



## Abnormal uterine bleeding (AUB) in adolescents

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### Definition

- Abnormal uterine bleeding refers to bleeding that is excessive (heavy) or occurs outside of normal cyclic menstruation in the absence of hormonal therapy
- Heavy AUB is defined as menstrual blood loss greater than 80 ml (sanitary towels change every 1-2 hours), longer than 8 days, or causing symptomatic anemia.
- At 1 year post-menarche, around 75 % of cycles occur every 21- 45 days and towards the 5th year of gynecological age, 95% occur every 21 - 40 days.

### Prevalence

- It is the most frequent gynecologic condition in adolescents.
- Prevalence rates may be as high as high as 30% among adolescent females presenting to the gynecologist.
- Heavy menstrual bleeding has been reported in up to a third of adolescents

### Etiology

- The most common cause of abnormal uterine bleeding in adolescents is the dysfunctional bleeding due to ovulatory dysfunction of the PALM-COEIN FIGO Classification, related to immaturity of the hypothalamic-pituitary-gonadal axis (95% of AUB). The diagnosis is made by exclusion of other etiologies.
- Pregnancy must always be excluded as a possible cause of AUB, as should injuries related to sexual assault, or STIs
- Structural causes are infrequent in adolescents, as are other causes encompassed by PALM-COEIN FIGO Classification, with the exception

of the coagulation disorders, which are a common cause of heavy menstrual bleedings in adolescent population.

- A detailed list of cause is presented in Table 1.

**Table 1. Causes of Abnormal Uterine Bleeding in Adolescent Girls**

Endocrinologic	Hematologic	Pregnancy
<ul style="list-style-type: none"> <li>• Immaturity of the HPO</li> <li>• Anovulation               <ul style="list-style-type: none"> <li>○ Thyroid dysfunction</li> <li>○ Polycystic ovary syndrome</li> </ul> </li> </ul> <p>RARE:</p> <ul style="list-style-type: none"> <li>• Hyperprolactinemia</li> <li>• Adrenal disorders</li> <li>• Hypothalamic dysfunction (due to excessive exercise RED-s, eating disorders, stress)</li> <li>• Premature Ovarian insufficiency (POI)</li> </ul>	<ul style="list-style-type: none"> <li>• Von Willebrand disease</li> <li>• Thrombocytopenia</li> <li>• Platelet dysfunction</li> <li>• Clotting factor deficiency</li> <li>• Coagulation disorders</li> </ul>	<ul style="list-style-type: none"> <li>• Ectopic pregnancy</li> <li>• Implantation bleeding</li> <li>• Spontaneous abortion (Incomplete, threatened, septic)</li> <li>• Trophoblastic disease</li> </ul>
Secondary to drugs	Trauma	Reproductive tract pathology

<ul style="list-style-type: none"> <li>• H o r m o n a l contraceptives</li> <li>• LNG-IUS</li> <li>• Antipsychotics</li> <li>• Anticoagulants</li> <li>• Platelet inhibitors</li> </ul>	<ul style="list-style-type: none"> <li>• Sexual abuse</li> <li>• Foreign body</li> <li>• Laceration from consensual intercourse</li> <li>• Accidental injury</li> <li>• Related to induced abortion or other surgical procedure</li> </ul>	<ul style="list-style-type: none"> <li>• Congenital uterine malformations</li> <li>• Leiomyoma</li> <li>• Polyps</li> <li>• Endometriosis</li> <li>• I n f e c t i o u s (including STIs)</li> <li>• Ovarian and uterine tumors (e.g. granulosa cell or Sertoli-Leydig)</li> <li>• Malignancy</li> </ul>
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## Presentation

- Presentation may be with irregular menses (too frequent or too infrequent), heavy acute bleeding, or chronic heavy menstrual bleeding; signs and symptoms of underlying disease may accompany menstrual symptoms:
  - PCOS: acne, hirsutism, alopecia, obesity, acanthosis nigricans
  - Thyroid dysfunction: heat or cold intolerance, palpitations, fatigue, changes in hair/skin/nail changes, or weight gain or loss.
  - Pituitary disease: headaches, vision field changes, galactorrhea
  - Hematological disorders: easy bruising, hematomas, prolonged bleeding after minor surgeries, bleeding gums, nose bleeds

