

# Abnormal Uterine Bleeding in Adolescents: A Multidisciplinary Approach

## Hemorragia Uterina Anormal em Adolescentes: Uma Abordagem Multidisciplinar



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### ABSTRACT

Abnormal uterine bleeding is the most common complaint that motivates female adolescents to seek medical advice. Abnormal uterine bleeding has a significant impact on quality of life, promoting school absenteeism and limitations in social life. Moreover, episodes can vary from mild to life threatening events if not recognized and treated promptly. Healthcare providers should be able to distinguish between a normal and abnormal menstrual pattern, as this may provide early diagnosis of a potential health concern. The PALM-COEIN classification system should be used in the evaluation. Anovulation is the most frequent cause, frequently due to immaturity of the hypothalamic-pituitary-ovarian axis. A careful history and physical examination are crucial in the differential diagnosis. Management is based on both the underlying cause and the severity of bleeding. Most patients improve with pharmacological treatment, frequently requiring a multidisciplinary approach. First line treatment consists of hormonal therapy. Surgery is rarely needed. Although the prevalence of abnormal uterine bleeding is higher in adolescents compared to adults, most recommendations are not specific for this age, which makes the diagnosis and management challenging. The literature reveals lack of standardized care for adolescents and regimens vary widely. Future studies on efficacy and safety of treatments specifically in adolescents are needed.

**Keywords:** Adolescent; Blood Coagulation Disorders; Menorrhagia; Metrorrhagia; Uterine Hemorrhage

### RESUMO

A hemorragia uterina anormal constitui a queixa que mais frequentemente leva as adolescentes a procurar cuidados de saúde. Esta situação tem um impacto significativo na qualidade de vida, levando a absentismo escolar e limitações na vida social. Os episódios podem variar de ligeiros a potencialmente fatais, se não reconhecidos e tratados rapidamente. Os prestadores de cuidados de saúde devem ser capazes de distinguir um padrão menstrual anormal, uma vez que isto poderá permitir o diagnóstico precoce de um grave problema de saúde. A classificação de PALM-COEIN deve ser usada na avaliação. A causa mais frequente é a anovulação, frequentemente associada a imaturidade do eixo hipotálamo-hipófise-ovário. A história clínica e um exame objetivo cuidadoso são cruciais no diagnóstico diferencial. A abordagem terapêutica deve ser baseada na etiologia subjacente e gravidade da hemorragia, sendo frequentemente necessária uma intervenção multidisciplinar. A maioria das doentes melhora com tratamento farmacológico, cuja primeira linha é constituída pela terapêutica hormonal. O tratamento cirúrgico é raramente necessário. Apesar da prevalência ser superior em adolescentes, a maioria das recomendações não são específicas desta idade, o que dificulta o diagnóstico e abordagem. A literatura revela falta de uniformização de condutas em adolescentes e os esquemas posológicos são muito variáveis. Por este motivo, é fundamental a realização de estudos sobre a eficácia e segurança dos tratamentos nesta faixa etária.

**Palavras-chave:** Adolescente; Hemorragia Uterina; Menorragia; Metrorragia; Perturbações da Coagulação Sanguínea

### INTRODUCTION

As abnormal uterine bleeding (AUB) is a common scenario that gynaecologists, paediatricians and primary care providers face in the care of adolescent patients.<sup>1,2</sup> It is the single most common complaint that makes reproductive age women seek medical help.<sup>2,3</sup> This problem has a huge impact on quality of life, promoting school absenteeism and limitations in social life.<sup>4-6</sup>

AUB may be either acute or chronic, and therefore patients may present in either an emergency or outpatient setting.<sup>4</sup> Acute AUB requires immediate intervention, in contrast with chronic AUB, that refers to abnormal bleeding in volume, regularity and/or timing present for the majority of the past six months.<sup>3,7</sup> Although the prevalence of this condition is higher in adolescents compared to adults (37% vs 10% - 20%),<sup>4</sup> most recommendations are not specific to this age group, which makes the diagnosis and management challenging.<sup>8</sup> Caution is thus required, as the management

is guided by evidence established in adults and there is no substantial direct evidence to support the extrapolation.<sup>9</sup> Besides, some studies identified variations in acute AUB treatment strategies among different specialities, which reflects a lack of standardized care.<sup>10</sup>

