Repeated use of pre- and postcoital hormonal contraception for prevention of pregnancy

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An updated version of this systematic review has been published and can be found online at www.cochrane.org. We will soon update the below RHL summary to reflect the updated findings of the systematic review.

This review suggests that repeated use of 0.75 mg levonorgestrel is not only safe but also effective in preventing pregnancy. However, the effect of emergency contraceptive pills on pregnancy outcomes is unknown. Precoital use of emergency contraceptives is currently not recommended by WHO and, as the data in this review show, taking emergency contraceptive pills prior to intercourse was not effective in preventing pregnancy.

RHL Commentary by Gaffield ME

1. INTRODUCTION

Worldwide, an estimated 80 million unplanned pregnancies occur each year (1). Emergency contraception (EC) – either contraceptive pills or copper-bearing intrauterine devices – refers to a back-up method of contraception for preventing unplanned pregnancy in the event of unprotected sex, contraceptive failure, or sexual assault. Emergency contraceptive pills (ECPs) are the most commonly used EC method and are registered in more than 117 countries (1). The mechanism of action for single use of ECP is primarily thought to be due to suppression of ovulation (2).

Current WHO guidance recommends a single dose of levonorgestrel (LNG) (1.5 mg) for emergency use within first 120 hours after unprotected sex; taking a repeat dose does not pose any known health risks, although this is not recommended by WHO. Owing to concerns about side-effects, and the lower level of effectiveness of EC compared with other modern methods of contraception, EC is not recommended for use as a regular method of contraception (3, 4). Nevertheless, reports from a variety of settings suggest that repeated use of ECPs for contraception is common, particularly among women who have sex infrequently. This Cochrane review (5) aims to evaluate the effectiveness and safety of repeated pre- and postcoital use of hormonal contraception for pregnancy prevention.
2. METHODS OF THE REVIEW

The review authors conducted a comprehensive and exhaustive search of eight electronic databases for published and unpublished studies, in all languages, reporting on repeated precoital or immediate postcoital use of oral steroid hormonal drugs for contraception, where pregnancy was measured as an outcome. The Pearl Index (number of pregnancies per 100 women–years of use) was used to measure the treatment effect. Secondary outcomes of interest included side-effects that were related to ECP use, bleeding patterns, and discontinuation rates. For inclusion, studies were required to report on the time of follow-up of study participants as well as the drug regimen and dosage. Non-randomized trials were eligible for inclusion. To ensure data extraction accuracy and completeness, two authors independently extracted and entered the data in RevMan. The GRADE system was used to appraise the quality of evidence. Most studies reported Pearl Indices; however, when this measure was not provided, the review authors computed Pearl Indices based upon available data. In the event of missing data, the authors attempted to contact researchers of studies conducted within the previous decade. Owing to extensive heterogeneity across the included studies – with respect to their study design, study populations, interventions, and measured outcomes – the review authors did not conduct a meta analysis of pregnancy risk. Pooled Pearl Indices with 95% confidence intervals (CI) were estimated across several studies, where possible. Overall, the review methods clearly report how the review was conducted, as well as the data available upon which the authors base their findings.

3. RESULTS OF THE REVIEW

The review identified 21 trials (involving 12,323 women from Europe, Asia, Central and South America) that evaluated the effectiveness of repeated pre- or postcoital use of hormonal contraception to prevent pregnancy. The timing of use and pill formulations varied across these trials: nine trials examined postcoital use of LNG 0.75mg; four trials studied postcoital LNG use in doses other than 0.75 mg; six trials reported on pericoital use of progestogen-only or combined hormonal pills (megestrol acetate – a progestogen; dienoestrol – an estrogen; dienoestrol plus ethynodiol-diacetate; and quingestanol acetate – a progestogen); one trial postcoital use of quingestanol acetate and LNG 0.35 mg; and one trial studied use of LNG 0.4 mg and LNG 0.75 both pre- and postcoitally.

