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A randomised trial comparing low dose vaginal misoprostol and dinoprostone for labour induction

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Objective To compare vaginal misoprostol with dinoprostone for induction of labour.

Design Randomised multicentre trial.

Setting Labour wards of one university hospital and two teaching hospitals.

Population Six hundred and eighty-one women with indication for labour induction at ≥36 weeks of gestation, singleton pregnancy and no previous ceasarean section.

Methods Misoprostol (25 mcg, hospital-prepared capsule) in the posterior vaginal fornix, every four hours, maximum three times daily or dinoprostone gel (1 mg) every four hours. Oxytocin was administered if necessary.

Main outcome measures Primary: 'adverse neonatal outcome' (5-minute Apgar score <7 and/or umbilical cord pH <7.15). Secondary: labour duration, mode of delivery and patient satisfaction.

Results Three hundred and forty-one women received misoprostol and 340 dinoprostone. The median induction–delivery interval was longer in the misoprostol group compared with the dinoprostone group (25 *versus* 19 hours, $P = 0.008$). The caesarean section rate was lower in the misoprostol group: 16.1% *versus* 21%, but this difference was not statistically significant RR = 0.8 (95% CI 0.6–1.04). 'Adverse neonatal outcome' was found to be similar in both groups: 21% in the misoprostol and 23% in the dinoprostone groups. Significantly fewer neonates were admitted to NICU in the misoprostol group compared with dinoprostone 19% *versus* 26% (RR = 0.7, 95% CI 0.5–0.98).

Conclusions Misoprostol in this dosing regimen is a safe method of labour induction. NICU admission rates were lower in the misoprostol group. No difference could be detected in patient satisfaction between groups.

INTRODUCTION

Induction of labour has become a common obstetric intervention in western countries, with induction rates as high as 44%.[1] Labour induction in the presence of an unfavourable cervix used to be associated with high incidences of prolonged labour, instrumental delivery and caesarean section in the pre-prostaglandin era.[2,3] For these reasons, extensive research has been directed towards the development of agents for efficient cervical ripening. The use of prostaglandins for cervical ripening turned out to have a positive effect on the spontaneous vaginal delivery rate, and thus women were less likely to require a caesarean section.[4] Vaginal prostaglandin E_2 preparations are effective in inducing labour in patients with an unripe cervix; however, they are expensive and unstable at room temperature.

In the past few years misoprostol, a synthetic prostaglandin E_1 analogue, has been used extensively and there has been a growing interest in using misoprostol as a cervical ripening and labour induction agent. Thus far, greater than 200 studies including more than 16,000 women have evaluated its effectiveness in pregnant women.[5]

Most research has concentrated on finding optimum dosing, shortening labour, reducing operative delivery and not on neonatal outcome and maternal satisfaction. Therefore, the aim of this randomised trial was to compare the safety and maternal satisfaction, as well as efficacy of a low dose of vaginal misoprostol with vaginal dinoprostone (our standard regimen) for labour induction after 36 weeks of gestation, in the presence of an unfavourable cervix.

METHODS

This randomised trial, comparing vaginal misoprostol and dinoprostone for labour induction, was carried out between 1 November 1999 and 31 December 2002 in

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The Netherlands. Women requiring induction of labour for medical, obstetric or other indications at Leiden University Medical Centre were asked to participate. St Franciscus Hospital, Rotterdam (from 15 September 2001) and St Antonius Hospital, Nieuwegein (from 1 December 2001), also participated in the study.

Inclusion criteria were (1) singleton pregnancy, (2) cephalic or breech presentation, (3) gestational age at least 36 completed weeks and (4) Bishop score $\leq$6. Only women with a viable fetus were included. Patients were excluded if there was (1) a contraindication to use prostaglandins, (2) previous caesarean section or other uterine incision or (3) no informed consent.

