Ultrasound Obstet Gynecol 2001; **18**: 629–635

Randomized study of vaginal misoprostol (PGE_1) and dinoprostone gel (PGE_2) for induction of labor at term

G. K. PANDIS, A. T. PAPAGEORGHIOU, C. M. OTIGBAH*, R. J. HOWARD† and K. H. NICOLAIDES

*Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, *Department of Obstetrics and Gynaecology, Harold Wood Hospital, Romford and †Department of Obstetrics and Gynaecology, King George Hospital, Goodmayes, UK*

KEYWORDS: Cervical assessment, Dinoprostone, Induction of labor, Misoprostol, Randomized study

ABSTRACT

Objectives *To investigate the efficacy and safety of misoprostol in the induction of labor at term by comparing this agent with the commonly used dinoprostone gel.*

Patients and methods *A randomized clinical trial of vaginal misoprostol, 50 μg 6-hourly, and dinoprostone gel, 1–2 mg 6-hourly, in 435 women undergoing induction of labor at term. The women, 210 in the misoprostol group and 225 in the dinoprostone group, were compared to determine whether there was a significant difference in achieving vaginal delivery within 24 h, the incidence of hyperstimulation syndrome, Cesarean section rate and adverse neonatal outcome. They were also offered the option of preinduction sonographic cervical assessment.*

Results *Misoprostol, compared to dinoprostone gel, was associated with a significantly shorter median induction-to-delivery interval (14.6 h vs. 19.0 h;* P = *0.0014), a higher incidence of vaginal delivery within 24 h of induction (65.7% vs. 54.2%;* P = *0.019) and a reduced need for oxytocin augmentation during labor (20.5% vs. 29.8%;* P = *0.034). The groups did not differ significantly in the rates of Cesarean section (18.1% vs. 19.1%;* P = *0.88) and hyperstimulation syndrome (2.4% vs. 0.9%;* P = *0.27). None of the cases of hyperstimulation required treatment with tocolysis. All nine cases of excessive uterine contractility occurred after the first dose of the drug. There were no significant differences in maternal and neonatal morbidity between the two groups. There was a significant association between preinduction cervical length and the induction-to-delivery interval in both those receiving misoprostol and those treated with dinoprostone.*

Conclusions *The use of misoprostol is associated with a shorter duration of labor and a higher rate of vaginal delivery within 24 h from induction without an increase in maternal and neonatal morbidity. Transvaginal sonographic measurement of cervical length is useful in the prediction of the likelihood of vaginal delivery within 24 h of induction and of the induction-to-delivery interval and may be useful in the stratification of patients participating in randomized studies that examine the effectiveness of inducing agents.*

INTRODUCTION

Induction of labor is performed in about 20% of pregnancies[1]. Although in the majority of cases there is successful vaginal delivery, in about 20% of cases there is failure of induction necessitating Cesarean section[2,3]. Another important complication of induction is hyperstimulation, which is associated with both maternal and perinatal mortality and morbidity[4].

The success of induction is primarily dependent on the preinduction condition of the cervix. When the cervix is favorable the usual method of induction is amniotomy and oxytocin, whereas with an unfavorable cervix vaginal prostaglandins are commonly used. Although prostaglandins licensed for obstetric applications have been used extensively, they are expensive and unstable, requiring refrigerated storage. In the UK and many other countries the only prostaglandin preparations licensed for induction of labor at term are prostaglandin E_2.

Recent interest in inducing agents has focused on misoprostol, a synthetic prostaglandin PGE_1 analog, which was first introduced for the treatment of gastric and duodenal ulcers. Misoprostol is about 100 times cheaper than PGE_2 preparations and is stable at room temperature. Several randomized studies have demonstrated that misoprostol may be more effective than other inducing agents, with a higher rate of vaginal delivery within 24 h of induction (Table 1)[5–14]. However, the use of vaginal misoprostol has been associated with increased uterine hypercontractility, although there is no apparent increase in operative delivery rates or neonatal morbidity[15].

