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EFFICACY OF EMERGENCY CONTRACEPTION AND BODY WEIGHT: Current Understanding and Recommendations

Summary

- **Research has raised the question of whether emergency contraceptive (EC) pills may be less effective for users with higher weight or body mass index.** Some data show that levonorgestrel EC (LNG EC, sold in the U.S. as Plan B One-Step®, Take Action™, and others) may be less effective for individuals weighing over 165 pounds. The effectiveness of ulipristal acetate EC (UPA EC, sold in the U.S. as ella®) may also be reduced for users weighing more than 194 pounds.
- **Regardless of body weight, the most effective form of EC is the copper IUD. The next most effective method is ulipristal acetate.** All patients (but particularly those at higher weights) should be offered the copper IUD or UPA EC if these options are accessible and acceptable.
- **No one should be refused or discouraged from using EC based on weight.** LNG EC is usually the most accessible, and sometimes the only, EC option. Patients at higher body weights should be advised that 1.5 mg LNG EC may not work for them and be informed if other, more effective methods are available.
- **For users with BMI >30, a double dose of LNG EC may improve efficacy.** Two recent studies showed that clinical obesity reduces the bioavailability of LNG EC. Early evidence suggests that, for users with BMI >30kg/m^2 (those who are clinically considered obese), taking 3.0 mg LNG EC may produce similar blood concentration levels as 1.5 mg LNG EC in users with BMI>25, although clinical trials are needed to confirm if this is effective at preventing pregnancy.
- **Advocates should work to disseminate information about all EC options** and encourage individuals with higher body weights to consult a clinician if they are at risk of pregnancy after unprotected sex.

Background

Research

In 2011, an article based on two clinical trials concluded that "the limit of efficacy was reached at a weight of 70 kg [154 lbs] for LNG compared with 88 kg [194 lbs] in women having taken UPA."[1] These findings are of potential clinical significance, yet there are important limitations to the data. These trials were not specifically designed to study the relationship between efficacy and weight, and at one of the study sites, weight and height were self-assessed [as is the case when EC is purchased over the counter (OTC)], not measured. The numbers of participants in the "overweight" and "obese" categories were small, and the number of pregnancies in the highest weight category was extremely small.[2] An analysis

of four World Health Organization (WHO) studies, conducted primarily among populations of African and Asian women, also found an increased risk of pregnancy among those with BMI >30kg/m^2, although the findings appear to be driven by incongruous findings from one study.[3]

Two recent pharmacokinetic studies support the theory that clinical obesity reduces the bioavailability of LNG EC. One study (involving 10 women) found that the serum concentration in those who took LNG 1.5 mg was about 50% lower in women with BMI of 30 kg/m^2 or greater compared to those with BMI less than 25 kg/m^2. In this study, doubling the dose in the higher BMI group brought the serum concentration to a level equaling that of women with lower BMI who had taken the standard dose (1.5 mg).[4] Another pharmacokinetic study (involving 32 women) similarly found that, throughout 24 hours after ingesting LNG EC, serum concentration levels were 50% lower among women with BMI of 30 kg/m^2 or greater. Following use of UPA EC, however, blood levels were similar among both BMI groups.[5]

Regulatory Decisions

The manufacturer of NorLevo (a 1.5 mg LNG emergency contraceptive pill (ECP)) conducted additional analyses of the data from the 2011 article and requested that European regulatory authorities allow a change to the product label indicating that higher weight may reduce its effectiveness. In November 2013, European authorities granted a label change warning that "in clinical trials, contraceptive efficacy was reduced in women weighing 75 kg [165 lbs] or more and levonorgestrel was not effective in women who weighed more than 80 kg [175 lbs]."[6] (These different weight limits resulted from further analyses of the clinical trial data referenced above.) Shortly thereafter, Health Canada (the Canadian regulatory authority) authorized the same label change for LNG EC. In July 2014, the European Medicines Agency completed a review of all available data (including data from trials conducted by WHO) and found that "the data were too limited and not robust enough to conclude with certainty that contraceptive effect is reduced with increased bodyweight," and such statements should be removed from product labels.[7] In May 2016, the US Food and Drug Administration (FDA) announced completion of a review of the available data and also concluded that "the data are conflicting and too limited to reach a definitive conclusion as to whether effectiveness is reduced in [women who weigh more than 165 pounds or have a BMI above 25]."[8] It should be noted that all of this regulatory activity took place before the publications of the most recent WHO study and the pharmacokinetic studies showing a reduction of bioavailability of LNG EC in clinically obese women.

