Cochrane for Clinicians

Putting Evidence into Practice

Emergency Contraception: Safety and Effectiveness

Sajeewane Seales, MD, MPH
Naval Medical Training and Readiness Command, Virginia Beach, Virginia

Paul Seales MD, MS, Fleet Surgical Team 4, U.S. Navy, Norfolk, Virginia

Author disclosure: No relevant financial affiliations.

Clinical Question

Which form of emergency contraception is the safest and most effective for preventing pregnancy after a single episode of unprotected intercourse?

Evidence-Based Answer

Oral mifepristone (Mifeprex), ulipristal (Ella), levonorgestrel-releasing emergency contraception (Plan B One-Step), ethinyl estradiol/levonorgestrel, and the copper intrauterine device (IUD; Paragard) are safe and effective for emergency contraception.[1] (Strength of Recommendation [SOR]: B, based on inconsistent or limited-quality patient-oriented evidence.)

In head-to-head comparisons, a one-time dose of mifepristone is more effective than any dose of oral levonorgestrel, with moderate-dose mifepristone (25 to 50 mg) being more effective than low-dose mifepristone (less than 25 mg; relative risk [RR] = 0.61). (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) All other forms of emergency contraception are more effective than ethinyl estradiol/levonorgestrel (RR = 0.57). (SOR: A, based on consistent, good-quality patient-oriented evidence.) Ulipristal is more effective than oral levonorgestrel alone (RR = 0.59). (SOR: A, based on consistent, good-quality patient-oriented evidence.)

The copper IUD is not inferior to any dose of mifepristone, but no direct comparison has been made between the copper IUD and other types of emergency contraception. (SOR: C, based on consensus, disease-oriented evidence, usual practice, expert opinion, or case series.) Adverse effects most often include nausea and vomiting for oral medications and abdominal pain and menorrhagia for the copper IUD.[1]

Practice Pointers

Emergency contraception is the use of a medication or device to prevent pregnancy following unprotected intercourse. Although the likelihood of pregnancy after a single episode of unprotected intercourse is highly variable depending on timing and other factors, emergency contraception can be more than 95% effective at preventing pregnancy when used within five days of intercourse. Nearly one-half of pregnancies in the United States are unintended, and they are associated with increased health risks to both mother and fetus.[2] The authors of this review sought to identify the safest and most effective emergency contraception.

This Cochrane review included 115 randomized controlled trials, 92 of which were performed in China, and involved 60,479 women who had engaged in a single act of unprotected intercourse.[1] Both one-time low-dose (less than 25 mg) and moderate-dose (25 to 50 mg) oral mifepristone were superior when compared with one-time oral levonorgestrel, 1.5 mg (RR for low-dose mifepristone = 0.72; 95% CI, 0.52 to 0.99; n = 8,752; RR for moderate-dose mifepristone = 0.61; 95% CI, 0.45 to 0.83; n = 6,052). For example, if the chance of pregnancy following unprotected intercourse and subsequent treatment with oral levonorgestrel is 20 women per 1,000, the chance following treatment with low-dose mifepristone would be between 10 and 20 women per 1,000. In a different cohort, if the chance of pregnancy following treatment with oral levonorgestrel is 35 women per 1,000, then the chance after taking moderate-dose mifepristone is between 16 and 29 women per 1,000. One study confirmed that oral levonorgestrel can be given as a single dose or as two doses 12 hours apart, but no difference in effectiveness was

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demonstrated between single and split dosing; other studies compared single-dose regimens.

All one-time doses of oral ulipristal, most often 30 mg, were more effective than oral levonorgestrel alone (RR = 0.59; 95% CI, 0.35 to 0.99; n = 3,448). If the chance of pregnancy following unprotected sex and treatment with oral levonorgestrel is 22 women per 1,000, the chance following treatment with ulipristal is eight to 22 per 1,000.

Ethinyl estradiol/levonorgestrel was found to be inferior to one-time oral levonorgestrel (RR = 0.57; 95% CI, 0.39 to 0.84; n = 4,750) and one-time mifepristone (RR = 0.14; 95% CI, 0.05 to 0.4; n = 2,144). In other words, if the chance of pregnancy following treatment with ethinyl estradiol/levonorgestrel is 29 women per 1,000, then the chance following treatment with oral levonorgestrel is between 11 and 24 women per 1,000. In the mifepristone studies, if the chance of pregnancy after taking ethinyl estradiol/levonorgestrel is 25 women per 1,000, the chance after taking a single dose of mifepristone is one to 10 per 1,000.

