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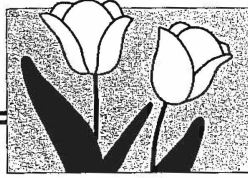
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Special Uses of Oral Contraception: The Progestin-Only Minipill Emergency Contraception

ORAL CONTRACEPTION is a phrase which appropriately denotes a vast body of knowledge (Chapter 2) pertaining to the combined estrogen-progestin "birth control pill." However, there are two special types of oral contraception which deserve separate consideration, the progestin-only minipill and emergency contraception.

The Progestin-Only Minipill

The minipill contains a small dose of a progestational agent and must be taken daily, in a continuous fashion.^{1,2} There is no evidence for any differences in clinical behavior among the available minipill products.

Minipills available worldwide:

1. Micronor, Nor-QD, Noriday, Norod -----0.350 mg
norethindrone
2. Microval, Norgeston, Microlut -----0.030 mg
levonorgestrel
3. Ovrette, Neogest -----0.075 mg
norgestrel
(equivalent to 0.0375 mg levonorgestrel)
4. Exluton -----0.500 mg
lynestrenol
5. Femulen -----0.500 mg
ethynodiol diacetate.
6. Cerazette -----0.075 mg
desogestrel

Mechanism of Action

After taking a progestin-only minipill, the small amount of progestin in the circulation (about 25% of that in combined oral contraceptives) will have a significant impact only on those tissues very sensitive to the female sex steroids, estrogen and progesterone. The contraceptive effect is more dependent upon endometrial and cervical mucus responses, because gonadotropins are not consistently suppressed. The endometrium involutes and becomes hostile to implantation, and the cervical mucus becomes thick and impermeable.^{3,4} Approximately 40–50% of patients will ovulate normally. Tubal physiology may also be affected, but this is speculative.

Because of the low dose, the minipill must be taken every day at the same time of day. The change in the cervical mucus requires 2–4 hours to take effect, and, most importantly, the impermeability diminishes 22 hours after administration, and by 24 hours sperm penetration is essentially unimpaired. This time schedule reflects the rise and fall of the blood progestin level.

Ectopic pregnancy is not prevented as effectively as intrauterine pregnancy. Although the overall incidence of ectopic pregnancy is not increased (it is comparable to the incidence in women not using a contraceptive method), when pregnancy occurs, the clinician must suspect that it is more likely to be ectopic. A previous ectopic pregnancy should not be regarded as a contraindication to the minipill.

There are no significant metabolic effects (lipid levels, carbohydrate metabolism, and coagulation factors remain unchanged),^{5,8} and there is an immediate return to fertility on discontinuation (unlike the delay seen with the combination oral contraceptive). Only one disturbing observation has been reported; progestin-only oral contraception was associated with about a 3-fold increased risk of diabetes mellitus in lactating women with recent gestational diabetes (an observation that is difficult to explain).⁹ Because this increased risk is not observed with the use of combined oral contraceptives, it is speculated that the low levels of estrogen associated with breastfeeding allow an unimpeded progestin effect on insulin resistance.

Efficacy

Failure rates have been documented to range from 1.1 to 9.6 per 100 women in the first year of use.¹⁰ The failure rate is higher in younger women (3.1 per 100 woman-years) compared with women over age 40 (0.3 per 100 woman-years).¹¹ In motivated women, the failure rate is comparable to the rate (less than 1 per 100 woman-years) that can be achieved with combination oral contraception.^{12,13}

Pill Taking

The minipill should be started on the first day of menstruation if the method is not necessary. The pill should be taken at the same time each day. The 24-hour period of action, evening is better than morning administration (one of the daily mealtimes may serve as a cushion if pill taking is late. If pills are missed, the minipill should be taken as soon as possible and a back-up method should be used (condom or withdrawal) until the pills have been taken for 7 consecutive weeks. If more pills are missed in a row and the woman is not sure if she is pregnant, a pregnancy test should be obtained. *taking a pill, a backup method should be used.*

Problems

In view of the unpredictable effect on the menstrual cycle, irregular menstrual bleeding is the most common problem. The progestational impact on the endometrium is minimal. Patients can expect to have normal menstrual cycles (40%), or a total lack of menstruation, or irregular bleeding to spotting and amenorrhea. Women who discontinue the minipill method should expect a return to their normal menstrual cycle.