Among 10 trials (2628 women) evaluating postcoital use of 0.75 mg LNG, the Pearl Indices ranged from 0 to 18.6 pregnancies per 100 women–years, resulting in a pooled Pearl Index of 5.1/100 women–years (95% CI 3.8–6.7). Coital frequency among women in these trials ranged from 1–15 acts of unprotected sexual intercourse per month. Because the quality of most of these trials was poor, the review authors computed a pooled estimate from three trials of higher methodological quality. The Pearl Indices in those trials ranged from 6.8 to 18 pregnancies per 100 woman–years, with a pooled estimate of 8.9/100 woman–years (95% CI 5.1–14.4). Evaluation of the occurrence of side-effects across the LNG 0.75-mg trials was not possible because reporting of menstrual irregularities was not consistent and minimal to no information was available on pregnancy outcome(s). Discontinuation of this method due to side-effects was rare.

Among the six trials that examined different doses of LNG use postcoitally, the Pearl Indices ranged from 0 to 9.0 pregnancies per 100 woman–years, giving a pooled estimate of 4.9 pregnancies/100 woman–years (95% CI 4.3–5.5). The relation between LNG dose or frequency of pill intake and the incidence of bleeding could not be established.

A pooled Pearl index of 5.3 pregnancies per 100 W-Y (95% CI 3.5 to 7.8) was estimated for quingestanol from two trials, as a third trial did not provide sufficient pregnancy data. Pericoital use of other progestogens resulted in higher rates of pregnancy (most Pearl indices > 15), and precoital use of megastrol acetate up to 22 hours resulted in a Pearl Index over 400.

Substantial methodological shortcomings across the majority of trials were noted by the review authors.
Moreover, the reporting of results within trials was considered to be of poor quality. Methodological limitations included: high levels of loss-to-follow-up in many trials; limited evaluation of potential confounders; peer-review status of nine trials could not be established; lack of information on statistical testing; and inadequate information on inclusion or exclusion criteria used to select study participants, collect study measures, and to assess fertility.

4. DISCUSSION

4.1. APPLICABILITY OF THE RESULTS

While findings from this review present reassuring evidence that earlier safety concerns regarding repeated use of postcoital hormonal contraception may need to be re-considered, it is not clear whether these findings can be applied to the currently recommended ECP regimen of LNG 1.5 mg. For women using LNG postcoitally immediately after intercourse (or shortly thereafter), the effectiveness of repeated LNG 0.75 mg use compared favourably with the effectiveness of either male or female condoms. It is not known whether these trial results can be reproduced in real-life settings. Reports of side-effects and bleeding irregularities were minimal; thus, in general, it appears that repeated postcoital use ECP was well-tolerated. The effect of ECPs on pregnancy outcome is unknown; however, several studies have not observed any increased risk of teratogenic outcomes resulting from exposure in early pregnancy to the higher doses of progestogens in either combined hormonal contraceptives (6) or to depot-medroxyprogesterone acetate (7). Finally, precoital use of EC is currently not included in WHO recommendations for pregnancy prevention.

4.2. IMPLEMENTATION OF THE INTERVENTION

In settings where LNG 0.75 mg is available and used for EC, results from this review provide reassurance that repeated use of this drug dose is not only safe but also efficacious in preventing pregnancy, at similar rates to the male or female condom. This evidence may be particularly useful for women who have infrequent sexual intercourse and want to have a supply of EC on hand, in the event they need protection from pregnancy. Health-care providers at all levels of the health system should have the capacity to counsel women about EC and offer it in advance of need, keeping in mind that women should be informed also about the effectiveness of other modern methods of contraception as well as about methods of protection against sexually transmitted infections.

4.3. IMPLICATIONS FOR RESEARCH

The trials included in this review were not only conducted using formulations and dosages that are currently not recommended by WHO, but also suffered from numerous methodological weaknesses that limited the interpretation of their results. Further research is needed to address whether repeated use of LNG 1.5 mg is safe and effective, and efforts must be made to ensure that these studies are of high quality. Evidence on the safety of repeated use of newer ECPs, such as ulipristal acetate is also warranted. Although results of this review show that precoital use of older EC formulations was not effective in preventing unintended pregnancy, high-quality studies are needed to determine whether precoital use of LNG could provide effective protection against pregnancy.

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References

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• Halpern V, Raymond EG, Lopez LM. Repeated use of pre- and postcoital hormonal contraception for prevention of pregnancy. Cochrane Database of Systematic Reviews 2010;Issue 1. Art. No.: CD007595; DOI: 10.1002/14651858.CD007595.pub2

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