INDUCTION OF LABOUR WITH MISOPROSTOL - A PROSTAGLANDIN E₁ ANALOGUE

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ABSTRACT

The purpose of our study was to compare the safety and efficacy of intravaginal misoprostol versus existing hospital protocol of intracervical dinoprostone and oxytocin for cervical ripening and induction of labour. 200 patients with indication for induction of labour were randomly assigned to receive either intravaginal misoprostol or dinoprostone/oxytocin combination. In first group twenty five micrograms of misoprostol was placed intravaginally every 6 hours till the patient reached active stage of labour. In second group dinoprostone gel 0.5 mg was placed in the endocervix at night and oxytocin induction was started in the early morning. The average interval from start to induction of vaginal delivery was shorter in misoprostol group (1315±811 minutes) compared to dinoprostone/oxytocin group (1512±712 minutes) ($p < 0.01$). There was no significant difference in route of delivery. 18% of misoprostol treated patients and 23% of dinoprostone/oxytocin treated patients required Caesarean section. Complications such as uterine tachysystole were significantly higher in misoprostol group ($p < 0.01$) but it was not associated with increased incidence of uterine hyperstimulation. Perinatal outcome was similar in both groups.

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Introduction

Induction of labour is indicated frequently in modern obstetrics. But labour induction when performed in patients with unripe cervix is associated with a higher incidence of prolonged labour, instrumental delivery and caesarean delivery. To minimize these complications, a number of agents have been used to ripen the cervix before labour induction; this includes laminaria tents, oxytocin, prostaglandin and nitric oxide etc [1-4]. Labour induction with prostaglandins offers the advantage of promoting cervical ripening while stimulating myometrial contractility.

Misoprostol a prostaglandin E₁ analogue is one of the few drugs whose use has been taken up very enthusiastically by obstetricians. The most recent Medline database produced more than 200 publications using the subject heading 'pregnancy' and 'misoprostol'. This is more unusual as misoprostol was developed by Searl in 1973 for treatment of peptic ulcer and its effect on the pregnant uterus was considered a major side effect. However in due course of time, use of this drug for medical termination of pregnancy and induction of labour has over shadowed its therapeutic value in gastrointestinal diseases.

Labour induction with misoprostol is being investi-

gated intensely all over the world. There are various studies that report on its excellent efficacy, minimal side effects and cost saving benefits [5,6]. However dose schedules and methods of administration are yet to be standardized. Present study of 100 cases of induction of labour with intravaginal misoprostol and its comparison with induction of labour with intracervical PGE₂ gel and oxytocin is based against this background.

Material and Methods

The present study was conducted in INHS Asvini from Jan 99 to Jan 2000, criteria for enrolment included a) obstetric indications for labour induction including hypertensive disorders of pregnancy, intrauterine growth retardation of fetus (IUGR), post-datism. b) medical complications including diabetes and renal disease; c) no history of previous caesarean section or uterine surgery; d) absence of active labour or fetal distress; e) singleton pregnancy with vertex presentation and no contraindication for vaginal delivery.

Patients were randomly assigned to misoprostol group and dinoprostone/oxytocin group. Cervical ripeness (Bishop Score) was assessed before administration of drugs. Women allocated to misoprostol group were administered 25 micrograms of misoprostol in posterior fornix. The dose was repeated every six hours until adequate uterine contractions were achieved (at least three uterine contractions in 10 minutes, lasting for atleast 45 seconds). The patients in active phase of labour (cervical dilation 5 cm or more) with arrest of dilation (no change in cervical dilation for more than 2 hours) received oxytocin for augmentation.

Women randomized to dinoprostone/oxytocin group were ad-

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ministered standard INHS Asvini protocol consisting of dinoprostone gel and oxytocin. Dinoprostone gel 0.5 mg (cerviprime, Astra-IDL) was instilled intracervically at 8 PM. In absence of effective uterine contraction oxytocin was started in the morning at 0600 hrs. The starting dose of oxytocin was 2.5 miu/minute, the dose was doubled every 45 minutes until adequate uterine contractions were achieved. Once patients reached active phase of labour, same intra-partum guidelines were followed in each group. Labour induction was considered successful if participant delivered within 36 hours of initiation of misoprostol or dinoprostone/oxytocin. Uterine contractions pattern was monitored to assess the frequency of tachysystole or hyperstimulation syndrome. Tachysystole was defined as at least six contractions in 10 minutes for two consecutive 10 minute period. Hyperstimulation syndrome was defined as presence of tachysystole with fetal tachycardia. Recognized episodes of hyperstimulation were managed with left lateral maternal repositioning, oxygen administration by nasal catheter and subcutaneous terbutaline 250 micrograms.

Results

200 patients who met the criteria were enrolled in the study. The distribution of age, parity, gestational age, Bishop score was in two groups (Table-1). Similarly the indications for labour induction were similar in both groups (Table-2). All the patients in misoprostol group developed effective uterine contractions without requiring oxytocin. In this group oxytocin was required for secondary arrest or ineffective uterine contractions in 11 patients after commencement of active phase of labour. Sixty percent of the women in this group required no more than two doses. The maximum number of doses required to achieve active phase labour was five. Maternal side effects associated with prostaglandin use including nausea, vomiting, diarrhoea were not noted in the patients receiving misoprostol. Only 1 patient receiving dinoprostone gel had fever following instillation.