The Medical Ethics Committees of all three hospitals approved the study. Eligible women were approached for participation, and written informed consent was obtained. Women were randomised by means of sequentially numbered opaque, sealed envelopes. The envelopes were assigned to either misoprostol or dinoprostone by the first author with the use of a random number table. Randomisation was stratified by hospital.

Women allocated to the misoprostol group received 25 mcg of a pulverised misoprostol tablet (Cytotec, Searle, Maarsen, The Netherlands) with cellulose in a capsule, prepared by the hospital pharmacy, placed in the posterior fornix. A Bishop score was assessed just before randomisation. Misoprostol was administered every four hours, maximum of three times a day. The attending physician performed amniotomy if deemed necessary. If amniotomy could not be performed after a maximum of six doses of misoprostol, a switch was made to dinoprostone gel.

Women allocated to the dinoprostone gel group received 1 mg of dinoprostone gel (Prostin, Pharmacia Upjohn, Leiden, The Netherlands) every four hours, maximum of three times a day, no maximum total dose. A switch could be made to 2 mg dose of dinoprostone if deemed necessary by the delivery room physician. The Bishop score was assessed just before randomisation. Amniotomy and the use of oxytocin was performed as in the misoprostol group.

Intravenous oxytocin augmentation was used after spontaneous or artificial rupture of membranes without adequate uterine contractions or failure to progress in active phase of labour. Oxytocin was started at a rate of 0.4 mu/min and was increased stepwise every 30 minutes by doubling the dose.

Continuous fetal heart rate monitoring and uterine activity monitoring were performed in all women from the moment they were considered to be in active labour. Evaluation of uterine activity was performed to assess the occurrence of hyperstimulation. Hyperstimulation was defined as the presence of more than four contractions in 10 minutes, with or without an abnormal fetal heart rate pattern.

Primary analysis consisted of all women included in the study after randomisation (intention-to-treat). As there were violations of the protocol, we also performed a secondary, 'protocol-compliant' analysis.

Baseline data included maternal age, gravidity, parity, underlying medical and obstetric disorders, gestational age, indication for induction and a Bishop score at randomisation.

The primary, predefined outcome variable was 'adverse neonatal outcome', defined as a 5-minute Apgar score <7 and/or an umbilical artery pH <7.15. Secondary outcomes included operative delivery rate, need for oxytocin, uterine hyperstimulation rate, meconium staining, use of pain relief, admission to NICU and maternal satisfaction. Maternal satisfaction was assessed by means of a semi-structured questionnaire to be filled in by the woman after delivery. The questionnaire has been developed especially for this study, in collaboration with the Department of Medical Decision Making of the Leiden University Medical Centre, and consisted of 32 questions.

A sample size calculation was performed on the assumption that misoprostol would not differ more than 10% from dinoprostone in the occurrence of 'adverse neonatal outcome'. Before the trial, primary outcome was found in 20% of neonates after induction of labour with dinoprostone gel in our hospital. On the basis of a type I error of 0.05 and a power of 80% (type II error 0.2), 294 women in both trial arms were required.

Statistical comparisons between the two groups were done, using the Student t, Mann–Whitney U or χ^2 test, whichever was appropriate. All tests were two-sided and a P value below 0.05 was considered significant. Logistic regression was used to assess the contribution of the induction agent to certain outcome variables, after adjusting for other potential contributory variables.

RESULTS

A total of 681 women were enrolled in the study. Although there were 31 violations of protocol, all these women were included in the primary analysis (Fig. 1). No woman was lost to follow up. Maternal satisfaction evaluation forms were obtained from 85% of the total group.

The distribution of maternal and gestational age, parity, Bishop score and indication for labour induction were similar in the misoprostol and dinoprostone groups (Table 1). In both groups, seven women with breech presentation were included.

