

Talking straight about emergency contraception

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Background

In this Commentary we review recent research about the mechanism of action of levonorgestrel emergency contraceptive pills (ECPs) and the population impact of emergency contraception (EC), and we examine the downside of making ECPs available directly from a pharmacist or other non-specialist provider without a prescription. We argue that better information-giving about EC is needed and that it is essential that emergency intrauterine device (IUD) insertion services are enhanced (Box 1).

Mechanism of action of ECPs

Early treatment with ECPs containing only the progestin levonorgestrel has been shown to impair the ovulatory process and luteal function;^{1–6} no effect on the endometrium was found in two studies,^{2,3} but in another study levonorgestrel taken before the luteinising hormone surge altered the luteal phase secretory pattern of glycodeilin in serum and the endometrium.⁷ Levonorgestrel also interferes with sperm migration and function at all levels of the genital tract.⁸ Studies in the rat and the *Cebus* monkey demonstrate that levonorgestrel administered in doses that inhibit ovulation has no post-fertilisation effect that impairs fertility.^{9–11} Whether these results can be extrapolated to women is unknown. Based on those animal studies and on their own studies in women (including their latest one in which no pregnancies were observed when levonorgestrel-only ECPs were taken before the day of ovulation whereas four to five would have been expected and three pregnancies were observed when ECPs were taken after ovulation when three to four would have been expected),¹² Novikova and colleagues have argued that most, if not all, of the contraceptive effect of both combined and levonorgestrel-only ECPs can be explained by inhibited or dysfunctional ovulation.

The reduced effectiveness with a delay in treatment, even when use is adjusted for cycle day of unprotected sex,¹³ is consistent with a contraceptive mechanism that is independent of effects on implantation. If ECPs did interfere directly with implantation, then delays in use should not reduce their effectiveness as long as they are used just before or during implantation.¹⁴ Nevertheless, it is unlikely that this question can ever be unequivocally answered, and we therefore cannot conclude that ECPs never prevent pregnancy after fertilisation.

To make an informed choice, women must know how ECPs work, when they won't, what their choices of emergency contraceptives are, and treatment risks, if any. Women should be informed that like all ongoing hormonal

Box 1: Factors that are key to a successful emergency contraception service

Women need to know:

- Emergency contraception pills *per se* carry almost no health risk no matter how often used.
- At certain times of the cycle or if delayed they are less effective.
- They are not a talisman. They work only if you swallow them!

The following elements need to be commissioned:

- Health promotion on emergency contraception and how/where/when to access it.
- Easy access from as many medical and non-medical providers as possible.
- Easy access to specialist services for emergency intrauterine devices through care pathways.
- Emergency contraception as an integral part of comprehensive sexual health care.

contraceptives such as the pill, patch, implant, injectable and ring,¹⁵ and even breastfeeding,^{16–19} ECPs may prevent pregnancy by delaying or inhibiting ovulation, inhibiting fertilisation, or inhibiting implantation of a fertilised egg. But, as a comprehensive review of the mechanism of action of levonorgestrel-only ECPs concluded: "At the same time, however, all women should be informed that the best available evidence is consistent with the hypothesis that their ability to prevent pregnancy can be fully accounted for by mechanisms that do not involve interference with post-fertilization events."¹⁴ Thus, an important clinical implication emerges from this review. If women are too near, at, or just past ovulation, then ECPs are less likely to work, if at all. It is no longer acceptable to say that 1.5 mg levonorgestrel will prevent about 84% (Levonelle One Step[®] package insert) or 89% (Plan B[®] package insert) of pregnancies when taken within 72 hours of intercourse without qualifying where in the cycle relative to ovulation it is taken. ECP dispensers need to take the best possible history and be able to offer the choice of an emergency insertion of a copper IUD if the client wishes to have the most effective EC. It is particularly important if the history clearly indicates that ECPs might not be effective or if the woman is unsure about where in her cycle she is (of course some clients will be dead sure, and dead wrong!) or if, regardless, she wishes to have the most effective EC. Emergency insertion of a copper IUD is always significantly more effective than use of ECPs, reducing the risk of pregnancy following unprotected intercourse by as much as 99%.^{20,21} This very high level of effectiveness implies that emergency insertion of a copper IUD must also be able to prevent pregnancy after fertilisation.

