

Emergency contraception for the South African healthcare professional

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Introduction

Unintended pregnancies are very common, and it is estimated that almost 45% of all pregnancies in 2011 in the USA were not planned.¹ In South Africa, the situation could even be worse as it is common knowledge that we have a very high teenage pregnancy rate. It puts the already overburdened health system under enormous pressure. The social and financial pressure of an unintended or even unwanted pregnancy can be devastating to a family and even more so to a single mother. It has been reported that the unintended pregnancy rate in Botswana is 52% and that only 22% had ever used emergency contraception (EC).²

Although EC is widely available in the public and private sectors, women are unaware of the options available to them. A study published in 2012 reported that only 50% of female university students had heard about EC.³ In rural populations, this number is even lower as it was previously estimated to be only 17%.⁴

What is even more concerning is that knowledge of EC amongst pharmacists and doctors is lacking. In Durban, KwaZulu-Natal, only 28% of doctors and 32% of pharmacists could correctly prescribe the Yuzpe regimen. The recognition of side-effects was even worse as only 27% of doctors and 22% of pharmacists could accurately diagnose or identify them.⁵

One can therefore expect that this lack of knowledge could lead to unsafe terminations of pregnancy and unnecessary maternal deaths. Unfortunately, at the population level, the use of EC has not reduced abortion rates, although the use of EC could be beneficial for individual woman.⁶

Indications for the use of emergency contraception

What are the indications for EC?

- Contraception failure (condom that slipped or broke, missed pills, the concomitant use of enzyme-inducing drugs or antibiotics in women using hormonal contraception or an expelled IUCD).
- Sexual assault.
- Sexual coercion.
- Unprotected consensual intercourse.¹

Emergency contraception options available in South Africa

EC can be divided into oral EC pills and copper-containing intrauterine contraceptive devices (IUCDs). The oral EC pills are:

- Yuzpe's method of combined oral contraceptives
- levonorgestrel (LNG)
- ulipristal acetate (UPA)

Each of these options will be discussed in greater detail. (Table I for a summary of EC options available in South Africa.)

Other options not registered for EC use will be briefly mentioned.

Yuzpe's method/regimen

Yuzpe's method is the use of 100 µg ethinylestradiol (EE) and 1 mg norgestrel (e.g. 2 Ovral® tablets) taken 12 hourly. Thus, 2 Ovral® tablets are taken stat and repeated 12 hours later. This regimen needs to be used within 72 hours of unprotected intercourse.⁷ Ordinary combined oral contraceptives can also be used as long as each 12-hourly dose contains at least 100–120 µg EE and a progestin of 0.5–0.6 mg LNG or 1.0–1.2 mg norgestrel.⁸

Another option is to use Nordette® as each tablet contains 30 µg EE and 0.15 mg LNG. To attain the acquired dose, the woman thus needs to take four Nordette® tablets stat and repeat the dosage 12 hours later. Four Nordette® tablets contain 120 µg EE and 0.6 mg LNG.

The yellow pills in a Triphasil® package could also be used as each yellow pill contains 30 µg EE and 0.125 mg LNG; four pills will thus give a total dose of 120 µg EE and 0.5 mg LNG.

Of all available methods, Yuzpe's is the least effective, but it was still shown to reduce the risk of pregnancy by 74%.⁹ Other studies have reported efficacy of 98–99% in preventing pregnancies.⁸

The sooner after unprotected coitus it is used, the more effective it is. This is also generally true for all methods of EC.⁹

Of all EC methods used, Yuzpe's method has the worst side-effect profile.⁹ The side-effects include:

- nausea,
- vomiting in up to 20% of women (the most common side-effect),

- headache,
- changes in the menstrual cycle (delay in onset of menstruation), and
- mastalgia.

