Guideline for the management of Heavy Menstrual Bleeding (HMB) in adolescents

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1.0 DEFINITION, BACKGROUND AND SCOPE

Abnormal uterine bleeding (AUB) is the most common gynaecological complaint of adolescents seen in secondary care. Heavy menstrual bleeding (HMB) is the most frequent clinical presentation of AUB. The prevalence of menorrhagia in the adolescent population has been reported as affecting up to 37% of teenage girls[1].

As per NICE guidance, heavy menstrual bleeding is defined as excessive menstrual blood loss that occurs regularly (every 24 to 35 days) which interferes with a woman's physical, emotional, social, and material quality of life[2].

The average age of menarche in the UK is between 12 and 13 years[3]. The normal cycle of an adolescent female occurs every 21-45 days with bleeding lasting between two and seven days[4,5]. Menstrual cycles are 21-34 days, similar to adults, in 60-80% of adolescents by the third year after menarche[5,6]. The average blood loss during a normal menstrual cycle is 30-40 mls, requiring the use of 3-6 pads or tampons per day or 10-15 soaked pads or tampons per cycle[7]. Chronic loss of ≥80 mL blood is associated with anaemia[8].

During the first two years after menarche, approximately half of menstrual cycles are anovulatory. However, at five years post-menarche 75% of cycles are ovulatory[9]. Delayed or absent ovulation, either physiological or due to polycystic ovaries, results in lack of progesterone and excessive oestrogen production from ovarian follicles, causing the endometrium to proliferate and to become prone to unpredictable bleeding in both timing and amount. For these reasons anovulatory cycles are the leading cause of HMB during adolescence.

Heavy menstrual bleeding at menarche and in adolescence may be representative of an underlying bleeding disorder. The frequency of bleeding disorders in the general population is approximately 1–2%, but bleeding disorders are found in approximately 20% of adolescent girls who present for evaluation of heavy menstrual bleeding and in 33% of adolescent girls hospitalised for heavy menstrual bleeding[10–12].

This guideline will focus on the investigations and management of HMB in adolescents.

2.0 HISTORY AND EXAMINATION

2.1 HISTORY

Ideally a history should be taken both with and without the parents/guardians being present because some of the questions asked may be difficult for patients to answer candidly in the presence of their parents/guardians, especially those relating to sexual activity.

History should include;

- Menstrual history - age of menarche, regularity, duration, number of pads/tampons per day, last menstrual period, painful periods
- Sexual history
- Past medical history - systemic illness, current/recent medication
- Family history – in particular coagulopathy, hormone sensitive cancers
- Social history – school attendance, are there any issues with missing days off school, concerns regarding bullying

A history of heavy menses since menarche, surgery related bleeding, bleeding associated with dental work, bruising or epistaxis with a frequency of at least once per month, frequent gum bleeding and bleeding symptoms in the family point to an underlying bleeding disorder[13].

2.2 EXAMINATION

A thorough "head to toe" examination should be performed with a chaperone present, taking into consideration the signs that would present with the differential diagnoses.

A basic examination includes:

- Assessment for pallor
- Evaluation for signs of androgen excess – hirsutism, acne
- Examination of the skin for acanthosis nigricans / petechiae / bruising
- Palpation of the abdomen for uterine or ovarian masses

3.0 INVESTIGATIONS

The following investigations should be considered first line in girls presenting with HMB:

- Full blood count
- Ferritin
- Coagulation screen – to include fibrinogen, prothrombin time, activated partial thromboplastin time if suspicion of bleeding/clotting disorder or anaemia needing iron/blood transfusion
- Urine pregnancy test (if sexually active)

Other investigations that may be considered:

- Pelvic ultrasonography –if there is suspicion on examination of a pelvic mass or in resistant menorrhagia (transabdominal scan only for non-sexually active girls).
- Thyroid function test – if accompanying symptoms suggestive of thyroid abnormality.
- Infection screen – if sexually active.
- Von Willebrand panel – includes plasma von Willebrand factor (Vwf) antigen and testing for factor VIII activity. Results can be affected by exogenous oestrogen therefore these tests should be performed before commencing oestrogen containing hormonal therapy and following discussion with a Haematologist.

