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CLINICAL ARTICLE

Oral misoprostol versus intracervical prostaglandin E2 gel for active management of premature rupture of membranes at term

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ABSTRACT

Objective: To compare the efficacy and safety of oral misoprostol with intracervical prostaglandin E2 (PGE2) gel for the active management of premature rupture of membranes (PROM) at term. *Methods:* Women with pregnancies between 37 and 42 weeks presenting with PROM at term and a Bishop score of 5 or less were randomly assigned to receive either a 4-hourly oral dose of 50 μg of misoprostol up to a maximum of 3 doses or 2 applications of intracervical PGE2 gel at a 6-hour interval. Oxytocin was given if labor had not started after 12 hours. *Results:* Twenty women in the misoprostol group (n = 31) delivered within 12 hours compared with 5 in the PGE2 group (n = 30) ($P<0.001$). The induction-to-delivery interval in the misoprostol group was shorter than in the PGE2 gel group (615 min vs 1070 min; $P<0.001$). The mode of delivery was comparable between the 2 groups ($P=0.821$). Abnormalities in uterine contractions and neonatal outcomes were also comparable. The requirement for oxytocin was lower and patient satisfaction was better in the misoprostol group. *Conclusion:* Oral misoprostol is a safe and efficacious alternative to intracervical PGE2 gel in the active management of PROM at term.

1. Introduction

Premature rupture of membranes (PROM) is common, occurring in 8%–10% of pregnancies at term [1]. A prolonged interval from rupture of membranes to delivery is associated with an increase in the incidence of chorioamnionitis and neonatal sepsis [2,3]. The optimum management of PROM is controversial [4]. Options include expectant care or induction of labor. Several reports have detailed an increase in maternal and neonatal morbidity with expectant management [5], whereas active management leads to a shorter interval from PROM to delivery, reducing the risk of postnatal infections [6]. In addition, active management is preferred by patients [7].

Prostaglandin E2 (PGE2) gel can be used to ripen the unfavorable cervix, but it is costly, unstable at room temperature, and carries the risk of ascending infections. Misoprostol, in comparison, is cheap and stable, and simultaneously ripens the cervix and stimulates uterine contractions [8]. Misoprostol given orally for PROM has additional possible advantages compared with PGE2 gel. These include less chance of hyperstimulation and tachysystole [8]; fewer vaginal examinations; a lower risk of sepsis in mother and neonate; greater freedom of movement for the mother, which might facilitate the progress of labor; and potentially better efficacy because a vaginally administered drug could partly flow out with the draining fluid.

A meta-analysis has documented the safety and efficacy of oral misoprostol for induction of labor [8], but few reports have compared oral misoprostol with conventional intracervical PGE2 gel regimens. The aim of the present study was to compare the safety and efficacy of oral misoprostol with PGE2 gel in women with PROM at term and an unfavorable Bishop score.

2. Materials and methods

This prospective study was carried out at Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital, New Delhi, from March 2006 to April 2007. The institution's ethics committee approved the study and informed consent was obtained from the participants. Women with a live singleton fetus at term (37–42 weeks of gestation) in cephalic presentation and a reactive nonstress test (NST) presenting with PROM and a Bishop score of 5 or less before the onset of labor were included in the study. Women in active labor or with previous uterine surgery, antepartum hemorrhage, chorioamnionitis, contraindication to prostaglandin use (bronchial asthma, glaucoma), contraindication to vaginal delivery, or major fetal anomalies were excluded from the study.

A detailed history was taken for all patients followed by clinical examination, and details were recorded on a standardized pretested proforma. The duration of leakage and color of the fluid were noted. The lie, presentation, and position of the fetus were recorded. The amniotic fluid content and the estimated birth weight were assessed clinically. The frequency, duration, and intensity of uterine contractions were

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recorded. An aseptic speculum examination was performed to confirm that the membranes had ruptured by noting the presence of pooling of amniotic fluid in the vaginal vault. A high vaginal swab was taken. A sterile digital examination was then carried out in all patients to note cervical effacement, dilation, consistency, and cervical length. If the patient was not in labor, a Bishop score was calculated.

Participants were randomized into 2 groups using computer-generated random numbers. Concealment of allocation was ensured using opaque envelopes containing treatment cards. After randomization, patients and staff were aware of the group allocation.

Patients in group 1 received a 4-hourly oral dose of 50 μg of misoprostol (maximum of 3 doses) until optimal uterine contractions occurred. If active labor was not established after 12 hours, an intravenous dose of 2 mIU/min of oxytocin was started; this was increased in increments of 2 mIU every 30 minutes to establish an effective contraction pattern up to a maximum of 32 mIU/min. Patients in group 2 received an intracervical dose of 0.5 mg of PGE2 gel, which was repeated 6 hours later if labor had not started. An infusion of oxytocin was given at 12 hours if labor had still not started. The dose and increments for the infusion were same as in group 1.

A partogram was maintained for all subjects. Onset of labor was determined by either regular uterine contractions or progressive cervical dilatation. Active labor was determined by moderate uterine contractions (3 or more contractions in 10 minutes) or 4 cm or greater cervical dilatation. Any adverse events, including tachysystole, hypertonus, hyperstimulation syndrome, chorioamnionitis, and postpartum endometritis, were recorded. Before discharge from hospital women were requested to categorize their satisfaction with the labor experience into fully satisfied, partly satisfied, or not satisfied. Neonatal birth weight and Apgar score were recorded and the neonate was followed-up for complications until discharge.