If a patient vomits within two hours after taking a dosage, that dosage needs to be repeated. Therefore, antiemetic drugs are recommended, such as prochlorperazine 5–10 mg, domperidone 10 mg or metoclopramide 10 mg, when Yuzpe's regimen is prescribed.^{8,9}

The method of action whereby Yuzpe's regimen prevents pregnancy is mostly by inhibiting ovulation. There may also be effects on the functioning of the endometrium and thus preventing implantation of the embryo.⁸ The cumulative effect on fertilisation, gamete transport and corpus luteum functioning is not clear, and due to ethical considerations, it is challenging to study in humans.¹⁰

There are almost no contraindications to the use of Yuzpe's regimen. Due to the high EE dosage, there may be a theoretical concern for the development of thromboembolic complications, but studies do not support this as the use of the EE is very brief.⁹ Studies also do not report increased risks to an existing pregnancy.⁹

Oestrogens are metabolised by the CYP450 enzymes which are mostly expressed in the liver. The first step is hydroxylation to hydroxyestradiol, which in turn is catalysed by CYP1A2 and CYP3A4 with the inactive metabolites excreted into faeces and urine.¹¹ It is thus logical that enzyme-inducing medication might decrease the efficacy of EC. Drugs known to be enzyme-inducing include rifampicin, griseofulvin, carbamazepine, phenytoin, St John's Wort, nevirapine and efavirenz.^{8,9}

Levonorgestrel

LNG as an EC is given orally in one of two dosages. It can be given as 0.75 mg 12 hourly for two doses or a single dose of 1.5 mg, which is now more commonly used – thus, two pills are taken stat.¹² LNG should be taken as soon as possible after unprotected intercourse and preferably before 72 hours have passed, although some studies report efficacy up to five days after sex.^{9,12} There is no reported difference in the effectivity of the single 1.5 mg dose compared to the two doses of the 0.75 mg tablets. Norlevo® is available as 0.75 mg tablets or Escapelle® as a single 1.5 mg tablet.

It is generally understood that a woman's fertile period is between five days prior to and one to two days post-ovulation. LNG is thought to inhibit ovulation as progesterone and progestins delay the LH surge.^{9,12} In order to be effective, it must be administered before the LH surge begins. It speaks for itself that it is less effective if given closer to ovulation.

LNG is more effective than the Yuzpe method in preventing pregnancies. LNG may prevent 85% of pregnancies,⁸ compared to the 74% mentioned for Yuzpe's regimen.⁹ Another comparison estimated the pregnancy rate to be 1.1% in the LNG group vs

3.2% in women employing the Yuzpe method as EC.⁹ When meloxicam, which is a COX-2 inhibitor, was added to 1.5 mg LNG, follicle rupture was delayed even in the presence of an LH surge.¹² Obesity has a negative effect on the efficacy of LNG EC. With a BMI > 30 kg/m², there is a definite increase in the failure rate, with an odds ratio (OR) of 4.41.⁹ Doubling the dose of LNG might be an option for obese women, and at present, it is being evaluated.¹

The side-effect profile of LNG is favourable compared to that of the combined oral contraceptive pill used for Yuzpe's method. Although the most common side-effect is nausea (23%), followed by vomiting (5.6%), side-effects are much less common compared to those accompanying the Yuzpe's regimen.⁹ LNG's mechanism of action predicts a delayed onset of menstruation because ovulation is delayed.

In a systemic review of 47 studies assessing the safety profile of LNG, it was reported that most side-effects were not serious. Uncommon adverse effects were anorexia, weight gain, ectopic pregnancy, ovarian cyst rupture, suicidal thoughts and even ovarian cancer.¹³ It is debatable if all of these are really due to LNG EC as it is used very briefly and often as a once-off only.

Breastfeeding women should be able to use LNG as it does not contain oestrogen; oestrogen inhibits breast milk production. It might be better though to discard the breast milk for 36 hours after taking LNG as an EC pill.

There are no absolute contraindications to the use of LNG as EC, and as with combined oral contraceptives, it does not negatively affect a pre-existing pregnancy.⁹ As a result, no pregnancy test or physical examination is required before taking the LNG EC pill.¹

As ovulation is delayed by LNG, a woman can still fall pregnant if she has unprotected intercourse a few days after the use of the EC pill. It is, therefore, of utmost importance to counsel the patient on the use of barrier methods for contraception after the use of an EC pill such as LNG (Norlevo®/Escapelle®).