The UK Faculty of Sexual and Reproductive Healthcare (FRSH, part of the Royal College of Obstetricians and Gynecologists) recently issued guidance recommending that patients with BMI greater than 26 kg/m^2 or weighing more than 154 pounds be offered a copper IUD, the first-line EC option, and UPA EC as a second-line option. If these options are not available, FRSH suggests considering 3.0 mg LNG, which may be more effective than a 1.5 mg dose.[9]

Significance

The U.S. Centers for Disease Control and Prevention reports that the average American woman weighs 166 pounds (75.3 kg);[10] therefore, millions of Americans fall into the weight category in which LNG ECPs (and for a smaller subset of users, possibly UPA ECPs) may not work. It is of vital importance that the most effective forms of EC (the copper IUD and UPA EC) be made widely available. However, both the

copper IUD and UPA EC can only be obtained with the involvement of a healthcare provider in the United States[1], while LNG EC is available over the counter without age or point-of-sale restrictions. Many consumers purchase EC directly from stores and pharmacies without consulting a healthcare provider, and many providers may not routinely include counseling about EC in their patient interactions. A 2011 study found that only 3% of US women reported ever having received counseling about EC from a healthcare provider;[11] another study found that only 52% of healthcare providers who treat women of reproductive age had heard of UPA EC, and 14% provide or recommend it.[12]

Recommendations and Conclusions

Although the evidence is not entirely clear, there appears to be a relationship between the efficacy of EC (particularly LNG) and the weight of the user, and emerging evidence suggests that biological processes may play a determining role. In its May 2016 communication on the subject, the FDA stated that "further research by the manufacturers of [LNG EC] products on the possible impact of weight or BMI on effectiveness should be a priority."[8] It must be noted that the FDA cannot require that manufacturers conduct such studies, and clinical trials with a rare outcome such as pregnancy after use of EC are large and expensive; therefore, it is unlikely that trials that definitively answer this question will be conducted in the near future. Those in need of EC and healthcare providers who serve patients of reproductive age will most likely need to make decisions about EC without complete information about precisely how weight impacts EC efficacy.

Those who serve patients of reproductive age in a clinical setting are in an excellent position to counsel on all options for EC. For everyone, the copper IUD is the most effective EC method. UPA is the next most effective option, and LNG is reasonable when these are not available. For patients at higher body weights, special emphasis should be placed on the benefits of the copper IUD or UPA (although for patients who weigh more than 194 pounds, the efficacy of UPA might be reduced as well). If UPA is not available, a double-dose of LNG EC might be considered (although there are currently no clinical data to support this approach). Providers should remind anyone choosing ECPs that the pill should be taken as soon as possible after sex, and all patients should be offered an ongoing contraceptive method if they wish. Hormonal methods can be started simultaneously with use of LNG and no sooner than 5 days after unprotected intercourse with use of UPA.

However, most individuals do not obtain EC from a clinic. The majority of EC sales take place in retail outlets now that LNG ECPs are available over the counter with no age or point-of-sale restrictions. Thus, advocates should work to spread information about all of the options for EC and encourage EC users with higher body weights to consult a clinician if they wish to obtain a more effective EC option after unprotected sex. Consumers should also be informed about the possibility of acquiring UPA EC online from a service such as Prjkt Ruby (www.prjktruby.com), and they may want to consider acquiring UPA EC prior to needing it, if possible. Individuals with higher body weights who are unable to access clinical care within 5 days of unprotected sex or who do not choose a copper IUD or UPA EC may consider taking a double dose of LNG EC, if it is not cost-prohibitive. Health care providers and pharmacists should never deny access to LNG ECPs because of the user's weight.

[1] In a small number of states in the US, ella® can be obtained directly from a pharmacist through collaborative practice agreements.

Options for Emergency Contraception in the U.S.

(listed in order of effectiveness)

Copper IUD

Benefits

✓ Nearly 100% effective[13] in preventing pregnancy after sex
✓ Provides up to 12 years of excellent ongoing contraceptive protection; maintenance-free
✓ Does not contain any hormones
✓ Efficacy is not influenced by weight

Challenges

– Must be inserted by a clinician; at least one office visit is required
– Some patients may find the insertion process uncomfortable or invasive; some experience unacceptable changes in menstrual bleeding patterns
– Not everyone is interested in a long-acting method
– Though many insurance plans now cover the costs of IUDs through the Affordable Care Act, cost remains a significant barrier for individuals without such insurance

Ulipristal acetate EC (30 mg)

Benefits

✓ Can work closer to the time of ovulation, after the luteinizing hormone surge has begun, when LNG is not effective.[14]
✓ May be more effective than LNG for individuals with heavier body weights.
✓ Can be purchased through an online prescription service (such as Prjkt Ruby, $67 with shipping).

