Hysterectomy, endometrial destruction, and levonorgestrel releasing intrauterine system (Mirena) for heavy menstrual bleeding: systematic review and meta-analysis of data from individual patients


CRD summary
This review concluded that more women were dissatisfied after endometrial destruction than after hysterectomy, although rates were low for both treatments. Hysterectomy was associated with increased length of hospital stay and a longer recovery period. Definitive evidence on Mirena versus more invasive procedures was lacking. These conclusions followed from the evidence presented and appear to be broadly reliable.

Authors' objectives
To evaluate the relative effectiveness of hysterectomy, endometrial destruction (both “first-generation” hysteroscopic techniques and “second-generation” non-hysteroscopic techniques), and the levonorgestrel releasing intrauterine system (Mirena) in the treatment of heavy menstrual bleeding.

Searching
The Cochrane Library, MEDLINE, EMBASE, and CINAHL databases were searched up to May 2010 for relevant evidence available in any language. Search terms were reported. This was supplemented by handsearching relevant bibliographies, trial registers (Meta-Register of Controlled Trials and International Standard Randomised Controlled Trial Number Register) and through contact with experts.

Study selection
Randomised controlled trials (RCTs) that evaluated the effects of hysterectomy, endometrial destruction techniques and Mirena, relative to one another, as treatment for heavy menstrual bleeding in women who were unresponsive to other medical treatment were eligible for inclusion in the review.

Among included trials, hysterectomy was performed abdominally, vaginally or laparoscopically. First-generation endometrial destruction hysteroscopic techniques included endometrial laser ablation, transcervical resection of the endometrium, and rollerball endometrial ablation; second-generation non-hysteroscopic techniques included thermal balloon (Cavaterm, Thermachoic, Vesta), microwave (Microsulis), laser (ELITT), bipolar radio frequency (NovaSure), cryoablation, and hydrothermal ablation.

The primary outcome of interest was dissatisfaction with outcome at 12 months, although a wide variety of outcomes were measured in the primary trials and summarised, including bleeding and pain scores, quality of life measures, duration of surgery/hospital stay, time to recovery, and complications.

The authors did not state how many reviewers performed the selection.

Assessment of study quality
The methodological quality of included trials was assessed according to seven criteria: adequacy of randomisation, description of target population, sample size calculation, comparability of groups at baseline, use of an intention-to-treat analysis, follow-up of at least 80%, and over 80% compliance with treatment in both arms at 12 months.

The authors did not state how many reviewers performed the assessment.

Data extraction
Authors of the included RCTs were contacted in order to obtain individual patient data. Where authors declined to take part or could not be contacted, two reviewers independently extracted aggregate data from available publications, with any disagreements resolved by a third reviewer. The primary outcome of dissatisfaction at 12 months was extracted as a...
Methods of synthesis
Individual patient data were reduced to aggregate data and combined with other trials using aggregate data. Odds ratios (ORs), with confidence intervals (CIs), were pooled using a fixed-effect (Peto) model. It was unclear whether 95% or 99% confidence intervals were calculated, as these were inconsistently reported in the publication. This abstract assumed 95% confidence intervals were calculated. Cochran's Q and the \( I^2 \) statistics were used to investigate statistical variability among pooled estimates. Weighted mean differences (WMDs) were calculated for continuous outcomes. Where direct within-trial comparisons were not available, indirect estimates were made using a logistic regression model allowing for trial and treatment. Individual patient data were used to examine the correlation of patient-level covariates with dissatisfaction.

Results of the review
Thirty RCTs (n=4,472 women) were included in the review; 17 (n=2,814 women) had available individual patient data. Trial quality was variable, with included RCTs meeting between two and seven of the assessment criteria.

Significantly more women were dissatisfied with first-generation hysteroscopic endometrial destruction than with hysterectomy (13% versus 5%; OR 2.46, 95% CI 1.54 to 3.93), but hospital stay (WMD 3.0 days, 95% CI 2.9 to 3.1) and mean time to resumption of normal activities (WMD 5.2 days, 95% CI 4.7 to 5.7) were longer for hysterectomy.

An indirect comparison suggested greater dissatisfaction rates with second-generation non-hysteroscopic techniques than with hysterectomy (11% versus 5%; OR 2.3, 95% CI 1.3 to 4.2).

There was no significant difference in dissatisfaction rate between first-generation and second-generation endometrial destruction techniques (14% versus 11%; OR 1.20, 95% CI 0.88 to 1.62).

There was no significant difference in dissatisfaction rate between Mirena and endometrial destruction techniques (17% versus 18%; OR 0.9, 95% CI 0.5 to 1.8). The results were similar for both first-generation and second-generation comparisons.

An indirect comparison suggested non-significantly greater dissatisfaction rates with Mirena than with hysterectomy (17% versus 5%; OR 2.2, 95% CI 0.9 to 5.3), although this analysis lacked statistical power.

Several other outcomes, as well as predictors of dissatisfaction and the association between dissatisfaction and quality of life, were also reported in the article.

Authors' conclusions
More women were dissatisfied after endometrial destruction than after hysterectomy, although rates were low for both treatments. Hysterectomy was associated with increased length of hospital stay and a longer recovery period. Definitive evidence on Mirena versus more invasive procedures was lacking.

CRD commentary
The review question was reasonably clearly defined in terms of the participants, interventions, comparators and study designs of interest. Multiple sources were searched to identify relevant evidence in any language, and attempts were made to collaborate with the authors of eligible trials. Attempts were made to minimise bias in the extraction of data from included trials, although it was unclear if similar efforts were made in the initial selection of trials.

Validity was assessed at trial level and reported outcomes were checked against individual patient data, where available. The review employed a mixture of aggregate and individual patient data, as well as direct and indirect analyses. The statistical methods used appeared broadly appropriate and pooled trials were statistically homogenous.

The authors’ conclusions followed from the evidence presented and appear to be broadly reliable.

Implications of the review for practice and research

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Practice: The authors stated that women eligible for treatment should be informed that dissatisfaction is lower with hysterectomy than with endometrial destruction and that hysterectomy may be offered if complete cessation of bleeding is sought. They added that although the evidence was not strong, Mirena should be offered before more invasive procedures.

Research: The authors stated that a further RCT of hysterectomy versus second-generation endometrial destruction would be of limited value. However, they stated that further evidence on the longer-term outcomes, particularly for Mirena versus surgical techniques, may be required. They also highlighted the need for consensus on optimal outcome measures among future studies.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.