## Diagnosis

- Detailed menstrual, sexual and medical history, with attention to signs of bleeding disorders
- Vital signs -orthostatic changes in blood pressure and pulse
- General physical examination with assessment of Tanner staging (minimum Breast T3 and above should be present), palpation of the abdomen, checking for signs of anemia, bleeding disorders (bruises

and petechia) and hyperandrogenism (acne of face, chest, back; excess hair of upper lip, sideburns, back, abdomen, periareolar area)

- Inspection of external genital organs and lower part of vagina can be considered, based on medical history and bleeding pattern
- If sexually active, speculum and bimanual exam can be performed with attention to signs of cervicitis or trauma
- Laboratory workout including: pregnancy test, complete blood count with platelets and peripheral blood smear, ferritin, coagulation tests, if applicable for heavy bleeding, hormonal workout with minimum TSH, PRL (if infrequent menses) and FSH, androgens if signs of androgen excess; in hemodynamically unstable patient blood type and crossmatch should be included.
  - the necessary laboratory studies should be obtained before initiation of hormone therapy or blood transfusion.
- Sexually transmitted diseases screening (can test urine, vaginal swab, or cervical), if applicable based on age and risk factors
- Pelvic ultrasonography does not need to be obtained solely for the workup of heavy menstrual bleeding in adolescents, but it can be considered for patients who do not respond to initial management or those with thrombocytopenia.
  - transabdominal ultrasonography is a method of choice in pediatric patients prior to first intercourse
  - evaluation of endometrial thickness and exclusion of other diseases (ovarian masses, Mullerian anomalies) facilitates more accurate management
  - transrectal / translabial ultrasonography may be considered in older girls when transabdominal ultrasonography is not optimal
- When a coagulation disorder should be suspected?
  - if acute AUB requires hospitalization, transfusion and/or the hemoglobin level is less than 10 g/dl (a coagulation disorder is diagnosed in 20% of the cases.
  - medical history positive for one of the following criteria:

- menstruations greater than 7 days with heavy bleeding, since menarche
- excessive bleeding in surgeries
- postpartum hemorrhage
- medical history positive for **two** of the following criteria:
  - Bleeding related to dental treatments
  - Hematomas once or twice a month
  - Epistaxis once or twice a month
  - Frequent gum bleeding
  - Family history of a bleeding disorder

## **Management**

### **General considerations**

1. Most cases of AUB in adolescents are caused by anovulation or coagulation disorder; therefore treatment of these conditions will be reviewed here. Before initiating treatment, pregnancy must be excluded. STIs should be considered.

2. Management depends on the:

- severity of bleeding (degree of anemia and hemodynamic stability)
- cause of bleeding
- presence of systemic disease
- availability and cost of treatment options (not all medications are available in all countries)
- patient's and family preferences due to cultural or religious factors

3. Objectives for AUB management include both initial and long-term goals.

Initial goals:

- Stop the bleeding
- Avoid or treat anemia
- Investigate underlying causes with labs

Long-term goals:

- Reestablish regular menstrual cycles
- Improve quality of life of adolescents (90% responds to medical treatment)

#### 4. Treatment options include

- Hormonal treatment options: Combine oral contraceptive pills (COCP), Progestogens, Estrogens, Intrauterine system with levonorgestrel (IUS-LNG), GnRH analogs.
- Non-hormonal treatment options: Non-steroidal anti-inflammatory drugs (NSAIDs), Antifibrinolytics, Desmopressin.

5. A 2012 systematic review found no relevant randomized trials evaluating progestin-only or combined estrogen-progestin therapy in the treatment of anovulatory uterine bleeding and no consensus about the optimal approach. The dose of estrogen, dose and type of progestin, and schedule of administration vary widely.

