INTRODUCTION

Prostaglandins have revolutionized obstetric practice. In particular, the advent of misoprostol has precipitated an enormous amount of innovative research as well as controversy. At present, misoprostol is being simultaneously investigated for its role in the management of postpartum hemorrhage (PPH), induction of labor, cervical ripening and termination of pregnancy. Initially, this drug was only approved by the US Food and Drug Administration (FDA) in 1988 for oral administration for the prevention and treatment of peptic ulcers associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs). Since the early 1990s, however, misoprostol has been viewed with increasing interest by obstetricians and gynecologists because of its uterotonic and cervical ripening activity. The multiple off-label uses for misoprostol, supported by a literature comprising thousands of individual articles, underlie its description as ‘one of the most important medications in obstetrical practice’\(^1\). Even as recently as 2005, misoprostol was not approved by the FDA for use in pregnant women, a stand strangely and yet strongly supported by its manufacturer\(^2\).

MISOPROSTOL

Misoprostol is a synthetic prostaglandin (PG) E1 analogue. Naturally occurring PGE1 is not orally sustainable, as it is unstable in acid media and is also not suitable for parenteral use because of its rapid degradation in the blood. Misoprostol, the synthetic PGE1 analogue, is produced by bringing about an alteration in the chemical structure of the naturally occurring compound, thereby making it orally stable and clinically useful. Misoprostol is otherwise called alprostadil and its chemical formula is \(C_{22}H_{38}O_5\) (\(\pm\)-methyl(13E)-11,16-dihydroxy-16-methyl-9-oxo-prost-13-enoate), as shown in Figure 1\(^3\).

Misoprostol is manufactured as oral tablets of 200 \(\mu\)g scored and 100 \(\mu\)g unscored. It possesses three major advantages – stability at ambient temperature, long shelf-life and low cost – that have made it a central focus of research in obstetrics and gynecology for the past 25 years\(^4\). Misoprostol is rapidly absorbed via the oral route and, although not formulated for parenteral use, can also be administered sublingually (buccally), rectally and vaginally\(^5\)–\(^7\).

Pharmacokinetics, physiology and teratogenicity profile

Misoprostol is extensively absorbed and undergoes rapid de-esterification to misoprostol acid; this latter compound is responsible for its clinical activity and, unlike the parent compound, it is detectable in plasma. After oral administration, the peak level of misoprostol acid is reached within 9–15 min, with a terminal half-life of 20–40 min. Plasma levels of misoprostol acid vary considerably between and within studies, but mean values after single doses show a linear relationship with the dose over the range of 200–400 \(\mu\)g. No accumulation of misoprostol acid was noted in multiple dose studies and a plasma steady state was achieved within 2 days. The bioavailability of misoprostol is decreased when administered with food or antacids\(^8\).

Misoprostol is primarily metabolized in the liver, and less than 1% of its active metabolite is excreted in the urine\(^9\). Patients with hepatic disease should receive smaller doses, whereas dose adjustment is not necessary for patients with renal disease not requiring dialysis. Misoprostol has no known drug interactions and does not induce the hepatic enzyme systems\(^9\).

Pharmacokinetic studies of misoprostol in pregnant women show that sublingual and oral doses used for first-trimester termination of pregnancy produce earlier and higher peak plasma concentrations than vaginal or rectal doses, resulting in earlier, more pronounced uterine tonus (oral misoprostol 7.8 \(\pm\) 3.0 min vs. vaginal misoprostol 20.9 \(\pm\) 5.3 min)\(^6\)\(^7\)\(^10\). These findings also have been validated in women after delivery\(^11\). The effects of misoprostol on the reproductive tract are increased and gastrointestinal adverse effects are decreased when it is administered vaginally\(^10\)\(^12\)\(^13\).

![Chemical structure of misoprostol](image)
When misoprostol tablets are placed in the posterior fornix of the vagina, plasma concentrations of misoprostol acid peak in 1–2 h and then decline slowly (Figure 2)\(^5\). Vaginal application of misoprostol results in slower increases and lower peak plasma concentrations of misoprostol acid than does oral administration, but overall exposure to the drug is increased (indicated by the increased area under the curve in Figure 2)\(^5\). The peak plasma levels of misoprostol are sustained for up to 4 h after vaginal administration\(^5\) (Figure 2). Among women who were 9–11 weeks pregnant and given misoprostol before a surgical termination of pregnancy, intrauterine pressure began to increase an average of 8 min after oral and 21 min after vaginal administration.

