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Induction of labour with a viable infant: a randomised clinical trial comparing intravaginal misoprostol and intravaginal dinoprostone

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Objective To compare the efficacy and safety of vaginal misoprostol (50μg) with vaginal dinoprostone.

Design Double-blind randomised trial.

Setting Obstetrics Department, Poissy Hospital, France.

Participants 370 patients with medical indications for induction of labour.

Outcome measures Vaginal deliveries within 24 hours, as well as time to vaginal deliveries, caesarean rates, costs, and fetal, neonatal and maternal condition.

Results Compared with vaginal dinoprostone, vaginal misoprostol resulted in greater efficacy in several areas: vaginal delivery within 24 hours; time to vaginal delivery; and vaginal delivery within 12 hours. There was a non-significant increase in the caesarean section rate for fetal distress in the misoprostol group, but fewer caesarean sections for failed induction. Fetal tolerance was similar in the two groups, although significantly more neonates had a cord pH <7.20 and (non-significantly) none had meconium stained amniotic fluid in the misoprostol group. The incidence of poor neonatal outcome was similar in both groups. Subgroup analysis by indication for induction showed that the higher rates of arterial cord pH <7.20 and of meconium-stained amniotic fluid with misoprostol persisted only in possible fetal compromise. Poor neonatal outcome was less frequent in the misoprostol group in cases of induction for non-fetal indications.

Conclusions Vaginal misoprostol resulted in successful and earlier induction of labour more often than dinoprostone, but the safety of misoprostol raises some concern in potentially compromised infants. Misoprostol should be preferred to dinoprostone in cases of induction for non-fetal indications.

INTRODUCTION

Induction of labour has several medical indications, including pregnancy-related hypertension, diabetes, intrauterine growth restriction, premature rupture of membranes after 34 weeks, and post-term pregnancies[1]. A national survey on obstetric practices in France has shown that induction for medical reasons accounted for up to 16.8%[2] of all deliveries. Intravenous oxytocin has been widely used for this purpose for many years. Nonetheless, if the cervix is unripe, cervical dystocia may occur and induction thereby fails[3]. The need for ripening agents before labour is induced is now generally accepted[4].

A meta-analysis[5] assessing the use of prostaglandins E_2 to induce labour concluded that the Bishop score increased rapidly among women who received prostaglandins vaginally. These women also underwent fewer failures of induction and fewer caesareans sections than women who received either a placebo or no treatment. Dinoprostone is currently the only prostaglandin approved for induction of labour with an unripe cervix, but is expensive (approximately £32.5–£42 per dose in France).

Misoprostol is a prostaglandin E_1 analog approved for protection of the gastric mucosa. It has also oxytocic effects that can induce labour. Its main advantages over dinoprostone include its low cost (roughly £0.10 per dose in France) and easier storage. Several randomised trials have demonstrated that misoprostol is either better than[6–15] or equivalent to[16–19] prostaglandin E_2 to induce labour. Neonatal tolerance appears to be similar with both drugs[6–19].

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Nonetheless, these randomised trials often included methodological inadequacies. Fourteen randomised trials have compared these two prostaglandins, but only one was double-blinded[18], three excluded patients who had been randomised from the analysis[8,9,18], and five included no more than 100 patients, too small a number to be able to show an excess of morbidity[8,9,11,17,18]. Two of these, however, suggested that misoprostol treatment is followed by a higher caesarean section rate for fetal heart rate anomalies[12,14] and a higher prevalence of meconium-stained amniotic fluid[6]. These raised concerns about fetal tolerance to misoprostol.

We therefore thought it would be useful to conduct a double-blind randomised trial with an adequate number of patients. By attempting to avoid the pitfalls of previous trials, we aimed to compare the efficacy and tolerance of misoprostol and dinoprostone in induction of labour for medical indications. It also appeared useful to complement this study with a clear economic assessment of the total cost of each strategy.

