SPHERE
NHMRC Centre of Research Excellence in Sexual and Reproductive Health for Women in Primary Care

Women's Sexual and Reproductive Health COVID-19 Coalition

A consensus statement on 52 mg Levonorgestrel-releasing IUD as emergency contraception: Examining the evidence

The recent US study examining whether a 52 mg Levonorgestrel-releasing intrauterine device (IUD; similar to the Mirena device available in Australia) was noninferior to the Copper-bearing T380A IUD for emergency contraception (EC) concluded that the 52mg Levonorgestrel-releasing IUD was non inferior to the Copper-bearing IUD and that the data supported quick-start of Copper-bearing and Levonorgestrel-releasing IUDs in those who have had recent unprotected sex and have a negative pregnancy test (1). While the results of this trial are encouraging, the study has a number of limitations: in particular, the estimated risk of unintended pregnancy of the participants. There is insufficient evidence to recommend changes to current guidelines. Further studies are needed, including head-to-head trials of oral EC with either the Copper-bearing IUD or the 52 mg Levonorgestrel-releasing IUD for EC.

The 52 mg Levonorgestrel-releasing IUD is not recommended as first line for EC. However, it can be carefully considered on a case-by-case basis when:

- *The person needing EC is aware that there is a strong evidence base for the use of the Copper-bearing IUD for EC and that the 52 mg Levonorgestrel-releasing IUD may not be as effective*
- *There has been documented informed consent of the potential risks, including a risk of ectopic pregnancy and risks to a continuing pregnancy if an unintended pregnancy occurs and the IUD cannot be removed*
- *The Levonorgestrel-releasing IUD is inserted within 5 days of predicted ovulation*
- *There are no anticipated barriers to a follow up pregnancy test in 3 weeks' time*

Note that the 19.5 mg Levonorgestrel-releasing IUD (Kyleena) has not been studied as EC.

Background

Current emergency contraception (EC) options in Australia include two types of oral EC (ulipristal acetate 30mg; levonorgestrel 1.5mg) or insertion of a Copper-bearing IUD. Oral EC works by preventing or delaying ovulation while Copper-bearing IUDs usually work by preventing fertilisation but may also prevent implantation of a fertilised egg. A recent randomised controlled trial considered whether the 52mg Levonorgestrel-releasing IUD was non-inferior to a Copper-bearing IUD as a method of post-coital EC (1). The study attracted worldwide attention because when choice of IUDs is available, users are

more likely to choose a Levonorgestrel-releasing than a Copper-bearing IUD for long term use (2, 3). It also has potential implications for increasing access to EC in Australia where Levonorgestrel-releasing IUDs, unlike the Copper-bearing IUD are easily available through pharmacies and are subsidised by the pharmaceutical benefits scheme. However, while the results from the trial are encouraging, Copper-bearing IUDs are considered the most effective method of EC (4). They have the added advantage over oral EC of efficacy being unaffected by the patient's weight or drug interactions as well as providing 5-10 years of ongoing contraception (5). A Copper-bearing IUD for EC is recommended to be inserted within 120 hours of unprotected sexual intercourse or within 5 days after the earliest estimated date of ovulation in order to confidently exclude an early pre-existing implanted pregnancy (6).

Pregnancies that occur as a result of failed oral EC or are undiagnosed at the time of initiating oral, injectable or implantable hormonal contraception do not require a different management approach to any other pregnancy as there is no evidence of any harmful effect on the pregnancy (5, 7). However, in the small likelihood of a failed IUD for EC, medical complications can occur. Around 50% of pregnancies that occur with a Levonorgestrel-releasing IUD and around 15% of those with a Copper-bearing IUD in place are ectopic (8-10), although it is unknown if this higher risk of ectopic pregnancy occurs when an IUD is inserted for EC. In addition, if the pregnancy is intrauterine and the IUD cannot be removed there is a risk of premature delivery or late miscarriage (11). A surgical procedure must be performed for those requesting abortion as medical abortion is contraindicated with an IUD in situ (12). For this reason, current guidelines do not support quick-start (starting the method without excluding pregnancy) of any IUD.

Key points

The recent US study examining whether a 52 mg Levonorgestrel-releasing IUD (similar to the Mirena device available in Australia) was noninferior to the Copper-bearing T380A IUD for EC concluded that the 52mg Levonorgestrel-releasing IUD was non inferior to the Copper-bearing IUD and that the data supported quick-start of Copper-bearing and Levonorgestrel-releasing IUDs in those who have had recent unprotected sex and have a negative pregnancy test (1). Over 10,000 women who presented for EC were invited to participate in a randomised controlled trial in which participants were offered either a Copper-bearing T380A IUD or a Levonorgestrel-releasing IUD. Overall a large majority of participants declined to take part and of the 711 enrolled and randomised, 328 had a Copper-bearing IUD inserted, of which 311 had confirmation of pregnancy status and 327 a 52 mg Levonorgestrel-releasing IUD of which 308 had confirmation of pregnancy status. There were no pregnancies in the Copper-bearing IUD group and 1 pregnancy in the Levonorgestrel-releasing IUD group. While these results are very promising there were a number of limitations to the study:

1. There was no calculation of the expected number of pregnancies if the participant had not taken EC and it is possible that this group represented those at low risk of unintended pregnancy.

