

## EMERGENCY CONTRACEPTION

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Emergency contraception refers to any device or drug that is used as an emergency procedure to prevent pregnancy after unprotected sexual intercourse.

The first method of emergency contraception was high dose of estrogen. Concern about side effects led to subsequent development of the so-called Yuzpe regimen which combined ethinil estradiol with levonorgestrel and levonorgestrel alone. Less convenient to use is the copper intrauterine contraceptive device.

It is known that in some women sexual steroids may inhibit or delay ovulation and may interfere with ovum and sperm transport and implantation. Copper intrauterine device causes a foreign-body effect on the endometrium and a direct toxic effect to sperm and blastocyst.

The Yuzpe regimen reduces the risk of pregnancy after a single act of sexual intercourse by about 75% and the levonorgestrel alone by about 85%. The copper intrauterine device is an extremely effective method for selected patients.

Nausea and vomiting are common among women using the Yuzpe regimen and considerably less common among women using levonorgestrel regimen alone.

Emergency contraception is relatively safe with no contraindications except pregnancy. It is ineffective if a woman is pregnant. There is no need for a medical history or a physical examination before providing emergency contraceptive pills. They are taken long before organogenesis starts, so they should not have a teratogenic effect.

Counseling should include information about proper use of the method, possible side effects and its preferences for regular contraception.

Unintended pregnancy is a great problem. Several safe, effective and inexpensive methods of emergency contraception are available including Yuzpe regimen, levonorgestrel-only regimen and copper intrauterine device. *Acta Medica Medianae* 2007;46(3):40-43.

**Key words:** emergency contraception, emergency contraceptive pills, Copper intrauterine device

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### Introduction

Emergency contraception refers to any device or drug that is used as an emergency procedure to prevent pregnancy after an unprotected sexual intercourse or possible contraceptive failure regardless of the point in the menstrual cycle (1,2,3,4,5).

The average fertile period of women (days in which an act of sexual intercourse can give rise to pregnancy) lasts only six days per menstrual cycle and it ends at the day of ovulation. Those

days are: the day of ovulation and five preceding days. Sperm can survive in the female up to 5 days and the mature egg may be fertilised over a 24-hours period. The pregnancy is expected in 15% of cases if an unprotected sexual intercourse took place 3 days before ovulation, in 30% if it happened 1-2 days before ovulation and in 12% if it happened on the day of ovulation (6). The implantation of blastocyst does not begin before the sixth day after the ovulation. The period from fertilisation till ovulation is the time for emergency contraception use. According to medical definition the pregnancy starts when implantation has occurred, therefore emergency contraception is not an abortifacient. The treatment will be ineffective if it takes place after the implantation of blastocyst in the endometrium. The Roman Catholic Church and some other opponents of artificial abortion state that pregnancy starts when the sperm and egg unite and they refuse to use this treatment, although Catholic

hospitals will prescribe emergency contra-ception for women who have been raped (7).

The most common reason for emergency contraception use is unexpected sexual intercourse with no contraceptive protection, after incorrect or inconsistent use of regular contraceptive method and after accidental or possible contraceptive failure.

### Methods

The method of choice for emergency contraception is the use of sexual steroids.

During the 1960s, high doses of estrogen were introduced for emergency contraception: 50 mg diethylstilbestrol and 5 mg etynil estradiol for 5 days within 72 hours since unprotected sexual intercourse. The effectiveness was high, but side effects were strong. This treatment is nearly abandoned today (5).

During the 1970s, the combination of estrogen and progestin was introduced for emergency contraception, the so-called Yuzpe regimen: 2 combined contraceptive pills containing 50 mcg etynil estradiol and 0,5 mg levonorgestrel each. The first dose within 72 hours since unprotected sexual intercourse and the second same dose 12 hours later. The alternative regimen is administration of 4 pills containing 30 mcg etynil estradiol and 1,15 mg or 0,125 mg levonorgestrel each (7,8). It has not been specially studied whether these doses are optimal and whether other progestin administered in similar way can be effective. The Yuzpe regimen has become gold standard for emergency contraception.

During 1990s, an independent administration of progestin levonorgestrel was introduced: 0,75 mg within 72 hours since unprotected sexual intercourse and the second same dose 12 hours later. The alternative regimen is administration of 1.5 mg in one dose. Registered preparations in the market are: Postinor 2 (Europe), Levoneller 2 (UK), Plan B (USA) (9,10).

The second-line form of emergency contraception is copper intrauterine device. It is an alternative to hormonal emergency contraception if sexual steroids are not available and/or if an unprotected sexual intercourse had taken place before more than 72 hours. The device is a good option for adequately selected women within 5 days since unprotected sexual exposure (11).