METHODS

Between July 1997 and April 1999 we offered participation in this randomised double-blind clinical trial to all patients at Poissy Hospital who required prostaglandin to induce labour for medical indications. The inclusion criteria were: singleton pregnancy, cephalic presentation, Bishop score ≤ 5, fewer than four spontaneous uterine contractions per hour, and signed written informed consent. Patients were not eligible if: they were younger than 18 years; a non-stress test prior to induction revealed acute fetal distress, fetal-pelvic disproportion, placenta praevia, breech or transverse lie had been diagnosed; they had previous caesarean section; or known allergy to prostaglandins. The study was approved by the ethics committee.

Randomisation, based on a computer-generated list and balanced in blocks of variable size (from 4 to 16), was carried out with sealed, opaque envelopes, which were stored in the pre-delivery unit of the maternity ward. The envelope was opened just before the allocated treatment was administered. After randomisation, dinoprostone or misoprostol was given in the posterior fornix by a midwife in the pre-delivery unit of the ward. These midwives did not otherwise participate in this trial and were instructed not to discuss the treatment with patients or any other staff members, in order to maintain the treatment blind of patients and staff investigators.

Patients in the misoprostol group received 50μg (1/4 of a 200μg tablet) of Cytotec (Monsanto, Paris-la Défense, France), repeated six hours later by the same midwife in the pre-delivery unit if regular painful uterine contractions had not started. At each Cytotec administration, the midwife held a syringe in her hand to ensure blinding of the patient, because of the different presentations of the two drugs. Patients in the dinoprostone group received 2mg of Prostine E_2 gel (Upjohn Guyancourt, France), and another 1mg was given six hours later if regular painful uterine contractions had not started. After prostaglandin administration, the patient was monitored continuously for one hour for contractility and fetal heart rate. Once active labour was established (regular painful contractions at a rate of at least two in 10 minutes), the patient was taken to the delivery room for monitoring of labour and delivery.

During labour, amniotomy was performed as soon as cervical dilatation reached or exceeded 2cm–3cm. An intravenous infusion of oxytocin intravenously (started at 2mU/minute and increased as needed by 1mU/minute every 30 minutes) was also given in cases with infrequent contractions (<3 contractions/10 minutes) or arrested labour for ≥ 2 hours at ≥ 4cm. Epidural analgesia was given at the patient's request, once regular contractions became painful.

A second dose was not given if fetal heart rate anomalies occurred. An abnormal fetal heart rate led to either a fetal blood sample for pH or emergency delivery, depending on the continuous cardiotocography analysis and cervical dilatation.

If labour had not started after 24 hours, women in the misoprostol group received another dose of 50μg, repeated every four hours until labour was established, up to a total dose of 150μg. This was done by the same midwife. The dinoprostone group received another dose of 2mg, supplemented by 1mg every four hours, up to a total dose of 4mg in 24 hours. They were thus given a maximum of two doses of 1mg dinoprostone.

If labour had not started after 48 hours, induction with a prostaglandin was abandoned and amniotomy and oxytocin infusion were carried out if the cervix was favourable (Bishop >6). If the cervix remained unfavourable, a caesarean section was performed.

Assessment and monitoring

Labour and delivery were monitored according to our delivery suite protocol with continuous CTG recording and external manometry. An internal pressure catheter was only used in cases with abnormal uterine contractility. The results of hourly cervical examination were recorded on a partogram. Fetal scalp pH was performed for an abnormal CTG. Apgar score was assessed at one and five minutes, and cord arterial pH was measured at birth.

Uterine activity was assessed to identify women with tachysystole (at least six uterine contractions per 10 minutes) and/or hypertonus (single contractions lasting ≥ 2 minutes). Only hyperstimulation associated with fetal heart rate anomalies was recorded. Fetal distress was defined as fetal heart rate abnormalities requiring

emergency delivery (forceps or caesarean section) or a scalp pH <7.20.

