

Review: The levonorgestrel-releasing intrauterine system prevents more pregnancies than intrauterine devices $\leq 250 \text{ mm}^2$ but not $> 250 \text{ mm}^2$

French RS, Cowan FM, Mansour D, et al. Levonorgestrel-releasing (20 $\mu\text{g}/\text{day}$) intrauterine systems (Mirena) compared with other methods of reversible contraceptives. *BJOG*. 2000 Oct;107:1218-25.

QUESTION

In women of reproductive age, is the levonorgestrel-releasing (20 $\mu\text{g}/\text{d}$) intrauterine system (LNG-20) more effective and tolerable than other reversible contraceptive methods?

DATA SOURCES

Studies were identified using MEDLINE, EMBASE/Excerpta Medica, PsycLIT, POPLINE, Cochrane Controlled Trials Register, and specialist databases between January 1974 and July 1998. Bibliographies of relevant articles were also reviewed. Experts in the field and organizations were contacted for unpublished data.

STUDY SELECTION

Randomized controlled trials were selected if participants were women of reproductive age, they compared LNG-20 with another reversible contraceptive, and they had predetermined outcomes.

DATA EXTRACTION

Data were extracted on predetermined outcomes of pregnancy as a result of method or user failure and continuation of contraceptive method. Data on these outcomes were extracted when either number of events per women months or single-decrement life-table probabilities were reported.

MAIN RESULTS

5 studies met the inclusion criteria. LNG-20 was compared with 2 groups of intrauterine

devices (IUDs), categorized by the surface area of the copper wire: $\leq 250 \text{ mm}^2$ (Nova-T, CuT 200, and CuT 220 IUDs) and $> 250 \text{ mm}^2$ (CuT 380 Ag IUD). At 5 years of follow-up, LNG-20 was more effective than IUDs $\leq 250 \text{ mm}^2$ for preventing unplanned pregnancy (rate ratio [RR] 0.08, 95% CI 0.04 to 0.18) but not more effective than IUDs $> 250 \text{ mm}^2$ (RR 0.66, CI 0.25 to 1.75) (Table). Overall, continued use was more likely with LNG-20 than with IUDs $\leq 250 \text{ mm}^2$ (RR 1.16, CI 1.02 to 1.31) and equally as likely with IUDs $> 250 \text{ mm}^2$ (RR 0.97, CI 0.83 to 1.14) (Table). LNG-20 users were more likely to discontinue use because of hormonal side effects than were users of IUDs $\leq 250 \text{ mm}^2$ (RR 5.2, CI 1.3 to 20.3) and IUDs $> 250 \text{ mm}^2$ (RR 4.2, CI 2.0 to 9.0). LNG-20 users were also more likely to discontinue use because of amen-

orrhea than were users of IUDs $\leq 250 \text{ mm}^2$ (RR 29.2, CI 1.7 to 488) and IUDs $> 250 \text{ mm}^2$ (RR 48.9, CI 16.9 to 141).

CONCLUSIONS

In women of reproductive age, the levonorgestrel-releasing (20 $\mu\text{g}/\text{d}$) intrauterine system (LNG-20) is more effective than intrauterine devices (IUDs) $\leq 250 \text{ mm}^2$ but as effective as IUDs $> 250 \text{ mm}^2$ for preventing pregnancy. LNG-20 is more likely to lead to discontinued use because of hormonal side effects and amenorrhea.

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Levonorgestrel-releasing (20 $\mu\text{g}/\text{d}$) intrauterine system (LNG) vs intrauterine devices $\leq 250 \text{ mm}^2$ (IUD ≤ 250) or $> 250 \text{ mm}^2$ (IUD > 250) in women of reproductive age at 5 years of use*

Outcomes	Comparison	Event rates	RRR (95% CI)	NNT:5 (CI)
Pregnancy	LNG vs IUD ≤ 250 †	0.009% vs 0.11%	92% (81 to 97)	17 (13 to 26)
	LNG vs IUD > 250	0.017% vs 0.026%	34% (-74 to 75)	Not significant
				RBI (CI)
Continued use	LNG vs IUD ≤ 250 †	1.11% vs 0.96%	16% (2 to 31)	12 (7 to 61)
	LNG vs IUD > 250	0.85% vs 0.88%	3% (-14 to 17)	Not significant
				RBR (CI)
				NNH:5 (CI)

*NNT:5 = NNT for a 5-year period of use. Other abbreviations defined in Glossary; RRR, RBI, RBR, NNT, NNH, and CI calculated from data in article.

†2 studies were meta-analyzed using a fixed-effects model and reported weighted event rates; other comparisons were based on 1 study.

COMMENTARY

The systematic review by French and colleagues addresses an important clinical question. The study methods reported were appropriate, and the search for relevant studies was comprehensive. The willingness by volunteers to be randomly allocated, however, implies that either contraceptive method was acceptable. The copper IUD comparative studies would therefore be unlikely to include women with heavy or painful menses, who are most likely to benefit from the "side effects" of LNG-20 (i.e., reduction of menstrual flow and pain). Some studies also noted the importance of preinsertion counseling to reduce concern about amenorrhea or the occurrence of irregular bleeding in the early months of use.

The category of IUDs $\leq 250 \text{ mm}^2$ could be misleading because the only studies that were analyzed related to the CuT 380 Ag IUD, which has copper on the side arms and in the center. No available comparisons existed with other high copper-load devices positioned

only centrally (e.g., Multiload 375). The distinction in the positioning of the copper may be one reason why the CuT 380 Ag IUD has such low pregnancy rates.

This review has a broader title than that of the abstract because a search was made for comparison with all reversible methods. Only 1 study not using a copper IUD was identified as eligible. This was a 3-year comparison with Norplant 2 that involved only 200 women and found no significant difference in measured outcomes other than fewer removals of devices because of bleeding with LNG-20.

The LNG-20 and the CuT 380 Ag IUD are equally effective and acceptable for women with normal menses. Questions remaining include which women are likely to benefit from a specific choice of 1 device or the other and the issue of cost-effectiveness.

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