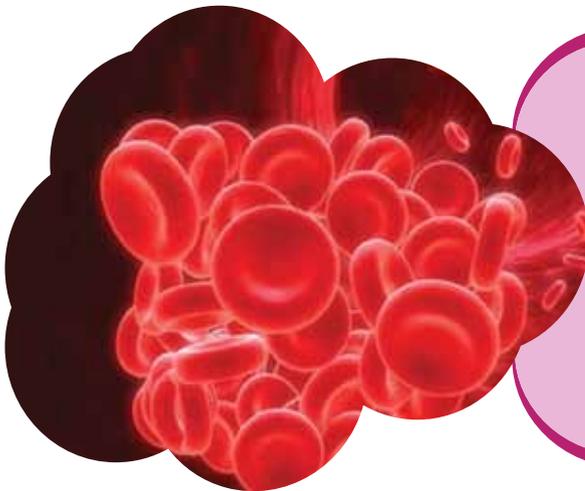


WOMEN'S HEALTH

Volume : 10, No. : 2 July-December 2017



**Don't Ignore
Heavy Menstrual
Bleeding**

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Editorial Note:

Dear Doctor

It is our immense pleasure to inform you that we have published our newsletter, "Women's Health". In this issue we are focusing on "Heavy menstrual bleeding".

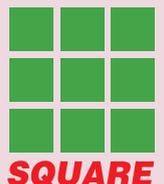
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Heavy menstrual bleeding



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Heavy menstrual bleeding

Menorrhagia or heavy menstrual bleeding (HMB) represents the most common gynecological presentation in women of reproductive age. Although there is no universally accepted definition for HMB, it is widely defined as menstrual blood loss (MBL) of 80 mL or more per cycle. However, in clinical practice, this value has been questioned. It is the perception of heavy MBL and the negative impact on quality of life that prompt women to seek medical attention. In 2011, the Federation of Gynecology and Obstetrics (FIGO) formally accepted a new classification system for causes of abnormal bleeding, including HMB. This was developed due to longstanding confusion concerning terminologies and definitions related to abnormal uterine bleeding. FIGO classify HMB as a woman's perception of increased menstrual volume, regardless of regularity, frequency or duration.

FIGO definition of abnormal uterine bleeding (AUB) includes:

- i. Disturbance of menstrual frequency and cycles shorter than 21 days are classified abnormal frequency of menses
- ii. Irregular menstrual bleeding - cycles when the onset of menses is unpredictable
- iii. Menstrual periods that exceed 8 days duration on a regular basis are classified as prolonged menstrual bleeding
- iv. Heavy menstrual bleeding (HMB)-describes increased menstrual volume regardless of regularity, frequency, or duration
- v. Inter-menstrual bleeding-episodes of bleeding that occur between normally timed menstrual periods

In the UK, the National Institute for Health and Clinical Excellence define HMB as excessive MBL which interferes with a woman's physical, emotional, social and quality of life, and which can occur alone or in combination with other symptoms. HMB increases the susceptibility to iron deficiency; if left untreated may progress to iron deficiency anemia, with associated morbidity. HMB results in increased use of health care resources including high rates of surgical interventions. It leads to decreased work productivity, or absence from work and school, which contributes to the overall economic burden. The aim of this article is to provide an up-to-date review on the assessment and management of HMB.

Assessment of heavy menstrual bleeding

In the UK, 5% of women aged between 30 and 49 years consult their general practitioner each year with HMB. In a European wide survey of 4506 women, 1225 (27%) reported two or more HMB symptoms; 661 (15%) required medical attention within the past year. Previous confirmed diagnosis or treatment for iron deficiency anemia was high (63%).

The first step in assessment of HMB is to ascertain a menstrual history, including cycle length and duration of menses, the passage of clots or flooding, and how frequently a change of sanitary towels and/or tampons is required. Irregular or inter-menstrual bleeding could be indicative of uterine pathology. The woman should be asked about symptoms of anemia. The impact of HMB on a

