

Fertility control by emergency contraception

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Emergency contraception is defined as any drug or device which can be used after intercourse to prevent pregnancy. It has been suggested that millions of unwanted pregnancies could be prevented if emergency contraceptives were widely accessible [1]. Yet despite considerable clinical evidence of both safety and efficacy, hormonal emergency contraception remains unlicensed in most developing and many developed countries. A number of different preparations can be used.

Combined estrogen and progestogen

The hormonal regimen most widely used for emergency contraception is a combination of 100 µg ethinylestradiol and 0.5 mg levonorgestrel taken twice with the two doses separated by twelve hours (the CEP regimen). A licensed product (PC4 or Tetragynon) is available in Germany, Finland, Switzerland, the UK and New Zealand. However, the same hormones are available in some brands of combined oral contraceptive pills and these are often used in countries where PC4 is unavailable such as the USA. Whether combined pills containing other progestogens are effective when administered in the same manner is not known.

Failure rates of between 0 and 5% have been reported when CEP is used mid-cycle [2]. Accurate estimates of efficacy are difficult to make. Many women are unsure of the exact date of their last menstrual period and most do not ovulate on exactly the same day each cycle. The majority of women who use emergency contraception are of unproven fertility and many use it after an accident with a condom which may not infact have resulted in the leakage of seminal fluid. The chance of conception following one act of intercourse has been calculated to be around 27% per cycle so that even without emergency contraception over 70% of women will not conceive.

Nausea (up to 50%) and vomiting (up to 20%) are the main side-effects of the combination regimen. Subsequent menses normally occur at the expected time but

may be heavier than usual, and some women experience mastalgia. Although the method is only used within 72 h of intercourse no one knows whether it is effective beyond this time limit.

The mode of action of CEP remains unclear but it probably works by either inhibiting, or in some way compromising, ovulation [3]. It has also been suggested that the CEP regimen may cause luteolysis or interfere with implantation but there is no good evidence for this and hormonal emergency contraception may be less effective after ovulation.

Estrogens

High doses of estrogens – usually ethinylestradiol or stilbestrol in a variety of regimens – given over five days were shown in the 1960s to be extremely effective postcoital agents with failure rates of between only 0.1% and 1% [4,5]. Side-effects – nausea (70%), vomiting (33%), mastalgia (23%) and menorrhagia (11%) – were more common than with the CEP regimen and many clinicians stopped using estrogens in the 1970s when the latter was introduced. Estrogen alone is still used in Holland where the so-called 5 by 5 regimen (five tablets of 1 mg ethinylestradiol given daily for five days) is thought to be more effective than the CEP regimen although no randomized comparison of the two regimens has ever been reported.

The intrauterine device (IUD)

The intrauterine device (IUD) is a highly effective postcoital contraceptive with failure rates of less than 1% [6]. In the United Kingdom it is used for up to five days after the estimated day of ovulation, which may of course be more than five days after intercourse. It is particularly appropriate for women who wish to continue the IUD as a long-term method of contraception. Most women requesting emergency contraception are however young and nulliparous and it can sometimes be difficult to insert a device. Used postcoitally the IUD's main method of action is to inhibit implantation.

Progestogen alone

Progestogen without estrogen has been tested as a post-coital agent. Ho and colleagues [7] working in Hong Kong gave 0.75 mg levonorgestrel (LNG) twice with the two doses separated by 12 h. Used within 48 h of unprotected intercourse, failure rates were similar to the CEP regimen (2.6% CEP versus 2.4% LNG). Side-effects were however significantly less common with LNG and further studies of progestogens alone are being undertaken. This regimen would be particularly useful for women who have relative contraindications to estrogen, and a progestogen-only method (Postinor) is already available from pharmacists in some Eastern European

and Far Eastern countries.

Danazol

A number of studies have been undertaken using the antigonadotropin Danazol as an emergency contraceptive. Zuliani and co-workers [8] reported failure rates of 1.7% for two doses of 400 mg given 12 h apart and 0.8% for three doses given at 0, 12 and 24 h. However a randomized study comparing CEP and Danazol (600 mg twice in 12 h) undertaken in the UK [9] suggested that Danazol may be ineffective when used after intercourse.

Antiprogestogens

The antiprogestogen mifepristone (mifegyne, RU486) has also been tested as an emergency contraceptive. Two randomized trials [9,10] comparing 600 mg mifepristone with the CEP regimen showed that, given within 72 h of intercourse to a total of almost 600 women, mifepristone was 100% effective. All side-effects were much less common when mifepristone was used; however, in one of the studies [10] 42% of women experienced a delay of more than three days in the onset of next menstrual bleed. This was particularly likely to occur if mifepristone was given in the follicular phase of the cycle when it is known to inhibit ovulation [11]. This is an obvious drawback of the method since the onset of menses reassures the woman who has used emergency contraception that she is not pregnant. A lower dose of antiprogestogen, or a compound with a shorter half-life than mifepristone, may have less of an effect on the timing of the onset of next menses.

