Emergency Contraception

INTRODUCTION

Emergency or post-coital contraception is used to prevent pregnancy after intercourse but before implantation. EC is used as a back-up method when regular contraception is not used, is used improperly, or when a contraceptive accident has occurred (e.g. condom slippage). It is not intended to be used as a regular method of contraception.

OPTIONS

There are 2 options for EC: hormonal methods, also known as emergency contraceptive pills, and post-coital insertion of a Cu-IUD. Hormonal EC options include LNG-EC, UPA-EC, and the Yuzpe regimen.

In Canada, commercial LNG-EC preparations include Plan B, Norlevo, Option 2, and Next Choice. All consist of 2 tablets of LNG 750 mcg to be taken together as a single 1.5 mg dose. They are approved for use up to 72 hours after UPI and there is evidence of efficacy up to 5 days.[1] They are available over-the counter in pharmacies across Canada without a prescription but are kept behind the counter in Saskatchewan and Quebec for reimbursement reasons. Pharmacies in other provinces may decide to keep LNG-EC behind the counter for various other reasons, for example concerns about theft.

The Yuzpe method uses combined oral contraceptives to deliver 2 doses of ethinyl estradiol (100 mcg) and LNG (500 mcg) 12 hours apart. This can be achieved using multiple pills of a variety of combined oral contraceptives (Table 5) but requires the use of prescription medication. The Yuzpe method is less effective and has more side effects than LNG-EC[2] or UPA-EC and is recommended only when other EC methods are not available.

UPA is a selective progesterone receptor modulator. The approved regimen for EC is one oral dose of 30 mg up to 5 days after UPI. In Canada, UPA-EC currently requires a prescription, but in Europe it was recently approved for over-the-counter use.[3] It may be directly available through pharmacists in provinces where EC prescription rights have been delegated to these professionals.[4,5]

The antiprogestin mifepristone (RU-486) is also highly effective as an emergency contraceptive,[1] but is not available in Canada and not approved elsewhere for EC.

Insertion of a Cu-IUD is highly effective for EC[1] and has the advantage of providing long-term contraception at a low cost. Several Cu-IUDs are approved in Canada for EC (Liberte, Mona Lisa, Flexi-T), although other Cu-IUDs may be provided off-label for EC use. LNG-IUS is not currently recommended or approved for EC.

EFFECTIVENESS

The effectiveness of all EC methods available in Canada is summarized in Table 6. The Cu-IUD is the most effective method of EC.[1] In a systematic review of 42 studies conducted in 6 countries between 1979 and 2011 on the EC use of 8 different Cu-IUDs in 7034 women, the global pregnancy rate was estimated to be 0.09% (95% CI 0.04% to 0.19%).[6] In these studies, the time from intercourse to insertion of the IUD ranged from 2 days to 10 or more days, but the majority of women had the IUD inserted within 5 days of intercourse. In a secondary analysis of data from a study on the use of the Copper T380A IUD for EC,[7] there were no pregnancies in the first month following emergency Cu-IUD insertion, regardless of the timing of insertion[8] Based on confidence intervals, the risk of pregnancy was estimated from 0% to 3% for insertions more than 5 days after the estimated day of ovulation and 0% to 5% for insertions 5 days after UPI.[8] More studies are needed to confirm the effectiveness of a Cu-IUD inserted more than 5 days after the estimated date of ovulation or of UPI.

LNG-EC and UPA-EC are less effective than the Cu-IUD, and their effectiveness is influenced by various factors. In the largest LNG-EC trial ever done in the 1990s, women using LNG-EC within 72 hours of UPI had a pregnancy rate of 1.1% compared to 3.2% with the Yuzpe regimen; this corresponded to an 85% reduction of the risk of pregnancy with LNG-EC compared with 57% with Yuzpe.[2] Subsequent studies have found higher pregnancy rates with LNG-EC (1.7%[9] and 2.6%[10]) such that it may reduce pregnancy risk by only 50%.[9,10] Although there is some conflicting research,[11] most studies have shown

Table 5. Combined oral contraceptive pills for use as EC

	Pills per dose	Ethinyl estradiol (mcg/dose)	Levonorgestrel (mcg/dose)
Alesse	5	100	500
Triquilar	4 yellow	120	500
Min-Ovral	4	120	600

Table 6. Summary table of risks of pregnancy with different methods of EC according to timing since UPI

Day since UPI	≤ 1	2	3	4	5	6	7
Methods, %				Risk of pregnancy			
Yuzpe EC[2]	3.2	3.2	3.2	> 3.2	> 3.2	NA	NA
LNG EC [9, 10]	2.3	1.6	2.7	2.8	3.0	NA	NA
UPA EC [9, 10]	0.9	2.2	0.9	0*	0*	NA	NA
Emergency, %							
Cu-IUD[6]	0.01	0.01	0.01	0.01	0.01	0.01	0.01

*Small sample size

Table 7. Effectiveness of UPA-EC versus LNG-EC (meta-analysis)

	Pregnancies, n/N (%)			
Interval between UPI and EC use	Ulipristal acetate	Levonorgestrel	Odds ratio	*P**
0–24 hours	5/584 (0.9)	15/600 (2.5)	0.35	0.035
0–72 hours	22/1617 (1.4)	35/1625 (2.2)	0.58	0.046
0–120 hours	22/1714 (1.3)	38/1731 (2.2)	0.55	0.025