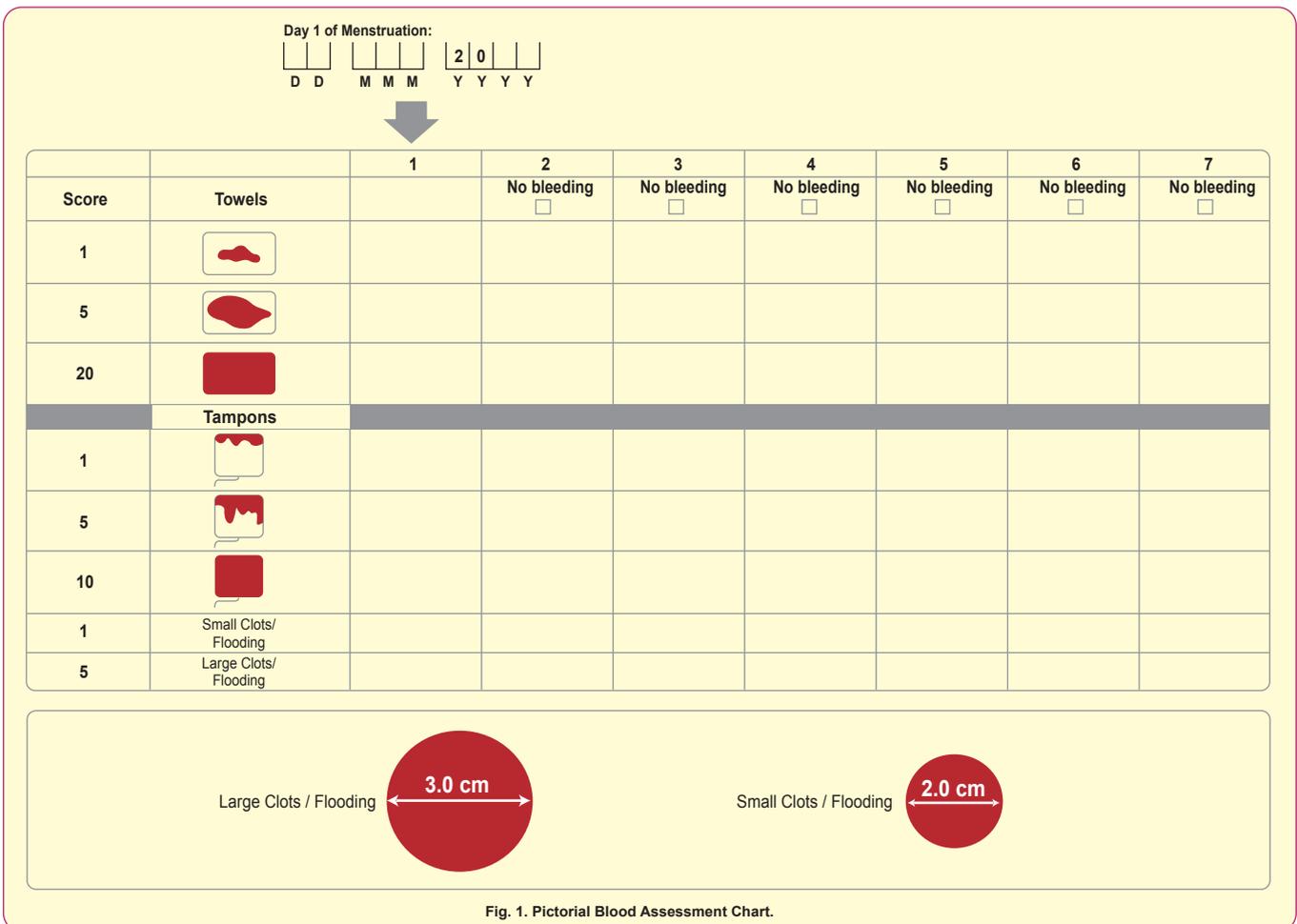
woman's quality of life, including limitations of work, exercise and social functioning should also be explored.

The subjective estimation of women's MBL can be inaccurate and there is limited correlation between self-assessment, quantity of sanitary protections required, and duration of menses with actual blood loss. The alkaline-haematin method is perhaps the most accurate method for quantification of MBL. Studies using this method indicate that maximum normal menstrual blood flow is 60–80 mL, with a mean of 30 mL. It involves the collection of all soiled sanitary products, incubation and absorbance measuring with a spectrophotometer to quantify blood loss represented by haematin-converted haemoglobin. However, this method is inconvenient, laborious and costly in clinical practice. In addition, there has been doubt as to the validity of the clinical usefulness of the 80 mL criterion. In a later study, the proportion of women with haemoglobin less than 12 g/dL and low ferritin levels were only significantly increased in the group with MBL >120 mL.