The aims of this randomized study were to investigate further the efficacy and safety of misoprostol in the induction of labor at term by comparing this agent with the commonly used dinoprostone gel.

Correspondence: Prof. K. H. Nicolaides, Harris Birthright Research Centre for Fetal Medicine, King's College Hospital Medical School, Denmark Hill, London SE5 8RX (e-mail: fmf@fetalmedicine.com)

Presented at The Fetal Medicine Foundation's meeting on Research and Developments in Fetal Medicine, London, August 30th–September 1st 2001.

Table 1 Randomized trials comparing 50 μg vaginal misoprostol with dinoprostone gel for induction of labor

Reference	n	*Misoprostol: regime*	*Dinoprostone: regime*	*Misoprostol: Vaginal delivery*		*Dinoprostone: Vaginal delivery*		*Misoprostol*		*Dinoprostone*	
				All (%)	*< 24 h (%)*	*All (%)*	*< 24 h (%)*	*Tachysystole (%)*	*Hyperstimulation (%)*	*Tachysystole (%)*	*Hyperstimulation (%)*
Sanchez-Ramos *et al.*[5]	129	50 μg 4-hourly	2 mg once	78	—	78	—	34	11	14	5
Tabor *et al.*[6]	127	50 μg 4-hourly	0.5 mg 6-hourly	75	—	75	—	—	—	—	—
Wing *et al.*[7]	135	50 μg 3-hourly	0.5 mg 6-hourly	85	71	81	48	37	7	12	3
Chuck and Huffaker[8]	99	50 μg 4-hourly	0.5 mg 6-hourly	80	—	80	—	—	2	—	4
Mundle and Young[9]	222	50 μg 4-hourly	0.5 mg 6-hourly or 1–2 mg 6-hourly	86	—	89	—	—	—	—	—
Buser *et al.*[10]	155	50 μg 4-hourly	0.5 mg 6-hourly	65	—	78	—	8	18	1	0
Surbek *et al.*[11]	100	50 μg 4-hourly	3 mg 6-hourly	88	—	86	—	8	0	14	2
Sanchez-Ramos *et al.*[12]	223	50 μg 3-hourly	10 mg 12-hourly	78	71	87	61	21	11	7	8
Kolderup *et al.*[13]	159	50 μg 4-hourly	0.5 mg 6-hourly	72	53	73	36	36	6	10	1
Danielian *et al.*[14]	211	50 μg 4-hourly	1 mg 6-hourly	89	—	87	—	5	0	4	1
Total	1560			79.7	65.4	82.3	50.0	20.7	7.3	8.0	3.1

The pooled odds ratio for vaginal delivery was 0.85 (95% confidence interval (CI): 0.66, 1.10), for vaginal delivery within 24 h was 1.96 (95% CI: 1.37, 2.81), for tachysystole was 3.08 (95% CI: 2.12, 4.47) and for hyperstimulation was 2.51 (95% CI: 1.45, 4.35).

METHODS

This was a randomized clinical trial of misoprostol and dinoprostone gel in women undergoing induction of labor at term. The study period was September 2000 to September 2001 and the participating centers were Universitäts-Frauenklinik, Kantonsspital, Basel, Switzerland and King George, Harold Wood and Southend Hospitals, Essex, UK. The entry criteria for the study were: women over the age of 16 years with singleton pregnancy at 37–42 weeks of gestation, live fetus in cephalic presentation, intact membranes, no history of antepartum hemorrhage, no previous Cesarean section or history of uterine surgery and no allergy or severe asthma in response to prostaglandins. Participants in the two groups were primarily compared to show significant difference in achieving vaginal delivery within 24 h, the incidence of hyperstimulation syndrome, Cesarean section rate and adverse neonatal outcome. The study was approved by the South Thames Multi-Centre Ethics Committee and subsequently by the local ethics committees.

