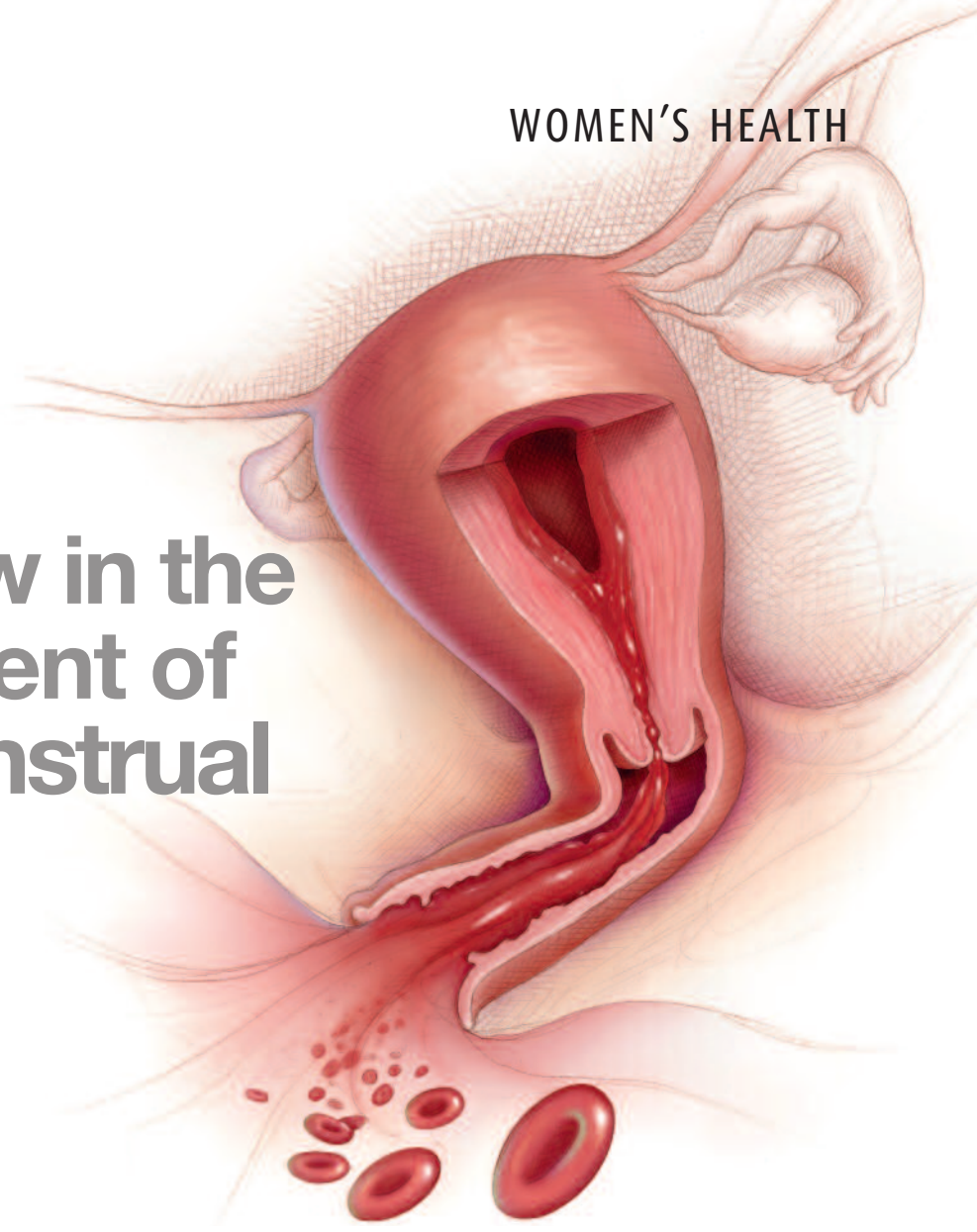

What's new in the management of heavy menstrual bleeding?

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A number of effective conservative treatment options are now available for women with heavy menstrual bleeding and these should be considered prior to surgical intervention.

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Abnormal uterine bleeding may be divided into two categories: organic and nonorganic. Nonorganic causes are usually attributed to a hormone imbalance, an unknown physiological process or end-organ response, or to causes such as stress. Organic causes include coagulopathies, endocrinopathies, adrenal disorders, polycystic ovarian syndrome, fibroids, polyps, endometrial hyperplasia and malignancy (see the box on page 62).