Pictorial blood assessment chart (PBAC) is a semi objective method that takes into account the number of towels and tampons used, the degree to which individual items are soiled, and the passage of clots and flooding (Fig. 1). From this information a score is ascertained, and a score >100 has a sensitivity and specificity of >80% for HMB (menstrual blood loss of 80 mL or more with the alkaline-haematin method). A drawback of the chart is that it should be completed prospectively for greater accuracy, as patient recall may be unreliable; therefore, results are not available at the initial consultation. In addition, the validity of the chart and its ease of use have been questioned by some investigators. Nevertheless, the PBAC is a simple and inexpensive tool that has been adopted readily for use in research as well as in clinical practice.

The menstrual cup is an alternative to using sanitary towels and tampons. A high satisfaction and continuation rate has been reported among users. The menstrual cup rated significantly higher than towels and tampons for comfort, quality, menstrual blood collection, appearance and preference in a randomised crossover trial in 124 women. This may provide a simple and more accurate method of measuring MBL, although studies have not yet been published to evaluate this method in women with HMB.

Bleeding history to assess other bleeding symptoms helps to discriminate those women who may have an underlying IBD and require further hematological investigation. Bleeding score is a systematic assessment that evaluates the severity of each bleeding symptom. There are several bleeding scores used in clinical practice, including the modified Molecular and Clinical Markers for the Diagnosis and Management of Type 1 VWD (MCMDM-1) and the International Society on Thrombosis and Hemostasis Bleeding Assessment Tool (ISTH BAT). The condensed MCMDM-1 bleeding score is relatively quick and straightforward to use, and has a sensitivity of 100% and specificity of 87% for the detection of VWD in the primary care setting. However, the validity of these bleeding scores has not been assessed in women with HMB.



Aetiology of heavy menstrual bleeding

The FIGO classification uses the acronym PALM-COEIN to categorise the important causes of HMB: polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial, iatrogenic; and not yet classified. In general, the components of the PALM group are discreet entities that can be visualized with imaging techniques, or through histopathological assessment. Conversely, entities within the COEIN group cannot be visualized through imaging or defined by histopathology.

Up to 20% of women with HMB have an underlying inherited bleeding disorder (IBD). HMB since menarche and a family history are predictive of an IBD. In addition, there may be a personal history of one or several additional bleeding symptoms (Table 1). The most common IBD resulting in HMB is Von Willebrand Disease (VWD), which occurs in up to 1% of the population. However, the prevalence of VWD in women with HMB is 13% (confidence intervals 11%, 15.6%) from a systematic review of 11 studies (Fig. 2). In a study of 150 women with HMB, the frequency of bleeding symptoms (including bruising, bleeding after tooth extraction and

postpartum and postoperative bleeding) was significantly higher in women with VWD compared to women without IBD (Table 2).

Inherited defects of platelet function are a heterogeneous group of disorders that result in bleeding symptoms that range from mild bruising to severe mucocutaneous haemorrhage. Platelet function disorders (PFDs) are classified according to their effect on the various steps of platelet thrombus formation including initiation, extension and cohesion, or based on their specific structural or functional deficiency. Mild PFDs are underestimated in women with HMB. Laboratory diagnosis of these disorders requires specialised laboratory facilities leading to under diagnosis in general.

Table 1: Additional bleeding symptoms indicative of an inherited bleeding disorder

- Epistaxis (usually bilateral and lasting >10 minutes duration)
- Notable bruising without injury (>2 cm in diameter)
- Minor wound bleeding (i.e. from trivial cuts lasting longer than 5 minutes)
- Bleeding of the oral cavity or gastro-intestinal tract without a lesion
- Excessive or prolonged bleeding following dental extraction

- Unexpected postsurgical bleeding
- Haemorrhage from ovarian cyst or corpus luteum
- Postpartum haemorrhage (especially delayed onset >24 hours)

The relatively few studies that assessed platelet function in women with HMB indicate that it is more common than VWD in such women. A multicenter study in the US included 232 women with unexplained HMB and a pictorial blood assessment chart (PBAC) score >100. The frequency of PFDs was 51.5%, (versus 17.3% in the control group). Carriers of hemophilia and women with other rare factor deficiencies (factor(s) V, VII, X, XI) may also present with HMB, and these are important diagnoses to establish, as they can have important implications in reproductive health.