In the dinoprostone group, 103 (30%) women received one dose of gel, 164 (48%) had two doses, 33 (10%) had three doses and the remaining 38 women (11%) received four or more doses. The median number of doses was two. In the misoprostol group, four women received no misoprostol (1%), 78 women (23%) received one capsule, 163 (48%) received two capsules, 41 (12%) three capsules and the other 55 women (16%) received four or more capsules (median number two). Six women (2%) in the misoprostol group had additional dinoprostone gel after they received

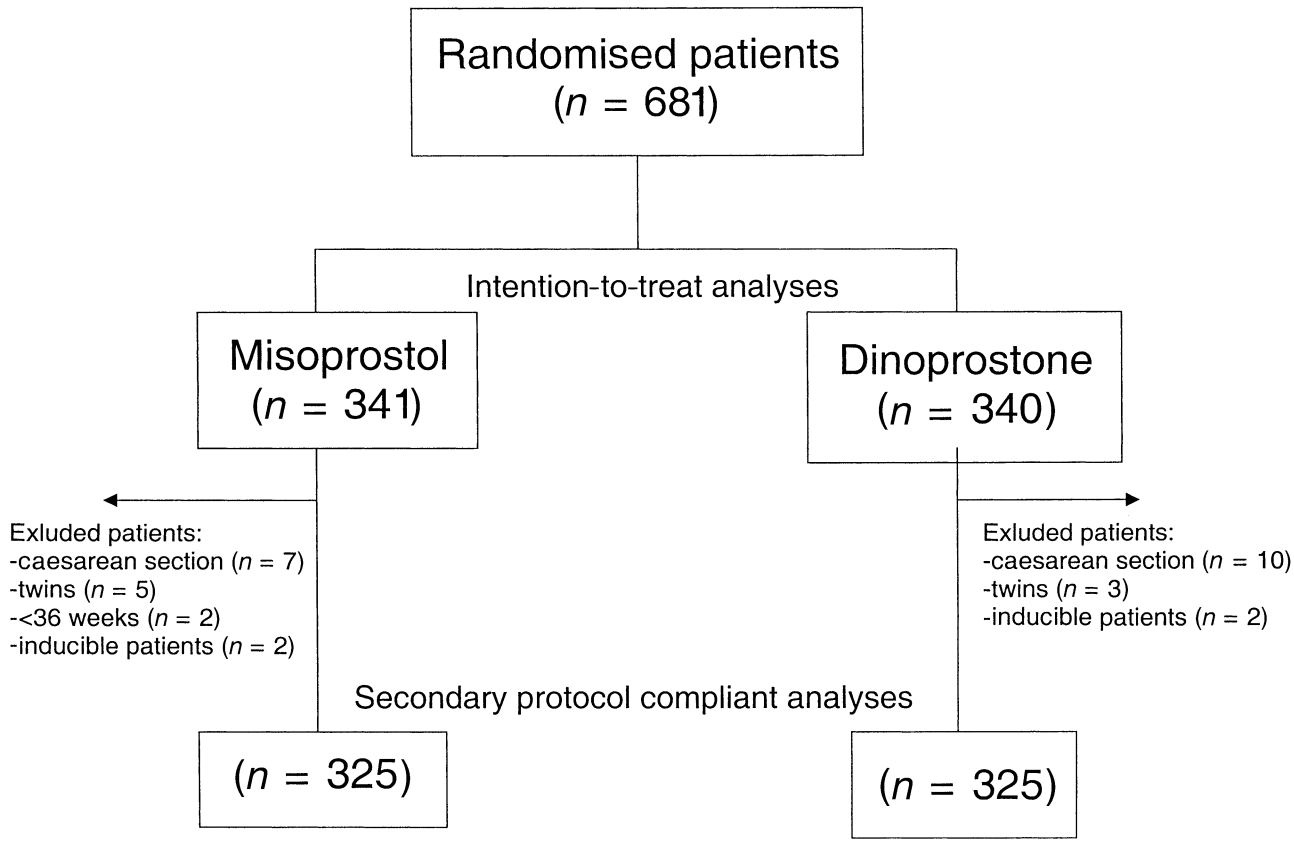

Fig. 1. Patient flow chart.

the assigned six doses of misoprostol, 323 women (95%) had no additional dinoprostone and 12 other women (4%) switched from misoprostol to dinoprostone before the assigned number of six doses of misoprostol, because of the woman's preference.

