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ORIGINAL ARTICLE

Comparative efficacy and safety of vaginal misoprostol versus dinoprostone vaginal insert in labor induction at term: a randomized trial

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Abstract
Objective To compare efficacy and safety of vaginal misoprostol (PGE_1 analog) with dinoprostone (PGE_2 analog) vaginal insert for labor induction in term pregnancies.
Study design A total of 112 women with singleton pregnancies of ≥37 weeks of gestation, and low Bishop scores underwent labor induction. The subjects were randomized to receive either 50 μg misoprostol intravaginally every 4 h to a maximum of five doses or a 10 mg dinoprostone vaginal insert for a maximum of 12 h. Time interval from induction to vaginal delivery, vaginal delivery rates within 12 and 24 h, requirement of oxytocin augmentation, incidence of tachysystole and uterine hyperstimulation, mode of delivery, rate of cesarean section due to fetal distress and neonatal outcome were outcome measures. Student's *t* test, Chi square test, Fischer's exact test were used for statistical analysis.
Results Time interval from induction to vaginal delivery was found to be significantly shorter in misoprostol group when compared to dinoprostone subjects (680 ± 329 min vs. 1070 ± 435 min, $P < 0.001$). Vaginal delivery rates within 12 h were found to be significantly higher with misoprostol induction [$n = 37$ (66%) vs. $n = 25$ (44.6%); $P = 0.02$], whereas vaginal delivery rates in 24 h did not differ significantly between groups [$n = 41$ (73.2%) vs. $n = 36$ (64.2%); $P = 0.3$]. More subjects required oxytocin augmentation in dinoprostone group [$n = 35$ (62.5%) vs. $n = 20$ (35.7%), $P = 0.005$] and cardiotocography tracings revealed early decelerations occurring more frequently with misoprostol induction (10.7 vs. 0%, $P = 0.03$). Tachysystole and uterine hyperstimulation, mode of delivery, rate of cesarean sections due to fetal distress and adverse neonatal outcome were not demonstrated to be significantly different between groups ($P = 1$, $P = 0.5$, $P = 0.4$, $P = 0.22$, $P = 0.5$).
Conclusion Using vaginal misoprostol is an effective way of labor induction in term pregnant women with unfavorable cervices, since it is associated with a shorter duration of labor induction and higher rates of vaginal delivery within 12 h. Misoprostol and dinoprostone are equally safe, since misoprostol did not result in a rise in maternal and neonatal morbidity, namely, tachysystole, uterine hyperstimulation, cesarean section rates and admission to neonatal intensive care units as reported previously in literature.

Keywords Misoprostol · Dinoprostone · Labor induction

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Introduction

Labor induction at term is applied in various fetal–maternal indications as required for 15–30% of pregnancies in obstetric practice [1–3]. This procedure, with low Bishop scores, may result in an exhausting labor course associated with higher rates of operative deliveries, longer hospitalization, and increased medical costs [4–6]. Cervical ripeners, namely, laminaria tents, estrogen gels, relaxin, prostaglandin (PG) analogs have been used with varying success [7, 8]. Various PG preparations including misoprostol vaginal tablets, dinoprostone vaginal gel and vaginal insert are commercially available to be used in labor induction [8].

Misoprostol is a synthetic prostaglandin E_1 analog and has been reported to be a considerably safe and efficacious cervical ripener [1, 9–11]. It is inexpensive, easy to administer, stable at room temperature, does not require refrigeration [12]. In spite of different doses and routes of administration (sublingual, oral, vaginal), ideal dosage and mode of administration still remain to be controversial. Potential complications such as uterine rupture, tachysystole and uterine hyperstimulation should be emphasized with respect to adverse maternal–neonatal outcome [10]. A considerable amount of work has concentrated on optimum dosing regimen that minimizes the risk while maintaining efficacy since both efficacy and side effects are suggested to be dose-dependent [10, 13].