Women meeting the study criteria were approached for participation and informed consent was obtained. There was a minimum 24-h period between recruitment and induction of labor so that subjects had adequate time to consider all available information on the trial.

Study protocol

In the participating centers the decision for induction of labor was taken by an obstetrician. All eligible women were invited to participate in the study. Those agreeing to take part were randomly allocated to one of the two inducing agents. Computer generated random number lists were drawn up by a medical statistician, with randomization in blocks of 10. The person recruiting the woman for the study was blinded to the trial drug. Allocation was performed by contacting the lead researcher who held the randomization code and each woman was then assigned a sequential study number corresponding to one of the inducing agents. Participants in the randomized trial were admitted to the antenatal or labor ward on the morning of induction of labor at 08.00 h. A 30-min admission cardiotocogram was recorded. Women were also offered the option of preinduction sonographic cervical assessment.

Pre-induction cervical assessment

Women had agreed to this part of the study at recruitment by signing a consent form. Transvaginal sonography was carried out by sonographers who had received The Fetal Medicine Foundation Certificate of Competence in Cervical Assessment. The probe was placed in the vagina approximately 3 cm proximal to the cervix to avoid any cervical distortion of its position or shape and a sagittal view of the cervix, with the echogenic endocervical mucosa along the length of the canal, was obtained. The calipers were used to measure the distance between the internal os and external os, the furthest points at which the cervical walls were juxtaposed[16–18]. Three measurements were obtained and the shortest, technically best measurement in the absence of uterine contractions was recorded.

Induction of labor

Induction of labor was performed according to the approved protocol. The Bishop score was assessed by an experienced obstetrician or midwife who was not aware of the sonographic findings. In the dinoprostone gel group, nulliparae with an unfavorable cervix (Bishop score < 5) received 2 mg dinoprostone gel (Pharmacia & Upjohn, Milton Keynes, UK) vaginally. Those with a Bishop score of 5 or 6 and all multiparae received 1 mg dinoprostone gel. Those with a Bishop score of ≥ 7 had artificial rupture of the membranes.

All women allocated to the misoprostol group received a 50-μg dose. The local pharmacy provided 100 μg misoprostol tablets (Cytotec, Searle, Canada imported into the UK by Idis Ltd, World Medicines, Surbiton, Surrey, UK) which were divided with a special cutter into two equal halves of 50 μg each. This was performed by an obstetrician or senior midwife with previous experience in the use of this particular misoprostol preparation (two of the obstetric units were familiar with the use of misoprostol for labor induction at term). Women in this group with a Bishop score of ≥ 7 also had artificial rupture of the membranes.

Monitoring and further management

Cardiotocography was performed for 40 min after the medication was administered, and if normal it was discontinued. In the event of contractions, monitoring was resumed and continued throughout the active phase of labor until delivery. The women were reviewed 6 h after the first administration of the inducing agent. A further dose of 1–2 mg dinoprostone gel or 50 μg misoprostol was repeated if necessary. The maximum dose over 24 h was 3 mg (4 mg in nulliparae with an unfavorable cervix) for the dinoprostone gel and 100 μg for misoprostol. The procedure was repeated the following day if labor did not ensue. If the procedure was not successful 48 h from the commencement of induction, the consultant obstetrician responsible for the care of the women made the decision on further management.

The study protocol included a standardized table for Bishop score evaluation printed on stickers and used before each dose administration to provide a record of each digital examination of the cervix and to secure accurate data keeping in the obstetric notes. Oxytocin augmentation was started in cases with unsatisfactory progress of labor (arrest of cervical dilatation for ≥ 2 h and/or inadequate uterine activity) or following amniotomy, at a rate of 1 mU/min. Oxytocin was not started for 6 h following administration of vaginal prostaglandins and was delivered via a syringe driver or infusion pump, increased at intervals of 30 min as needed to achieve an adequate contraction pattern. Surveillance of fetal heart rate and uterine activity was performed by external cardiotocography. Epidural anesthesia was given on request once labor was established.

