Medical Management of Abnormal Uterine Bleeding

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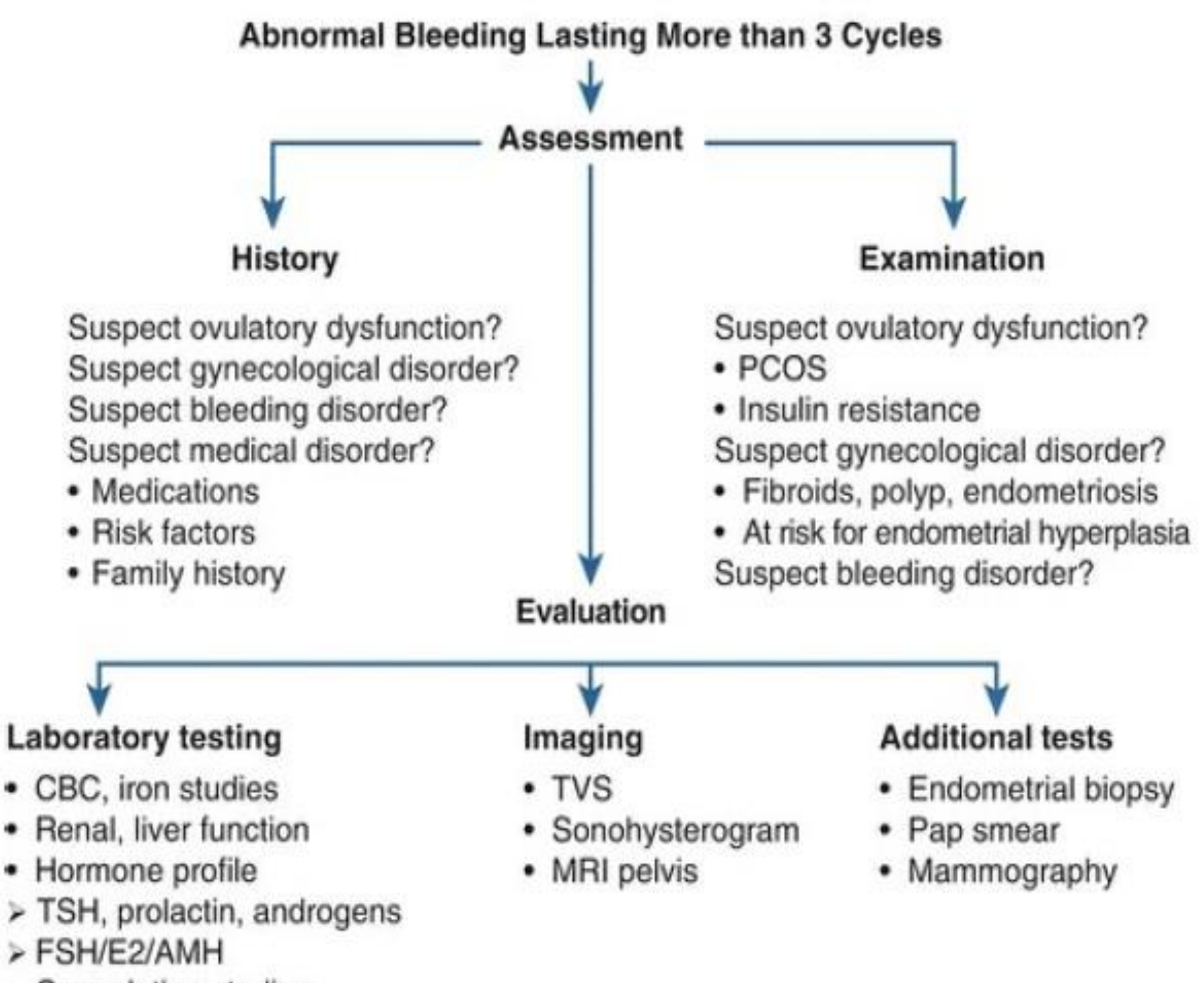
Abnormal Bleeding Lasting More than 3 Cycles
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Abnormal uterine bleeding in adolescents: Management

The treatment of anovulatory uterine bleeding varies with severity, which is classified as follows:

- **Mild – Longer than normal menses (>7 days) or shortened cycles (<24 days) for ≥2 months, with slightly or moderately increased menstrual flow; hemoglobin is usually normal (≥12 g/dL) but may be mildly decreased (10 to 12 g/dL)**

