FSRH
Clinical Effectiveness Unit

The Faculty of Sexual & Reproductive Healthcare of the Royal College of Obstetricians & Gynaecologists

FSRH CEU Statement: Response to Recent Publication Regarding Banh, et al.

"The effects on ovarian activity of delaying versus immediately restarting combined oral contraception after missing three pills and taking ulipristal acetate 30 mg"

17 November 2020

The journal *Contraception* recently published a well-designed and well-conducted randomised pharmacodynamic study investigating timing of combined oral contraceptive pill (COC) restart after missed pills and use of ulipristal acetate emergency contraception (UPA-EC)[1].

What was the study question?

If established COC users miss the 5th, 6th and 7th pills after a 7-day pill-free interval AND UPA-EC is taken on day 8, is ovulation more likely to occur if COC is restarted immediately after UPA-EC or if COC restart is delayed for 5 days?

What were the study findings?

In the study group restarting COC immediately after UPA-EC, no ovulation with theoretical risk of pregnancy was observed in the remainder of the cycle in any of the 26 subjects. In the study group restarting COC 5 days after UPA-EC, 4 out of 23 subjects ovulated between 7 and 9 days after taking UPA-EC. This difference in ovulation was statistically significant.

What can be concluded from the study?

In the specific scenario in which established users of 30mcg EE/LNG COC in a 21/7 regimen restart pill-taking for 4 days after a pill-free interval, miss the next 3 consecutive pills, and take UPA-EC, ovulation and theoretical risk of pregnancy later in the cycle is less likely if COC is restarted immediately after UPA-EC than if COC restart is delayed for 5 days after UPA-EC.

What don't we know from this study?

The study does not tell us what the risk of ovulation would be:

- if the same pills were missed and COC was restarted without use of any EC
- if the same pills were missed, levonorgestrel EC (LNG-EC) was taken, and COC was restarted immediately
- if a different number of COC pills was missed, or if pills were missed at a different time (e.g., immediately after the pill-free interval)
- if a different COC, patch, or ring or a different hormonal contraceptive was being used incorrectly

And we don't know how many of the subjects that ovulated would have become pregnant.

What do we know from previous studies: how is this different?

UPA-EC works by delaying ovulation until sperm from previous unprotected sex are no longer viable (5 days after sex). From previous studies, we know that individuals who take UPA-EC when they are close to ovulation in a natural menstrual cycle are significantly more likely to ovulate in the following 5 days if they

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start a COC or progestogen-only pill immediately after UPA-EC[2,3]. Delayed start of hormonal contraception is therefore recommended in this situation. This new study by Banh, *et al.* considers a different scenario, in which UPA-EC users are already established on COC. The findings can only be applied to that scenario.

What is the current guidance?

Current FSRH guidance *Recommended Actions after Incorrect Use of Combined Hormonal Contraception*[4] indicates that, for COC users, EC should be considered:

- if the pill-free interval is extended, or
- if 2-7 pills are missed in the first week following a pill-free interval, or
- if more than 7 pills are missed in any week of scheduled pill-taking (this situation is considered a new start rather than restart of COC)

EC is generally not advised if 1 pill is missed at any time during scheduled pill taking or if 2-7 pills are missed in week 2 or week 3 after the pill-free interval (or subsequent consecutive weeks of continuous pill-taking)[4].

The FSRH guideline *Emergency Contraception*[5] recommends that, if any progestogen (including progestogen in CHC) has been taken in the 7 days prior to EC, LNG-EC should be considered, with immediate quick start of suitable effective contraception. It recommends that, if UPA-EC is used in this situation, use of hormonal contraception should be delayed for 5 days after UPA-EC.

How does this study affect FSRH guidance?

On the basis of this new information, FSRH CEU makes the following recommendations:

- If EC is considered to be required ***in the specific situation in which an established CHC user restarts CHC after a hormone-free interval and then misses 2-7 pills in the first week of pill-taking (or makes an equivalent error with combined patch or ring use)***:
  - LNG-EC may be offered, with immediate restart of CHC and use of condoms for 7 days **(no change to guidance)**
  - if UPA-EC is preferred, it may be offered, now with immediate restart of CHC and use of condoms for 7 days **(new recommendation for this specific scenario only)**
- Unless an individual taking UPA-EC is an established CHC user in the specific situation described above, hormonal contraception should **not** be started for 5 days after UPA-EC. Situations in which hormonal contraception should **not** be started for 5 days after UPA-EC include:
  - established COC users who have extended the pill-free interval or missed more than 7 pills in any week of scheduled pill taking (or established combined patch or ring users who have made an equivalent error)
  - new starters of any hormonal contraceptive
  - established users of progestogen-only contraceptives who have used the method incorrectly

In these situations, LNG-EC with immediate quick start of hormonal contraception should be considered **(no change to guidance).**

We have convened an expert group to develop further guidance around choice of oral emergency contraceptive during established use of hormonal contraception.

Changes to FSRH CEU guidance (*Recommended Actions after Incorrect Use of Combined Hormonal Contraception* and *Emergency Contraception*) will be made to align with this statement.

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References

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5. Faculy of Sexual & Reproductive Healthcare. *Emergency Contraception*. 2017. Available at: https://www.fsrh.org/standards-and-guidance/fsrh-guidelines-and-statements/emergency-contraception/ [Accessed 17/11/2020]

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