Vaginal misoprostol in managing premature rupture of membranes

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المعالجة بالميزوبروستول عن طريق المهبل في التدبير العلاجي للتمزُّق الباكر للأغشية

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الخلاصة: تُقارن هذه الدراسة بين نجاعة الميزوبروستول ونجاعة البروستاغلاندين E_2 في إنضاج عنق الرحم وتحريض المخاض لدى المصابات بالتمزُّق الباكر للأغشية قبل الأسبوع السادس والثلاثين من الحمل. فقد تم توزيع 238 حاملاً من المصابات بالتمزُّق الباكر للأغشية قبل الأسبوع السادس والثلاثين من حملهن توزيعاً عشوائياً بحيث يتلقى بعضهن 50 ميكروغراماً من الميزوبروستول على شكل هلامة مهبلية، في حين يتلقى بعضهن الآخر 5 ميلي غرام من هلامة البروستاغلاندين E_2. وقد تم تقييم أحراز بيشوب قبل تطبيق المعالجة وبعدها بست ساعات وتسجيل المعطيات السريرية والنتائج في الفترة المحيطة بالولادة. وقد لوحظ أن كلاً من متوسط الفترة من بدء التحريض وحتى الولادة والحاجة للمعالجة بالأوكسيتوسين كانتا أقل بشكل يُعتدُّ به إحصائياً لدى المجموعة التي عولجت بالميزوبروستول. ولم تكن هناك أية فروق هامة في سرعة المخاض العفوي ونمط الولادة والنتائج في الفترة المحيطة بالولادة. وقد استنتج أن المعالجة بالميزوبروستول عن طريق المهبل مأمونة وأكثر فعالية من المعالجة بالبروستاغلاندين E_2 في تحريض إنضاج عنق الرحم في التدبير العلاجي للتمزُّق الباكر للأغشية بعد الأسبوع السادس والثلاثين من الحمل.

ABSTRACT We compared the efficacy of misoprostol with that of prostaglandin E_2 in cervical ripening and labour induction. Thus 238 women with rupture of membranes beyond 36 weeks gestation without labour were randomized to receive 50 μg misoprostol vaginal gel or 5 mg of prostaglandin E_2 gel. Bishop score was evaluated before drug application and 6 hours later. Clinical data and perinatal outcome were recorded. Mean time from induction to delivery and the need for oxytocin were significantly less in the misoprostol group. There were no significant differences in spontaneous labour rate, type of delivery and perinatal outcome. It is concluded that intravaginal misoprostol is safe and more effective than prostaglandin E_2 for preinduction cervical ripening in premature rupture of membranes beyond 36 weeks gestation.

Le misoprostol vaginal dans la prise en charge de la rupture prématurée des membranes
RESUME La présente étude compare l'efficacité du misoprostol et de la prostaglandine E_2 dans la maturation du col utérin et l'induction du travail chez des femmes ayant une rupture prématurée des membranes après 36 semaines de grossesse. Deux cent trente-huit femmes ayant une rupture des membranes après 36 semaines de grossesse sans travail ont été randomisées pour recevoir 50 μg de gel de misoprostol vaginal ou 5 mg de gel de prostaglandine E_2. Le score de Bishop a été évalué avant l'application du gel et six heures plus tard. Les données cliniques et l'issue périnatale ont également été consignées. Le temps moyen entre l'induction et l'accouchement et le besoin d'ocytocine étaient significativement moindres dans le groupe des patientes ayant reçu du misoprostol. Il n'y avait pas de différence significative en ce qui concerne le taux d'accouchement spontané, le type d'accouchement et l'issue périnatale. On conclut que le misoprostol intravaginal est sûr et plus efficace que la prostaglandine E_2 pour maturer le col avant l'induction standard en cas de rupture prématurée des membranes après 36 semaines de grossesse.

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Introduction

Spontaneous rupture of membranes beyond 36 weeks gestation occurs in about 10% of pregnant women. Many studies have compared the use of expectant management with active labour induction for treatment of this condition [*1–3*].