#### **Assessment of AUB severity**

**Mild AUB:** longer than normal menses (>7 days) or shortened cycles (<21 days) for  $\geq 2$  months, with slightly or moderately increased menstrual flow with Hb > 12 g/dl

**Moderate AUB:** prolonged or frequent menses (every 1-3 weeks), with moderate to heavy flow and Hb  $\geq 10$  g/dl

**Severe AUB:** Disruptive menstrual cycles with heavy bleeding causing Hb < 10 g/dl and may be accompanied by haemodynamic instability (includes life-threatening condition with Hb <7 g/dl and haemodynamic instability)

#### **Acute management of AUB/HMB**

**MILD AUB:** Hb > 12 g/dl (120 g/l)

- Education and reassurance of the patient and family
- Menstrual calendar
- NSAIDs and tranexamic acid can help decrease bleeding
- hormonal treatment optional, especially if the desire for contraception exist

- Follow-up in 3-6 months or earlier if AUB worsens

**MODERATE AUB:** Hb 10 - 12 g/dl (100 - 120 g/l)

Control of moderate anovulatory uterine bleeding may involve hormonal therapy and/or hemostatic agents.

**Not currently bleeding treatment regimens for moderate AUB:**

**Progestin-only regimen** (for patient who do not desire contraception) prescribed as a maintenance regimen of either:

- Micronized progesterone 200 mg orally nightly for the first 12 days of each calendar month (if not allergic to peanuts) - such scheduling makes it easy for teenagers to follow
- Norethindrone acetate 5 mg orally nightly for the first 5 to 10 days of each calendar month
- Medroxyprogesterone acetate 10 mg orally nightly for the first 10 days of each calendar month

**Combined oral contraceptive pills (COCP) regimen**

- Monophasic oral contraceptives with a minimum of 30 mcg ethinyl estradiol according to the usual schedule (i.e., one pill per day, including the pills that do not contain hormones)

**Tranexamic acid**

Can be an option for patients with normal, regular cycles but prolonged, heavy menses, who decline hormonal options.

- Oral: 1000-1300 mg 3 times daily for up to 5 days during monthly menstruation; maximum daily dose: 3,900 mg/day

**Currently bleeding treatment regimens for moderate AUB:**

**Combined oral contraceptive pill (COCP) regimen** using monophasic oral contraceptives containing minimum 30 mcg ethinyl estradiol with a second-generation progesterone (the pills that do not contain hormones should be discarded):

- one pill every eight hours until the bleeding stops (usually within 48 hours),

- then one pill every 12 hours for 2 days,
- then one pill once per day for a total of at least 21 days
- It may be prudent to continue pill as back-to-back therapy and then allow the withdrawal bleeding to occur

Alternative tapering regimens have been also described in the literature. Withdrawal bleeding should be allowed to occur prior to initiating continuous or cyclic hormonal regimens.

### **Progestin-only regimen**

- Norethindrone acetate 5 to 10 mg nightly until the bleeding stops and the anemia is resolved. Once anemia has resolved, the initial course of oral progestin should be followed by at least five to seven days of no hormonal therapy to permit shedding of the endometrium (withdrawal bleeding).
- Medroxyprogesterone acetate 20 mg orally every 6 - 12 hours (up to 80 mg/day) until the bleeding stops, and then tapering to 10 mg once daily until maintenance therapy is initiated after allowing withdrawal bleeding

### **Tranexamic acid**

Can be an initial option with close follow-up when the patient declines hormonal therapy. with close follow-up. Hormonal therapy may be warranted if hemoglobin concentration does not improve or continues to decrease.

- Oral: 1000-1300 mg 3 times daily for up to 5 days during monthly menstruation; maximum daily dose: 3,900 mg/day

### **SEVERE AUB: Hb < 10 g/dl**

Control of severe anovulatory uterine bleeding in a pediatric patient may involve hormonal therapy, hemostatic agents, and very rarely surgical intervention. Therapy may require hospitalization.

