10 mg of mifepristone prevented pregnancy as effectively as 600 mg within 5 days of unprotected intercourse

Task Force on Postovulatory Methods of Fertility Regulation. **Comparison of three single doses of mifepristone as emergency contraception: a randomised trial.** Lancet. 1999 Feb 27;353:697-702.

Question
In women who have had unprotected intercourse in the previous 5 days, what is the relative effectiveness of mifepristone in doses of 600, 50, and 10 mg in preventing pregnancy?

Design
Randomised, single-blind (patient), controlled trial with follow-up to the next menstrual cycle or confirmation of pregnancy.

Setting
11 family planning clinics in 6 countries.

Patients
1717 healthy women who had regular menstrual cycles and had requested emergency contraception within 120 hours of 1 act of unprotected intercourse, were willing to avoid further acts of unprotected intercourse during the present menstrual cycle, and were available for follow-up during the next 6 weeks. Exclusion criteria were pregnancy or breast-feeding, current use of hormonal contraception, uncertainty about the date of the last menstrual period, contraindications to mifepristone, or likeliness to continue pregnancy if treatment failed. 1684 women (98%) were included in the analysis (mean age 28 y).

Intervention
Women were allocated to oral mifepristone given in 3 tablets containing 600-mg (n = 570), 50-mg (n = 575), or 10-mg (n = 572) doses.

Main outcome measures
Unintended confirmed pregnancy, side effects, and delay in the onset of the next menstrual cycle.

Main results
20 women became pregnant after treatment. The groups did not differ in the proportion of pregnancies; the overall proportion of pregnancies prevented was 85% (Table). Delays in the onset of the next menstrual period were dose dependent: delay > 7 days occurred in 36%, 23%, and 18% of women who took 600, 50, and 10 mg of mifepristone, respectively ($P < 0.01$). Bleeding within 5 days of treatment was also dose dependent and occurred in 35%, 31%, and 15% of women who took 600-, 50-, and 10-mg doses ($P < 0.01$), respectively. No other side effects differed among groups.

Conclusion
In women who have had unprotected intercourse in the previous 5 days, mifepristone doses of 600, 50, and 10 mg were equally effective in reducing the likelihood of pregnancy.

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Mifepristone for preventing pregnancy up to 5 days after unprotected intercourse

Mifepristone dose	Proportion pregnant (95% CI)	RRR (CI)*
10 mg	1.2% (0.5 to 2.5)	85% (67 to 93)
50 mg	1.1% (0.4 to 2.3)	86% (69 to 94)
600 mg	1.3% (0.5 to 2.6)	84% (67 to 93)

*Abbreviations defined in Glossary; estimated reduction in expected pregnancies based on non-trial data.

Commentary

Effective, well-tolerated, and accessible emergency contraception is needed if unwanted pregnancies after unprotected intercourse are to be avoided. 600 mg of mifepristone is effective but costly, and many users have delayed menstruation (especially unwelcome by those already concerned about pregnancy). The trial from the World Health Organization Task Force on Postovulatory Methods of Fertility Regulation suggests that a 10-mg dose given within 5 days of unprotected intercourse is as effective as higher doses and has fewer side effects, including less delayed menses.

The trial was carefully designed, with few protocol violations (< 1%) and little loss to follow-up (< 2%). The size of the trial, however, was based on a smaller anticipated outcome rate than that observed (predicted proportion of pregnancies 0.5% vs 1.2% observed) (1, 2). This, and slower recruitment rates, resulted in restricted statistical power: A nearly 3-fold difference between doses could not be ignored, nor could important differences in outcome associated with timing of administration. Until more information is available, emergency contraception should be given as early as possible (3).

About 40% of trial participants requested emergency contraception because they had not used a contraceptive; another 57% reported condom failure. 25% of participants had used emergency contraception previously, and most had used another method of contraception. These data emphasise the continued need for effective emergency contraception.

Mifepristone is controversial because of its association with induced abortion. Further, because it may delay ovulation, mifepristone may be less effective than other hormonal postcoital contraceptives if couples continue to have unprotected intercourse. These concerns, however, may be offset by a lower incidence of side effects, especially at 10-mg doses. Further work is needed to determine the acceptability and role of mifepristone in emergency contraception.

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References

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