Ulipristal acetate

UPA (Ella®), as a second-generation antiprogestin, has antagonistic as well as partial agonistic effects on progesterone receptors, thus, it is a selective progesterone receptor modulator (SPRM).^{7,15} UPA also blocks glucocorticoid receptors.⁹ It has been marketed in Europe since 2009 and was approved for EC by the FDA in 2010.⁷ As an EC, it is shown to be more effective than the LNG EC pill as it can prevent ovulation even after a woman had an LH surge.¹² UPA can be given up to five days after unprotected coitus. As the LH surge is suppressed and ovulation is delayed, the menstrual cycle is prolonged.⁹ UPA also seems to be more effective in women with a BMI of > 30 with a failure rate of 2.6% compared to a 5.8% failure rate with LNG EC pills.¹² The most common side-effects of UPA are nausea, vomiting, headache and a prolonged cycle. Overall it is very well tolerated. There are no absolute contraindications to the use of UPA. Still, as it blocks glucocorticoid receptors, LNG is preferred in asthmatic women.¹ UPA is not an abortifacient. There has been no difference in the ability of embryos to implant

in endometrium that has been exposed to UPA compared to endometrium that has not been exposed.¹ It is taken orally as a single 30 mg dose.⁸

Copper-containing intrauterine contraceptive device

The copper-containing IUCD is regarded as the most effective of all EC options.^{1,9,12,14} Studies reported a failure rate of only 0.1%.^{7,14} The big drawback in using a copper-containing IUCD as EC is that a certain skill set and instrumentation are required for it to be inserted successfully. As a result, it is often overseen as EC.

The advantages of inserting a copper-containing IUCD as EC are numerous:

- It is cost effective.¹⁰
- It provides continuous/ongoing protection against pregnancy.¹⁰
- It does not have any hormonal effects and thus is not contraindicated in women with risk factors for deep venous thrombosis.
- It can be inserted up to 120 hours (five days) after unprotected intercourse.^{1,9}
- Increased BMI does not affect the effectiveness of a copper-containing IUCD.¹
- The efficacy of IUCDs is not affected by other medication such as enzyme-inducing drugs or antibiotics.
- Copper-containing IUCDs do not have an adverse effect on breast milk and may be safely used by lactating mothers.¹

The copper-containing IUCD releases copper ions into the uterine cavity. Copper reduces sperm motility.¹ It is also known to cause an inflammatory reaction (increase in white blood cells and enzymes) in the uterine cavity, which is hostile to sperm.^{1,9} If

fertilisation does occur, the inflammatory response may prevent implantation.⁹ There is also a change in the tubal environment. The copper-containing IUCD also prevents implantation,¹⁰ but it is important to note that the changes in the uterine cavity do not affect a blastocyst that is already implanted, and furthermore, copper-containing IUCDs are not implicated in birth defects.¹

Side-effects of a copper-containing IUCD include:

- Increased menstrual bleeding,⁹ which can be managed with the use of nonsteroidal anti-inflammatory drug (NSAIDs) and tranexamic acid.
- Discomfort and pain during its insertion can be minimised with the use of local analgesia and oral pain medication such as paracetamol and NSAIDs.⁹
- There is an increase in pelvic inflammatory disease (PID) in women with a copper-containing IUCD.¹⁰
- The risk of malposition or uterine perforation is always present,⁷ therefore, it is advisable to do a pelvic ultrasound examination to confirm the correct placement.

There are certain contraindications to the insertion of a copper-containing IUCD for EC:¹

- Women with active PID.
- Known congenital malformation of the uterus such as duplications.
- Wilson's disease.
- Cancer of the cervix or uterus, including gestational trophoblastic disease.
- The WHO warns against the use of copper-containing IUCDs in HIV-positive women who are not using antiretroviral (ARV)

Table I: Summary of EC options available in South Africa

Method	Timing after unprotected coitus	Side-effects	Contraindications	Special considerations	Effectivity
Copper-containing IUCD (Nova T 380®) Single insertion	Up to 5 days (120 hours)	Pain and discomfort with insertion Increased menstrual flow	Current pregnancy Uterine abnormality PID and pelvic TB Gynaecological malignancies Abnormal uterine bleeding Wilson's disease (rare)	Training needed to insert Risk of uterine perforation	Most effective Provides ongoing contraception
LNG (Norlevo®) (Escapelle®) Single dose of 1.5 mg or 2 doses of 0.75 mg 12 h apart	Within 72 hours	Nausea Vomiting Delayed menstruation	None	Less effective in obese women	Effective
Yuzpe's method Ovral® ii tabs stat and repeat after 12 h Nordette® / Triphasal® (yellow pills) iv tabs stat and repeat after 12 h	Within 72 hours	Severe nausea Vomiting Headache Mastalgia Delayed menstruation	No absolute contraindications Careful in women with known hypercoagulability	Less effective in obese women	Least effective Worst side-effect profile
Ulipristal acetate (Ella®) Taken as a single 30 mg dose	Up to 5 days after contraceptive failure/unprotected intercourse	Well tolerated Nausea and vomiting Headache Delayed menstruation	No absolute contraindications Careful in asthmatic patients as it blocks glucocorticoid receptors	More effective in preventing ovulation in obese women than LNG or Yuzpe's method	More effective than LNG, especially in obese women

therapy.

