ORIGINAL ARTICLE

Comparative Study of Efficacy of Misoprostol Vs Dinoprostone Gel For Induction of Labour

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Abstract

This study has been undertaken to compare the safety and efficacy of intra-vaginal misoprostol (PGE1 analogue) with intra-cervical dinoprostone (PGE2) in progress and induction of labour, the maternal side effects and the foetal outcome. Group I comprised of 50 patients who underwent induction with misoprostol vaginal tablets and Group II comprised of 50 patients who underwent induction with dinoprostone intra cervical gel. Labour induction was considered successful if subjects delivered within 24 hours of initiation of either of two methods. The maternal and foetal outcome were measured i.e., Bishop's score, time intervals from 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-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. Intravaginal 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 can be routinely used for induction of labour than dinoprostone gel.

Key Words

PGE_1, PGE_2, Induction of Labour

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 either to the mother (or) the foetus (1). Induction primarily refers to attempt to produce regular uterine contractions along with cervical changes to begin the active phase of labour (2). 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 (3). Cervical ripening is an essential prerequisite for induction and is assessed with Bishop scoring system. When Bishop score exceeds 8, the likelihood of a successful vaginal delivery approaches that of spontaneous labour, the duration of pregnancy being inversely correlated with score (4). For the choice of most optimal cervical ripening agent, the safety profile, efficacy and cost should figure into decision analysis. In order to improve cervical score and induce myometrial contractility, prostaglandins in various forms and preparations have been used (5). Misoprostol, a prostaglandin E1 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). This study was undertaken to compare the safety and efficacy of intra vaginal misoprostol with dinoprostone cervical gel for cervical ripening and for the induction of labour.

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Material and Methods

The present cross-sectional study was conducted on 100 patients requiring induction of labour, admitted in antenatal ward, Department of Obstetrics and Gynaecology, GMC Jammu. The patients were distributed in two groups: Group I - 50 patients who underwent induction with misoprostol vaginal tablets and Group II - 50 patients who underwent induction with dinoprostone intra cervical get (cerviprime).

Inclusion criteria : for induction of labour were singleton pregnancy with cephalic presentation more than 27 weeks with unfavourable cervix, with a fetal or maternal isoimmunizatioin, post dates, intra uterine growth retardation, intra uterine death, premature rupture of membranes and congenital malformations. *Exclusion criteria* : included cases with indications like fetopelvic disproportion, major degrees of placenta praevia, malpresentation, multifoetal gestations, grand multiparas, previous cesarean delivery, myomectomy, hypersensitivity to prostaglandins, renal, hepatic or cardiovascular disease.

The study was approved by the Institutional Ethics Committee and an informed written consent for enrolment was obtained from each patient. Each patient's name, age and parity were noted. Systemic examination was done to rule out any disease of heart, lungs and kidney. Obstetrical examination included perabdominal and pervaginal examination. On perabdominal examination, height of uterus, lie, presentation and position were noted and foetal heart auscultated. For pervaginal examination, perineal preparation was done. The vulval region was cleaned thoroughly with savlon (2.5%) solution and draped. The labia minora separated with gloved thumb and index fingers of left and index and middle fingers of right hand introduced into vagina until the cervix was reached. 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. The cervix was graded as a favorable cervix when the Bishop score was equal to or greater than six points. In Group I, each patient received misoprostol (Misoprost, Cipla) vaginal tablet in the dosage of 25 microg in the posterior fornix. The dose was repeated every 4 hours, until adequate uterine contractions were achieved (at least 3 contractions lasting 30-45 seconds in 10 minutes). The maximum total dose of misoprostol was 150 microg or 6 tablets. If labour did not ensure than after 4 hours following last dose or cervix was not favourable enough for artificial rupture of membrane it was considered a failed induction and other methods like oxytocin was tried for augmentation or referred for surgical intervention. In Group II, patient

was asked to evacuate bladder and lie down. Rate, rhythm and intensity of fetal heart sound noted. Blood pressure, pulse, temperature and respiratory rate of patient were noted. Lithotomy position was made and parts cleaned and draped. Posterior vaginal wall was retracted with sims speculum. Anterior lip of cervix was held with sponge holding forceps and dinoprostone (Cerviprime) gel (0.5 mg) in a preloaded syringe with catheter was instilled into the cervical canal. The gel was deposited entirely into the cervical canal beginning at the internal os and gently withdrawing the catheter to the level of external os while continuously injecting the gel.

