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FPIN's Clinical Inquiries

Vaginal Misoprostol for Cervical Ripening in Term Pregnancy

Clinical Question

How safe and effective is vaginal misoprostol (Cytotec) for cervical ripening in a term pregnancy?

Evidence-Based Answer

Low-dose (25 mcg) intravaginal misoprostol appears to be safe and effective for cervical ripening in term pregnancy for patients without a history of cesarean section. Compared with other cervical ripening methods, misoprostol has an increased rate of vaginal delivery within 24 hours without significant differences in cesarean section rates or fetal outcomes. (Strength of recommendation: B, systematic review of randomized controlled trials)

A 50-mcg dose of intravaginal misoprostol causes increased rates of uterine hyperstimulation and may be associated with an increased cesarean section rate. (Strength of recommendation: B, single prospective randomized controlled trial)

Because of a potential increased risk of uterine rupture, use of misoprostol for labor induction in women with a previous cesarean section is relatively contraindicated. (Strength of recommendation: B, large population-based retrospective cohort study)

Evidence Summary

Cervical ripening is a process that is intended to soften, dilate, and efface the cervix. An unripe cervix is generally not yet soft, is dilated less than 2 cm, and is less than 50 percent effaced. Procedures that ripen the cervix commonly are used in routine pregnancies (with an unripe cervix) that extend past 41 weeks or when complications dictate a delivery before the mother spontaneously goes into labor. Misoprostol is a synthetic prostaglandin E1 analogue commonly used for cervical ripening and labor induction; however, it is not approved by the U.S. Food and Drug Administration for this purpose. A recent Cochrane systematic review¹ of 70 studies, 13 of which were blinded, examined the use of vaginal misoprostol for cervical ripening and labor induction. Subgroup analysis of vaginal misoprostol versus other vaginal prostaglandins and versus intracervical prostaglandins found more patients delivering vaginally within 24 hours when misoprostol was used (>17 trials, number needed to treat [NNT] = 10).¹ Cesarean section rates for patients receiving vaginal misoprostol and other vaginal/intracervical prostaglandins

varied between studies, but no significant overall difference was found (38 trials).¹ This same review¹ reported that low-dose (25 mcg) misoprostol is associated with more need for oxytocin (Pitocin) augmentation (13 trials, relative risk [RR], 1.23; 95% confidence interval [CI], 1.08 to 1.40; number needed to harm [NNH] = 11) but results in less uterine hyperstimulation compared with 50-mcg doses (RR, 0.61; 95% CI, 0.49 to 0.76; NNT = 25). There also was a trend to fewer neonatal intensive care unit (NICU) admissions with lower doses compared with higher doses of intravaginal misoprostol.

In another systematic review of five high-quality randomized controlled trials involving 933 women,² there were no significant differences between 25- and 50-mcg misoprostol dose groups with respect to cesarean section rates (19.1 and 18.9 percent, respectively) or operative vaginal delivery. No dose-related differences were found with respect to abnormal Apgar scores, admissions to the NICU, or patients requiring cesarean section for fetal heart rate abnormalities. Oxytocin augmentation was used more often in the 25-mcg dose group (29 versus 13.2 percent). The 50-mcg dose did result in a faster time to vaginal delivery (five hours shorter)² but was associated with a higher incidence of uterine hyperstimulation (20.8 versus 8.9 percent in the 25-mcg dose group).

A more recent, high-quality, prospective double-blind randomized controlled study³ of 114 subjects comparing 25 versus 50 mcg of intravaginal misoprostol reported a significantly higher cesarean section rate with a 50-mcg dose of misoprostol (28.6 versus 10.3 percent; NNH = 6). This primarily was caused by abnormal fetal heart rate patterns. Oxytocin augmentation was required less often with 50 mcg of misoprostol (32.1 versus 63.8 percent; NNT = 4), but the rate of oxytocin use was still much higher than shown in the previously mentioned review.² The impact this had on the cesarean section rate was not explored.

One small (68 patients) randomized, double-blind, placebo-controlled trial⁴ recently reported that a single 25-mcg outpatient dose of misoprostol significantly decreased the interval to delivery compared with placebo (4.1 versus 9.2 days; $P = .04$).

Finally, a large, population-based, retrospective cohort analysis⁵ of more than 20,000 births demonstrated that induction of labor with prostaglandins (including misoprostol) among women with a previous cesarean section delivery is associated with an increased risk of uterine rupture (RR, 15.6; 95% CI, 8.1 to 30.0).

The published data appear to indicate that intravaginal misoprostol is safe and effective. Cervical ripening and subsequent labor induction is probably more effective with the 50-mcg dose; however, the currently available information reveals conflicting data on whether the higher dose is as safe as the 25-mcg dose.

Recommendations from Others

The American College of Obstetricians and Gynecologists recommends that low-dose misoprostol (25 mcg every three to six hours) is effective for cervical ripening but should not be used in women with previous cesarean delivery because of increased rates of uterine rupture.⁶ A

practice recommendation from the American Academy of Family Physicians supports the safety and effectiveness of vaginal misoprostol for cervical ripening and labor induction.⁷

Clinical Commentary

Methods for cervical ripening with subsequent labor induction at term vary greatly by physician and practice locale. Vaginal misoprostol appears to be well tolerated by patients and is a cost-effective alternative to intravaginal/intracervical prostaglandins. Misoprostol costs a few dollars for multiple doses compared with several hundred dollars per dose for an intracervical prostaglandin preparation such as dinoprostone (Cervidil). Vaginal misoprostol can be used effectively by family physicians either as a cervical ripening agent or for labor induction. Additionally, because vaginal misoprostol does not require connecting a patient to an intravenous line, patients may be more comfortable as they are able to move around more freely during labor. In summary, low-dose (25 mcg) intravaginal misoprostol appears to be safe and effective for cervical ripening in term pregnancy for women without a history of cesarean section.

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