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Heavy Menstrual Bleeding

Definition

Heavy menstrual bleeding (HMB) is defined menstrual blood loss $\geq 80\text{ml}$, or menstrual bleeding longer than 7 days, or both

Clinical assessment

<p>History</p>	<ul style="list-style-type: none"> • Bleeding pattern and whether it is considered abnormal • History of associated symptoms, such as persistent intermenstrual bleeding, pelvic pain and/or pressure symptoms These symptoms may indicate uterine cavity abnormality, adenomyosis or uterine fibroids • Factors that may alter treatment choice e.g. medical comorbidities, prior failed treatment
<p>Examination</p>	<ul style="list-style-type: none"> • If associated symptoms are present, physical examination is indicated to assess pelvic pathology

Investigations

Laboratory tests

- Complete blood count: for all women with HMB
- Coagulation profile: when coagulation disorders are clinically suspected e.g. HMB with menarche
- Thyroid function test: if signs and symptoms of thyroid disease are present

Routine assessment of serum ferritin, hormonal profile, or thyroid function is not indicated

Offer office hysteroscopy

- It is indicated if fibroids or endometrial pathology is suspected e.g.
 - ① Persistent intermenstrual bleeding
 - ② Risk factors of endometrial pathology
- Office hysteroscopy is the standard using vaginoscopy approach (the scope is 3.5 mm or less). Oral analgesia is administered prior to the procedure.
- If declined, hysteroscopy under regional or general anaesthesia may be offered. If both declined, pelvic Ultrasound may be offered after discussing limitations

Endometrial biopsy

- It is indicated at time of hysteroscopy in women at high risk of endometrial pathology:
 - ① Persistent Intermenstrual bleeding, irregular bleeding, infrequent bleeding with obesity and poly cystic ovary syndrome
 - ② Women on Tamoxifen
 - ③ Unsuccessful treatment
- No blind endometrial biopsy offered with HMB