Many terms have been used to describe nonorganic abnormal uterine bleeding, including dysfunctional uterine bleeding, menorrhagia, polymenorrhoea and metrorrhagia. However, heavy menstrual bleeding is now the preferred term over these historic descriptions.[1,2]

Heavy menstrual bleeding is common; imposes health, economic and quality of life concerns; and warrants treatment. It occurs in between 9 and 14% of women in the reproductive age group. Subjective reports of incidence range from 2% to as many as 52% of women who believe that their blood loss is excessive.[3] The quantitative definition of heavy menstrual bleeding is 'menstrual blood loss in excess of 80 mL per cycle', the normal blood loss being less than 40 mL. The National Institute of Clinical Excellence in the UK has defined heavy menstrual bleeding as 'excessive menstrual blood loss without identifiable cause which interferes with a woman's physical, emotional, social and material quality of life and which can occur alone or in combination with other symptoms'.[4] Therefore, any treatment for women with heavy menstrual bleeding should be aimed at improving these quality of life issues.

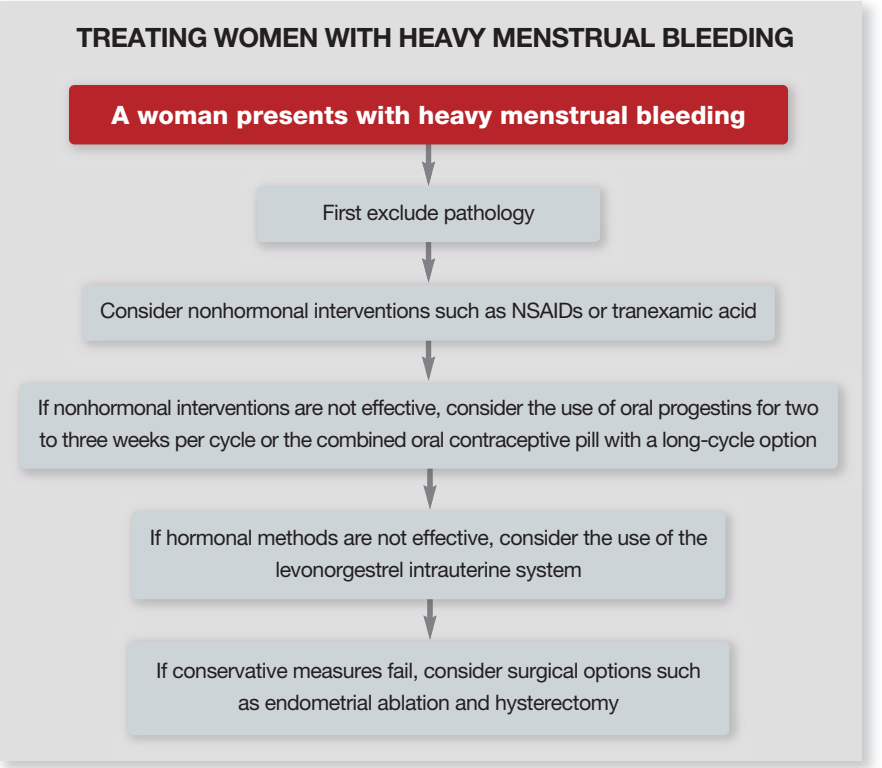
ORGANIC AND NONORGANIC CAUSES OF HEAVY MENSTRUAL BLEEDING

Organic

- Systemic causes (e.g. coagulopathy disorders, endocrinopathies, adrenal disorders, polycystic ovarian syndrome)
- Anatomical causes (e.g. malignancy, fibroids, polyps, hyperplasia)

Nonorganic

- Hormonal imbalance
- Unknown physiological processes
- End-organ response
- Other causes such as stress



AETIOLOGY

The aetiology of nonorganic heavy menstrual bleeding is not fully understood. Heavy menstrual bleeding may be anovulatory or ovulatory. Anovulatory heavy menstrual bleeding usually results from the disruption of the hypothalamic–pituitary–ovarian axis and is associated with menstrual irregularities. Ovulatory heavy menstrual bleeding is related to local loss of endometrial homeostasis due to abnormal vasodilatory or vasoconstrictive activity within the endometrium.

