

The efficacy of dinoprostone vaginal insert for active management of premature rupture of membranes at term: a randomized controlled trial

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Summary

Purpose: To evaluate the efficacy and safety of the vaginal insertion of dinoprostone in terms of achieving cervical ripening, shortening the length of labor, and lowering the cesarean delivery rate for term pregnancies complicated with premature rupture of membranes. **Methods:** A prospective, randomized, controlled trial enrolled 100 women with term pregnancies complicated with premature rupture of membranes. Each had a normal non stress test, unscarred uterus, a singleton pregnancy with cephalic presentation, and a Bishop score of less than 4. Patients were randomized to receive a 10 mg dinoprostone vaginal insert single dose or no medication. After cervical ripening, oxytocin induction was performed during labor for both the study and control group. Cervical ripening in the 12th hour, total delivery time and delivery mode were compared between the two groups. **Results:** More often cervical ripening was obtained in the study group women who used dinoprostone vaginal inserts compared to the control group ($p: 0.001$). Latent phase of labor and total delivery time was shorter in the study group women than the control group ($p: 0.022$ and $p: 0.026$). There was no difference in terms of delivery mode and indication of section between study and control groups. **Conclusion:** The use of dinoprostone vaginal inserts in patients with term pregnancy of premature rupture of membranes reduced both the latent phase of labor and total delivery time without increasing the rate of cesarean section.

Key words: Premature rupture of membranes; Dinoprostone vaginal insert; Cervical ripening; Labor induction.

Introduction

Premature rupture of membranes (PROM) is defined as rupture of membranes that occurs at term before the onset of labor. It occurs in 8-10% of pregnancies. The most significant risk of PROM is intrauterine infection, which increases with duration of rupture. The optimum management of term pregnancies with PROM and an unfavorable cervix is controversial. Management options are induction of labor or expectant care. Several reports showed that expectant management increased maternal and neonatal morbidity [1, 2]. Active management yields to a shorter interval from PROM to delivery, reducing the risk of maternal and neonatal infection, without changing the rate of cesarean delivery [1].

The dinoprostone vaginal insert has been shown to be safe and efficacious in promoting cervical ripening in women with term pregnancies and low Bishop scores. However, data related to the efficacy and safety of dinoprostone in term pregnancies complicated with PROM are scarce.

Therefore, the purpose of the study was to compare the efficacy and safety of vaginal insertion of dinoprostone and expectant management in terms of achieving cervical ripening, shortening the length of labor, and lowering the cesarean delivery rate in term pregnancies complicated with PROM.

Material and Methods

This prospective randomized controlled study was carried out at Izmir Ataturk Training and Research Hospital, 1st Gynecology and Obstetrics Department, from May 2009 to December 2009.

Women with prelabor rupture of amniotic membranes with the clinical decision to induce labor were asked to participate. The inclusion criteria were: a live singleton fetus at term (37-42 weeks of gestation), cephalic presentation, a reactive non stress test (NST), presenting with PROM and Bishop score of 4 or less. Women in active labor or with abnormal fetal heart rate, malpresentation, estimated fetal weight above 4,500 g, multiple pregnancies, cephalopelvic disproportion, more than four previous term pregnancies, with previous uterine surgery, antepartum hemorrhage, chorioamnionitis, and contraindication to prostaglandin use (bronchial asthma, glaucoma) were excluded from the study.

A detailed history was taken for all women followed. A dry aseptic speculum examination was performed to confirm that the membranes had ruptured. Then a sterile digital examination was carried out and Bishop score was calculated.

Randomization sequence was generated by a computerized random number generator in blocks of 8 and prepared by an investigator. The treatment allocation was placed into numbered, sealed envelopes each of which contained a piece of paper bearing the legend 'dinoprostone pessary' or 'no treatment'.