*Inferential statistics based on the logistic regression model including significant covariates and the study factor

Adapted from Table 2 in Glasier, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet* 2010;375(9714):555–62.[9]

that LNG-EC is more effective the earlier it is taken.[12–14] Although 3 RCTs also demonstrated that LNG regimens were effective when taken from 72 to 120 hours after UPI,[15,16] several studies found reduced efficacy from 72 to 120 hours (more likely on the fifth day) compared with < 72 hours.[1,9,16–19]

A meta-analysis of 2 large RCTs[9,10] reported that UPA-EC was significantly more effective than LNG-EC (Table 7).[9] For UPA, no significant relationship has been seen between efficacy and timing of EC.[9,10,20] The lower pregnancy rates seen with UPA are likely related to the fact that it can disrupt ovulation even after the LH surge has begun,[21] whereas LNG is ineffective after the start of the LH surge.[22,23]

Mifepristone

Two RCTs comparing the use of one 10 mg dose of mifepristone with 1.5 mg LNG or two doses of 0.75 mg LNG given 12 hours apart, within 120 hours of UPI, showed no significant difference in pregnancy rates between the 3 groups.[11,15] The pregnancy rate was 1.7% (95% CI 1.3% to 2.2%) in a study that combined data from 12 RCTs of mifepristone 10 mg for EC (10 989 women) for an estimate of 83.4% of pregnancies prevented.[24] A 2015 RCT reported a higher efficacy with mifepristone 10 mg than with mifepristone 5 mg, with a pregnancy rate of 0.7% (95% CI 0.3% to 1.4%) compared with 1.2% (95% CI 0.7% to 2.0%).[25]

FACTORS AFFECTING EFFECTIVENESS OF EC PILLS

Weight

A 2011 secondary analysis of data from 2 RCTs evaluating the effectiveness of UPA-EC versus LNG-EC showed significantly higher pregnancy rates for LNG-EC in women with a BMI ≥ 30 kg/m^2 (5.8%, 95% CI 3.5% to 9.5%) than in women with a normal BMI (1.3%, 95% CI 0.8% to 2.2%).[26] Pregnancy rates for women with a BMI

25 to 29 kg/m^2 (2.5%, 95% CI 1.3% to 4.6%) were not significantly higher.[26] A 2015 re-analysis of the same data reported a similar increase in pregnancy rates with increasing body weight or BMI in users of LNG-EC.[27] The 2011 secondary analysis also found that the pregnancy rate was not significantly higher in women with a BMI ≥ 30 kg/m^2 using UPA-EC (2.6%, 95% CI 1.2% to 5.6% vs. 1.1% CI 0.6% to 1.9%) or women with a BMI of 25 to 29 kg/m^2 (1.1%, 95% CI 0.4% to 2.7%) than in women with a normal BMI (1.1% CI 0.6% to 1.9%).[26] Another meta-analysis of these data showed that significantly more obese women had further acts of intercourse after taking EC than women who were not obese.[20] These data were the basis for a Health Canada warning on the LNG-EC label about the lack of efficacy of the product for women over 80 kg in March 2014.[28] After examining data from WHO that contradicted the previous study's findings,[26,27] the European Medicines Agency concluded that "the data available are too limited and not robust enough to conclude with certainty that contraceptive effect is reduced with increased bodyweight" and that "emergency contraceptives can continue to be taken after unprotected intercourse or contraceptive failure, regardless of the woman's bodyweight."[29] Until new data are available, health care providers should not withhold LNG-EC for the reason of body weight. No population studies have been conducted to determine whether increasing the LNG-EC dose would improve its effectiveness, so offering a higher dose is not currently recommended. However, after considering access and cost, it would be reasonable to offer UPA-EC to women with BMI ≥ 25 kg/m^2 because of its better effectiveness.

Data from an RCT comparing the effectiveness of LNG-EC and mifepristone showed no significant association between the effectiveness of EC and age, BMI, method of contraception used, circumstances leading to EC request, interval between UPI and treatment, or day in the menstrual cycle on which UPI occurred for the 2 EC methods used.[11] Pharmacokinetic studies have shown that hormone serum levels may be slightly reduced among obese women taking hormonal contraceptives.[30,31] In the case of EC, reduced serum levels of LNG can reduce the length of time that ovulation is delayed[32] and may put obese women more at risk for pregnancy with subsequent acts of intercourse.

Timing of UPI and EC Administration

Hormonal EC (LNG and UPA) has not been shown to be effective if given the day of or the day just prior to ovulation.[23,26] and it has no effect if given after ovulation.[23,33] A meta-analysis of the mechanism of action of LNG-EC suggests that LNG-EC will not delay ovulation if administered the day before or the day of ovulation.[21]

Further acts of UPI

For all types of EC, women who have further unprotected acts of intercourse are 4 to 26 times more likely to get pregnant after taking EC than those who do not.[1,2,14–16,24,26,34–36] A meta-analysis of studies on UPA-EC confirmed that the most significant contributor to decreased effectiveness was subsequent UPI.[20]

MECHANISM OF ACTION

Conception is only possible during a limited period in the menstrual cycle because of the limited life span of sperm in the female reproductive tract (up to 5 days) and the length of oocyte survival post-ovulation (12 to 24 hours).[37] Thus the fertile window extends from 5 days before ovulation to 1 day after, with the highest rates of conception when intercourse occurs within 2 days prior to ovulation.[38]