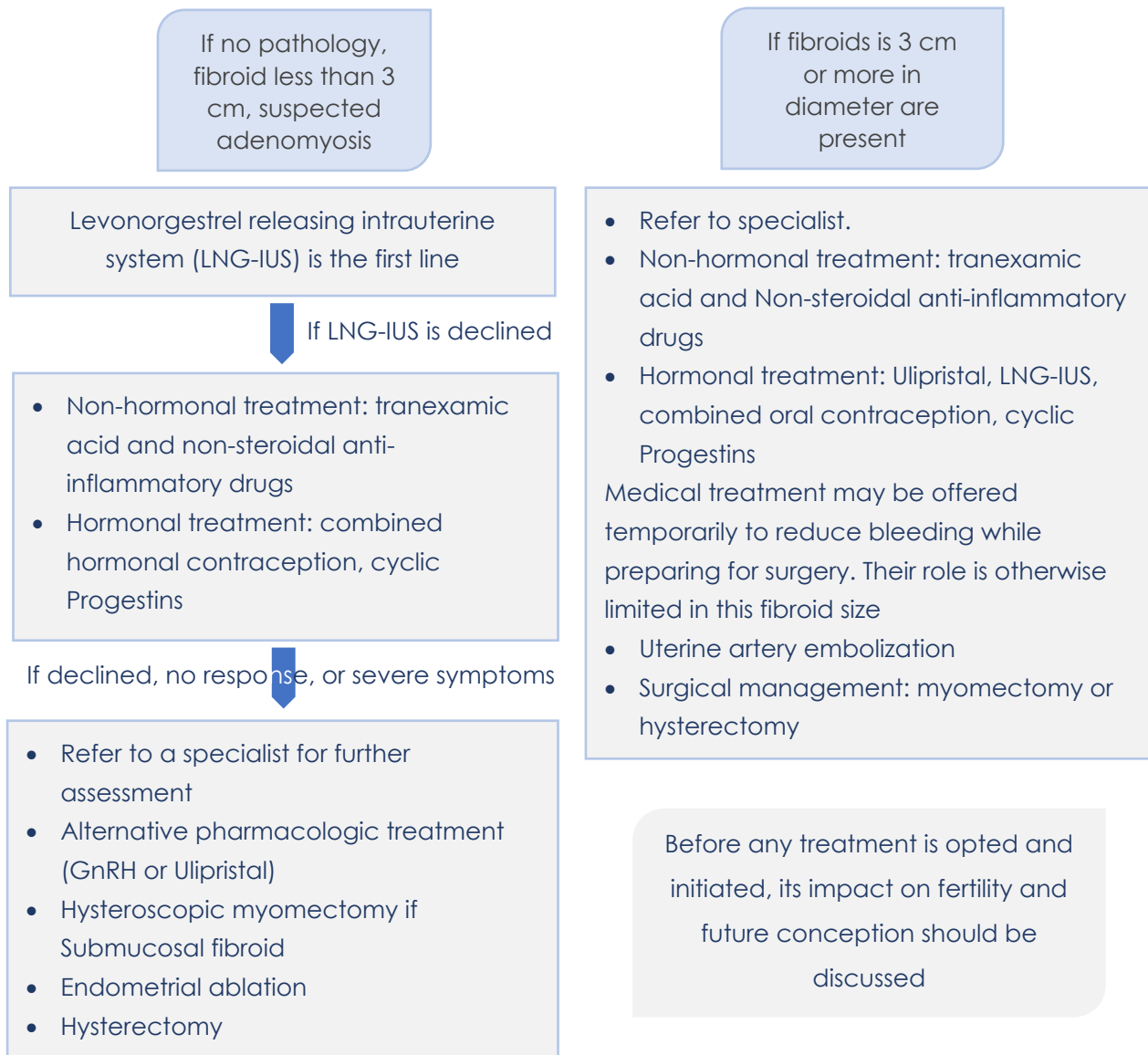
Pelvic ultrasound

Pelvic ultrasound is indicated if:

- Fibroids are suspected:
 - ① Uterus is felt abdominally
 - ② Pelvic mass
 - ③ Inconclusive examinations e.g. obese patients
- Adenomyosis is suspected:
 - ① Significant dysmenorrhea
 - ② Bulky tender uterus

Treatment

- Treatment decision depends on:
 - ① Patient preference and conception plans
 - ② Presence of comorbidities
 - ③ Presence of fibroids
 - ④ Other symptoms e.g. pressure, pain
- Women with HMB without associated symptoms are initially treated medically. Physical examination and imaging are not necessary



Method	Precautions and instructions
LNG-IUS	Patients should be advised that the first few cycles may be associated with abnormal bleeding patterns. They should be advised that this may continue for up to 6 months and that they should give LNG-IUS up to 6 cycles to appraise benefits of this method
Ulipristal acetate	<ul style="list-style-type: none"> • Ulipristal acetate 5 mg is given for up to 4 courses in the presence of: <ol style="list-style-type: none"> ① Heavy menstrual bleeding ② Fibroids ≥ 3 cm in diameter ③ Haemoglobin ≤ 102 g/L Ulipristal may serve as a preoperative treatment for large fibroids • Liver function should be monitored during administration (liver injury is rare, but serious with ulipristal)
GnRH analogue	Like ulipristal, it may be considered as a preoperative for large fibroids
Uterine artery embolization	<ul style="list-style-type: none"> • Uterus and fibroids should be assessed by ultrasound prior to the procedure. MRI may be required • Patients should be informed that fertility is retained
Endometrial ablation	<ul style="list-style-type: none"> • "Dilation and curettage" is not offered as a treatment. However, it is performed preoperatively to assess endometrial pathology since endometrial assessment after endometrial ablation is limited • Endometrial ablation is not a contraception. Pregnancy following endometrial ablation is not safe and therefore, a good contraceptive method should be used
Myomectomy	Ultrasound is the standard method of assessment. MRI may be needed to better delineate these fibroids
Hysterectomy	Before hysterectomy is selected, discuss impact on fertility, sexual function, ovarian function, bladder function, and surgical complications

Uterine Fibroids

Definition

Uterine fibroids (leiomyomas) are benign neoplasms arising from the smooth muscle fibres of the myometrium

