E1 (PG E1) which was initial registered for the treatment of peptic ulcers[15], later found it's use in labour induction by cervical ripening and has been gaining worldwide interest.

There are very limited studies in Indian settings comparing the effect of intravaginal misoprostol tablet and intracervical dinoprostone gel for labour induction at term among patients with unfavourable cervix. The purpose of this study is to compare the safety and efficacy intravaginal misoprostol tablet and intracervical dinoprostone gel for induction of

labour at term, requirement of oxytocin augmentation, delivery time, maternal side effects, rate of caesarean section among mother and birth asphyxia, Apgar score and neonatal outcome.

Materials and Methods

The present study was conducted in a tertiary care hospital in New Delhi among pregnant females with singleton pregnancy in the age bracket of 18 to 32 years at term requiring induction of labour for various indications. The mean duration of labour (from induction to delivery) was taken into consideration and in a study conducted by Sundari Lakshmidevi et al [16] the mean duration of labour in misoprostol group was 11.3 ± 2.9 hours and the same in dinoprostone group was 15.1 ± 4.1 hours. At 95% confidence interval and an error of 5% (power of the study at 95%) the minimum sample size was calculated to be 24 cases per group.

Primigravida and multigravida with singleton pregnancy at term with cephalic presentation were considered for the study. Cases with gestational diabetes at 38 weeks of gestation or above, PROM with Bishop's score of less than six, postdated pregnancies, IUGR pregnancies and gestational hypertension were also considered for the study. Patients with previous caesarean section, uterine scar, cephalon-pelvic disproportion, ante-partum haemorrhage, malpresentation, grand multigravida, multiple pregnancies, umbilical cord prolapse, foetal weight of more than 4000 grams, known allergy to prostaglandins or any other complication that hampers vaginal delivery were excluded from the study. Patients with cervical dilation of 3 cm or more at the time of examination were also excluded from the study. The present study was conducted from 01 Jun 2018to 30 May 2019. Ethical approval was obtained from institutional ethical committee. All study subjects were informed in detail about the study in the language they could understand and an informed written consent was obtained from all the study participants. We enrolled a total of 100 females for the study and were further allocated to both the study groups (50 cases in each group) through randomization (computer generated). The study subjects were enrolled in group A (misoprostol group) were administered 25 mcg of misoprostol through intravaginal route every 4th hourly to a maximum of 5 doses and in group B (dinoprostone) study subjects were administered 0.5 mg of dinoprostone through intracervical route every 6th hourly to a maximum of 4 doses. Continuous monitoring of foetal heart rate and uterine activity was carried out throughout labour in both the study groups. I/V Oxytocin augmentation was administered in case of spontaneous or artificial rupture of membranes or in absence of adequate uterine contractions. Evaluation of uterine activity was performed to assess occurrence of hyperstimulation (4 contractions in 10 min) and/or abnormal foetal heart rate pattern.

The data collected was entered in the MS Excel master sheet and analyzed using Statistical Package for Social Sciences (SPSS) version 22. Categorical data have been presented as numbers and percentages (%) and quantitative data in terms of mean and standard deviation. Categorical variables have been analysed using Pearson's chi-square test and Fisher exact tests (when the expected count of 20% of cells is less than 5). Quantitative variables have been analysed using Student T test. A p value of <0.05 has been considered as statistically significant.

Results

A total of 50 cases were enrolled in both the study groups. The baseline parameters among both the study groups were comparable. The mean age of participants in misoprostol group was 24.41 ± 3.0 years and that of subjects in dinoprostone group was 24.35 ± 2.95 years. The similar number of participants in both the groups had a parity of one and two with 10% (5 cases) with a parity of three. Most common reasons for induction of labour in both the groups was post term, gestational diabetes mellitus, hypertensive disorders in pregnancy, foetal growth restriction and premature rupture of membrane. There was statistically no significant difference between the two groups (p value > 0.05) with respect to baseline parameters (table 1).

Table 1: Comparison of baseline parameters among study groups

Parameters	Misoprostol group	Dinoprostone group	p-value
Age (in years)			
Mean ± SD	24.41 ± 3.0	24.35 ± 2.95	0.92
Parity (Frequency/ percentage)			
One	22 (44%)	20 (40%)	0.91
Two	23 (46%)	25 (50%)	
Three	05 (10%)	05 (10%)	
Indication for induction of labour (Frequency/ percentage)			
Post-term	12 (24%)	11 (22%)	0.99
Gestational diabetes mellitus	11 (22%)	12 (24%)	
Hypertensive disorders of pregnancy	10 (20%)	10 (20%)	
Premature rupture of membranes	08 (16%)	08 (16%)	
Foetal growth restriction	07 (14%)	08 (16%)	
Oligohydramnios	02 (4%)	01 (2%)	
Total	50 (100%)	50 (100%)	

On comparison of time from induction of labour to delivery (interval of delivery), it was observed that nearly two-third of study subjects (30 cases, 60%) in misoprostol group delivered within first 12 hours and the remaining 20 cases (40%) delivered in next 12 hours whereas in dinoprostone group nearly three-fourth (36 cases, 72%) delivered between 13 to 24hours and only six cases (12%) had delivered in first 12 hours. Eight cases (16%) in dinoprostone group delivered after one day of induction of labour. The mean interval of delivery was 11.7 ± 2.8 hours in misoprostol group and 18.5 ± 4.8 hours in dinoprostone group. The interval of delivery was significantly lower (p value < 0.01) in misoprostol group when compared to dinoprostone group (table 2).