Population impact of ECPs

Reported evidence demonstrates convincingly that making ECPs more widely available does not increase risk-taking or adversely affect regular contraceptive use.^{22–35} In the three studies that examined the impact of easier access to ECPs on rates of sexually transmitted infections (STI), women randomly assigned to the group given advance supplies of ECPs for later use should the need arise had the same incidence of infection as did women in the control group who had to obtain ECPs from a clinic.^{27,29,34,35} Conversely, no published study has yet demonstrated that

J Fam Plann Reprod Health Care 2007; **33**(3): 139–142

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increasing access to ECPs can reduce pregnancy or abortion rates in a population,^{35–37} although one demonstration project³⁸ and three clinical trials^{29,30,34} were specifically designed to address this issue. The explanation for this result is that even when provided with ECPs in advance, women do not use the treatment often enough after the most risky incidents to result in a substantial population impact. In the demonstration project, 78% of women with advance supplies who got pregnant did not use ECPs. In the San Francisco trial, almost half of the women in the advance provision group who had unprotected intercourse did not use ECPs. In the Chinese trial, 30/38 pregnancies in the advance provision group occurred in women who did not use ECPs in that cycle. Finally, in the Nevada/North Carolina trial, 57/74 pregnancies in the advance provision group occurred in women who did not use ECPs in that cycle.

Effectiveness of ECPs

The chance that pregnancy would occur in the absence of EC has been estimated indirectly using published data on the probability of pregnancy on each day of the menstrual cycle.^{39,40} This estimate is compared to the actual number of pregnancies observed after treatment in observational treatment trials. Effectiveness is calculated as the reduction in women's chance of pregnancy: $1 - O/E$, where O and E are the observed and expected number of pregnancies, respectively. Eight studies of the levonorgestrel regimen that in total included more than 9500 women reported estimates of effectiveness between 59% and 94%.^{41–48} Calculation of effectiveness, and particularly the denominator of the fraction, involves many assumptions that are difficult to validate. Therefore, reported figures on the efficacy of EC may be underestimates or, more probably, overestimates.⁴⁹ Nevertheless we have excellent evidence that levonorgestrel-only ECPs work. Combined data from two randomised trials that directly compared the levonorgestrel-only regimen and levonorgestrel-ethinylestradiol (Yuzpe) regimen showed a relative risk of pregnancy of 0.51 for the levonorgestrel-only regimen (95% CI 0.31–0.83), indicating that the chance of pregnancy was about half that among those who received the combined regimen.^{44,45,50} If we assume that the Yuzpe regimen is totally ineffective, then the estimate of levonorgestrel-only ECP effectiveness would be 49%. If we assume that the effectiveness of the Yuzpe regimen is 50%, then the implied effectiveness of the levonorgestrel-only regimen would be 74%. Of course, these estimates are averages and do not reflect differential efficacy by timing of ECP ingestion relative to the day of ovulation. As noted above, it is likely that the failures occur when ECPs are not taken far enough in advance of ovulation, and this explanation would also be consistent with the finding that the risk of failure increases with delay in treatment.¹⁴

Hence, we can be confident that levonorgestrel-only ECPs do substantially reduce the risk of pregnancy when they are actually used. The lack of a population level effect on reducing unintended pregnancy is due to insufficient use. But if there is insufficient use in groups of women given an advance supply of ECPs at no cost, it is highly unlikely that there will be a major public health impact when women have to obtain and pay for ECPs. ECPs are a tiny cork floating on a vast sea of unprotected sex! There is an apt analogy with condoms and HIV. A meta-analysis has demonstrated that in HIV-discordant couples in which the male was infected and the female was not, no reduction in the risk of acquiring HIV was seen unless condoms were used during 100% of acts of intercourse.⁵¹ Just making treatment available does not change human nature or

behaviour, nor does only occasional use when at risk provide any long-term benefit.