A single study comparing the effectiveness of the copper IUD and moderate-dose mifepristone (25 to 50 mg) at preventing pregnancy revealed no significant difference between the two treatments (RR = 0.33; 95% CI, 0.04 to 2.74; n = 395).

No serious adverse effects were reported in any of the studies. Nausea and vomiting were most common in patients taking oral medications, with mifepristone and oral levonorgestrel having lower rates than ethinyl estradiol/levonorgestrel. Menstrual delay occurred most often in those taking mifepristone vs. any other intervention, and this appeared to be dose-dependent. Users of ulipristal were more likely to experience delayed resumption of menses compared with those who took oral levonorgestrel (RR = 1.65; 95% CI, 1.42 to 19.2; n = 3,593). Women who used copper IUDs were at risk of uterine perforation and/or expulsion, abdominal pain, and menorrhagia.[3,4]

The 2015 American College of Obstetricians and Gynecologists practice bulletin on emergency contraception recommends ulipristal, oral levonorgestrel, and the copper IUD as effective forms of emergency contraception.[3] (SOR: A, based on consistent, good-quality patient-oriented evidence.) Because ethinyl estradiol/levonorgestrel is often the only method available, physicians should be familiar with its dosing regimens. They should also be educated on all of the available methods so that they can provide compassionate and timely emergency contraception to their patients.

The practice recommendations in this activity are available at http://www.cochrane.org/CD001324.

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Potential of Fetal Fibronectin Testing to Prevent Preterm Birth

Tyler Barreto, MD, MPH, Sea Mar Marysville Family Medicine Residency, Marysville, Washington

Author disclosure: No relevant financial affiliations.

Clinical Question

Does testing for fetal fibronectin in patients with signs and symptoms of preterm labor help to prevent preterm birth (i.e., birth before 37 weeks' gestation)?

Evidence-Based Answer

Fetal fibronectin testing may reduce preterm birth, although the evidence is not strong enough to recommend regular testing. Knowing the results of fetal fibronectin testing does not lead to a reduction in secondary outcomes such as preterm birth before 34 weeks' gestation, admission to the neonatal intensive care unit, or perinatal death.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Preterm birth affects about one in 10 births in the United States and is the second most common cause of infant mortality.[2,3] Tools to identify the risk of preterm birth are limited. One potential marker, fetal fibronectin, is a glycoprotein produced by amniocytes and cytotrophoblasts and is found at the maternal-fetal interface. It is believed that fetal fibronectin keeps the amniotic sac attached to the uterine lining. In practice, a positive test result indicates that the mother is at increased risk of preterm birth during the ensuing seven days.[4] This review focuses on the potential of fetal fibronectin testing to prevent preterm birth in patients with signs and symptoms of preterm labor.

The authors assessed six trials with 546 women who had a singleton pregnancy and signs and symptoms of preterm labor at 23 weeks' to 34 6/7 weeks' gestation.[1] Only studies evaluating outcomes based solely on fetal fibronectin test results were included. Interventions based on additional methods of preterm delivery prediction, such as cervical length measurement, were not included. One trial was completed in the United Kingdom, and five were completed in the United States.

Management of preterm labor based on fetal fibronectin results did not reduce the overall rate of preterm birth (relative risk = 0.72; 95% CI, 0.52 to 1.01). However, when excluding one of the smallest trials (n = 77), which was called into question based on unclear risk of allocation concealment, fetal fibronectin results appeared to significantly reduce the risk of preterm birth (relative risk = 0.67; 95% CI, 0.46 to 0.97), leading authors to suggest that there may be a benefit from fetal fibronectin testing.

Fetal fibronectin testing results did not affect any of the secondary outcomes, including preterm birth at less than 34 weeks' gestation, gestational age at delivery, perinatal death, maternal hospitalization, tocolysis, use of steroids for fetal lung maturity, neonatal intensive care unit admission, or maternal well-being.

This review was limited to studies using only fetal fibronectin testing. In clinical practice, fetal fibronectin results would not be used alone. The clinician would likely seek additional information such as a thorough history and cervical length. A lack of demonstrable change in secondary outcomes also indicates that fetal fibronectin testing alone should not change management.

A 2016 American College of Obstetricians and Gynecologists practice bulletin notes that although fetal fibronectin and cervical length may predict preterm birth, there is no evidence to support the use of these measures to guide management of preterm labor.[5] Further studies are needed to determine if fetal fibronectin testing can lead to prevention of preterm birth. Physicians may consider fetal fibronectin testing in patients with signs and symptoms of preterm labor to aid in predicting the risk of preterm birth.

The practice recommendations in this activity are available at http://www.cochrane.org/CD006843.

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