The foetal heart sound was heard immediately after the procedure and patient was asked to remain recumbent for about half an hour. Her blood pressure, pulse and respiratory rate were noted every 10 minutes. Foetal heart sound was auscultated every 10 minutes.

If the Bishop's score remained <7 after 6 hours, reapplication was done. When the score remained below 7 after 6 hours of second application and if there was failure to induce labour in 24 hours or evidence of maternal or fetal compromise then it was taken as a failure. Labour was augmented with oxytocin in patients with arrest of cervical dilatation due to poor contractions. Augmentation was delayed for 6 hours after administration of drug. Artificial rupture of the membrane was performed when clinically indicated. Once the subjects reached active phase of labour, the same intrapartum management guidelines were followed in each group. In all, cases of tachysystole (defined as at least six uterine contractions in 10 minutes for two consecutive 10 minutes periods) and fetal distress, were managed as follows: left lateral maternal repositioning, removal of tablets in Group I, oxygen administration via nasal catheter and 250 microg of subcutaneous terbutaline.

All patients were kept under continuous supervision and progress of labour was recorded on a partograph. Vaginal examination was done 4 hourly or earlier as required. Partograph of each patient was made and following things were noted: blood pressure, pulse and temperature of mother, concentration and rate of oxytocin drip, any drug given to mother throughout labour and intravenous fluids given, frequency and duration of uterine contractions, FHS ausculated every 30 minutes in 1st stage and every 15 minutes in 2nd stage of labour. Colour of liquor was noted in partograph as 'C' (clear) or 'M' (meconium stained). Rate of cervical dilatation, descent of head was noted, urine for albumin and sugar was tested and oxytocin drip was continued for 1 hour after delivery in all cases. Labour induction was considered successful if subjects delivered within 24 hours of initiation of either

Table 1. Time Taken for Initiation of Labour After Induction

Time for IOL (in hours)	Group I (n=50) No. (%)	Group II (n=50) No. (%)	Total (n=100) No. (%)
≤6	45 (90.00)	26 (52.00)	71 (71.00)
>6	5 (10.00)	24 (48.00)	29 (29.00)
Total	50 (100.00)	50 (100.00)	100 (100.00)
	$_{(1)}x^2$ = 17.53; p<0.001; Significant		

Table 2. Induction-Delivery Interval

Induction-delivery interval (in hours)	Group I (n=50) No. (%)	Group II (n=50) No. (%)	Total (n=100) No. (%)
<12	20 (40.00)	8 (16.00)	28 (20.00)
12-24	22 (44.00)	22 (44.00)	44 (44.00)
>24	0	7 (14.00)	7 (14.00)
Total	42 (84.00)	37 (74.00)	79 (79.00)
$_{(1)}x^2$ Yates corrected = 4.73; p=0.02; Significant; For the purpose of analysis, >24 hours category has been clubbed with 12-24 hours category			

Table 3. Outcome of Induction of Labour

Outcome	Group I (n=50) No. (%)	Group II (n=50) No. (%)	Total (n=100) No. (%)
Successful	42 (84.00)	30 (60.00)	72 (72.00)
Unsuccessful	8 (16.00)	20 (40.00)	28 (28.00)
Total	50 (100.00)	50 (100.00)	100 (100.00)
	$_{(1)}x^2$ = 7.14; p<0.007; Significant		

Table 4: Mode of Delivery

Mode of delivery	Group I (n=50) No. (%)	Group II (n=50) No. (%)	Total (n=100) No. (%)
Vaginal	42 (84.00)	37 (74.00)	79 (79.00)
LSCS	8 (16.00)	13 (26.00)	21 (21.00)
Total	50 (100.00)	50 (100.00)	100 (100.00)
	$_{(1)}x^2$ = 1.50; p=0.22; Not significant		

of two methods. The analyzed 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 where data was in number and percentages. The two tailed probability value (p < 0.05) was considered as statistically significant.