The neonatal evaluation was performed by the midwife or the obstetrician attending the delivery, or by the paediatrician in cases of neonatal distress requiring resuscitation. None knew which treatment group the patient had been allocated to.

Outcome measures

The primary outcome was the rate of vaginal deliveries within 24 hours. The secondary outcomes were: 1. obstetric criteria: vaginal deliveries rate within 12 hours, time interval from randomisation to delivery, Bishop score after 12 hours, type of delivery (spontaneous vaginal, forceps, caesarean section); 2. fetal criteria: presence of thick meconium in the amniotic fluid, fetal distress as defined by abnormal CTG prompting emergency delivery or a scalp pH <7.20; 3. neonatal criteria: Apgar score at one and five minutes, arterial cord pH, meconium aspiration (defined by the presence of meconium below the vocal cords after laryngoscopic examination), transfer to the neonatal intensive care unit, poor neonatal outcome (defined by Apgar score <7 at five minutes, arterial pH <7.10, or meconium aspiration); 4. maternal safety and tolerance criteria: hypertonus or tachysystole, vaginal pain, nausea, vomiting, diarrhoea, fever, chorioamnionitis; 5. economic criteria: total cost of each strategy.

Sample size

Anticipating a 65% success rate of dinoprostone for vaginal delivery within 24 hours and aiming for an 80% success rate with misoprostol, we estimated that 185 women should be included in each group to obtain a power of 90% and a type I error (α) of 5% in a two-tailed test. We therefore sought to enrol a total of 370 women.

Statistical and economic analysis

We conducted an intention-to-treat analysis. The main outcome, rate of delivery within 24 hours, was estimated

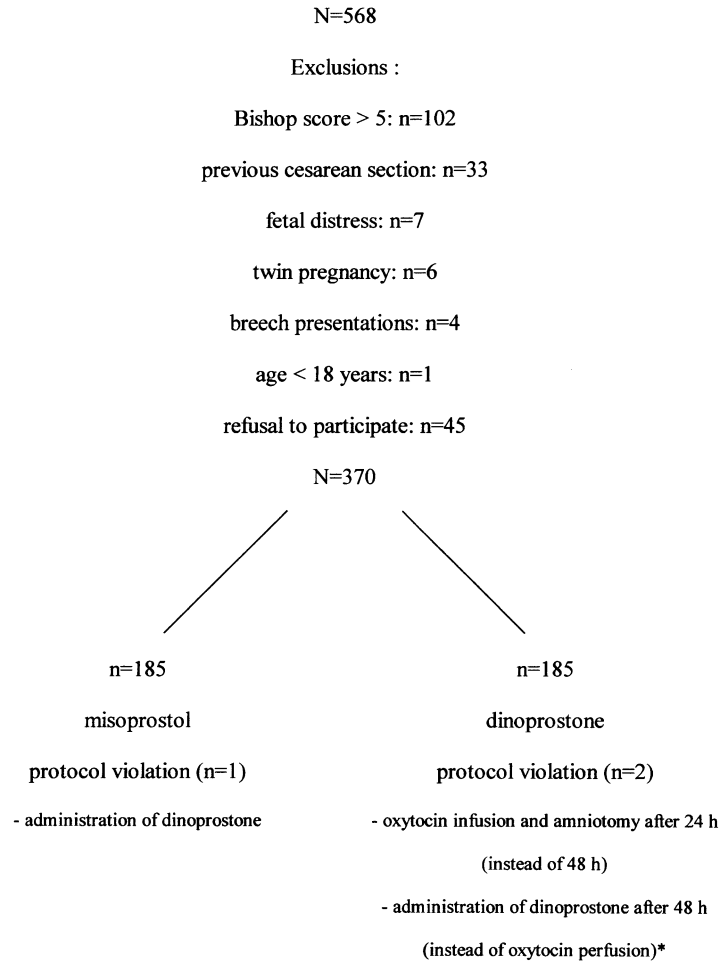

Fig. 1. Study design and protocol deviations.

and compared between the randomised groups by Fisher's exact test. The strength of the association between the treatment group and the outcome was measured by relative risk (RR), with computed 95% confidence interval.

