An Update on the Management of Heavy Menstrual Bleeding

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Heavy menstrual bleeding is a common problem in reproductive-aged women. It impairs the quality of life and is a common cause of anaemia. Pharmaceutical interventions continue to be first-line treatment, but when these fail it is usual to offer surgical options. In the early 1990s, at least 60% of women presenting with heavy menstrual bleeding would have a hysterectomy as the treatment of choice. Since then, newer therapeutic modalities such as the levonorgestrel intra-uterine device and endometrial ablation techniques have become available. In this article, we provide an overview of the diagnostic and therapeutic options and review the efficacy and acceptability of the pharmaceutical and surgical treatments that are available worldwide and locally.

Introduction

The National Institute for Health and Clinical Excellence (NICE) published a management guideline on heavy menstrual bleeding (HMB) in 2007[1]. It was defined as excessive menstrual blood loss that interferes with the woman's physical, emotional, social, and material quality of life, and which can occur alone or in combination with other symptoms. The current definition differs from previous definitions used in research studies[2], which quantified menorrhagia as more than 80 ml of blood loss per cycle.

HMB is a common problem. According to a postal survey involving 1513 women in the UK, in a 12-month period the incidence of menorrhagia was 25%[3]. Patients with HMB make up to 12% of gynaecological referrals. In the early 1990s, at least 60% of women presenting with HMB would have hysterectomy as the treatment. Since then, newer modalities of treatment such as hormonal intra-uterine devices and different techniques for endometrial ablation have become available. These have provided safe and effective alternatives.

This review provides an overview of the diagnosis and management of menorrhagia, based on the NICE guidelines for HMB published in 2007[1], the Cochrane library and a local attitudes study[4].

History and Physical Examination

In assessing patients presenting with HMB, a history and physical examination can (1) define the nature of bleeding, (2) define its likely pathology, and (3) identify associated ideas, concerns, expectations, and needs.

A diagnostic study in UK involving 2500 women with HMB showed that majority (50%) had no histological abnormality that could be implicated as a cause. Uterine fibroids (30%) and polyps (10%) are the most commonly found pathology[5]. Rarer causes include endometrial hyperplasia, cancer, or medical conditions including coagulation and thyroid disorders. Remarkably, a systematic review in women with menorrhagia found that the prevalence of inherited blood disorders, such as von Willebrand disease, was up to 13%[6].

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Investigations

Investigations should therefore aim to differentiate dysfunctional uterine bleeding from the above-mentioned pathologies and assess the impact of HMB on the physical, mental, and social life of the patient. These include:

1. Blood tests: a complete blood count can reveal anaemia, and can be used to monitor response to treatment.

2. Imaging studies: these are performed when (a) the uterus is palpable abdominally, (b) a pelvic mass is noted on vaginal examination, and (c) medical treatment fails. Pelvic ultrasound should be the first-line imaging modality to detect structural uterine abnormalities. In a previous systematic review[7], it was shown to have variable sensitivity (48-100%) and specificity (12-100%). Notably, saline infusion sonography further improved the detection of pathologies inside the uterine cavity. Magnetic resonance imaging should be reserved for patients in whom ultrasound provided indeterminate results, or when malignancy or adnexal pathology was suspected.

3. Endometrial biopsy: this should be undertaken in women aged 40 years or more with treatment failure, persistent intermenstrual bleeding, or to exclude endometrial cancer or atypical hyperplasia. The latter could be encountered in patients who were obese, had polycystic ovary syndrome, and those with a family history of breast or endometrial cancer.

4. Hysteroscopy: this is less sensitive than ultrasound in detecting fibroids, but more sensitive in detecting endometrial polyps and endometrial cancer (sensitivity 86%, specificity 99%)[8]. Women often found this procedure 'unpleasant' and in many, the examinations are aborted due to patient discomfort.

5. Other tests:
   - Cervical smear should be taken when the woman is due for cervical cancer screening.
   - Tests for coagulation disorders should be considered in women with menorrhagia since menarche, or if there is a suspicious personal or family history.
   - Ferritin level and female hormone levels should not be routinely tested. Thyroid function test should only be carried out when other features of such disease are present.