In these cases induction of labour was suggested because of the increased incidence of maternal and neonatal infections with an increasing interval between membrane rupture and delivery [*4*]. The incidence of chorioamnionitis and neonatal sepsis is increased when premature rupture of membranes (PROM) is present more than 24 hours before delivery than when delivery occurs within 24 hours. For such reasons the accepted management of such patients has been induction of labour [*5*].

More recently the use of prostaglandins and prostaglandin analogues has been advocated for cervical ripening and induction of labour in patients with PROM. The two prostaglandin analogues receiving the most popular attention are vaginal misoprostol and intracervically administered prostaglandin E2 analogues. Misoprostol, a synthetic prostaglandin E1 (PGE1) analogue; has continued to gain favour as a cervical ripening and labour induction agent [*6–11*]. Advantages of misoprostol include effectiveness, low cost and ease of administration because it is given intravaginally rather than in the endocervix.

Prostaglandin E2 (PGE2) used as intravaginal gel preparations (0.5 mg of PGE2 mixed with methylcellulose) has been the preferred cervical agent because of its local tissue absorption with excellent efficacy and minimal side effects [*12–14*].

This investigation was undertaken to compare vaginally administered misoprostol with intravaginal PGE2 gel for cervical ripening and labour induction in women with PROM beyond 36 weeks gestation.

Methods

From February 1999 to February 2000, women meeting the eligibility criteria were offered entry into this randomized trial of labour induction. Eligibility criteria were singleton pregnancy at > 36 weeks with PROM of less than 24 hours duration, Bishop score < 8, vertex presentation and fewer than 12 contractions per hour. Exclusion criteria were prior caesarean delivery, parity > 5 and nonreassuring fetal monitoring (i.e. fetal bradycardia or tachycardia). Informed consent was obtained from all the participants.

After randomization, Bishop score was determined at the start and 6 hours after drug administration. Fetal head at the start was at –3 station. Patients were given intravaginal misoprostol 50 μg inserted into the posterior fornix of the vagina (group 1). Group 2 were given 0.5 mg of pharmacy-prepared PGE2 gel applied in the endocervix.

Induction started a minimum of 6 hours after the spontaneous rupture of membranes in the absence of adequate uterine contractions (> 3 contractions in a 10-minute window of observation). Women had continuous fetal and uterine monitoring. Oxytocin was started if the patient was not in adequate labour 6 hours after the drug application in each group, and was administered according to our protocol; dosing started at 1 mU/min and increased by 1 to 2 mU/min every 15 minutes if contractions were not adequate, to a maximum of 22 mU/min.

Study outcomes were caesarean delivery, induction to delivery time, hyperstimulation syndrome and fetal distress requiring

delivery. Hyperstimulation syndrome was defined as tachysystole with fetal bradycardia or abnormal fetal heart rate requiring treatment. Tachysystole was defined as > 6 contractions in a 10 minute period for at least 10 minutes in a row.

Results

There were 238 patients randomly assigned to receive either misoprostol (n = 118) or PGE2 (n = 120). There was no difference in maternal age, parity, gestational age and preinduction Bishop score between the two groups.

Misoprostol was associated with a significantly shorter time from the start of induction to delivery (14.2 ± 6.4 hours for group 1 compared with 20.5 ± 10.2 hours for group 2; P = 0.005) and with significantly fewer women requiring oxytocin than with PGE2 use (47% compared with 70%) Table 1. The maximum dose of oxytocin used was significantly lower in the misoprostol group than in the PGE2 group.

Caesarean delivery rate and operative delivery rate (forceps and vacuum) were not significantly different in the groups (Table 2) [*13*].

Regarding the complication rates, misoprostol was associated with a significantly more frequent occurrence of tachysystole but not hyperstimulation syndrome (Table 3) [*15*]. Neonatal admissions to intensive care nursing were similar in the two treatment groups (Table 4).