Results

A total of 100 patients in the age group of 18 to 35 years admitted for induction of labour were equally distributed in two groups - in Group I induction was administered with misoprostol vaginal tablets and in Group II induction was administered with dinoprostone intracervical gel (Cerviprime). Out of 100 patients, 60% belonged to age group of 21-25 years, followed by 27% in the 26-30 years and 9% in the age group of <20 years, while 4% of patients were in 31-35 years age group. Mean age was 22.53 years. Maximum inductions were done in age groups of 21-25 years both in Group I and Group II (60% each). In the study, 54% patients were nulliparas and 46% were multiparas. In Groups I and II, 48% and 60% respectively were nulliparas. Maximum

induction (52%) was done in term (37-40 weeks) patients, 39% at >40 weeks and 9 patients underwent induction of labour at 33-36 weeks of gestation. Groupwise, 56% and 48% patients underwent induction of labour in Group I and Group II respectively. Among 100 patients, the common indications for induction of labour were postdated pregnancy (39%), followed by preeclampsia (31%). In 14% patients, there were other indications like intrauterine growth retardation, polyhydramnios, isoimmunization, chronic hypertension, intrauterine death, congenital malformations. In Group I, 40% patients had indication of postdated pregnancy, 28% mild to moderate pregnancy induced hypertension, 16% PROM, 12% others and 4% oligohydramnios. In Group II, 38% patients had indication of postdate pregnancy, 34% preeclampsia, 16% others and 12% oligohydramnios. In Group I, Bishop score was <4 in 56% patients and between 4 and 6 in 44%. In Group II, the score was <4 in 40% patient and between 4 and 6 in 60% patients. Overall, Bishop score was <4 in 48% patients and between 4 and 6 in 52% patients. In both Groups, I and II, initiation of labour was

not initiated within 2 hours. In Group I, majority of patients (90%) had gone into labour within six hours, whereas in Group II, 52% had gone into labour within 6 hours. The difference of time taken in the two groups was statistically significant (p<0.001) (*Table 1*).

The mean induction delivery interval was 11.23 hours in Group I and 18.5 hours in Group II. In Group I, 40% of patients delivered within 12 hours, while 44% patients delivered within 12-24 hours. In Group II, 16% of patients delivered within 12 hours, whereas 44% patients delivered within 12-24 hours. In comparison to Group I, where no patient delivered after 24 hours, 14% of patients delivered vaginally after 24 hours in Group II. The difference of induction-delivery interval was statistically significant (p=0.02) (*Table 2*). Labour induction was considered successful if patients delivered vaginally within 24 hours. In Group I 84% and in Group II 60% patients had successful induction, the difference between the two groups being statistically significant (p=0.007) (*Table 3*).

In Group I, 84% patients had vaginal delivery, while LSCS rate was 16%. In Group II, 74% patients had vaginal delivery and LSCS rate was 26%. The difference in mode of delivery in two groups was statistically not significant (*Table 4*). All the patients in Group I reached active phase of labour without requiring oxytocin which was required by 62% of patients in Group II. Applying Fisher's exact test, the difference between the two groups was statistically significant (p<0.001). Indications for caesarean section in Group I was non-progress of labour in 4%, foetal distress in 8% and abnormal uterine action in 4%. In Group II, non-progress of labour was present in 8%, foetal distress in 4%, undiagnosed cephalopelvic disproportion in 4% and abnormal uterine action in 10% patients. In Group I and Group II, 10% and 8% respectively babies had Apgar score <7 at 1 minute and 2% and 4% had Apgar score <7 at 5 minutes. The difference of Apgar score in two Groups at 1 and 5 minutes was statistically not significant (p=0.55). Rate of tachysystole (>6 contraction/10 minutes) was higher in Group 1 (18%) as compared to Group II (6%). Also, fetal distress was higher in Group I (8%) as compared to Group II (4%). One (2%) patient in Group II had fever. However, rate of complications in both the groups were comparable (p=0.07).