Women on progestin-only oral contraception may develop ovarian follicular cysts.^{14,15} Nearly all, if not all, are asymptomatic and a problem of any significance. Women who discontinue the minipill method should expect a return to their normal menstrual cycle.

The levonorgestrel minipill can be associated with a decrease in SHBG similar to that seen with Norplant. This decrease decreases the circulating levels of free testosterone (SHBG).¹⁶ Therefore free steroid levels will be increased despite the low dose of testosterone. This is not a problem with combined oral contraception where the increase in SHBG by the estrogen-induced increase in SHBG is not great, and a clinical manifestation is not seen in women who are extremely sensitive to small changes in testosterone levels.

The incidence of the other minor side effects is similar to that which would be encountered with combination oral contraception.

minipill, the small amount of progestin in it (that in combined oral contraceptives) will act on those tissues very sensitive to the female progesterone. The contraceptive effect is more on vaginal and cervical mucus responses, because they are more readily suppressed. The endometrium is involuntarily suppressed, and the cervical mucus becomes thin and watery. Approximately 40–50% of patients will ovulate normally, but this is speculative.

minipill must be taken every day at the same time. The cervical mucus requires 2–4 hours to take effect. If taken late, the impermeability diminishes. Within 24 hours sperm penetration is essentially normal. The cycle reflects the rise and fall of the blood

is considered as effectively as intrauterine pregnancy. The incidence of ectopic pregnancy is not increased (it is 1% in women not using a contraceptive method). The clinician must suspect that it is more likely to be a clinical pregnancy should not be regarded as a failure.

Metabolic effects (lipid levels, carbohydrate tolerance factors remain unchanged),^{5,8} and there is no weight gain on discontinuation (unlike the delay seen with combined oral contraceptive). Only one disturbing observation with combined oral contraception was associated with diabetes mellitus in lactating women with insulin resistance (an observation that is difficult to explain),⁹ which was not observed with the use of combined oral contraceptive. The low levels of estrogen associated with the low levels of progestin effect on insulin resistance.

The failure rate is estimated to range from 1.1 to 9.6 per 100 woman-years.¹⁰ The failure rate is higher in younger women (1–10 years) compared with women over age 40.¹¹ In motivated women, the failure rate is less than 1 per 100 woman-years that can be expected with combined oral contraception.^{12,13}

Pill Taking

The minipill should be started on the first day of menses, and a backup method is not necessary. The pill should be keyed to a daily event to ensure regular administration at the same time of the day. Because of the limited 24-hour period of action, evening is best avoided as the time of administration (one of the daily mealtimes is better), thus providing a small cushion if pill taking is late. If pills are forgotten or gastrointestinal illness impairs absorption, the minipill should be resumed as soon as possible, and a back-up method should be used immediately (unless fully breastfeeding) and until the pills have been resumed for at least 2 days. If 2 or more pills are missed in a row and there is no menstrual bleeding in 4–6 weeks, a pregnancy test should be obtained. *If more than 3 hours late in taking a pill, a backup method should be used for 48 hours.*

Problems

In view of the unpredictable effect on ovulation, it is not surprising that irregular menstrual bleeding is the major clinical problem. The daily progestational impact on the endometrium also contributes to this problem. Patients can expect to have normal, ovulatory cycles (40–50%), short, irregular cycles (40%), or a total lack of cycles ranging from irregular bleeding to spotting and amenorrhea (10%). This is the major reason why women discontinue the minipill method of contraception.¹³

Women on progestin-only oral contraception develop more functional, ovarian follicular cysts.^{14,15} Nearly all, if not all, regress. This is not a clinical problem of any significance. Women who have experienced frequent ovarian cysts would be happier with methods that effectively suppress ovulation (combined oral contraceptives and depot-medroxyprogesterone acetate).