4.0 MANAGEMENT

A clinician should assess a young person's competence to consent to treatment by their ability to understand information provided, to weigh up the risks and benefits, and to express their own wishes. Competence to consent to treatment should ideally be assessed and documented at each visit where relevant. The choice of management for HMB should be a joint decision between the clinician, patient and parent (where applicable) taking into consideration factors such as pill compliance.

4.1 NON-PHARMACOLOGICAL MANAGEMENT

Reassurance that HMB is common in adolescents is helpful. Regular exercise and maintenance of a healthy BMI should be recommended to every adolescent. Although the evidence for cause and effect is limited, a high BMI will increase the risk of ovulatory dysfunction and subsequent heavy or irregular menstrual loss[14,15].

A healthy diet will also help limit iron deficiency anaemia, raise energy levels and improve quality of life.

4.2 PHARMACOLOGICAL MANAGEMENT

The medical management options are displayed in Tables 1-3. The most commonly occurring side effects are listed, however for a full list of known side effects please refer to the British National Formulary (BNF). For the full list of contraindications for each drug group please refer to the BNF and UK Medical eligibility criteria (UKMEC) guidance provided by the FSRH.

It is important to know that although UKMEC criteria is a useful tool, the recommendations are based on use for contraceptive purposes only and one should use clinical judgements if prescribing it therapeutically for non-contraceptive indications such as HMB.

4.2.1. NON-HORMONAL MANAGEMENT

Table 1. Non-hormonal options for HMB management

Drug	Dose	Timing and duration of therapy	Efficacy rates	Common side effects	Contraindications
NSAIDS **(Mefenamic Acid)**	500mg TDS (licensed for girls 12-17years)	To be taken on first day of heavy bleeding, maximum duration 3 days.	25-50% reduction in menstrual blood loss[16].	GI discomfort, diarrhoea (discontinue if occurs), nausea, vomiting, headache, dizziness.	History of GI bleed, recurrent GI ulcers, IBD
Tranexamic Acid	1g TDS or QDS (licensed for girls 12-17years)	To be initiated when menstruation has started, to be taken for up to 4 days; maximum 4g per day.	50% reduction in menstrual blood loss[17-18].	Diarrhoea (reduce dose if occurs), nausea, vomiting	Fibrinolytic conditions, history of convulsions, thromboembolic disease

4.2.2. HORMONAL MANAGEMENT

Combined hormonal options

Combined hormonal contraceptives (CHC) are available as tablets (COC), transdermal patches (CTP), and vaginal rings (CVR). The ethinylestradiol content of COCs range from 20–40 micrograms. A monophasic preparation containing 30 micrograms or less of ethinylestradiol in combination with levonorgestrel or norethisterone is generally used as the first line option.

Girls should be counselled that weight gain is not associated with CHC, but some can get fluid retention and increased appetite.

BMI and blood pressure should be checked prior to initiation and annually for all girls taking CHCs.

Table 2. Combined hormonal preparation options for HMB management

NB: *Please use UKMEC criteria judiciously for non-contraceptive indications*

Drug	Dose	Timing and duration of therapy	Efficacy rates	Common side effects	Contraindications	Additional information
Microgynon / Rigevidon	30mcg Ethinylestradiol + 150mcg Levonorgestrel	Tailored regimens with shortened, or no hormone free interval (HFI) have been shown to be the most beneficial for reducing HMB. Extended use (tricycling): 9 weeks of continuous use followed by a 4 or 7 day HFI. Alternatively, can be taken continuously without any HFI. If breakthrough bleeding occurs, should	Over six months the COC reduces HMB in women with unacceptable HMB from 12% to 77% (compared to 3% in women taking placebo)[19]. 70-80% amenorrhoea at the end of 1year continuous use[20,21].	Headaches, nausea, dizziness, breast tenderness, unscheduled bleeding, mood changes.	Personal or family (1st degree relative) history of VTE, migraines with aura, hypertension, BMI ≥35. Should not prescribe for girls taking enzyme-inducing medication. See UKMEC guidance for all contraindications.	Should be considered as first line COC option.

		take a 4 day pill break and then resume as normal.				
Lizinna (replace-ment for discontinued Cilest)	35mcg Ethinylestradiol + 250mcg Norgestimate	As above	As above	As above	As above	Contains highest EE content, should be considered for girls where acne is an issue. Should also be considered where breakthrough bleeding is a problem.
Yasmin	30mcg Ethinylestradiol + 3mg Drospirenone	As above	As above	As above	As above	Contains anti-androgen, should be considered for girls where acne is an issue.