Table 1. Patient characteristics. Values are given as *n* (%) or average [range].

	Misoprostol ($n = 341$)	Dinoprostone ($n = 340$)
Median maternal age (years)	31 [18–44]	31 [16–42]
Nullipara	201 (59)	199 (59)
Median gestational age (weeks)	40 [34–43]	39.7 [36.4–43.3]
Initial Bishop score ≤3	270 (81)	278 (84)
Median initial Bishop score	2 [0–8]	2 [0–7]
Indications for induction of labour		
Postdate pregnancy	75 (22)	92 (27)
Hypertension*	95 (28)	81 (24)
Diabetes mellitus	9 (3)	14 (4)
Intrauterine growth restriction	13 (4)	15 (5)
Psychosocial	68 (20)	50 (15)
PROM	29 (9)	28 (8)
Oligohydramnios	34 (10)	34 (10)
Red cell immunisation, (NA) ITP	11 (3)	17 (5)
Congenital malformation	2 (0.6)	6 (2)
Other	5 (1)	3 (1)

PROM = premature rupture of membranes.
* Including pre-eclampsia.

Peripartum data are shown in Table 2. There were more spontaneous births in the misoprostol group (RR = 1.1; 95% CI 1.0–1.3) (Table 2). The number of caesarean sections was lower in the misoprostol group (RR = 0.8, 95% CI 0.6–1.04) (Table 2), although this difference was not statistically significant. Fifteen women from the misoprostol group and seven from the dinoprostone group had an induction to delivery interval longer than 96 hours. All of these women had a vaginal birth. When these women are excluded, the difference in induction-to-delivery interval is 23 and 19 hours, respectively ($P = 0.05$).

The vaginal birth rate within 24 hours was significantly lower in the misoprostol group, but vaginal delivery rates within 36 hours were similar (Table 2). The rate of caesarean sections performed for poor progress of labour was similar: 42% in the misoprostol and 40% in the dinoprostone group. Caesarean section performed for fetal distress was also similar: 45% in the misoprostol and 39% in the dinoprostone group.

Outcomes for infants in breech presentation were not different between groups: 5 babies (18%) in the misoprostol group were admitted to NICU compared with 4 (15%) in the dinoprostone group, but there were no adverse neonatal outcomes.

Table 2. Peripartum data. Values are given as *n* (%), median {range}, *P* value or RR [95% CI].

	Misoprostol ($n = 341$)	Dinoprostone ($n = 340$)	*P*/RR (95% CI)
Oxytocin use	199 (58)	154 (45)	1.3 [1.1–1.5]
Epidural use	69 (21)	74 (24)	0.9 [0.7–1.2]
Opioids	120 (35)	117 (34)	1.0 [0.8–1.3]
Scalp pH done	58 (17)	69 (20)	0.8 [0.6–1.2]
Med. scalp pH (range)*	7.3 (7.0–7.5)	7.3 (7.0–7.5)	$P = 0.70$
Meconium at time of amniotomy	46 (14)	45 (13)	1.0 [0.7–1.4]
Hyperstimulation	29 (8)	26 (8)	1.2 [0.7–1.9]
Vaginal birth within 24 hours	164 (48)	199 (59)	0.8 [0.7–0.95]
Vaginal birth within 36 hours	255 (75)	271 (80)	0.9 [0.9–1.02]
Induction–delivery interval (hours)	25 {3–686}	19 {3–199}	$P = 0.008$
Spontaneous birth	231 (68)	206 (61)	1.1 [1.0–1.3]
Caesarean section	53 (16)	70 (21)	0.8 [0.6–1.04]
Blood loss (mL)	350 {50–3000}	350 {30–11000}	$P = 0.37$
Blood loss >1000 mL	20 (6)	27 (8)	0.7 [0.4–1.3]
Stay >1 day after birth	206 (60)	227 (67)	0.9 [0.8–1.01]

* Lowest pH per patient recorded.

