South African Family Practice 2019; 61(2):46-48

S Afr Fam Pract
ISSN 2078-6190 EISSN 2078-6204

REVIEW

The use of emergency hormonal contraception in South Africa: current and future perspectives

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Emergency hormonal contraceptives play an important role in preventing unplanned pregnancies in South Africa. In this review, we discuss the levonorgestrel emergency contraceptive, the combined estrogen and progestin regimen (also known as the Yuzpe method) and the use of Ulipristal acetate. The levonorgestrel and the combined estrogen, progestin regimen are available in South Africa. The specific mechanisms of action of each of these emergency hormonal contraceptives will be discussed as well as their efficacy, the side effects associated with each of these preparations and the drug interactions. Levonorgestrel can be used as a single dose (1.5 mg) instead of two doses (0.75 mg) 12 hours apart. Levonorgestrel is very effective, with fewer adverse effects than the combined estrogen and progestogen administration. Levonorgestrel and the Yuzpe method have demonstrated good efficacy when utilised within 72 hours after unprotected intercourse or contraceptive failure. These emergency hormonal contraceptives should not be used as regular contraception. It is essential that all health professionals and educators inform women of reproductive age about the risks and common side effects of emergency hormonal contraceptives.

Keywords: Emergency Hormonal Contraception, Contraceptive Failure, Levonorgestrel, Yuzpe method, Ulipristal acetate

Introduction

Despite the recent advances in modern hormonal contraceptive developments, ill-timed and unintended pregnancies continue to be a concern worldwide. Between 2010 and 2014, approximately 44% of pregnancies were unintended due to various reasons. In developing regions, the unintended pregnancy rate fell 16% (90% UI 5–24), from 77 (74–88) per 1000 women aged 15–44 years to 65 (62–76). The decline in developing regions coincided with a declining unintended birth rate. In 2010–14, 55% of unintended pregnancies ended in abortion in developing regions.[1] Abortion in many African countries is risky and unsafe, resulting in almost 9% of all maternal deaths. This is where the importance of emergency hormonal contraceptives plays a significant role in preventing unwanted pregnancies. Emergency hormonal contraceptives (EC) are safe methods that can be used to prevent unwanted pregnancies if they are used within an exact time period.[2,3]

Indications and types of emergency hormonal contraception

Emergency hormonal contraceptives should be used in the following situations: after having unprotected sexual intercourse, when a woman has improperly used regular contraceptives, in the event of sexual assault, or in situations where a condom has broken, slipped, or has been used incorrectly.[3,4]

The available methods of emergency hormonal contraception in South-Africa include levonorgestrel (LNG) or the combined estrogen and levonorgestrel/norgestrel method commonly known as the Yuzpe method.[5] LNG is a synthetic progestin which is administered orally as a single dose of 1.5 mg or it can be taken in two doses of 0.75 mg each within 12 hours. Studies have shown that a single dose of 1.5 mg is as effective as two 0.75 mg doses taken 12 hours apart.[6] The LNG method is utilized more often than the Yuzpe method.[5,6]

The Yuzpe method involves the use of estrogen combined with levonorgestrel/norgestrel and requires the pills to be taken at 12-hour interval in two divided doses starting as soon as possible after unprotected intercourse or contraceptive failure.[5] This method must be utilized within 72 hours of unprotected sexual intercourse or contraceptive failure.[5] Each dose must contain estrogen (usually 100–120 mcg ethinyl estradiol) and progestin (either 0.50–0.60 mg levonorgestrel or 1.0–1.2 mg norgestrel).[7]

Ordinary birth control pills containing both estrogen and progestin may be used in specified combinations as emergency contraception.[8] Depending on the brand available and the concentrations of the estrogen and progestin, each dose consists of 4, 5, or 6 pills.[8] If vomiting occurs within two hours of taking a dose, the dose should be repeated.[8] Any brand of combined oral contraceptives can be used provided it contains the amount of estrogen and progestin discussed above.

Ulipristal acetate is a novel, selective progesterone receptor modulator (SPRM). Ulipristal acetate is taken as a single oral dose of 30 mg.[9] Clinical trials have demonstrated that ulipristal acetate is highly effective and well tolerated. It may be utilized within 120 hours (5 days) after unprotected sexual intercourse or contraception failure.[9] The United States Food and Drug Administration (US FDA) and the Medicine Regulatory Authority in the United Kingdom have approved ulipristal acetate for emergency contraception; however, it is unavailable in South Africa.