Loestrin 20	20mcg Ethinylestradiol + 1mg Norethisterone acetate	As above	As above	As above	As above	Contains lowest EE content, should be considered for girls with low BMI to reduce chances of side effects. Likely lower VTE risk.
Qlaira	Estradiol valerate + dienogest (Multiphasic 28day preparation COC)	28 day regimen with a monthly withdrawal bleed during the 2 day hormone free interval (HFI)	No specific studies comparing efficacy of Qlaira to monophasic COCs for HMB.	As above	As above	The only CHC which contains natural oestrogen (17B-oestradiol) and is licensed for HMB. Is the most expensive CHC.

Co-cyprindiol (Dianette)	35mcg Ethinylestradiol + 2mg Cyproterone acetate	1 tablet daily for 21 days, to be started on day 1 of menstrual cycle; subsequent courses repeated after a 7-day interval (during which withdrawal bleeding occurs), time to symptom remission, at least 3 months. Should consider alternatives with lower VTE risk for use >2 years.		Abdominal pain, breast abnormalities, depression, headaches, altered mood, nausea, weight changes from fluid retention	Acute porphyrias, gallstones, migraines with aura, personal or family history (1st degree relative) of VTE	Contains anti-androgen, is indicated for management of hirsutism and acne, should not be prescribed for HMB alone. Higher VTE risk (1.5-2x) than second generation progesterone Levonorgestrel containing CHC.
Combined transdermal patch (CTP) Evra CTP	Releases 33.9mcg ethinylestradiol and 203mcg norelgestromin per 24 hours	One patch is applied to the skin below waist and replaced every 7 days for two further weeks. The fourth week is patch-free to allow a withdrawal bleed. A new patch is then	No randomised trials have evaluated the use of CTP for HMB.	As for COC	As for COC	Patch is less effective in girls or young women who weigh >90kg.

		applied after 7 patch-free days. Tailored regimens can also be considered. Tricycling (9 patches used consecutively with 4-7 day HFI). Continuous use, no HFI.	However extended cycle has shown fewer days of breakthrough bleeding than monthly use[22].			Risk of VTE is higher than with pill.
Combined vaginal ring (CVR) Nuvaring	Releases ethinylestradiol and etonogestrel at daily rates of 15mcg and 120mcg, respectively	One ring is inserted into the vagina and left in place continuously for 21 days. After a ring-free interval of 7 days to induce a withdrawal bleed, a new ring is inserted. Tailored regimens can also be considered. Tricycling (3 rings used consecutively with 4-7 day HFI). Continuous use, no HFI.	Similar efficacy for HMB compared with COC[19]. No reduction in spotting symptoms with cyclical or extended use[20].	As for COC	As for COC	Recommended to avoid use in those who are not sexually active.

Progesterone only options

Table 3. Progesterone only options

Drug	Dose	Timing and duration of therapy	Efficacy rates	Common side effects	Contraindications	Additional information
Norethist-erone (NET)	5mg TDS	Can be taken as a short cycle or long cycle. Short-cycle for 7 to 10 days, starting from day 15 or day 19. Long cycle from day 5 to day 26 of the menstrual cycle. Should consider other options for long term use.	No randomised studies comparing cyclical progestogens to placebo, but efficacy shown to be less than LNG-IUS for reducing HMB[23]. Amenorrhoea rates up to 76% at high doses at 2 years[24].	Menstrual cycle irregularities, dizziness, headache, hypersensitivity, nausea, skin reactions, increased weight.	Acute porphyrias, arterial disease	NET is metabolised to ethinyl oestradiol (EE). It has been suggested that a daily dose of NET 5mg TDS might be equivalent to taking 20-30mcg COC[25]. Therefore, if COC is contraindicated then NET should also **not** be prescribed. Long term high dose (10-20mg/day) use of NET has also been linked with increased risk of hepatic adenoma[26].