Table 2: Comparison of interval of delivery among study groups

Interval of delivery	Misoprostol group	Dinoprostone group	p-value
≤ 12 hours	30 (60%)	06 (12%)	<0.01
13-24 hours	20 (40%)	36 (72%)	
≥ 25 hours	0	08 (16%)	
Total	50 (100%)	50 (100%)	
Mean ± SD	11.7 ± 2.8 hours	18.5 ± 4.8 hours	<0.01

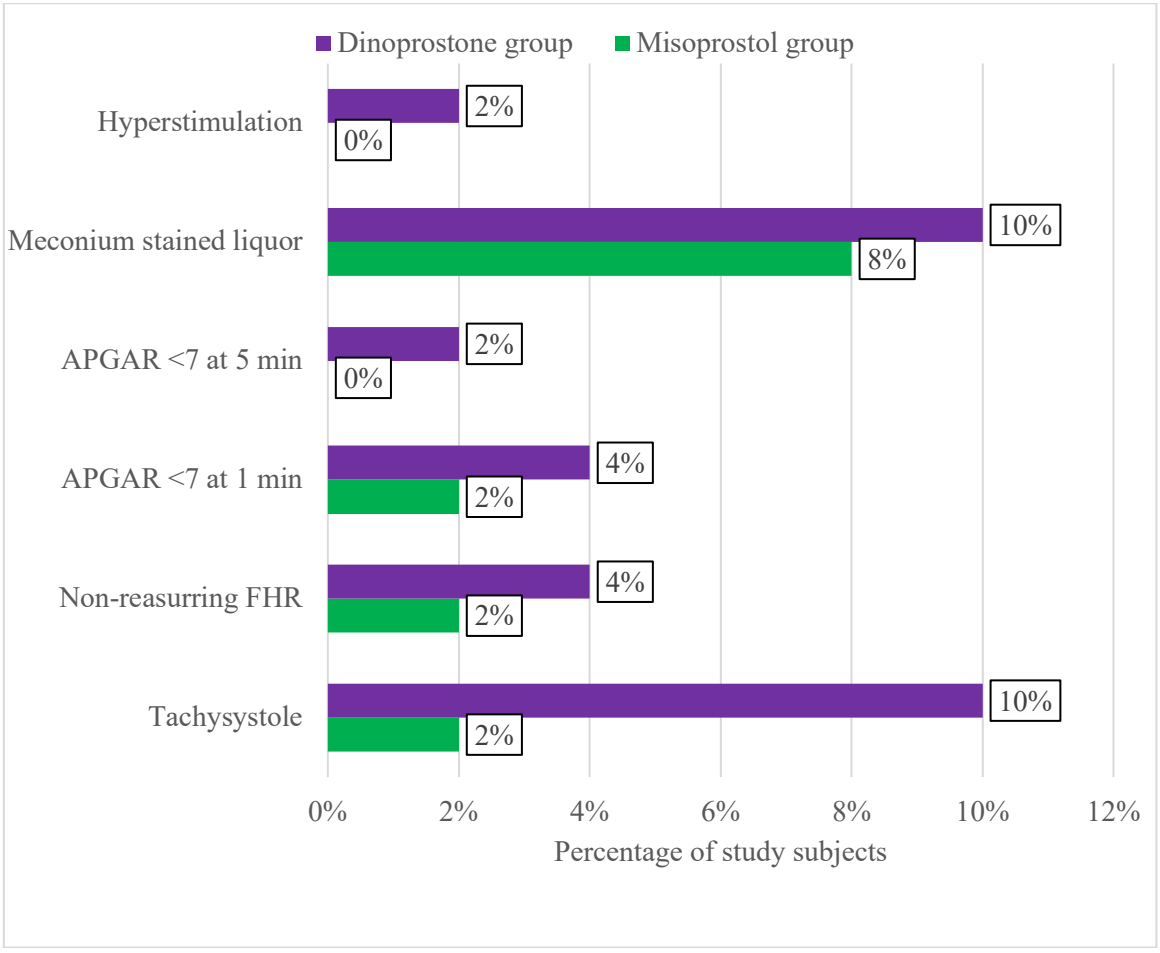

Figure 1: Comparison of complications among study groups

Tachysystole was significantly higher (p value < 0.01) in dinoprostone group when compared to misoprostol group whereas incidence of non-assuring foetal heart rate (FHR), hyperstimulation, meconium-stained liquor, APGAR score at one minute and APGAR score at five minutes were comparable between the groups (p value > 0.05) (Fig 1).