LNG acts by interfering with ovulation. It affects follicular development after selection of the dominant follicle but before the beginning of the pre-ovulatory rise in LH. Once the LH rise begins, LNG fails to inhibit ovulation.[21,22,37,39] The addition of a single oral dose of meloxicam 15 mg has been shown to improve the delay of ovulation by LNG.[21,40] LNG also influences muscular contractility of the Fallopian tubes[37] and concentrations of glycodelin-A (known as an inhibitor of sperm binding to the zona pellucida).[41] LNG does not affect endometrial receptivity or implantation[37,39] thus it is not an abortifacient. The best available evidence suggests that its ability to prevent pregnancy is not related to post-fertilization events.

UPA has a longer window of effectiveness than LNG-EC because it has a direct inhibitory effect on follicular rupture that allows it to be effective even when given shortly before ovulation. When given before the onset of the LH surge, it inhibits 100% of follicular ruptures versus 0% with placebo.[42] In a meta-analysis of 3 small RCTs, UPA-EC was significantly more effective than LNG-EC in delaying follicular rupture (UPA: 58.8% versus LNG: 14.6%; $P = 0.0001$), particularly after the initial LH rise but before the LH surge (UPA: 79% versus LNG: 14%; $P = 0.0018$).[21] Both treatments were ineffective when administered on the day of the LH surge. UPA has little or no effect on the endometrium.[37,39]

Mifepristone administered during the pre-ovulatory phase either blocks or delays ovulation in a dose–dependent fashion.[37,39] Mifepristone induces minor effects on the endometrium and influences muscular contractility of the Fallopian tubes.[37,39]

Cu-IUDs induce a sterile inflammatory reaction in the uterine cavity.[43] Copper ions and by-products of

inflammation are toxic for spermatozoa and oocytes,[43] increase Fallopian smooth muscle activity, and stimulate myometrial contractility.[37] Copper can alter molecules such as cytokines and integrins in the endometrial lining and thereby inhibit implantation in the event that a blastocyst reaches the uterus.[37] Studies have rarely shown increased hCG and early pregnancy factor in IUD users.[43] In vitro studies showed that Cu-IUDs adversely affect the viability and fertilizing capacity of human spermatozoa, both in culture medium and in cervical mucus.[37]

INDICATIONS

EC should be considered for women wishing to reduce their risk of pregnancy after UPI or a contraceptive accident such as:

- failure to use any method of contraception
- condom slippage, breakage, or leakage
- missed hormonal contraception (pill, patch, vaginal ring, or medroxyprogesterone acetate injection)[44]
- error in using withdrawal (ejaculation in vagina or on external genitalia)
- dislodgement, incorrect insertion, or premature removal of a diaphragm or cervical cap
- mistimed fertility awareness (intercourse occurred on fertile cycle day)
- sexual assault when the woman is not using reliable contraception.

It is difficult to determine with certainty the fertile time of a women's cycle, thus EC should be offered regardless of the cycle day on which UPI occurred if a woman is concerned about her risk of pregnancy. The risk of pregnancy is very low for the first 3 days after the onset of menses, then rises significantly until ovulation, after which is falls. However, a US study estimated a persistent small risk of pregnancy of 1% late in the cycle and even when menses were delayed.[45]

Contraindications

There are no evidence-based absolute contraindications to any EC pills with the exception of pregnancy and hypersensitivity to the product or to any ingredient in the formulation. Known pregnancy is a contraindication because the medication will not work; accidentally ingesting LNG-EC while pregnant will not cause harm to the fetus nor will it disrupt an established pregnancy.[46,47] Women who have contraindications to regular use of combined oral contraceptive pills can safely use any of the hormonal EC methods as the duration of action is very brief. LNG-EC or UPA-EC is generally preferred because it is better tolerated and carries no theoretical risk, particularly in women with strong contraindications to estrogen such as those at higher risk of venous thromboembolism.

Contraindications to use of the Cu-IUD for EC are the same as for its use for contraception (please refer to the IUD Chapter). A pre-existing pregnancy should be excluded prior to insertion. As an EC method, the Cu-IUD can be provided safely to women who are nulliparous, to adolescents, and to those with a history of multiple sexual partners unless there is evidence of current or recent pelvic infection or current purulent cervicitis.[48]

Side Effects

LNG-EC is associated with a significantly lower incidence of nausea (23.1%), vomiting (5.6%), dizziness (11.2%), and fatigue (16.9%) than the Yuzpe regimen.[2] UPA is associated with side effects similar to LNG-EC.[9] Both LNG-EC and UPA-EC may be associated with a change in timing of the next menses. The next menses might be early, on time, or late.[9,49] In one study, when menses did occur it was within 7 days of the expected time in 75% of women using UPA-EC and 71% of women using LNG-EC.[9]

Risks

Although there have been case reports of ectopic pregnancy following use of LNG-EC, a systematic review found no increase in ectopic pregnancy rates with LNG-EC or mifepristone compared with the general population.[50] Because EC prevents some pregnancies, its use actually lowers the risk of ectopic pregnancy after UPI. There is no evidence that the high dose of LNG used for EC is harmful to adolescents[48]; therefore, access to EC should not be limited by age. There is no effect on physical growth, mental development, or occurrence of birth defects in children born after LNG-EC exposure.[51] Data are limited on pregnancy outcomes with UPA-EC failure,[50] but in utero exposure does not appear to increase the risk of birth defects.[52]

The risks of the Cu-IUD are believed to be the same whether it is used for EC or for ongoing contraception. These risks include uterine perforation, infection, expulsion, and, with continued use, an increase in menstrual flow and cramping.