The time interval to delivery was estimated by the Kaplan-Meier method, and the two randomised groups were compared by the log-rank test. A second analysis compared the groups after caesarean sections were censored. The hazard ratio (HR) of the event was computed (as well as its 95% CI) from the use of a Cox model in which the randomisation group was introduced as a binary covariate.

The other secondary criteria including costs and resources were compared in both groups by Fisher's exact test and the non-parametric Wilcoxon sum rank test. Note that in the analysis, the Bishop score value for women in labour or who had given birth within the first 12 hours was recorded as 13. The costs of each strategy were estimated from the viewpoint of the payer (national health care system) for the duration of the index admission[20]. We computed a cost per patient, which included the cost for the mother and for the newborn: cost of the drug, cost for the delivery (vaginal uncomplicated or complicated, or caesarean section) and the hospital admission, costs for any intensive care treatment for mother or baby. The costs of hospital procedures were derived from the national hospital cost database, which uses accounting data to estimate a cost per related diagnostic group. We supplemented data from the national database with specific data collected for this study, from the viewpoint of the hospital. Costs in 2000 French francs were converted into pounds using a 10/1 rate (OECD purchasing power parity index).

Finally, besides the intention-to-treat analysis on the whole sample, we also performed a *post hoc* explanatory analysis to compare the caesarean section rate according to the indications for induction, distinguishing: 1. possible fetal compromise (e.g. postdate, intrauterine growth restriction with or without severe pre-eclampsia, nonreassuring fetal testing); and 2. non-fetal indications (e.g. premature rupture of the membranes, isolated hypertension with normal fetal testing, maternal disease with normal fetal testing). All tests were two-tailed. Statistical significance was defined by P values of ≥ 0.05. Statistical analysis was performed with SAS 6.12 (SAS Inc, Cary, North Carolina, USA) software package.

RESULTS

In all, 568 women required induction of labour during the study period. Among them, 370 met the inclusion criteria and were randomised (Fig.1). Two patients, one in each group, went into labour spontaneously before receiving the assigned treatment. Three protocol violations also occurred (Fig.1). All randomised women were included in all analyses according to their assigned treatment, regardless of the treatment they actually received (intention-to-treat). One woman randomised to the misoprostol group subsequently withdrew her consent and was not included in the analysis, as this was specifically requested by the ethics committee. At randomisation, the two groups were well-balanced and comparable for general and obstetric characteristics (Table 1).

Of the 369 women, 229 (62.1%) delivered vaginally within 24 hours, namely 124 (67.4%) in the misoprostol group,compared with 105 (56.8%) in the dinoprostone group (RR = 1.19, 95% CI 1.01–1.40). Indeed, time interval to delivery was significantly shorter in the misoprostol group (Table 2). This remained true after caesarean sections were censored (Figs. 2 and 3). The percentage of patients delivered vaginally within 12

Table 1. General and obstetrical characteristics of the population. Values are given as median [1st and 3rd quartiles]or *n* (%).

	Misoprostol ($n = 184$)	Dinoprostone ($n = 185$)
Age (years)	29.0 [26.3; 32.6]	29.2 [26.7; 32.9]
Weight	72 [65; 81]	72 [67; 81]
Gestational age (weeks)	39.9 [38.6; 41.3]	39.7 [38.3; 41.1]
Nulliparas	128 (69.6)	127 (68.7)
Bishop score ≤ 3	95 (51.6)	93 (50.3)
Indication for induction		
Possible fetal compomise		
Post term	52 (28.3)	45 (24.3)
IUGR	20 (10.9)	19 (10.3)
Nonreassuring testing	20 (10.9)	17 (9.2)
Non-fetal indications		
Premature rupture of membranes	30 (16.3)	36 (19.5)
Pregnancy-related hypertension	28 (15.2)	30 (16.2)
Diabetes	9 (4.9)	15 (8.1)
Thrombocytopenia	11 (6.0)	5 (2.7)
Others	14 (7.6)	18 (9.7)
Epidural analgesia	169 (91.9)	173 (93.5)

Table 2. Obstetric criteria for each treatment group. Values are given as *n* % or median [95% CI]. HR = hazard ratio; RR = relative risk.