- **Moderate – Moderately prolonged (eg, >7 days) or frequent menses every one to three weeks, with moderate to heavy menstrual flow and hemoglobin ≥10 g/dL**

- **Severe – Disruptive menstrual cycles with heavy bleeding that causes a decrease in hemoglobin (to <10 g/dL) and may or may not cause hemodynamic instability**

The treatment of anovulatory uterine bleeding varies with severity, which is classified as follows:

GOALS OF MANAGEMENT

Establishment and/or maintenance of hemodynamic stability

●Correction of acute or chronic anemia

●Return to a pattern of normal menstrual cycles

●Prevention of recurrence

●Prevention of long-term consequences of anovulation (eg, anemia, infertility, endometrial cancer

GENERAL PRINCIPLES

Pretreatment evaluation — It is important to exclude pregnancy and pelvic infections before initiating treatment of anovulatory uterine bleeding .

In addition, causes of AUB and anovulatory uterine bleeding other than an immature hypothalamic-pituitary-ovarian axis should be evaluated as indicated based upon clinical findings.

The necessary laboratory studies should be obtained before initiation of hormone therapy or blood transfusion.

Appropriate management of underlying causes of AUB may prevent potential short- and long-term sequelae such as anemia and endometrial cancer

Thus, it is crucial to establish the correct diagnosis before any therapy is administered.

Appropriate treatment of the underlying problem usually permits return to a normal menstrual pattern.

GENERAL PRINCIPLES

Management of iron deficiency — Patients with anovulatory uterine bleeding are at risk for iron deficiency anemia and should be monitored and treated as indicated .

●For those with mild or moderate anovulatory uterine bleeding and mild, asymptomatic anemia (eg, hemoglobin 10 to 12 g/dL), we initiate iron supplementation with 60 mg elemental iron per day.

●For those with severe anovulatory uterine bleeding, we initiate iron supplementation as soon as the patient is stable and able to take pills by mouth. Depending upon the severity of iron deficiency, we use 60 mg of elemental iron once or twice per day.

GENERAL PRINCIPLES

- **Hormone effects — In adolescents with anovulatory uterine bleeding and sustained acyclic estrogen secretion, bleeding occurs when the endometrium proliferates beyond the ability of endogenous estrogen to maintain the integrity of the endometrium.**

- **Administration of exogenous estrogen permits additional endometrial proliferation which heals the sites of endometrial bleeding, and provides hemostasis. Administration of progestin stabilizes the endometrial lining .**

GENERAL PRINCIPLES

- Clinicians may be concerned that the high doses of estrogen that are sometimes necessary to control severe AUB may cause premature closure of the growth plates, reducing ultimate adult height.

- However, by the time of menarche, most female adolescents have already undergone their growth spurt and achieved approximately ≥95 percent of adult height.

- Oral contraceptive therapy has not been associated with reductions in expected height.

GENERAL PRINCIPLES

Monitoring response — Adolescents who are being treated for anovulatory uterine bleeding should maintain a menstrual calendar to monitor response to therapy and subsequent episodes of anovulatory uterine bleeding.

ACUTE MANAGEMENT OF MILD ANOVULATORY UTERINE BLEEDING

- **Mild anovulatory uterine bleeding is characterized by longer-than-normal menses or shortened cycles for ≥2 months, with slightly to moderately increased flow.**

- **Hemoglobin is usually normal (≥12 g/dL) but may be mildly decreased (eg, 10 to 12 g/dL).**

- **Decisions regarding management of mild anovulatory bleeding are individualized according to the preferences of the patient and guardian and the need for contraception .**

ACUTE MANAGEMENT OF MILD ANOVULATORY UTERINE BLEEDING

- **For those with mild anovulatory uterine bleeding, normal hemoglobin, and no desire for contraception who report that their quality of life is not affected by bleeding, we suggest observation and reassurance.**

ACUTE MANAGEMENT OF MILD ANOVULATORY UTERINE BLEEDING

- **For those with mild anovulatory uterine bleeding and hemoglobin between 10 and 12 g/dL, observation and reassurance or hormonal therapy to stabilize endometrial proliferation and promote cyclic shedding are both acceptable options.**

