Heavy menstrual bleeding

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Abstract

Heavy menstrual bleeding is defined as excessive menstrual blood loss which interferes with the woman's physical, emotional, social and material quality of life, and which can occur alone or in combination with other symptoms. In the majority of cases, an accurate history may indicate the cause of the bleeding. Common investigations include haematological blood tests, ultrasound scan and endometrial biopsy. Management may be medical or surgical, depending on the patient's age, pathology identified and fertility wishes. All interventions should aim to improve quality of life rather than focussing on menstrual blood loss alone. This review considers the intricacies involved when managing women with heavy menstrual bleeding.

Keywords abnormal uterine bleeding; endometrial ablation; heavy menstrual bleeding; hormonal treatment; hysterectomy; long acting injectable progestogens

Introduction

Heavy menstrual bleeding (HMB) is defined as excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life. It can occur alone or in combination with other symptoms. The term heavy menstrual bleeding has replaced the term menorrhagia. The objective definition of HMB is no longer used except for research purposes.

Prevalence

The true incidence of HMB globally is not known but some estimates suggest inter country and inter racial variation between 4% and 51%. Heavy menstrual bleeding affects one in three women of reproductive age. In the UK, almost 1.5 million women consult their GP each year with menstrual complaints and the annual treatment cost exceeds £65 million.

Causes of heavy menstrual bleeding

The possible causes of HMB can be divided into local, systemic and iatrogenic causes as highlighted in Table 1.

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In the majority of cases of HMB, the cause of heavy bleeding lies at the level of the endometrium. This was previously termed dysfunctional uterine bleeding (DUB) and is a diagnosis of exclusion. Sub mucosal and intramural fibroids are particularly associated with HMB, although about 50% of fibroids cause no symptoms.

Coagulopathy should be considered in women who fail to respond to medical management or women who present at a young age. Coagulopathy may be inherited or acquired and most common inherited disorder is von Willebrand's disease. Endometrial and cervical carcinomas are potential causes of intermenstrual and post coital bleeding and rarely HMB. Untreated hypothyroidism may be associated with HMB. Chronic endometrial infection may cause intermenstrual bleeding or HMB. *Chlamydia trachomatis* has also been proposed as a cause of HMB.

Arteriovenous malformations in the uterus may be congenital or acquired and are a rare cause of HMB. Acquired AVM may occur following uterine curettage after pregnancy. Colour Doppler imaging is a useful diagnostic modality if AV malformation is suspected. Acute heavy bleeding from an AVM may be required to be managed with uterine artery embolisation.

Iatrogenic causes include the use of anticoagulants in women with thromboembolic disease and copper intra uterine device (IUD). Table 1 summarizes the main causes of HMB

Obesity and HMB

Obesity is associated with abnormal uterine bleeding. There is clear association between obesity, endometrial polyps, endometrial hyperplasia (subsequently developing into carcinoma) and ovulatory dysfunction.

At cellular level, raised circulating oestrogen levels, as a consequence of peripheral conversion of androgens by adipose tissue aromatase enzyme have been implicated in the increased proliferative activity of endometrial cells. Circulating adipokines have also been associated with increased angiogenesis as well as cell proliferation.

History, examination and investigations for HMB

A history should be taken to identify the nature of bleeding and related symptoms that might suggest structural or histological abnormality, impact on the quality of life and other factors that may determine treatment options (such as presence of co-morbidity). The menstrual cycle duration, frequency and blood loss must be established. A menstrual diary is often helpful to determine the amount and timing of the bleeding. Flooding and clots indicate significant loss, particularly if compounded by systemic symptoms of anaemia – such as tiredness or breathless at rest. Inter menstrual and post coital bleeding may also suggest an anatomical cause which should be investigated. Furthermore pressure symptoms, including bowel and urinary symptoms, can indicate the presence of a large fibroid.

A coagulation disorder may be suggested by history of excessive bleeding since menarche, and/or history of postpartum haemorrhage, and surgery related bleeding. Coagulation disorder should also be suspected if there is a history of two or more of the following: bruising greater than 5 cm, epistaxis once a month, or a family history of bleeding disorders.

Summary of causes of HMB/DUB

Classification	Subtype
Local uterine pathology	Uterine fibroids
	Uterine polyps
	Chronic endometrial infection
	Uterine cancer
	Endometrial hyperplasia
	Arteriovenous malformation
Local pelvic pathology	Polycystic ovary syndrome
Systemic disorders	Hypothyroidism
	Coagulopathy e.g. von Willebrand's disease
Iatrogenic causes	Anticoagulation therapy
	IUD

Table 1

Examination

A general physical examination should be performed to exclude signs of anaemia, evidence of systemic coagulopathy and thyroid disease.