	Misoprostol ($n = 184$)	Dinoprostone ($n = 185$)
Main end point		
Vaginal delivery within 24 h	124 (67.4)	105 (56.8)
RR (95% CI)	1.19 (1.01-1.40)	1.00
Secondary end points		
Time to delivery (min)	843 [760-920]	1093 [1025-1220]
HR (95% CI)	1.46 (1.18-1.79)	1.00
Time to vaginal delivery (min)	910 [835-978]	1128 [1070- 1265]
HR (95% CI)	1.52 (1.21-1.92)	1.00
Vaginal delivery within 12 h	55 (29.9)	37 (20.0)
RR (95% CI)	1.50 (1.04-2.15)	1.00

hours was also significantly higher in the misoprostol group (RR = 1.90, 95% CI 1.04–2.15). Among the women who did not give birth within 12 hours of the first treatment administration, the Bishop score was ≤5 in 36 (19.8%) misoprostol patients, and in 55 (30.6%) dinoprostone patients. By contrast, the mode of delivery was similar (Table 3) in both groups, although the indications for caesarean section were different. The main indication for caesarean section in the misoprostol group was fetal distress, and this occurred more often than in the dinoprostone group (13.0% *vs* 7.0%, RR = 1.86, 95% CI 0.98–3.53). Conversely, caesarean sections were performed more often for failed induction in the dinoprostone group than in the misoprostol group (3.2%% *vs* 0%, respectively, RR = 0.08, 95% CI 0.004–1.36).

One hundred and seventy-three women (94.0%) received fewer than three doses of treatment in the misoprostol group, compared with 147 (79.5%) in the dinoprostone group. An oxytocin infusion was required for five (2.7%) and 14 (7.6%) women in the misoprostol and dinoprostone groups, respectively.

Tables 4 and 5 summarise the fetal and neonatal results, either on the whole sample or according to the main indication for labour induction. When a caesarean section was performed for fetal distress, one of the 24 infants (4.2%) in the misoprostol group and three of the13 infants (23.1%) in the dinoprostone group had a poor neonatal outcome.

Tachysystole was observed twice as often in the misoprostol group, compared with the dinoprostone group, but this difference was not statistically significant (Table 6). The rate of hypertonus was similar in each group. Of the 24 caesarean sections performed for fetal distress in the misoprostol group, five (20.8%) were associated with uterine tachysystole, indicating hyperstimulation syndrome. In the dinoprostone group, hyperstimulation was also present in two of the 13 women delivered by caesarean section for fetal distress (15.4%). The other indicators examined to assess the maternal tolerance did not differ significantly between groups, except for vaginal pain, which was reported significantly more often with dinoprostone.

The actual mean (standard deviation) costs for patients included in the study in our Paris metropolitan area teaching hospital were: £2202 (£595) and £2134 (£574) in the dinoprostone and misoprostol groups, respectively. Median costs were £1212 and £1200, respectively. Accordingly the two treatments did not differ significantly in either resource use or total cost ($P = 0.12$), although misoprostol tended to be cheaper.