Indications for hospitalization include:

- hemodynamic instability (tachycardia, hypotension, dyspnea)



- symptomatic anemia (lethargy, fatigue, syncope, tachypnea)
- Hb <7 g/dL or <10 g/dL with active heavy bleeding
- necessity of intravenous or surgical intervention

If the patient's Hb concentration is between 8-10 g/dl and she is hemodynamically stable, and the family is reliable and able to maintain phone contact, ambulatory management with oral hormonal therapy may be sufficient

### **Hormonal therapy**

#### **COCP regimen**

The initial management is hormonal therapy with monophasic oral contraceptives containing 50 mcg (if available) or a minimum of 30-35 mcg ethinyl estradiol with a second-generation progesterone (the pills that do not contain hormones should be discarded):

- one pill every six hours until the bleeding stops (usually within 24 hours),
- then one pill every 8 hours for 3 days,
- then one pill every 12 hours for 3 days (up to 2 weeks)
- then one pill once per day continuously until Hb concentration is > 11 g/dl; at that time withdrawal bleeding can be allowed (by discontinuing therapy for at least 3 days).

Alternative tapering regimens have been also described in the literature.

#### **Progestin-only regimen**

Can be an option when estrogens are contraindicated or a patient declines therapy with oral contraceptives. The following regimens can be used

- Norethindrone acetate 5 to 10 mg twice per day for 7 days, then 5 to 10 mg once per day until maintenance therapy is initiated
- Norethindrone acetate 5 to 10 mg three times per day for 3 days, then 5 to 10 mg twice per day for 7 days, then 5 to 10 mg once per day until maintenance therapy is initiated

- Medroxyprogesterone acetate 20 mg orally every 8 hours (up to 80 mg/day) for 7 days, or until bleeding stops and then begin progestin taper to reach 10 mg once daily, maintenance therapy.
- Treatment should be continued until Hb concentration is > 11 g/dl; at that time withdrawal bleeding can be allowed (by discontinuing therapy for at least 3 days).

### **Intravenous estrogens**

- IV estrogen therapy may be indicated if bleeding is not controlled after 24 hours of combination hormonal therapy or patient is not able to take oral medications, or surgical intervention is considered (rare)
- Consideration should be given to ultrasonography (particularly in patients with platelet dysfunction) to assess for a hematometrium (or clot/tissue within the uterus) which may be preventing adequate hemostasis
- The following regimen is most often indicated:
- Conjugated estrogen 25 mg every four hours, no more than 6 dosages should be administered
- Bleeding decrease or stop within up to 48 hours; if it does not subside after 24 hours, hemostatic therapy may be warranted and the progestins should be added if it persists after 48 hours.
- When the bleeding subsides, the COCP regimen for severe AUB should be initiated (as described above)

### **Hemostatic therapy**

May be warranted for severe AUB which persists after 24 hours of IV estrogens, and in patients with platelet dysfunction. Although there is a theoretical risk of thrombosis with the concomitant administration of tranexamic acid and COCPs, the review of the existing literature has not identified an increased risk of venous thromboembolism in this setting, although studies are very limited.

### **Tranexamic acid**

- Oral: 1000-1300 mg 3 times daily for up to 5 days during monthly menstruation; maximum daily dose: 3,900 mg/day

**Aminocaproic acid:**

- IV or orally 5 g during first hours, followed by continuous infusion of 1g/hour until bleeding stops or up to 8 hours

**Desmopressin**

- IV 0.3 mcg/kg over 15-30 minutes; the dose maybe repeated during next 48 hours is bleeding persist

**Surgical intervention**

Surgical interventions should be reserved as a last resort in case of life-threatening bleeding refractory to other therapies