Clinicians need to explain to their patients and their caretakers what to expect of a first menstrual period, especially in patients with known bleeding disorders.<sup>11</sup> These girls should have a consultation with a gynaecologist or haematologist prior to menarche.<sup>1,2,8</sup> At every consultation after menarche, the last menstrual period, menstrual patterns and amount of blood loss should be assessed as if they were a clinical vital signs.<sup>2</sup> A smartphone application may facilitate recording and may be preferred over paper by adolescents.<sup>12</sup>

It has been demonstrated that a multidisciplinary protocol for work-up in adolescents with heavy menstrual bleeding

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(HMB) can reduce time to diagnosis and improve outcomes.<sup>4,13</sup>

## MENARCHE AND BLEEDING PATTERN

Patient menstrual history can help on the differential diagnosis of AUB.<sup>14</sup> Menarche is one of the most significant milestones in a woman's life.<sup>15</sup> The median age of menarche is around 12 - 13 years old, typically within 2-3 years after telarche.<sup>11,14</sup> During the first years, cycles may be irregular due to immaturity of the hypothalamic-pituitary-ovarian axis, but by the third year after menarche, on average, cycles become more regular.<sup>3,11,15</sup> The suggested normal limits for frequency are 21 - 45 days.<sup>16</sup> In adolescents, approximately half of menstrual cycles are anovulatory.<sup>17</sup>

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" by the National Institute for Health and Clinical Excellence (NICE) and is endorsed by The International Federation of Gynecology and Obstetrics (FIGO).<sup>18,19</sup> Although subjective, clinical features strongly associated with HMB include: 1) need to change sanitary protection every 1 - 2 hours or more than seven per day; 2) blood clots greater than 2 cm; 3) need to change protection during the night; 4) need to use double protection (pad and tampon); 5) anaemia and low ferritin levels.<sup>4,5,20</sup>

In 2011, the International Federation of Gynaecology and Obstetricians (FIGO) proposed a standardized terminology. The term menorrhagia was replaced by AUB/HMB and the term metrorrhagia by AUB/intermenstrual bleeding.<sup>21</sup>

## ETIOLOGY

FIGO has developed a classification system that should be used in the evaluation of AUB, the PALM-COEIN (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified).<sup>5,22</sup> The first part of the acronym refers to structural causes, that are rare in adolescents, and the second part to non-structural, which includes most of the causes in this population.<sup>21,22</sup> AUB secondary to an ovulatory dysfunction is described as AUB-O, which is the most common cause of AUB in adolescents.<sup>2,5,21</sup> Anovulation frequently results from the immaturity of the hypothalamic-pituitary-ovarian axis, but can also be due to hypothalamic hypogonadism or endocrinopathies, such as polycystic ovarian syndrome.<sup>5,14,21</sup> During anovulatory cycles, there is no formation of corpus luteum and therefore no progesterone production during the second half of the menstrual cycle. Estrogen promotes endometrium proliferation, but without the stabilizing influence of progesterone, it can lead to unpredictable bleeding and/or HMB.<sup>8,23</sup> It is a diagnosis of exclusion.<sup>3,20</sup> The presence of an underlying bleeding disorder can exacerbate this situation.<sup>3</sup>

