



## Non-surgical management options for menorrhagia

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Menorrhagia is a common problem in women and increasing numbers are seeking help and advice regarding management. In many cases, surgery is not appropriate and so awareness of alternative treatments is important. The aim of this review is to summarise the evidence available regarding current medical therapies.

Menorrhagia is a largely benign condition but can be emotionally and socially debilitating. It is defined as excessive menstrual bleeding with a loss of more than 80ml of blood per month. The condition may be caused by an underlying pathology, such as malignancy, uterine fibroids, polyps, infection or haematological disorders.

However, no obvious reason for the heavy bleeding is found in the majority of cases (approximately 80 per cent) and it is then described as dysfunctional uterine bleeding. Heavy, prolonged or frequent bleeding may be

associated with anovulation in 10-20 per cent of cases, particularly at the extremes of reproductive life when changes in the length of the menstrual cycle lead to disturbances of the hypothalamo-pituitary-ovarian axis. In cases where menorrhagia is associated with anovulation, menstrual cycles tend to be irregular due to unopposed oestrogen production and consequent prolonged endometrial stimulation, causing a build-up of endometrium followed by erratic bleeding as it breaks down and is expelled.

Each year, one in 20 women between the ages of 30 and 49 years presents to her GP with heavy menstrual periods (Vessey et al, 1992) and about 21 per cent of all referrals to gynaecologists are for menstrual disorders (Coulter et al, 1991). Various surgical techniques are used to treat menstrual disorders.

The aim of any therapy is to reduce menstrual blood loss to an acceptable level, with as little inconvenience as possible and minimal side-effects. The Royal College of Obstetricians and Gynaecologists (1998a; 1998b) has issued guidelines on the management of menorrhagia and recommends that medical treatments be tried in the first instance before surgical procedures are considered. The National Institute for Clinical Excellence has issued a referral advice booklet (2001) which states that many women with menorrhagia can initially be managed medically in the primary care setting and need not be referred to a gynaecologist unless there is:

- A suspicion of cancer;
- Severe anaemia;
- Persistent heavy bleeding despite three months of drug therapy.

A range of medications is available to reduce heavy menstrual bleeding, but there is no evidence to suggest an optimum regimen (Lethaby et al, 2001a).

### Treatment options Antifibrinolytic agents

Increased endometrial fibrinolysis may be a contributing factor for menorrhagia (Bonnar et al, 1983). Studies show reduced menstrual blood loss after treatment with antifibrinolytic agents (Dockeray et al, 1987; Ylikorkala and Viinikka, 1983). The agent most commonly used in the treatment of menorrhagia is tranexamic acid.

One review evaluated seven trials of women of reproductive age being treated with antifibrinolytic agents versus those given placebo, no treatment or any other non-surgical treatment (Lethaby et al, 2001a). Antifibrinolytic therapy showed a significant reduction in mean blood loss and a significant change in mean reduction of blood loss compared with placebo. However, one

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### BOX 1. SUMMARY OF FINDINGS

- Antifibrinolytics reduce heavy menstrual bleeding
- Non-steroidal anti-inflammatory drugs have also been shown to be effective in reducing heavy menstrual bleeding, but they are less effective than antifibrinolytics and danazol
- Progestogens taken during the luteal phase of menstruation have no advantage over other medical therapies in the management of menorrhagia. However, the evidence shows that when taken for 21 days of the cycle, they do significantly reduce menstrual blood loss
- The levonorgestrel-releasing interuterine system is more effective than cyclical norethisterone taken over 21 days of the cycle in treating menorrhagia
- There is little evidence to determine whether the oral contraceptive pill is an effective medical therapy for reducing menorrhagia or whether it is more effective and has fewer side-effects than other medications
- There is no evidence of effectiveness or acceptability of progestogens alone or a combination of oestrogens and progestogens in the management of irregular bleeding associated with

of the studies reviewed, which looked at patient-perceived improvement of symptoms, showed a significant reduction in mean blood loss for antifibrinolytic agents compared with other medical treatments, such as mefenamic acid, norethisterone (administered orally during the luteal phase) and etamsylate. This was mirrored by patients' perceived reduction of blood loss. Antifibrinolytics were not associated with an increase in side-effects compared with placebo or the other medical treatments. Flooding and leakage were shown to be significantly improved after antifibrinolytic therapy.