- **The hormonal therapy regimens for mild anovulatory uterine bleeding are the same as for moderate anovulatory uterine bleeding.**

- **We also recommend iron supplementation for patients with mild anovulatory uterine bleeding and hemoglobin between 10 and 12 g/dL.**

ACUTE MANAGEMENT OF MILD ANOVULATORY UTERINE BLEEDING

- **They should follow up in three to six months**
- **Unless bleeding becomes more severe or prolonged, in which case they should be seen acutely.**
- **We obtain a complete blood count in patients whose initial hemoglobin was <12 g/dL.**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Moderate anovulatory uterine bleeding is characterized by moderately prolonged (eg, >7 days) or frequent menses every one to three weeks, with moderate to heavy menstrual flow and hemoglobin ≥10 g/dL

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Moderate anovulatory uterine bleeding usually can be managed in the outpatient setting.**
- **Treatment typically involves hormonal therapy to stabilize endometrial proliferation and shedding.**
- **The hormonal therapy regimen depends upon whether the patient is currently bleeding.**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

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.

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Most adolescents with anovulatory uterine bleeding respond to hormonal therapy.**
- **Among those who do not, an alternative diagnosis (eg, bleeding disorder, polycystic ovary syndrome, infection, uterine pathology) should be considered.**
- **Additional evaluation and consultation may be warranted if bleeding cannot be controlled despite hormonal therapy .**
- **Patients with moderate anovulatory uterine bleeding often have mild anemia (hemoglobin 10 to 12 g/dL), which should be treated with iron supplementation .**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Not currently bleeding — Decisions regarding management of moderate anovulatory bleeding in patients who are not currently bleeding are individualized according to the preferences of the patient and guardian and the need for contraception.**

- **For patients with moderate anovulatory uterine bleeding who are not actively bleeding, we suggest either progestin-only hormone therapy or combined estrogen-progestin oral contraceptives.**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Progestin/progesterone-only regimen – Among the oral progestin-only regimens for patients with moderate to severe anovulatory bleeding who are not actively bleeding , we suggest a maintenance regimen of either:**

- **Norethindrone acetate 5 mg orally nightly for the first 5 to 10 days of each calendar month, or**

- **Oral micronized progesterone 200 mg nightly for the first 12 days of each calendar month, or**

- **Medroxyprogesterone acetate 10 mg orally nightly for the first 10 days of each calendar month**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Norethindrone helps to stabilize the endometrium and, in our experience, is usually rapidly effective.**
- **Oral micronized progesterone is chemically identical to endogenous progesterone for those patients who prefer a more bioidentical approach.**
- **Medroxyprogesterone is another commonly used option based on patient insurance coverage.**
- **Scheduling the pills to start on the first day of each calendar month is easy for teenagers to follow.**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

We warn patients that irregular spotting is common initially

But, if heavy vaginal bleeding occurs while the patient is taking progesterone, they should see their provider to discuss whether oral progestin is the optimal regimen.

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Combination estrogen-progestin regimen – For patients who are not actively bleeding and choose combination estrogen-progestin therapy, we suggest monophasic oral contraceptives (ie, pills that contain the same dose of estrogen and progestin in each of the hormonally active pills) with a minimum of 30 mcg ethinyl estradiol to ensure a sufficient amount of estrogen to prevent breakthrough bleeding**

We generally initiate combination estrogen-progestin oral contraceptives according to the usual schedule (ie, one pill per day, including the pills that do not contain hormones).

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Currently bleeding — For patients with moderate anovulatory uterine bleeding who are actively bleeding, we suggest combined estrogen-progestin oral contraceptives rather than progestin-only hormone therapy because estrogen provides hemostasis.

Progestin-only therapy

Tranexamic acid

Combination estrogen-progestin regimen

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Progestin-only therapy is an alternative for patients who cannot tolerate, dislike, or have a contraindication to estrogen therapy:

- migraine with aura,
- systemic lupus erythematosus,
- arterial or venous thromboembolic disease,
- estrogen-dependent tumors,
- hepatic dysfunction or
- disease or who object to taking combination oral contraceptives.

Treatment with tranexamic acid may be an option for patients with moderate anovulatory bleeding who are currently bleeding and decline hormonal options.

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Combination estrogen-progestin regimen –

For combined estrogen-progestin therapy in patients with moderate to severe anovulatory bleeding.