Discussion

In the present study, maximum number of patients requiring induction was in the age group of 21-25 years (60%) which is comparable to that reported by Shivarudraiah and Palaksha (10). In the present study, nulliparas constituted 54% and multiparas 46%. Maximum inductions (52%) were done at gestational age of 37-40

weeks with mean period of gestation for induction of labour being 39.36 weeks which is comparable to studies by Shivarudraiah and Palaksha (10) (39.4 weeks) and Kulshreshtha *et al.* (11) (38.9 weeks). In our patients, maximum number of patients was induced for postdated pregnancy (39%), followed by preeclampsia (31%). 90% patients in Group I went into labour after induction within 6 hours as compared to 52% in Group II, the difference being statistically significant (<0.001). This shows that misoprostol has shorter induction to onset of labour interval as compared to Cerviprime. These results are quiet consistent with the study conducted by Kudagi *et al.* (1), Buser *et al.* (12), Nunes *et al.* (13), Belfrage *et al.* (14), Neiger and Greaves (15) and Rozenberg *et al.* (16).

Again, in the present study, induction-delivery interval was also shorter in misoprostol group with 40% patients delivering within 12 hours as compared to 16% in Cerviprime group. The difference between the two groups being statistically significant (p=0.02). The mean induction-delivery interval was 11.23 hours in Group I and 18.5 hours in Group II. This is comparable with the results of Nanda *et al.* (17) who reported mean induction-delivery interval of 13.3 hours in misoprostal group and 18.53 hours in dinoprostone group (p=0.01). Similarly, Leuva *et al.* (18) also reported mean induction-delivery interval of 12 hours in misoprostal group versus 16 hours in dinoprostone group (p<0.001). Successful outcome of induction of labour i.e. vaginal deliveries within 24 hours was found in 84% patients in Group I as compared to 60% patients in Group II. The difference being statistically significant (p=0.007). Gupta *et al.* (19) also reported that spontaneous vaginal deliveries were 86% in misoprostol group compared to 68% in dinoprostone gel, which is comparable to our study. Kudagi *et al.* (1) reported number of vaginal deliveries as 75% in misoprostol group compared to 60% in dinoprostone gel group.

Thus from the above results it is obvious that 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. In Group I, 84% patients had vaginal delivery, while LSCS rate was 16%. In Group II, 74% patients had vaginal delivery and LSCS rate was 26%. The difference in mode of delivery was statistically not significant. A difference of 10% in favour of misoprostol group although not statistically significant might have clinical importance in terms of patient's health and cost effectiveness. Kudagi *et al.* (1) also reported rates of caesarean sections less in misoprostol group (25% vs 40%) than dinoprostone gel group but statistically insignificant. Leuva *et al.* (18) also found that in both

misoprostol and dinoprostone groups, the majority of women had vaginal delivery, 92% vs 88%. There was no statistically significant difference between the two groups with regard to the cesarean section rate. In the present study, no patient required augmentation of labour in Group I as compared to 62% patients requiring augmentation in Group II, the difference being statistically significant (p<0.001). Kudagi *et al.* (1) found in their study that 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. Leuva *et al.* (18) also reported reduced need for oxytocin augmentation in labour with misoprostol 64% vs 84% with dinoprostone (p < 0.05), while Danielian *et al.* (20) mentioned 21% in the misoprostol group as compared to 47% in the dinoprostone gel group. In the above studies it is evident that vaginal misoprostol is more effective than dinoprostone and serves the dual purpose of cervical priming as well as inducing labour without the need for augmentation to oxytocin. In the present study, Apgar score (<7) in new born babies at 1 minute was found in 10% patients in Group I and 8% in Group II, while at 5 minutes it as found in 2% in Group I and 4% in Group II. The difference between the two groups was statistically not significant (p=0.55). Kudagi *et al.* (1) also reported no significant statistical difference in Apgar scores at 1 minute and 5 minutes between misoprostol and dinoprostone groups. Our result showed that rate of tachysystole was higher in Group 1 (18%) as compared to Group II (6%). Also, fetal distress was higher in Group I (8%) as compared to Group II (4%). One (2%) patient in Group II had fever. However, rate of complications in both the groups were comparable (p=0.07), similar to the study of Kudagi *et al.* (1). In the present study, although there is higher incidence of tachysystole in misoprostol group but this does not lead to increased fetal distress or lower Apgar scores in newly born babies.

Conclusion

Misoprostol an analogue of PGE1 appear to be perfect substitute for induction of labour. Its use was found to be associated with reduced time to delivery and high rate of vaginal delivery within 12 and 24 hours of induction. The requirement for oxytocin in augmentation was substantially reduced.

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