At present, the only agent specifically approved by US Food and Drug Administration (FDA) for labor induction is dinoprostone [14]. Dinoprostone; a PGE_2 analog has been shown to be an efficacious agent of cervical ripening and labor induction, available as gel, tablet, pessary or suppository [13]. However, it is expensive, requires refrigeration, endocervical administration, and mostly oxytocin augmentation [3]. It is suggested to be safer than misoprostol as it is not associated with increased incidence of uterine hyperstimulation and cesarean delivery rates.

In this study, we aimed to compare safety and efficacy of vaginal misoprostol with that of dinoprostone vaginal insert for labor induction in term pregnancies.

Material and methods

The study was conducted at Kocaeli University, School of Medicine, Department of Obstetrics and Gynecology between July 2005 and December 2006. The study was approved by Local Ethics Committee of the University and performed in accordance with the ethical standards for human research established by the Declaration of Helsinki. Written informed consents were obtained.

A total of 112 pregnant women over 37 weeks of gestation, undergoing labor induction were enrolled. Inclusion criteria were singleton pregnancy ≥37 weeks of gestation (37–42 weeks), a maternal–fetal indication of labor induction, cephalic presentation, intact amniochorionic membranes, a cervical Bishop score of ≤4, reassuring fetal heart rate. Exclusion criteria were fetal congenital abnormalities, parity >5, any contraindication for vaginal delivery, antepartum bleeding of unknown etiology, cardiopulmonary, renal, hepatic disease, glaucoma, known hypersensitivity to prostaglandins, cephalopelvic disproportion, estimated fetal birth weight over 4,500 g in nondiabetic and over 4,000 g in diabetic patients, placenta previa, known or suspected chorioamnionitis, previous uterine scar (myomectomy or cesarean delivery).

The subjects were randomized to receive either 50 μg misoprostol (PGE_1 analog) ($n = 56$) intravaginally in the posterior fornix every 4 h to a maximum dose of 250 μg (Cytotec®, Searle, Chicago, IL, USA) until regular painful uterine contractions had been achieved or a 10 mg dinoprostone (PGE_2 analog) vaginal insert ($n = 56$) for a maximum of 12 h (Propess vaginal insert®, Ferring Pharmaceuticals, Berkshire, UK). Randomization was done by means of a computer-generated randomization table, and allocations were placed in consecutively numbered and sealed, opaque envelopes.

Dinoprostone vaginal insert is a preparation of PGE_2 packaged in a hydrogel polymer matrix and designed for intravaginal release of 10 mg dinoprostone at a rate of 0.3 mg/h over 12 h. It is placed transversely in the posterior vaginal fornix for 12 h or removed earlier if regular painful uterine contractions were recorded or rupture of membranes occured.

The fetal heart rate was monitored 30 min before and 1 h after administration of prostaglandin analogs. Intermittent auscultation was performed at least hourly before the onset of active labor and then continuously in active labor.

Intravenous oxytocin augmentation was commenced at 2 mU/min and increased as required by 1 mU/min every 20 min to a maximum of 30 mU/min in cases with infrequent uterine contractions (<3/10 min) or arrested labor ≥2 h at ≥4-cm cervical dilatation. Oxytocin infusion was not started until at least 30 min after removal of the insert or at least 4–6 h after misoprostol and was given for a maximum of 8 h [15]. Amniotomy was performed at cervical dilatation of 4 cm. Epidural analgesia was given at the subject's request.

Fetal well-being was confirmed by cardiotocography (CTG). Fetal heart rate (FHR) patterns were reviewed by a single observer (S.Ö.).

Nonreassuring patterns were classified as follows [16]:

Any of the following for >15 min:

1. Persistent late decelerations (>50% of uterine contractions);
2. Sinusoidal pattern;
3. Variable decelerations with ≥1 of the following:
   - Relative drop of ≥70 beats/min or absolute drop to ≤70 beats/min for >60 s;
   - Persistent slow return to baseline;
   - Long-term variability <5 beats/min;
   - Tachycardia >160 beats/min;
4. Recurrent prolonged decelerations (≥2 below 70 beats/min for >90 s);
5. Any of the following for >60 min:
   a. Tachycardia >160 beats/min with long-term variability <5 beats/min;

b. Persistent decreased variability (≤5 beats/min for >60 min).

