Therapeutics

Review: the levonorgestrel releasing intrauterine system prevents more pregnancies than intrauterine devices (IUDs) ≤ 250 mm² but not IUDs > 250 mm²


QUESTION: In women of reproductive age, is the levonorgestrel releasing (20 µg/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 Experts in the field and organisations were contacted for unpublished data.

Study selection
Randomised 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), categorised by the surface area of the copper wire: ≤ 250 mm² (Nova-T, CuT 200, and CuT 220 IUDs) and > 250 mm² (CuT 380 Ag IUD). At 5 years of follow up, LNG-20 was more effective than IUDs ≤ 250 mm² for preventing unplanned pregnancy (rate ratio [RR] 0.08, 95% CI 0.04 to 0.18) but not more effective than IUDs > 250 mm² (RR 1.16, CI 1.02 to 1.31) and equally as likely with IUDs > 250 mm² (RR 0.97, CI 0.83 to 1.14) (table). LNG-20 users were more likely to discontinue use because of hormonal side effects and amenorrhea than were users of IUDs ≤ 250 mm² (RR 5.2, CI 1.3 to 20.3) and IUDs > 250 mm² (RR 4.2, CI 2.0 to 9.0). LNG-20 users were also more likely to discontinue use because of amenorrhoea than users of IUDs ≤ 250 mm² (RR 29.2, CI 1.7 to 488) and IUDs > 250 mm² (RR 48.9, CI 16.9 to 141).

Conclusions
In women of reproductive age, the levonorgestrel releasing (20 µg/d) intrauterine system (LNG-20) is more effective than intrauterine devices (IUDs) ≤ 250 mm² but as effective as IUDs > 250 mm² for preventing pregnancy. LNG-20 is more likely to lead to discontinued use because of hormonal side effects and amenorrhea.

Levonorgestrel releasing (20 µg/d) intrauterine system (LNG) v intrauterine devices ≤ 250 mm² (IUD ≤ 250) or >250 mm² (IUD >250) in women of reproductive age at 5 years of use*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Comparison</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT:5 (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>LNG v IUD ≤250†</td>
<td>0.009% v 0.11%</td>
<td>92% (81 to 97)</td>
<td>17 (13 to 26)</td>
</tr>
<tr>
<td>LNG v IUD &gt;250</td>
<td>0.017% v 0.026%</td>
<td>34% (74 to 75)</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td>Continued use</td>
<td>LNG v IUD ≤250†</td>
<td>1.11% v 0.96%</td>
<td>16% (2 to 31)</td>
<td>12 (7 to 61)</td>
</tr>
<tr>
<td>LNG v IUD &gt;250</td>
<td>0.85% v 0.88%</td>
<td>3% (14 to 17)</td>
<td>Not significant</td>
<td></td>
</tr>
</tbody>
</table>

* NNT5 = 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-analysed using a fixed-effects model and reported weighted event rates; other comparisons were based on 1 study.

COMMENTARY
The systematic review by French et al 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 (ie, reduction of menstrual flow and pain). Some studies also noted the importance of pre-insertion counselling to reduce concern about amenorrhea or the occurrence of irregular bleeding in the early months of use.

The category of IUDs ≤ 250 mm² could be misleading because the only studies that were analysed related to the CuT 380 Ag IUD, which has copper on the side arms and in the centre. No available comparisons existed with other high copper load devices positioned only centrally (eg, 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.

Rosemary Kirkman, MB, ChB
Palatine Centre
Manchester, UK