One uterine rupture occurred in the dinoprostone group in a woman without previous uterine surgery. A postpartum haemorrhage developed after vaginal birth of a healthy infant. After inspection in the operation room and embolisation of the uterine arteries without success, laparotomy was performed and uterine rupture detected. Repair failed and hysterectomy had to be performed. Total blood loss 11 L. The woman recovered uneventfully after blood transfusion. One woman with a previous caesarean section in the misoprostol group had a uterine rupture. She had one dose of misoprostol, followed by one dose of dinoprostone gel four hours later. Five hours later oxytocin was started. Thirteen hours after the first dose of misoprostol, an emergency caesarean section had to be performed, the old scar had ruptured and the cord and shoulder of the baby protruded through the old scar. A healthy infant (birthweight 2830 g, Apgar score 9 at 5 minutes, umbilical pH 7.13) was born. The uterus was repaired without difficulty, with a total blood loss of 350 mL.

No difference in 'adverse neonatal outcome' was found between both groups (Table 3). Umbilical artery pH was not performed in 43 cases, in the misoprostol group and in 41 cases in the dinoprostone group, explaining why 'adverse outcome' could not be ascertained in these cases. In 12 cases umbilical pH was not performed because the clamp on the cord had been removed during caesarean section and in 11 cases umbilical cord blood had to be used for other reasons. In the remaining cases, blood sampling was not performed due to logistic reasons; those babies were born in good condition.

A cord pH <7.0 was found in 9 (3%) and 6 (2%) neonates in the misoprostol and dinoprostone groups, respectively. This difference is statistically not significant ($P = 0.42$). Significantly fewer neonates were admitted to NICU in the misoprostol group (Table 3). The indications for NICU admission are shown in Table 4.

Three neonatal deaths were found in this study: one in the misoprostol and two in the dinoprostone group. All three were related to severe congenital malformations.

In the dinoprostone group, two babies died. In one baby, antenatally, bradycardia was found, which was diagnosed neonatally as a 'long QT syndrome'. A pacemaker was implanted but the baby died at the age of one month because of ventricle fibrillation. The other baby died 19 days after delivery because of an not understood combination of hepatosplenomegaly with severe liver dysfunction,

Table 3. Neonatal outcomes. Values are given as *n* (%), median {range}, *P* value or RR [95% CI].

	Misoprostol ($n = 341$)	Dinoprostone ($n = 340$)	*P*/RR [95% CI]
Birthweight	3440 {1545–5285}	3448 {1560–5460}	$P = 0.48$
5-minute Apgar score	10 {5–10}	10 {4–10}	$P = 0.49$
5-minute Apgar score <7	8 (2)	8 (2)	1 [0.4–2.6]
Cord pH	7.2 {6.9–7.4}	7.2 {6.9–7.5}	$P = 0.95$
Cord pH <7.15	56 (19)	63 (21)	0.9 [0.7–1.2]
'Bad outcome'*	56 (22)	68 (23)	0.9 [0.7–1.2]
Admission to NICU	67 (20)	89 (26)	0.8 [0.6–0.99]
Duration of stay (days)	4 {1–42}	4 {1–31}	$P = 0.38$
Neonatal mortality	1 (0.3)	2 (0.6)	0.5 [0.1–5.5]

* Bad outcome is not known in 43 cases (13%) in the misoprostol group and in 41 cases (12%) in the dinoprostone group because umbilical pH was not performed.

Table 4. Indications for admission to NICU. Values are given as *n* (%) or RR [95% CI].