HMB is also common in women taking anticoagulation medication. In a study of 90 Swedish women taking oral anticoagulants (OA)

the duration of menses increased from 5.6 to 6.1 days, with an increase in the incidence of HMB (no specific definition supplied) from a baseline of 44% to 71%. A more objective assessment of change in MBL using a PBAC was applied to fifty-three women of reproductive age receiving OA. The mean duration of menses increased from 5 to 7 days, and thirty-one women (66%) had HMB (defined by PBAC score >100) after the commencement of OA treatment. The proportion of women who experienced flooding and clots during menstruation also increased.

Direct oral anticoagulants (DOACs) were recently introduced for prevention and treatment of VTE, and for stroke prevention in atrial fibrillation. A recent meta-analysis of gender-related bleeding rates suggests that DOAC therapy in women is associated with increased rate of HMB compared to Warfarin.

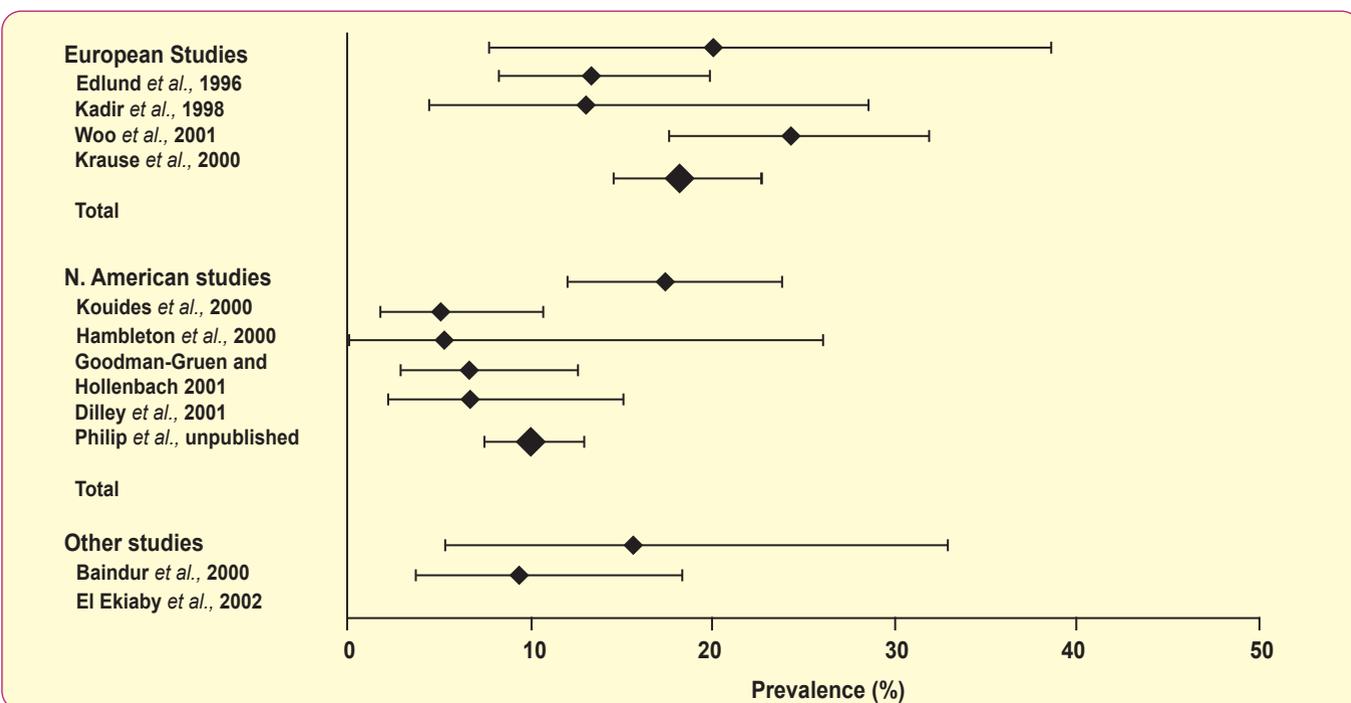


Fig. 2. Prevalence rates of von Willebrand Disease in women with HMB.

Table 2: Frequency of bleeding symptoms in women with HMB; with von Willebrand disease versus those with no inherited bleeding disorder.