In the presence of FHR abnormality, a number of measures were undertaken such as oxygen supplementation by mask, maternal positioning to the left lateral side, intravenous hydration, cessation of oxytocin infusion or removal of the remainder of prostaglandin analogs, infusion of tocolytic agent.

Active labor was defined as recording minimum three uterine contractions of 40–50 s of duration in 10 min. Labor induction was accepted to be successful if active labor could be achieved, while unsuccessful if active labor could not be initiated. If the cervix was not favorable for artificial rupture of membranes after five doses of misoprostol or 12 h of dinoprostone or oxytocin augmentation, labor induction was considered to have failed, and the women were offered cesarean section.

Tachysystole was defined as at least six contractions in 10 min for two consecutive 10 min. A single contraction of at least 2 min was determined as uterine hypertonus.

Tachysystole or hypertonus associated with nonreassuring fetal heart rate tracings was named as uterine hyperstimulation.

Age, parity, gestational age, indication of labor induction, Bishop score, route of delivery, time interval from induction till active labor, time intervals to delivery and vaginal delivery, vaginal delivery rates within 12 and 24 h, cesarean section rates for fetal distress and unsuccessful labor induction, oxytocin requirement, intrapartum complications such as uterine hyperstimulation, tachysystole, fetal distress and meconium stained amnios, adverse effects due to administered medical agents such as nausea, vomiting, diarrhea, fever, neonatal outcome measures; umbilical arterial pH recordings below 7.10, Apgar scores, admission to neonatal intensive care unit (NICU), meconium aspiration (presence of meconium below the vocal cords after laryngoscopic examination) and fetal birth weights were recorded.

Two study groups were compared by means of those variables in order to determine safety and efficacy of misoprostol and dinoprostone for labor induction. Vaginal delivery within 24 h was the primary outcome measure of this study while time interval to delivery, time interval to vaginal delivery, delivery and vaginal delivery rates within 12 h, uterine hyperstimulation and tachysystole, cesarean section rates due to fetal distress and neonatal outcome were suggested as secondary outcome measures.

On the basis of current literature, a total sample size of 103 women was required to provide 90% power to show a difference of 15% between groups for successful vaginal delivery within 24 h. This calculation was based on the success rate of 68% with misoprostol and 38% for dinoprostone vaginal insert [8].

Statistical analysis was performed by SPSS programme (Chicago IL 11). Continuous variables were assessed by Student's *t* test, whereas categoric variables were analyzed by Chi square and Fisher exact tests; $P < 0.05$ was considered to be statistically significant.

Results

Nulliparous pregnant women constituted of 51.8% ($n = 29$) and 57.1% ($n = 32$) of misoprostol and dinoprostone groups respectively ($P = 0.56$).

The indications of labor induction were similar in misoprostol and dinoprostone groups (Table 1).

Hypertensive disease of pregnancy, diabetes mellitus, history of infertility, postterm pregnancy, preterm labor, oligohydramnios, meconium stained amnios, intrauterine growth restriction (IUGR) did not appear to be occurring significantly more frequently in one group ($P = 0.13$, $P = 0.5$, $P = 0.5$, $P = 0.15$, $P = 0.37$, $P = 0.4$, $P = 0.71$, $P = 0.48$).

In misoprostol group, 14 (25%) women received 1 dose, 27 (48.21%) women received 2 doses, 12 (21.42%) cases received 3 doses, 3 (5.35%) cases required 4 doses of misoprostol.

Intrapartum variables, induction success rates and laboring data are shown in Table 2.

Delivery route was not significantly different between groups ($P = 0.403$). Cesarean section was performed due to fetal distress in 8 (14.3%) and 4 (7.1%) misoprostol and dinoprostone subjects, respectively, ($P = 0.222$). Failed induction [$n = 3$ (5.35%) vs. $n = 7$ (12.5%)] and arrest of dilatation/descent [$n = 3$ (5.35%) vs. $n = 7$ (12.5%)] were other cesarean section indications in misoprostol and dinoprostone groups, respectively.

