Is the vaginal or buccal route more effective when administering prostaglandins for cervical ripening at term?

Vaginal administration of misoprostol (25 μg initial dose, 50 μg subsequent doses) may be superior to the buccal route, according to results of the IMPROVE trial, a prospective randomized placebo-controlled study of 300 women with a singleton vertex fetus requiring cervical ripening for induction of labor at term. Women treated with vaginal misoprostol (VM) had more rapid vaginal delivery, more vaginal deliveries within 24 hours, and fewer urgent cesarean deliveries for nonreassuring fetal testing (although the overall cesarean delivery rate was not significantly different) compared with those treated with buccal misoprostol (BM).


EXPERT COMMENTARY
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Cervical ripening is routine practice in women undergoing induction of labor who have an unfavorable cervical examination. This is because generating contractions against a long thick cervix is more likely to lead to failed induction and cesarean delivery. Cervical ripening can be achieved using mechanical or pharmacologic methods.

Misoprostol (a prostaglandin E, [PGE], analog) is approved by the US Food and Drug Administration for the treatment of peptic ulcer disease, but it also is widely used off-label for cervical ripening, partly due to its low cost. Misoprostol’s optimal dosing regimen and route of administration are not known. The IMPROVE trial was designed to address this knowledge gap, specifically to compare the efficacy and safety of VM versus BM in women undergoing labor induction at term.

Details of the study
The IMPROVE trial was a prospective, randomized, noninferiority, triple-masked,
Cervical ripening and risk of cesarean delivery among overweight patients

While a number of studies have evaluated the risk of cesarean delivery (CD) with the use of cervical ripening agents by different routes of administration, Handal-Orefice and colleagues studied this outcome specifically in a predominantly overweight population at a tertiary care center.1

The retrospective study included 276 women, of whom 91% had a body mass index (BMI) of 25 kg/m² or more and 61% had a BMI of 30 kg/m² or more at the time of delivery.

For cervical ripening, 138 women received vaginal misoprostol (25 µg) and 138 received oral misoprostol (50 µg). The frequency of CD (the primary study outcome) was significantly higher with oral compared with vaginal misoprostol use (32% vs 21%; P = .04). When the analysis was adjusted for age, BMI, parity, indication for induction, and Foley catheter use, the risk of CD remained significantly higher for the oral misoprostol group (adjusted odds ratio [aOR], 2.01; 95% confidence interval [CI], 1.07–3.76).

Other key findings:
- frequency of CD among nulliparous women: 41% in the oral misoprostol group, 28% in the vaginal misoprostol group (aOR, 2.79; 95% CI, 1.26–6.19)
- time to vaginal delivery: 41 hours for the oral misoprostol group, 31 hours for the vaginal misoprostol group (P = .01)
- uterine tachysystole: 11% in the oral misoprostol group, 20% in the vaginal misoprostol group (P = .04).

The authors noted that the strengths of the study, including the racial and ethnic diversity of the population (72% of women were of either black or Hispanic race or ethnicity), the commonly used doses of misoprostol, and the performance of inductions outside a research protocol, add to the generalizability of the results.

Reference
The study has good generalizability as it included both elective and medically indicated inductions; however, patients with ruptured membranes were excluded. Although there was no difference in the overall cesarean delivery rates, the study was underpowered to look at this outcome. The authors included a patient satisfaction survey, but this is hard to interpret since study participants all received tablets orally and vaginally. The study did not address efficacy of VM versus BM administration at different doses or time intervals.

**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

Labor induction has doubled over the past 2 decades, with almost 25% of parturients currently undergoing induction in the United States. This number is likely to increase given recent data suggesting that routine induction at 39 weeks may significantly decrease cesarean delivery rates. It is critical, therefore, that we identify the optimal technique for cervical ripening, including the ideal dosing regimen and route of administration. Results of the IMPROVE trial suggest that vaginal administration of misoprostol (25 μg initial dose, 50 μg subsequent doses) may be superior to the buccal route, with more rapid vaginal delivery, more vaginal deliveries within 24 hours, and fewer urgent cesareans for non-reassuring fetal testing (although the overall cesarean delivery rate was not significantly different).

**References**