2. More participants in the Copper-bearing IUD group did not use any method of contraception at the time of last unprotected sex than in the Levonorgestrel-releasing IUD group. Potentially this could be associated with a reduced risk of unintended pregnancy in the Levonorgestrel-releasing IUD group.

3. More participants in the Levonorgestrel-releasing IUD group reported a broken condom as the reason for requesting emergency condom. As there was no included information as to whether ejaculation occurred, this could cause bias either way.

4. Participants who had intercourse 6-14 days prior to EC and potentially had an undetectable pregnancy were also included, however no data on how many in each arm fell into this group was used in the analysis.

*The Coalition uses *women* as an inclusive and broad term that refers to and acknowledges the diversity in needs and experiences of all people who may access and use abortion and women's sexual and reproductive health services including other people who do not identify as women but can experience pregnancy and abortion and may need to access these.

REFERENCES

1. Turok DK, Gero A, Simmons RG, Kaiser JE, Stoddard GJ, Sexsmith CD, et al. Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception. N Engl J Med. 2021 Jan 28;384(4):335-44. PubMed PMID: 33503342. Epub 2021/01/28.
2. Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, et al. Continuation and satisfaction of reversible contraception. Obstet Gynecol. 2011 May;117(5):1105-13. PubMed PMID: 21508749. PMCID: 3548669.
3. Turok DK, Sanders JN, Thompson IS, Royer PA, Eggebroten J, Gawron LM. Preference for and efficacy of oral levonorgestrel for emergency contraception with concomitant placement of a levonorgestrel IUD: a prospective cohort study. Contraception. 2016 Jun;93(6):526-32. PubMed PMID: 26944863.
4. 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. Human reproduction. 2012 May 8;27(7):1994-2000. PubMed PMID: 22570193. PMCID: 3619968. Epub 2012/05/10. Eng.
5. FSRH Guideline. Emergency Contraception: Faculty of Sexual & Reproductive Healthcare Statement. Clinical Effectiveness Unit; 2017 [updated December 2020; cited 2021 6 April]. Available from: https://www.fsrh.org/documents/ceu-clinical-guidance-emergency-contraception-march-2017/fsrh-guideline-emergency-contraception03dec2020.pdf.
6. eTG. Contraception [published 2020 Dec]. In: eTG complete [digital]. Melbourne: Therapeutic Guidelines Limited; [cited 2021 17 March]. Available from: https://www.tg.org.au.
7. FSRH Guideline. Quick Starting Contraception: Faculty of Sexual & Reproductive Healthcare Statement. Clinical Effectiveness Unit; 2017 [cited 2021 6 April]. Available from: https://www.fsrh.org/standards-and-guidance/documents/fsrh-clinical-guidance-quick-starting-contraception-april-2017/.
8. Gemzell-Danielsson K, Apter D, Dermout S, Faustmann T, Rosen K, Schmelter T, et al. Evaluation of a new, low-dose levonorgestrel intrauterine contraceptive system over 5 years of use. Eur J Obstet Gynecol Reprod Biol. 2017 Mar;210:22-8. PubMed PMID: 27930941.
9. Heinemann K, Reed S, Moehner S, Minh TD. Comparative contraceptive effectiveness of levonorgestrel-releasing and copper intrauterine devices: the European Active Surveillance Study for Intrauterine Devices. Contraception. 2015 Apr;91(4):280-3. PubMed PMID: 25601350.
10. Intrauterine Contraception: Faculty of Sexual & Reproductive Healthcare Clinical Effectiveness Unit; 2015 [updated September 2019; cited 2021 14 March]. Available from: https://www.fsrh.org/standards-and-guidance/documents/ceuguidanceintrauterinecontraception/.
11. Ozgu-Erdinc AS, Tasdemir UG, Uygur D, Aktulay A, Tasdemir N, Gulerman HC. Outcome of intrauterine pregnancies with intrauterine device in place and effects of device location on prognosis. Contraception. 2014 May;89(0):426-30. PubMed PMID: 24508123.
12. eTG. Medical Abortion [published 2020 Dec]. In: eTG complete [digital]. Melbourne: Therapeutic Guidelines Limited; [cited 2021 17 March]. Available from: https://www.tg.org.au.