Use of emergency contraception

Trussel and Stewart [12] have calculated that even based on a conservative 75% efficacy, the widespread use of emergency contraception in the USA each year could prevent over one million abortions and two million unintended pregnancies which presently end in childbirth. Health economists in the UK have estimated that every pregnancy prevented by the use of hormonal emergency contraception saves the National Health Service (ignoring the cost to society of bringing up a child) at least £500, so that the method is also cost-effective [13]. Despite these calculations which are published and widely quoted, emergency contraception is still not widely used. In a consensus statement resulting from a meeting of experts held in Italy last year [1] the reasons for this were discussed. Firstly women and providers are by and large poorly informed about the methods. Since currently available hormonal preparations must be used within 72 h of intercourse a woman has to know about the method before she needs to use it. Secondly, there are few marketed products for emergency contraception and pharmaceutical companies appear to be reluctant to enter the

market. This may be particularly true for the antiprogestogens presumably because of the tendency of the anti-abortion lobby to condemn this group of compounds for all reproductive technologies. Thirdly, service providers in many countries seem reluctant to provide emergency contraception because it is confused with abortion. It cannot be stressed too strongly that if hormonal emergency contraception works largely by interfering with ovulation then it cannot be regarded as an abortifacient. Even in countries where hormonal emergency contraception is licensed and free of charge, such as the United Kingdom, its use is limited by difficulty of access. Although recent surveys undertaken in the UK have suggested that the majority of women are aware that hormonal emergency contraception exists [14], knowledge of the practical details is still, however, poor. Many women continue to be misled by the use of the term 'morning after pill' and are surprised to learn that PC4 can be used up to 72 h after intercourse. In the UK emergency contraception must be prescribed by a doctor and necessitates a visit to the family doctor or family planning clinic. Increasingly emergency contraception is becoming available from genitourinary medicine or accident and emergency departments but in the latter the wait for attention may be extremely long. Unprotected intercourse tends to occur at weekends, particularly in the case of young people, when clinics are closed and calling out the emergency doctor seems inappropriate. Women are often too embarrassed to ask for emergency contraception particularly if they have had to ask for it on a previous occasion, fearing that professionals will accuse them, implicitly or explicitly, of failing to 'learn their lesson'.

Not all doctors in the UK will prescribe emergency contraception and some will only do so rather grudgingly. There is a tendency – among both the providers and the users – to believe that it can only be given once and many teenagers are under the misapprehension that it is dangerous to use. Theoretically use of the CEP regimen once every month exposes a woman to less risk from contraceptive steroids than if she were to use the combined oral contraceptive pill – although of course it exposes her to a greater risk of pregnancy. Few data are available on the safety of the CEP regimen, but recently both the World Health Organization and the International Medical Advisory Panel of the International Planned Parenthood Federation have advised that there are no absolute contraindications to its use.

Over the last two or three years in the United Kingdom the proposal that PC4 should be taken off prescription and sold over-the-counter in pharmacies has been widely discussed [14]. Despite support for the proposal from the Royal Colleges of Obstetricians and Gynaecologists and General Practitioners and from the Royal Pharmaceutical Society it has not happened yet. The manufacturers are concerned about the potential for misuse and presumably about the possibility of litigation – and who can blame them? It has been reported [15] that the Ministry of Health in New Zealand expects emergency contraception to be available over-the-counter in July of 1996. The New Zealand Medical Association and the Royal New Zealand College of General Practitioners are opposed to the move, as are Schering who are concerned about misuse, incorrect use and medicolegal risks. Neither Wyeth (who market an appropriate combined pill preparation in New Zealand) nor Schering have plans to repackage a product for over-the-counter (OTC) use but the Ministry of

Health will allow pharmacists to cut up packets of pills and label them appropriately if the pharmaceutical companies do not respond. When PC4 was made available OTC in Denmark some years ago the manufacturers removed the drug from the market and it is possible that this might happen in New Zealand.

Increasing knowledge and improving availability will not have much of an impact on the rates of unwanted pregnancy until women (and their partners) equate unprotected sex with a risk of pregnancy. A number of studies [16,17] have demonstrated that even when they do know about emergency contraception and know where to get it from, many women still choose – although it may not be a conscious choice – to take the risk of falling pregnant rather than to go through the hoops involved in obtaining emergency contraception.

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MS received 20 June 96.

Accepted for publication 1 July 96.

Resumé

La méthode contraceptive d'urgence est définie comme reposant sur un médicament ou un dispositif à utiliser éventuellement après des rapports sexuels pour éviter une grossesse. On a suggéré que des millions

de grossesses non désirées pourraient être évitées si les contraceptifs d'urgence étaient plus largement accessibles. Pourtant, malgré le nombre considérable de preuves cliniques relatives à leur efficacité et leur innocuité, la contraception hormonale d'urgence demeure illicite dans la plupart des pays en développement et dans de nombreux pays développés. Il existe dans ce domaine différents produits utilisables.

Resumen

La anticoncepción de emergencia se define como cualquier fármaco o dispositivo que puede utilizarse después del coito para prevenir el embarazo. Se ha sugerido que podrían prevenirse millones de embarazos no deseados si hubiera acceso amplio a anticonceptivos de emergencia. Sin embargo, a pesar de las considerables pruebas clínicas tanto de seguridad como de eficacia, los anticonceptivos hormonales de emergencia continúan no siendo objeto de licencias en la mayoría de los países desarrollados y muchos países en desarrollo. Se pueden utilizar diferentes preparaciones.