- Intrauterine balloon: a 30-mL Foley balloon, after calculating the volume of the uterus by ultrasound measurements, can be used for the tamponade effect; it usually can be kept in place for 12-24 hours, after which time a gradual deflation by 5 mL increments is recommended; antibiotics use can be considered while balloon stays in the uterine cavity
- suction (preferred) or sharp curettage, if used, need to be done with special caution to prevent scarring of the endometrial lining with risk of subsequent Asherman syndrome
  - concomitant placement of a LNG-IUD for long-term management should be considered in this setting
- Endometrial ablation, uterine artery embolization, and hysterectomy are invasive measures that can cause infertility and should not be considered in the adolescent population unless absolutely necessary, as in life-threatening situations

**Additional considerations and follow-up schedule:**

- When the bleeding returns during tapering of the COCP, an increase in dosage to the previously effective dose usually results in cessation of bleeding

- Blood transfusion may be needed, and is considered based on hemoglobin concentration, amount of blood loss and clinical parameters
  - Healthy adolescents usually tolerate Hb levels < 7 g/dL, and a decision to transfuse should be based on hemodynamic status and presence of active bleeding, not only the hemoglobin level.
- Administration of antiemetics (e.g., promethazine 12.5 to 25 mg or ondansetron 8 mg orally, IV, or per rectum) one hour before each dose of COCP or IV estrogen may alleviate the side effects of nausea and vomiting.
- Patients should be counseled that breakthrough bleeding is common during the first three months of continuous hormonal therapy and possibly longer. Consistent daily pill taking is required, although it may not obviate the risk of breakthrough bleeding in the initial months of use.
- Maintenance of an accurate menstrual calendar (paper charting or with an app) will guide therapy.
- Iron supplementation with 60 mg of elemental iron should be initiated immediately for Hb < 12 g/dl, once or twice per day based on the severity of anemia. There is some evidence that every other day use of iron may improve absorption.
- **Follow-up schedule**
  - First follow-up after hospitalization for severe AUB should be scheduled in 7 to 14 days, and then every month until Hb is >10 g/dl and menstrual pattern is stable
  - Patients with severe AUB treated in an ambulatory setting should be seen in 7 days, and then every month until Hb is >10 g/dl and menstrual pattern is stable.
  - Patients with moderate AUB should be followed every 3 to 6 months until menstrual pattern is stable, and annually thereafter.
- **Specific management in case of coagulation disorder**
  - Interdisciplinary management with hematology should be implemented.

- ACOG Committee on Adolescent Health recommends the use of the screening tool for identification of patients with bleeding disorders among those presenting with AUB/HMB. Freely available from <https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2019/09/screening-and-management-of-bleeding-disorders-in-adolescents-with-heavy-menstrual-bleeding>
- The screening tool is positive if 1 of the following 4 criteria is met:
  1. menses  $\geq$  7 days and the patients report “flooding” or bleeding through the tampon or pad in 2 hours or less with most periods
  2. a history of treatment of anemia
  3. a family history of diagnosed bleeding disorder
  4. a history of excessive bleeding with tooth extraction, surgery, miscarriage or delivery
- In adolescents with known bleeding disorders, the pictorial blood assessment chart may help to assess response to treatment, although it may not be predictive of bleeding disorders
- Tests to order, when bleeding disorder is suspected: smear to evaluate platelet morphology, Prothrombin time, APTT, fibrinogen, von Willebrand factor antigen (VWF), ristocetin cofactor activity, factor VIII activity
- If the above results are normal: test for platelet aggregation and secretion is recommended
- Consider that hormonal treatment alters the results of the hematologic tests, so ideally, even in the face of heavy bleeding that will require immediate treatment, it is recommended to do testing prior to the administration of treatment.
- In girls and adolescents with underlying bleeding disorders, continuous use of combined OCs or the use of a LNG-IUS may be optimal.

### **Long-term management of AUB/HMB**

Long-term management is usually required up to 6 months after acute moderate or severe AUB and may be stopped at that time to evaluate if the normal menstrual pattern has been established if no underlying cause of anovulation (e.g. PCOS) has been found, and there is no need for contraception.