	Total (n - 150)	No bleeding disorders (n - 123)	von Willebrand's disease (n - 120)	p value
Bleeding symptoms				
Bruising	88 (58.7%)	66 (53.7%)	16 (80%)	0.05
Nose bleeding	22 (14.7%)	17 (13.8%)	5 (25.0%)	0.20
Gum bleeding	54 (36%)	41 (33.3%)	9 (45.0%)	0.45
Bleeding after tooth extraction*	13/98 (13.3%)	6/81 (7.4%)	6/13 (46.2%)	0.001
Postoperative bleeding*	18/109 (16.5%)	7/90 (7.8%)	8/13 (61.5%)	<0.001
Postpartum bleeding*	29/27 (29.9%)	17/80 (21.3%)	8/13 (61.5%)	0.005
Symptom score				
0	40 (26.7%)	39 (31.7%)	0	
1-2	78 (52.0%)	65 (52.9%)	11 (55.0%)	
3-4	28 (18.7%)	17 (13.8%)	7 (35.0%)	
5-6	4 (2.7%)	2 (1.6%)	2 (10.0%)	<0.001
Median (range)	1 (0-5)	1 (0-5)	2 (1-5)	<0.001

* Expressed as a percentage of women who had the event or procedure.

HMB in adolescents is most often related to an immature hypothalamic-pituitary axis, which results in anovulatory cycles and months to years of unpredictable ovulation after menarche. The establishment of regular cyclic productions of progesterone appears to lag behind gonadotrophin-releasing hormone and estrogen. Up to 85% of cycles are anovulatory in the first year following menarche. Thus, adolescents with IBD suffer more from HMB; often with anemia and episodes of acute menorrhagia requiring blood transfusion.

Investigations

Since HMB may be indicative of underlying uterine pathology, a full gynecological evaluation is required prior to instigating treatment. This usually entails pelvic examination, transvaginal ultrasound, and/or histological sampling of the endometrium depending on the initial findings.

In women whose symptoms warrant further hematological assessment, the initial investigations should include a full blood count, ferritin to exclude iron deficiency anemia and blood group. Correction of iron depletion and treatment for anemia is an important aspect of management. Correction of iron status alleviates symptoms, leads to improvement of quality of life, reduces the requirement for blood transfusion and reduces operative morbidity.

A full hemostasis evaluation is neither necessary nor practical for all women with HMB. However, it should be considered in women with suspected IBD (e.g. those with family history, HMB since menarche, or a high bleeding score). Initial bleeding state work up should include activated partial thromboplastin time (aPTT), prothrombin time (PT), assessment of VWF (measured with ristocetin cofactor activity and antigen) and FVIII levels. If these tests are normal, platelet function (aggregation and release) tests should be performed if available. Further hemostatic investigations, including testing for specific coagulation factor deficiencies are considered on the basis of the degree and severity of bleeding symptoms (and bleeding score). Collaboration between the gynecological team and hematology department are important to ensure the bleeding status has been thoroughly investigated in women with suspected IBD.

Management of heavy menstrual bleeding

The management of HMB will depend on a woman's age; desire to maintain fertility, the presence or absence of pelvic pathology, and/or underlying IBD.

Medical management

Non-surgical management for HMB entails both hormonal and hemostatic therapies. Nonsurgical therapies allow a woman to retain reproductive potential, improve quality of life, and reduce the burden of unnecessary surgical procedures.

(I) Hormonal

(a) Progestogen-releasing intrauterine systems

The levonorgestrel-releasing intrauterine system (LNG-IUS) provides the most effective non-surgical treatment for HMB and is

considered first line treatment if contraception is required. The data is evident from numerous randomised controlled trials (RCTs) and systematic reviews. The mean reported reduction in PBAC scores from 17 RCTs involving 712 patients, and 10 non-randomised trials involving 380 patients exceeded 70% during the first 3 months of treatment, with further reductions during the first year of treatment that were sustained throughout the four years of use. Where reported, the one-year continuation rate was 71%. The need for further surgical intervention, although inconsistently reported across studies, was around 9%. In another systematic review, five studies that reported efficacy of LNG-IUS were included. Two compared the LNG-IUS with combined oral contraceptive (COC) pill, and found that the decrease in MBL was significantly greater (83% versus 68%, $p = 0.02$, and 87% versus 35%, $p = 0.01$) in the LNG-IUS versus COC pill, respectively after 12 months of treatment.

