FPIN's Clinical Inquiries

Misoprostol Dosing for First-Trimester Abortion

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Clinical Question

What is the most effective way to dose misoprostol (Cytotec) for evacuating the uterus of first-trimester products of conception?

Evidence-Based Answer

Vaginal, oral, and sublingual misoprostol in single doses of 600 to 800 mcg are equally effective for promoting completed abortion in patients with an incomplete first-trimester spontaneous abortion. (Strength of Recommendation [SOR]: A, based on consistent meta-analyses of randomized controlled trials [RCTs].) When combined with mifepristone (Mifeprex), a single 800-mcg dose of vaginal or buccal misoprostol is more effective than a single 800-mcg dose of oral misoprostol for first-trimester therapeutic abortion. (SOR: A, based on a meta-analysis of RCTs.) Vaginal dosing is better tolerated than oral, buccal, or sublingual dosing. (SOR: A, based on meta-analyses of RCTs.)

Evidence Summary

INCOMPLETE SPONTANEOUS ABORTION: SINGLE-DOSE MISOPROSTOL

Two 2017 systematic reviews evaluating misoprostol in women with incomplete first-trimester spontaneous abortion found that doses of at least 600 mcg were equally effective for uterine evacuation, regardless of the route of administration. The first review evaluated all options for the medical treatment of spontaneous abortion and included five RCTs of single-dose misoprostol regimens.[1] One RCT (n = 198) comparing vaginal and oral misoprostol, 800 mcg, found similar success rates for complete uterine evacuation (relative risk [RR] = 0.94; 95% CI, 0.76 to 1.16). Two RCTs (n = 464) compared different doses of oral misoprostol: 600 mcg vs. 1,200 mcg. Both doses resulted in similar rates of complete uterine evacuation (RR = 1.00; 95% CI, 0.93 to 1.07). Two additional RCTs (n = 358) compared sublingual misoprostol, 400 to 600 mcg, with oral misoprostol, 600 mcg. Oral and sublingual administration produced similar rates of complete uterine evacuation (RR = 0.99; 95% CI, 0.94 to 1.05).

The second review[2] evaluated 18 RCTs (N = 1,802), only one of which was included in the first review. The trials were primarily from India and Thailand and compared different misoprostol regimens in women with incomplete spontaneous abortions. In individual comparisons (unknown number of trials or patients), the authors found no significant differences in effectiveness between vaginal misoprostol, 800 mcg, vs. sublingual misoprostol, 600 mcg (RR = 1.01; 95% CI, 0.86 to 1.19); vaginal misoprostol, 800 mcg, vs. vaginal misoprostol, 600 mcg (RR = 1.22; 95% CI, 0.93 to 1.59); or vaginal misoprostol, 600 mcg, vs. sublingual misoprostol, 600 mcg (RR = 1.23; 95% CI, 0.99 to 1.55). Doses of less than 600 mcg were less effective than those of 600 to 800 mcg.

THERAPEUTIC ABORTION: MISOPROSTOL PLUS MIFEPRISTONE

A 2011 systematic review and meta-analysis evaluating medical therapeutic abortion in the first trimester found that oral dosing was the least effective route of administration.[3] The included RCTs used misoprostol in combination with mifepristone. Two RCTs (n = 1,407) comparing oral and vaginal misoprostol, 800 mcg, found that oral administration resulted in more incomplete abortions (RR = 3.05; 95% CI, 1.98 to 4.70). One RCT (n = 442) comparing buccal and vaginal

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This series is coordinated by John E. Delzell Jr., MD, MSPH, associate medical editor.

A collection of FPIN's Clinical Inquiries published in *AFP* is available at https://www.aafp.org/afp/fpin.

Author disclosure: No relevant financial affiliations.

misoprostol, 800 mcg, found no significant difference between the groups. Two RCTs (n = 490) comparing sublingual misoprostol, 600 to 800 mcg, with vaginal misoprostol, 800 mcg, found no difference in effectiveness. One RCT (n = 480) comparing sublingual and oral misoprostol, 400 mcg, found that sublingual administration was more likely to result in complete abortion (RR = 4.76; 95% CI, 1.38 to 16.7).

ADVERSE EFFECTS

In the 2017 review of five RCTs, rates of nausea and vomiting were similar for all comparisons, but rates of diarrhea sometimes differed.[1] One RCT (n = 198) comparing vaginal and oral misoprostol, 800 mcg, found that patients had less diarrhea with vaginal administration (RR = 0.21; 95% CI, 0.12 to 0.36). Two RCTs (n = 358) comparing sublingual misoprostol, 400 to 600 mcg, with oral misoprostol, 600 mcg, found no difference in rates of diarrhea.

In the 2017 meta-analysis of 18 RCTs, different dosing regimens and routes of administration generally yielded similar adverse effect profiles.[2] However, women who received vaginal misoprostol, 400 mcg, had less diarrhea and fever than those receiving sublingual misoprostol, 400 mcg (RR = 0.54; 95% CI, 0.32 to 0.90).

The 2011 review of RCTs combining misoprostol with mifepristone for therapeutic abortion found that vaginal dosing tended to be better tolerated.[3] In two RCTs (n = 1,407) comparing vaginal and oral misoprostol, 800 mcg, diarrhea and nausea occurred more often with oral dosing (RR for oral dosing = 1.80; 95% CI, 1.49 to 12.18; RR for vaginal dosing = 1.13; 95% CI, 1.02 to 1.25). In one RCT (n = 442) comparing buccal and vaginal misoprostol, 800 mcg, buccal administration resulted in more diarrhea (RR = 1.51; 95% CI, 1.12 to 2.03). In one of two RCTs (n = 150) comparing sublingual misoprostol, 600 to 800 mcg, with vaginal misoprostol, 800 mcg, sublingual dosing resulted in more diarrhea (RR = 2.5; 95% CI, 1.55 to 4.04), nausea (RR = 1.67; 95% CI, 1.21 to 2.29), and vomiting (RR = 2.93; 95% CI, 1.69 to 5.06). In the other (n = 340), more patients expressed dissatisfaction with sublingual dosing than with vaginal dosing (RR = 2.81; 95% CI, 1.15 to 6.87). One RCT (n = 480) comparing sublingual and oral misoprostol, 400 mcg, found no significant difference in adverse effects.

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