Prevalence

Lifetime incidence is 30%

Risk factors

- Age: the risk increases with age before the menopause
- Nulliparity or low parity
- Race: more common in black women
- Obesity
- Hypertension
- Family history and genetic predisposition

Clinical picture

Approximately 30% of patients are asymptomatic, and fibroids may be incidentally diagnosed. Symptoms include abnormal uterine bleeding, pelvic pain and pressure and abdominal distension

Investigations

- Standard imaging modality is pelvic and abdominal ultrasound
- Saline infusion sonography or hysteroscopy may be considered in submucous fibroids to determine treatment plan
- MRI: it may be considered in certain clinical situations:
 - ① Surgical decision for challenging fibroids (e.g. interstitial fibroids)
 - ② Differentiating leiomyomas from leiomyosarcomas if malignancy is suspicious (suggestive but not conclusive)
 - ③ Prior to uterine artery embolization

Classification

Grade	Description (FIGO classification)
Grade 0	• Pedunculated intracavitary leiomyoma
Grade 1	• Leiomyoma is less than 50% intramural
Grade 2	• Leiomyoma is 50% or more intramural
Grade 3	• Leiomyoma is 100% intramural, contact the endometrium.
Grade 4	• Leiomyoma is 100% intramural, no endometrial contact
Grade 5	• Leiomyoma is subserosal, 50% or more intramural
Grade 6	• Leiomyoma is subserosal, less than 50% intramural
Grade 7	• Leiomyoma is subserosal, pedunculated
Grade 8	• Other types (e.g., cervical, parasitic)

Treatment

- **Pharmacological treatment:**

- **Indications:**

Medical treatment is a short-term option that is appropriate for:

- ① Premenopausal women
- ② Women who are unsuitable for or decline surgery
- ③ Prior to surgery (GnRH or ulipristal)
- ④ some women with infertility

- **Treatment lines:**

Oral hormonal treatment	<ul style="list-style-type: none"> • Effect on fibroids is inconclusive • These drugs act by inducing endometrial atrophy, thus, decrease menstrual blood loss
Levonorgestrel-releasing intrauterine system (LNG-IUS)	<ul style="list-style-type: none"> • This option is suitable if contraception is desired as well • This option is superior to oral hormonal treatment in reducing menstrual blood loss and improving haemoglobin level
Tranexamic acid	<ul style="list-style-type: none"> • It decreases both menstrual blood loss and perioperative blood loss in women undergoing surgery • It may induce necrosis and infarctions in large fibroids
Medroxyprogesterone injectables	<ul style="list-style-type: none"> • They may decrease menstrual blood loss and fibroid size after 6 months of treatment
GnRH analogues	<ul style="list-style-type: none"> • It should be limited to 6 months of treatment. Add-back therapy is given in conjugation • Its use for 3 months is associated with significant improvement of symptoms and 36% reduction in fibroid • Following cessation, menstruation returns in 1-2 months and fibroid size is restored in 4-6 months • Preoperative administration may allow vaginal hysterectomy, decrease perioperative blood loss and hospital stay. • Its use may cause loss of fibroid plane and missing small fibroids during surgery

Selective progesterone receptor modulators (SPRMs)	<ul style="list-style-type: none"> • These agents may be clinically useful e.g. ulipristal, mifepristone, telapristone • Ulipristal: <ul style="list-style-type: none"> ▪ It induces 40% reduction in size that is maintained for 6 months after discontinuation ▪ It decreases menstrual blood loss in 90% of patients ▪ It is comparable to GnRH but is more tolerated ▪ Endometrial changes are observed in 2/3 of patients and they resolve within 6 months. These changes are not prevented by progestins ▪ Liver damage is a rare complication • Mifepristone: It is still under research
Aromatase inhibitors	<ul style="list-style-type: none"> ▪ Treatment is still experimental. It may be comparable to GnRH in initial results