LNG-IUS has proven benefit in women with IBD and those taking oral anticoagulant therapy. LNG-IUS has been assessed in women with leiomyoma ($n = 484$ patients), and adenomyosis ($n = 72$ patients). The available data suggest that the LNG-IUS is also effective for managing HMB in women with these pathologies. In a RCT of the LNG-IUS and low dose COC pill in women with HMB and leiomyoma, the reduction in MBL was more significant in the LNG-IUS group, measured with both the alkaline haematin and PBAC score.

The main adverse side effects reported with the use of LNG-IUS include irregular spotting and hormonal symptoms; breast tenderness, abdominal/pelvic pain, headache and ache. The National Institute for Health and Clinical Excellence (NICE) have advised that up to 60% of women discontinue use of LNG-IUS within 5 years due to unscheduled bleeding, pain and / or systemic progestogenic adverse effects, when provided for contraception. However, discontinuation due to hormonal side effects are rare, as these symptoms often resolve spontaneously by 6 months of use and in general LNG-IUS has high rates of patient satisfaction and tolerability when its use is for treatment of HMB. In the systematic review the 1-year continuation rate of LNG-IUS to treat HMB was 79%, reported from 14 studies. Expulsion of the IUS from the uterine cavity can occur after insertion, usually within the first 6 weeks. Women are encouraged to check the threads by digital examination, or if they are not happy to do so, by speculum examination 6 weeks following insertion to ensure the IUS is correctly in place. Uterine perforation is a rare but potentially serious complication of LNG-IUS insertion, occurring in 1 in 1000 cases. The LNG-IUS is contraindicated in unexplained vaginal bleeding and uterine sepsis.

(b) Combined hormonal contraceptives

Combined oestrogen and progestin oral contraceptive pills are considered safe, effective and well tolerated, and have many non-contraceptive benefits. In addition to the oral pill, combined contraceptives can also be administered via dermal patch, or vaginal ring. They reduce MBL by inducing shorter, regular shedding of a thinner endometrium, as well as reducing menstrual pain or dysmenorrhea. CHCs are of particular benefit in young women and adolescents who require contraception in addition to management of HMB.

A systematic review of eight studies among 438 women, including 6 RCTs (5 in the COC pill, 1 in the vaginal ring), assessed the effect of combined contraceptive in treatment of HMB. All six studies reported a reduction in MBL (measured through either the alkaline-haematin method or PBAC score) following 7 cycles or 6 months of treatment. However, hormonal side effects including breast tenderness, headache, mood changes/depression, nausea/vomiting and weight gain resulted in 1-year continuation rates that ranged between 72–84%. The new estradiol valerate and dienogest (E2V/DNG) COC pill is the only formulation that has provided sufficient evidence to receive U.S Food and Drug Administration (FDA) and European Union (EU) approval to treat HMB. Two placebo-controlled trials assessed efficacy of E2V/DNG in 269 women with HMB for 7 menstrual cycles. A pooled analysis reported a significant reduction in median MBL by the end of treatment relative to baseline (88% in the E2V/DNG treatment group versus 24% in placebo). Combined hormonal contraceptives are not suitable for all women, and are contraindicated in women with increased risk of VTE, migraine with aura, and breast cancer.

(c) Cyclical oral progestogens

The available data on short-phase (administered for <14 days per cycle) oral progestogens is generally inconsistent, or shows limited efficacy in reducing MBL. In a systematic review, involving 157 patients in 4 studies, the median MBL reduction ranged from between 2% to 30% with a 6-month treatment course. One study that assessed efficacy of short-phase medroxyprogesterone acetate (MPA) 10 mg daily reported mean PBAC score reductions of 25% and 41% after one and two months of treatment, respectively, but a 12% mean increase after 3 months of treatment. In one comparison study with tranexamic acid, short-phase progestogens were associated with a 20% increase in MBL ($p < 0.001$). In contrast to short-phase, the longer course (>3 weeks per cycle) oral progestogens consistently reduced PBAC scores in the systematic review including 4 studies among 178 women.

In a randomised trial comparing the LNG-IUS to norethisterone (5 mg twice daily) the reported median MBL reduction was 63%, and 78% during cycles 1 and 3 of treatment. Adverse side effects reported with oral progestogens include headaches, breast tenderness and erratic bleeding problems. Of note, none of the studies included in the systematic review were placebo-controlled studies and thus it was not possible to ascertain whether these side effects could be attributed to the placebo effect. However, the discontinuation rate with long-phase cyclical oral progestogen treatment is high (78% after 3 months), suggesting that tolerability is a problem with this method of treatment.