All cardiotocograms were reviewed by one of the authors (G.K.P.) to identify and classify abnormal patterns. Uterine hyperstimulation syndrome was defined as uterine hyperstimulation (tachysystole: > five contractions per 10 min for at least 20 min, or hypersystole: contraction lasting ≥ 2 min) with fetal heart abnormalities, such as persistent decelerations, tachycardia, or reduced short-term variability. The suggested regime in the treatment of hyperstimulation was 0.25 mg subcutaneous terbutaline with positioning of the pregnant woman in the left lateral position and administration of oxygen via a facial mask.

Outcome measurements and collection of data

Patient characteristics including maternal age, gestational age, parity, body mass index, indication for induction and preinduction Bishop score were compared between the two study groups. The primary outcome measurement was vaginal delivery within 24 h from the first prostaglandin administration. Secondary outcome measurements included delivery within 24 h, Cesarean section rate, uterine hyperstimulation with or without fetal heart rate abnormalities, and maternal/neonatal outcomes such as uterine rupture, instrumental delivery rate, maternal side effects (nausea, vomiting, diarrhea, pyrexia), postpartum hemorrhage (blood loss > 500 mL), presence of meconium in the amniotic fluid, Apgar score < 7 at 5 min and admission to the neonatal intensive care unit. Outcomes were documented by the local trial co-ordinator on a specially designed data collection sheet and stored in an anonymous electronic database protected by a password known only by the trial co-ordinator.

Power calculations and statistical methods

A systematic review on randomized studies comparing vaginal misoprostol and dinoprostone for induction of labor reported that vaginal delivery within 24 h of induction was achieved in 60% and 40% of women, respectively[15]. On the basis of these data we calculated that to demonstrate a significant difference in efficacy between the two drugs it would be necessary to randomize about 400 women (test of significance at the 1% level, power 90%).

For comparison of results with previous studies a literature search was carried out that identified 10 randomized studies comparing 50 μg vaginal misoprostol with dinoprostone (Table 1).

Statistical analysis

The groups were compared by the chi-square or Fisher's exact tests for categorical variables and Student's *t*-test or the Mann–Whitney *U*-test for continuous variables where appropriate. All *P*-values are reported two sided and with Yates correction in chi-square tests. Pooled odds ratios were calculated using a fixed effects model (Mandel-Haenzsel method).

RESULTS

During the 1-year study period 670 women were recruited to the study and 335 were randomized into each group. Excluded from the study were 110 in the dinoprostone group

Table 2 Reasons for exclusion of patients from the study

	Dinoprostone (n)	*Misoprostol* (n)
Randomized (*n* = 670)	335	335
Excluded (*n* = 235)	110	125
Patient withdrew from the study	0	1
Spontaneous delivery before induction	86	95
Induction by amniotomy (Bishop score ≥ 7)	11	21
Cesarean section prior to induction*	4	4
Long delays in assessment after induction	8	3
Erroneous drug administration	1	1
Analyzed (*n* = 435)	225	210

*Abnormal fetal heart rate pattern or breech presentation before induction.

Table 3 Demographic characteristics of the two study groups

Characteristic	*Dinoprostone* (n = *225*)	*Misoprostol* (n = *210*)	P
Age (years, mean (SD))	29.7 (5.4)	29.5 (5.5)	0.69
Race (*n* (%))			0.91
White	176 (78.2)	167 (79.5)	
Black	23 (10.2)	19 (9.1)	
Asian	26 (11.6)	24 (11.4)	
Body mass index (mean (SD))	28.6 (6.0)	28.6 (6.1)	0.93
Smoker (*n* (%))	35 (15.6)	36 (17.1)	0.75
Nulliparous (*n* (%))	123 (54.7)	117 (55.7)	0.90
Gestational age (weeks, mean (SD))	40.6 (1.2)	40.6 (1.2)	0.93
Bishop score (mean (range))	3 (0–6)	3.2 (0–6)	0.17
Birth weight (g, mean (SD))	3589.0 (483.8)	3599.6 (525.3)	0.83

SD, standard deviation.