Treatment

Iron deficiency anaemia due to HMB should be treated accordingly with iron supplements. According to a local survey, medication was the preferred first-line treatment in 87% of Chinese women with menorrhagia[4]. Pharmaceutical treatment can be broadly divided into hormonal and non-hormonal, as shown in Table 1.

Danazol, also known as 17alpha-ethinyl testosterone, and depot progestogen are less commonly used to treat HMB, because of side-effects (virilisation with Danazol and irregular cycles and amenorrhoea with depot-progestogen injections).

The levonorgestrel intra-uterine device (LNG-IUD) releases 20 µg of the drug each day (Fig), and prevents endometrial proliferation and thickening of cervical mucus, and occasionally suppresses ovulation. Mean menstrual blood loss reduction ranges between 71% and 96% when used for 6 months or longer[9].

In a previous cohort study in Chinese women with HMB, the LNG-IUD was highly acceptable, the main side-effect being prolonged spotting. Efficacy was good and the reduction in menstrual blood loss was up to 95%, when used for up to 6 months[10]. However, only 3% of Chinese women with HMB considered the LNG-IUD as first-line treatment, while 45% would choose it as second-line treatment when other drug therapy failed[4].

The NICE guideline[1] recommended consideration of pharmaceutical treatment when there was no structural or histological abnormality, or for fibroids less than 3 cm in diameter without cavity distortion. The effectiveness of the LNG-IUD, non-steroidal anti-inflammatory drugs, tranexamic acid and the combined oral contraceptive pills were similar. However, the LNG-IUD was the preferred treatment option whenever long-term treatment was required, or when the patient opted for long-term reversible contraception. This was also the recommendation of the NICE guideline that advocated its use for at least 12 months.

Table 1. Pharmaceutical treatment options

Treatment option	Estimated mean blood loss reduction	Remarks
Non-hormonal		
Tranexamic acid (2.0-4.5 g daily for 4-7 days per cycle)	34-59% over 2-3 cycles	No reports of deep vein thrombosis
Non-steroidal anti-inflammatory drugs	20-49%	Evidence lacking for efficacy in presence of fibroids
Hormonal		
Combined oral contraceptive pills (30 μg ethinyl estradiol and 150 μg levonorgestrel for 21 days per cycle)	43%	Provide contraception as well
Norethisterone 15 mg per day from D5-26 of each cycle when used long term (at least 3 months)	83%	Requires a long course regimen rather than luteal phase progestogen alone Limited by tolerability
Gonadotrophin releasing hormone analogues	Significantly	89% amenorrhoea Reduction in size of fibroids Limited by side-effects Add-back therapy prevents adverse effects, does not affect efficacy
Levonorgestrel releasing intrauterine device	71-96% when used for 6 months or longer	Main side-effects being prolonged spotting Low acceptance rate for the first-line treatment An option when long-term treatment or reversible method of contraception is required

Surgical Options

Surgical options for treating HMB may or may not entail hysterectomy. Non-hysterectomy surgery includes: endometrial ablation, myomectomy, and uterine artery embolisation in the presence of fibroids. Surgery, especially hysterectomy, was shown to reduce menstrual bleeding at 1 year more effectively than medical treatments, but conferred no advantage in terms of quality of life compared to the LNG-IUD.