(d) Progesterone only contraceptives

The progesterone only pill (POP) taken continuously without a break is usually associated with irregular and unpredictable MBL, therefore not usually considered a treatment for HMB. However, it is a safer alternative to oestrogen containing hormonal contraceptives for some women. Desogestrel containing POP may induce amenorrhea in up to 20% of women, and may be considered an effective treatment for women in whom the COC pill is contraindicated.

Intramuscular or subcutaneous injection of high dose depot medroxyprogesterone acetate (DMPA) can induce amenorrhea in up to 50% of women. Injection is given every 12 weeks to ensure exposure to progesterone and contraceptive efficacy. However, due to follicular suppression, long-term oestrogen production is reduced resulting in reduction in bone mineral density and increased risk of fracture, limiting their use in adolescent girls and perimenopausal women with HMB.

The progesterone-only subdermal implant is a highly effective form of long-acting contraception that alters menstrual bleeding patterns and may result in amenorrhea in a small proportion of women. However, their use as a treatment for HMB has not been studied.

(e) Danazol

Danazol, a synthetic androgen that has anti-oestrogen and anti-progestogen actions, is used primarily for the treatment of endometriosis. It is rarely used for the treatment of HMB due to perceived and real adverse effects including low mood, irritability, weight gain, hirsutism and irreversible voice changes. In the systematic review, ten studies in 170 women reported mean MBL reduction of >80% assessed through the PBAC and alkaline-haematin method. The reported duration of treatment was 3 months or less in most studies due to concerns regarding the above side effects.

(f) Ulipristal acetate

Ulipristal acetate is a selective progesterone receptor modulator (SPRM) that is clinically proven to reduce size of uterine fibroids (leiomyoma and myomas), reduce MBL (or induce amenorrhea), and improve quality of life. In the PEARL IV study, an RCT involving 46 centers across Europe, women with symptomatic fibroids (at least one fibroid >3 cm, and non >12 cm, PBAC score >100, uterus size <16 weeks gestation) were administered 10 mg/day ulipristal acetate or placebo for up to four three month courses. Treatment with 10 mg demonstrated amenorrhea in 89%, 88% and 90% for the 131, 119 and 107 women who received treatment course 2, 3 and 4 respectively. In addition there was significant reduction in fibroid volume from baseline of -63%, -67% and -72% after treatment courses 2, 3 and 4 respectively. Common side effects reported included headache and breast tenderness. In some patients abnormal bleeding (prolonged, frequent or irregular) was reported in women with submucous fibroids, which could limit the efficacy of Esmya® at controlling bleeding. Endometrial thickness increased after the first course (>16 mm in 7.4%), but returned to below screening levels (4.9%) in subsequent treatment courses.

(ii) Hemostatic therapies

Tranexamic acid an antifibrinolytic agent, has been shown to significantly reduce MBL in women with HMB. However, it does not reduce the duration of menses or regulate the cycle. In a systematic review of 12 studies involving 690 women, the reduction in MBL ranged from 34% to 56% in those treated with >3 mg tranexamic acid for 5 days. In a prospective crossover trial in women with IBD and HMB, intranasal desmopressin was compared with oral tranexamic acid. There was a significant reduction in PBAC scores (-106 (95% confidence interval; 131–81) in the tranexamic acid group.

In addition, tranexamic acid has a superior reduction in MBL over three cycles compared to mefenamic acid (54% versus 10%, $p < 0.001$). In the systematic review comparing 5 studies of tranexamic acid use versus placebo, the mean MBL reduction was 26–54%.

DDAVP (1-deamino-8-D-arginine) is a synthetic vasopressin analogue that enhances endogenous levels of VWF and FVIII. It is specifically indicated to treat HMB in women with mild IBD, mainly type 1 VWD and carriers of haemophilia A. A test does is usually required to assess effectiveness prior to instigating treatment. DDAVP can be administered easily via a nasal spray, which has been shown to significantly reduce PBAC scores. Combined use of DDAVP and oral tranexamic acid is more effective (greater reduction in PBAC score), compared to use of DDAVP alone. DDAVP has also proved to be an effective treatment of HMB in women a prolonged bleeding time, but no definably IBD. Women with severe IBD (e.g. type 3 VWD) may require regular prophylactic treatment with factor concentrates for several days during menstruation, or throughout their cycle to prevent ovulation bleeding.