- **Uterine artery embolization:**

	Uterine artery embolization	Surgical management
Satisfaction rate	No significant difference in both options	
Major complications	Less common	More common
Minor complications	More common	Less common
Hospital stay	Shorter	Longer
Readmission	More (pain and vaginal discharge)	Less common
Post-treatment Intervention	More common (5-fold increase in the first 2-5 days)	Less common
Ovarian failure	No significant difference in both options	
Maternal mortality	1:10.000	3:10.000

- **MRI-guided focused ultrasonography:**

- This approach is associated with 90% satisfaction rate
- Less vascular fibroids with low signal intensity are more likely to respond to treatment
- 25% may require further intervention (specially with Hyperdense fibroids)
- The procedure is generally safe and is associated with minor side effects:
 - ① Mild skin burn

- ② Nausea
- ③ Transient buttock or leg pain
- ④ Transient sciatic nerve palsy
- Compared to uterine artery embolization:
 - It achieves similar relief of symptoms.
 - Risk of intervention is 7-folds higher in the first year

- **Surgical treatment:**

- **Myomectomy:**

it may be indicated in women with heavy menstrual bleeding, recurrent miscarriage or infertility (after exclusion of all other possible causes)

Hysteroscopic myomectomy	<ul style="list-style-type: none"> • This approach is indicated for grade 0 and 1 fibroids: <ul style="list-style-type: none"> ▪ Grade 0 fibroid: it is managed by resectoscope and slicing ▪ Grade 1 and 2 fibroid: there is no standard approach. Myolysis and cryomyolysis may be used. However, they do not provide a sample for histopathology, and they may be associated with higher risk of adhesions and reintervention • Safety of this procedure with grade 2 fibroids depends on uterine thickness between the fibroid and the serosa • The procedure may be combined with endometrial ablation (90% of patients experience significant reduction in blood loss within 1 year of treatment)
Laparoscopic myomectomy	<ul style="list-style-type: none"> • Compared to open surgery, laparoscopic surgery is associated with: <ul style="list-style-type: none"> ▪ Longer surgical time ▪ Less blood loss ▪ Less postoperative pain, fever, and hospital stay • It is superior to open surgery in women who want to retain fertility

Techniques to decrease blood loss include preoperative GnRH or SPRM, intraoperative use vasopressin and uterine tourniquet

- **Laparoscopic uterine artery occlusion:** It is generally **less effective** than myomectomy or uterine artery embolization
- **Endometrial ablation:** it may be used to treat heavy menstrual bleeding in the presence of **small fibroids that do not significantly distort the cavity**

- **Hysterectomy:**

- It is the last resort if other methods fail or inappropriate
- One third of hysterectomies are indicated of uterine fibroids

Premenstrual Syndrome

Definition

Premenstrual syndrome (PMS) is a spectrum of cyclic physical and psychologic symptoms that occur in the second half of the menstrual cycle and impact life quality

Epidemiology

PMS affects **40%** of women in; **5-8%** suffers from severe PMS

Clinical picture

Patients report recurrent symptoms in the last week of each cycle. These symptoms are most significant within 4 days prior to menstruation and in the first 2 days of the cycle

- **Psychological symptoms:** e.g. depression, anxiety, irritability, mood swings
- **Physical symptoms:** e.g. mastalgia, bloating

Diagnosis

- Diagnosis should be made by prospective recording of symptoms using a menstrual diary for 2 successive cycles
- If the menstrual diary is inconclusive, GnRH analogues should be tried for 3 months to reach a definitive diagnosis. A good response to GnRH is diagnostic

Classification

Physiological premenstrual disorder (mild)	<ul style="list-style-type: none"> • Cyclic symptoms relieved by menses with symptom-free week • No interference with quality of life
Core premenstrual disorder (premenstrual syndrome, premenstrual dysmorphic disorder)	<ul style="list-style-type: none"> • Cyclic symptoms relieved by menses with symptom-free week • Symptoms should include depression and fulfill at least 5 out of 11 criteria of PMS
Progestogen-induced PMD	<ul style="list-style-type: none"> • Clinical features of core premenstrual disorder are associated with progestins in hormonal therapy or with combined oral contraceptives (COCs)
Premenstrual disorder with absent menstruation	<ul style="list-style-type: none"> • PMS features associated with functioning ovaries. However, menses are absent due to endometrial ablation, hysterectomy, levonorgestrel releasing intrauterine system
Premenstrual exacerbation of underlying condition	<ul style="list-style-type: none"> • Cyclic symptoms relieved by menses with NO symptom-free week, • It is associated with an underlying condition e.g. diabetes, epilepsy, migraine, depression, asthma

