The effect of the levonorgestrel releasing intrauterine system on endometrial hyperplasia: an Australian study and systematic review

Buttini MJ, Jordan SJ, Webb PM

CRD summary
The review found that levonorgestrel releasing intrauterine system was an effective treatment for non-atypical hyperplasia. The consistency of the evidence supported the authors’ conclusions. However, in view of the lack of controlled evidence and methodological limitations in the review (in particular the failure to assess study validity), a degree of caution is advised in interpreting the findings.

Authors' objectives
To evaluate the use of the levonorgestrel releasing intrauterine system (LNG-IUS) for endometrial hyperplasia.

Searching
MEDLINE (1966 to August 2008) and Cochrane Menstrual Disorders and Subfertility Group Specialised Register of controlled trials (Cochrane Library, Issue 3 2008) were searched. Search terms were reported. Reference lists of retrieved articles were checked.

Study selection
Studies that reported histological follow-up of women diagnosed with endometrial hyperplasia and treated with an LNG-IUS were eligible for inclusion. Outcomes of interest in the review were complete response (return to normal endometrium), partial response (change from atypical to non-atypical hyperplasia) and endometrial carcinoma.

About half of the studies in the review included women with either atypical or non-atypical hyperplasia; the other studies were restricted to women with one or other diagnosis (where reported). Diagnoses were made by dilatation and curettage, hysteroscopy and biopsy, pipelle biopsy or suction biopsy. Most studies used LNG-IUS systems that released 20 micrograms over 24 hours (μg/24h). Frequency of follow-up varied widely, from one-off to ongoing two-monthly visits. Maximum duration of follow-up ranged from three to 90 months (where reported).

The authors did not state how the papers were selected for the review.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Response rates were extracted from each study and reported as percentages. Data on atypical and atypical hyperplasia were extracted separately, where feasible. Data were extracted by a single reviewer.

Methods of synthesis
Studies were combined by pooling response rates across studies reported as a percentage of the overall sample.

Results of the review
Twelve studies were included in the review: nine observational studies (n=321, range five to 105) and three case reports (n=4).

Among women with non-atypical hyperplasia, LNG-IUS was associated with a regression rate of 96% (194 out of 202); there was one case of endometrial carcinoma, detected at 12 months. Among women with atypical hyperplasia, LNG-IUS was associated with combined (complete or partial) response rate of 89% (31 out of 35). Two of the 29 responders achieved partial response only. There was one case of endometrial carcinoma, detected at six months.

Two studies (n=21 and n=66) did not distinguish between types of atypia. In one (n=21) LNG-IUS was associated with
a regression rate of 62% at five months and in the other (n=66) it was associated with a 100% complete response rate at six months.

**Authors' conclusions**

LNG-IUS was an effective treatment for non-atypical hyperplasia.

**CRD commentary**

The objectives and inclusion criteria of the review were clear in most respects, although it appeared that the exclusion of one study (which used an obsolete device and vague histological criteria) was decided retrospectively. Relevant sources were searched for studies. Relevant sources were searched for studies. It was not reported whether the search was limited by language or publication status (in which case some studies may have been missed). It did not appear that steps were taken to minimise the risk of reviewer bias and error by having more than one reviewer independently select studies and extract data. It did not appear that study quality was systematically assessed. Very little information was provided about the design of the included studies. These factors made it difficult to assess the reliability of the evidence presented. The technique of pooling data by simple summary was of questionable validity in view of the differences between the studies (such as sample size and follow-up time). The consistency of the review findings supported the authors’ conclusions, but in view of the lack of controlled evidence and methodological limitations of the review (in particular the failure to describe review processes or assess study validity), some caution may be required in interpreting the findings.

**Implications of the review for practice and research**

**Practice:** The authors stated that among women with atypical hyperplasia, LNG-IUS should be used only where the patient desired non-surgical treatment for maintenance of fertility or where the risk of hysterectomy may exceed the risk of progression to endometrial cancer. Women must be fully informed of the risks and need for adequate histological follow-up. Clinicians should be aware that pipelle biopsy had lower diagnostic accuracy for endometrial pathology than hysteroscopy with dilation and curettage.

**Research:** The authors stated that further research was required to determine whether LNG-IUS was a safe and cost-effective alternative to hysterectomy for treatment of atypical endometrial hyperplasia.

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