PROVIDING EMERGENCY CONTRACEPTION

All EC methods should be initiated as soon as possible after UPI. Due to its superior efficacy in EC and ongoing contraception, the emergency Cu-IUD should be offered as a first choice to all eligible women (see Contraindications to Copper IUD in the IUD Chapter). However, knowledge

of the Cu-IUD for EC is limited among women and health care providers[53–55] and even experienced family planning providers rarely offer it as an option.[55,56] Barriers to its use may include lack of provider availability for urgent IUD insertion and the immediate cost of the IUD. Women for whom EC pills are likely to be less effective should be encouraged to consider a Cu-IUD (women with BMI ≥ 30, women delayed in presentation, and those presenting one day prior to, on the day of, or after presumed ovulation for hormonal EC). Because the date of ovulation is difficult or often impossible to assess in women consulting for EC, a Cu-IUD can be inserted up to 7 days after UPI provided that a pregnancy test is negative. Studies have shown that women who choose the Cu-IUD for EC have very low odds of pregnancy 4 weeks after insertion.[7,8]

LNG-EC is available from pharmacies without a prescription and should be taken as soon as possible within 5 days of UPI. UPA-EC is taken as a single 30 mg dose within 5 days of UPI. UPA-EC is more effective than LNG-EC, especially at days 4 and 5 after UPI.[9]

ASSESSMENT

Very little information is required to determine whether EC is indicated. History taking must determine that UPI occurred within the time when EC is effective. The woman's risk for having a pre-existing pregnancy should be assessed by determining the timing and normalcy of her last menstrual period, prior acts of UPI, and whether or not she is currently overdue for an expected period. A urine pregnancy test is only required if there is uncertainty and a Cu-IUD is to be inserted.[8] If the woman has a negative urine pregnancy test and there are no other contraindications, a copper IUD can be inserted up to 7 days after UPI.[6–8]

A woman who had UPI earlier in the cycle may be at risk of pregnancy because the EC therapeutic window has passed, but she should not be denied EC pills if she also had UPI within the 5-day window. She also can be offered a Cu-IUD if UPI occurred within the 7-day window and her urine pregnancy test is negative. For example, if a woman had UPI on days 8 and 13 of her menstrual cycle and presents on day 17 for EC, she can be offered a post-coital IUD if her urine pregnancy test is negative. Repeated use of LNG 0.75 mg in a cycle does not appear to be associated with any serious adverse events.[57] Repeated use of UPA has not been specifically studied.

Health care providers should also discuss broader sexual health concerns, such as whether the UPI was coerced, the need for ongoing contraception, the risk of STIs, and the need for post-exposure prophylaxis. Screening for chlamydia and gonorrhea should be offered to all women and recommended for those at higher risk.[58] If a Cu-IUD is chosen in a woman at high risk for STIs, swabs for chlamydia and gonorrhea should be taken at the time of IUD insertion and prophylactic antibiotics that cover chlamydia and gonorrhea can be considered.[59] Women using EC pills should be advised that they do not prevent pregnancy if UPI occurs in the days or weeks after treatment and that a reliable ongoing method of contraception should be used. Women who want to start oral contraceptives, the patch, the ring, or medroxyprogesterone acetate can begin using it the day of or the day following LNG-EC (the "quick start" method).[60] There is some concern that quick start of regular hormonal contraceptives or continuation of hormonal contraceptives after missed pills may interfere with the action of UPA-EC.[61] For this reason it is prudent to wait 5 days before starting or continuing hormonal contraceptives after UPA-EC.[61] There is no evidence that quick start of hormonal contraceptives after EC harms a pregnancy in the event of EC failure.[62] Back-up contraception/abstinence should be used for 7 days after LNG-EC even if a woman has started another method of hormonal contraception or is using her usual hormonal contraception.[60] Women who choose UPA-EC must use back-up contraception/abstinence for the first 5 days after taking UPA-EC and then for the first 14 days after starting hormonal contraception.[61] If delaying initiation of hormonal contraception until the next menses, abstinence or a barrier method should be used in the interim.

DRUG INTERACTIONS

Although certain enzyme-inducing medications may theoretically reduce the efficacy of LNG-EC, UPA-EC, and the Yuzpe regimen,[63,64] the World Health Organization in its last Medical Eligibility Criteria for Contraceptive Use of 2015[65] does not consider these drugs as a contraindication to the use of any EC pill. Some guidelines[66] recommend doubling the dose of LNG-EC to 3.0 mg in women using enzyme-inducing medication, but there is currently no evidence to support this statement. Women taking one of these medications also have the opportunity to choose a Cu-IUD for EC.

