# Cochrane Corner

# At last an effective treatment for heavy menstrual bleeding

*A review of the Cochrane review and the New Zealand guideline on the management of heavy menstrual bleeding*

*Associate Professor Bruce Arroll, Department of General Practice and Primary Health Care, University of Auckland*

*This review should be cited as: Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding (Cochrane Review). In: The Cochrane Library, Issue 4, 2001. Oxford: Update Software and Guidelines for the management of heavy menstrual bleeding (www.nzgg.org.nz).*

*Two of the NZGG writers were also the first two authors on the Cochrane review on fibrinolytics. The guidelines can be downloaded from the NZGG site but may require an update of your winzip file.*

*For access to the Cochrane site as a member of the RNZCGP see the end of this article.*

My initial reaction to the publication of the New Zealand Guidelines Group (NZGG) Management of heavy menstrual bleeding was one of horror. For almost 20 years I had been using a therapy that was ineffective, namely luteal phase progestagens. What was effective was oral progestagens from Day 5 to 25; much longer than I had been using. The NZ guidelines also mentioned a progestagen containing intrauterine device (Mirena) which is available through some hospital Obstetric and Gynaecology clinics. I also learnt that there was a medication that was specialist only at the time of publication and that NSAIDs were equally as effective. The medication concerned is tranexamic acid (Cyklokapron) which only needs to be taken during days of heavy menstruation. Heavy menstrual bleeding is defined as more than 80 mLs/cycle. In the NZGG guidelines there is a diagram which can facilitate an estimation of cycle volume (Figure 6.1). Since January 1st 2002 tranexamic acid is fully funded for prescription by general practitioners.

## The Cochrane review

Heavy menstrual bleeding (HMB) is an important cause of ill health in women. In New Zealand it is estimated that 2.3% of GP consultations for women less than 50 years are for heavy menstrual bleeding. Medical therapy, with the avoidance of possibly unnecessary surgery, is an attractive treatment option. A wide variety of medications are available to reduce heavy menstrual bleeding but there is considerable variation in practice and uncertainty about the most appropriate therapy. Plasminogen activators are a group of enzymes that cause fibrinolysis (the dissolution of clots). An increase in the levels of plasminogen activators has been found in the endometrium of women with heavy menstrual bleeding compared to those with normal menstrual loss. Plasminogen activator inhibitors (antifibrinolytic agents, i.e. tranexamic acid) have therefore been promoted as a treatment for heavy menstrual bleeding. Eighty per cent of women treated for menorrhagia have no anatomical pathology and over a third of the women undergoing hysterectomies for heavy menstrual bleeding have anatomically normal uteri. Hence medical therapy, with the avoidance of possibly unnecessary surgery, is an attractive alternative.

All studies which might describe randomised controlled trials of antifibrinolytic therapy for the treatment of heavy menstrual bleeding were obtained by electronic searches of electronic databases including the Cochrane Controlled trials register (now regarded as the best source of randomised controlled trials). The review selected papers which were randomised controlled trials in women of reproductive age treated with antifibrinolytic agents versus placebo, no treatment or any other medical (non-surgical) therapy for regular heavy menstrual bleeding within either the primary, family planning or specialist clinic settings. Women with post menopausal bleeding, intermenstrual bleeding, iatrogenic or pathological causes of heavy menstrual bleeding were excluded.

## Results

Tranexamic acid compared to placebo showed a significant reduction in mean blood loss of 94 mLs/cycle with the 95% confidence interval from 151.4 mLs to 36.5 mLs. Tranexamic acid was compared to two other medical (non-surgical) therapies: mefenamic acid and norethisterone administered in the luteal phase. In all instances, there was a significant reduction in mean blood loss. Change in the quality of life measures, flooding and leakage and sex life, were significantly improved in the tranexamic acid group when compared to the oral progestagen group. These findings are based in most cases on only one trial. This treatment is not associated with an increase in side effects compared to placebo, NSAIDS or oral luteal phase progestagens.

## Safety

As these medications slow the breakdown of clots, there has been concern that antifibrinolytic agents may have an associated increased risk of thrombogenic disease (deep venous thrombosis). Long term studies in Sweden, however, have shown that the rate of incidence of thrombosis in women treated with tranexamic acid is comparable with the spontaneous frequency of thrombosis in women. There are no data available within randomised controlled trials which record the frequency of thromboembolic events.

## Clinical bottom line

For women who are not at high risk of endometrial cancer (see NZGG for how to assess this) then tranexamic acid, the Levonorgestrel intrauterine system, non-steroidal anti-inflammatory agents (menstruating days only), oral contraceptive pill (Day 5–25) and long courses of high dose norethisterone (Day 5–25) are all effective treatments for heavy menstrual bleeding. The good news is that tranexamic acid is now fully funded on a GP prescription.

## References

References are available from B Arroll or from the Cochrane library.

Associate Professor Bruce Arroll, Department of General Practice and Primary Health Care, University of Auckland, Private Bag 92019, Auckland; email: b.arroll@auckland.ac.nz

*For the access codes to the Cochrane library contact Cherylyn Pearson cpearson@rnzcgp.org.nz at the College.*