The second most common cause is coagulopathy (AUB-C), such as von Willebrand disease (vWD), Glanzmann thrombasthenia, idiopathic thrombocytopenic pur-

pura, platelet dysfunction and thrombocytopenia related to malignancy or treatment for malignancy.<sup>3</sup> A wide range of prevalence rates of bleeding disorders has been reported in adolescents with AUB (7% - 62%).<sup>8,9</sup> Conversely, 76% of women with a known bleeding disorder have HMB. The frequency of bleeding disorders in the general population is approximately 1% - 2%, but in adolescents with HMB is approximately 20%, and 33% in the ones who need hospitalization.<sup>16</sup> VWD is the most common inherited bleeding disorder in adolescents.<sup>21</sup> A history of HMB during menarche is suggestive of a bleeding disorder and can be its first manifestation.<sup>24</sup> Signs and symptoms that might be suggestive must be recognized: trivial wounds that lead to prolonged bleeding; heavy, prolonged and recurrent bleeding after surgery or dental procedures; bruising with minimal trauma; frequent and/or prolonged epistaxis; HMB with iron deficiency and family history of bleeding disorders.<sup>5</sup>

Other causes of AUB include problems related to pregnancy, sexually transmitted infections (*Chlamydia trachomatis* and *Neisseria gonorrhoeae*), genital trauma, foreign bodies and medications.<sup>2,3,15,25</sup> Malignancy is rare in adolescents, but there are some case reports in the literature, such as endometrial cancer or botryoid sarcoma.<sup>3</sup> Risk factors for endometrial cancer include severe obesity and chronic AUB unresponsive to therapy.<sup>3</sup>

The most common causes of AUB in premenarcheal girls are foreign bodies, trauma, and infection.<sup>3</sup> In postmenarcheal girls, anovulatory bleeding, coagulopathies, infections, hormonal contraception and complications of pregnancy are the most common causes.<sup>3</sup> The diagnosis in adolescents is often delayed due to the difficulty in recognizing the problem. The cycle-to-cycle variability, the inconsistency in evaluation and the embarrassment of discussing menstruation and sexual activity contribute to this.

## EVALUATION

Once it is confirmed that the patient has AUB, it should be determined if it is acute or chronic, and a focused history and physical examination will help guide the differential diagnosis.<sup>4</sup>

Patients should be questioned about menarche, bleeding pattern, medical history, current medication and sexual history.<sup>3</sup> Symptoms of anaemia (e.g. dizziness and fatigue) should be screened. A personal and family history to rule out any contraindication to hormonal treatment should be obtained, as it is the first line treatment for AUB and many patients will also need contraception in future.<sup>26</sup>

A physical examination will sometimes reveal an explanation for the AUB. It should include orthostatic blood pressure, pulse measurements to evaluate hemodynamic stability and signs of anaemia.<sup>15</sup> Examination should exclude extrauterine sources for abnormal bleeding, as urethra, vagina, cervix, vulva and anus.<sup>3</sup> Speculum and bimanual examination should only be done in sexually active adolescents.<sup>5</sup> Assessment for signs of hyperandrogenism (e.g. acne, hirsutism), petechiae, ecchymosis and thyroid palpation may help in determining the etiology.<sup>7</sup>

Laboratory evaluation allows the assessment of anaemia as well as an investigation of potential AUB causes. It should start with complete blood count and pregnancy test (urine or serum); coagulation testing (i.e., prothrombin and an activated partial thromboplastin time and fibrinogen) and iron status (ferritin).<sup>3,4,13,15</sup> Blood type and cross match must be immediately obtained in cases of unstable patients.<sup>5</sup> Adolescents with heavy menses since menarche or who have a personal or family history suggestive of a coagulation disorder should undergo testing for vWD.<sup>4,13,24</sup> The vWD profile consists of vWD factor antigen, ristocetin cofactor assay, factor VIII, and multimer analysis. Testing for vWD is recommended before initiating hormonal therapy, because estrogen may elevate vWD factor into the normal range and yield a false negative result.<sup>9</sup> Consultation with a haematologist is recommended for interpretation of abnormal results and for further evaluation if there is evidence of a bleeding disorder and initial testing is inconclusive (i.e., platelet function and aggregation testing).<sup>3,5,20,27</sup> Selected patients should undergo a second-tier laboratory evaluation (liver function tests, TSH if symptoms of thyroid disease and screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* if sexually active).<sup>24</sup>