FOLLOW-UP

Women should have a pregnancy test if they do not have normal menstrual bleeding by 21 days following EC treatment (LNG-EC, UPA-EC, or Cu-IUD) or by 28 days if cyclic hormonal contraception was initiated and withdrawal bleeding does not occur. Women who start

medroxyprogesterone acetate or continuous hormonal contraception should do a pregnancy test 21 days after using EC to rule out EC failure. Women who obtain an emergency Cu-IUD should come for a follow-up visit 4 to 6 weeks after the insertion to check that the IUD is in place and that there are no other concerns.

ACCESS TO EMERGENCY CONTRACEPTION

Emergency contraception is a woman's last chance to prevent an unintended pregnancy. To maximize the potential for EC to reduce the number of unintended pregnancies, women at risk of pregnancy and their partners need to be knowledgeable about both hormonal EC and the post-coital IUD *before they need it* and must be able to access it quickly should they need it.

Possible barriers to EC use include lack of knowledge, negative attitudes, fear of side effects, judgemental attitudes from providers, overstating of associated health risks, impractical business hours of medical clinics and pharmacies, cost of EC, unavailability of the product in some pharmacies, and lack of Health Canada approval for all EC methods. Although women are increasingly familiar with and using hormonal EC, specific knowledge is often poor[67,68] and knowledge of IUDs is even more limited.[69] Pharmacy availability of LNG-EC has been shown to increase access and use and to reduce the time to use.[70] Systematic reviews and meta-analyses have shown that women with advance provision of EC used it more frequently and with less delay than those accessing EC through the usual channels.[71–73] Most studies have shown that women and adolescents receiving LNG-EC in advance did not differ from those receiving usual care in their use of hormonal contraception or in subsequent sexual risk-taking behaviours.[71,72] Increased access to EC pills through pharmacies and advance provision has not been shown to reduce population pregnancy rates in individual studies or meta-analyses.[71–73] However, a recent observational study found that women receiving post-coital IUDs were more likely to be using an effective method of contraception and less than half as likely to have had a pregnancy in the following year compared with those who received LNG-EC.[74] Despite evidence for its superior effectiveness, the Cu-IUD may be difficult for women to access. Even clinics specializing in sexual health services seldom offer this option.[55] Organized efforts are warranted to make this option available to all Canadian women in need.

Summary Statements

12. The copper intrauterine device is the most effective method of emergency contraception. (II-2)
13. A copper intrauterine device can be used for emergency contraception up to 7 days after unprotected intercourse provided that pregnancy has been ruled out and there are no other contraindications to its insertion. (II-2)
14. Levonorgestrel emergency contraception is effective up to 5 days (120 hours) after intercourse; its effectiveness decreases as the time between unprotected intercourse and ingestion increases. (II-2)
15. Ulipristal acetate for emergency contraception is more effective than levonorgestrel emergency contraception up to 5 days after unprotected intercourse. This difference in effectiveness is more pronounced as the time from unprotected intercourse increases, especially after 72 hours. (I)
16. Hormonal emergency contraception (levonorgestrel emergency contraception and ulipristal acetate for emergency contraception) is not effective if taken on the day of ovulation or after ovulation. (II-2)
17. Levonorgestrel emergency contraception may be less effective in women with a body mass index > 25 kg/m^2 and ulipristal acetate for emergency contraception may be less effective in women with a body mass index ≥ 35 kg/m^2. However, hormonal emergency contraception may still retain some effectiveness regardless of a woman's body weight or body mass index. (II-2)
18. Hormonal emergency contraception is associated with higher failure rates when women continue to have subsequent unprotected intercourse. (II-2)
19. Hormonal contraception can be initiated the day of or the day following the use of levonorgestrel emergency contraception, with back-up contraception used for the first 7 days. (III)
20. Hormonal contraception can be initiated 5 days following the use of ulipristal acetate for emergency contraception, with back-up contraception used for the first 14 days. (III)

Recommendations

16. All emergency contraception should be initiated as soon as possible after unprotected intercourse. (II-2A)
17. Women should be informed that the copper intrauterine device (IUD) is the most effective method of emergency contraception and can be used by any woman with no contraindications to IUD use. (II-3A)
18. Health care providers should not discourage the use of hormonal emergency contraception (EC)

on the basis of a woman's body mass index (BMI). The copper intrauterine device for EC should be recommended for women with a BMI > 30 kg/m^2 who seek EC. If access and cost allow, ulipristal acetate for EC should be the first choice offered to women with a BMI ≥ 25 kg/m^2 who prefer hormonal EC. (II-2B)

19. Health care providers should discuss a plan for ongoing contraception with women who use pills for emergency contraception (EC) and should provide appropriate methods if desired. Hormonal contraception should be started within 24 hours of taking levonorgestrel for EC, and back-up contraception or abstinence should be used for the first 7 days after starting hormonal contraception. (III-B) Women who use UPA-EC should start hormonal contraception 5 days after using UPA-EC. UPA-EC users must use back-up contraception or abstinence for the first 5 days after taking UPA-EC and then for the first 14 days after starting hormonal contraception. (III-B)
20. Ulipristal acetate and levonorgestrel should not be used together for emergency contraception. (III-B)
21. A pregnancy test should be conducted if the woman has no menstrual period within 21 days of using pills or inserting a copper intrauterine device for emergency contraception. (II-B)
22. Health services should be developed to allow Canadian women to have timely access to all effective methods of emergency contraception. (III-A)