Pressure was maximal 25 min after oral administration and 46 min after vaginal administration. Uterine contractility initially increased and reached a plateau 1 h after oral administration, whereas it increased on a continuous basis for 4 h after vaginal administration. Maximal uterine contractility was significantly higher after vaginal administration\(^10\). Maximum serum concentration was achieved 23 min later in rectal administration, and peak levels were lower compared with oral administration of misoprostol (Figure 2)\(^7\).

In the pharmacokinetic study by Tang and colleagues, the peak plasma level of misoprostol acid was highest and earliest after administration of misoprostol by the sublingual route\(^6\). Misoprostol tablets dissolved in water and taken orally also have been shown to produce a faster onset and stronger uterotonic effect than either oral or rectal tablet administration\(^14,15\). However, no significant difference was present when misoprostol was used in the form of moistened compared with dry tablets for first-trimester termination of pregnancy\(^16\).

### Adverse effects

Common side-effects of misoprostol include shivering, diarrhea and abdominal pain. Less common side-effects include headache, abdominal cramps, nausea and flatulence, chills and fever, all of which are dose dependent. Interestingly, before its use in pregnant women, chills, shivering and fever were not commonly reported side-effects, suggesting that these are dose dependent.

Package warnings prepared by the manufacturer and based on the original indication for which this drug was marketed clearly state that misoprostol is not to be taken by pregnant women, and that non-pregnant women should use contraceptives while taking misoprostol and should be warned about the effects of misoprostol if taken by pregnant women. Misoprostol should also be avoided in nursing mothers because of concern over causing diarrhea in the baby\(^8,11\).

Congenital anomalies sometimes associated with fetal death have been reported subsequent to the unsuccessful use of misoprostol for termination of pregnancy, but the drug’s teratogenic mechanism has not been elucidated\(^17,18\). Several reports associate the use of misoprostol during the first trimester of pregnancy with skull defects, cranial nerve palsies, facial malformations (Mobius syndrome) and limb defects\(^19\). Misoprostol is listed as a pregnancy category X drug.

Toxic doses of misoprostol have not been determined; however, pregnant women have tolerated cumulative doses up to 2200 µg administered over a period of 12 h without any serious adverse effects\(^20\). A dose of 6000 µg of misoprostol (which is far greater than necessary), taken orally to induce termination of pregnancy (with trifluoperazine), resulted in abortion with hyperthermia, rhabdomyolysis, hypoxemia and a complex acid–base disorder\(^21\).

### MISOPROSTOL IN THE FIRST TRIMESTER

For first-trimester medical termination of pregnancy, misoprostol has been used most extensively in conjunction with mifepristone or methotrexate. Both regimens are effective. In the initial studies of mifepristone and misoprostol for medical termination of pregnancy, both drugs were administered orally. Only regimens of mifepristone in combination with oral misoprostol have been licensed for abortion in many countries. Administration of 600 mg of oral mifepristone followed 48 h later by 400 µg of oral misoprostol resulted in 91–97% complete abortion in women who were no more than 49 days pregnant, compared with 83–95% of women who were no more than 56 days pregnant\(^22–25\).

Lowering the dose of mifepristone to 200 mg and increasing the dose of oral misoprostol to 600 µg increases the efficacy, with abortion rates of 96–97% among women no more than 49 days pregnant and 89–93% among women 50–63 days pregnant\(^26,27\). The dose of mifepristone can be lowered to 200 mg without significantly decreasing efficacy\(^28\).

---

**Figure 2** Mean (standard deviation) plasma concentrations of misoprostol acid after oral and vaginal administration of misoprostol in 20 women. Reprinted from Zieman M, et al.\(^5\), with permission.
A combined regimen of mifepristone and misoprostol results in complete abortion in 94–95% of women who are 9–13 weeks pregnant but is associated with high incidence of heavy bleeding29,30. The timing of administration of misoprostol after mifepristone for medical termination of pregnancy ranges from 6 to 48 h. Studies report high efficacy with shorter intervals of 24 h, 6–8 h and even the simultaneous administration of mifepristone and misoprostol, although one study carried out in Scotland showed reduced efficacy with a shorter interval of 6 h compared with a 36–48 h interval31,32. Complete abortion rates improve with one or two additional doses of misoprostol.