The dinoprostone vaginal insert is a preparation of PGE₂ packaged in a hydrogel polymer matrix and designed for intravaginal release of 10 mg of dinoprostone at a rate of 0.3 mg/h over 12 hours. It was inserted into the posterior fornix of the study group women. The control women were followed spontaneously until effective uterine contractions began. Continuous cardiotocogram monitoring was maintained throughout the induction and labor. After cervical ripening was provided, oxy-

tocin infusion was started for both the study and control group women. The dinoprostone pessary was removed after a maximum of 12 hours. In the event of uterine hyperstimulation or a non reassuring cardiotocogram, cervical ripening or effective uterine contraction was achieved, the pessary was removed earlier.

Hyperstimulation was defined as more than five contractions per ten minutes or a contraction lasting at least two minutes. Cervical ripening was defined as Bishop score more than 9. Oxytocin infusion (5 mU oxytocin in 500 ml of Ringer's lactate solution) was started at a rate of 2 mU/min and increased by 2 mU/min every 20 minutes. The contractions were considered effective if they reached a frequency of four per ten minutes for two consecutive 10-minute periods; the oxytocin dose was not increased further.

Antibiotic prophylaxis against Group B streptococcal infection was routinely administered in case PROM lasted for 18 hours or more; 2 g of ampicillin IV was started as a standard prophylactic regimen followed by 1 g ampicillin IV every four hours until delivery.

Primary outcomes were the duration of latent and active phase of labor and total delivery time, and the rate of cervical ripening at the 12th hour. The length of the latent phase was defined as the lapse of time to cervical dilatation reaching 4 cm. The length of the active phase was defined as the lapse of time from cervical dilatation equal to 4 cm to complete dilatation. Total delivery time was defined as the time from beginning the enrolment to delivery.

Statistical analysis was carried out using SPSS 11.0 for Windows (SPSS Inc, Chicago, IL, USA) statistical software. Categorical variables were described using frequency distribution and compared by chi-square and Fisher's exact test. For continuous variables, descriptive statistics were calculated and reported as mean \pm standard deviation. The Student's t-test was used to compare mean scores of continued variables between the two groups; $p < 0.05$ was accepted as the level of significance.

Results

One hundred women were randomly assigned: 50 to dinoprostone pessary and 50 to expectant management. There was no significant difference between the study and control group women in terms of age, gestational age, body mass index, Bishop score, and the rate of multigravida. There was no distinction between study and control groups in terms of the duration from PROM to admission. The dinoprostone pessary was removed before the 12th hour in 31 women, one of whom showed deceleration at cardiotocogram and four of whom had hyperstimulation. The other reasons for earlier removal were achievement of effective uterine contractions in seven women and cervical ripening in 19 women. In women where the pessary was removed before the 12th hour, the pessary stayed in the vagina an average of 6.68 hours (range 1-11 hours). There was no difference between the groups in terms of uterine hyperstimulation.

There were no significant differences in mean birth weight, the rate of Apgar score at 5 min and the route of delivery.

Cesarean section was performed in three women of the study group. In two of these, hyperstimulation and fetal

Table 1. — Comparison of the study and control group patients.

		Study group (Dinoprostone)	Control group (No medication)	<i>p</i> value
		Mean \pm SD	Mean \pm SD	
Age		28.16 \pm 4.36	25.56 \pm 5.50	0.052
Gestational age		38.71 \pm 1.49	38.52 \pm 1.34	0.987
Body mass index		28.14 \pm 2.95	27.38 \pm 2.49	0.216
		Number (percent)	Number (percent)	
Multigravida		5 (10%)	6 (12%)	0.706
Bishop score	1	19 (38%)	18 (36%)	0.580
	2	19 (38%)	24 (48%)	
	3	12 (24%)	8 (16%)	
Deceleration				
in cardiotocogram		5 (10%)	4 (8%)	0.679
Hyperstimulation		4 (8%)	3 (6%)	0.568
Cervical ripening				
at the 12 th hour		47 (94%)	29 (58%)	0.001
Cesarean section		3 (6%)	1 (2%)	0.365
		Mean \pm SD	Mean \pm SD	
Duration of PROM		5.10 \pm 3.33	4.83 \pm 3.13	0.709
Apgar score		9.00 \pm 0.85	9.14 \pm 0.70	0.425
Birth weight		3118.39 \pm 363.12	3172.00 \pm 392.25	0.540
Latent phase of labor		9.37 \pm 2.96	11.10 \pm 5.71	0.022
Active phase of labor		5.22 \pm 1.69	5.52 \pm 2.03	0.499
Total delivery time		14.72 \pm 3.94	16.82 \pm 6.89	0.026

