



C-Obs 12

The use of misoprostol in obstetrics and gynaecology

There is considerable evidence in published studies about the use of misoprostol in obstetrics and gynaecology. There are in excess of 200 randomised controlled trials included in Cochrane Systematic Reviews, involving more than 35,000 women where misoprostol has been administered for obstetric or gynaecological indications, involving 16,000 women in over 200 studies by 2001.

Use in first and second trimesters

In general, the evidence demonstrates advantages of misoprostol over available alternatives for use in medical management of miscarriage and termination of pregnancy in the first and second trimesters. The advantages are that it is at least as effective as alternatives, has fewer side effects, is more practical to use and is cheaper. Recent research reports suggest that alternatives to misoprostol are used with diminishing frequency. The occurrence of maternal side effects is reduced when using lower doses of misoprostol, when compared with higher cumulative doses.

Use for cervical ripening and induction of labour

The considerable literature evaluating the use of misoprostol for cervical ripening and induction of labour.

The Cochrane Review relating to vaginal misoprostol indicates that vaginal misoprostol is more effective when compared with other standard methods of induction of labour in terms of women achieving vaginal birth within 24 hours, but it is at the expense of an increase in the occurrence of uterine hyperstimulation (without associated fetal heart rate changes).

The studies have not been large enough to exclude low risks of serious adverse events and further research is warranted. The doses used in the early studies may have been higher than necessary/appropriate.

The Cochrane Review relating to oral misoprostol indicates that oral misoprostol is at least as effective as vaginal dinoprostone, with no evidence to suggest that it is inferior to vaginally administered misoprostol. Additionally, oral administration is associated with a lower risk of uterine hyperstimulation. The recommended dose for use of oral misoprostol should not exceed 50mcg. The effective use of lower doses of misoprostol (20mcg, 40mcg) has been demonstrated in randomised controlled trials using oral misoprostol solution (Dodd et al 2006; Hofmeyr et al 2001; Dallenbach et al 2003; Moodley et al 2003).

There is currently insufficient information available to make a recommendation relating to the use of buccal misoprostol (Muzonzini 2004).

Attitude of pharmaceutical industry

The company which markets an oral formulation of misoprostol (Cytotec) has not researched and does not support its use in pregnancy, nor does it intend to do so. Since it is readily available for other indications and widely used in obstetrics and gynaecology in Australia as in other countries, there is already an established market. In addition to the low cost associated with production it could therefore be argued that there is no incentive for the company to invest in such research and support.

As the use of misoprostol in pregnancy is "off-label", clearly no liability would be accepted by the company for any adverse events.

Use in clinical practice

As with all new therapeutic agents, Fellows should take particular care to use misoprostol according to regimens for which evidence is available and to ensure that appropriate informed consent is obtained from women prior to its use. Where misoprostol is the most appropriate therapeutic option, it should be available for use according to established medical evidence.

Particular caution is recommended with the use of misoprostol for cervical ripening and induction of labour. The potential risks and benefits in each individual case should be carefully evaluated and attention paid to the published information regarding minimization of dosage. As with all prostaglandin preparations, caution is recommended with the use of misoprostol in the presence of a uterine scar.

There may be a role for the use of misoprostol in the management of post partum haemorrhage. The use of misoprostol in properly approved clinical trials is supported.

The references which follow include information about dosage regimens evaluated.

References

Goldberg AB, Greenberg MB, Darney PD. Drug Therapy: Misoprostol and Pregnancy. New England Journal of Medicine 2001;344:38-47 (95 references).

Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion. RCOG Press, 2004 (176 references).
<http://www.rcog.org.uk/index.asp?PageID=662>

Chong Y-S, Su L-L & Arulkumaran, S. Misoprostol: A Quarter Century of Use, Abuse and Creative Misuse. CME Review Article, Obstetrical and Gynaecological Survey 2004; 59(2):128-140.

Alfirevic Z. Oral misoprostol for induction of labour. The Cochrane Database of Systematic Reviews 2006 Issue 2. Art. No.: CD001338. DOI: 10.1002/14651858.CD001338.

Dodd JM, Crowther CA. Elective repeat caesarean section versus induction of labour for women with a previous caesarean birth. (Review The Cochrane Database of Systematic Reviews 2006 Issue 4. Art. No.: CD004906. DOI: 10.1002/14651858.CD004906.

Dodd JM, Crowther CA. Misoprostol for induction of labour to terminate pregnancy in the second or third trimester for women with a fetal anomaly or after intrauterine fetal death. (Protocol) The Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004901. DOI: 10.1002/14651858.CD004901. In press.

Dodd JM, Crowther CA. Misoprostol versus cervagem for the induction of labour to terminate pregnancy in the second and third trimester for women with a fetal anomaly or after intra-uterine fetal death: A systematic review. Eur J Obstet Gyn Reprod Biol 2005.

Hofmeyr GJ, Gülmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour. The Cochrane Database of Systematic Reviews 2003, Issue 1 Art. No.: CD000941. DOI: 10.1002/14651858.CD000941.

Kulier R, Gülmezoglu AM, Hofmeyr GJ, Cheng LN, Campana A. Medical methods for first trimester abortion. The Cochrane Database of Systematic Reviews 2004, Issue 2. Art. No.: CD002855. DOI: 10.1002/14651858.CD002855.pub3.

Weeks A, Fiala C, Safar P. Misoprostol and the debate over off-label drug use. BJOG. 2005 Mar;112(3):269-72.

*Dodd JM, Crowther CA, Robinson JS. Oral misoprostol for the induction of labour at term: a randomised controlled trial. British Medical Journal 2006.

*Hofmeyr GJ, Alfirevic Z, Matonhodze B, Brocklehurst P, Campbell E., Nikodem VC. Titrated oral misoprostol solution for induction of labour: a multi-centre, randomised trial. British Journal of Obstetrics and Gynaecology 2001;108:952-959.

*Dallenbach P, Boulvain M, Viardot C, Irion O. Oral misoprostol or vaginal dinoprostone for labor induction: a randomized controlled trial. American Journal of Obstetrics & Gynecology 2003;188:162-167.

*Moodley J, Venkatachalam S, Songca P. Misoprostol for cervical ripening at and near term - a comparative study. S Afr Med J 2003;93(5):371-374

**Dodd JM, Crowther C Induction of labour for women with a previous caesarean birth: a systematic review of the literature. ANZJOG 2004;44(5):392-395

Muzonzini G, Hofmeyr GJ Buccal or sublingual misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews 2004; Issue 4; CD004221.

Key

* *References describe the use of low dose oral misoprostol solution for induction of labour at term.*

** *Reference describes a meta-analysis of preparations used for induction of labour in the presence of a prior caesarean section.*

Disclaimer

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