The means (standard deviation) of total costs were as

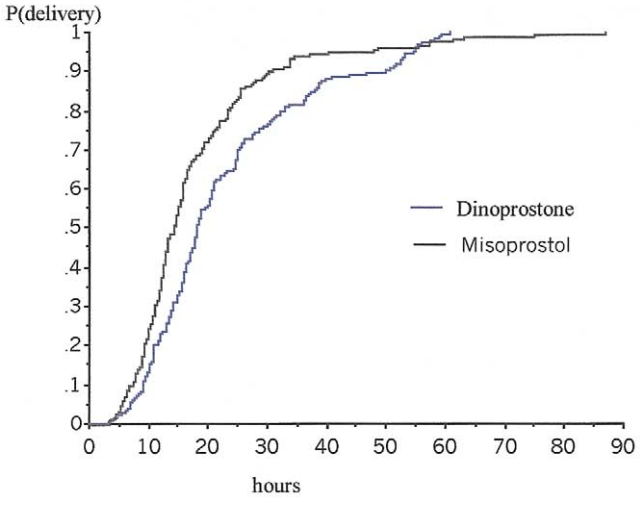

Fig. 2. Estimated time to delivery from randomisation according to treatment group.

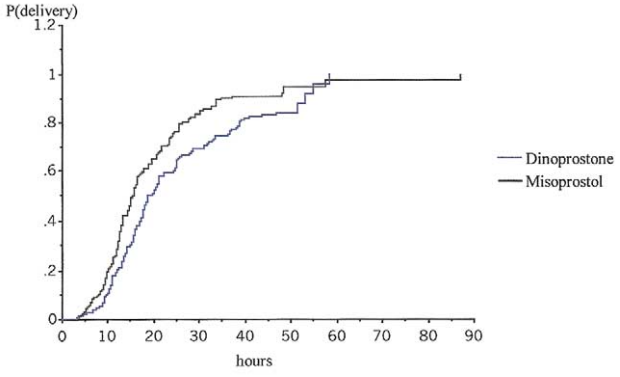

Fig. 3. Estimated time to vaginal delivery from randomisation according to treatment group.

Table 3. Mode of delivery according to treatment group. Values are given as *n* (%). SVD = spontaneous vaginal delivery.

n (%)	Misoprostol ($n = 184$)	Dinoprostone ($n = 185$)	RR (95% CI)
SVD	104 (56.5)	99 (53.5)	1.06 (0.88-1.27)
Forceps	47 (25.5)	56 (30.3)	0.84 (0.61-1.17)
Fetal distress	20 (10.9)	20 (10.8)	1.00 (0.56-1.81)
Non-progression	27 (14.7)	36 (19.5)	0.75 (0.46-1.12)
CS	33 (17.9)	30 (16.2)	1.11 (0.71-1.74)
Induction failed	0	6 (3.2)	0.08 (0.004-1.36)
Failure to progress	6 (3.3)	10 (5.4)	0.60 (0.22-1.63)
Obstructed labor	3 (1.6)	0	7.04 (0.37-135.3)
Fetal distress[a]	24 (13.0)	13 (7.0)	1.86 (0.98-3.53)
Suspected uterine rupture	0	1 (0.6)	0.34 (0.014-8.17)

[a] Abnormal fetal heart rate requiring delivery or scalp pH < 7.20.

follows. Costs directly related to the use of either dinoprostone or misoprostol were drug and personal costs: £353 [225–470] and £312 [249–390] for dinoprostone and misoprostol patients, respectively, of which drug costs were £81 and £0.3, respectively. Maternal-related costs, including the admission, delivery (vaginal and caesarean section weighted by their respective proportions): £1431 (449) and £1433 (474) for dinoprostone and misoprostol patients, respectively. Neonatal costs included neonatal intensive care unit and ordinary neonatal care during the admission: £418 (431) and £389 (331) for dinoprostone and misoprostol patients, respectively.