The interval from the start of induction to vaginal delivery (ITD) was evaluated as the primary outcome variable. Secondary maternal outcomes included interval from induction to active labor (ITAL); interval from induction to full dilatation (ITFD); the duration of the 1st, 2nd, and 3rd stages of labor; mode of delivery; incidence of vaginal delivery within 24 hours of induction; operative vaginal delivery; cesarean delivery for fetal distress; dose of misoprostol used; use of oxytocin for augmentation; maternal infection; adverse effects; and maternal satisfaction. Secondary neonatal outcomes included Apgar scores; birth weight; meconium aspiration; ventilation; admission to the neonatal intensive care unit (NICU); culture proven sepsis; and other perinatal morbidity and mortality.

On the basis of previous reports (mean ITD interval 720 ± 240 minutes [9]), it was estimated that a sample size of 28 patients in each group would be required to detect a difference of 180 minutes between the 2 groups with 80% power and an α error of 0.05. Post-trial estimates showed that the study had 99.9% power for the difference observed in the study (455 minutes).

Data were analyzed using Epi Info (CDC, Atlanta, GA, USA) and SPSS version 13.0 (SPSS; Chicago, IL, USA). The 2 groups were compared using χ^2 and unpaired t test where applicable. Correlation and regression analysis were used where necessary.

3. Results

Sixty-one consecutive women presenting to the labor ward on scheduled days of the week were recruited to the study. The baseline characteristics of the 2 groups were comparable (Table 1). A comparison of the labor characteristics (Table 2) revealed that 20 of the 31 women (64.5%) in the misoprostol group had delivered within 12 hours compared with 5 of 30 (16.7%) women in the PGE2 group ($P<0.001$). The ITD interval in the misoprostol group was 10 hours 15 minutes compared with 17 hours 50 minutes in the PGE2 group resulting in a statistically significant, average difference of 7 hours 34 minutes ($P<0.001$). The duration of stage 1 of labor in the misoprostol group was significantly less than in the PGE2 group (8 hours 27 minutes vs 12 hours 47 minutes; $P=0.002$). The duration of the 2nd and 3rd stages of labor was comparable between the 2 groups.

In the misoprostol group, 5 (16.1%) women required oxytocin augmentation compared with 27 (90%) in the PGE2 group ($P<0.001$). The mean maximum dose of oxytocin used was also significantly lower in the misoprostol group compared with the PGE2 gel group (3.42 vs 30.87 mIU/min; $P<0.001$). The neonatal outcomes in the misoprostol and PGE2 groups were comparable, including the birth weight (2.84 vs 2.89 kg; $P=0.597$), Apgar scores, resuscitation requirement at delivery (1 case in each group), admission to the NICU (1 vs 2; $P=0.534$), meconium aspiration syndrome (0 vs 1; $P=0.492$), or phototherapy (0 vs 2; $P=0.238$). A significantly higher proportion of women in the misoprostol group compared with the PGE2 gel group were completely satisfied with the method used (71.0% vs 43.3%; $P=0.020$).

There was no significant difference in the mode of delivery between the 2 groups ($P=0.821$). Twenty-seven of 31 women (87.1%) in the misoprostol group and 25 of 30 women (83.3%) in the PGE2 group had a normal vaginal delivery (Table 2). Two women in the PGE2 gel group had an operative vaginal delivery by vacuum extraction, and 1 woman in the misoprostol group required an outlet forceps delivery. Three women in each of the 2 groups underwent a cesarean delivery. The indications for cesarean delivery in the misoprostol group were 1 patient with meconium-stained fluid with unfavorable cervix, 1 patient with meconium-stained fluid with fetal heart rate abnormalities, and 1 patient with deep transverse arrest. In the PGE2 gel group, the indications for cesarean delivery were failed induction in 1 patient and nonprogress of labor in 2 patients. Both groups were comparable with regard to the occurrence of abnormal uterine contractions (1 case of hypertonus in the misoprostol group, and 1 case of tachysystole in the PGE2 group). There were 2 cases of passage of intrapartum meconium in each group. One patient in the PGE2 group developed high grade fever, and tachycardia with purulent vaginal discharge several hours after the second dose of PGE2; this patient was diagnosed with chorioamnionitis. There were no similar cases in the misoprostol group. Three patients had primary

Table 1
Baseline characteristics of the participants[a].

Characteristics	Total study (n = 61)	Misoprostol (n = 31)	Prostaglandin E2 (n = 30)	*P* value
Maternal age, y	24.97 ± 3.17	25.29 ± 2.99	24.63 ± 3.36	0.423
Gravidity	1.80 ± 1.04	1.90 ± 1.01	1.70 ± 1.08	0.453
Parity	0.57 ± 0.84	0.74 ± 0.89	0.40 ± 0.77	0.115
Primigravida	62.3	51.6	73.3	0.305
Pregnancy, completed weeks	38.59 ± 1.30	38.55 ± 1.15	38.63 ± 1.47	0.802
Body mass index	25.33 ± 1.9	25.09 ± 1.84	25.57 ± 1.99	0.337
Systolic blood pressure, mm Hg	123.4 ± 11.6	125.94 ± 13.14	120.87 ± 9.40	0.089
Diastolic blood pressure, mm Hg	79.05 ± 7.6	80.52 ± 6.90	77.53 ± 8.23	0.130
Hemoglobin, g/dL	10.3 ± 1.5	10.36 ± 1.54	10.26 ± 1.54	0.799
Leaking to recruitment, min	594 ± 633	492 ± 370	699 ± 815	0.203

[a]Values are given as mean ± SD or percentage.