

Emergency Contraception : What is it and How it works ?

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Abstrak

Para akseptor yang mengalami kegagalan atau tidak cocok dengan kontrasepsi yang telah lama dikenal (reguler), membutuhkan cara kontrasepsi jenis lain agar mereka tetap dapat membatasi kelahirannya. Kontrasepsi 'darurat' atau 'pasca senggama', adalah kontrasepsi yang digunakan sesudah senggama tanpa proteksi, untuk mencegah terjadinya kehamilan. Ada beberapa jenis kontrasepsi ini yang aman dan efektif, antar alain kontrasepsi oral tipe kombinasi (pil KB) dan AKDR bertembaga (CuIUD). Levonorgestrel dan mifepriston dapat pula digunakan sebagai kontrasepsi darurat, meski yang terakhir yang merupakan antiprogestin, masih belum digunakan secara luas. Efektivitas kontrasepsi darurat dalam mencegah kehamilan diperkirakan sekitar 75-90%.

Abstract

Women need access to secondary contraceptives they can use in case of failures of regular methods, or in cases where other methods are not suitable for them. Emergency contraception are methods that can be used after unprotected intercourse to prevent pregnancy. Emergency contraceptives are sometimes called post-coital or morning-after contraceptives. Several safe and effective emergency contraception methods are available. These include regular combined hormonal ethinyl estradio/levonorgestrel contraceptives, simply given in a higher dose (the Yuzpe regimen), and the copper intrauterine device (IUD). These regimens avert approximately 75 to 99 percent of pregnancies expected among women seeking treatment. Levonorgestrel may also be used, and mifepristone is a promising antiprogestin that works well as emergency contraception.

Keywords : Emergency contraception, secondary contraception.

INTRODUCTION

All contraceptive methods that are available in family planning programs today are appropriate for use before intercourse. The term emergency contraception refers to methods that can prevent pregnancy when used shortly after unprotected intercourse. They are often called *post-coital contraception* or *morning-after-pills* or *morning-after treatment*. To dispel the idea that the user must take *treatment* immediately after unprotected intercourse or must wait until the morning, in order not to be too late if she doesn't use any contraception until afternoon or the night after, these methods are better named *secondary contraception* or *emergency contraception*.

The name emergency contraception also stresses that the methods, while better than nothing in the emergency of unprotected intercourse, are typically less effective than all ongoing method of contraceptives.

The historical evolution of the regimens began in the 1920s when estrogenic ovarian extracts were first found to interfere with pregnancy. The most recent developments in emergency contraception include the discovery that mifepristone, also known as RU-486, is very effective for this indication.^{1,2,3,4}

Many accidental pregnancies have been occurring to contraceptive users because they do not use the methods properly. For instance, forget to take pill regularly, condom breakage, miscalculation of fertile-period, overdue to have the next injection or IUD expulsion. Unintended pregnancies are also experienced by non users. For couples who live in different cities, if the spouse comes unexpectedly, an emergency contraception will be useful, or for couples who have sexual intercourse very infrequent, less than

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four times a month. Above are the real life situations where emergency contraception might be useful.^{5,6}

The objectives of this paper are : to describe the use of emergency contraception including regimens and indications, and to discuss the research needs.

REGIMENS

Emergency contraception may be divided into two types : mechanical and medicinal.

Mechanical

The only mechanical type of emergency contraception is Copper IUD. When inserted up to seven days after unprotected intercourse, Copper IUDs can prevent pregnancy. The device releases Copper ions which is spermatotoxic and causes endometrial changes that prevent implantation. A meta-analysis of 20 studies of the post-coital insertion of a Copper IUD reveals that the failure of this method was probably not higher than 0.1%. The IUD offers an additional advantage of providing up to 10 years of protection. This method is contraindicated for women suffering from sexually transmitted disease.^{1,2,3}

Medicinal

There are at least five major regimens of emergency contraception that have been widely studied. They are all belong the hormonal contraception, given orally. Although trials are underway for vaginal administration, the published literature is still confined to oral medication.^{1,2}

Combined oral contraceptive (Yuzpe regimen)

In total, the regimen consists of 200 µg ethinyl estradiol and 1.0 mg levonorgestrel. Half of the dose (100 µg ethinylestradiol and 0.5 mg levonorgestrel) should be taken within 72 hours after unprotected intercourse. The other half (100 µg ethinyl estradiol and 0.5 mg levonorgestrel) is to be taken twelve hours later. One reason for the popularity of the Yuzpe method is that the composition of the regimen are nothing other than the active ingredients found in several brands of ordinary combined oral contraceptives. The brand that contains the exact Yuzpe regimen is marketed as Microgynon 50 ED in Asia (including Indonesia) and Europe or Ovral in the United States and Canada. Each tablet of Ovral contains 50 µg of ethinyl estradiol and 0.25 mg of levonorgestrel.