#### **Patients with Hb < 10 g/dl**

- Continuous COCP with minimum 30-35 mcg for 3 months or until Hb level > 10 g/dl, followed by 3 months of cyclic COCP
  - two Cochrane Reviews found that extended cycling as compared with monthly cycling offered more favorable bleeding profiles, a decrease in estrogen withdrawal symptoms, reliable ovulation suppression, and a decrease in unscheduled bleeding episodes over time.
- Monitoring of hemoglobin monthly until it is  $\geq 10$  g/dL and then every three to six months until it is >12 g/dL.

#### **Patients with Hb $\geq 10$ g/dl**

- Monophasic COCP with minimum 30 mcg in a cyclic manner for 3 to 6 months
- Continuous extended COCP
- Continuous extended progestogen therapy
- If bleeding occurs while the patient is taking maintenance progesterone, she should discontinue progesterone and allow menses to occur. Cyclic progestogen therapy:
  - Micronized progesterone 200 mg orally nightly for the first 12 days of each calendar month (if not allergic to peanuts) - such scheduling makes it easy for teenagers to follow
  - Norethindrone acetate 5 mg orally nightly for the first 5 to 10 days of each calendar month
  - Medroxyprogesterone acetate 10 mg orally nightly for the first 10 days of each calendar month

- For patients needing contraception, progestin-only regimen includes continuous progestin-only contraceptive pills, depot medroxyprogesterone acetate, progestin implants, and levonorgestrel-releasing IUDs .
  - In 2018 prospective study in adolescents levonorgestrel-releasing IUD was shown to have the highest rate of successful control of bleeding, and was especially effective in the patients with the bleeding disorder
- Monitoring of hemoglobin every 3 to 6 months until it is >12 g/dL.

### **Prognosis**

- The long-term prognosis for girls with AUB depends upon the underlying cause
- AUB due to immaturity of the hypothalamic-pituitary-ovarian axis usually resolves with maturation of HPO axis, which may take up to 6-8 years since menarche
- Girls with PCOS or other specific cause of anovulation, or those with significant dysmenorrhea, or who need contraception may benefit from ongoing COCP
- The long-term follow-up is needed to avoid relapse and adverse sequelae

### **Summary characteristic of pharmacological AUB treatment options**

#### **1. Combined oral contraceptive pills (COCP)**

COCPs are the first-line treatment of AUBs. COCPs can be administered cyclically or in extended mode. There are no studies that prove one type of COCP to be more effective over another or patches or rings in the management of AUB.

Most authors suggest COCP with minimum 30 or 35 mcg ethinylestradiol (EE2).

In our practice we often start with COCP consisting of 30 mcg (EE2) and either 150 mcg levonorgestrel or 2 mg dienogest.

During AUB treatment the COCP dose varies from 1 pill once a day up to 2 - 4 per day (hemostatic dose) depending of severity of bleeding.

Exogenous estrogen and progestin permits additional endometrial proliferation, which heals the sites of endometrial bleeding, and provides hemostasis by stimulating the synthesis of coagulation factors. Estrogen promotes initial hemostasis while progestogen stabilizes the endometrium. COCPs can decrease bleeding by 50-60%.

## 2. Cyclical oral progestins are an option:

- in very young girls
- if contraception is not required
- if estrogen use is contraindicated
- if a patient declines therapy with oral contraceptives

Chronic AUB	Acute AUB
5-10mg medroxyprogesterone acetate (MPA) 10-14 days per cycle.	10-20mg MPA PO every 4-6 hours (max. 80mg/d)
Norethindrone acetate 2.5 - 5mg/d 10-14 days per cycle	Norethindrone acetate 5 - 10mg every 6 hours (up to 40mg/day) to stop bleeding and then gradually decrease
Depot MPA 150mg IM every 10-13 weeks	Long - acting depot MPA is not recommended
Micronized oral progesterone 100-200 mg 12-14 days per month	
Dydrogesterone 10-20 mg 12-14 days per month	

**Micronized oral progesterone** is chemically identical to endogenous progestin and thus is more physiological. Oral progestin is given for 12 days every month and bleeding occurs 2-7 days after cessation. If bleeding does



not start within one week the patient should be re-evaluated and the possibility of pregnancy considered

**Dydrogesterone** appears to be a highly selective progestin which, due to its structure, binds almost exclusively to the progesterone receptor.