Ultrasound, suprapubic, transrectal or ideally transvaginal, if sexually active, should be done to rule out structural abnormalities.<sup>5</sup> Despite being rare in adolescents, in cases of high index of suspicion for a structural cause and inconclusive examinations and ultrasound, a magnetic resonance may be carried out.<sup>9</sup>

## MANAGEMENT

In acute AUB, treatment is focused on the hemodynamic stability of the patient and bleeding control.<sup>5</sup> Identification of the underlying cause is important to determine treatment.<sup>2,9</sup> Most patients with anovulatory bleeding improve with pharmacological treatment, which is divided into hormonal and nonhormonal medicines. Surgery is rarely needed.<sup>7</sup>

Although many adolescents can be managed effectively on an outpatient basis, acute AUB may be severe enough to require hospitalization and emergency treatment.<sup>3</sup> Hospitalization is indicated for patients with severe anaemia (Hb < 7 g/dL) or moderate anaemia (Hb 8 - 10 g/dL) with active bleeding, hemodynamic instability or symptomatic anaemia and those with a serious underlying medical illness.<sup>28</sup> A multidisciplinary approach, including gynaecology, paediatric, hematology and transfusion medicine can greatly benefit patient care. After achieving hemodynamic stability and bleeding has stopped, the patient may be discharged, but close follow-up should be maintained.

Chronic AUB does not require immediate intervention and treatment may be similar to long-term treatment for acute AUB.<sup>18</sup>

We will discuss in detail the approved pharmacologic agents to treat acute AUB in adolescents, followed by a pharmacological management algorithm, taking in consideration the hemodynamic stability and the haemoglobin level.<sup>8,9,15</sup>

## Pharmacologic treatment of acute AUB

### Intravenous fluids and blood products

In hemodynamically unstable patients, intravenous crystalloid or blood products may be necessary.<sup>4</sup> Transfusion criteria include hemodynamic instability and severe symptoms of anaemia.<sup>16</sup> Restrictive red blood cell transfusion practices (one unit of packed red cells) are recommended in patients with haemoglobin < 6 - 7 g/dL in order to limit complications of allogenic transfusion.<sup>16,28</sup> Otherwise, healthy adolescents usually respond quickly and tolerate anaemia better than an adult.<sup>16</sup> Platelets may be necessary in cases of severe thrombocytopenia (< 50 000) or platelet disorders.<sup>4</sup> Clotting factor replacement with plasma-derived concentrate or recombinant agents may be required in cases of clotting factor deficiencies.<sup>4,9</sup>

### Hormonal treatment

Hormonal treatment is the first line of medical therapy.<sup>27</sup> Acute anovulatory bleeding can be treated with combination estrogen and progestin oral contraceptives (COC), progestin only (PO) or estrogen therapy. The goal is to stabilize the endometrium.<sup>2,3,15</sup> The best choice depends primarily on the current condition of the endometrium. Contraindications need to be considered before administration.<sup>3,15,27</sup> Counseling about possible adverse effects is important to ensure good compliance.<sup>3</sup>

- **Estrogen-progestin therapy:** COC are the first line therapy for AUB in adolescents. However, there are several contraindications, that clinicians should be aware before starting, such as history of thromboembolic events, uncontrolled chronic hypertension, systemic lupus erythematosus, hepatic dysfunction and migraines with aura.<sup>3,29</sup>
- **Progestin therapy:** Patients who cannot tolerate or have contraindications to estrogens can be treated with PO regimens.<sup>2,4,15</sup> Two commonly used oral PO in adolescents include medroxyprogesterone acetate (MPA) and norethisterone acetate.<sup>2,10,30</sup> These can be administered as a taper or used daily.<sup>15</sup>
- **Estrogen therapy:** If the endometrium is very thin, it becomes unstable and heavy bleeding may occur. In this scenario, PO therapy is unlikely to control bleeding and may aggravate the problem.<sup>15</sup> A high-dose estrogen therapy is the best choice to stimulate endometrial proliferation, since it serves as the foundation for the actions of progestin, and promotes clotting at the capillary level.<sup>3</sup> The benefits of this treatment must be weighed against its potential risks of thromboembolism.<sup>3</sup>