distress developed within the first hour after the pessary insertion, and then one woman underwent cesarean section. The other women who developed hyperstimulation responded rapidly to removal of the pessary or stopping of the infusion. In one case of the control group, progress of labor arrested at 6-cm cervical dilatation. A healthy 3,900 g neonate was delivered by cesarean section. There were no women with intrapartum chorioamnionitis or postpartum endometritis. There were no maternal or neonatal adverse outcomes in either group.

More often cervical ripening was obtained in the study group women who used dinoprostone vaginal inserts than the control group. Latent phase of labor and total delivery time were shorter in study group women than controls.

Discussion

When rupture of fetal membranes occurs before the onset of labor, most cases go into labor spontaneously within 24 hours. Expectant management of term pregnancies with PROM and an unfavorable cervix could increase adverse events related to infection. Early induction of labor could shorten the delivery time and thus reduce the risk of maternal and fetal morbidity related to infection in term pregnancies complicated with PROM and low Bishop scores [2].

Previous studies showed that PGE₂ is effective for the total delivery time to shorten labor in term pregnancies complicated with PROM. It improves success rates and reduces morbidity associated with labor induction [3]. Induction of labor with a PGE₂ insert was also demonstrated to be successful in women with post-term pregnancies, without any serious complications. However the rate of cesarean section was increased [4].

Some studies have investigated the efficacy and safety of vaginal PGE₂ inserts in term pregnancies complicated with PROM and low Bishop scores [5, 6]. In a multicenter study, 100 pregnancies with PROM and unfavorable cervixes were compared to 180 pregnancies with intact membranes. All patients were treated with dinoprostone vaginal inserts [5]. The rate of labor within 24 hours in the PROM group was higher than in the intact membrane group. The rates of cesarean section, tachysystole or neonatal asphyxia did not differ in either group. In the term pregnancies not only with intact membranes but also with PROM, dinoprostone vaginal inserts were safe and efficient for cervical ripening and induction of labor.

Studies comparing PGE₂ vaginal inserts with oxytocin for labor induction in pregnancies with PROM reported that oxytocin induction yielded a shorter latent phase of labor and total delivery time, while the rate of cesarean section remained unchanged [6].

In a retrospective cohort study, Park *et al.* compared use of dinoprostone and oxytocin for labor induction in term pregnancies with PROM and with intact membranes and unfavorable cervixes in nulliparous women. They found that labor induction for PROM in term nulliparous women with an unfavorable cervix was associated with longer mean duration of second stage and a higher risk of cesarean delivery for failure to progress than those with intact membranes [7].

Concurrent oxytocin and prostaglandin for labor induction have been used both in pregnancies with PROM and pregnancies with intact membranes. When comparing concurrent oxytocin and dinoprostone pessary versus dinoprostone pessary in labor induction of nulliparas with an unfavorable cervix, cesarean rate did not differ [8]. When a similar trial was done in women with PROM, no distinction was found in vaginal delivery and hyperstimulation rate between concurrent oxytocin and dinoprostone pessary versus dinoprostone pessary in labor induction of pregnancies with PROM [9].

In their retrospective non-randomized study, Larrañaga-Azcárate *et al.* compared dinoprostone and expectant management of women with a single pregnancy at term, PROM, and Bishop test < 4. They had started oxytocin at the 12th hour after PROM. The duration from dilatation to labor was shorter and the rate of cesarean section was lower in the dinoprostone group than expectant management group [10]. Our study was planned as randomized and prospective. Oxytocin infusion was started when cervical ripening was provided. Hence, the rate of hyperstimulation was lower than concurrent use of dinoprostone and oxytocin treatment. Not performing power analysis was the limitation of this study.

Conclusion

Vaginal dinoprostone inserts following oxytocin infusion to induce labor in term PROM decreased the latent phase of labor and total delivery time without increasing cesarean rate compared with expectant management following oxytocin infusion.

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