Discussion

There was a significant difference in the mean time interval from start of induction to delivery in women with PROM beyond 36 weeks of gestation in the two groups The use of misoprostol was associated with achieving delivery more quickly and with less need for oxytocin.[*2–7*]

Table 1 **Labour characteristics of the women**

Characteristic	Misoprostol (n = 118)	PGE2 (n = 120)	Statistical significance
Induction to delivery time (hours)	14.2 ± 6.4	20.5 ± 10.2	P = 0.0005
Oxytocin use, No. (%)	55 (47%)	84 (70%)	χ^2 = 13.4, P = 0.002

Table 2 **Rates of caesarean and operative deliveries**

Type of delivery	Misoprostol (n = 118)	PGE2 (n = 120)	Statistical significance
Caesarean	33 (28%)	21 (18%)	χ^2 = 3.72, P = 0.054
Operative	19 (16%)	12 (10%)	χ^2 = 1.96, P = 0.162

Table 3 Intrapartum complications

Complication	Misoprostol	PGE2	Statistical significance
Tachysystole	34 (29%)	9 (8%)	$\chi^2 = 18.26$, $P = 0.0002$
Hyperstimulation	5 (4%)	1 (1%)	FET = 0.12

FET= Fisher exact test.

Table 4 Neonatal outcomes and neonatal intensive care unit (NICU) admissions

Outcome	Misoprostol	PGE2	Statistical significance
Birth weight (g)	3200 ± 536	3150 ± 590	$t = 0.68$, $P = 0.49$
Apgar score < 7	10 (9%)	10 (8%)	$\chi^2 = 0.01$, $P = 0.94$
Neonatal resuscitation	22 (19%)	25 (21%)	$\chi^2 = 0.24$, $P = 0.63$
Admission to NICU	24 (20%)	30 (25%)	$\chi^2 = 0.74$, $P = 0.39$

Table 5 Primigravid outcomes

Outcome	Misoprostol ($n = 78$)	PGE2 ($n = 74$)	Statistical significance
Caesarean delivery	23 (30%)	31 (42%)	$\chi^2 = 2.55$, $P = 0.11$
Operative delivery	16 (20%)	11 (15%)	$\chi^2 = 0.83$, $P = 0.36$
Oxytocin use	31 (40%)	59 (80%)	$\chi^2 = 25.14$, $P < 0.01$
Induction to delivery (hours)	16 ± 6.5	24 ± 9	$t = 6.306$, $P < 0.01$

There was no significant difference in the percentage of women having successful induction, defined as vaginal delivery within 24 hours after initiation of induction in the two groups.

When primigravid women were evaluated separately, there was a significantly shorter time to delivery and less need for oxytocin augmentation in the misoprostol group than the PGE2 group (Table 5). There was also a significantly greater change in the median Bishop score in the primigravid women receiving misoprostol.

Unfortunately, the caesarean section rate (22%) was not significantly reduced in the misoprostol group. The majority of caesarean sections in the misoprostol group were performed for labour dystocia,

rather than in the PGE2 group, where failed induction was the main indication for caesarean section. This indicates that misoprostol is more effective than PGE2 in bringing about cervical dilatation and effacement and inducing labour in patients with PROM.

This study shows an increased frequency of fetal tachysystole, but in spite of this there was no measurable compromise of neonatal well-being [*15*]. Neonatal outcomes were similar in both groups. No significant differences existed for mean birth weight, Apgar score, requirement for neonatal resuscitation and admission to neonatal intensive care unit. Most of the admissions to the neonatal intensive care unit were for suspected sepsis.

Maternal side-effects in both groups, including nausea and vomiting, were uncommon: one misoprostol patient had nausea (1%) and one had vomiting (1%). Nausea and vomiting were not noted in the PGE2 group. There were no reports of diarrhoea or fever in either group.

This study shows that misoprostol is more effective for labour induction than PGE2 [*16–18*]. Nearly every measure of adequacy of labour induction was significantly better with misoprostol, including time from induction to delivery and lack of necessity for oxytocin; these findings are similar to those reported in other publications [*2–7*].

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