Second generation endometrial ablation techniques for heavy menstrual bleeding: network meta-analysis

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CRD summary
The authors concluded that bipolar radio frequency and microwave ablative devices were more effective than thermal balloon and free fluid ablation in the treatment of heavy menstrual bleeding. Some concerns about the synthesis and the unknown quality of included data and trials warrants a degree of caution when interpreting the reliability of this review.

Authors’ objectives
To evaluate the relative effectiveness of second generation ablation techniques for treating women with heavy menstrual bleeding.

Searching
The Cochrane Library, MEDLINE, EMBASE and PsycINFO were searched from inception to April 2011. There were no language restrictions. Full search strategies were reported. Bibliographies of relevant articles and reviews were searched for additional studies. Experts were contacted to locate grey literature.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared second generation endometrial ablation techniques in women with heavy, abnormal, excessive or prolonged uterine bleeding who had not responded to initial medical treatment.

The included women varied in terms of uterine pathologies and presence and size of fibroids. Ablation device manufacturers were reported in some cases. Various outcomes were reported. Chosen outcome measures for this review were rates of amenorrhoea or heavy bleeding (as reported in the studies or converted from pictorial bleeding assessment scores) and rate of dissatisfaction with treatment (defined elsewhere, see Other Publications of Related Interest) at 12 months or two years.

Two reviewers independently selected the studies for inclusion. Disagreements were resolved by consensus or arbitration by a third reviewer.

Assessment of study quality
The authors did not describe any methods to assess the quality of included trials or individual patient data (IPD) in this review.

Data extraction
Data were extracted to enable calculation of point estimates and 95% confidence intervals (CI). Where possible, IPD were obtained from study authors.

Two reviewers independently extracted the aggregate data. Disagreements were resolved by consensus or arbitration by a third reviewer.

Methods of synthesis
Meta-analyses were conducted to provide pooled odds ratios (OR) with 95% CIs. It appeared that this represented stage one of a two-stage model. Statistical heterogeneity was assessed using Cochrane's Q and $I^2$. A network meta-analysis (combining direct and indirect estimates) was subsequently carried out by fitting a linear mixed model to the log odds ratio from each trial using maximum likelihood to estimate treatment effects. Estimates of incoherence (standard deviation of the random effect) in the network model were calculated and were explored in sensitivity analysis. It appeared that aggregate data were combined with point estimates calculated from IPD.

Results of the review
Nineteen trials (3,287 women) were included in the review. It appeared that 10 trials had available IPD. There were five head-to-head comparisons (744 women) of second generation devices and 14 comparisons (2,543 women) of second and first generation (hysteroscopic) devices. Fixed-effect and random-effects meta-analyses showed similar results (random-effects results presented here).

Direct comparisons showed that bipolar radio frequency ablation was associated with an increased rate of amenorrhoea compared with thermal balloon ablation (OR 4.56, 95% CI 2.24 to 9.26; I²=0%). Bipolar radio frequency ablation was also favourable when compared with free fluid thermal ablation where this showed a reduced rate of amenorrhoea (OR 0.36, 95% CI 0.18 to 0.73; one trial) and increased heavy bleeding (OR 4.88, 95% CI 1.32 to 18.11; one trial). There were no other substantial differences and (where more than one trial was included in the analysis) there was generally no evidence of statistical heterogeneity.

The network meta-analysis was concurrent with the direct evidence. Indirect comparisons showed increased rates of amenorrhoea in favour of radio frequency ablation when compared with cryoablation (OR 0.20, 95% CI 0.09 to 0.49) and favouring microwave ablation over thermal balloon ablation (OR 1.66, 95% CI 1.01 to 2.71; one trial) and cryoablation (OR 0.31, 95% CI 0.13 to 0.74). Radio frequency ablation was preferable to free fluid ablation in reducing heavy bleeding (OR 2.91, 95% CI 1.23 to 6.88).

In general, rates of dissatisfaction with treatment or on-going heavy bleeding were low. Direct comparisons showed reduced rates of dissatisfaction with bipolar radio frequency ablation when compared with thermal balloon ablation (OR 0.39, 95% CI 0.16 to 0.91; I²=0%), although this was not statistically significant in the network meta-analysis. Increased rates of dissatisfaction were noted for free fluid thermal ablation compared with bipolar radio frequency ablation (OR 9.40, 95% CI 1.14 to 77.18; one trial) and this was mirrored in the network meta-analysis. There were no other substantial differences.

Estimates of incoherence were high in the network analysis regarding rate of amenorrhoea. This was influenced by one trial that compared microwave ablation to thermal balloon ablation, but removal of this trial did not alter any directions of effect.

**Authors’ conclusions**

Bipolar radio frequency and microwave ablative devices were more effective than thermal balloon and free fluid ablation in the treatment of heavy menstrual bleeding with second generation endometrial ablation devices.

**CRD commentary**

The review question was clear and inclusion criteria were potentially replicable for all aspects apart from outcomes. The authors accessed a range of relevant data sources and attempts were made to locate unpublished material. Efforts were made to minimise language bias. The processes of study selection and extraction of aggregate data included steps to minimise error and bias. There was no reported quality assessment of included trials or reference to checking the integrity of individual patient data in this review. This limits judgement about the overall reliability. Study details demonstrated some clinical variation, although statistical heterogeneity was reported to be low.

The evidence was robust and the authors’ conclusion reflects what was presented. However, the lack of sensitivity analyses around model form and structure and the unknown quality of trials/data suggests a degree of caution is warranted when interpreting the reliability of this review, especially where results were based solely on indirect comparisons as there was likely to be uncertainty around the effect estimates.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that large scale rigorous randomised controlled trials were needed to compare existing and emerging ablative techniques. Trials should use standardised measures relating to satisfaction and menstrual bleeding and be conducted independently from the device manufacturers.

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