The levonorgestrel minipill can be associated with acne. The mechanism is similar to that seen with Norplant. The androgenic activity of levonorgestrel decreases the circulating levels of sex hormone-binding globulin (SHBG).¹⁶ Therefore free steroid levels (levonorgestrel and testosterone) will be increased despite the low dose. This is in contrast to the action of combined oral contraception where the effect of the progestin is countered by the estrogen-induced increase in SHBG. However, the SHBG changes are not great, and a clinical manifestation is probably limited to women who are extremely sensitive to small changes in androgens.

The incidence of the other minor side effects is very low, probably at the same rate that would be encountered with a placebo.

Clinical Decisions

There are two situations where excellent efficacy, probably near total effectiveness, is achieved: lactating women and women over age 40. In lactating women, the contribution of the minipill is combined with prolactin-induced suppression of ovulation, adding up to very effective protection.¹⁷ In breastfeeding, overweight, Latina women with prior gestational diabetes, the progestin-only minipill was associated with a 3-fold increased risk of non-insulin dependent diabetes mellitus.⁹ It is not known whether this might be a risk in all women who have experienced gestational diabetes; a prudent course would be to advise other methods for this special group of women. In women over age 40, reduced fecundity adds to the minipill's effects.

There is another reason why the minipill is a good choice for the breastfeeding woman. There is no evidence for any adverse effect on breastfeeding as measured by milk volume and infant growth and development.¹⁸⁻²⁰ In fact, there is a modest positive impact; women using the minipill breastfeed longer and add supplementary feeding at a later time.²¹ *Because of the slight positive impact on lactation, the minipill can be started soon after delivery, but at least a 3-day postpartum delay is recommended to allow the decline in pregnancy levels of estrogen and progesterone and the establishment of lactation.*²²

The minipill is a good choice in situations where estrogen is contraindicated, such as patients with serious medical conditions (diabetes with vascular disease, severe systemic lupus erythematosus,²³ cardiovascular disease), and in women with significant cardiovascular risk factors, such as smoking or hypertension. It should be noted that the freedom from estrogen effects, although likely, is presumptive. Substantial data, for example on associations with vascular disease, blood pressure, and cancer, are not available because relatively small numbers have chosen to use this method of contraception. On the other hand, it is logical to conclude that any of the progestin effects associated with the combination oral contraceptives can be related to the minipill according to a dose-response curve; all effects should be reduced. Both the World Health Organization case-control study and the Transnational case-control study could find no indication for increased risks of stroke, myocardial infarction, or venous thromboembolism with oral progestin-only contraceptives.^{24,25} No impact can be measured on the coagulation system.^{5,26} The minipill can probably be used in women with previous episodes of thrombosis, and the package insert in the United States was revised, eliminating vascular disease as a contraindication.

The minipill is a good alternative for diminished libido on combination or decreased androgen levels. The mini few patients who report minor side (tenderness, headaches) of such a deceptive is not acceptable.

Because of the relatively low doses using medications that increase liver of contraception. These drugs include

- Carbamazepine (Tegretol)
- Felbamate
- Oxcarbazepine
- Phenobarbital
- Phenytoin (Dilantin)
- Primidone (Mysoline)
- Rifabutin,
- Rifampicin (Rifampin)
- Topiramate
- Vigabatrin
- Possibly* ethosuximide, griseof

Do the noncontraceptive benefits acceptance apply to the minipill? Studies again because of the relatively small progestin impact on cervical mucus one to think the benefits will be pre endometrial cancer, and ovarian numbers, one case-control study endometrial cancer was even greater combination oral contraceptives.²⁷

Good efficacy with the minipill each same time each day. There is less for minipill is probably not a good choice average adolescent.

