

MISOPROSTOL

Use

Although gastric ulcer prevention is currently the only marketed indication for misoprostol in most countries, it is now widely used to terminate pregnancy, and is a valuable alternative to oxytocin (q.v.) in the control of serious postpartum bleeding (a problem that currently kills one woman every 4 minutes in resource-poor countries) and does not need refrigeration. It also has a role (if the dose is kept low) in the induction of labour.

Pharmacology

The only officially recognised use of misoprostol, an orally active prostaglandin E₁ analogue first synthesised in 1973, is to prevent and treat the gastric ulcers that are sometimes caused by nonsteroidal anti-inflammatory drug (NSAID) use. The drug's original manufacturer (Searle Pharmaceuticals) has never recommended use for any other purpose, or supported the studies needed to evaluate any other use, and only makes the drug available in 100 and 200 microgram tablets (a higher dose than is usually appropriate when attempting to induce labour in late pregnancy). It is, however, widely accepted that a 400 microgram vaginally administered dose of misoprostol is an effective way of preparing the first trimester cervix for suction termination, while a 800 microgram dose given 48 hours after a 200 mg dose of oral mifepristone will effect non-surgical termination of pregnancy in any woman less than 8 weeks pregnant. Nausea, abdominal pain, diarrhoea, shivering and fever are the commonest transient, dose dependent, side effects.

Much lower doses usually suffice to induce labour at term, and dangerous uterine hyperstimulation was a common problem before this was recognised. Indeed uterine rupture has been reported so often in women with a uterine scar that any such use is now considered very unwise. In fact there is probably nothing specifically dangerous about the use of misoprostol in this situation – it is probably the dose used that has been the problem, because other strategies for induction can also cause uterine rupture. The active metabolite, misoprostol acid, is rapidly cleared by the liver, and the half life with oral administration is less than an hour. Placing a tablet in the posterior fornix of the vagina increases the drug's bioavailability, and its half life, but most women prefer oral treatment and, while the optimum oral dose still requires further study, this (or sublingual use) is now the generally preferred option. Misoprostol should never be used for other reasons during pregnancy, not only because it stimulates uterine activity, but also because high dose first trimester use can cause fetal deformity. There are no reports of complications with use during lactation.

Treatment

Inducing labour: One approach is to give up to three 25 microgram oral (or sublingual) doses once every 2 hours, doubling the dose to 50 micrograms every 2 hours if necessary after 6 hours. Treatment is stopped once the uterus is contracting regularly (three 30-second contractions every 10 minutes). An alternative strategy has been to give up to five 100 microgram doses at four hourly intervals. The existence of a uterine scar is a contraindication to *either* of these strategies, as is the simultaneous use of IV oxytocin.

Postpartum haemorrhage: While IV oxytocin is the drug of choice to control early postpartum bleeding, 600 micrograms of oral (or sublingual) misoprostol is (once absorbed) extremely effective at controlling serious, sustained, and life-threatening, post partum bleeding because of its longer half life.

Supply and administration

The only product currently available in the UK is a 200 microgram tablet which costs 17p. Smaller doses can however be given by crushing the tablet and dissolving it in tap water. Any such solution must then be used within 12 hours. Misoprostol has not yet been licensed for obstetric use but, unlike oxytocin, it does not have to be stored in the dark, or kept at 4°C, to maintain its potency. It is also much cheaper than dinoprostone vaginal gel and now the drug's patent has expired France plans to manufacture a low dose product

References

See also the relevant Cochrane reviews ©

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