

# Single dose mifepristone, single dose levonorgestrel, or 2 dose levonorgestrel were effective emergency contraceptives

von Hertzen H, Piaggio G, Ding J, et al. *Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. Lancet* 2002;360:1803–10.

**QUESTION:** In women requesting emergency contraception, what is the relative effectiveness of a single dose of mifepristone, a single dose of levonorgestrel, or 2 separate doses of levonorgestrel in emergency contraception?

## Design

Randomised (allocation concealed\*), blinded (clinicians, patients, monitoring committee, {data collectors, outcome assessors, and data analysts}†),\* controlled trial with 6 weeks of follow up.

## Setting

15 family planning clinics in China, Finland, Georgia, Hungary, India, Mongolia, Slovenia, Sweden, Switzerland, and the UK.

## Patients

4136 women (mean age 27 y) who presented for emergency contraception within 120 hours of 1 act of unprotected coitus in their present menstrual cycle. Women had to be healthy, have regular (24–42 d duration) menstrual cycles, and be willing to abstain from unprotected intercourse during the menstrual cycle. Women who had been pregnant or had recently discontinued hormonal contraception had to have had  $\geq 1$  complete and normal menstrual cycle before the current cycle. Exclusion criteria were pregnancy, breast feeding, use of hormonal contraception or the rhythm method in the current cycle, uncertainty about date of last menstrual period, and contraindication to mifepristone. 4071 women (98%) were included in the efficacy analysis and 4084 (99%) in the safety analysis.

## Intervention

Women were allocated to a single 10 mg dose of mifepristone (n=1380), a single 1.5 mg dose of levonorgestrel (n=1379), or 2 separate doses of 0.75 mg of levonorgestrel given 12 hours apart (n=1377).

## Main outcome measures

Unintended pregnancy. Secondary outcomes were side effects in the week after the start of treatment and time to first menstruation after treatment.

## Main results

Analysis was by intention to treat. 65 women (1.6%) became pregnant. The 3 groups did not differ for pregnancy rates (p=0.83) (table). Effectiveness was not affected by a delay in treatment > 72 hours. Side effects were generally mild and did not differ among groups except that more women who received levonorgestrel than mifepristone had bleeding within the first 7 days of treatment (31% v 19%, p < 0.001) and more women who received mifepristone than levonorgestrel had a delay of > 7 days in menses (9% v 5%, p < 0.001).

## Conclusion

In women requesting emergency contraception, a single dose of mifepristone, a single dose of levonorgestrel, or 2 separate doses of levonorgestrel given 12 hours apart were similarly effective in preventing pregnancy if taken within 5 days.

\*See glossary.

†Information provided by author.

*Mifepristone, single dose levonorgestrel, and 2 doses of levonorgestrel for emergency contraception at 6 weeks‡*

Drug	Pregnancy rate	Comparison	Relative risk (95% CI)
Mifepristone	1.55%	v 2 dose levonorgestrel	0.87 (0.49 to 1.56)
Single dose levonorgestrel	1.47%	v 2 dose levonorgestrel	0.83 (0.46 to 1.50)
		v mifepristone	0.95 (0.52 to 1.75)
2 dose levonorgestrel	1.77%	v mifepristone	1.15 (0.64 to 2.05)
Levonorgestrel 2 regimens combined	1.62%	v mifepristone	1.05 (0.63 to 1.76)

‡All values are not significant.

## COMMENTARY

Every day millions of women risk pregnancy because they have coitus without using contraception or the method they are using fails. Hormonal emergency contraception substantially reduces this risk. A previous trial showed the superior efficacy and side effect profile of levonorgestrel over the Yuzpe method, when taken 12 hours apart within 3 days of unprotected intercourse.<sup>1</sup> Another trial has shown that single low dose mifepristone taken within 5 days of unprotected intercourse is as effective as high dose preparations.<sup>2</sup>

The trial by von Hertzen *et al* directly compared the efficacy and side effects of mifepristone and levonorgestrel when used within 5 days of unprotected intercourse, levonorgestrel being taken in single or divided doses. The study showed similar, low pregnancy rates in each group. The number of women lost to follow up was small, but if some had become pregnant, their exclusion from the efficacy analysis would have underestimated the true pregnancy rate in each group (although comparisons between groups are likely to remain valid).

These theoretical considerations aside, this rigorously done trial has important clinical implications. Firstly, it supports the case for levonorgestrel as the first choice in hormonal emergency contraception. Although side effects were generally infrequent and similar in each group, levonorgestrel users had more bleeding and earlier menses than mifepristone users, and mifepristone users had more delayed menses. Minimising the interval between treatment and menstruation is important, partly because intercourse during this period increases the risk of pregnancy, even with additional contraception. Secondly, it simplifies levonorgestrel use; single doses are effective and do not increase side effects. Thirdly, it extends the period within which levonorgestrel can be used (although delay to treatment analyses highlight the maxim that earlier is better than later when using this method). The challenge now is to widen the availability of this valuable contraceptive.

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- 1 Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 1998;352:428–33.
- 2 Task Force on Postovulatory Methods of Fertility Regulation. Comparison of three single doses of mifepristone as emergency contraception: a randomised trial. *Lancet* 1999;353:697–702.