In some countries (e.g. China and Israel) the antiprogesteron mifepriston is used for emergency contraception: 600 mg in single dose within 72-120 hours since unprotected sexual intercourse. It can disturb an early pregnancy if it is administered after implantation, so this method is between emergency contraception and artificial abortion (1).

### Mechanism of action

The mechanism of action of emergency contraception by sexual steroids has been studied for a long time, but it is not completely clear till today. It is considered that the main mechanism is achieved through inhibition of hypothalamus

and hypophysis and results by anovulation, ovulatory dysfunction or delayed ovulation (1,12,13,14). The Yuzpe regimen will lead to anovulation in 80% of cases if the diameter of leading follicle is 12-15 mm, but in 50% if the diameter is 15-17 mm. The treatment will result in ovulatory dysfunction or the ovulation will be delayed if the follicle is bigger. That means that the Yuzpe regimen is at least successful at the days of the highest fertility (12). The administration of Yuzpe regimen significantly before ovulation creates histological and biochemical endometrial changes which do not allow the implantation, although it is not known which endometrial perfection is necessary for successful implantation (15). The levonorgestrel regimen does not cause significant endometrial changes (16).

The possible mechanisms of sexual steroids are: a direct inhibition of fertilisation, a creation of insufficient corpus luteum, formation of dense cervical mucus which is unpenetrable for sperm, some alterations in tubal motility or ovum tubal transport, some alternations of sperm or early conceptus (1,5,17).

The copper intrauterine device creates an intense inflammatory reaction of the endometrium and, therefore, it becomes inappropriate for implantation. Copper ions provoke direct toxic effect on spermatozoa and blastocyst (18).

Mifepriston administered before ovulation postpones gonadotropines surges, but if administered after ovulation it leads to inhibition of secretory endometrial transformation and creates substantial morphological and biochemical changes which disrupt the implantation of the blastocyst (1).

### Effectiveness

The effectiveness of emergency contraception is very difficult to assess. The exact time of ovulation is not known and its relationship with the unprotected sexual intercourse. On the other hand, it is not ethical to create a control-group or to give a placebo treatment (1,3,15,19). The effectiveness can be expressed by the rate of pregnancy which occur after the emergency contraception use (failure rate) (18). It is better to express the effectiveness by the proportion of pregnancies that were prevented by the emergency contraception use, that means the possibility for pregnancy with emergency contraception use compared with the possibility without its use (19). It is estimated that if 100 women have an unprotected sexual intercourse during two middle weeks of menstrual cycle, 8 of them will get pregnant, with Yuzpe regimen use 2 women and with Levonorgestrel regimen use only 1 woman. The conclusion may be: that Yuzpe regimen can prevent 6 but levonorgestrel regimen 7 pregnancies (20,21).

It is estimated that failure rate with Yuzpe regimens 3% and with levonorgestrel regimen 1.1%. At the same time, the proportion of prevented pregnancies are 57% and 85%, respectively. The ideal use of Yuzpe regimen can prevent 76% of pregnancies and levonorgestrel regimen 89%.

The conclusion is that levonorgestrel regimen is more effective than Yuzpe one. The risk of getting pregnant with levonorgestrel regimen is only one third of the risk with Yuzpe one (22).

The effectiveness of sexual steroids, which are given as emergency contraception is better if they are used sooner after sex. The effectiveness is the best if they are administered within 12 hours, although the application is recommended within 72 hours. The effectiveness is moderately decreased if sexual steroids are administered between 73 and 120 hours after sexual exposure (23).

The use of Yuzpe regimen within 25-48 and 49-72 hours after an unprotected sexual intercourse is followed with failure rates of 2.0%, 4.1% and 4.7%, but levonorgestrel regimen is followed of 0.4%, 1.2% and 2.7%, respectively. At the same time, the proportions of pregnancies which have been prevented with Yuzpe regimen are 77%, 36% and 31%, but with levonorgestrel regimen are 95%, 85% and 58%, respectively (22).

The emergency contraception by copper intrauterine device is extremely high. Failure rate is less than 1% and by mifepristone 1.3% (1,3,11,18).

### Side effects

Around 50% of women using Yuzpe regimen have nausea and 20% of them have vomiting. The incidence is much lower with levonorgestrel regimen (1,7,24).

It is a good practice to use an antiemetic medication 1 hour before each dose in order to improve the compliance. It is not necessary with levonorgestrel regimen (1,7,24). If vomiting occurs within 24 hours after taking a dose, it is common practice to repeat it. However, there is no evidence that this improve the effectiveness (10). In case of vomiting, further pills may be administered vaginally (9). On the other hand, vomiting can be an indication that the hormones have been absorbed and that vomiting presents their effect on central nervous system, so it is not necessary to repeat the dose (21).

Other less common side effects are: breast tenderness, fatigue, headache, dizziness and abdominal pain (1).

