Does self-administered misoprostol prime the cervix for hysteroscopy?

YES **in a premenopausal woman.** However, the ideal dosage is yet to be determined.

In this randomized, placebo-controlled trial by Oppegaard and colleagues, when 1,000 µg of vaginal misoprostol was self-administered by premenopausal women at least 12 hours before operative hysteroscopy, significant cervical ripening occurred, with increased cervical dilatation and less difficulty with dilatation, compared with women given placebo.

The drug was ineffective in postmenopausal women.

Oppegaard K, Nesheim B, Istre O, Qvigstad E. Comparison of self-administered vaginal misoprostol versus placebo for cervical ripening prior to operative hysteroscopy using a sequential trial design. BJOG. 2008;115:663–e9.

FAST TRACK

1,000 µg of misoprostol self-administered at least 12 hours before operative hysteroscopy caused significant cervical ripening in premenopausal women

EXPERT COMMENTARY
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Operative hysteroscopy is a common, minimally invasive procedure used to treat a number of gynecologic pathologies.[1] The procedure requires that the cervical canal be dilated enough to allow passage of the hysteroscope.

Misoprostol is a prostaglandin E_1 analog. It also is an effective cervical-ripening and labor-induction agent used during pregnancy in the second and third trimesters.[2,3] Earlier studies suggested that misoprostol may be promising as a cervical-ripening agent before hysteroscopy in premenopausal women, although further research is needed to determine the ideal dosage, route, and timing of administration.[1,4–6] Most of the studies demonstrating benefit with misoprostol before hysteroscopy have involved intravaginal dosages of 200 to 400 µg given 8 to 12 hours before the procedure.[1,4–6]

Misoprostol enabled greater dilatation in more women

Oppegaard and colleagues found greater mean cervical dilatation with misoprostol in premenopausal women than with placebo (6.4 ± 2.4 mm, compared with 4.8 ± 2.2 mm), more women achieving at least 5-mm cervical dilatation (88% versus 65%), and fewer women being difficult to dilate for hysteroscopy (20% versus 32%). As in previous studies, they also found misoprostol to be an ineffective cervical-ripening agent in postmenopausal women.

Strengths of this study

Because this study was randomized and placebo-controlled, bias in the evaluation of outcomes was minimized. The sample size was based on a sequential trial design, which ensures adequate power to answer the question of interest using as few women as possible.

The medication was self-administered and therefore more convenient than physician administration. In addition, women were questioned afterward to determine the acceptability of the self-administered medication, and 83% of premenopausal subjects found self-administration fairly or completely acceptable.

Shortcomings

Oppegaard and colleagues recommend that 1,000 µg of vaginal misoprostol be offered to nulliparous premenopausal women before operative hysteroscopy, but they do not present data specific to nulliparous women.

Moreover, the use of 1,000 µg of misoprostol is higher than in most previous studies, and Oppegaard and colleagues do not compare different dosages. The use of a higher dosage (1,000 µg) may be expected to cause more side effects. Indeed, researchers found a higher incidence of vaginal bleeding

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with misoprostol, compared with placebo (21% versus 3%), and 42% of women receiving misoprostol experienced mild or moderate abdominal pain, with 7% reporting severe abdominal pain.

WHAT THIS EVIDENCE MEANS FOR CLINICAL PRACTICE

The use of self-administered vaginal misoprostol 12 hours before operative hysteroscopy in premenopausal women increases cervical dilatation and reduces the difficulty of dilatation. Oppegaard and colleagues used 1,000 µg of misoprostol, although earlier studies suggested benefit with 200 µg to 400 µg.

Although the route and timing of misoprostol for cervical ripening before hysteroscopy appears evident from the literature (vaginal administration 12 hours before the procedure), the ideal dosage is still unclear. Furthermore, misoprostol carries potential side effects, including vaginal bleeding and abdominal pain.

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Can intrauterine growth restriction be present in the first trimester?

POSSIBLY In this retrospective cohort study from Sweden, when the expected date of delivery was postponed more than 7 days as a result of early (<14 weeks' gestation) or late (>16 weeks) ultrasonographic dating, the risk of a small-for-gestational-age infant increased (odds ratio [OR], 1.77; 95% confidence interval [CI], 1.13–2.78 and OR 2.09; 95% CI, 1.59–2.73). This study involved a population of 28,776 singleton pregnancies dated between 1998 and 2004.

Thorsell M, Kaijser M, Almstron H, Andolf E. Expected day of delivery from ultrasound dating versus last menstrual period—obstetric outcome when dates mismatch. BJOG. 2008;115:585–589.

FAST TRACK

When the expected date of delivery was postponed more than 7 days as a result of ultrasonographic dating, the risk of a small-for-gestational-age infant increased

▸ **EXPERT COMMENTARY**

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Conventional perinatal wisdom, since the inception of obstetric ultrasonography (US), has been that disordered growth in utero occurs only in the second half of pregnancy; growth in the first half of pregnancy is believed to be uniform, with little variation among individuals. This assumption of uniform growth at the beginning of gestation allows us to create growth curves for populations and generate estimates of gestational age for individual fetuses from their growth parameters. Utilization of US for dating has pushed the mean gestational age at delivery back a few days, tightened the distribution around the mean, and lowered the prevalence of postdatism.

In this new study, Thorsell and colleagues question conventional wisdom and introduce a new notion that disordered intrauterine growth may be present in the first half of pregnancy as early as the first trimester. Women whose US evaluation at 16–18 weeks moved their due date forward more than 6 days were at increased risk of intrauterine growth restriction, preterm birth, and preeclampsia. Those whose due date was moved forward more than 6 days as a result of US dating at 12–14 weeks were at increased risk of growth restriction, but not preterm birth or preeclampsia. The authors call for increased surveillance for growth restriction in pregnancies in which US evaluation changes dates.

Weaknesses of the study

These findings are intriguing, but take them with a grain of salt. "Intendedness" of conception can, of course, be a marker of higher social status and resources, thereby linking "unintendedness" to poor dates (dates that need to be adjusted by US) and poor pregnancy outcomes. To prove their point, Thorsell and associates would have to repeat the study in women using ovulation-prediction methods or assisted reproduction (which would be confounded by subfertility and its link to poor perinatal outcomes). Such a study would not be feasible, given that a sample size of more than 27,000 women was required to demonstrate very mild effects in this investigation (risk ratios from 1.1 to 1.5).

WHAT THIS EVIDENCE MEANS FOR CLINICAL PRACTICE

This provocative study challenges convention but is not ready for incorporation into clinical practice routines. However, it may be prudent to monitor pregnancies in which US dating significantly changes the due date, keeping in mind a potential for intrauterine growth restriction.

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