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Comparison of Prostaglandin E_1 (Misoprostol) with Prostaglandin E_2 (Dinoprostone) for Labor Induction

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OBJECTIVE – To evaluate the efficacy and safety of intravaginal misoprostol and intracervical dinoprostone for labor induction. **MATERIAL AND METHODS** – Fifty women needing induction of labor with singleton term pregnancy and cervix with Bishop score ≤ 5, were randomly assigned to receive intravaginal misoprostol or intracervical dinoprostone. The outcome variables were change in Bishop score, time from first application to active phase of labor and delivery, fetal and maternal morbidity and the incidence of cesarean deliveries. **RESULTS** – The interval from application of the initial dose to the beginning of the active phase of labor was 5.6 hours in misoprostol group and 6 hours in dinoprostone group and the interval from initial dose to delivery was 11.5 hours in misoprostol group and 13 hours in dinoprostone group. Delivery before 12 hours from the initial dose occurred in 16 cases in misoprostol group and in 8 cases in dinoprostone group ($P<0.02$). There were no significant differences in Bishop score change, cesarean delivery rate and the incidence of tachysystole, hypersystole and hyperstimulation. Apgar score < 7 was seen only in dinoprostone group. CS rate was more in the dinoprostone group than in the misoprostol group. **CONCLUSION** – Intravaginal misoprostol is safer, effective and less costly than intracervical dinoprostone gel for labor induction in low risk cases with unfavorable cervix.

Key words : induction of labor, misoprostol, dinoprostone

Introduction

Many maternal and fetal conditions exist in which there is a need to terminate pregnancy before the patient goes to spontaneous labor. When the induction of labor is necessary and the cervix is unripe, the obstetrician is faced with a management that frequently ends in cesarean delivery. A great amount of research has been directed in the last few years towards the development of effective cervical ripening agents which can induce labor also[1]. Induction of labor wih prostaglandins offers the advantage of promoting cervical ripening with stimulation of myometrial contractility.

The prostaglandin E_2 derivative dinoprostone is the only pharmacological agent approved by the FDA for cervical ripening and labor induction. This preparation is expensive, and its cost is further increased because many patients require two or more doses to achieve adequate cervical ripening. Recently a prostaglandin E_1 analogue, misoprostol has been approved by FDA to be taken orally for the prevention and treatment of gastric ulcers associated with the use of NSAIDS. It has also become an important drug in obstetric practice, because of its uterotonic and cervical ripening action[2] This medication has the advantages of being inexpensive, easy to store and stable at room temperaure. Numerous recent reports have been found that misoprostol safely and effectively ripens the cervix and induces labor in patients with unfavorable cervix[3].

The objective of the present study was to compare the safety and efficacy of misoprostol administered intravaginally with those of intracervical dinoprostone gel for cervical ripening and induction of labor.

Material and Methods

The present study was carried out from January to April 2002. The study population consisted of 50 pregnant women admitted for induction of labor. The indications for induction are shown in Table I. The inclusion criteria were singleton term pregnancy with vertex presentation, Bishop score of ≤ 5, intact membranes and a fetal heart rate (FHR) monitoring tracing considered reassuring. We excluded women with multiple pregnancy, parity of > 4, breech presentation, probable CPD, previous uterine scar, hypersensitivity to prostaglandins, vaginal bleeding in second half of pregnancy, asthma, renal or hepatic dysfunction, heart disease, non-reassuring FHR pattern and vaginal or cervical infection.

The study was approved by the hospital ethical committee and informed consent was obtained from all participants. A detailed history, general and obstetric examination and necessary investigations

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were carried out. The women were randomly allocated to group A (misoprostol group) and group B (dinoprostone group). In group A, 50 µg of misoprostol (i.e. one fourth of 200 µg tablet or one half of 100 µg tablet was kept in the posterior fornix of the vagina. The dose was repeated once after 6 hours if necessary. In group B, 0.5 mg of dinoprostone gel was inserted intracervically. If necessary a second dose was given after 6 hours.

In both the groups cervical ripening was assessed by the change in Bishop score after 6 hours and if there was no change, a second dose was given. Twelve hours after the initial dose, if there were less than two uterine contractions in 10 minutes or any protraction or arrest disorder occurred, oxytocin infusion was started. Throughout the procedure, FHR and maternal uterine contractions were monitored periodically.

The efficacy of the medication was evaluated by predetermined outcome variables for induction of labor and delivery. Cervical ripening was assessed by change in Bishop score after 6 hours of initial application. Labor induction was assessed by measuring the time interval from the initial dose to the beginning of the active phase of labor. The beginning of the active phase of labor was defined as the sudden increase in the slope of cervical dilatation that usually happens when the cervix reaches a dilatation of three to four cms. The time from initial application to delivery and the number of subjects that underwent vaginal delivery 12 and 24 hours after the first dose of medication were considered. Hypersystole was defined as one uterine contraction with a duration of > 90 seconds, tachysystole as > 5 contractions in 10 minutes for two consecutive 10 minute periods, and hyperstimulation as tachysystole associated with an abnormal FHR pattern. There was no specific protocol for artificial rupture of membranes, which was performed at the discretion of attending obstetricians.