DISCUSSION

This is the largest randomised double-blind trial to date which compares misoprostol and dinoprostone for induction of labour for medical indications with a viable fetus. In contrast to previous studies, the sample size, double-blind design, and intention-to-treat analysis of this trial allowed the treatment effects to be compared without bias. Indeed, of the 14 prospective randomised trials already published on this subject[6–19], only one was double-blinded[18]. As stressed by Hofmeyr *et al.*[21], there is a substantial possibility of inadvertent bias in these studies. The decision to perform a caesarean section for fetal heart rate anomalies and the assessment of Apgar scores are subjected to inter- and intra-observer variability that can be influenced by unintentional knowledge of the allocated treatment. The drugs, however, should be used in their intended but different forms, for two reasons: 1. misoprostol is stable only as a powder, and its dilution in a gel or suppository[18] may alter the active component and therefore influence the results of the study; 2. to increase the clinical value of this study we wanted to test misoprostol in the form most likely to be used in routine clinical practice. Treatment was therefore administered by medical staff not involved in subsequent management of the patient.

Our results confirm that the efficacy of misoprostol was better than that of dinoprostone, both for time interval to delivery and for the rate of vaginal delivery within 12 or 24 hours.

Although the rate of caesarean section performed for acute fetal distress was higher with misoprostol (albeit non-significantly), one cannot exclude a lack of power of this study (RR = 1.86, 95% CI 0.98–3.53). The higher rate of fetal heart rate abnormalities following misoprostol administration has already been reported[12,14]. However, hyperstimulation was responsible for only five of 33 caesarean sections, and therefore it is difficult to understand the underlying mechanism of fetal distress in the misoprostol group. Nonetheless, we did not collect

Table 4. Fetal and neonatal results. Denominators vary due to missing data. Values are shown as n (%) or median [1st and 3rd quartiles].CS = caesarean section; NICU = neonatal intensive care unit.

	Misoprostol ($n = 184$)	Dinoprostone ($n = 185$)	RR (95% CI)
Meconium-stained liquor	17/183 (9.3)	8/184 (4.4)	2.14 (0.95-4.83)
CS for fetal distress	24 (13.0)	13 (7.0)	1.86 (0.98-3.53)
Birthweight (g)	3285 [2890-3680]	3200 [2860-3540]	—
1-min Apgar < 7	34 (18.5)	25 (13.5)	1.37 (0.85-2.20)
5-min Apgar < 7	2 (1.1)	3 (1.6)	0.67 (0.11-3.97)
PH < 7.20	23/177 (13.0)	12/182 (6.6)	1.97 (1.01-3.84)
PH < 7.10	2/177 (1.1)	4/182 (2.2)	0.51 (0.10-2.77)
Transfer to NICU	15 (8.2)	16 (8.7)	0.94 (0.48-1.85)
Meconium aspiration	3 (1.6)	3 (1.6)	1.00 (0.21-4.92)
Poor neonatal outcome[a]	6 (3.3)	9 (4.9)	0.67 (0.24-1.85)

[a] Apgar at 5 mn < 7; arterial pH < 7.10; meconium aspiration.

Table 5. Fetal and neonatal tolerance according to the type of indication. Values are shown as *n* (%).

Indication of labor induction	Misoprostol ($n = 184$)	Dinoprostone ($n = 185$)	RR (95% CI)
Possible fetal compromise	$n = 95$	$n = 84$	
Meconium-stained liquor	11/94 (11.7)	2/83 (2.4)	4.86 (1.11-21.3)
pH < 7.20	15/93 (16.1)	4/84 (4.8)	3.39 (1.17-9.80)
CS for fetal distress	17 (17.9)	7 (8.3)	2.15 (0.94-4.92)
Poor neonatal outcome	6 (6.3)	3 (3.6)	1.77 (0.46-6.85)
Non fetal indications	$n = 89$	$n = 101$	
Meconium-stained amniotic fluid	6/89 (6.7)	6/101 (5.9)	1.14 (0.38-3.39)
pH < 7.20	8/84 (9.5)	8/98 (8.2)	1.17 (0.46-2.97)
CS for fetal distress	7 (7.9)	6 (5.9)	1.32 (0.46-3.79)
Poor neonatal outcome	0	6 (5.9)	0.09 (0.005-1.526)

quantitative data on contraction intensity and therefore we cannot exclude the possibility that uterine hyperstimulation might have been the cause of these abnormalities. Two previous studies also reported an increased rate of fetal heart rate abnormalities with misoprostol, but the interpretation of the abnormal traces remains controversial. In the first study[12], fetal heart rate abnormalities were directly associated with an excess of contractions, while in the second[14], the rate of fetal bradycardia or late deceleration was much higher (41%) than that of hyperstimulation syndrome (6%).