Monophasic oral contraceptives (ie, pills that contain the same dose of estrogen and progestin in each of the hormonally active pills) with a minimum of 30 mcg ethinyl estradiol to ensure a sufficient amount of estrogen to prevent breakthrough bleeding .

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Randomized trials regarding the treatment of anovulatory uterine bleeding in adolescents are lacking .**

- **However, in a systematic review of randomized trials in adult women with AUB presumed to be secondary to endometrial dysfunction, a variety of combined estrogen-progestin contraceptive regimens appeared to be equally effective (with 35 to 65 percent reductions in menstrual blood loss) .**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

For patients who are actively bleeding, we use the following regimen (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**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Close follow-up (in person or by phone) is essential while the pills are being taken two or three times per day.

High-dose estrogen therapy can cause nausea, which may result in decreased adherence.

If nausea occurs, we suggest antiemetic therapy (eg, promethazine 12.5 to 25 mg orally or per rectum or ondansetron 4 to 8 mg orally) before each combination estrogen-progestin pill .

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Management of hormonal therapy after the initial 21-day course

- **Progestin-only regimen**
- **Tranexamic acid**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Progestin-only regimen – In patients with mild-to-moderate anovulatory uterine bleeding, progestin-only therapy may be used to mature and slough the endometrium .**

- **Among the oral progestin-only regimens for acute management , we suggest norethindrone acetate.**

- **Norethindrone provides enough estrogenic activity to minimize side effects but not enough to stimulate endometrial bleeding.**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Among the oral progestin-only regimens for acute management

Norethindrone acetate

Norethindrone 5 to 10 mg nightly until the bleeding stops and the anemia is resolved.

We warn patients that irregular spotting is common initially, but, if heavy vaginal bleeding occurs while the patient is taking progesterone, they should see their provider to discuss whether oral progestin is the optimal regimen.

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.

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

- **Tranexamic acid – Treatment with cyclic tranexamic acid may be an option for patients with moderate anovulatory bleeding who are currently bleeding and decline hormonal options .**

- **The regimen is 1300 mg orally up to three times per day for the first one to five days of each menstrual cycle.**

- **It is uncertain how long adolescents with heavy menstrual bleeding should be treated with cyclic tranexamic acid. We ask patients to follow up in one to three months to monitor hemoglobin.**

- **A switch to hormonal therapy may be warranted if hemoglobin continues to decline or fails to stabilize.**

ACUTE MANAGEMENT OF MODERATE ANOVULATORY UTERINE BLEEDING

Cyclic tranexamic acid does not regulate menstrual cycles.

However, in a small pilot study, it appeared to be as effective in reducing menstrual blood loss and improving quality of life as combined estrogen-progestin in adolescents with heavy menstrual bleeding .

A systematic review of randomized trials in women with heavy menstrual bleeding found low quality evidence that tranexamic acid and progestin therapy were similarly effective in reducing mean menstrual blood .

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

- **Severe anovulatory uterine bleeding is defined by disruptive menstrual cycles with heavy bleeding that causes a decrease in hemoglobin (to <10 g/dL) with or without hemodynamic instability .**

- **Control of severe anovulatory uterine bleeding may involve hormonal therapy, hemostatic agents, and (rarely) surgical intervention.**

- **We initiate iron supplementation as soon as the patient is stable and able to take pills by mouth.**

- **Depending upon the severity of iron deficiency, we use 60 mg of elemental iron once or twice per day.**

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Indications for hospitalization:

- Hemodynamic instability (eg, tachycardia, hypotension, orthostatic vital signs)
- Hemoglobin concentration <7 g/dL or <10 g/dL with active heavy bleeding
- Symptomatic anemia (eg, fatigue, lethargy)
- Need for intravenous conjugated estrogen (eg, cannot take oral medications, continued heavy bleeding after 24 hours of estrogen-progestin combination therapy)
- Need for surgical intervention

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Additional evaluation —

Patients who require hospitalization for anovulatory uterine bleeding should:

Evaluation for a bleeding disorder

Pelvic ultrasonography to evaluate pelvic pathology (eg, polyps, ovarian tumors)

particularly if they do not respond to initial therapy.

Any underlying disorder that is detected should be promptly treated.