Table 3: Comparison of oxytocin augmentation, mode of delivery and indication for LSCS among study groups

Parameters	Misoprostol group	Dinoprostone group	p-value
Requirement of oxytocin augmentation			
Yes	09 (18%)	08 (16%)	0.79
No	41 (82%)	42 (84%)	
Mode of delivery			
Normal vaginal delivery	46 (92%)	44 (88%)	0.70
Vacuum delivery	02 (4%)	02 (4%)	
LSCS	02 (4%)	04 (8%)	
Indication for LSCS			
Foetal distress	01 (50%)	02 (50%)	0.69
Non-progress of labour	01 (50%)	01 (25%)	
Failed induction	0	01 (25%)	

Requirement of oxytocin augmentation of labour was nearly similar in both the study with 18% of cases in misoprostol group and 16% cases in dinoprostone group requiring it. Mode of delivery was also comparable with majority of the study participants in both the study groups having had a normal vaginal delivery (92% in misoprostol group and 88% in dinoprostone group). Of the two subjects who underwent LSCS in misoprostol group, one was because of foetal distress and the other due to non-progress of labour. In dinoprostone group four study subjects underwent LSCS of which two were because of foetal distress and one each due to non-progress of labour and failed induction. All the above parameters were similar in both the study groups with no statistical significance (p value >0.05) (table 3).

Discussion

Labour induction is a crucial medical intervention that plays a significant role in ensuring the health and safety of both the mother and the baby during delivery. It is recommended in certain situations when the natural onset of labour is delayed or when there are potential risks to the well-being of either the mother or the baby. Labour induction can prevent complications such as foetal distress, meconium aspiration, or placental abruption, which can be life-threatening and also minimize the risk of stillbirth [17]. Dinoprostone and misoprostol are two commonly used medications in labour induction, both are considered safe and well-tolerated medications which help initiate labour in cases where it may be delayed or when there is a medical indication for induction by promoting cervical ripening and uterine contractions and ensuring the well-being of both the mother and the baby [18-19].

In the present study mean age group of vaginal titrated misoprostol group was 24.41 ± 3.0 years and the intracervical dinoprostone group was 24.35 ± 2.95 years with the p value of 0.92, which make both the groups comparable. The groups were also comparable with respect to parity status and indication for induction of labour. The time interval from the 1st dose to vaginal delivery was 11.7± 2.8hours in misoprostol group versus 18.5 ± 4.8 hours in dinoprostone group. Number of deliveries in the first 12 hrs were 30 patients (60%) in misoprostol group whereas only 12% deliveries occurred in first 12 hours in dinoprostone group. These results are similar to a RCT published by Cheng et al [20], cross-sectional study by Raval BM et al [21] and a prospective interventional study Das D et al [22] who also observed that duration from induction time to delivery was significantly lower in misoprostol group when compared to dinoprostone group.

The rate of tachysystole was significantly higher in the intracervical dinoprostone group (10%) in comparison to vaginal misoprostol group (2%). Occurrence of non-assuring foetal heart rate (FHR), hyperstimulation, meconium-stained liquor, APGAR score at one minute and APGAR score at five minutes though slightly higher in dinoprostone group there was statistically no significant difference. The findings are almost the same as the Cochrane review by Alfirevic Z et al [8]. In cases of vaginal misoprostol further doses were stopped while in the intracervical dinoprostone group 06 patients required tocolysis. This can be explained by the sustained peak level in case of vaginal application as demonstrated by Khan R et al [23]. Das D et al [22] also observed similar findings in their study with respect to complications among the study groups (foetal distress, APGAR score). Raval BM et al. [21] also observed similar incidence of foetal distress in both the study groups whereas contrary to our study the authors observed higher hyperstimulation rate in misoprostol group. Higher rate of tachysystole in the dinoprostone group further supports the fact that action of dinoprostone cannot be immediately stopped as compare to vaginal method where the removal of intra vaginal tablet can stop the incidence of tachysystole. Despite higher incidence of tachysystole the neonatal outcomes in terms of APGAR scores at

birth and NICU admission were comparable in the two groups.

In the present study we also observed that the requirement of oxytocin requirement and percentage of patients undergoing LSCS were comparable in the study groups though the former was slightly higher in misoprostol group and later slightly more in dinoprostone group. Contrary to the findings in our study Das D et al [22] observed higher requirement of oxytocin in dinoprostone group when compared to misoprostol group. Similar were the findings in study by Raval BM et al [21] wherein 22% of cases in misoprostol group required oxytocin requirement and the same was 24% in dinoprostone group, but the difference was statistically not significant. Suman et al in [24] in their randomised comparative trial observed caesarean section was relatively lower in misoprostol group (16%) compared to dinoprostone group (26%), though the difference was not found to be statistically significant. This is consistent with the study of Kundodyiwa TW et al [25] and Raval BM et al [21].

This study shows that low dose vaginal misoprostol is associated with a lower incidence of uterine tachysystole and a lower caesarean delivery rate (though not statistically significant) than intracervical dinoprostone for labour induction in patients with unfavourable cervix. Misoprostol is a good alternative especially in low resource setting as it is economical and does not require cold chain maintenance. Fewer adverse effects observed with low dose vaginal misoprostol tablet is a promising method of labour induction for both nulliparous and multiparous women, though further studies with larger number of patients are required to validate these findings.

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