Medroxyprogesterone Acetate (MPA) oral (Provera)	10mg BD or TDS	Can be taken as a short cycle or long cycle. Short-cycle for 7 to 10 days, starting from day 15 or day 19. Long cycle. To take from day 5 to day 26.	Amenorrhoea rates up to 76% at high doses at 2years[24].	Alopecia, breast abnormalities, low mood, dizziness, fluid retention, insomnia, menstrual cycle irregularities, nausea, skin reactions, weight changes, increased appetite, constipation, fatigue, headache, vomiting.	Acute porphyrias, arterial disease	Can be used as alternative to NET for preventing menses or treatment of HMB in longer term use if other options not desired.
Desogestrel (Cerazette or Cerelle)	75mcg	To be taken continuously. Can be increased to double dose if HMB not improving on single	By 11–13 months of use almost 50% will have infrequent bleeding or amenorrhoea[27].	Breast abnormalities, low mood, headache, reduced libido,	Acute porphyrias, arterial disease	Should be first-line option for HMB where COC is not wanted or contraindicated.

		dose (150mcg daily). This is off license but found to be effective.	30-40% will have irregular bleeding in long term use[28].	menstrual cycle irregularities, altered mood, nausea, skin reactions, increased weight.		
Etonogestrel-releasing implant (Nexplanon)	68mg	To be changed every 3 years.	After 6 months use, 30% have infrequent bleeding; 10-20% have prolonged bleeding[29]. In longer term use, 20% are amenorrhoeic, 50% have infrequent or prolonged bleeding which may not settle[29].	Abdominal pain, alopecia, anxiety, increased appetite, breast abnormalities, low mood, dizziness, flatulence, menstrual irregularities, ovarian cysts, skin reactions, weight changes	Acute porphyrias, arterial disease	Is commonly associated with bleeding disturbances. Not licensed for females under 18.

Medroxyprogesterone Acetate injection (Depo-Provera, Sayana Press)	Depo-Provera 150mg. Sayana Press 104mg	150mg every 12 weeks. 104mg every 13weeks. Should review every 2 years if this is the method of choice.	Amenorrhoea rates 50-60% at 1 year; up to 70% at 2 years[30].	In addition to side effects with oral MPA: anxiety, gastrointestinal discomfort, vulvovaginal infection.	Acute porphyrias, arterial disease	Should be used only in adolescents when other methods of contraception are inappropriate. Concerns with reversible osteopenia with prolonged use (>2years) and highest association with weight gain (2-3kg in 1year).
Intra-uterine progestogens Levonorgestrel intrauterine system (LNG-IUS): Mirena, Levosert	20mcg/ 24hours	Effective for 5 years.	HMB is reduced significantly within 3–6 months of insertion. It is more effective than oral medication as a treatment for	Back pain, breast abnormalities, low mood, device expulsion, hirsutism, increased risk of infection, ovarian cysts, vulvovaginal	Active trophoblastic disease, acute vaginitis, distorted uterine cavity	Consider insertion under general anaesthetic or sedation if not sexually active.

			HMB[31]. 65% have amenorrhoea or reduced bleeding at 1 year[29]. A 90% reduction in menstrual blood loss seen over 12months use [32,33.]	disorders		

FOLLOW UP FOR GIRLS ON HORMONAL THERAPY

Adolescents should be counselled that hormonal therapy can take up to 6 months to have an effect; irregular bleeding and spotting frequently gets better after the first 3 months of treatment. The importance of compliance should also be discussed with both patient and parent (where applicable).

A medical review should be undertaken after 6 months of initiating treatment for HMB to reassess symptoms and determine if treatment can continue or if alternatives should be considered.

4.3 SURGICAL OPTIONS

On the rare occasions where a structural abnormality (i.e. polyp or submucous fibroid) is thought to be the cause of the HMB these should be treated surgically, the same as for adult women. Appropriate consent should be obtained as for all adolescent surgery cases.

5.0 RECOMMENDATIONS FOR RESEARCH

- *A randomised trial of CTP versus COC for HMB*. There is currently no trial which has looked at the efficacy of CTP for HMB. We feel that in a population where pill taking is a common problem, the use of patches for HMB needs to be explored.
- *A randomised trial of single dose versus double dose desogestrel.* A retrospective study suggested greater benefit in reducing HMB from starting double dose in place of single dose; however, a prospective randomised trial is needed to provide conclusive evidence.

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