Emergency Postcoital Contraceptive

The use of large doses of estrogen to Morris and van Wageningen at Yale in led to the use of high doses of di ethinyl estradiol in women.²⁸ It extremely large doses of estrogen

an excellent efficacy, probably near total effectiveness in women and women over age 40. In lactating women, the minipill is combined with prolactin-inhibiting hormone, adding up to very effective protection.¹⁷ In addition, Latina women with prior gestational diabetes and the minipill was associated with a 3-fold increased risk of diabetes mellitus.⁹ It is not known whether women who have experienced gestational diabetes would be advised to use other methods for this population. For women over age 40, reduced fecundity adds to

the minipill is a good choice for the breast-feeding woman. There is no evidence for any adverse effect on milk volume and infant growth and development, and a modest positive impact; women using the minipill may add supplementary feeding at a later time.²¹ *Impact on lactation, the minipill can be started immediately after delivery; a 3-day postpartum delay is recommended to allow levels of estrogen and progesterone and the estab-*

in situations where estrogen is contraindicated by serious medical conditions (diabetes with retinopathy, systemic lupus erythematosus,²³ cardiovascular disease, or significant cardiovascular risk factors, such as hypertension, hyperlipidemia, and smoking), should be noted that the freedom from estrogen is presumptive. Substantial data, for example on hypertension, blood pressure, and cancer, are not available. In women who have chosen to use this method of contraception, it is logical to conclude that any of the benefits of the combination oral contraceptives can be attributed to a dose-response curve; all effects should be similar. The World Health Organization case-control study and the Nurses' Health Study could find no indication for increased risk of myocardial infarction, or venous thromboembolism with oral contraceptives.^{24,25} No impact can be measured on the use of the minipill can probably be used in women with hypertension, and the package insert in the United States lists hypertension as a contraindication.

The minipill is a good alternative for the occasional woman who reports diminished libido on combination oral contraceptives, presumably due to decreased androgen levels. The minipill should also be considered for the few patients who report minor side effects (gastrointestinal upset, breast tenderness, headaches) of such a degree that the combination oral contraceptive is not acceptable.

Because of the relatively low doses of progestin administered, patients using medications that increase liver metabolism should avoid this method of contraception. These drugs include the following:

- Carbamazepine (Tegretol)
- Felbamate
- Oxcarbazepine
- Phenobarbital
- Phenytoin (Dilantin)
- Primidone (Mysoline)
- Rifabutin
- Rifampicin (Rifampin)
- Topiramate
- Vigabatrin
- Possibly* ethosuximide, griseofulvin, and troglitazone.

Do the noncontraceptive benefits associated with combination oral contraception apply to the minipill? Studies are unable to help us with this issue, again because of the relatively small numbers of users. However, the progestin impact on cervical mucus, endometrium, and ovulation leads one to think the benefits will be present (reduced risks of pelvic infection, endometrial cancer, and ovarian cancer). Although limited by small numbers, one case-control study indicated that protection against endometrial cancer was even greater with progestin-only pills than with combination oral contraceptives.²⁷

Good efficacy with the minipill requires regularity, taking the pill at the same time each day. There is less room for forgetting, and, therefore, the minipill is probably not a good choice for a disorganized adult or for the average adolescent.

Emergency Postcoital Contraception

The use of large doses of estrogen to prevent pregnancy was pioneered by Morris and van Wageningen at Yale in the 1960s. The initial work in monkeys led to the use of high doses of diethylstilbestrol (25–50 mg/day) and ethinyl estradiol in women.²⁸ It was quickly appreciated that these extremely large doses of estrogen were associated with a high rate of

gastrointestinal side effects. Yuzpe developed a method utilizing a combination oral contraceptive, resulting in an important reduction in dosage.²⁹ The following treatment regimens have been documented to be effective:

Ovral: 2 tablets followed by 2 tablets 12 hours later.

Alesse: 5 tablets followed by 5 tablets 12 hours later.

Lo Ovral, Nordette, Levlen, Triphasil, Tri-Levlen:
4 tablets followed by 4 tablets 12 hours later.

Levonorgestrel in a dose of 0.75 mg given twice, 12 hours apart, is more successful and better tolerated than the combination oral contraceptive method, but this dose is equivalent to 20 pills of the norgestrel progestin-only minipill.^{30,31} In many countries, special packages of 0.75 mg levonorgestrel are available for emergency contraception. Greater efficacy and fewer side effects make low-dose levonorgestrel the treatment of choice.

