ARTICLE

Misoprostol in obstetrics and gynaecology — benefits and risks

Medical Research Council/University of Natal Pregnancy Hypertension Research Unit and Department of Obstetrics and Gynaecology, Nelson R Mandela School of Health Sciences, University of KwaZulu-Natal, Durban
G Essilfie-Appiah, MB ChB
G J Hofmeyr, MB ChB, FCOG

Department of Obstetrics and Gynaecology, Frere and Cecilia Makiwane hospitals, Effective Care Research Unit, University of the Witwatersrand, Johannesburg, and Fort Hare University, Alice, Eastern Cape
J Moodley, MB ChB, FRCOG, FCOG, MD

Misoprostol is currently being used for induction of labour at or near term and also for termination of pregnancy. Its use without proven dosage regimens is possibly associated with an increase in the incidence of uterine hyperstimulation, preterm labour, induced abortion above 20 weeks' gestation, meconium-stained liquor in the latent phase of labour, fetal distress and cases of uterine rupture as demonstrated by these case reports and literature review. Its use for these purposes must be under controlled circumstances, using minimum doses.

The well-documented effectiveness of misoprostol in several gynaecological and obstetric applications has resulted in enthusiasm for its use that has overtaken the need for careful assessment of potential risks.

Since misoprostol has become freely available for termination of pregnancy (TOP) and for induction of labour at or near term, we have seen an increase in the incidence of uterine hyperstimulation, preterm labour, induced abortion above 20 weeks' gestation, meconium-stained liquor in the latent phase of labour, fetal distress and cases of uterine rupture associated with the use of high doses of misoprostol.

The purpose of these case reports and brief literature review is to highlight the benefits and risks associated with the current unregistered use of misoprostol in clinical practice and in the community.

Case reports

Case 1

In September 2002, a 28-year-old woman, para 2, gravida 3, was admitted with severe abdominal pain and vaginal bleeding. She was haemodynamically stable. An ultrasound examination revealed a live term baby and a normally situated placenta. A tablet of misoprostol (200 µg) was found in the vagina. The patient had inserted the tablet herself (obtained from a neighbour). Emergency caesarean section was performed for suspected abruptio placentae and fetal heart rate decelerations, detected by electronic fetal heart rate monitoring. A ruptured uterus was found at caesarean section; a live baby was delivered and the uterus repaired. Mother and baby were well on discharge from hospital.

Case 2

In April 2003, a 25-year-old woman, para 1, gravida 2, 38 weeks' gestation, with a previous caesarean section, was admitted in labour with severe lower abdominal pain and draining meconium-stained liquor. Upon vaginal examination, two tablets of misoprostol were found in the posterior fornix of the vagina. She said she had used misoprostol tablets given to her by a friend. Emergency caesarean section was performed. A dehisced caesarean section scar was found. A baby with very low Apgar scores was delivered, but died after a few hours.

Case 3

In August 2003, a 19-year-old primigravid woman at term was admitted in labour. Uterine hyperstimulation and fetal tachycardia were detected on electronic fetal heart rate and external uterine pressure monitoring. A tablet (200 µg) of misoprostol was found in the posterior vaginal fornix. The tablet was removed, 10 µg of intravenous ipradol given and labour managed expectantly, with normal delivery of a healthy baby. She informed us that

the tablet was inserted by her general practitioner.

Case 4

In December 2003, a 25-year-old woman, para 2, gravida 3, 20 weeks' gestation was admitted with a 1-day history of lower abdominal pain and vaginal bleeding. A tablet of misoprostol was found in the posterior vaginal fornix and she had clinical features of an inevitable miscarriage. She said she had used misoprostol given to her by a friend whose pregnancy had been terminated previously at the hospital.

Discussion

Misoprostol (Cytotec, Pharmacia) is a prostaglandin E_1 analogue. It is marketed for oral use in the prevention and/or treatment of prostaglandin synthetase inhibitor-induced gastro-intestinal damage. It has been shown to be an effective myometrial stimulant,[1] and is widely used off-licence for obstetric and gynaecological indications,[2] mainly orally, buccally/sublingually, vaginally and rectally.

Complications include uterine hyperstimulation, precipitate labour, fetal distress in labour, meconium passage, nausea, vomiting, diarrhoea, abdominal pains, shivering, and pyrexia. Teratogenic effects associated with the use of misoprostol have been identified, particularly limb reduction defects following unsuccessful TOP.[3]

Community use of misoprostol for TOP and induction of labour

Over the past 2 years, it is our clinical impression that a number of women presenting with threatened, inevitable and incomplete miscarriage admit to using misoprostol given to them by friends whose pregnancies had previously been terminated using misoprostol, as illustrated by the fourth case report. These were often women who had been denied legal abortion because their pregnancies were above 20 weeks' gestation.

We have also found that in unexplained cases of early pre-term labour, a tactfully elicited history sometimes reveals that misoprostol is used with the intent of inducing early labour. These women knew that if their babies were delivered preterm they might not survive.

In one study most women requesting TOP preferred home administration of misoprostol.[4] In many hospital services, women requesting TOP are given misoprostol tablets for self-administration at home. Often they do not return unused tablets to the hospital. The result is that these tablets become available to other pregnant women.

Uterine sensitivity to misoprostol increases greatly with increasing duration of pregnancy. Vaginal doses of up to 800 µg (4 tablets) are routinely used for early pregnancy termination. Systematic review of 62 randomised trials of vaginal misoprostol for induction of labour found the range of dosage used to be enormous (25 µg 6-hourly - 100 µg 2-hourly).[5] Vaginal dosages as low as 25 µg 3-hourly were more effective than oxytocin or dinoprostone for induction of labour, but were associated with increased uterine hyperstimulation, fetal heart rate changes and increased meconium passage.

At term it has been recommended that if used at all, the dose should not exceed 25 µg (1/8 of a tablet) 4-hourly. Uterine rupture in nulliparous women has been documented with as little as a single 100 µg dose.[5]

It is not surprising that misoprostol is inadvertently used in dangerously high doses by women and even by doctors.

Labour induction with misoprostol is associated with an increased incidence of meconium-stained liquor.[6] This could be due to a direct stimulant effect of misoprostol on fetal bowel.[7] Commonly used substances such as the herbal uterine stimulant *isihlambezo* have also been associated with meconium passage. It is possible that misoprostol and *isihlambezo* may act synergistically to potentiate the problem and increase the risk of meconium aspiration syndrome.

Misoprostol is commonly used in women with previous caesarean section for pregnancy termination in the first trimester and up to 20 weeks' gestation. The use of misoprostol above 24 weeks in women who have had a previous caesarean section carries an increased risk of uterine rupture.

Conclusion

Misoprostol has the potential to be an extraordinarily useful drug in obstetric and gynaecological practice, particularly in developing countries where conventional prostaglandin preparations are unaffordable.

As commercial registration for use in pregnancy appears unlikely, clear guidelines from the health authorities regarding its use are urgently needed, coupled with indemnity against complications that may be associated with its use within these guidelines.

There is an urgent need to educate the public and health professionals on the risks of misoprostol used at the wrong time in the wrong dosage.

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