Women using Ovral as an emergency contraception therefore take two pills as the first dose, and then take two more pills after 12 hours. The original studies of this method by a Canadian physician, Albert Yuzpe,⁷ reported on this means by ingesting four Ovral tablets.

The same hormonal preparation studied in the Yuzpe article are also available in several other brands of combined oral contraceptions. Because some manufacturers have lowered the dose of hormones in newer formulations, women have to take more than two pills of some brands in order to get the same amount of the active ingredients as that of 2 Ovral tablets.⁸

In the United States there is no special contraceptive preparation marketed and packaged as emergency contraception. Instead, many clinicians simply cut up packages of Ovral or the other brands that contain the same hormones. In several European countries, Ovral tablets are available in four-pill strips labeled explicitly for emergency use. The packages are known as PC-4 in Britain, and as Tetragynon in Germany and Switzerland.^{1,2}

Efficacy studies of the Yuzpe regimen have yielded a widely varying results, in part because of the definition of efficacy was slightly different when applied to a post-coital method. In one efficacy study, the women using a given method were observed for a certain length of time and the number of pregnancies was noted. The resulting calculation dividing the pregnancies by the exposure did not account for the fact that several of the women in the trial, would not have become pregnancy even without contraception. When studied in this fashion, the efficacy of the Yuzpe regimen ranges from about 97% to 99%. This value is useful for clinicians in the sense that of all the women treated by this regimen, presenting on different cycle days, only 1 to 3% of them would become pregnant.

Yet emergency contraception is not used by women cycle after cycle as a primary method. Instead, the method is only sporadically used and at times, such as midcycle intercourse, when the probability of pregnancy is high. For this reason, better studies of the method are needed to proof their security for women of proven fertility and regular cycles. For such women, an expected number of pregnancies can be calculated using fertility tables from the published literature if the cycle day of intercourse is recognised. Based on the available studies that are conducted in the optimal fashion, it is possible to calculate a proportionate reduction in preg-

nancy associated with the use of the Yuzpe regimen. By comparing observed to expected pregnancies, investigators have demonstrated that the Yuzpe regimen reduces the chances of pregnancy by about 75 percent.⁹

General consensus stated that the regimen has no contraindication and there is no evidence linking its use to the risk of fetal malformation.^{10,11} However, since the Yuzpe regimen contain the same active ingredients as certain combined oral contraceptives, and the regimen has never been regulated specifically, there are still some clinicians put the contraindication for the Yuzpe regimen which simply adopted from those stated for combined oral contraceptives: current or past thromboembolic disorders, cerebral-vascular disease or coronary-artery disease, known or suspected carcinoma of the breast or endometrium, jaundice, and hepatic adenomas or carcinomas. Clinicians should also ensure that women are not yet pregnant from an unprotected intercourse prior to 72 hours from the first dose of the Yuzpe regimen. Although there is no known teratogenic effect of the regimen, too few births resulting from failure of the Yuzpe regimen have been observed to support confident conclusions of this point.¹

Side effect of the Yuzpe regimen are also the same as those of short term use of combined oral contraceptives: nausea (including vomiting in about 20 percent of cases), headaches, breast tenderness, abdominal pain and dizziness. Nausea is by far, the most common side effect, with typically 50 percent of women reporting this event. Nausea may be reduced by taking the tablets with food or with milk. Some clinicians also routinely accompany the Yuzpe regimen with anti-emetic or anti-nausea medication such as dimenhydrinate or cyclizine hydrochloride.¹²

Progestin

The progestin emergency contraceptive regimen consists of 0.75 mg levonorgestrel taken in two doses, twelve hours apart started within 48 hours of unprotected intercourse. Although the regimen was one of the first discovered, few published studies have analyzed the regimen in a way it controls cycle day of unprotected intercourse.^{1,2} The best and the most recent levonorgestrel trial indicated a failure rate of 2.4 percent and a proportionated reduction in pregnancy of 60 percent. The study randomized women to either Yuzpe or levonorgestrel treatment within 48 hours of unprotected intercourse. During the trial, 410 women

used the levonorgestrel method. Investigators did not detect any statistical significant difference between the levonorgestrel and Yuzpe method.¹³