In the United States, a kit is available (Preven) containing 4 tablets, each containing 50 µg ethinyl estradiol and 0.250 mg levonorgestrel, to be used in the usual fashion, 2 tablets followed by 2 tablets 12 hours later. A package (Plan B) containing only levonorgestrel (two 0.75 mg tablets of levonorgestrel) is also available, one tablet taken within 72 hours of intercourse and the second 12 hours later.

This method has been more commonly called postcoital contraception, or the "morning after" treatment. Emergency contraception is a more accurate and appropriate name, indicating the intention to be one-time protection. It is an important option for women, and should be considered when condoms break, sexual assault occurs, if diaphragms or cervical caps dislodge, or with the lapsed use of any method. In studies at abortion units, 50–60% of the patients would have been suitable for emergency contraception and would have used it if readily available.^{32,33} In the U.S., it is estimated that emergency contraception could annually prevent 1.7 million unintended pregnancies and the number of induced abortions would decrease by about 40% to 800,000 per year.³⁴

Many women do not know of this method, and it has been difficult to obtain.^{33,35} In Europe and New Zealand, special packages with printed instructions have been marketed specifically for emergency contraception, and this is now available in the U.S. Even if women are aware of this method, accurate and detailed knowledge is lacking.³⁶ A favorable attitude toward this method requires knowledge and availability. Women who have used emergency contraception are very satisfied with the method, and most importantly, do not express an intention to substitute this method for regular contraception.³⁷

Information for patients and clinicians can be obtained from the following by the Office of Population Research

<http://opr.princeton.edu/ec/>
Telephone Hotline: 1-888-NO

Clinicians should consider providing (a kit can be a simple envelope containing a number of oral contraceptives) to be a contribution to our efforts to avoid unintended pregnancy without contraindications to oral contraception available for use when needed more effectively in reducing the need for a call. In two studies of self-administered emergency contraception, younger women in California increased their use without adverse effects such as increased weight gain.

"Collaborative drug therapy agreements between pharmacists to write prescriptions based upon a kit in the state of Washington allows women to obtain emergency contraception directly from pharmacists. Since the implementation of participating pharmacies, awareness of the method has increased in the public, and the number of emergency contraceptive kits dispensed has steadily increased.⁴⁰

Mechanism and Efficacy

The mechanism of action is not known with justification that this treatment combined with a local effect on the endometrium is confirmed in large clinical trials and the literature.^{44,46} Treatment with high-dose levonorgestrel yields a failure rate of approximately 2–3%. The failure rate of ethinyl estradiol given within 72 hours of intercourse with combination oral contraceptives at general clinical use, the method can reduce the failure rate to 75%; this degree of reduction in pregnancy risk is a relatively low chance, about 8%, for postcoital use⁴⁷ yields the 2% failure rate measured in clinical studies (in other studies with levonorgestrel will be even better). The risk of pregnancy was 60% lower compared with the oral contraceptive

uzpe developed a method utilizing a combination of 2 tablets 12 hours later, followed by 5 tablets 12 hours later. Levlen, Triphasil, Tri-Levlen: 4 tablets 12 hours later.

0.75 mg given twice, 12 hours apart, is more effective than the combination oral contraceptive equivalent to 20 pills of the norgestrel progestin-only countries, special packages of 0.75 mg for emergency contraception. Greater efficacy of low-dose levonorgestrel the treatment of choice.

is available (Preven) containing 4 tablets, each containing 0.02 mg ethinyl diethyl ether and 0.250 mg levonorgestrel, to be used as follows: 1 tablet followed by 2 tablets 12 hours later. A pack of 12 tablets containing 2 tablets of levonorgestrel (two 0.75 mg tablets of ethinyl diethyl ether, one tablet taken within 72 hours of intercourse later.

is commonly called postcoital contraception, or emergency contraception. Emergency contraception is a more accurate method, indicating the intention to be one-time use. It is an option for women, and should be considered in cases of sexual assault, if diaphragms or cervical caps are used. In studies at abortion clinics, emergency contraception would have been suitable for emergency use if readily available.^{32,33} In the U.S., it is estimated that emergency contraception could annually prevent 1.7 million pregnancies and the number of induced abortions from 1.7 million to 800,000 per year.³⁴