	Misoprostol ($n = 341$)	Dinoprostone ($n = 340$)	RR [95% CI]
Birth asphyxia	18 (5)	19 (6)	0.9 [0.5–1.8]
Small for gestational age	10 (3)	19 (6)	0.5 [0.3–1.1]
Congenital malformation	5 (2)	5 (2)	1.0 [0.3–3.4]
Red cell immunisation/ITP	9 (3)	19 (6)	0.5 [0.2–1.03]
Neonatal infection	3 (1)	3 (1)	1.0 [0.2–4.9]
Suspected infection	10 (3)	10 (3)	1.0 [0.4–2.4]
Meconium aspiration	1 (0.3)	1 (0.3)	1.0 [0.1–15.9]
Glucose regulation	6 (2)	10 (3)	0.6 [0.2–1.6]
Other	5 (2)	3 (1)	1.7 [0.4–6.9]

Infection suspected: cultures sterile.
Glucose regulation: babies from diabetic mothers.

most probably resulting in severe anaemia and thrombocytopaenia, intracranial bleeding and perinatal asphyxia. At autopsy, a giant cell hepatitis was found. All probable causes like infection and metabolic complications were ruled out. The perinatal death in the misoprostol group was a baby who died 11 days after delivery because of the complications of an antenatally diagnosed meningomyelocele in combination with a hydrocephalus and an Arnold Chiari malformation type II.

The crude OR for admission to NICU for dinoprostone *versus* misoprostol was 1.4 (95% CI 1–2). Logistic regression was used to adjust for other potential contributory variables to the NICU admission rate, including induction agent, complications in pregnancy, indication for induction, gestational age at induction, meconium, Bishop score, maternal age, caesarean section, use of opioids, duration of labour and birthweight (Table 4). Although the OR did not change essentially, in the multivariate model, the induction agent was no longer significant ($P = 0.13$, OR = 1.4, 95% CI 0.9–2.2). Variables that significantly influenced the admission to NICU were complication in pregnancy (OR = 1.9, 95% CI 1.02–3.6), gestational age (OR = 0.7, 95% CI 0.5–0.8), meconium (OR = 2.1, 95% CI 1.1–3.8) and indication for induction (overall *P* value for indication for induction <0.001).

Patient satisfaction was measured by a questionnaire, filled in by the woman as soon as possible after delivery. In the misoprostol group, 291 women (85%), and in the dinoprostone group, 286 women (84%) completed the questionnaire. If questionnaires were not returned during the stay in hospital after delivery, a questionnaire was sent to the home address. In both groups, 71% of women answered the questions within the first two days after delivery. One question concerned the choice for the same medication in the same circumstances in a new pregnancy. In the misoprostol group, 179 women (64%) said they would probably or certainly choose for the same method next time. In the dinoprostone group, 58% (164 women) chose this option. Sixty-eight (23%) and 73 (26%) women answered 'no preference', respectively. When women were asked if the method of inserting the tablets or gel was annoying, only 29 (10%) and 36 (13%) women, respectively, said 'yes'.

The duration of labour was judged as 'much too slow' or 'too slow' by 101 (36%) and 95 (35%) women in both groups. It was judged as 'too fast' or 'much too fast' by 43 women (15%) in the misoprostol group and 39 women (14%) in the dinoprostone group.

Five statements, such as, 'I went through hell', 'Pain was so bad I would not even wish this for my worst enemy', 'The pain was bad, but I could handle it', 'The pain goes on and on, I had no rest', 'The pain was not as bad as I expected after stories from others', were scored in the same way in both groups. No significant difference in pain experience could be found.

Nausea was reported by 165 women (57%) in the misoprostol group and 158 women (57%) in the dinoprostone group. Vomiting was reported by 84 (29%) and 78 (28%) women in both groups, respectively. There was no significant difference in the number of times women were vomiting; however, one woman in the misoprostol group said she vomited more than 50 times. Diarrhoea (varying from light to severe diarrhoea) was reported more often in the dinoprostone group (15% and 9%, respectively, $P = 0.05$). On the whole, no significant differences or trends could be found in this evaluation of patient satisfaction.