Data from a previous randomised study showed that the LNG-IUD and endometrial ablation had similar efficacy in reducing menstrual blood loss[11]. However, a local randomised study in Chinese women with menorrhagia yielded a higher success rate using endometrial ablation than the LNG-IUD. The former also conferred a perception of better general and mental health[12]. Compared to oral medications, endometrial resection was significantly more effective in controlling bleeding and less likely to cause side-effects[13].
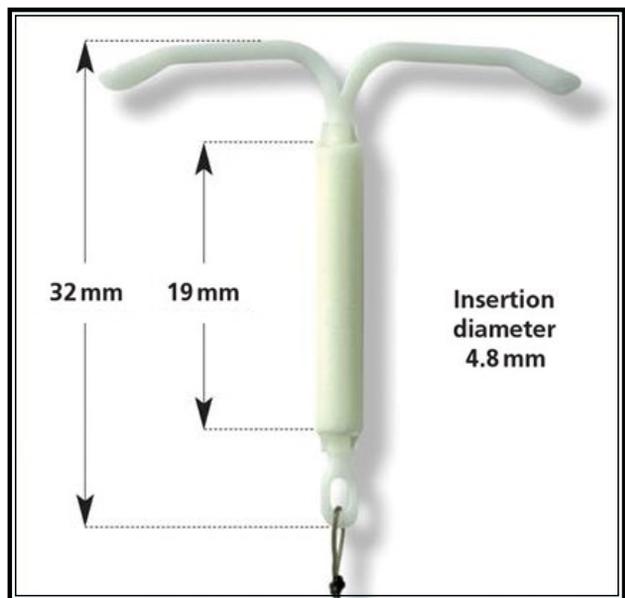

Figure. The physical structure of the levonorgestrel intra-uterine device; 20 μg of levonorgestrel is released daily

Non-hysterectomy Surgery

Endometrial ablation aims to destroy the

Table 2. Different endometrial ablation techniques

First-generation	Second-generation
- Rollerball endometrial ablation - Transcervical resection of the endometrium	- Impedance-controlled bipolar radiofrequency ablation - Thermal balloon endometrial ablation - Microwave endometrial ablation - Endometrial cryotherapy - Free fluid thermal endometrial ablation

endometrium along with the superficial layer of the myometrium, thereby reducing or stopping menstrual loss.

First-generation ablative techniques required hysteroscopic guidance (Table 2). They were associated with longer operating times, higher risk of fluid overload, uterine perforation, cervical lacerations, and haematometra, compared to second-generation ablation techniques. Overall, the success rates and complication profiles of newer techniques compare favourably with transcervical resection of the endometrium, but are associated with higher rates of equipment failure. Second-generation techniques are suitable for women who have a uterus that is not greatly enlarged and devoid of large fibroids that distort the cavity[14].

In the MISTLETOE study[15], it was shown that techniques of endometrial destruction, namely by laser, loop diathermy, rollerball and radiofrequency ablation were associated with low morbidity and mortality.

Endometrial ablation provides a safe and effective alternative to hysterectomy. While the latter was less invasive, of shorter duration, involved faster recovery and shorter hospital stays, hysterectomy conferred more improvement in HMB and satisfaction rates that lasted up to 4 years. Patients should continue reliable contraception after endometrial ablation[16].

In women who have completed their families, and whose quality of life was severely affected by HMB, endometrial ablation may have a role as a first-line treatment and should be considered in patients with a normal uterus or fibroids of less than 3 cm in diameter. According to a local survey however, only 3% of Chinese women with HMB consider endometrial ablation as their first-line treatment[4]. In Hong Kong, several second-generation endometrial ablation techniques were used (thermal balloon, microwave endometrial ablation and impedance-controlled bipolar radiofrequency ablation). None of these were very popular and only the impedance-controlled bipolar radiofrequency ablation (Novasure) is in use now.

Hysterectomy

Hysterectomy has been the traditional surgical treatment for HMB. However, it is associated with significant morbidity and occasionally mortality. In a local study involving 200 Chinese women, none of them preferred hysterectomy as the first-line treatment. Even if medical therapy failed, only 5% would prefer hysterectomy[4].

Hysterectomy should be considered only when (1) other treatment options have failed, (2) there is a wish for amenorrhoea, and (3) the woman no longer wishes to retain her uterus and fertility, and has been fully informed of risks and alternatives.

Surgical Approach

Hysterectomy can be performed abdominally, vaginally, or laparoscopically. The abdominal approach (AH) was the traditional one for gynaecological malignancy, when other pelvic pathology (endometriosis or adhesions) was present, or in the context of an enlarged uterus. The vaginal approach (VH) was originally used only for prolapse. However, the latter has become more widely used for menstrual abnormalities, such as dysfunctional uterine bleeding, provided the uterus is not grossly enlarged[17].