Demedicalisation of access to ECPs

Access to levonorgestrel-only ECPs from a pharmacist without prescription in the UK and USA bears comparing. Unlike in the UK, pharmacists in the USA do not have to receive any training whatsoever to dispense levonorgestrel-only ECPs without a prescription. It is evident from e-mails to the Emergency Contraception Website 'not-2-late.com' that some pharmacists in the USA are woefully ignorant about EC. Also, in the USA, there has been an increase in cost [from about \$25 (£12.50) to \$40–\$45 (£20.00–£22.50)], presumably to cover the expense of advertising to consumers, accompanied by a loss of insurance coverage, even for women aged 18 years and over who obtain a prescription (since the ECP Plan B is over-the-counter and does not require a prescription, most insurance companies no longer cover it). It is clear that in the UK many (a third of) women prefer to pay £25 for the convenience of getting Levonelle One Step from a pharmacist even though Levonelle 1500® is free on prescription, from a community contraception clinic, or a scheme where the drug can be dispensed free by Patient Group Direction (PGD)²² (e.g. from pharmacists or school nurses). It is not hard to understand why. Access to general practitioner (GP) appointments can be difficult and community contraception clinics are being closed.⁵² Women (particularly young women) are often shy of sitting in a GP's waiting area for hours in full potential view of their neighbours wondering why they are there, and women of all ages worry about being told they are feckless, stupid or promiscuous.

In both countries, a predictable adverse consequence is the loss of contact with a clinician. When women were required to see a clinician to obtain ECPs there was a potential bridging opportunity to discuss the relative effectiveness of ECPs versus an emergency IUD, provide the said emergency IUD, initiate effective regular methods of ongoing contraception if ECPs were chosen, and assess and manage STI risk. Admittedly that opportunity was only potential because there is no requirement for professionals in general practice to be post-basic trained in contraception. Nevertheless, for women who would have seen a specialist clinician or a GP who would have initiated such a discussion, that bridging opportunity is lost. Pharmacists are neither trained nor paid to provide ongoing contraception, although some UK schemes provide free condoms and chlamydia tests with ECPs by PGD. Of particular note is that among women who buy ECPs directly from a pharmacist or via PGD, the opportunity for immediate emergency insertion of a copper IUD is now lost, and with it up to 10 additional years (depending on the device) of highly effective contraceptive protection. The demedicalisation of access to ECPs has been successful in improving access, a laudable accomplishment. Advance provision would be further progress. But such increased access demands an informed discussion regarding choice of method of EC, particularly now given the evidence available on ECP effectiveness (or lack of) in different times of the cycle, and at least the broaching of ongoing contraception, especially long-acting reversible methods,⁵³ and STI prevention and detection. In the UK, this need can best be addressed by updating the written and verbal information women should be given on effectiveness, and involving community pharmacists and other non-specialist providers in care pathways within managed clinical networks so women can be 'signposted on' for an emergency IUD insertion and full contraceptive and sexual health care.

Conclusions

Access, care pathways and specialist provision are critical areas that must be brought to the attention of Primary Care Trust commissioners: easy access to ECPs today may reduce the risk of pregnancy from an act of unprotected intercourse last night, if taken early enough in the cycle, but not from the STI acquired during the same episode or the recurring risk with the next and subsequent episodes. ECPs are but one piece in the jigsaw of comprehensive sexual health care.

Editor's note

Readers are referred to Sam Rowlands' review of the 2007 *Contraception* article authored by Novikova *et al.* on page 145.

Statements on funding and competing interests

Funding None identified.

Competing interests None identified.

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