Mechanism of action

Several studies have demonstrated that levonorgestrel exerts its contraceptive effects by preventing or delaying ovulation thus reducing luteal function when administered before ovulation. Levonorgestrel also increases the thickness of the cervical mucus and hinders sperm motility, ultimately leading to the prevention of a fertilized egg.[10] The Yuzpe method works by inhibiting implantation of a fertilized egg. Other mechanisms by which this method works include delaying or suppressing ovulation, interfering with corpus luteum function and making changes in the endometrium that prevents implantation.[11]

Ulipristal acetate is thought to inhibit or delay ovulation. Clinical trials have demonstrated that ulipristal acetate can delay ovulation for 24–48 hours even on the day of the luteinizing hormone (LH) surge. When ulipristal was given before or immediately after the LH surge, it inhibited 100% of the follicular ruptures.[12] Other contraceptive mechanisms of ulipristal acetate include reducing the endometrial thickness, delayed endometrial maturation, and alterations in the progesterone–dependent markers required for implantation. These effects may subsequently inhibit implantation because the uterus will be less receptive to the trophoblast.[13]

Efficacy of emergency hormonal contraceptives

The LNG and Yuzpe method are effective when used within 72 hours after unprotected intercourse or contraceptive failure. Nonetheless, the earlier treatment is initiated, the more likely it is for the treatment to be successful. This does not apply to ulipristal. Within 72 hours of unprotected coitus or contraceptive failure, ulipristal was as effective as levonorgestrel and estimated to have an efficacy of between 98.2–99.1%.[13,14] The Yuzpe regimen of emergency contraception has been reported to be between 97–98 % effective in preventing pregnancy.[15,16]

A multi-centre double blind randomized trial of 1998 women, comparing the use of levonorgestrel with the Yuzpe combination noted that the LNG method was associated with better pregnancy prevention when compared to the Yuzpe method.[16] The levonorgestrel regimen reduced the average predicted pregnancy rate by approximately 85% compared to the Yuzpe regimen which only reduced the predicated pregnancy rate by 57%.[16,17]

The use of ulipristal acetate upholds a reliable effectiveness of up to 5 days (120 hours) following unprotected intercourse or contraceptive failure, whereas the effectiveness of levonorgestrel starts to decline when given more than 48 hours after unprotected sexual intercourse or contraceptive failure.[18,19,20] Within 72 to 120 hours, ulipristal acetate is more effective than levonorgestrel.[15,20] A meta-analysis of the two clinical trials involved involving ulipristal acetate demonstrated that the risk of pregnancy with ulipristal acetate was significantly reduced compared to levonorgestrel (p=0.046).[13]

Adverse effects of emergency hormonal contraception

Emergency hormonal contraceptive pills have an excellent safety profile.[21,22] The side effects associated with the use of emergency hormonal contraceptives are comparable to those of oral contraceptive pills, such as the nausea and vomiting, irregular vaginal bleeding, and fatigue.[12] The use of emergency hormonal contraception has been known to delay the users period by up to 7 days.[5,12] If vomiting occurs within 2 hours of taking a dose, the recommendation is that the dose be repeated. Levonorgestel and ulipristal acetate are preferred to the Yuzpe method because these two methods are less likely to cause nausea and vomiting.[23]

Other uncommon side effects associated with both the progestin and the Yuzpe regimens include headache, bloating, and uterine cramping.[5,23] Taking each dose of emergency contraceptive with food and using antiemetics such as domperidone and prochlorperazine 30 minutes before, may reduce the likelihood of nausea and vomiting.[5,23]

Potential drug interactions

Cytochrome p450 (CYP450) enzyme inducers that metabolize both the progestins, and the estrogens may decrease their plasma concentration levels and can therefore decrease the efficacy of the emergency hormonal contraception.[24] Examples of cytochrome p450 enzyme inducers include carbamazepine, rifampicin, phenytoin, and griseofulvin. Co-administration of levonorgestrel with HIV protease inhibitors or with non-nucleoside reverse transcriptase inhibitors has shown to produce significant changes (increase or decrease) in the plasma levels of levonorgestrel.[25] The metabolism of ulipristal acetate also involves cytochrome p450 specifically CYP 3A4 so the co-administration of CYP 3A4 enzyme inducers is not recommended.[26] Concomitant use of ulipristal acetate with CYP3A4 inducers such as phenytoin, fosphenytoin, carbamazepine, oxcarbazepine, rifampicin, rifabutin, griseofulvin, efavirenz and nevirapine will thus reduce the plasma concentrations of ulipristal acetate and may decrease the efficacy of this method of EHC. For woman who have used these enzyme inducing drugs in the past 4 weeks, ulipristal acetate is not recommended.[27]

Conclusions

Emergency hormonal contraceptives are effective in preventing unplanned pregnancies and should be initiated as soon as possible following unprotected sexual intercourse or contraceptive failure. The availability of emergency hormonal contraception is a benefit to all women who are at risk for pregnancy following unprotected intercourse or contraceptive failure. For both the levonorgestrel containing and the Yuzpe method, efficacy of emergency hormonal contraception decreases after 72 hours; thus, the sooner they are taken, the better the chances of preventing an unplanned pregnancy. Ulipristal, on the other hand, has no decreased efficacy and works for up to 120 hours. The progestin containing regimens are more effective and better tolerated than the estrogen-containing regimens. Emergency contraceptives should not be used as a regular form of contraception and do not protect against sexually transmitted infections, including HIV/AIDS.

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