

comparable with other IUDs. Even though there was no direct comparison, the side effect profile was not dissimilar to that shown by similar studies with other IUDs.

This phase III trial did not include women who were nulliparous or under the age of 18 years. As with any other product, when used in clinical practice the pregnancy rates and removal rates will vary according to the population using the method. The initial results suggest that the product is similar to IUDs already in established use.

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**Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial.** von Hertzen H, Piaggio G, Ding J, et al. *Lancet* 2002; **360**(9348): 1803–1810

Levonorgestrel (LNG) taken in divided doses has replaced the Yuzpe regimen for emergency contraception (EC) where it is available. This World Health Organization (WHO) trial was designed to see if LNG can be given as a single dose, and to compare both regimens with single-dose mifepristone, used up to 5 days after unprotected intercourse.

In this triple-blind study, using a secure method or randomisation, 4136 women were

allocated to 10 mg mifepristone, a single dose of 1.5 mg LNG or two doses of 0.75 mg LNG taken 12 hours apart. It was an international study with just over half the participants coming from China. The loss to follow-up rate was low at 1.5%.

The pregnancy rates were similar with the three treatments: 1.5% each for mifepristone and single-dose LNG and 1.8% with the two-dose LNG. The relative risk of pregnancy of single-versus two-dose levonorgestrel was 0.83 (95% CI 0.46–1.50). When restricted to women who had treatment within 1–3 days of intercourse, the same comparisons gave a similar result (relative risk 0.79, 95% CI 0.41–1.52, difference in risk of pregnancy –0.4%, 95% CI –1.3%–0.6%, calculated from data in the paper).

There was a significant rising trend in pregnancy rates, for all treatments combined, in the five successive days from the time of intercourse ( $p = 0.02$ ), although the pregnancy rate with LNG was numerically higher following treatment delay of 1 day compared to a delay of 2 or 4 days. The authors estimated that around 60% of expected pregnancies were prevented with each of the regimens when treatment was started 4–5 days after intercourse. The side effect profiles with the three regimens were very similar, the only difference being less frequent bleeding after treatment, and a delay in menses, with mifepristone.

This is a well-designed trial minimising opportunities for systematic bias. Together with

its large size, it allows a confidence in using the results in clinical practice. A single dose of LNG can replace the standard two-dose treatment, up to 3 days after intercourse, with no loss of efficacy and no change in side effects. The remarkably similarity of reported side effects with mifepristone and LNG with different pharmacodynamics suggests that a placebo arm may have had similar effects. The simplification of the treatment is welcome.

The efficacy of LNG used beyond 72 hours after intercourse is as uncertain as ever. Even in this large trial fewer than 500 women attended 4–5 days after treatment and the wide confidence intervals for pregnancies prevented include no effect. Estimates of pregnancies prevented, however, have very limited validity as the method used to calculate 'expected pregnancies' is derived from different women in different circumstances and based on crude estimates of day of ovulation. Ultimately, the real efficacy can only be answered by a placebo-controlled randomised trial at a coitus-to-treatment interval where there is uncertainty about efficacy, and an intrauterine device (IUD) is inappropriate.

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