Challenges

– Sold by prescription only in the U.S.
– Awareness among providers and stocking in pharmacies may be low
– Efficacy may also be reduced in individuals weighing more than 196 pounds.
– Interactions with progestins may reduce efficacy. Do not start hormonal contraceptives sooner than 5 days after unprotected intercourse if UPA is used or when EC is needed due to missed or late pills, patches or rings (or if any hormonal method has been used within 7 days before EC is needed).[15]

Levonorgestrel EC (1.5 mg)

Benefits

✓By far the most widely-available EC option; available for sale at retail outlets to anyone of any age, with no prescription or proof of age requirement.
✓Hormonal contraceptives can be immediately started after use of LNG EC; can be used when EC is needed because of missed or late pills, patches or rings (no interaction with hormonal contraception used prior to EC).

Challenges

– Less effective than other EC methods
– May be less effective in particular for users with heavier body weights. A double dose of LNG EC may improve efficacy for users with BMI >30kg/m^2
– Price may be a significant barrier; the branded product (Plan B One-Step®) costs an average of $48, while the generic products cost about $41[16] (less expensive options are available at www.afterpill.com and www.prjktruby.com)
– Some health plans may not cover OTC products or will cover them only with a prescription

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References

1. Glasier A, Cameron ST, Blithe 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(4):363-367.

2. Cleland K, Wood S. A tale of two label changes. *Contraception*. 2014;90(1):1-3.

3. Festin MP, Peregoudov A, Seuc A, Kiarie J, Temmerman M. Effect of BMI and body weight on pregnancy rates with LNG as emergency contraception: Analysis of four WHO HRP studies. *Contraception*. 2017;95(1):50-54.

4. Edelman AB, Cherala G, Blue SW, Erikson DW, Jensen JT. Impact of obesity on the pharmacokinetics of levonorgestrel-based emergency contraception: Single and double dosing. *Contraception*. 2016;94(1):52-57.

5. Praditpan P, Hamouie A, Basaraba CN, et al. Pharmacokinetics of levonorgestrel and ulipristal acetate emergency contraception in women with normal and obese body mass index. *Contraception*. 2017;95(5)464-69.

6. Irish Medicines Board. Norlevo 1.5mg, summary of product characteristics. http://www.medicines.ie/history/11933/SPC/Norlevo+1.5mg+tablet. Updated 2014. Accessed August 9, 2016.

7. European Medicines Agency. Levonorgestrel and ulipristal remain suitable emergency contraceptives for all women, regardless of bodyweight. http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/07/news_detail_002145.jsp&mid=WC0b01ac058004d5c1. Updated 2014.

8. US Food and Drug Administration. FDA communication on levonorgestrel emergency contraceptive effectiveness and weight. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm109775.htm. Updated 2016. Accessed May 24, 2017.

9. Faculty of Sexual and Reproductive Healthcare. FRSH guideline: Emergency contraception. March 2017.

10. Fryar CD, Gu Q, Ogden CL. Anthropometric reference data for children and adults: United States, 2007–2010. *Vital and Health Statistics*. 2012;11(252).

11. Kavanaugh ML, Williams SL, Schwarz EB. Emergency contraception use and counseling after changes in United States prescription status. *Fertil Steril*. 2011;95(8):2578-2581.

12. Batur P, Cleland K, McNamara M, Wu J, Pickle S, EC Survey Group. Emergency contraception: A multispecialty survey of clinician knowledge and practices. *Contraception*. 2016;93(2):145-152.

13. 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(7):1994-2000.

14. Glasier AF, Cameron S, Fine P, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: A randomised non-inferiority trial and meta-analysis. *Lancet*. 2010;375:555-562.

15. American Society for Emergency Contraception. Providing ongoing hormonal contraception after use of emergency contraceptive pills. http://americansocietyforec.org/uploads/3/4/5/6/34568220/asec_fact_sheet-_hormonal_contraception_after_ec.pdf. Updated 2016. Accessed April 19, 2017.

16. American Society for Emergency Contraception. The cost of emergency contraception: Results from a nationwide survey. http://americansocietyforec.org/uploads/3/2/7/0/3270267/asecpricingreport.pdf. Updated 2013. Accessed June 24, 2014.