Treating menorrhagia in primary care: an overview of drug trials and a survey of prescribing practice
Coulter A, Kelland J, Peto V, Rees M C

Authors' objectives
To examine the efficacy of drugs used to treat menorrhagia, and survey British general practitioners (GPs) to discover the extent to which they prescribe the most effective drugs for this condition.

Searching
MEDLINE, and EMBASE on CD-ROM were searched using the terms 'menorrhagia', 'menstrual blood loss' and 'dysfunctional uterine bleeding'; search dates and publication language restrictions are unclear. Citations in the retrieved papers were examined to identify additional trials.

Study selection
Study designs of evaluations included in the review
Only randomised trials were included. The type of designs used were crossover, double-blind, placebo-controlled and double dummy. Half the trials were not placebo-controlled.

Specific interventions included in the review
The specific interventions included in the review are aminocaproic acid (3 g), danazol (200 mg), diclofenac sodium (50 mg), ethamsylate (500 mg), flurbiprofen (100 mg), ibuprofen (600, 1200 and 1,600 mg), meclofenamate sodium (100 mg), mefenamic acid (500 mg), naproxen (5, 250, 500, 750 and 1,250 mg), norethisterone (5 mg), oral contraceptive (low dose), tranexamic acid (1, 12 and 24 g), interuterine devices (IUDs) and hormone-releasing IUDs.

Participants included in the review
Women with menorrhagia. Some trials included all patients with a subjective complaint of menorrhagia, others gave thresholds of blood loss ranging from 60 to 80 mL. Patients using IUDs were to have been doing so for contraception before entry into the trial or as a treatment for menorrhagia.

Outcomes assessed in the review
Reduction in menstrual blood loss, as measured by the alkaline hematin method or other equally reliable technique.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not report the criteria used to assess validity, or how the validity assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
For each trial of each drug, the percentage reduction in mean menstrual blood loss from the pretreated to the active treatment, was calculated. The weighted average of these was used to estimate the overall improvement with treatment;
group sizes were used as weights.

How were differences between studies investigated?
The following inconsistencies in the trials were noted: varying entry criteria in terms of objective versus subjective measures of blood loss, reporting of side-effects; trial design, dosages and length of follow-up. No tests of heterogeneity were presented.

Results of the review
A total of 31 studies were included in the review, some of which studied 2 or more interventions: aminocaproic acid (1 study, 12 women); danazol (5 studies, 110 women); diclofenac sodium (2 studies, 28 women); ethamsylate (4 studies, 79 women); ibuprofen (3 studies, 48 women); meclofenamate sodium (1 study, 29 women); mefenamic acid (11 studies, 279 women); naproxen (5 studies, 95 women); norethisterone (2 studies, 39 patients ); oral contraceptive (1 study, 15 women); tranexamic acid (7 studies, 154 women); and IUDs (4 studies, 87 women).

The interventions produced the following percentage reductions in menstrual blood loss:

- hormone-releasing coil 58.6 (95% confidence interval, CI: 56.7, 60.6);
- danazol 49.7 (95% CI: 47.9, 51.6);
- tranexamic acid 46.7 (95% CI: 45.0, 46.7);
- mefenamic acid 29.0 (95% CI: 27.9, 30.2);
- diclofenac 26.9 (95% CI: 23.2, 30.6);
- naproxen 26.4 (95% CI: 24.6, 28.3);
- ibuprofen 16.2 (95% CI: 13.6, 18.7);
- ethamsylate 13.1 (95% CI: 10.9, 15.3); and
- norethisterone -3.6 (95% CI: -6.1, 1.1).

No randomised controlled trials of the use of hormone replacement therapy were identified.

Cost information
It is noted that danazol is expensive. It is estimated that the total annual cost of the 821,700 UK prescriptions issued to patients complaining of this conditions is £37,176,595. Norethisterone was the most commonly used drug, prescribed to 38% of patients, followed by mefenamic acid (27%).

Authors' conclusions
This comparison showed that hormone-releasing coils, danazol and tranexamic acid could lead to significant reductions in menstrual blood loss. The coils are not registered for use in Britain as a treatment for menorrhagia, and the serious side-effects of danazol make it unacceptable for long-term use; it is also very expensive. The evidence from the trials suggests that tranexamic acid is the most effective and acceptable treatment. Tranexamic acid is seldom used by British GPs, whereas the least effective drug, norethisterone, is the most frequently prescribed.

CRD commentary
The search is weak and no details are given about the validity criteria used in this review. The disparate nature of the included studies is mentioned but not further analysed, even though the authors state that there were a number of methodological problems with the trials and the trials were weighted according to group sizes.
Bibliographic details

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Clinical Trials as Topic; England; Family Practice /statistics & numerical data; Female; Humans; Menorrhagia /drug therapy; Middle Aged; Practice Patterns, Physicians'; Randomized Controlled Trials as Topic

Accession Number
11995002772

Date bibliographic record published
31/10/1996

Date abstract record published
31/10/1996

Record Status
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.