Vaginal administration of misoprostol was more effective and better tolerated than oral administration for the induction of first trimester abortion33,34. However, some studies concluded that both oral and vaginal misoprostol were of similar efficacy. Sublingual administration of misoprostol had a success rate of 92%35.

A single dose of intramuscular or oral methotrexate (50 mg/m² body-surface area) followed 5–7 days later by 800 µg of vaginal misoprostol resulted in complete abortion in 88–100% of women provided with this regimen; 53–60% of women aborted within 24 h after one dose of misoprostol was administered36–42. If complete abortion did not occur within that interval, however, repeating the misoprostol dose resulted in complete termination of pregnancy in 19–32% of women within 24 h after the second dose36,37. The remaining 10–30% of women who aborted successfully had a delayed response, with the abortion completed over an average period of 24–28 days36,37. This regimen is presently not commonly used, as safer regimens with other drugs are available.

Misoprostol has also been used alone for medical termination of pregnancy, albeit with variable efficacy. The earliest studies of misoprostol induced termination of pregnancy in the first trimester and reported complete abortion rates of 5–11% among women given a total dose of 400 µg of oral misoprostol13-44. Up to three 800 µg doses of vaginal misoprostol given every 48 hours resulted in complete termination of pregnancy in up to 96% of women who were no more than 63 days pregnant13.

Misoprostol alone was almost equally effective as combined mifepristone plus misoprostol. However, in a randomized trial comparing methotrexate plus vaginal misoprostol alone, only 47% of the women given misoprostol alone had complete termination of pregnancy, as compared with 90% of the women given methotrexate plus misoprostol (p < 0.001)46. With regard to the use of misoprostol as a cervical-priming agent before vacuum aspiration of the uterus, numerous randomized, controlled studies have shown that misoprostol is more effective than placebo and vaginal PGE2 in terms of the degree of cervical dilatation achieved47,48. As cervical priming facilitates surgical vacuum aspiration, the risks of dilatation and evacuation of the uterus are therefore minimized.

These results were replicated by numerous randomized, controlled trials involving a large number of participants. The best regimen for cervical ripening in the first trimester is 400 µg of vaginal misoprostol given 3–4 h before suction curettage47,49,50. In one study, misoprostol, when administered with mifepristone for termination of early pregnancy in scarred uterus, was safe and effective, but further randomized trials are essential to confirm this51. Sublingual misoprostol was effective in facilitating cervical dilatation before surgical abortion, and its use significantly decreased the time of surgical evacuation and minimized blood loss during the procedure52,53.

**MISOPROSTOL IN EARLY PREGNANCY FAILURE**

Single or repeated doses of misoprostol result in complete expulsions with minimal side-effects and complications in evacuation of first trimester missed abortions54,55. Vaginal misoprostol is more effective than oral administration56. Misoprostol is also effective in incomplete termination of pregnancy, and it is safer than the surgical method57,58.

Based on a review, a single dose of 800 µg vaginal or 600 µg sublingual misoprostol is an effective, safe and acceptable alternative to the traditional surgical treatment for missed abortion. Bleeding may last up to or more than 14 days with additional days of light bleeding or spotting. However, in case of excessive bleeding or any evidence of infection the woman should report to her provider. A follow-up is recommended after 1–2 weeks for confirmation of complete expulsion of products of conception59.

**MISOPROSTOL IN THE SECOND TRIMESTER**

Indications for second trimester termination of pregnancy include chromosomal and structural fetal abnormalities as well as social reasons. Surgical evacuation of the uterus, still being practiced in some centers, is associated with greater morbidity, mortality and complications. Intra-amniotic hypertonic saline/urea instillation, intra-amniotic PGE2 infusion, extra-amniotic ethacridine lactate, oxytocin infusion and vaginal PGE2 all were practiced before the introduction of misoprostol.

Intravaginal misoprostol in the dose of 400 µg is effective and associated with fewer side-effects56. Vaginal misoprostol was as effective as or more effective than PGE2. Misoprostol was equally as effective as extra-amniotic prostaglandin60-64. Misoprostol in the dose of 400 µg every 3 hours was more effective in terms of a significantly shorter drug administration-to-abortion interval and a higher percentage of successful abortion within 48 h compared with misoprostol 400 µg every 6 hours, and the incidence of side-effects was similar in both groups except for that of fever. However, the fever returned to normal within 24 h after the last dose of misoprostol65. In late second
trimester, it is safer to use the less frequent dosage regimen. Vaginal misoprostol was significantly more effective as judged by drug administration-to-abortion interval and the need to augment therapy with oxytocin infusion when compared with oral misoprostol.