REFERENCES

1. Cheng L, Che Y, Gulmezoglu AM. Interventions for emergency contraception. Cochrane Database Syst Rev 2012;8:CD001324.
2. [No authors listed]. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. Task Force on Postovulatory Methods of Fertility Regulation. Lancet. 1998;352(9126):428–33.
3. European Medicines Agency. EMA recommends availability of EllaOne emergency contraceptive without prescription. EMA/710569/2014. 21 November 2014.
4. Ordre des pharmaciens du Québec. La contraception d'urgence, plus facilement accessible au Québec puisque les pharmacies peuvent la prescrire [Emergency contraception: more accessible in Quebec because pharmacies are permitted to prescribe]. Montreal (QC): Ordre des pharmaciens du Quebev; 2011. Available at: http://www.opq.org/fr-CA/presse/communiques-de-presse/communiques-2001/2001-12-19-la-cou-plus-facilement-accessible-au-quebec-. Accessed on February 17, 2015.
5. Saskatchewan College of Pharmacists. Emergency post-coital contraception—standards and guidelines for pharmacists prescribing. Regina (SK): Saskatchewan College of Pharmacists; 2003. Avaiilable at: http://scp.in1touch.org/uploaded/58/web/refmanual/Emergency-Post-Coital-Contraception-Standards-and-Guidelines-04-18-12.pdf. Accessed on February 17, 2015.
6. Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. Hum Reprod 2012;27:1994–2000.
7. Wu S, Godfrey EM, Wojdyla D, Dong J, Cong J, Wang C, et al. Copper T380A intrauterine device for emergency contraception: a prospective, multicentre, cohort clinical trial. BJOG 2010;117:1205–10.
8. Turok DK, Godfrey EM, Wojdyla D, Dermish A, Torres L, Wu SC. Copper T380 intrauterine device for emergency contraception: highly effective at any time in the menstrual cycle. Hum Reprod 2013;28:2672–6.
9. Glasier AF, Cameron ST, Fine PM, Logan SJ, Casale W, Van Horn J, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. Lancet 2010;375:555–62.
10. Creinin MD, Schlaff W, Archer DF, Wan L, Frezieres R, Thomas M, et al. Progesterone receptor modulator for emergency contraception: a randomized controlled trial. Obstet Gynecol 2006;108:1089–97.
11. Hamoda H, Ashok PW, Stalder C, Flett GM, Kennedy E, Templeton A. A randomized trial of mifepristone (10 mg) and levonorgestrel for emergency contraception. Obstet Gynecol 2004;104:1307–13.
12. Piaggio G, von Hertzen H, Grimes DA, Van Look PF. Timing of emergency contraception with levonorgestrel or the Yuzpe regimen. Task Force on Postovulatory Methods of Fertility Regulation. Lancet 1999;353:721.
13. Cheng L, Gulmezoglu AM, Piaggio G, Ezcurra E, Van Look PF. Interventions for emergency contraception. Cochrane Database Syst Rev 2008(2):CD001324.
14. Arowojolu AO, Okewole IA, Adekunle AO. Comparative evaluation of the effectiveness and safety of two regimens of levonorgestrel for emergency contraception in Nigerians. Contraception 2002;66:269–73.
15. von Hertzen H, Piaggio G, Ding J, Chen J, Song S, Bártfai G et al. Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. Lancet 2002;360:1803–10.
16. Ngai SW, Fan S, Li S, Cheng L, Ding J, Jing X, et al. A randomized trial to compare 24 h versus 12 h double dose regimen of levonorgestrel for emergency contraception. Hum Reprod 2005;20:307–11.
17. Ashok PW, Stalder C, Wagaarachchi PT, Flett GM, Melvin L, Templeton A. A randomised study comparing a low dose of mifepristone and the Yuzpe regimen for emergency contraception. BJOG 2002;109:553–60.
18. Olukayode AD, Godfrey E, Piaggio G, von Hertzen H. A randomized, double-blind, noninferiority study to compare two regimens of levonorgestrel for emergency contraception in Nigeria. Contraception 2010;82:373–8.
19. Piaggio G, Kapp N, von Hertzen H. Effect on pregnancy rates of the delay in the administration of levonorgestrel for emergency contraception: a combined analysis of four WHO trials. Contraception 2011;84:35–9.
20. Moreau C, Trussell J. Results from pooled Phase III studies of ulipristal acetate for emergency contraception. Contraception 2012;86:673–80.
21. Brache V, Cochon L, Deniaud M, Croxatto HB. Ulipristal acetate prevents ovulation more effectively than levonorgestrel: analysis of pooled data from three randomized trials of emergency contraception regimens. Contraception 2013;88:611–8.
22. Noé G, Croxatto HB, Salvatierra AM, Reyes V, Villarroel C, Muñoz C, et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. Contraception 2011;84:486–92.

23. Novikova N, Weisberg E, Stanczyk FZ, Croxatto HB, Fraser IS. Effectiveness of levonorgestrel emergency contraception given before or after ovulation—a pilot study. Contraception 2007;75:112–8.

24. Piaggio G, Heng Z, von Hertzen H, Bilian X, Linan C. Combined estimates of effectiveness of mifepristone 10 mg in emergency contraception. Contraception 2003;68:439–46.

