EMERGENCY POSTCOITAL CONTRACEPTION

This Committee Opinion has been reviewed and approved by the Reproductive Endocrinology and Infertility Committee and approved by its Council in June 1996.

STRUCTURED ABSTRACT

Objective: A major reduction in the number of unwanted pregnancies and pregnancy terminations could be achieved if an effective method of emergency pregnancy interception (postcoital contraception) was readily available to women. This policy statement describes a method which is the Yuzpe 2 + 2 regimen, the use of two tablets of estradiol/levonorgestrel, with an antiemetic, followed by a second identical dose 12 hours later.

Opinions: It must be stressed that this is the method of emergency contraception. Treatment should be reserved for those who have been exposed to unprotected coitus within the previous 72 hours only.

Outcomes and Benefits: The success rate is 98 percent and is heralded by menstrual bleeding by the 21st day following treatment. For those women who do not qualify for this regimen, or with exposure in the previous seven days, the insertion of a copper intrauterine device (IUD) is highly effective in preventing pregnancy.

Contraindications are those of the oral contraceptive pill.

Evidence: Clinical trials have supported this statement.

Harm and Costs: The rates of mild side effects, headaches, bloating and nausea and/or vomiting have been reduced by the reduction of the steroid dosage and the accompanying antiemetic.

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**Recommendations:** Although the Yuzpe 2+2 method has been widely marketed in Europe and used in North America at physicians' discretion, there is currently no specific approval by the Health Protection Branch (HPB) or the Food and Drug Administration (FDA).

However, the SOGC recommends this method to consumers as a highly effective method of emergency contraception.

**Sponsors:** The SOGC is the sponsor of this practice guideline produced by the Reproductive Endocrinology Committee of SOGC and approved by the SOGC Council in June 1996.

**INTRODUCTION**

It is well established that many unwanted pregnancies occur as a result of either unprotected intercourse, inadequate contraceptive measures, or failure of a method. Such pregnancies are, in part, preventable and such prevention could result in a major reduction in either the number of unwanted pregnancies or pregnancy terminations if an effective method of pregnancy interception (postcoital contraception) were readily available to women. Such availability depends upon both physician and patient education.

**METHODS**

The use of high-dose estrogen preparations (ethinyl estradiol, conjugated estrogens, or diethylstilbestrol) was at one time common. Their use is associated with a very high incidence of side effects, including nausea and/or vomiting, and failures also occur. In the early 1970s, reports appeared in the literature confirming the safety and efficacy of a combination of ethinyl estradiol and levonorgestrel as a pregnancy interceptive. Failure rates have been reported ranging from zero to five percent, with the majority of studies indicating a failure rate of approximately 1.5 percent to two percent. Two tablets containing 50 pg of ethinyl estradiol and 250 pg of levonorgestrel per tablet are administered at once, followed by two tablets 12 hours later. Both doses are administered concomitantly with a tablet of an antiemetic such as a 50 mg dose of dimenhydrinate. This method has commonly been referred to as the Yuzpe 2+2 regimen.

The Yuzpe 2+2 method involves the administration of a total of 200 pg of ethinyl estradiol and one mg of levonorgestrel (in two equally divided doses), compared to the previous high-dose estrogen methods. This significant reduction in steroid administration using the Yuzpe 2+2 method has resulted in a reduced incidence of nausea and/or vomiting, especially when combined with an antiemetic. No cases of teratogenesis or an increased risk of an ectopic pregnancy have been demonstrated with this method.

Although there are anecdotal reports of the use of other oral contraceptive preparations containing different progestins, only the ethinyl estradiol/levonorgestrel preparation has been evaluated in clinical trials. Comparative studies of this regimen with mifepristone (RU486) employed as a pregnancy interceptive have shown very little difference in efficacy. Since mifepristone is not available in Canada, the Yuzpe 2+2 method is therefore the method of choice for emergency postcoital contraception or pregnancy interception.
This method is proposed as an emergency method only to prevent pregnancy as a result of a single unprotected or inadequately protected coital exposure and is not to be used as an ongoing method of contraception, since a failure rate of even two percent per treatment cycle can be translated to a cumulative failure rate of as much as 24 percent annually, a rate which is totally unacceptable as an ongoing method of contraception.