Table 4 Indications for induction of labor of the two study groups

Indication	*Dinoprostone* (n = *225*) (n)	*Misoprostol* (n = *210*) (n)
Prolonged pregnancy (> 41 weeks)	141	126
Pre-eclampsia	27	28
Fetal growth restriction	8	6
Fetal abnormality	2	1
Macrosomia	5	4
Oligohydramnios	3	2
Polyhydramnios	2	4
Reduced fetal movements	6	5
Maternal disease*	9	11
Maternal minor complaints/social†	14	19
Past obstetric complications	8	4

*Diabetes mellitus, cholestasis, hypothyroidism, renal disease, epilepsy, and systemic lupus erythematosus. †Nausea and vomiting, pruritus, symphysiopubic dysfunction, persistent abdominal pain and generally feeling unwell.

and 125 in the misoprostol group (Table 2). Thus, the remaining 435 women completed the study successfully and comprised the final sample for statistical analysis (225 had dinoprostone gel and 210 had misoprostol). Due to the high rate of spontaneous onset of labor between recruitment and scheduled day of induction (27%) analysis of the data was not by 'intention to treat' as this would have compromised the results on the performance of the two tested inducing agents.

There were no significant differences between the groups in demographic characteristics (Table 3) or indications for induction of labor (Table 4). Misoprostol, compared to dinoprostone, was associated with a significantly shorter induction to delivery interval and the incidence of vaginal delivery within 12 h and 24 h of induction (Table 5). The groups did not differ significantly in the rate of Cesarean section or hyperstimulation syndrome. None of the cases of hyperstimulation required treatment with tocolysis. All nine cases of excessive uterine contractility occurred after the first dose of the drug. In the dinoprostone group more women required repeated doses of the inducing agent before achieving active labor and were less likely to deliver following administration of a single dose. A significantly smaller proportion of women in the misoprostol group required oxytocin augmentation during labor.

There was no significant difference between the two groups in serious maternal morbidity (Table 6) or perinatal outcome (Table 7). In total, nine neonates were admitted to the neonatal intensive care unit, three in the dinoprostone group (two because of feeding problems and one with low Apgar scores and possible infection) and six in the misoprostol group (two because of feeding problems, two with transient tachypnea, one with low Apgar score but normal cord blood pH and base deficit, and one with possible infection). The duration of stay in the neonatal unit ranged from 1 to 3 days and all babies were discharged home with their mothers.

Table 5 Mode of delivery and course of labor in the two groups

Delivery/labor	*Dinoprostone* (n = *225)*	*Misoprostol* (n = *210)*	P
Interval (h, median (range))	19.0 (2.2–113.7)	14.6 (1.7–85.8)	0.0014
Delivery within 24 h (*n* (%))	140 (62.2)	153 (72.9)	0.024
Vaginal delivery (*n* (%))	182 (80.9)	172 (81.9)	0.88
within 24 h (*n* (%))	122 (54.2)	138 (65.7)	0.019
within 12 h (*n* (%))	45 (20.0)	69 (32.9)	0.0033
spontaneous (*n* (%))	146 (64.9)	140 (66.7)	0.77
instrumental (*n* (%))	36 (16.0)	32 (15.2)	0.93
Cesarean delivery (*n* (%))	43 (19.1)	38 (18.1)	
for fetal distress (*n* (%))	18 (8.0)	19 (9.0)	0.88
for failure to progress (*n* (%))	25 (11.1)	19 (9.0)	
Fetal distress during labor (*n* (%))*	66 (29.3)	61 (29.0)	0.99
Tachysystole (*n* (%))	1 (0.4)	1 (0.5)	1.0
Hyperstimulation syndrome (*n* (%))	2 (0.9)	5 (2.4)	0.27
Doses of agent (*n*, median (range))	2 (1–7)	1 (1–3)	< 0.0001
Single dose (*n* (%))	85 (37.8)	129 (61.4)	< 0.0001
Epidural analgesia (*n* (%))	89 (39.6)	80 (38.1)	0.83
Oxytocin augmentation (*n* (%))	67 (29.8)	43 (20.5)	0.034

*Abnormal cardiotocography.