### Nonhormonal treatment

- **Anti-inflammatory medication:** Non-steroidal anti-inflammatory drugs (NSAIDs) decrease menstrual blood loss in adult patients and may be used in cases of mild bleeding.<sup>7,15</sup> However, it is not as effective as other therapies.<sup>4,15,31</sup> Examples of regimens include: mefenamic acid 500 mg every eight hours,

ibuprofen from 600 to 1200 mg daily and naproxen from 250 to 500 mg every 12 hours).<sup>2,7</sup> Patients with bleeding disorders should avoid them, due to their negative effect on platelet aggregation and clotting factor enhancement.<sup>2,9,13,30</sup>

- **Hemostatic therapy:** Antifibrinolytic agents act by decreasing fibrinolysis and promoting clot formation, reducing menstrual blood loss significantly (40% - 50%).<sup>4,5,13,15,21,32-34</sup> When patients have been unresponsive to hormones alone, hormonal therapy can be associated with antifibrinolytics.<sup>5,20</sup> Tranexamic acid is as effective as COC in reducing menstrual bleeding and should be prescribed 10 mg/kg intravenous (IV) every to eight hours or 1300 mg orally three times per day, up to five days.<sup>4,5,35</sup> Although less potent and with more side effects, aminocaproic acid is another option, and it can be used 3 - 6 g every six hours orally or 100 - 200 mg/kg (maximum 30 g/d) IV.<sup>4,5,28</sup> Antifibrinolytic agents are contraindicated in patients with disseminated intravascular coagulation, venous or arterial thromboembolism, macroscopic haematuria, severe renal impairment, early pregnancy or colour vision deficiency.<sup>35,36</sup> Clinicians should be aware that the prescribing information for tranexamic acid lists concurrent use of oral contraceptives as a contraindication, due to the theoretical risks of thrombosis.<sup>16,37</sup> However, the concomitant administration has been used when monotherapy has failed, and available literature does not suggest increased risk of thrombosis in this setting.<sup>13,16,31,32,37</sup> Desmopressin acetate, a synthetic analogue of the antidiuretic hormone vasopressin, has been used to treat abnormal uterine bleeding in women with coagulation disorders, especially those with von Willebrand disease and mild haemophilia A.<sup>3</sup> It stimulates release of vWD and factor VIII from the endothelium and increases platelet adhesiveness.<sup>3,9,20,21,35</sup> It is typically prescribed and managed by hematologists.<sup>2,4,20</sup>

## Other medical treatment

### GnRH agonists

GnRH agonists can be used in severe cases of HMB as they are effective in achieving temporary relief.<sup>3,20,38</sup> However, their side effect profile (vasomotor symptoms and bone mineral density loss) discourages its use in adolescents.<sup>4</sup> As a final option, it can be used with add-back therapy (addition of estrogen and/or progestin therapy) for girls with severe bleeding disorders, such as Glanzmann thrombasthenia, Bernard-Soulier syndrome or oncologic related cases, not responding to other measures.<sup>2,4,9,15,30,39</sup>

### Acute AUB pharmacological management algorithm

Pharmacological management will be based on the severity of the patient's anemia.<sup>7</sup> Randomized trials regarding treatment in adolescents are lacking. There is no clear consensus in the literature, and the dose of estrogen and

progestin, as well as the schedule of administration, vary widely.

### Normal haemoglobin

Observation and reassurance are usually enough. NSAIDs may help to decrease flow.<sup>15</sup> Patients should be encouraged to keep an accurate menstrual calendar that will guide maintenance therapy.<sup>27,28,37</sup>

### Mild anaemia (Hb 10 - 12 g/dL)

A monophasic COC containing 30-35 mcg ethinylestradiol should be given twice daily until bleeding stops and then daily for 21 days.<sup>7,15</sup> As a progestin alternative, norethisterone acetate can be administered 5 - 10 mg orally until the bleeding stops. The association with NSAIDs may be useful.<sup>15</sup> Iron supplementation is recommended.<sup>2,7,15</sup>