Statistical analysis was done by Chi-square test as indicated.

Results

Among the 50 women who presented for labor induction during the study period, 24 were randomized to receive misoprostol and 25 to receive dinoprostone. The two groups were comparable in age, parity, gestational age and the indications for induction of labor (Table I). The initial median Bishop score was similar in both the groups. Bishop score after 6 hours was same in both the groups. Twenty-eight percent of the women in group A and 32% in group B required a second dose of medication. Maternal side effects associated with prostaglandin like nausea, vomiting, fever and diarrhea were not noted in any of the two groups. Ten women in group A and 16 in group B required oxytocin to reach active phase of labor. Table II and III compare the intrapartum course, complications, mode of delivery and neonatal outcome in each of the two groups.

The interval from initiation of induction to vaginal delivery and induction to delivery overall was shorter in group A than in group B (10.3 hours vs 13.1 hours and 11.5 hours vs 13 hours respectively). Successful induction was 100% in group A 92% in group B. More patients in the misoprostol group delivered vaginally within 12 hours of induction initiation than those receiving dinoprostone ($P < 0.02$). Hypersysto was seen in two cases of misoprostol and in one cas of dinoprostone. Tachysystole was seen in one case in each group. Hyperstimulation was seen in one case of dinoprostone group only. Cesarean delivery rate was higher in the dinoprostone group than in the misoprostol group (5 vs 2). Out of five cases needing cesarean section in the dinoprostone group, three needed it for fetal distress and other two for cervical dystocia. Both the cases in the misoprostol group needed cesarean section for cervical dystocia.

Table III shows the neonatal outcome in both the groups. Birthweights were similar in both the grou Apgar score < 7 was seen in three cases dinoprostone group out of which two had to b admitted to NICU. Apgar score <7 was not seen any case in misoprostol group. The mean overa induction cost in misoprostol group was Rs.22/-. In contrast, the mean overall induction cost in dinoprostone group was Rs. 265/-.

Table I : Demographic Characteristics of Patients

	Misoprostol group (n=25)	Dinoprostone group (n=25)
Age (years)	22.4	23.6
Gestational age (weeks)	40.14	40.0
Nulliparity	13	14
Indication for induction		
- Prolonged pregnancy	15	16
- PIH	6	5
- Rh -ve	2	3
- IUGR	2	1
Initial median Bishop's score	4	4

Table II : Intrapartum Variables

	Misoprostol Group	Dinoprostone Group	P Value
Interval from start to vaginal delivery (hours)[a]	10.3	13.1	0.1
Interval from start to delivery (hours) [a]	11.5	13	0.1
Induction to onset of active labor interval (hours) [a]	5.6	6	NS
Successful induction	100%	92%	NS
Vaginal delivery in < 12 hours	16	8	0.02
Vaginal delivery in < 24 hours	23	18	-
Need for oxytocin	10	16	NS

Values are mean.

Table III : Intrapartum Complication, Mode of Delivery and Neonatal Outcome

	Misoprostol group (n=25)	Dinoprostone group (n=25)
Complication		
Hypersystole	2	1
Tachysystole	1	1
Hyperstimulation	0	1
Mode of delivery		
Vaginal	22	16
Forceps	1	2
Cesarean	2	5
Mean birth weight (kg.)	3.0	2.9
Apgar score < 7		
1 minute	0	3
5 minute	0	2
Admission in NICU	0	2

Discussion

The present study shows that induction of labor with misoprostol was more effective than that with dinoprostone in respect to vaginal delivery within 12 hours and also within 24 hours. Studies by Sanchez-Ramos et al[4] and Nunes et al[5] and Busor et al[6] show the same results. In our study the incidence of cesarean section was more in dinoprostone than in misoprostol group (20% vs 8%). Nunes et al[5], show the same cesarean section rate in both the groups. Sanchez-Ramos et al[4]., had greater cesarean section rate in misoprostol group than in dinoprostone group (22.2% v/s 13.0%). Busor et al[6] also had a greater cesarean section rate in misoprostol group than in dinorpostone group (35.5% v/s 21.5%). Hyperstimulation and fetal distress were seen more in dinoprostone group than in misoprostol group in our study. Nunes et al[5] found abnormal pattern incidence to be more in dinoprostone group and Apgar < 7 to be more in misoprostol group. Sanchez Ramos et al[4] found greater incidence of fetal distress in misoprostol group than in dinoprostone group. Buser et al[6] showed that FHR abnormalities were greater in misoprostol group than in dinoprostone group.

We found that both misoprostol and dinoprostone were useful and safe for induction of labor in cases with unfavorable cervix. However, misoprostol offers the advantage of more rapid labor, lower cesarean section rate and less effect on fetal and neonatal outcome than those offered by dinoprostone. Misoprostol has an additional advantage of being cheaper for induction than dinoprostone (Rs.22/- vs Rs.265/-).

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