Use of this method, and it has been difficult to implement in New Zealand, special packages with printed instructions were developed specifically for emergency contraception, and in the U.S. Even if women are aware of this method, their knowledge is lacking.³⁶ A favorable attitude toward emergency contraception and its availability. Women who have been educated are very satisfied with the method, and they do not express an intention to substitute this method for

Information for patients and clinicians, including the latest available products, can be obtained from the following web site and hot line maintained by the Office of Population Research at Princeton University:

<http://opr.princeton.edu/ec/>
Telephone Hotline: 1-888-NOT-2-LATE (1-888-668-2528)

Clinicians should consider providing emergency contraceptive kits to patients (a kit can be a simple envelope containing instructions and the appropriate number of oral contraceptives) to be taken when needed. It would be a major contribution to our efforts to avoid unwanted pregnancies for all patients without contraindications to oral contraceptives to have emergency contraception available for use when needed. In our view, this would be much more effective in reducing the need for abortion than waiting for patients to call. In two studies of self administration, adult women in Scotland and younger women in California increased the use of emergency contraception without adverse effects such as increasing unprotected sex.^{38,39}

"Collaborative drug therapy agreements" provide a mechanism for pharmacists to write prescriptions based upon written protocols. A pilot project in the state of Washington allows women to receive emergency contraception directly from pharmacists. Since this project was initiated, the number of participating pharmacies, awareness of emergency contraception by the public, and the number of emergency contraception prescriptions have steadily increased.⁴⁰

Mechanism and Efficacy

The mechanism of action is not known with certainty, but it is believed with justification that this treatment is mainly a delay of ovulation combined with a local effect on the endometrium.⁴¹⁻⁴³ The efficacy has been confirmed in large clinical trials and summarized in complete reviews of the literature.⁴⁴⁻⁴⁶ Treatment with high doses of estrogen or with levonorgestrel yields a failure rate of approximately 1%, with the combination oral contraceptive, about 2-3%. The failure rate is lowest with high doses of ethinyl estradiol given within 72 hours (0.1%), but the side effects make combination oral contraceptives and levonorgestrel better choices. In general clinical use, the method can reduce the risk of pregnancy by about 75%; this degree of reduction in probability of conception (given the relatively low chance, about 8%, for pregnancy associated with one act of coitus⁴⁷) yields the 2% failure rate with combination oral contraceptives measured in clinical studies (in other words, 98% effective).^{48,49} Results with levonorgestrel will be even better; in the worldwide WHO study, the risk of pregnancy was 60% lower with the levonorgestrel-only method compared with the oral contraceptive method.³¹

Treatment Method

Treatment should be initiated as soon after exposure as possible, and the standard recommendation is that it be no later than 72 hours. Careful assessment of the reported experience with emergency contraception indicated that the method is equally effective when started on the first, second, or third day after intercourse (which would allow user-friendly scheduling), and that efficacy might extend beyond 72 hours.⁵⁰ Data from the WHO randomized, clinical trial, however, support the importance of timing, finding a reduction in efficacy after 72 hours, and the greatest protection occurring when the medication is taken within 24 hours of intercourse.⁵¹ Postponing the dose by 12 hours raises the chance of pregnancy by almost 50%. For this reason, the treatment should be initiated as soon as possible after sexual exposure, an important argument in favor of advance provision.

Because of possible, but unlikely, harmful effects of these high doses to a fetus, an already existing pregnancy should be ruled out prior to use of postcoital hormones. Furthermore, the patient should be offered induced abortion if the method fails. This patient encounter also provides an important opportunity to screen for STDs, and to discuss future contraception.