It is paradoxical that a greater dose (800 µg) of vaginal misoprostol is essential for abortion in the first trimester, whereas doses in the range of 25–50 µg induce labor in the third trimester. The optimal dose of vaginal misoprostol for induction of labor in the second trimester probably lies somewhere between 50 and 800 µg. Within this range, higher doses may be needed to cause termination of pregnancy early in the second trimester, whereas lower doses may be sufficient later in the second trimester. Higher and more frequent doses are associated with shorter drug administration-to-abortion interval compared with lower and less frequent doses (Figure 3).1,67

MISOPROSTOL IN THE THIRD TRIMESTER

Induction of labor

Labor induction is one of the common obstetric interventions primarily performed with the aim of reducing maternal and perinatal morbidity and mortality. The success of induction of labor not only lies with replication of physiological mechanisms, but also depends upon cervical status. An unfavorable cervix presents the greatest challenge to successful induction. The development of effective, safe (to both mother and fetus) and less expensive pharmacological agents to accomplish this task has been the focus of much clinical research.

The results of the first study (1993) in this area suggested that misoprostol was a cost-effective and safe alternative for induction of labor at term. Later studies, including randomized trials, not only confirmed this finding, but also documented that misoprostol is more effective than placebo or other prostaglandins; moreover, it is associated with a higher rate of vaginal delivery within 24 h, a shorter induction-to-delivery interval and significantly lower cesarean section rates than pooled figures for the control groups.

Studies of different routes of misoprostol administration (oral, vaginal, intracervical and sublingual) were conducted for induction of labor. Although all were successful, vaginal misoprostol is associated with a shorter induction-to-delivery interval, lower number of doses and diminished oxytocin use. Misoprostol gel is associated with fewer uterine contraction abnormalities and longer induction-to-labor and delivery interval when compared with misoprostol tablets.

The safety of misoprostol is crucial, as some studies have shown a high frequency of uterine tachysystole and hyperstimulation, including some reports of uterine rupture during the induction of labor with misoprostol. A vaginal dose of 25 µg is often recommended as the more prudent dose, as it is associated with lower incidence of uterine hyperstimulation and is comparable with the 50 µg dose in achieving delivery within 24 hours. Doses higher than 50 µg have been associated with increased risk of complications. The interval of administration of misoprostol ranges from every 3 to 6 h. It is better to use 6-h dosing intervals to avoid the possible risk of tachysystole. Misoprostol is also effective as a cervical ripening agent for prelabor rupture of the membranes.

Oral misoprostol not only induced labor, but also resulted in delivery within 24 h without increasing maternal or neonatal complications.

Misoprostol is not recommended for induction in cases of previous cesarean section, as it is associated with higher frequency of disruption of prior uterine incisions compared with use of PGE2 or oxytocin. Misoprostol use is associated with a 5.6% rate of uterine rupture compared with 0.2% in patients attempting vaginal birth after cesarean delivery without stimulation, as shown by meta-analysis. Misoprostol use in grand multiparas is not associated with adverse maternal or neonatal outcome. However, its use in such patients warrants strict vigilance. The use of prostaglandins including misoprostol increases the uteroplacental resistance but does not affect the umbilical blood flow in a Doppler velocimetry study of umbilical, uterine and arcuate arteries immediately before and 2–3 h after the administration of vaginal misoprostol or cervical PGE2, thus suggesting misoprostol is as safe as PGE2 gel. Available data suggest that vaginal misoprostol in a dose of 25 µg every 6 h is as safe as PGE2 in patients with a live fetus for induction of labor.

Induction of labor after fetal death

Misoprostol is an ideally suited agent for induction of labor after fetal death, as there is no concern about the adverse effects of uterine hyperstimulation on the fetus. For fetal death at term, a dose as low as 50 µg every 12 h may be adequate for induction of labor, whereas higher doses are necessary in patients with fetal death in the second trimester and early in the third trimester. It is safer to use the lowest effective dose.