Table 6 Maternal outcome in the two study groups

Outcome	*Dinoprostone* (n = *225)*	*Misoprostol* (n = *210)*	P
Minor complaints (*n* (%))*	17 (7.6)	19 (9.0)	0.70
Hospital stay (days, median (range))	3 (1–12)	3 (1–14)	0.33
Postpartum complication (*n* (%))	57 (25.3)	46 (21.9)	0.47
Postpartum hemorrhage (*n* (%))	45 (20.0)	37 (17.6)	0.61
Postpartum pyrexia (*n* (%))	6 (2.6)	4 (1.9)	0.75
Estimated blood loss (mL, median (range))	300 (50–2000)	250 (50–1700)	0.44

*Nausea, vomiting, diarrhea, pyrexia.

Table 7 Neonatal outcome in the two study groups

Outcome	*Dinoprostone* (n = *225)*	*Misoprostol* (n = *210)*	P
Apgar score at 5 min (median)	10	10	0.25
Apgar score < 7 at 5 min (*n* (%))	3 (1.3)	2 (1.0)	
Cord blood pH (median (range))	7.30 (6.96–7.45)	7.30 (7.06–7.48)	0.60
Cord blood pH < 7.15 (*n* (%))	13 (5.8)	8 (3.8)	0.38
Meconium staining of amniotic fluid (*n* (%))	24 (10.7)	29 (13.8)	0.39
Admission to neonatal unit (*n* (%))	3 (1.3)	6 (2.9)	0.32

Table 8 Vaginal delivery within 24 h in the two study groups by cervical length

	Dinoprostone		*Misoprostol*		
Cervical length (mm)	n	*Vaginal delivery < 24 h* (n (%))	n	*Vaginal delivery < 24 h* (n (%))	P
0–10	7	7 (100.0)	5	5 (100.0)	—
11–20	49	36 (73.5)	52	52 (100.0)	< 0.0001
21–30	81	54 (66.7)	75	54 (72.0)	0.58
31–40	55	14 (25.5)	54	17 (31.5)	0.63
41–50	14	0 (0.0)	9	0 (0.0)	—
Total	206	111 (53.9)	195	128 (65.6)	0.022

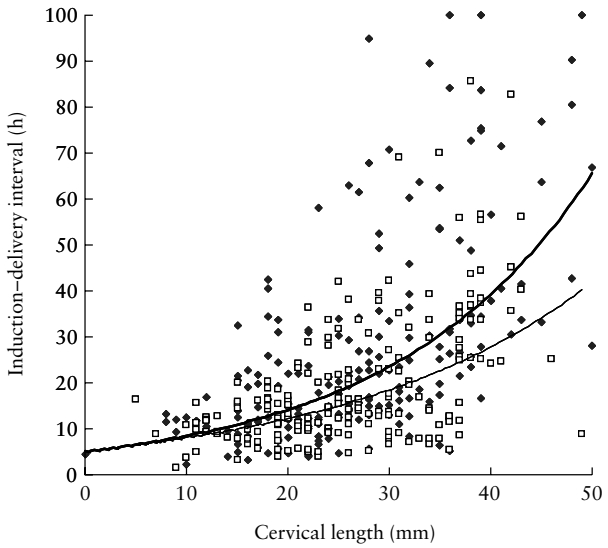

Figure 1 Sonographic cervical assessment in the prediction of time to delivery. ◆, dinoprostone gel (bold line); □, misoprostol (thin line).