If the symptoms are not cyclic and not associated with a symptom-free week, it is unlikely PMS and psychiatric referral is indicated

Management

- **Complementary medicine:**
 - The role of these medications is controversial. They may be helpful. However, they may be associated with drug interactions
 - Examples include calcium, magnesium, vitamin D, Primrose oil and Ginkgo
- **Integrated holistic approach:** it is recommended in all women with PMS
- **Cognitive behavioural therapy (CBT):** should be considered routinely in **severe PMS**

- **Medical treatment:**

- **Drospirenone-containing COCs:**

- It is the first line of treatment and the most effective in women with PMS
- It should be given continuously not cyclically
- The lowest dose of progestogen is used to reduce side effects (PMS-type side effects).
- Alternative to oral route, percutaneous oestrogen with cyclic progestogen may be used
- Micronized progesterone is less likely to produce PMS-like symptoms
- Progesterone alone should not be used to treat PMS

- **Selective serotonin reuptake inhibitors (SSRIs):**

- One of the first line treatments of severe PMS
- *Dose:* sertraline 25 mg and 50 mg
- *Regimen:*

Luteal regimen	Continuous regimen
<ul style="list-style-type: none"> • lower total premenstrual score while higher mood swings and tension effects than continuous. • Luteal regimen is associated with fewer SEs & higher efficacy using newer agents 	<ul style="list-style-type: none"> • It should be withdrawn gradually • Nausea, insomnia, somnolence, fatigue, reduction in libido

Symptoms typically improve in pregnancy, therefore: these medications should be discontinued if pregnancy is confirmed. If pregnancy occurs while the patient is on these medications, congenital malformation risk is small, if any

Patients are referred to a gynaecologist if Refer if Failed COCs, vit B6, SSRIs and /or severe symptoms

- **Danazol:**

- It improves physical symptoms, particularly breast tenderness
- It may be used in a low dose (200mg)
- It induces irreversible virilization and therefore, an effective contraception should be used to prevent female foetus virilization if unintentional pregnancy occurs

- **Spironolactone:**

It may be used to treat physical symptoms

- **GnRH analogue:**

- It is reserved to the most severe symptoms
- Treatment should be limited to 6 months. If treatment must extend beyond 6 months: add-back therapy should be given (continuous hormonal therapy OR tibolone)
- If long-term treatment is decided, DEXA bone scan should be done every year
- If bone marrow density declines significantly, treatment should be stopped immediately

- **Surgical treatment:**

- If all options fail, or if long term GnRH is considered, or if there are other indications of surgery, surgery should be considered
- In women with PMS, who are younger than 45 years, and who do not have any other indications of surgery, preoperative GnRH should always be given to predict response of surgery
- Preferred surgery is total hysterectomy and bilateral salpingectomy. Preservation of the ovaries is not recommended as symptoms will likely continue and preservation of the uterus is not recommended because hormonal replacement therapy should include progestins to protect the endometrium, which are likely to cause PMS-like symptoms
- Women should receive hormonal replacement after surgery particularly if younger than 45 years

Menstrual disorders

Abstract

Menstrual disorders are the most common cause of outpatient gynaecologic visits worldwide. They significantly impact quality of life and they may result in significant health sequelae. Menstrual disorders may be caused by alternation of endogenous hormonal regulation or may result from structural abnormalities. Therefore, management spectrum is wide, ranging from simple treatment,

such as non-steroidal anti-inflammatory drugs, to hysterectomy. In this chapter, we will discuss types and causes of menstrual disorders and outline diagnosis and management approaches.

Keywords

Abnormal uterine bleeding, fibroids, hysterectomy, endometrial ablation, myomectomy

Further readings

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