Contraindications to the use of the Yuzpe 2+2 method include those which exist for the use of any oral contraceptive or estrogen/progestin containing preparation or previous unprotected intercourse prior to the 72-hour window of effectiveness.

Studies evaluating the efficacy of the Yuzpe 2+2 regimen have been confined to patients exposed to a single unprotected coital act within the previous 72 hours. No data exist with respect to efficacy in those women who have had multiple exposures both within and immediately prior to the previous 72 hours. Consequently, for those women who do not qualify for the Yuzpe 2+2 regimen and whose exposure(s) have been within the previous seven days, the insertion of a copper intrauterine device (IUD) has also been shown to have a high rate of efficacy in preventing pregnancy. When the copper IUD is selected as the most appropriate method, care must be taken to exclude those women who are not suitable candidates for IUD use, i.e. those with a previous history of pelvic inflammatory disease and those with a history of multiple partners especially during the exposure period in question.

Multiple mechanisms of action have been suggested for the efficacy of the Yuzpe 2+2 method. When the medication is administered at or immediately prior to the luteinizing hormone surge, obliteration or a significant delay in the surge has been demonstrated. In addition, endometrial effects have been shown with an "out-of-phase" appearance between the development of endometrial glands and stroma. Enzymatic changes in the endometrium as well as ovarian steroidal alterations have also been noted.

Side effects with the Yuzpe 2+2 method are primarily associated with nausea and/or vomiting. The use of the antiemetic preparation has greatly reduced this problem. However, if patients do experience vomiting within an hour after the administration of the medication, the dosage should be repeated. Studies have shown that high estrogen levels are obtained from vaginal absorption. Although this has never been tested clinically, in patients with severe vomiting, a vaginal preparation could be offered. Other side effects have been reported but are uncommon and are mainly associated with headaches, bloating and uterine cramps.

The success of treatment with the Yuzpe 2+2 method is heralded by the onset of menstrual bleeding. In early studies, 98 percent of patients will have experienced menstrual bleeding by the 21st day following treatment. If bleeding does not occur, the patient should be reassessed in order to establish whether she has merely experienced a delay in the onset of menses or whether treatment failure has occurred and she is, in fact, pregnant. Thus, a serum β-hCG pregnancy test should be performed if no bleeding occurs by the 21st day following treatment. In the majority of cases, bleeding occurs at the time of the expected menses or even before. The patient should be counselled regarding an acceptable ongoing method of contraception. Thus, the use of the postcoital interceptive method should be considered not only for the purposes of preventing an unwanted pregnancy, but also as an opportunity to initiate contraceptive counselling and prescription.
Although the Yuzpe 2+2 method is widely employed in North America, there is currently no specific approval by the Health Protection Branch or the Food and Drug Administration. However, since the medication is approved for contraception, physicians may offer this method at their discretion. In European countries and in other parts of the world, this preparation is marketed specifically as a pregnancy interceptive under various trade names, including Tetragynon (ethinyl estradiol/norgestrel).

SUMMARY

The use of two tablets containing ethinyl estradiol and levonorgestrel combined with an antiemetic followed by a second identical dose 12 hours later has been shown to be an effective method of emergency postcoital contraception or pregnancy interception. Treatment should be reserved for those women exposed to unprotected coitus within the previous 72 hours only. The use of a copper IUD for those women exposed between 72 hours and seven days prior to seeking medical help has also been shown to be extremely effective in preventing pregnancy. Physicians should be familiar with this method and be available to provide this treatment for those individuals who are candidates for treatment. Consumers should be educated that there is a medical method which can be used and, although not universally effective, it carries a high rate of efficacy.

REFERENCES