### Moderate anaemia (hb 8 - 10 g/dL)

One pill of a monophasic COC (30 - 35 mcg ethinylestradiol) should be given every six hours for two days, followed by one pill every eight hours for two day. Then, one pill every 12 hours for two more days, and continued once a day, skipping placebo pills and starting a new pack with active pills.<sup>2,15</sup> If bleeding resumes as the dose is decreased, pills can be taken twice daily until completing the 21 day cycle.<sup>2</sup> An antiemetic drug, such as promethazine 12.5 - 25 mg or ondansetron 4 - 8 mg, is recommended before the patient receives high dose hormonal treatment to avoid nausea and vomiting.<sup>9,15,27</sup> PO regimens include a progestin every 8 to 12 hours until bleeding stops, and then be tapered down every week until daily dosing.<sup>7</sup> Tranexamic acid may be an option in patients declining hormonal therapy.<sup>5</sup> All patients should receive iron supplementation.<sup>7,15</sup> Close follow-up is essential.<sup>15</sup>

### Severe anemia (Hb ≤ 7 g/dL)

Blood transfusion should be considered.<sup>15</sup> Guidance for hormonal therapy is similar to that for moderate anaemia, but may require one COC pill every four to six hours until bleeding decreases, up to 24 - 36 hours. If bleeding significantly decreases, one pill every eight hours for three days and then one pill every 12 hours until haematocrit is above 30%.<sup>2</sup> High-dose estrogen therapy is another possibility: 4 mg every six hours until bleeding stops (maximum 24 hours), followed by 2 mg every six hours for two days every eight hours for two days, every 12 hours and then daily. An oral progestin must be added to estrogen for 10 to 14 days to stabilize the estrogen-stimulated endometrial growth.<sup>3,28</sup> Antiemetics should be prescribed before starting.<sup>2,7</sup> If bleeding recurs during tapering, dosage can be temporarily increased to the lowest dosage that controls bleeding. As a progestin alternative, norethisterone acetate can be administered 5 - 10 mg orally every six hours for four days, every eight hours for three days and every 12 hours for two weeks.<sup>2</sup> MPA 10 - 20 mg orally every six to eight hours for one week, followed by one tablet twice daily for a week and then daily is another option.<sup>2,4</sup> Addition of

haemostatic agents may be warranted if bleeding persists. Consultation with a haematologist is essential to improve clinical outcomes. GnRH analogues may be used as last pharmacological option. Surgery may be needed in cases of refractory AUB.<sup>15</sup>

### Surgical procedures

Surgery is reserved for cases in which medical therapy has failed within 24 to 36 hours, or in a life-threatening emergency.<sup>15,37</sup> Some therapies are more appropriate for adolescents for whom fertility preservation is desired. An examination under anaesthesia may be easier and reveal some laceration that could not be seen with the patient awake.<sup>4,13,37</sup> Mechanical tamponade within the uterus is used to control postpartum haemorrhage and has been suggested in adolescents with persistent bleeding.<sup>5,16</sup> After evacuation of clots, a 16 or 18 Foley catheter with a 30-cc balloon is placed inside the uterine cavity and is inflated with saline until bleeding is controlled by compression.<sup>4,5,9,13</sup> Cervical dilatation may be required.<sup>1,2,5,9,13</sup> It may be helpful to use a rigid instrument fitted in the tip of the catheter to guide its insertion.<sup>9</sup> The balloon is then inflated with saline until resistance is achieved and bleeding ceases.<sup>9,16</sup> Its position should be confirmed by ultrasound and kept in situ for no more than 24 hours.<sup>9</sup> Some authors recommend the use of prophylactic antibiotics.<sup>9</sup> Curettage is rarely needed in adolescents but may be therapeutic and provides tissue sampling.<sup>9,13,21</sup> Uterine embolization should be considered a life-saving measure and a last resort to avoid hysterectomy.<sup>9,13,15,21</sup>

### LONG TERM MANAGEMENT

Maintenance treatment is crucial to prevent future events, establish a regular menstrual cycle and improve quality of life.<sup>7</sup> In adolescents with anovulatory bleeding, the main objective is to induce or restore orderly growth and shedding of a structurally stable endometrium.<sup>3</sup> Decisions involve consideration of the patient's preference and the need for contraception.<sup>9,40</sup> Options include COC, PO or long-acting reversible contraceptive methods (LARCs).

