



PIC QUESTION OF THE WEEK: 5/08/06

Q: Can misoprostol tablets be inserted vaginally?

A: Misoprostol (Cytotec), a synthetic analogue of prostaglandin E₁, is FDA labeled for the prevention of gastric ulcers associated with the administration of nonsteroidal anti-inflammatory drugs (NSAIDs). It is also available in combination with diclofenac (Arthrotec) for the treatment of osteo- and rheumatoid arthritis in patients at high risk of developing gastric and duodenal ulcers. The drug is currently included in the protocol for termination of intrauterine pregnancy after treatment with mifepristone (Mifeprex). Misoprostol has also been frequently administered to stimulate cervical ripening prior to hysteroscopy and the induction of labor. It is generally prescribed for oral administration (available as 100 and 200 mcg tablets) with dosage based on the specific indication. Intravaginal use of misoprostol tablets was initially investigated approximately ten years ago. This occurred because of the relatively high incidence of adverse effects with oral misoprostol in gynecologic procedures and the more rapid onset of effect with this route of administration. Initial studies for induction of labor utilized intravaginal doses of 25 mcg every 4-6 hours. Higher doses produce a shorter time to induction of labor and delivery, but can also result in hyperstimulation of the uterus and adverse effects in the newborn. Misoprostol can be administered intravaginally by inserting a carefully cut portion (usually one-quarter to one-half) of a 100 mcg tablet into the posterior vaginal fornix. It is recommended to avoid using gels or lubricants as they may prevent proper dissolution of the tablet. The American College of Obstetrics and Gynecology currently recommends intravaginal misoprostol for use in cervical ripening and induction of labor. It cautions that women with a previous cesarean delivery have an increased risk of uterine rupture if treated with intravaginal misoprostol. The American Academy of Family Physicians also supports this practice guideline. A recent review of published studies also confirms that intravaginal misoprostol is safe and effective for the induction of labor. Doses of 50 mcg may be associated with a greater frequency of adverse effects. Intravaginal administration of 400 to 800 mcg of misoprostol can result in spontaneous abortion. These doses may produce effects comparable to the combination of mifepristone plus misoprostol. A recent FDA Public Health Advisory cautions against the use of intravaginal misoprostol in combination with mifepristone for termination of pregnancy. This was prompted by the report of five deaths (possibly attributed to sepsis associated with *Clostridium sordellii*) after administration of intravaginal misoprostol for this indication. Although not FDA labeled, there is extensive documentation to support the safety and efficacy of intravaginal misoprostol for cervical ripening and induction of labor.

References:

- U.S. Food and Drug Administration. FDA Public Health Advisory. <http://www.fda.gov/cder/drug/advisory/mifepres200603.htm> (accessed 2006 May 4).
- Colon I, Clawson K, Hunter K, et al. Prospective randomized clinical trial of inpatient cervical ripening with stepwise oral misoprostol vs. vaginal misoprostol. *Am J Obstet Gynecol* 2005;192:747-52.
- Weaver S, Cook J, Nashelsky J. Vaginal misoprostol for cervical ripening in term pregnancy. *Am Fam Physician* 2006;73:511-2.

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