### Non-steroidal anti-inflammatory drugs

A reduction in menstrual blood loss has been found to occur when non-steroidal anti-inflammatory drugs (NSAIDs), such as mefenamic acid and flufenamic acid, are taken during menstrual bleeding (Anderson et al, 1976). NSAIDs reduce prostaglandin levels by inhibiting the enzyme cyclo-oxygenase. Deranged haemostasis, as a result of altered levels of prostaglandin activity in the endometrium, is suggested as one of the causes of heavy menstrual bleeding and has led to the use of prostaglandin synthetase inhibitors in treating menorrhagia.

Sixteen trials comparing NSAIDs with placebo or other medical therapies in women of reproductive age with regular, heavy periods with no identifiable pathological or iatrogenic cause were reviewed (Lethaby et al, 2001b). NSAIDs were found to reduce heavy menstrual bleeding when compared with placebo but were less effective than either tranexamic acid or danazol. However, adverse side-effects were more severe with danazol. No significant difference in efficacy was demonstrated between NSAIDs and other medical treatments such as oral progestogens given in the luteal phase, etamsylate, the oral contraceptive pill (OCP) and the progesterone-releasing intrauterine system (IUS).

### Oral contraceptive pill

The OCP is believed to induce regular shedding of a thinner endometrium and to inhibit ovulation. It is, therefore, used to achieve good cycle control in women with menorrhagia.

A trial of 45 women of reproductive age with regular, heavy periods (Iyer et al, 2001) compared those taking the OCP with those taking mefenamic acid, low-dose danazol and naproxen. There was no significant difference between reduction in blood loss at two months in patients treated with the OCP and danazol, and those given OCP and mefenamic acid, or OCP and naproxen. However, the data from this one small trial is not sufficient to conclude whether the OCP is an effective treatment for menorrhagia and if it is more effective or has fewer side-effects than other non-surgical therapies.

### Cyclical progestogens and progestogen-releasing intrauterine system

During the early part of the menstrual cycle, oestrogen causes proliferation of the endometrium. Progestogens inhibit this effect, which is the rationale for using cyclical

progestogens to provoke a regular withdrawal bleed. Continuous progestogen induces endometrial atrophy preventing oestrogen-stimulated endometrial proliferation.

Seven randomised controlled trials compared oral progestogen therapy with other medical treatments in women of reproductive age with regular, heavy periods (Lethaby et al, 2001c). No trials comparing progestogens with placebo were found.

Mean menstrual blood loss was significantly greater with luteal-phase progesterone therapy when compared with danazol, tranexamic acid and the progestogen-releasing IUS.

It was concluded that progestogens administered from day 15 or 19 to day 26 of the menstrual cycle offered no advantage over other medical therapies such as danazol, tranexamic acid, NSAIDs and the progestogen-releasing IUS in the treatment of menorrhagia.

Five trials of the use of IUS versus no treatment, placebo or other therapy for heavy menstrual bleeding in women of reproductive age showed that the levonorgestrel-releasing IUS is more effective than cyclical norethisterone (21 days) as a treatment for heavy menstrual bleeding (Lethaby et al, 2001c).

Women with a levonorgestrel-releasing IUS were more satisfied and willing to continue with treatment but experienced more side-effects such as intermenstrual bleeding and breast tenderness. Treatment resulted in a smaller mean reduction in menstrual blood loss than transcervical resection of the endometrium and women were not as likely to become amenorrhoeic, but there was no difference in satisfaction.

Women with a levonorgestrel-releasing IUS experienced more progestogenic side-effects compared with women having transcervical resection for treatment of their heavy menstrual bleeding, but there was no difference in their perceived quality of life. There is no data available from randomised controlled trials comparing progesterone-releasing intrauterine systems with either placebo or other commonly used medical therapies for heavy menstrual bleeding.

### Danazol

Danazol is an androgen derivative, which causes a change in the release of gonadotrophins which, in turn, induces a hypo-oestrogenic and hypo-progestogenic state. Chimbira et al (1979) found that danazol in many cases caused women to become amenorrhoeic.

### Conclusion

The aim of any therapy for menorrhagia is to reduce menstrual blood loss to an acceptable level, with as little inconvenience as possible and minimal side-effects. In view of this, non-surgical therapies may be more effective than surgery. However, the evidence for non-surgical management of menorrhagia is more limited than one might imagine and, clearly, further research into this area is required before a consensus can be reached on the optimum treatment regimen for heavy menstrual bleeding. ■

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