Cervical length measurement

There was a significant association between preinduction cervical length and the induction to delivery interval in both those receiving misoprostol ($r = 0.546$; $P < 0.0001$) and those treated with dinoprostone ($r = 0.588$; $P < 0.0001$) (Figure 1). Vaginal delivery within 24 h of induction occurred in 65.6% (128 of 195) of cases in the misoprostol group and in 53.9% (111 of 206) of cases in the dinoprostone group ($P < 0.022$). The two groups are compared according to preinduction cervical length in Table 8. Essentially, in both groups delivery occurred within 24 h of induction in all patients with cervical length of ≤ 10 mm and in none with cervical length of > 40 mm. Significant differences between the groups were observed for those with cervical lengths of 11–20 mm.

DISCUSSION

This randomized study has compared vaginal misoprostol (50 μg 6-hourly) with dinoprostone gel (1–2 mg 6-hourly) for induction of labor at term. The findings have demonstrated that the use of misoprostol is associated with a shorter duration of labor, higher rate of vaginal delivery within 24 h from induction (65.7 vs. 54.2%) and less need for oxytocin augmentation, without an increase in the rate of Cesarean section or maternal and neonatal morbidity.

There are 10 previous randomized studies, which compared vaginal misoprostol (50 μg) with dinoprostone for induction of labor at term (Table 1). In general, there was no significant difference between the groups in the incidence of vaginal delivery but in the three studies that provided data on the incidence of vaginal delivery within 24 h of induction this was higher in the misoprostol group. Misoprostol was associated with a higher rate of tachysystole but the incidence of hyperstimulation syndrome was not significantly different between the two groups, although this may simply reflect the small number of cases examined.

Our findings suggest that uterine tachysystole and hyperstimulation syndrome may be avoided by administering misoprostol every 6 hours with a maximum of two doses in 24 h, rather than at a higher frequency. In our study all cases of tachysystole and hyperstimulation syndrome followed the administration of a single dose of the inducing agent. Excessive uterine contractility may be partially a primary myometrial effect and partially a cumulative effect secondary to frequent dosage of misoprostol[7]. Administration of 50 μg misoprostol, 6-hourly, seems to eliminate the latter effect. Previous studies have suggested that the incidence of hyperstimulation can be further reduced by the administration of a smaller dose of misoprostol (25 μg rather than 50 μg) without compromising the effectiveness of the drug[15]. However, such low-dose regimes are difficult to introduce because the drug is currently available in 100–200 μg tablets and the use of 25 μg would require multiple cutting of the tablet.

Preinduction sonographic measurement of cervical length helps in the prediction of the likelihood of vaginal delivery within 24 h of induction and of the induction-to-delivery interval[19]. Furthermore, this measurement may be useful in the stratification of patients participating in randomized studies that examine the effectiveness of inducing agents. In our study vaginal delivery within 24 h of induction occurred in all patients with a cervical length of ≤ 10 mm and in none with a cervical length of > 40 mm, irrespective of the inducing agent. Consequently, the significant improvement observed with misoprostol was due to the beneficial effect in those with a preinduction cervical length of 11–40 mm.

ACKNOWLEDGMENT

The study was funded by The Fetal Medicine Foundation (Registered Charity 1037116).