25. Carbonell JL, Garcia R, Gonzales A, Breto A, Sanchez C. Mifepristone 5 mg versus 10 mg for emergency contraception: double-blind randomized clinical trial. Int J Womens Health 2015;7:95–102.

26. Glasier A, Cameron ST, Blithe D, Scherrer B, Mathe H, Levy D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. Contraception 2011;84:363–7.

27. Kapp N, Abitbol JL, Mathé H, Scherrer B, Guillard H, Gainer E, et al. Effect of body weight and BMI on the efficacy of levonorgestrel emergency contraception. Contraception 2015;91:97–104.

28. Health Canada. Healthy Canadians. Emergency contraceptive pills to carry warnings for reduced effectiveness in women over a certain body weight. Ottawa (ON): Health Canada; 2014. Available at: http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38701a-eng.php. Accessed on June 25, 2015.

29. European Medicines Agency. Levonorgestrel and ulipristal remain suitable emergency contraceptives for all women, regardless of bodyweight. EMA/440549/2014. July 24, 2014.

30. Edelman AB, Cherala G, Munar MY, Dubois B, McInnis M, Stanczyk FZ, et al. Prolonged monitoring of ethinyl estradiol and levonorgestrel levels confirms an altered pharmacokinetic profile in obese oral contraceptives users. Contraception 2013;87:220–6.

31. Westhoff CL, Torgal AH, Mayeda ER, Pike MC, Stanczyk FZ. Pharmacokinetics of a combined oral contraceptive in obese and normal-weight women. Contraception 2010;81:474–80.

32. Croxatto HB, Brache V, Pavez M, Cochon L, Forcelledo ML, Alvarez F, et al. Pituitary-ovarian function following the standard levonorgestrel emergency contraceptive dose or a single 0.75-mg dose given on the days preceding ovulation. Contraception 2004;70:442–50.

33. International Federation of Gynecology and Obstetrics (FIGO), International Consortium for Emergency Contraception. Mechanism of action: how do levonorgestrel-only emergency contraceptive pills (LNG ECPs) prevent pregnancy? London (GB): FIGO; 2011. Available at: http://www.figo.org/sites/default/files/uploads/MOA_FINAL_2011_ENG.pdf. Accessed on February 9, 2015.

34. Ellertson C, Webb A, Blanchard K, Bigrigg A, Haskell S, Shochet T, et al. Modifying the Yuzpe regimen of emergency contraception: a multicenter randomized controlled trial. Obstet Gynecol 2003;101:1160–7.

35. [No authors listed]. Comparison of three single doses of mifepristone as emergency contraception: a randomised trial. Task Force on Postovulatory Methods of Fertility Regulation. Lancet 1999;353:697–702.

36. Xiao B, Zhao H, Piaggio G, von Hertzen H. Expanded clinical trial of emergency contraception with 10 mg mifepristone. Contraception 2003;68:431–7.

37. Gemzell-Danielsson K, Berger C, Lalitkumar PGL. Emergency contraception—mechanisms of action. Contraception 2013;87:300–8.

38. Wilcox AJ, Baird DD, Dunson DB, McConnaughey DR, Kesner JS, Weinberg CR. On the frequency of intercourse around ovulation: evidence for biological influences. Human Reprod 2004;19:1539–43.

39. Gemzell-Danielsson K. Mechanism of action of emergency contraception. Contraception 2010;82:404–9.

40. Massai MR, Forcelledo ML, Brache V, Tejada AS, Salvatierra AM, Reyes MV, et al. Does meloxicam increase the incidence of anovulation induced by single administration of levonorgestrel in emergency contraception? A pilot study. Hum Reprod 2007;22:434–9.

41. Durand M, Koistinen R, Chirinos M, Rodríguez JL, Zambrano E, Seppälä M et al. Hormonal evaluation and midcycle detection of intrauterine glycodelin in women treated with levonorgestrel as in emergency contraception. Contraception 2010;82:526–33.

42. Brache V, Cochon L, Jesam C, Maldonado R, Salvatierra AM, Levy DP, et al. Immediate pre-ovulatory administration of 30 mg ulipristal acetate significantly delays follicular rupture. Hum Reprod 2010;25:2256–63.

43. Ortiz ME, Croxatto HB. Copper-T intrauterine device and levonorgestrel intrauterine system: biological bases of their mechanism of action. Contraception 2007;75(6 Suppl):S16–30.

44. Guilbert E, Black A, Dunn E, Senikas V. Missed hormonal contraceptives—new recommendations. J Obstet Gynaecol Can 2008;20:1050–62.

45. Wilcox AJ, Dunson DB, Weinberg CR, Trussell J, Baird DD. Likelihood of conception with a single act of intercourse: providing benchmark rates for assessment of post-coital contraceptives. Contraception 2001;63:211–5.

46. Zhang L, Chen J, Wang Y, Ren F, Yu W, Cheng L. Pregnancy outcome after levonorgestrel-only emergency contraception failure: a prospective cohort study. Hum Reprod 2009;24:1605–11.

47. De Santis M, Cavaliere AF, Straface G, Carducci B, Caruso A. Failure of the emergency contraceptive levonorgestrel and the risk of adverse effects in pregnancy and on fetal development: an observational cohort study. Fertil Steril 2005;84:296–9.