The levonorgestrel regimen has also been studied as an ongoing method of post-coital contraception. The Hungarian company, Gedeon Richter, markets a 10 pill strip containing ten doses of 0.75 mg each for this use, although the pills could equally be used sporadically for emergencies or as a secondary method of contraception. The brand, called Postinor, is advertised for women with infrequent intercourse, or intercourse fewer than four times a month. Unlike commercial formulations of the Yuzpe method, Postinor is available in many developing countries, and is even sold *over the counter* in some places.¹

Certain brands of progestin-only oral contraceptive can also be adapted for emergency use. A minipill known as Ovrette, for example, contains 0.075 mg norgestrel, equivalent to 0.0375 mg levonorgestrel, per tablet. A woman could therefore take 20 such tablets, to make up the complete regimen. Although such an option is impractical for most women, the option may be important for women with estrogen contraindications.²

High-dose estrogens

Post-coital treatment with several of the high dose estrogens was the standard method during the 1960s and early 1970s before being replaced by the better tolerated, Yuzpe regimen. The high-dose estrogen regimens consisted of diethylstilbestrol (DES), esterified estrogen, conjugated estrogen, estrone or high dose ethinyl estradiol. The over high-dose estrogen regimens are at least as effective as the Yuzpe method, but produce a more inconvenient side effect profile. In each case, high dose estrogen must be initiated within 72 hours of unprotected intercourse. Patients take the pill twice daily for five days. Each of the twice daily doses must be equivalent to 25 mg DES: ethinyl estradiol requires 2.5 mg per dose, esterified and conjugated estrogens each require 10 mg per dose, and 5 mg estrone provides the needed equivalent.

The best example of a high-dose estrogen prescribed as an emergency contraceptives is Lynoral, marketed and used in family planning programs in the Netherlands Commercial products and typically used for estrogen replacement therapy. Conjugated estrogen Premarin can also be easily adapted for use as emergency contraception.^{2,3}

What are the mechanism of actions of these steroid (estrogen, progestin and estrogen + progestin) methods of emergency contraception? Several hypothesis have been proposed. Among other is a more rapid transport of fertilized ova through the oviduct, and moreover, a slower maturation of the endometrium, as shown by endometrial biopsies. Basal vacuoles usually not found after the 4th day of the secretory phase, remained clearly visible throughout the second phase of cycle, which reflect the avoidance of implantation. Once implantation has taken place, however, the method has no effect on the pregnancy.³

Mifepristone

The progesterone dependency of the implanted blastocyst is a new target in fertility regulation, since antiprogestins bind competitively to progesterone receptors and nullify the effect of endogenous progesterone. Administration of the antiprogestin Mifepristone, also known as RU 486, during the luteal phase of the menstrual cycle, produces a dramatic drop in the plasma levels of the endogenous steroids, progesterone and estradiol. Interception and the administration of antiprogestins within the menstrual cycle are closely related to and are therefore, included in post-coital interception studies. Because of the interference with early gestation, this method termed post-coital contraception, filling the "window" from day 21 to 28 of the cycle.

This new method using antiprogestins, however, can be used irrespective of the time lapse following unprotected intercourse, with the dates and number of exposures also being unimportant. When antiprogestins are given in the luteal phase, uterine bleeding resembling menstruation is induced in approximately 2 days. This bleeding occurs irrespective of the presence of an early conceptus, and whether or not it is implanted. Since there were no known contraindications for the use of antiprogestins and because the prevention of unwanted pregnancy is so important to the individuals concerned, no exclusion criteria for age, body weight, general good health, etc, are considered.^{3,14}

Only two studies have evaluated mifepristone for use as an emergency contraceptive. In each case, the regimen showed great promise: not a single pregnancy was observed in the mifepristone arm of either trial, despite enrolment of nearly 600 women. The side effect profile of mifepristone was also favourable, although menstrual disturbances not associated with the Yuzpe regimen may result. The mifepristone

method investigated to date consists of 600 mg of the drug, taken in a single dose within 72 hours of unprotected intercourse. It is possible that lower doses of the drug may be effective, and that the time limit in which the therapy may be used could extend beyond 72 hours.^{1,2}

Danazol

Danazol is an androgen agonist with anti gonadotropin effect which can be used as an emergency contraceptive. The danazol regimen consists of two doses of 400 mg each, taken twelve hours apart, as with the Yuzpe regimen. A variant of this regimen, involving three doses of 400 mg each, with each taken 12 hours after the last, has also been investigated. The advantages of danazol are that its side effects are less prevalent and less severe than those of the Yuzpe regimen, and that danazol can also be taken by women in the case where combined oral contraceptives or estrogen is contraindicated. Its disadvantages are that there is less information available about the regimen, and that some of the data indicate that the regimen is not effective.^{1,3} Table 1 summarizes the regimen of emergency contraception.