Figure 3  Safe single doses of misoprostol for producing uterine contractions at various gestations.67
PPH is a major cause of maternal morbidity and mortality. It is sudden, dramatic and unpredictable. In developing countries, approximately 28% of total maternal deaths are caused by PPH each year. Based on the uterotonic effects of misoprostol, the drug has been evaluated for both prevention and treatment of PPH. The WHO misoprostol multicenter trial concluded that use of an oral tablet of 600 µg was associated with a higher risk of severe PPH, the need for additional uterotonic agents, shivering and pyrexia compared with intramuscular or intravenous oxytocin. However, the dose of misoprostol used in these trials varied from 400 to 600 µg (orally and rectally). Moreover, the frequency of PPH (blood loss more than 1000 ml) was not lower in the misoprostol group than in the control group in any of the trials. Nonetheless, there was higher use of oxytocin in the control groups. In many reports, misoprostol 600 µg oral or 400 µg rectal is significantly less effective than injectable uterotonic in preventing PPH. Misoprostol at the dose of 400–600 µg is associated with risk of shivering, and doses more than 400 µg also significantly increase the risk of pyrexia. At present, oral or rectal misoprostol is not as effective as conventional injectable uterotonic agents, and the high rates of shivering and fever associated with its use make it undesirable for routine use to prevent PPH, especially for low-risk women, when injectable oxytocics (oxytocin or methylergometrine) are available. There is some evidence of increased uterotonic effect with the administration of misoprostol, either by the sublingual route or as an oral solution. Use of buccal misoprostol in a placebo-controlled trial to prevent hemorrhage at cesarean delivery was not associated with a significant difference between the two groups, both in the incidence of PPH and a difference in pre- and postoperative hemoglobin level. However, misoprostol reduced the need for additional uterotonic agents during cesarean delivery. In all of these studies, it is important to note that misoprostol was compared with conventional uterotonics. It is tragic but true, however, that these latter drugs are not available in many parts of the world where women deliver with no medical assistance whatsoever.

Despite the reduced efficacy of misoprostol compared with conventional injectable oxytocics and the potential to cause side-effects, several factors – ease of use, stability in field conditions, longer shelf-life and less expense – underlie its continued evaluation as a uterotonic agent. It remains of great interest, especially for use in home deliveries by traditional birth attendants and minimally qualified nurse midwives in less developed areas where administration of injectable uterotonics may not be feasible or may not be available. It offers a plausible preventive strategy in such areas for reducing maternal mortality related to PPH. Trials with misoprostol versus placebo for prevention of PPH showed superiority of misoprostol.

Misoprostol for treatment of PPH

Current evidence suggests that misoprostol is less effective than injectable oxytocics especially versus oxytocin. However, misoprostol was almost equally effective in the treatment of PPH where oxytocin was used for prophylaxis compared with when oxytocin was not used earlier. It is reasonable to ask why misoprostol is effective for women with PPH, but has little effect on normal bleeding (in contrast to oxytocin). Oral misoprostol is absorbed more slowly than intramuscular oxytocin, and by the time it reaches its peak at 20 min, the third stage is over for most women (see Figure 4). Thus, the more prolonged the bleeding (i.e. the PPH), the more effective is misoprostol.

Hence, it is important to note that the injectable oxytocin acts more rapidly than misoprostol, so this latter agent in reality cannot be as effective as oxytocin. Future research with misoprostol must address this issue, as currently available misoprostol is recommended for oral use and takes more time to act. Newer formulations with sublingual/buccal route may probably act equal to oxytocin or injectable oxytocics.

OTHER USES

Cervical priming with misoprostol facilitates transcervical procedures and reduces side-effects.

Oral misoprostol in the dose 600 µg was associated with lower incidence of measured blood loss 500 ml or more and lower incidence of reduced postpartum hemoglobin (reduction of hemoglobin by 2 g/dl or more was 16.4% with misoprostol and 21.2% with ergometrine), but this difference was not statistically significant. Shivering was significantly more common with misoprostol, whereas vomiting was more common with ergometrine in a randomized, controlled trial with misoprostol 600 µg and ergometrine (0.5 mg, four tablets) in home delivery settings of rural Gambia.