Table 1 Indications for labor induction are shown

Indication of labor induction	Misoprostol ($n = 56$) (n, %)	Dinoprostone ($n = 56$) (n, %)	P
Hypertensive disease	16 (28.6)	16 (28.6)	1
Postterm pregnancy	14 (25)	8 (14.3)	0.15
IUGR	13 (23.2)	10 (17.9)	0.48
Oligohydramnios	6 (10.7)	9 (16.1)	0.40
Diabetes mellitus	2 (3.6)	1 (1.8)	0.55
Maternal disease	2 (3.6)	3 (5.35)	0.66
Psychosocial	1 (1.8)	4 (7.14)	0.16
Past obstetric complications	1 (1.8)	3 (5.35)	0.62
Impending macrosomia	1 (1.8)	2 (3.57)	0.57

IUGR intrauterine fetal growth restriction

* $P < 0.05$ statistically significant

Table 2 Intrapartum variables, laboring data and induction success rates are shown

	Misoprostol ($n = 56$) (n, %)	Dinoprostone ($n = 56$) (n, %)	P
Time interval to onset of labor (min)	389.8 ± 179	649.8 ± 322	<0.01*
Time interval to delivery (min)	629 ± 322	1023 ± 457	<0.001*
Time interval to vaginal delivery (min)	680 ± 329	1070 ± 435	<0.001*
Delivery within 12 h	43 (76.8)	27 (48.2)	0.002*
Vaginal delivery within 12 h	37 (66)	25 (44.6)	0.02*
Delivery within 24 h	54 (96.4)	48 (85.7)	0.047*
Vaginal delivery within 24 h	41 (73.2)	36 (64.2)	0.3
Delivery route (vaginal)	42 (75)	38 (67.9)	0.403
Cesarean section due to fetal distress	8 (14.3)	4 (7.1)	0.222
Early decelerations on CTG tracings	6 (10.7)	0	0.03*
Tachysystole	5 (8.9)	5 (8.9)	1
Uterine hyperstimulation	2 (3.6)	1 (1.8)	0.50
Successful induction	47 (83.9)	40 (71.4)	0.112
Requirement for oxytocin augmentation	20 (35.7)	35 (62.5)	0.005*
Hospitalization period (days)	1.89 ± 0.824	2.41 ± 1.07	0.005*

CTG cardiotocography

* $P < 0.05$ statistically significant

There were no significant differences in maternal outcome with respect to abruptio placenta, postpartum atonia, estimated blood loss between the two groups. No maternal death and uterine rupture were reported. Minor complications such as nausea, vomiting, diarrhea, fever, infection were not determined to occur more frequently in one of the groups. Incidence of vaginal lacerations and requirement of episiotomy were not significantly different between groups ($P = 1$, $P = 0.84$). Epidural analgesia application was also similar between groups.

Neonatal weight, 5-min Apgar score <7, cord blood pH <7.10, meconium stained amnios, requirement for resuscitation, requirement for intubation, NICU admission did not differ significantly between groups (Table 3). Perinatal death and hypoxic ischemia were not reported in neither misoprostol nor dinoprostone subjects.

Table 3 Neonatal outcome

	Misoprostol ($n = 56$)	Dinoprostone ($n = 56$)	P
Birth weight (g)	3250 ± 519	3119 ± 622	0.23
Apgar score <7 at 5 min	2 (3.6%)	2 (3.6%)	1
Cord blood pH <7.10	1 (1.78%)	1 (1.78%)	1
Meconium stained amniotic fluid	5 (8.9%)	3 (5.4%)	0.71
Requirement for resuscitation	2 (3.6%)	2 (3.6%)	1
Requirement for intubation	2 (3.6%)	1 (1.78%)	0.55
NICU admission	2 (3.6%)	3 (5.4%)	0.5

NICU neonatal intensive care unit

* $P < 0.05$ statistically significant

Discussion

A growing body of evidence regarding prostaglandin use for cervical ripening and labor induction pointed out that misoprostol might be more efficacious than the other induction agents with higher rates of vaginal delivery within 24 h [17, 18]. However, increased incidence of tachysystole and uterine hyperstimulation although not suggested to cause increased operative deliveries or adverse maternal–neonatal outcome, represents a major safety concern [10, 14]. Tachysystole and uterine hyperstimulation were reported in up to 30–70 and 7–8% with 50 μg dose of misoprostol administered 3–4 hourly, respectively [17, 18]. Even a lower dose of 25 μg misoprostol was shown to cause tachysystole with an incidence of 1.8–8.3% [11, 18].