A diagnosis of heavy menstrual bleeding can usually only be made once organic causes are excluded and depending on the circumstances in which the patient presents. Investigations may include ultrasound, blood tests for anaemia and endocrinopathies, office endometrial biopsy or hysteroscopy, and dilation and curettage.

CURRENT TREATMENTS

Currently used therapies for women with heavy menstrual bleeding may be divided into nonhormonal, hormonal and surgical options. These options are discussed below. The flowchart on this page also shows a series of steps that may be used in the treatment of women with heavy menstrual bleeding.

Nonhormonal treatments

Nonhormonal treatments for heavy menstrual bleeding include NSAIDs, which have been shown in clinical trials to reduce blood loss by up to 39%.[5] Prostanoids are involved in the vascular and myometrial changes that occur during menstruation, and altered synthesis and production of these may cause heavy menstruation.[6,7] By inhibiting prostaglandin synthesis, NSAIDs may therefore reduce blood loss and reduce menstrual pain. These preparations are taken orally three times daily during the bleeding period. Side effects may include diarrhoea, gastric irritation and asthma.

Antifibrinolytics, such as tranexamic acid, are also used to treat women with heavy menstrual bleeding and will reduce blood loss by 20 to 44%.[8] Tranexamic acid acts as a competitive inhibitor of plasminogen activation. A dose of two tablets four times daily should be taken for the first three days of menstrual bleeding. Side effects may include indigestion, diarrhoea and headaches.

Hormonal treatments

Oral progestins

Oral progestins are widely used to treat women with heavy menstrual bleeding. They may be useful in regulating a menstrual cycle; however, clinical trials have found them less effective in the treatment of heavy menstrual bleeding.[8] A Cochrane review of randomised trials investigating progestins for heavy menstrual bleeding found that when administered to women from day 15 to 26 of their cycle, they offered no advantages over the use of NSAIDs, tranexamic acid or levonorgestrel intrauterine system and were less effective than these modalities in reducing menstrual blood loss.[9] Oral progestins administered to women from day 5 to 26 of their cycle did result in a

significant reduction in menstrual blood loss; however, this was less than that seen with the use of the levonorgestrel intrauterine system. Adverse side effects of progestins, including weight gain, bloating, breast tenderness, headaches, acne and depressed mood, were more common with the longer regimen rendering it suitable only for short-term therapy. The progestin most commonly tested in the trials analysed in the Cochrane review was norethisterone.

If progestins are used off-label in higher doses (e.g. 5 mg norethisterone three times daily for three weeks out of every four) then efficacy rates are much higher, reducing menstrual blood loss by 87%.[10] However, side effects are dose related.

Danazol has also been used to treat women with heavy menstrual bleeding. A Cochrane review of various oral interventions for treatment of heavy menstrual bleeding found that danazol appeared to be more effective than placebo, progestins, NSAIDs and the oral contraceptive pill (OCP) at reducing menstrual blood loss; however, the confidence intervals were wide.[11] Treatment with danazol caused more adverse events than treatment with NSAIDs (odds ratio, 7.0; 95% confidence interval 1.7–28.2) or other progestins (odds ratio, 4.05; 95% confidence interval 1.6–10.2).[11] Therefore, the use of danazol is likely to be limited by its side-effect profile, its acceptability to women and the need for continuing treatment.

Combined oral contraceptive pill

The combined OCP is commonly used off-label for the treatment of women with heavy menstrual bleeding. Monophasic OCPs are also often used by women with long cycles to minimise episodes of menstruation. In the few clinical trials to have accurately evaluated their efficacy, a reduction in bleeding of up to 43% was reported, which is not materially different from that reported for NSAIDs or tranexamic acid.[5] The combined OCP has the advantages of being a contraceptive, short-acting and reversible, and is usually able to regulate a woman's cycle. OCPs are well tolerated although side effects may include mood changes, headaches, nausea, fluid retention and breast tenderness. The risk of venous thromboembolic disease is increased with use of the OCP. In absolute terms this increase is between one and three extra cases per 10,000 women per year compared with nonusers. The OCP is not suitable for older women who are obese, have hypertension or are smokers.