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Additional evaluation —

Heavy menstrual bleeding requiring hospitalization or transfusion may be the initial presentation of a coagulation disorder, particularly von Willebrand disease.

It is estimated that up to 20 percent of adolescents with heavy menstrual bleeding have von Willebrand disease or platelet dysfunction

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

The laboratory evaluation for patients who require hospitalization for heavy menstrual bleeding generally includes:

Screening for pregnancy

Hypothyroidism (with thyroid stimulating hormone),

A complete blood count (to include a platelet count),

Prothrombin time, activated partial thromboplastin time, plasma von Willebrand factor (VWF) antigen,

Plasma VWF activity (ristocetin cofactor activity),

Factor VIII activity, and blood group typing

Of note, blood group O is associated with lower levels of VWF.

Evaluation in conjunction with a hematologist is suggested, especially if there is a concern that requires testing for additional bleeding disorders .

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Hormonal therapy :

Combination therapy

Progestin-only pills

Intravenous estrogen

Addition of hemostatic therapy

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Combination therapy —

Combination oral contraceptive pills are the first-line hormonal therapy for the acute management of severe anovulatory uterine bleeding.

Progestin-only therapy and IV conjugated estrogen are potential alternatives for patients who cannot take combination oral contraceptive pills.

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

In adolescents who have severe anovulatory bleeding and anemia or who are at risk for anemia

Starting with a monophasic combination oral contraceptive pill with a higher dose of estrogen (ie, 50 mcg ethinyl estradiol, which is equivalent to the dose in intravenous estrogen) and either 0.5 mg norgestrel or 1 mg norethindrone to promote control of bleeding as soon as possible

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Tapering according to the regimen below:

- One pill every four to six hours until the bleeding subsides (usually within 24 hours), then
- One pill every eight hours for three days, then
- One pill every 12 hours for up to two weeks, then one pill once per day.

Once the patient is weaned to one pill per day and their anemia has resolved, they should be allowed to have a withdrawal bleed (ie, by discontinuing hormones for at least three days).

The adolescent must be instructed to discard the pills that do not contain hormones.

Antiemetic therapy (eg, promethazine 12.5 to 25 mg orally or per rectum or ondansetron 4 to 8 mg orally) may be required for patients who are taking more than one pill per day.

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Progestin-only pills —

Oral progestin-only therapy is an alternative to combination oral contraceptive pills in the acute management of patients with severe anovulatory bleeding in whom estrogen is contraindicated :

Migraine with aura, systemic lupus erythematosus, arterial or venous thromboembolic disease, estrogen-dependent tumors, and hepatic dysfunction or disease) or who refuse to take combination oral contraceptives

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Norethindrone provides enough estrogenic activity to minimize side effects but not enough to stimulate endometrial bleeding.

Norethindrone 5 to 10 mg can be given up to four times a day based on the severity of the patient's bleeding. Once bleeding has stopped, it can be tapered over several days.

Two commonly used tapering regimens are provided below :

- **Norethindrone 5 to 10 mg twice per day for seven days, followed by 5 to 10 mg once per day until maintenance therapy is initiated**

- **Norethindrone 5 to 10 mg three times per day for three days, followed by 5 to 10 mg twice per day for seven days, followed by 5 to 10 mg once per day until maintenance therapy is initiated**

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Intravenous estrogen —

IV conjugated estrogen therapy is reserved for patients with severe anovulatory uterine bleeding who are unstable and cannot take oral medications.

In addition, IV conjugated estrogen therapy may be indicated if bleeding is not controlled after 24 hours of combination hormonal therapy.

The dose of IV conjugated estrogen is 25 mg every four to six hours until the bleeding stops.

No more than six doses should be administered.

Thromboembolism is a potential complication

Administration of antiemetics (eg, promethazine 12.5 to 25 mg orally, transdermally ,one hour before each dose of IV estrogen may alleviate the side effects of nausea and vomiting.

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

- **Bleeding usually subsides within 4 to 24 hours of the initiation of IV estrogen .**
- **Hemostatic therapy may be warranted if bleeding persists beyond 24 hours**
- **If bleeding lasts longer than 24 to 48 hours after initiation of IV estrogen, oral progesterone should be added to stabilize**
- **Oral progesterone should be discontinued when oral contraceptive pills are initiated**

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

After the bleeding subsides, the patient should be switched to a taper of combination monophasic oral contraceptive.