Dinoprostone is suggested to be safer than misoprostol with respect to uterine contraction abnormalities. However, dinoprostone preparations are expensive and require refrigeration [1, 13].

Misoprostol administered orally or vaginally did appear to be more efficacious than dinoprostone achieving vaginal delivery within 24 h, reducing oxytocin augmentation in women at term with intact membranes and unfavorable cervix [9–11]. The issue of major concern was increased risk of tachysystole and uterine hypersensitivity of misoprostol use without fortunately increasing adverse outcome. However, some studies concluded that uterine contraction abnormalities did not occur more frequently with misoprostol. Rosenberg et al. [12] concluded that 50 μg misoprostol in comparison with dinoprostone has shortened time interval to vaginal delivery and tacysystole was not more frequently observed. Sanchez also concluded that dinoprostone vaginal insert was associated with lower rates of active

labor and increased time interval to vaginal delivery, whereas incidences of cesarean delivery and uterine contraction abnormalities were not significantly different in comparison with misoprostol induction [7]. Leukomage has also suggested more efficacious labor with shorter interval to delivery, more intrapartum CTG changes fortunately related with no abnormal maternal–neonatal outcome [19]. Our findings were in accordance with those findings that misoprostol provided shorter time intervals to onset of labor, shorter time intervals to delivery and vaginal delivery, more vaginal deliveries within 12 h, less oxytocin augmentation, shorter hospitalization period without increasing the incidence of tachysystole and uterine hyperstimulation.

Some others found no significant differences with respect to efficacy of those two agents. Wing and colleagues [11] reported that none of induction to delivery interval, oxytocin augmentation, delivery route and neonatal–maternal outcome was significantly different when they compared 25 μg vaginal misoprostol with dinoprostone. Langenegger [2] suggested that vaginal delivery rates within 24 h were not different in his study comparing oral misoprostol and dinoprostone. Hughes and Dällenbach [1, 20] found no significant differences regarding those parameters in their studies comparing vaginal misoprostol and dinoprostone and oral misoprostol and dinoprostone, respectively. Le Roux [21] compared three induction agents: oral misoprostol, vaginal misoprostol, and dinoprostone. Vaginal delivery rates were lower with oral misoprostol and the incidence of tachysystole was not increased, whereas the efficacies of vaginal misoprostol and dinoprostone were similar although vaginal misoprostol led to tachysystole and cesarean sections due to fetal distress more frequently.

Several investigators have reported excessive uterine activity and abnormal FHR patterns with misoprostol [14, 22]. Despite no increase in cesarean rates, increased incidence of nonreassuring CTG patterns with misoprostol was disturbing patient satisfaction in terms of both patient and physician anxiety [19]. Garry and Buser [8, 22] both in their studies concluded that misoprostol induction resulted in higher frequency of nonreassuring FHR patterns associated with hyperstimulation and increased cesarean rates due to FHR abnormalities. Hemodynamic changes secondary to misoprostol may be explained by increased resistance in uterine vessels after oral misoprostol in early pregnancy [23]. Chen et al. [24] demonstrated that labor induction with misoprostol lacks the normal fetal adaptation to labor which is declining impedance in both umbilical artery and middle cerebral artery. No increase in neonatal morbidity–mortality was identified, but the involved studies in this manner were not large enough to adequately assess relatively infrequent but serious complications such as neonatal asphyxia or death. Some investigators such as Langenegger [2] observed no significant differences with respect to FHR patterns in his study in which oral misoprostol and dinoprostone were compared. In our study, incidences of tachysystole and uterine hyperstimulation did not differ significantly between groups. Early decelerations were more frequently recorded with misoprostol induction without leading to increased abdominal delivery and adverse neonatal outcome.