- The risk of expulsion and uterine perforation is increased if it is inserted within four to six weeks postpartum.

We have all been taught that copper-containing IUCDs increase the risk for an ectopic pregnancy, but recently it has been shown that in women not using contraception the absolute risk for an ectopic pregnancy is between 3 and 4.5 per 1 000 women years compared to 0.2 in women using copper-containing IUCDs.

Given the above copper-containing IUCDs are still safe for the majority of women in need of EC.¹⁴

At present, the use of an LNG-containing intrauterine system (Mirena[®]) is not recommended. Currently, there are studies underway evaluating its efficacy as EC intrauterine device. Unfortunately, limited data is available.¹

EC contraception option not registered for use in South Africa

Mifepristone

Mifepristone (RU4860, Mifegyne[®]) is a synthetic steroid and is an antiprogesterin.^{1,7,9} The mechanism of action is complex and in the follicular phase it delays the rise in oestrogen and consequently the LH surge and therefore prevents ovulation. Once ovulation has taken place, it blocks the endometrial receptors resulting in an immature endometrium not suitable for embryo implantation.⁹ In doses of 200–600 mg, it is a known abortifacient, and in this context, its use as an EC pill is controversial. Studies have shown that mifepristone has an efficacy comparable to LNG and UPA.⁹ It should be noted that, as with all other EC options that delay ovulation, mifepristone also prolongs the menstrual cycle. Other side-effects include headache and dizziness, nausea and vomiting, abdominal cramping and diarrhoea.⁹ Absolute contraindications to the use of mifepristone are:⁹

- adrenal insufficiency,
- steroid therapy,
- asthma,
- porphyria, or
- hypersensitivity to prostaglandins.

Mifepristone is not registered for use in South Africa.

Ethics in emergency contraception

For EC to be a viable option, healthcare providers should be knowledgeable and non-judgemental.¹⁶ Misconceptions abound, and often EC is seen as preventing implantation or as an abortifacient, but as seen from the discussion above, it prevents fertilisation and does not interfere with an existing pregnancy.^{17,18} When seen in this context, EC pills may prevent abortion.¹⁸ By preventing women the right to EC pills, the ethical principles of autonomy, non-maleficence, beneficence and justice are violated.¹⁷

Practical considerations

EC can be obtained in private and public sectors from pharmacies and clinics without prescription.

A copper-containing IUCD is the most effective form of EC, it also provides long-term contraception.

There are no absolute contraindications to the use of LNG EC pills.

LNG EC pills are more effective than Yuzpe's method.

UPA is more effective than LNG in obese woman.

All methods that delay ovulation should only be used for a single episode of unprotected intercourse.

If a woman has a second episode of unprotected intercourse in the same menstrual cycle, a copper-containing IUCD should be considered.

After taking EC pills which delay ovulation, a woman should be reminded to use additional barrier methods for contraception.

When prescribing Yuzpe's regimen, it is important to add an antiemetic drug.

The sooner EC is instituted, the lower the failure rate, i.e. less unintended/unwanted pregnancies.

EC pills should be given within 72 hours, except UPA which can be taken up to 5 days after unprotected coitus.

A copper-containing IUCD should be inserted within five days.

Healthcare professionals working in emergency rooms and those involved with sexual assault victims should have protocols in place for the provision of EC.

It should be remembered that EC is not a long-term solution to women having unprotected sex and that long-term options should be discussed with women.

EC does not prevent sexually transmitted diseases.

If a woman's menstrual period is delayed by more than one week after her usual period should start, or if her menstruation does not commence within three weeks of taking EC pills, she should do a pregnancy test and seek medical attention.⁹

It is important to note that pregnancy should be excluded before inserting an IUCD.¹⁰ It can be done by a urine pregnancy test, a serum β -hCG or pelvic ultrasound.

When inserting an IUCD, it is the ideal opportunity for doing a Papanicolaou smear or liquid-based cytology (LBC) of the cervix.¹⁰

Not one of all the methods of EC can prevent each and every pregnancy.

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