INDICATIONS

Emergency contraception is indicated to prevent pregnancy of unprotected intercourse:^{5,15}

1. When there is a contraceptive accident or misuse which include :
 - * condom rupture, slippage or misuse
 - * diaphragm or cap dislodgement, breakage or tearing or early removal
 - * failed coitus interruptus (e.g. ejaculation in vagina or on external genitalia)
 - * misulation of the periodic abstinence method
 - * IUD expulsion
 - * missed more than two oral pills
 - * overdue more than two weeks for the next injection
2. In cases of sexual assault
3. When there is no contraception has been used

Research needs

From articles published on emergency contraception the basic question about the safety, efficacy and side-effects, are still not answered satisfactorily. Therefore researchers investigating emergency contraceptive regimens should make sure to follow several guidelines when designing and conducting research.^{2,6}

Table 1. Regimens for emergency contraception

Regimen	Brandnames	Doses required	Timing of administration
I. Mechanical Copper-IUD	Copper T Multiload Nova T	One insertion	Within 7 days of unprotected intercourse
II. Medicinal Oral-Combined Pill (Yuzpe)	Microgynon 50 Ovral Neogynon Nordion Eugynon	Two doses of two tablets	First dose within 72 hours of unprotected intercourse Second dose 12 hours later
	Microgynon 30 Microdiol Nordette	Two doses of four tablets	First dose within 72 hours of unprotected intercourse Second dose 12 hours later
Progestin Only	Portinor	Two doses of one tablet	First dose within 72 hours of unprotected intercourse Second use 12 hours later
Estrogen	Lynoral Premarin Progynova	2.5 mg/dose 10 mg/dose 10 mg/dose	First dose within 72 hours of unprotected intercourse Two doses per day for five days
Mifeprystone	RU-486	Single dose of 600 mg	Within 72 hours of unprotected intercourse
Danazol	Danocrine	Two doses of four tablets	First dose within 72 hours of unprotected intercourse Second dose 12 hours later

Efficacy studies

In order to evaluate efficacy, an observed number of pregnancies should be compared to an expected in a group of fecund women which is primarily a function of the cycle day of unprotected intercourse. Yet perhaps the most neglected feature of most published trials is that the trials failed to control the cycle day of intercourse. In all trials of emergency contraception, researchers should record the cycle day of unprotected intercourse. In order to make this determination, the study should be first limited to women with regular cycles.

Another problem with many of the published literatures on emergency contraception is that some of the women who participate in the trial may already be pregnant. Where feasible, ultrasensitive pregnancy tests should be used to establish whether the women participating in the trial are already pregnant or not from an unprotected intercourse occurring prior to 72

hours before the start of treatment with emergency contraception. Analysis of failure should be limited to those women who did not have further acts of unprotected intercourse during the treatment cycle. Several trials have made willingness to abstain or use condoms for the rest of the cycle as condition of inclusion.

Analysis should also be limited to women of proven fertility. Such an analysis might afford more precise estimates of the efficacy of the regimens.

Other impact studies

Several avenues of important research uncharted to establish the acceptability of emergency contraceptives and how women could best use the method to suit their needs.

How do people like the method ?

Should be pills be available over the counter or from vending machines ?

Should they be routinely prescribed at every family planning or medical visit for the woman to keep in case of a later emergency ?

Should women be issued ID cards, equivalent to a standing prescription, entitling them to the purchase of a regimen of emergency contraceptives once they had been screened and counseled about the use of the therapy ?

Would women prefer a specially packaged product to plain cycle or part of a cycle of oral contraceptives ?

To answer these questions, and many others, many researches are needed to determine the Information, Education and Communication (IEC) program, which distribution system and use patterns would best help women to avoid unwanted pregnancy.

Further research

Additional basic research could clarify the mechanism of action of various regimens. These mechanism are poorly understood. Preliminary research indicating the exact mechanism of action, and particularly the timing of the action in the process of pregnancy, may be an important piece of information for women in making their ethical considerations about the use of the regimens.

CONCLUSION

Any woman at risk of unwanted pregnancy may need emergency contraception occasionally. Millions of unwanted pregnancies could be averted if emergency contraceptives were widely accessible.

Existing regimens are usually inexpensive, often consist simply of altered doses of widely available medications, and have been used for decades.

So why are emergency contraceptives not used more widely ? The answer may well be ignorancy. Both from providers and the community.

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