Some studies reported meconium stained amnios with misoprostol [12, 18]; however, some others attributed this to a direct effect of misoprostol on fetal gastrointestinal tract rather than being a sign of fetal distress [1]. In our study, meconium stained amnios was not more frequently observed in either group.

In order to compare misoprostol and dinoprostone in terms of delivery route, some investigators concluded that more or equal vaginal delivery occurred with misoprostol [21], whereas some reported less vaginal delivery and increased cesarean rates with misoprostol [3]. Rosenberg et al. [12] reported increased cesarean rates due to fetal distress with misoprostol. Megalo [14] concluded that there was a trend towards increased cesarean rates for failed induction or arrest of labor in dinoprostone group, whereas misoprostol led to significantly increased abdominal delivery due to fetal distress. In our study, delivery route and cesarean section rates due to fetal distress did not differ significantly between groups.

As a conclusion, vaginal misoprostol 50 μg when compared to dinoprostone vaginal insert provides shorter time interval to onset of labor, shorter time intervals to both delivery and vaginal delivery, higher vaginal delivery rates within 12 h, less oxytocin augmentation and shorter hospitalization without causing increased tachysystole, uterine hyperstimulation, cesarean rates due to fetal distress, adverse maternal–neonatal outcome. Its cost benefit is apparent; less oxytocin further saves costs. It requires no refrigeration and has a long shelf life. It may be recommended as an efficacious and safe option of labor induction. As the present trial was not blinded which should be considered as somewhat a limit for our conclusions, further investigation is required to focus on optimal dosage and intervals to decrease tachysystole, uterine hyperstimulation, and uterine rupture reported in literature.

Conflict of interest statement None.

References

1. Dällenbach P, Boulvain M, Viardot C, Irion O (2003) Oral misoprostol or vaginal dinoprostone for labor induction: a randomized controlled trial. Am J Obstet Gynecol 188:162–167. doi:10.1067/mob.2003.108
2. Langenegger EJ, Odendaal HJ, Grove D (2005) Oral misoprostol versus intracervical dinoprostone for induction of labor. Int J Gynaecol Obstet 88:242–248. doi:10.1016/j.ijgo.2004.12.005