In a randomized, double-blind, placebo-controlled trial with sublingual misoprostol (600 µg) at a primary health center in Bissau, Guinea-Bissau, West Africa, the incidence of PPH was not significantly different between the two groups. However, significantly fewer women in the misoprostol group experienced a blood loss of 1000 ml or more or 1500 ml or more. The decrease in hemoglobin concentration tended to be less in the misoprostol group, the mean difference between the two groups being 0.16 mmol/l (=0.01 to 0.32 mmol/l). From this study, it was concluded that sublingual misoprostol reduces the frequency of severe PPH.

Editor’s note: These clinical findings, even without statistical differences, are of great practical importance in areas where blood supplies are insufficient or totally lacking. L.G.K.]
it is ideal for induction of labor in patients with intrauterine fetal death.

Misoprostol may also prevent PPH when injectable uterotonic agents are either impractical or unavailable. On the other hand, misoprostol should not be the preferred uterotonic for prevention of PPH where injectable oxytocics are readily available. Its use in the treatment of PPH in regions of the world where the standard of care is delivery without uterotonic agents (i.e. delivery with no uterotonic medication) needs further evaluation. The oral route is associated with faster effect and with more side-effects. The other routes, such as vaginal and rectal, have sustained and longer effects with less side-effects. The sublingual and buccal routes and doses need further evaluation.

Finally, after considerable discussions between the American College of Obstetricians and Gynecologists (ACOG) and Searle, the manufacturer of misoprostol, the FDA has approved a new label for the use of misoprostol during pregnancy. The new labeling revises the contraindications and the precaution that misoprostol should not be used in pregnant women by stating that the contraindication is only for pregnant women who are using the medication to reduce the risk of NSAIDs. Misoprostol is now a legitimate part of the FDA-approved regimen for use with mifepristone to induce abortion in early abortion and the label warns of the complications/risks of its use for induction and augmentation of labor\(^{120}\). Uses in obstetrics and gynecology continue to be off-label.

**WHO has also approved misoprostol for the prevention of PPH where oxytocin is not available or cannot be safely used and included the drug in the Model List of Essential Medicines\(^{122}\).** Currently, misoprostol is registered by the national regulatory agencies of 17 countries for prevention and/or treatment of PPH. Consequently, several non-USA manufacturers are now marketing the drug with this indication included in the label.

**References**


---

**Figure 4** Comparison of concentrations of misoprostol and oxytocin in blood with duration of physiological third stage in 12,979 women\(^ {117}\)

Cervical priming is recommended by several evidence-based guidelines prior to surgical abortion, dilatation and curettage, hysteroscopy and intrauterine device insertion\(^ {118}\). It is effective in pregnant as well as in non-pregnant women, whereas the results in postmenopausal women are conflicting\(^ {118}\). Various doses, routes and time intervals between misoprostol application and the intervention have been evaluated. A single dose of 400 µg given sublingually or vaginally 3 h before the intervention has given the best efficacy with the least side-effects. Higher doses or longer intervals do not improve the effect on the cervix. Pain is a frequent side-effect, but usually responds well to NSAIDs. Other side-effects are rare\(^ {118}\). Its use in cervical pregnancy is documented with one case report; however, extreme caution is recommended with this approach and methotrexate is favored by most authorities\(^ {119}\).

**CONCLUSION**

Misoprostol is one of the most important medications in obstetric practice. As of the time of writing, its use in pregnant women remains unapproved by the US FDA, except in conjunction with mifepristone (or, in some cases, methotrexate) for first-trimester medical termination of pregnancy. Despite this, the international literature is replete with innumerable favorable reports in many languages of off-label uses. For example, there is strong and consistent evidence to support the use of misoprostol for cervical ripening before surgical abortion in the first trimester and for induction of labor in the second and third trimesters. Whereas lower dose and strict vigilance are required for use of misoprostol for induction of labor with a live fetus,


**Editorial note:** A randomized controlled trial by Bellad et al. comparing sublingual misoprostol and intramuscular oxytocin for the prevention of postpartum haemorrhage demonstrates that a relatively low dose of sublingual misoprostol is more effective than standard intramuscular administration of oxytocin for vaginal deliveries. This is the first study to demonstrate sublingual misoprostol’s superiority over intramuscular oxytocin and it is easier to administer. (Bellad M, Tara D, Ganachari M, et al. Prevention of postpartum haemorrhage with sublingual misoprostol or oxytocin: a double-blind randomised controlled trial. BJOG 2012;119:975–86). M.K.