An abdominal examination should be performed to exclude a pelvic mass (fibroid); a speculum examination should be performed to assess vulva, vagina and cervix (this may reveal sources of bleeding, such as a tumour, polyp or a foul smelly discharge suggestive of infection). A bimanual examination should be performed to elicit uterine enlargement.

A physical examination should be carried out before

- All levonorgestrel-releasing intrauterine System (LNG-IUS) fittings.
- All investigations for structural abnormalities by speculum examination and a pelvic ultra sound.
- All investigations for histological abnormalities such as endometrial sampling.

Investigations (Table 2)

- Laboratory tests

A full blood count test should be carried out on all women with HMB. Testing for coagulation disorders (for example, von Willebrand's disease) should be considered in women who have had HMB since menarche and have personal or family history of a coagulation disorder. Estimation of serum ferritin, LH, and FSH should not be routinely carried out. Thyroid function test should be carried out only when other signs and symptoms of thyroid disease are present.

- Endometrial biopsy

The primary indication for an endometrial biopsy is age – i.e. women over the age of 45, or in those at high risk of endometrial hyperplasia/carcinoma (e.g. PCOS patients). Blind sampling methodologies (outpatient pipelle endometrial biopsy) are reasonable screening techniques but they are less effective at diagnosing focal lesions. Where focal pathology is suspected, hysteroscopy and endometrial biopsy is a better option in these circumstances than endometrial biopsy alone.

- Role of imaging

Ultrasound (ideally transvaginal) is the first line diagnostic tool for identifying structural uterine abnormalities associated with HMB. Common findings include uterine polyps, fibroids or a grossly thickened endometrium suggestive of malignancy.

Treatment for HMB

Women with HMB should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. Treatment can be medical or surgical; medical management does not impact on future fertility in the long-term.

1) Pharmacological treatments (Table 3)

Pharmacological treatment should be considered where no structural or histological abnormality is present, or for fibroids less than 3 cm in diameter which do not distort the uterine cavity.

Hormonal and non-hormonal treatments are available and should be considered in the following order.

1) Levonorgestrel-releasing intrauterine system (LNG-IUS) provided long-term (at least 12 months) use is anticipated.
2) Tranexamic acid or non-steroidal anti-inflammatory drugs (NSAIDs) or combined oral contraceptives (COCs).
3) Norethisterone (5 mg tds) daily from days 5 to 26 of the menstrual cycle, or injectable long-acting progestogens.

Other treatment options include:

GnRH analogues-administered either by injections or by nasal inhalation.

Danazol, ethamsylate and gestrinone – no longer routinely used in clinical practice for the treatment of HMB because of their unacceptable side effects such as weight gain, acne, voice change, increased risk of hirsutism and mood changes.

a) **Non-hormonal treatments**

These treatments can be used if hormonal treatments are not acceptable to the woman, women wishing to become pregnant or whilst awaiting investigations and definitive treatment.

- Antifibrinolytics

Antifibrinolytics such as tranexamic acid reduce blood loss by 58% by inhibiting endometrial fibrinolysis. Side effects are rare but may include indigestion, diarrhoea or headache. Cochrane reviews concluded that antifibrinolytic therapy causes a greater reduction in objective measurements of heavy menstrual bleeding when compared to placebo or other medical therapies (NSAIDS, oral luteal phase progestogens and ethamsylate). This treatment is not associated with an increase in side effects compared to placebo, NSAIDS, oral luteal phase progestogens or ethamsylate as described above.

NSAIDs

Non-steroidal anti-inflammatory drugs are prostaglandin synthetase inhibitors and act by inhibiting endometrial prostaglandin production leading to reduction in menstrual blood loss. Mefenamic acid is the most frequently used agent and reduces blood loss by approximately 25%. This drug should be taken during menstruation and is associated with gastrointestinal side effects such as indigestion, diarrhoea, worsening of asthma and peptic ulcer disease. When HMB coexists with dysmenorrhoea, NSAIDs are preferable to tranexamic acid. There have been isolated reports of NSAID-associated reversible female infertility and probable mechanism is ovulatory failure due to non rupture of mature follicle, often after a prolonged use of NSAID.