3. Agarwal N, Gupta A, Kriplan A, Bhatla N (2003) Six hourly vaginal misoprostol versus intracervical dinoprostone for cervical ripening and labor induction. J Obstet Gynaecol Res 29(3):147–151. doi:10.1046/j.1341-8076.2003.00091.x
4. Gregson S, Waterstone M, Norman I, Murrels T (2005) A randomised controlled trial comparing low dose vaginal misoprostol and dinoprostone vaginal gel for inducing labour at term. BJOG An Int J Obstet Gynaecol 112:438–444. doi:10.1111/j.1471-0528.2004.00496.x
5. van Gemund N, Scherjon S, le Cessie S, van Leeuwen SJH, van Roosmaln J, Kanhai HHH (2004) A randomised trial comparing low dose vaginal misoprostol and dinoprostone for labour induction. BJOG An Int J Obstet Gynaecol 111:42–49. doi:10.1046/j.1471-0528.2003.00010.x
6. Chang YK, Chen H, Yu MH, Liu HS (2003) Intracervical misoprostol and prostaglandin E_2 for labor induction. Int J Gynaecol Obstet 80:23–28. doi:10.1016/S0020-7292(02)00333-8
7. Sanchez-Ramos L, Kaunitz AM, Delke I, Gaudier FL (1999) Cervical ripening and labor induction with a controlled release dinoprostone vaginal insert: a meta-analysis. Obstet Gynecol 94:878–883. doi:10.1016/S0029-7844(99)00320-8
8. Garry D, Figueroa R, Kalish RB, Catalano CJ, Maulik D (2003) Randomized controlled trial of vaginal misoprostol versus dinoprostone vaginal insert for labor induction. J Matern Fetal Neonatal Med 13:254–259. doi:10.1080/713605867
9. Sanchez-Ramos L, Kaunitz AM (2000) Misoprostol for cervical ripening and labor induction: a systematic review of the literature. Clin Obstet Gynecol 43:475–488. doi:10.1097/00003081-200009000-00008
10. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL (1997) Misoprostol for cervical ripening and labor induction: a meta-analysis. Obstet Gynecol 89:633–642. doi:10.1016/S0029-7844(96)00374-2
11. Wing DA (1999) Labor induction with misoprostol. Am J Obstet Gynecol 181:339–345. doi:10.1016/S0002-9378(99)70558-2
12. Rosenberg P, Chevret S, Senat MV et al (2004) A randomized trial that compared intravaginal misoprostol and dinoprostone vaginal insert in pregnancies at high risk of fetal distress. Am J Obstet Gynecol 191:247–253. doi:10.1016/j.ajog.2003.12.038
13. Shetty A, Livingstone I, Acharya A, Rice P, Danielian P, Templeton A (2004) A randomised comparison of oral misoprostol and vaginal prostaglandin E_2 tablets in labour induction at term. BJOG An Int J Obstet Gynaecol 111:436–440. doi:10.1111/j.1471-0528.2004.00107.x
14. Megalo A, Petignat P, Hahlfeld P (2004) Influence of misoprostol or prostaglandin E_2 for induction of labor on the incidence of pathological CTG tracing: a randomized trial. Eur J Obstet Gynecol Reprod Biol 116:34–38. doi:10.1016/j.ejogrb.2004.01.038
15. American College of Obstetricians and Gynecologists (1995) Induction of labor. ACOG Technical Bulletin No.217, ACOG, Washington, DC
16. Garite TJ, Dildy GA, McNamara H et al (2000) A multicenter controlled trial of fetal pulse oximetry in the intrapartum management of nonreassuring fetal heart rate patterns. Am J Obstet Gynecol 183(5):1049–1058. doi:10.1067/mob.2000.110632
17. Sanchez-Ramos L, Kaunitz AM, Del Vale GO, Delke I, Schoeder P (1993) Labor induction with the prostaglandin E_1 methyl analogue misoprostol versus oxytocin: a randomized trial. Obstet Gynecol 81:332–336
18. Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH (1995) A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. Am J Obstet Gynecol 172:1804–1810. doi:10.1016/0002-9378(95)91415-3
19. Leukomage AU, Forsyth SF, Sullivan KR, El Refaey H, Rodeck CH (2003) Dinoprostone versus misoprostol. A randomized study of nulliparous women undergoing induction of labor. Acta Obstet Gynecol Scand 82:133–137. doi:10.1034/j.1600-0412.2003.00066.x
20. Hughes EG, Kelly AJ, Kavanagh J (2001) Dinoprostone vaginal insert for cervical ripening and labor induction: a metaanalysis. Obstet Gynecol 97:847–855. doi:10.1016/S0029-7844(00)01216-3
21. Le Roux PA, Olaragun JO, Penny J, Anthony J (2002) Oral and vaginal misoprostol compared with dinoprostone for induction of labor: a randomized controlled trial. Obstet Gynecol 99:201–205. doi:10.1016/S0029-7844(01)01681-7
22. Buser D, Mora G, Arias F (1997) A randomized comparison between misoprostol and dinoprostone for cervical ripening and labor induction in patients with unfavorable cervices. Obstet Gynecol 89:581–585. doi:10.1016/S0029-7844(97)00015-X
23. Yip SK, Tse AO, Haines CJ, Chung TK (2000) Misoprostol's effect on uterine arterial blood flow and fetal heart rate in early pregnancy. Obstet Gynecol 95:232–235. doi:10.1016/S0029-7844(99)00472-X
24. Chen WH, Lai HC, Tang YH, Liu HS (1999) Fetal Doppler hemodynamic changes in spontaneous versus prostaglandin induced active labor. Acta Obstet Gynecol Scand 78:599–604. doi:10.1034/j.1600-0412.1999.780707.x