A total of 31 women did not meet the inclusion criteria for this study (see Fig. 1). Four women had a favourable Bishop score and therefore did not receive the medication; two women in the misoprostol group and two in the dinoprostone group. Two women had a gestational age <36 weeks. They were both allocated to receive misoprostol. They both received the assigned medication, both had a caesarean section. Eight women had a multiple pregnancy (five from the misoprostol group, three from the dinoprostone group). Four of the misoprostol group and all three from the dinoprostone group received the assigned medication. Three women from the misoprostol group and one from the dinoprostone group had a caesarean section. Another 17 women had a previous caesarean section and should not have been randomised. Ten of these women were in the dinoprostone group. All these women received

Table 5. *Post hoc* analysis: nulliparous and multiparous women. Values are given as *n* (%) or RR [95% CI].

	Nulliparous women			Multiparous women		
	Misoprostol ($n = 201$)	Dinoprostone ($n = 199$)	RR [95% CI]	Misoprostol ($n = 140$)	Dinoprostone ($n = 141$)	RR [95% CI]
Oxytocin use	127 (63)	108 (54)	1.2 [0.99–1.4]	72 (51)	46 (33)	1.6 [1.2–2.1]
Spontaneous birth	104 (52)	91 (46)	1.1 [0.9–1.4]	127 (91)	115 (82)	1.1 [1.0–1.2]
Caesarean section	41 (20)	54 (27)	0.7 [0.5–1.1]	12 (9)	16 (11)	0.8 [0.4–1.5]
Vaginal birth <36 h	137 (69)	146 (74)	0.9 [0.8–1.1]	118 (84)	125 (89)	0.9 [0.9–1.0]
'Adverse outcome'*	49 (27)	45 (25)	1.1 [0.8–1.5]	12 (10)	23 (19)	0.5 [0.3–1.0]
5-minute Apgar <7	7 (4)	6 (3)	1.2 [0.4–3.4]	1 (0.7)	2 (1.4)	0.5 [0.1–5.5]
Umbilical pH <7.15	45 (25)	40 (22)	1.1 [0.8–1.6]	11 (9)	23 (19)	0.5 [0.3–1.0]
Admission NICU	46 (23)	48 (24)	0.9 [0.7–1.4]	21 (15)	41 (29)	0.5 [0.3–0.8]

* 'Adverse outcome' is adverse neonatal outcome.

the assigned medication. Three women had a repeated caesarean section, one a vaginal operative delivery. The other six had normal vaginal delivery. The other seven women were randomised to receive misoprostol. All seven received one or more doses of misoprostol before the wrongful inclusion was discovered. They then switched to dinoprostone, three also received oxytocin. Four had a caesarean section, the other three had a spontaneous vaginal birth. If all these women ($n = 31$) are excluded from analysis, the spontaneous birth rate in the misoprostol group was 70% (226 women), compared with 61% in the dinoprostone group (198 women). This difference was statistically significant (RR = 1.1, 95% CI 1.02–1.3). In the misoprostol group, 44 women had a caesarean section (14%), compared with 20% in the dinoprostone group, 65 women (RR = 0.7, 95% CI 0.5–0.96). The occurrence of neonatal adverse outcome was not different between groups, 58 (20%) and 64 (22%) in the misoprostol and dinoprostone groups, respectively. However, a significant difference in admission to neonatal care was found, 59 (18%) and 84 (26%) in the misoprostol and dinoprostone groups, respectively (RR = 0.7, 95% CI 0.5–0.9).

A separate analysis according to parity (nulliparous/multiparous) is presented in Table 5.

DISCUSSION

We found no significant difference in neonatal morbidity or mortality, defined as 'adverse neonatal outcome'. This is consistent with the literature, although this outcome is not specified in all studies.[6,7] The difference in admissions to the neonatal intensive care unit was statistically significant with more babies in the dinoprostone group being admitted. However, in the logistic regression analysis, although the absolute OR did not change, induction agent was no longer a significant risk factor for NICU admission after adjusting for other possible risk factors.