The mifepristone use is associated with rare occurrence of nausea and vomiting than Yuzpe regimen, but with longer delay in the onset of menses which provokes longer anxiety for the patient (1).

### Safety

Before the recommendation of emergency contraception by sexual steroids, it is sufficient to take the history, but clinical or laboratory checking is not necessary. Menses usually occurs at expected time, some days before or later, nevertheless it can occur the day after medication (10).

According to recent information, there is no data to suggest teratogenicity or harm effect on pregnancy if sexual steroids have been administered

accidentally. The incidence of major congenital anomalies is as in general population. Emergency contraception is almost always given less than 15 days after possible ovulation when cells are pluripotential and organogenesis has not started yet. There is no absolute contraindication to emergency contraception use other than known pregnancy or a doubt about it, because the treatment will not be effective (1,9).

The Yuzpe or levonorgestrel regimen can be used by women with contraindication for combined oral contraception, because the exposure to sexual steroids is short but the risk of unwanted pregnancy is considerable. It is better for these women to use levonorgestrel regimen (4, 15).

The repeated administration of Yuzpe or levonorgestrel regimen is not harmful. There are no data about safety if emergency contraception is used frequently during a long period of time.

Multiparous are the ideal candidate for emergency contraception by copper intrauterine device with only one sexual partner and with low risk for sexually transmitted infections who want effective, long-lasting and economic regular contraception. This regimen is less practical than those with sexual steroids, because an intrauterine device must be placed by an experienced practitioner and there is usually little time for screening about sexual transmitted infections. Nulliparous are not ideal candidates for this method. Nevertheless, the risk of pelvic inflammatory disease is directly related with the risk of sexually transmitted infections but not with parity. If the regimen has not been effective and the pregnancy occurred, but a woman wants to continue the pregnancy, it is necessary to remove the device as soon as possible. The teratogenicity is not expected, but there is a danger of late septic spontaneous abortion if the device is in the uterine cavity (1,15).

### Counseling

The counseling about emergency contraception should be done on time, without any prejudice, by giving emotional support and information about the need of regular contraception use. It is extremely important to give those information to young women who have not given birth or who are not finished with bearing. It is necessary to emphasize that emergency contraception by sexual steroids does not give a protection against sexually transmitted infections. Condom should be used till next menstruation in case if she wants new sexual intercourse. It is not necessary if copper intrauterine device had been used.

It is necessary to check the presence of pregnancy if the menses delays longer than 7 days or it does not occur 3-4 weeks after the treatment date.

Emergency contraception should be recommended for the woman who uses combined oral contraceptives, when she has forgotten to take the pill more than 24 hours during the first

week of treatment and if she had an unprotected sexual intercourse within 120 hours before, or if she has forgotten to take more than 3 pills in any time of the treatment cycle. The administration of the combined oral contraceptives can be started a day after the second dose of emergency contraception. Anyway, additional condom protection is recommended during the first 7 days.

The copper intrauterine device can be removed just when the next menses starts, if it is used for emergency contraception and the woman does not want to use it as a regular contraceptive method.

Emergency contraception by Yuzpe or levonorgestrel regimen should be acceptable to women within 24 hours/day, 7 days/week and it is better to be acceptable without prescription. Therefore, it can be used whenever women need

it, as soon as possible with its greatest effectiveness. The suggestions have been made that easy availability of the emergency contraception is not connected with its abuse and women do not use it more often than it is necessary.

### Conclusion

There is large economical and psychological need for emergency contraception use because an unwanted pregnancy is great individual and social problem which can be simply and effectively avoided with saving the fertility. It has been postulated that optimal use of this treatment would significantly reduce the number of unwanted pregnancies and risks which are usually followed by artificial abortion.

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## HITNA KONTRACENCIJA

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Hitna (postkoitalna) kontracepcija je primena leka ili sredstva posle nezaštićenog polnog odnosa ili uočene kontraceptivne greške u cilju sprečavanja pojave neželjene trudnoće bez obzira na fazu menstrualnog ciklusa. Danas se u ovu svrhu najčešće koriste seksualni steroidi, a znatno ređe bakarni intrauterini uložak. Efikasnost hitne kontracepcije je velika, ali manja od efikasnosti regularne kontracepcije, zato hitna kontracepcija nije zamena za regularnu, već hitan tretman u vanrednim situacijama.

Hitna kontracepcija deluje u preimplantacionom periodu i nije abortivno sredstvo. Ako se desila implantacija, tretman ostaje neefikasan. Očekuje se da adekvatna primena hitne kontracepcije doprinese smanjenju broja neželjenih trudnoća i namernih pobačaja. *Acta Medica Medianae* 2007;46(3): 40-43.

**Ključne reči:** hitna kontracepcija, seksualni steroidi, bakarni intrauterini uložak