REFERENCES

1 RCOG. Induction of labour. Evidence-based Clinical Guideline Number 9. London: RCOG Clinical Support Unit, 2001
2 Arulkumaran S, Gibb DM, Tambyraja RL, Heng SH, Ratnam SS. Failed induction of labour. *Aust NZ J Obstet Gynaecol* 1985; 25: 190–3
3 Crowley P. Interventions for preventing or improving the outcome of delivery at or beyond term. (Cochrane Review). *The Cochrane Library*. Oxford: Update Software, 2001: Issue 3
4 Graves G, Baskett T, Gray JH, Luther ER. The effect of vaginal administration of various doses of prostaglandin E2 gel on cervical ripening and induction of labor. *Am J Obstet Gynecol* 1985; 151: 178–81
5 Sanchez-Ramos L, Kaunitz AM, Del Valle GO, Delke I, Schoeder P. Labor induction with the prostaglandin E1 methyl analogue misoprostol versus oxytocin: a randomized trial. *Obstet Gynecol* 1993; 81: 332–6
6 Tabor B, Anderson J, Stettler B, Wetwiska T. Misoprostol versus prostaglandin E2 gel for cervical ripening. *Am J Obstet Gynecol* 1995; 172: 425 (S605)
7 Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. *Am J Obstet Gynecol* 1995; 172: 1804–10
8 Chuck FJ, Huffaker BJ. Labor induction with intravaginal misoprostol versus intracervical prostaglandin E2 gel (Prepidil Gel): Randomized comparison. *Am J Obstet Gynecol* 1995; 173: 1137–42

9 Mundle WR, Young DC. Vaginal misoprostol for induction of labor: a randomized controlled trial. *Obstet Gynecol* 1996; 88: 521–5
10 Buser D, Mora G, Arias F. A randomized comparison between misoprostol and dinoprostone for cervical ripening and labor induction in patients with with unfavorable cervices. *Obstet Gynecol* 1997; 89: 581–5
11 Surbek DV, Boesiger H, Hoesli I, Pavic N, Holzgreve W. A double-blind comparison of the safety and efficacy of intravaginal misoprostol and prostaglandin E2 to induce labor. *Am J Obstet Gynecol* 1997; 177: 1018–23
12 Sanchez-Ramos L, Peterson DE, Delke I, Gaudier FL, Kaunitz AM. Labor induction with prostaglandin E1 misoprostol compared with dinoprostone vaginal insert: a randomized trial. *Obstet Gynecol* 1998; 91: 401–5
13 Kolderup L, McLean L, Grullon K, Safford K, Kilpatrick SJ. Misoprostol is more efficacious for labor induction than prostaglandin F2 but is it associated with more risk? *Am J Obstet Gynecol* 1999; 180: 1543–50
14 Danielian P, Porter B, Ferri N, Summers J, Templeton A. Misoprostol for induction of labour at term: a more effective agent than dinoprostone vaginal gel. *Br J Obstet Gynaecol* 1999; 106: 793–7
15 Hofmeyr GJ, Gulmezoglou AM, Alfirevic Z. Misoprostol for induction of labour: a systematic review. *Br J Obstet Gynaecol* 1999; 106: 798–803
16 Sonek JD, Iams JD, Blumenfeld M, Johnson F, Landon M, Gabbe S. Measurement of cervical length in pregnancy: comparison between vaginal ultrasonography and digital examination. *Obstet Gynecol* 1990; 76: 172–5
17 Anderson HF, Nugent CE, Wanty SD, Hayashi RH. Prediction of risk for preterm delivery by ultrasonographic measurement of cervical length. *Am J Obstet Gynecol* 1990; 163: 859–67
18 Sonek J, Shellhaas C. Cervical sonography: a review. *Ultrasound Obstet Gynecol* 1998; 11: 71–8
19 Pandis GK, Papageorghiou AT, Ramanathan VG, Thompson MO, Nicolaides KH. Preinduction sonographic measurement of cervical length in the prediction of successful induction of labor. *Ultrasound Obstet Gynecol* 2001; 18: 623–8

APPENDIX

Local co-ordinators of The Fetal Medicine Foundation Induction of Labour Project:
Universitäts-Frauenklinik, Kantonsspital, Basel, Switzerland: E. Visca, A. Gairing, I. Hösli; King George Hospital, Essex, UK: J. Webber, R. Howard; Harold Wood Hospital, Essex, UK: C. Yu, C. Otigbah; Southend General Hospital, Essex, UK: T. Smith, M. Hassanaien.