The combination oral contraceptive method delivers significantly less steroid hormone than estrogen alone, and this reduction in the total dose and the number of doses reduces the side effects and limits them to a shorter time period. It is worth adding an antiemetic, oral or suppository, to the treatment; a long-acting nonprescription agent, 25 or 50 mg meclizine (Bonine, Dramamine II, Antivert), is recommended, to be taken one hour before the emergency contraception treatment. Side effects reflect the high doses used: nausea (50%), vomiting (20%), breast tenderness, headache, and dizziness. If a patient vomits within an hour after taking pills, additional pills must be administered as soon as possible. It should be noted that an analysis of the U.K. General Practice Research Database could find no evidence for an increased risk of venous thromboembolism with the short-term use of oral contraceptives for emergency contraception (Indeed, no cases were found for as long as 60 days after use in more than 100,000 episodes of use).⁵² Although short-term treatment with combined oral contraceptives has been documented to have no effect on clotting factors,⁵³ in our view the usual contraindications for oral contraception apply to this use. *Because of the high dose of estrogen, emergency contraception with combined oral contraceptives should not be provided to women with either a personal or close family history (parent or sibling) of idiopathic thrombotic disease.*

For women with a contraindication only minipill can be used for emergency contraception. 20 norgestrel tablets (each tablet is for each of the two doses, or in special package with levonorgestrel). Levonorgestrel-only emergency contraception has significantly less side effects, especially nausea, than the standard oral contraceptive method.

A 3-week follow-up visit should be scheduled for routine contraception.

Could other combination oral contraceptives be used for other doses and other formulations? The answer is unknown. It would not be appropriate to recommend a failure rate.

The 3 major problems with the availability of emergency contraception are the high rate of side effects, the need for treatment within 72 hours after intercourse, and the need for a single dose. Mifepristone (RU486) in a single dose is markedly less nausea and vomiting. Mifepristone is used for emergency contraception as 50 mg. In a worldwide randomized trial, mifepristone was as effective as 50 mg or 600 mg, achieving a 95% efficacy was not diminished by delayed treatment after intercourse.⁵⁶ Because the next method of emergency contraception should be iron pills, mifepristone, around which make an effective contribution to induced abortions.

Another method of emergency contraception, the IUD, up to 5 days after unprotected intercourse (number of studies) is very low, 0.1% failure rate. Intrauterine implantation, but it is not suitable for intrauterine contraception, e.g., mifepristone.

The use of danazol for emergency contraception is not recommended.

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For women with a contraindication to exogenous estrogen, the norgestrel-only minipill can be used for emergency contraception; e.g., administering 20 norgestrel tablets (each tablet is equivalent to 37.5 µg levonorgestrel), for each of the two doses, or in some countries using the special commercial package with levonorgestrel (each tablet contains 750 µg). Levonorgestrel-only emergency contraception is associated with significantly less side effects, especially nausea and vomiting, compared with the standard oral contraceptive method.^{30,31}

A 3-week follow-up visit should be scheduled to assess the result, and to counsel for routine contraception.

Could other combination oral contraceptive products be used? Because other doses and other formulations have never been tested, the efficacy is unknown. It would not be appropriate to expose patients to an unknown failure rate.

The 3 major problems with the available methods of emergency contraception are the high rate of side effects, the need to start treatment within 72 hours after intercourse, and the small, but important, failure rate. Mifepristone (RU486) in a single oral dose of 600 mg is associated with markedly less nausea and vomiting and an efficacy rate of nearly 100%.^{34,35} Mifepristone is used for emergency contraception in China in a dose as low as 50 mg. In a worldwide randomized trial, 10 mg mifepristone was as effective as 50 mg or 600 mg, achieving a pregnancy rate of only 0.9%, and efficacy was not diminished by delaying treatment as long as 5 days after intercourse.³⁶ Because the next menstrual cycle is delayed after mifepristone, contraception should be initiated immediately after treatment. Ironically, mifepristone, around which swirls the abortion controversy, can make an effective contribution to preventing unwanted pregnancies and induced abortions.

Another method of emergency contraception is the insertion of a copper IUD, up to 5 days after unprotected intercourse. The failure rate (in a small number of studies) is very low, 0.1%.^{44,45} This method definitely prevents implantation, but it is not suitable for women who are not candidates for intrauterine contraception, e.g., multiple sexual partners or a rape victim.

The use of danazol for emergency contraception is not effective.³⁴

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