Besides being a contraceptive, COC allows cycle regulation and improvement of menstrual pain.<sup>3,15</sup> A monophasic COC can be prescribed for three weeks followed by one hormone-free week to allow withdrawal bleeding, or be given in extended regimens (for three months) to reduce the number of withdrawal bleeding episodes.<sup>2,9,30</sup> Continuous use to induce amenorrhea can be helpful in anaemic patients.<sup>2,9,30</sup>

For girls who desire contraception, progestin alternatives include continuous PO pills or LARCs.

LARCs are an excellent option for adolescents. MPA injections lead to reductions in blood loss, up to 50% result in amenorrhea, resulting in anemia improvement.<sup>4</sup> It is administered every 12 weeks as an intramuscular injection, or subcutaneous in patients with bleeding disorders to prevent hematoma formation.<sup>4</sup> The 52 mg levonorgestrel-releasing intrauterine system (LNG-IUS) is considered to be the most

effective medical treatment for HMB, causing a decrease in blood loss of 86% after three months use and 97% after one year.<sup>21,30,41</sup> The available data highlights its safety in adolescent girls and is considered, even for those who are nulliparous, among first line options.<sup>9,13,21,41</sup>

For adolescents who don't need contraception, progestins can be prescribed cyclically - norethisterone acetate 5 mg orally for the first 10 days of each month, dihydrogesterone 10 mg orally for the first 10 days or oral micronized progesterone 200 mg for the first 12 days.<sup>15</sup> Starting on the first day of each month is easier for adolescents.

Iron supplementation should be given simultaneously and continue until anaemia is solved. A ferritin level should be obtained to confirm the complete resolution of iron deficiency.<sup>16</sup>

### FOLLOW-UP

The frequency of follow-up depends upon severity of bleeding and anaemia. If mild bleeding, patients should be seen in six months. Adolescents with moderate anaemia can be seen in three months, or earlier if there is lack of improvement. In cases of patients with severe anaemia who did not require hospitalization, monthly follow-up until menstrual pattern and haemoglobin (> 10 g/dL) are stable. Patients who have required hospitalization should be seen in two weeks after discharge and then monthly.<sup>28</sup> Adolescents and their parents should be provided a 24-hour phone number to report urgent questions and unusual symptoms.<sup>37</sup> Duration of therapy should be guided by patient's response to treatment and severity of anaemia.<sup>16</sup>

### CONCLUSION

AUB is a common complaint in adolescents and interferes with quality of life. In these patients it is more likely to be due to non-structural causes. A history of HMB during menarche is suggestive of a bleeding disorder and can be its first manifestation.<sup>24</sup> Clinicians should provide guidance to premenarcheal and postmenarcheal girls and their families about issues related with menses in order to recognize an abnormal pattern earlier, particularly all patients with known bleeding disorders,

Treatment strategies can be categorized in acute and maintenance therapies, according to the severity of the situation, prioritizing hemodynamic stability, bleeding cessation, correction of anaemia and subsequent regulation of menses. The first-line treatment consists of hormonal therapy. HMB may require combined regimens with hemostatic agents.

Consultation with a haematologist is frequently necessary, mostly in case of bleeding disorders and difficult cases that are unresponsive to first-line medical treatment.

A multidisciplinary approach and standard protocols for work-up improve time for diagnosis and bleeding control, which can reduce its physical and psychological impact in young women.

Long term treatment is crucial to prevent future events, establishing a regular menstrual cycle and improve quality

of life.

Future prospective studies on the efficacy and safety of treatments in adolescents, as well as standardized protocols, are required.

### PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

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### DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

### COMPETING INTERESTS

The authors have declared that no competing interests exist.

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