A new form of the combined OCP

containing oestradiol valerate plus dienogest has recently been approved for the treatment of heavy menstrual bleeding in women without organic pathology who desire oral contraception. In two multinational, randomised, double-blind, placebo-controlled trials, patients were investigated for the effect of oestradiol valerate plus dienogest treatment on prolonged, frequent and excessive menstrual bleeding. All women recruited to the study underwent a 90-day run-in period to confirm the diagnosis and then a further 196 days randomised to therapy or placebo, of which the last 90 days was assessed for efficacy. Confirmation of diagnosis and assessment of treatment was based on subjective patient assessment with E-diaries and objective quantification of menstrual blood loss using the alkaline haematin method.

Pooled data from these two trials have recently been published.[12] Median menstrual blood loss per cycle in the treatment arm was reduced from 142 mL per month at baseline to 17 mL per month at cycle seven, an 88% reduction.[12] In the placebo group menstrual blood loss was reduced from 154 to 117 mL at cycle seven, a 24% reduction.[12] Median reduction in menstrual blood loss was consistent and substantial irrespective of the baseline menstrual blood loss, which ranged from 80 mL per cycle to more than 200 mL per cycle. The treatment arm was associated with statistically significant reduction in the number of sanitary items used, a statistically significant increase in both haemoglobin and ferritin values and a high level of user satisfaction.[12]

Levonorgestrel intrauterine system

Out of all the previously available treatment modalities for women with heavy menstrual bleeding, the levonorgestrel intrauterine system has proven the most successful. Randomised clinical trials have shown a 71% reduction in menstrual blood loss for users of this modality, which also provides contraception for five years.[13] Approximately 50% of users of the levonorgestrel intrauterine system will have complete amenorrhoea after one year of therapy. However, users who do not have complete amenorrhoea cannot be assured of any menstrual cycle regularity and intermittent breakthrough bleeding is a common characteristic of this form of treatment for the first several months of therapy.

Surgery

Surgery remains the final option for women experiencing heavy menstrual bleeding. Dilation and curettage remains diagnostic but has no therapeutic value.

Endometrial ablation

Endometrial ablation involves a variety of techniques aimed at destroying the basalis layer of the endometrium and therefore inducing amenorrhoea. Techniques may be classified as first and second generation. First-generation techniques involve hysteroscopically-guided modalities such as resection, laser or rollerball electrocautery, whereas second-generation techniques involve microwave or thermal devices such as the thermal balloon ablation device. Endometrial ablation significantly reduces menstrual blood loss for most women, with reductions in the range of 45 to 80% being reported and with approximately 50% of women becoming amenorrhoeic after one year.[14]

A Cochrane review found the second-generation techniques of endometrial ablation less likely to be associated with fluid overload, uterine perforation and cervical laceration than first-generation techniques, but more likely to be associated with nausea, vomiting and uterine cramping.[15] Meta-analyses have shown that 25 to 30% of women undergoing endometrial ablation (whether first or second generation) will undergo a second procedure, and 18 to 20% will go on to have a hysterectomy.[15]

Hysterectomy

Hysterectomy is the gold standard therapy for women with heavy menstrual bleeding but should be reserved as a last resort. It is suitable for women who have significant uterine enlargement, thus disqualifying themselves from the diagnosis of nonorganic heavy menstrual bleeding. Hysterectomy may be performed using a vaginal approach, laparoscopically or abdominally. Morbidity from hysterectomy includes the usual surgical complications together with an increased incidence of later surgery for urinary incontinence and prolapse repair. These specific complications appear more common after vaginal surgery, although this may be a reflection of the underlying pathology that led the surgeon to elect that approach.[16] Although techniques of hysterectomy have improved and diversified dramatically over recent years, mortality rates still range between 0.02 and 0.4% and morbidity is also an issue to be considered.[17]

SUMMARY

Heavy menstrual bleeding is common and can affect a woman's quality of life. The diagnosis of nonorganic heavy menstrual bleeding should be made after possible organic causes of abnormal uterine bleeding have been excluded. Heavy menstrual bleeding may be ovulatory or anovulatory.

Treatment of women with heavy menstrual bleeding should be aimed at improving quality of life. Treatments include nonhormonal, hormonal and surgical options. A number of effective conservative treatment options are now available for this condition and these should be considered before surgical intervention. MT

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A list of references is available on request to the editorial office.

COMPETING INTERESTS: None.

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