If we consider the most important indicators of perinatal asphyxia (5-minute Apgar score <7, arterial pH cord <7.10 and meconium aspiration), tolerance was similar in both groups. These results contrast with the higher rate of fetal distress observed with misoprostol. This discrepancy in the results (fetal distress associated with healthy babies) has also been reported previously[12]. The rates of arterial cord pH <7.20 and of meconium-stained amniotic fluid were also more common at birth in the misoprostol group. The difference in meconium-stained amniotic fluid rates could be due to chance, although this increase in the prevalence of antenatal meconium excretion has also been reported previously[6]. It may indicate fetal compromise or reflect the direct effect of misoprostol on fetal intestinal motility[6,21].

Subgroup analysis by indication for induction shows that the higher rate of caesarean section performed for fetal distress with misoprostol persists only in potential fetal compromise in the group of fetal indications for induction. Nonetheless, this difference fails to reach the significance. However, the rates of arterial cord pH <7.20 and of meconium-stained amniotic fluid were significantly higher than in the dinoprostone group. Finally, all six infants with a poor neonatal outcome in the misoprostol group belonged to this subgroup. It could therefore well be that the healthy fetuses show a better tolerance to the powerful ripening effect of misoprostol. However, the incidence of poor neonatal outcome in both groups after induction for fetal indications was similar.

Among non-fetal indications for induction, this analysis failed to show any difference in tolerance between the two subgroups. Nonetheless, these conclusions must be guarded in view of the absence of initial stratification by indication for induction which led to *post hoc* analysis.

Total costs, from the viewpoint of either the payer or the hospital, did not differ significantly, because the additional cost of dinoprostone was partly offset by reduced personnel costs. In addition, although the hospital's pharmacists may disagree, drug costs are a minor component since dinoprostone accounted for 6% of total costs. The lower cost of misoprotol resulted in a tendency to lower total costs.

In conclusion, the efficacy of misoprostol as a ripening and oxytocic agent was greater than that of dinoprostone. The main analysis of fetal and neonatal safety does not show any difference between the two groups. However, *post hoc* analysis suggests that there could be a higher incidence of arterial cord pH <7.20, and meconium-stained amniotic fluid at birth in the misoprostol group in cases of induction for fetal indications. Fetal/neonatal tolerance to misoprostol should therefore be assessed in a

Table 6. Maternal tolerance. Values are given as *n* (%). PPH = postpartum haemorrhage.

	Misoprostol ($n = 184$)	Dinoprostone ($n = 185$)	RR (95% CI)
Hypertonus	8 (4.3)	8 (4.4)	1.00 (0.38-2.62)
Tachysystole	12 (6.5)	6 (3.2)	2.01 (0.77-5.24)
Hyperstimulation	5 (2.7)	2 (1.1)	2.51 (0.49-12.8)
Nausea, vomiting, diarrhea	7 (3.8)	9 (4.9)	0.78 (0.30-2.06)
Fever	2 (1)	0	5.03 (0.24-107.0)
Chorioamnionitis	1 (0.5)	0	3.02 (0.12-73.6)
Vaginal pain	3 (2)	34 (18)	0.09 (0.03-0.28)
PPH	16 (9)	17 (9)	0.95 (0.49-1.82)

subset of potentially compromised fetuses. In the meantime, misoprostol should be preferred to dinoprostone in non-fetal indications for induction, such as premature rupture of membranes. Cost considerations do not appear to be relevant in this decision-making process, which can be entirely based on medical criteria.

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