Hysterectomy can also be undertaken laparoscopically. Depending on the part of operation being performed laparoscopically, it is further subcategorised into three types[18]:

(1) Laparoscopic-assisted vaginal hysterectomy is where part of the hysterectomy is performed laparoscopically and part vaginally, but the former

component of the operation does not involve division of the uterine vessels.

(2)   Laparoscopic hysterectomy (LH) in which uterine vessels are ligated via the laparoscope, and part of the operation is performed vaginally.

(3)   Total LH is where the entire operation (including suturing of the vaginal vault) is performed laparoscopically, and there is no vaginal component.

When performed laparoscopically, hysterectomy requires greater surgical expertise. Its main advantages are that it facilitates: (1) the diagnosis and treatment of other pelvic diseases, such as endometriosis, (2) adnexal surgery, including the removal of the ovaries, (3) securing intraperitoneal haemostasis, and (4) more rapid recovery from surgery compared to AH[19].

Individual assessment is essential when deciding the route of hysterectomy. The following factors need to be taken into account: (a) presence of other gynaecological conditions or disease, (b) uterine size, presence and size of uterine fibroids, (c) mobility and descent of the uterus, (d) size and shape of the vagina, and (e) history of previous surgery.

When technically feasible, VH should be performed in preference to AH, because of more rapid recovery and fewer postoperative febrile episodes. Where VH is not possible, LH has some advantages over AH (including less operative blood loss, more rapid recovery, fewer febrile episodes, as well as fewer wound or abdominal wall infections). However, these advantages are offset by longer operating times, and more bladder and ureteric injuries. In one study, there were no advantages of LH over VH, and the former took longer[17]. Under circumstances such as morbid obesity, or the need for oophorectomy during VH, the laparoscopic approach should be considered whenever appropriate expertise is available.

Total Versus Subtotal Hysterectomy

When hysterectomy is opted for both the total (removal of the uterus and the cervix) and subtotal (removal of the uterus and preservation of the cervix), operations should be discussed with the patient.

Subtotal hysterectomy is significantly faster, blood loss and postoperative febrile morbidity are reduced, but ongoing cyclical vaginal bleeding is more likely for up to a year after surgery[20]. One rationale for total as opposed to subtotal hysterectomy is to avoid the risk of cervical cancer, as the cervix is also removed. The risk of cervical cancer in women who have had subtotal hysterectomy is fairly low. According to a Danish study, the risk of cancer in the cervical stump of patients undergoing subtotal hysterectomy was low and not higher than that of the general population[21]. Moreover, this risk of cervical stump cancer is not an issue for women in countries that have routine cervical screening programmes. Nevertheless, it may be prudent to advise against subtotal hysterectomy in women with a history of high-grade cervical lesions, a fear of developing cervical cancer, or cervical cancer screening that is not up to date or unlikely to occur regularly[20].

Removal of Ovaries (Oophorectomy) with Hysterectomy

Removal of healthy ovaries at the time of hysterectomy should not be undertaken unless explicitly requested and consented to[1]. Whether to perform a prophylactic bilateral oophorectomy at the time of a hysterectomy in premenopausal women, is currently at the discretion of the clinician and not based on evidence from randomised controlled studies. The benefits or harmful effects of bilateral oophorectomy remain unclear. Therefore this option should be approached with great caution. Due consideration should be given to the individual's baseline risk of developing breast or ovarian cancer, coronary heart disease, and osteoporotic hip fracture[22]. Women with a significant family history of breast or ovarian cancer should be referred for genetic counselling prior to opting for oophorectomy. If removal of ovaries is being considered, the impact on well-being, and the possible need for hormone replacement therapy should also be discussed[1].

The choice of surgical treatment should be jointly decided by the woman and her clinician, and made after informed discussion about outcomes, the relative benefits and possible disadvantages, and viewed in the context of all other treatment options.

Conclusion

Heavy menstrual bleeding is a common gynaecological condition. Given the large number

of treatment modalities available for this condition, gynaecologists should discuss the most suitable options with the patient and her relatives. Such discussion should take into account the patient's wish, the cause and severity of the menorrhagia, and the likely response to alternative treatments. Non-surgical treatment should always be considered first before resorting to surgery.

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