Surgical interventions for treatment of heavy menstrual bleeding

Surgical procedures are offered usually when medical therapies have failed to provide adequate treatment, in women who have no desire to preserve ongoing fertility. They include endometrial ablation and hysterectomy. Rates for surgical interventions for HMB in women are 14.3 per 10,000 in the UK.

(a) Endometrial ablation

Endometrial ablation employs a variety of methods to destroy the endometrium. They are frequently used as an alternative to hysterectomy as they are minimally invasive, with shorter operating time, recovery period, and associated with fewer complications. First-generation techniques included rollerball ablation, transcervical resection and laser ablation performed under direct hysteroscopic vision, performed under light general anaesthetic. Second-generation techniques involve devices that destroy the endometrium using the application of high temperature fluid within a balloon (Thermachoice®), bipolar radiofrequency electrical energy (Novasure®) or less frequently cyroablation (HerOption®). The second-generation techniques are generally safer, can be performed under local anaesthetic as an outpatient procedure and involve shorter length of hospital stay.

A meta-analysis of RCTs found that second-generation techniques were at least as effective, in terms of patient satisfaction. However, the majority of these studies did not report objective measurement of MBL through PBAC scores or alkaline-haematin method. Bipolar radio frequency ablation demonstrated a higher rate of amenorrhoea compared with thermal balloon ablation (odds ratio (OR) 2.51, 95% CI: 1.53–4.12; $p < 0.001$), free-fluid ablation (OR 2.77, 95% CI: 1.49–5.14; $p = 0.004$) and cryoablation (OR 0.2, 95% CI: 0.09–0.49; $p = 0.002$). In a meta-analysis of 14 RCTs comparing first and second-generation endometrial ablation, the number of women requiring hysterectomy was lower for second compared to first-generation techniques. Long-term outcome data are still lacking

on second-generation techniques, an important consideration as the early reported benefits may not be sustained, or unknown complications may become apparent. Endometrial ablation has been used successfully to treat HMB in women with IBD; twelve women who underwent the procedure reported a significant reduction in PBAC score, improved haemoglobin levels, and quality of life scores at 32 month follow-up post-ablation ($p < 0.01$).

(b) Hysterectomy

Hysterectomy remains the most common major gynaecological operation, and by the age of 60, 1 in five women in the UK, and 1 in 3 women in the US have undergone hysterectomy. It is a major surgical procedure and carries risks of serious morbidity and death. A mortality rate of 0.38 per 1000, a major operative complication rate of 3%, and post-operative complication rate of 9% have been reported. Rates of hysterectomy have fallen, as expected, due to the advent of novel techniques with their reduced risk, rate of complications, and shorter recovery. However, it is still regarded as being definitive treatment, when all other measures have failed. Hysterectomy is performed via abdominal, vaginal or laparoscopic route. The choice depends of the size of the uterus/fibroids, the presence of other gynaecological abnormality, and the surgeon's experience. Vaginal and laparoscopic hysterectomy have a faster recovery and lower operative morbidity compared to abdominal hysterectomy.

Conclusion

HMB is an important global issue that impacts on a woman's quality of life, work and social functioning. The common aetiologies were defined by FIGO into two categories depending on the presence or absence of discreet "PALM" entities. Coagulopathy, including both inherited and acquired bleeding disorders secondary to anticoagulant therapy also play an important role in the underlying pathophysiology of HMB.

The assessment of HMB entails a detailed menstrual and gynaecological history, as well as bleeding history. MBL measurement using the PBAC score is a practical and easy method, which can also be used to help monitor response to treatment. Investigations include gynaecological to exclude pelvic pathology and hematological to exclude an IBD, and identify and treat women with iron deficiency anemia.

There is a range of medical alternative therapies available to treat HMB, which are usually offered prior to undergoing a surgical procedure if the woman is amenable. The most effective method is the LNG-IUS that results in the highest reduction of MBL and patient satisfaction rates. Fibroid disease of the uterus can be successfully treated with ulipristal acetate. Endometrial ablation is an alternative, safer option to hysterectomy, which is still used as definitive treatment, when other methods have failed.

Ref. : J. Davies, R.A. Kadir / *Thrombosis Research* 151, Suppl. 1 (2017) S70–S77



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