48. Glasier A. Emergency contraception: clinical outcomes. Contraception 2013;87:309–13.

49. Gainer E, Kenfack B, Mboudou E, Doh AS, Bouyer J. Menstrual bleeding patterns following levonorgestrel emergency contraception. Contraception 2006;74:118–24.

50. Cleland K, Raymond E, Trussell J, Cheng L, Zhu H. Ectopic pregnancy and emergency contraceptive pills: a systematic review. Obstet Gynecol 2010;115:1263–6.

51. Zhang L, Ye W, Yu W, Cheng L, Shen L, Yang Z. Physical and mental development of children after levonorgestrel emergency contraception exposure: a follow-up prospective cohort study. Biol Reprod 2014;91:27.

52. Levy DP, Jager M, Kapp N, Abitbol JL. Ulipristal acetate for emergency contraception: postmarketing experience after use by more than 1 million women. Contraception 2014;89:431–3.

53. Wright RL, Frost CJ, Turok DK. A qualitative exploration of emergency contraception users' willingness to select the copper IUD. Contraception 2012;85:32–5.

54. Turok DK, Gurtcheff SE, Handley E, Simonsen SE, Sok C, North R, et al. A survey of women obtaining emergency contraception: are they interested in using the copper IUD? Contraception 2011;83:441–6.

55. Harper CC, Speidel JJ, Drey EA, Trussell J, Blum M, Darney PD. Copper intrauterine device for emergency contraception: clinical practice among contraceptive providers. Obstet Gynecol 2012;119(2 Pt 1):220–6.

56. Moss E, Reynolds T, Kundu A. Emergency contraception: patterns of use in community sexual health clinics. J Obst Gynaecol 2009;29:337–9.

57. Raymond EG, Halpern V, Lopez LM. Pericoital oral contraception with levonorgestrel. Obstet Gynecol 2011;117:673–81.

58. Caddy S, Yudin MH, Hakim J, Money DM. Best practices to minimize risk of infection with intrauterine device insertion. J Obstet Gynaecol Can 2014;36:266–74.

59. Kettle H, Cay S, Brown A, Glasier A. Screening for Chlamydia trachomatis infection is indicated for women under 30 using emergency contraception. Contraception 2002;66:251–3.

60. Salcedo J, Rodriguez MI, Curtis KM, Kapp N. When can a woman resume or initiate contraception after taking emergency contraceptive pills? A systematic review. Contraception 2013;87:602–4.

61. Jensen J. Emergency contraception. OB/GYN Clinical Alert 2014;30:81–4.

62. Yovich JL, Turner SR, Draper R. Medroxyprogesterone acetate therapy in early pregnancy has no apparent fetal effects. Teratology 1988;38:135–44.

63. Robinson JA, Jamshidi R, Burke AE. Contraception for the HIV-positive woman: a review of interactions between hormonal contraception and antiretroviral therapy. Infect Dis Obstet Gynecol 2012;2012:890160.

64. Carten ML, Kiser JJ, Kwara A, Mawhinney S, Cu-Uvin S. Pharmacokinetic interactions between the hormonal emergency contraception, levonorgestrel (Plan B), and Efavirenz. Infect Dis Obstet Gynecol 2012;2012:137192.

65. World Health Organization. Medical eligibility criteria for contraceptive use. 5th ed. Geneva (CH): WHO; 2015: pp i–xiii.

66. Royal College of Obstetricians and Gynaecologists. Faculty of Sexual & Reproductive Healthcare. Emergency contraception. Clinical effectiveness unit. London (GB): RCOG; 2011 (updated 2012). Available at: http://www.fsrh.org/pdfs/CEUguidanceEmergencyContraception11.pdf. Accessed on Jun 25, 2015.

67. Whelan AM, Langille DB, White SJ, Asbridge M, Flowerdew G. Knowledge of, beliefs about, and perceived barriers to the use of the emergency contraception pill among women aged 18–51 in Nova Scotia. Pharm Pract (Granada) 2011;9:148–55.

68. Daniels K, Jones J, Abma J. Use of emergency contraception among women aged 15–44: United States, 2006–2010. NCHS Data Brief 2013;(112):1–8.

69. Schwarz EB, Kavanaugh M, Douglas E, Dubowitz T, Creinin MD. Interest in intrauterine contraception among seekers of emergency contraception and pregnancy testing. Obstet Gynecol 2009;113:833–9.

70. Raymond EG, Trussell J, Polis CB. Population effect of increased access to emergency contraceptive pills: a systematic review. Obstet Gynecol 2007;109:181–8.

71. Rodriguez MI, Curtis KM, Gaffield ML, Jackson E, Kapp N. Advance supply of emergency contraception: a systematic review. Contraception 2013;87:590–601.

72. Polis CB, Schaffer K, Blanchard K, Glasier A, Harper CC, Grimes DA. Advance provision of emergency contraception for pregnancy prevention (full review). Cochrane Database Syst Rev 2007(2):CD005497.

73. Meyer JL, Gold MA, Haggerty CL. Advance provision of emergency contraception among adolescent and young adult women: a systematic review of literature. J Pediatr Adolesc Gynecol 2011;24:2–9.

74. Turok DK, Jacobson JC, Dermish AI, Simonsen SE, Gurtcheff S, McFadden M, et al. Emergency contraception with a copper IUD or oral levonorgestrel: an observational study of 1-year pregnancy rates. Contraception 2014;89:222–8.