### **3. Estrogens**

In cases with very severe and prolonged bleeding and thin endometrium, estrogen therapy is indicated to promote endometrial growth, and to stimulate clotting at the capillary level.

In patients with acute or heavy bleeding and those requiring hospitalization, 25 mg of conjugated estrogen is administered intravenously every 4 hours until the bleeding is under control, or for 12 hours. Oral estrogen can also be used, 1.25 mg of conjugated estrogens or 2 mg estradiol every 4 hours for 24 hours, followed by 1.25 mg conjugated estrogens or 2 mg estradiol daily for 7-10 days.

After the course of estrogen therapy, progestins are added concomitant with the estrogen therapy or after the estrogen therapy. This is more physiological treatment for adolescents and very well tolerated.

One can also choose the estrogen-progestin combination from cyclic combined hormone regimen of menopausal hormone replacement therapy. These are administered in regular doses.

### **4. Levonorgestrel-releasing intrauterine system (LNG-IUS)**

It reduces bleeding in patients with chronic AUB by more than 80% in three months and 97% in one year. More effective than NSAIDs, COCs and progestogens. Excellent therapeutic alternative for adolescents who are sexually active with benefit of contraception. Very useful in patients with coagulopathies and those with significant dysmenorrhea or endometriosis.

### **5. GnRH analogs**

Second line treatment. Useful in patients receiving chemotherapy who develop low platelet count with heavy uterine bleeding or blood dyscrasias when other treatments have failed.

### **6. Non-steroidal anti-inflammatory drugs (NSAIDs)**

More effective than placebo but less than tranexamic acid or LNG-IUS. NSAIDs can reduce blood loss by 30% to 50%, when administered during menses. To start 1-2 days before bleeding and until it subsides, total course should not exceed five days. Advantage: simultaneous treatment of dysmenorrhea. They would not be top of the line for the treatment of AUB.

- Ibuprofen: 200 - 400 mg, every 6 - 8 hours
- Naproxen 250 - 500 mg, every 12 hours. The longer duration of action is particularly helpful for adolescents, as it lasts the entire school day.
- Mefenamic acid 500 mg, every 8 hours

**7. Antifibrinolytics:** useful in acute bleeding due to their rapid effect, and when hormonal treatment is contraindicated, or in patients with coagulopathy.

Equally effective in adolescents as combined oral contraceptives although with fewer adverse effects and higher adherence. The literature does not suggest an increased risk of thrombosis when used in combination with COCP. They reduce bleeding by 25-50%. Contraindications: acute thromboembolic disease or prothrombotic states. A small randomized study in adolescents with AUB, showed tranexamic acid as effective in reducing menstrual blood loss and improving quality of life as combined estrogen-progestin. A 2018 systematic review of randomized trials in adult women with heavy menstrual bleeding found low quality evidence that tranexamic acid and oral progestin therapy were similarly effective in reducing mean menstrual blood flow.

- Tranexamic acid 1 - 1.3 g PO every 8 hours for 5 days
- Aminocaproic acid 2 - 4g PO 4 - 6 times a day for 5 days

## Desmopressin

Useful in patients with type 1 VWD, hemophilia or platelet defects. It increases VWF and factor VIII and platelet adhesion.

## Treatment options of acute and severe AUB

Treatment	Dose	Mode	Frequency
Conjugated estrogens	25mg	IV *	4-6 h
17-beta estradiol	2mg	PO*	4-6 h
COCP 30-35mcg EE	1 pill	PO	6h
Norethindrone acetate	5-10mg	PO	6hs
Medroxyprogesterone acetate	10-20mg (80mg/d max)	PO	6-12hs
Tranexamic acid	10mg/k	IV	6-8hs

\*IV - intravenously \*PO - orally

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