The mean induction/delivery interval (Table-3) was 1315 minutes in misoprostol group and 1512 minutes in dinoprostone/oxytocin group ($P < 0.01$). This group also had higher number of suc-

cessful vaginal delivery than dinoprostone/oxytocin group (82% and 77% respectively) though the difference is not statistically significant ($P > 0.05$). Caesarean section rate was almost similar in both the groups ($P > 0.05$).

TABLE 3

Intrapartum characteristics and mode of delivery

	Misoprostol group	Dinoprostone/oxytocin group	p value
Induction delivery interval (minutes)	1315 $\pm$ 812	1512 $\pm$ 712	< 0.01
Vaginal delivery within 12 hrs.	38	24	< 0.05
Vaginal delivery 13-24 hrs	36	46	> 0.05
Vaginal delivery 25-36 hrs.	08	07	> 0.05
Need for oxytocin	11	45	< 0.01
Total vaginal deliveries	82 (82%)	77 (77%)	> 0.05
Caesarean sections	18 (18%)	23 (23%)	> 0.05

Tachysystole (Table-4), occurred more frequently in misoprostol group (20%) compared to dinoprostone/oxytocin group (5%), ($p < 0.01$). No significant difference was found in incidence of hyperstimulation in two groups. Statistically no difference was noted in birth weights of the babies and Apgar scores at one minute and five minutes (Table-5). Admissions to NICU (neonatal intensive care unit) were similar in both groups.

TABLE 4

Intrapartum complications

	Misoprostol group	Dinoprostone/oxytocin group	p value
Tachysystole	20	5	< 0.01
Hyperstimulation	07	6	> 0.05
Use of tocolytics	02	Nil	> 0.05

TABLE 5

Neonatal outcome

	Misoprostol group	Dinoprostone/oxytocin group	p value
Birth weight (gm)	2700 $\pm$ 650	2715 $\pm$ 708	> 0.05
Apgar score < 7			
At 1 minute	12	8	> 0.05
At 5 minutes	3	2	
Admission to NICU*	7	6	> 0.05

NICU* - Neonatal intensive care unit.

Discussion

Induction of labour is a common practice in obstetrics and is often indicated for a variety of maternal and fetal conditions. Our study compared the induction of labour by misoprostol with existing labour induction

TABLE 1

Demographic characteristics of patients

	Misoprostol group (n=100)	Dinoprostone/oxytocin group (n=100)
Age	22 $\pm$ 5.8	22 $\pm$ 5.5
Gestational age (weeks)	39 $\pm$ 2.8	38.2 $\pm$ 2.5
Nulliparity	60	55
Multiparity	40	45
Bishop score 4 or less	30	35
Bishop score 5 or more	70	65

TABLE 2

Indication for labour induction

	Misoprostol group (n=100)	Dinoprostone/oxytocin group (n=100)
Post date	23	27
Hypertensive disorders	33	32
Gestational diabetes	05	03
Abnormal biophysical profile including oligohydramnios	13	15
Others	26	23

protocol (dinoprostone and oxytocin) in our hospital. The study confirms the effectiveness and safety of misoprostol for induction of labour as observed by other workers [4,5,6]. The efficacy and safety of dinoprostone gel has already been established by various studies [7,8]; no difference was noted in our study either.

Being a relatively new drug for induction of labour, the researchers used different doses of misoprostol, varying from 50 micrograms 3 hourly to 25 micrograms 4-6 hourly in an attempt to find out the optimum dose [9,10]. In a pilot study before carrying out the present study we used 50 micrograms of misoprostol intravaginally 3 hourly but this was associated with higher number of precipitate labour, therefore we decided in favor of lower doses (25 micrograms/6 hourly). Misoprostol may be used by oral or vaginal route [11], we used vaginal route keeping in mind the proven safety of the route, and also because the tablet can be removed from the vagina in case of uterine hyperstimulation.

In present study the use of misoprostol was associated with reduced induction delivery interval and high rate of vaginal delivery in first 12 hours. However if we take into account vaginal deliveries in first 24 hours, the rates were similar in both groups. These results were consistent with those obtained by Wing et al 1977 [12]. On the contrary Sanchez-Ramos et al in 1998 [9] reported much shorter induction delivery interval compared to our study. The explanation of this difference could be that we used lower doses of misoprostol (25 micrograms/6 hourly) in contrast to the dose of 50 micrograms/3 hourly used by the author.

Vaginal deliveries occurred more frequently in misoprostol group compared to dinoprostone/oxytocin group, similarly caesarean section rate was also lower in misoprostol group though the difference was not statistically significant. Meta-analysis of various trials has also shown decreased caesarean section rates in the patients who were induced with misoprostol [6]. However compared to overall caesarean section rate of 15% in our hospital, higher caesarean section rates were noted in both the groups selected for induction of labour in this study.

Tachysystole occurred more frequently in misoprostol group even with lower doses of drug used in this study. However the frequency was similar to other studies [7,9]. Higher incidence of tachysystole was not associated with a significant increase in the rate of uterine hyperstimulation. Furthermore, in most

of the patients hyperstimulation resolved spontaneously, only 2 patients required tocolysis with terbutalin. Adverse perinatal outcome occurred at similar rates in each treatment group. These rates were also similar to those reported with different labour inducing agents including oxytocin and prostaglandins E₂ [9,13].

It can therefore be concluded that misoprostol is an effective agent for induction of labour. The drug is easy to use, effective and safe to mother and the fetus. It has the potential to replace oxytocin and dinoprostone as an ideal agent for induction of labour.

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