We did not find a difference in meconium-stained liquor, nor did we find a higher incidence of hyperstimulation in the misoprostol group, which is in contrast to the literature.[8–10] Side effects and maternal discomfort in relation to the use of prostaglandins in general and misoprostol in particular turn out to be dose-dependent phenomena.[9,11] In a study by Herabutya and O-Prasertsawat[11] concerning second trimester pregnancy termination, misoprostol doses of 200, 400 and 600 mcg every 12 hours were used. The higher doses had a faster action, but were accompanied by an increasing rate of side effects, such as nausea, vomiting, diarrhoea and rise in temperature. Since misoprostol has been used for induction of labour at term, the doses used have gradually decreased from 100 mcg every 12 hours to the now commonly used 25 mcg every four to six hours.[12–16] While lower doses are effective, hyperstimulation and meconium passage are found less frequently. Using this low dose is safe. The low dose used in this study is effective, although a little bit slower than dinoprostone.

The median induction to delivery interval in the present study in the misoprostol group is longer and fewer women had a vaginal delivery within 24 hours than is generally found in other studies using 25 mcg.[16–18] Possible explanation for this difference is the number of doses administered in 24 hours. In our study, a maximum of three doses in 24 hours were permitted, while in most other studies four to six doses were given. However, we found a lower operative delivery rate in the misoprostol group, especially when women with a previous caesarean section were excluded (protocol-compliant analysis). At the expense of a slightly longer induction delivery interval, higher spontaneous birth and lower caesarean section rates along with less NICU admissions are observed in the misoprostol group.

Another interesting observation is made in the group of women who did not go into active labour within two to three days. Intervals longer than 96 hours can be explained by the fact that after two or three days of induction without success, the indication for induction is sometimes reconsidered. The decision can be made to wait a few days before trying again or even await spontaneous onset of labour (depending on the indication for induction). All

these women eventually had a spontaneous birth. Of course, one can debate whether these women should have been induced in the first place if the indication was apparently not that strong, but it is worthwhile not to persevere on the induction path if it is not effective.

Patient satisfaction does not seem to be different between the two groups (i.e. there is no reason in that respect to have a preference for one of these two methods of induction). The questionnaire used for this study was specially designed for this study. The fact that we did not find a difference in patient satisfaction does not necessarily mean that there is no difference, but the difference may be too subtle to measure with this questionnaire. On the other hand, in a study where two methods are compared that both comprise vaginal administration of medication, followed by intravenous medication, and where the use of pain relief is not different in both groups, it is unlikely to find big differences in patient satisfaction between groups. Recall bias may certainly play a role in our study design, but there is no difference in timing of filling in the questionnaire between groups.

Although a potential point of criticism is the fact that this study is not double blind in its design, physicians making intrapartum decisions to perform a caesarean section, however, were in general not involved in this study, thereby reducing possible bias. The use of oral misoprostol for labour induction seems promising. Some interesting trials have been performed in this field, but the proper dosing regimen has not been found yet.[19–21] It is plausible that oral administration would lead to higher patient satisfaction. Although in our study only approximately 5% of women found the vaginal insertion of the medication undesirable, a lot of women might prefer oral administration, although vaginal examinations are still needed to evaluate progress of induction. In a study by Shetty *et al.,*[22] patient acceptability of both oral and vaginal misoprostol was evaluated by a questionnaire. Satisfaction rates were 89% for the vaginal group and 75% for the oral group. This difference seemed to be caused mainly by the slower action of oral misoprostol in this study. Future research should be directed towards more randomised trials, using not more than 25 mcg misoprostol. Unfortunately, misoprostol in women with a uterine scar is a field of research that not many investigators will dare to consider.

In conclusion, misoprostol in this low dose regimen of 25 mcg two to three times daily at an interval of at least four hours, in women with a term pregnancy, without previous caesarean section, is a safe, effective and cheap method of labour induction.

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