We use a monophasic oral contraceptive that contains at least 50 mcg estradiol and suggest the following schedule:

- **One pill every four to six hours until the bleeding stops**
- **One pill every eight hours for three days, then**
- **One pill every 12 hours for two weeks**

Antiemetic therapy (eg, promethazine 12.5 to 25 mg orally or per rectum or ondansetron 4 to 8 mg orally) may be required for patients who are taking more than one pill per day.

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Addition of hemostatic therapy —

The addition of hemostatic therapy to hormonal therapy may be warranted for severe anovulatory uterine bleeding that continues after 24 hours of hormonal therapy and in patients with platelet dysfunction.

Hemostatic therapies include tranexamic acid, aminocaproic acid, and desmopressin, which is classically used for the treatment of von Willebrand disease .

Among these agents, we prefer tranexamic acid unless the patient has increased risks for thromboembolism .

Aminocaproic acid should be avoided in patients with renal impairment.

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

- **Tranexamic acid** is administered orally: 1300 mg three times per day for up to five days

- **Aminocaproic acid** may be administered orally or IV as follows:

- Aminocaproic acid 5 g orally during the first hour, followed by a continuous dose of 1 to 1.25 g per hour; treatment is continued for approximately eight hours or until the bleeding has been controlled, or

- Aminocaproic acid 4 to 5 g IV during the first hour of treatment, followed by a continuous infusion at a rate of 1 g per hour; treatment is continued for approximately eight hours or until the bleeding has been controlled

- **Desmopressin** is administered IV as follows:

- Desmopressin 0.3 mcg/kg IV over 15 to 30 minutes; the dose may be repeated in 48 hours if there is no response

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Refractory uterine bleeding —

In the rare cases in which treatment with hormones and antifibrinolytics agents fails, additional evaluation (examination under anesthesia, endometrial sampling) may be necessary to assess causes of AUB other than anovulatory uterine bleeding.

Dilation and curettage (D&C) also may be used as a therapeutic intervention. However, therapeutic D&C is rarely required in adolescents with AUB. It should be reserved as a last resort for the rare patient who continues to have life-threatening bleeding despite other therapies .

If D&C is performed in adolescents, care must be taken to prevent scarring of the endometrial lining (Asherman syndrome).

ACUTE MANAGEMENT OF SEVERE ANOVULATORY UTERINE BLEEDING

Maintenance therapy —

Management after the acute episode of bleeding is controlled and the initial course of hormonal therapy is complete depends upon the initial hormonal regimen, the patient's desire for contraception, and whether they remain anemic.

Long-term follow-up is essential —

Hormonal treatment should be continued for at least three to six months when possible.

Hormonal therapy that has been discontinued can be restarted if heavy menstrual bleeding recurs.

Alternatively, patients who go more than three months without a period (and are not pregnant) should undergo an endocrinology workup and receive a course of progesterone to induce withdrawal bleeding.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Chronic heavy or prolonged uterine bleeding can result in anemia, interfere with daily activities, and is the most common presenting symptom in patients with endometrial hyperplasia or carcinoma.

Most patients with chronic AUB requiring medical attention can be managed in an outpatient setting.

Occasionally, an exacerbation of chronic AUB is severe enough to necessitate emergency medical care.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

MANAGEMENT GOALS — The main goals of AUB management are as follows:

- **Correct the underlying primary etiology, if present and feasible.**
- **Improve quality of life.**
- **Prevent an episode of acute uterine bleeding.**
- **Prevent, or treat, anemia.**
- **Establish a regular bleeding pattern (or amenorrhea).**
- **Prevent endometrial hyperplasia/carcinoma.**

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

CONSIDERATIONS PRIOR TO INITIATING TREATMENT — To help determine which treatment is best for a particular patient, clinicians should consider several patient factors. These include:

- **Etiology**

The timing of initiating treatment of AUB should be individualized.

In patients in whom AUB is not interfering with daily activities, it may be appropriate to delay initiation of treatment until results of diagnostic testing (eg, blood count, imaging, endometrial biopsy) are available.

By contrast, when AUB is interfering with daily activities and/or marked anemia is present, it is appropriate to immediately initiate treatment, while pursuing diagnostic testing.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Severity of bleeding**

Most patients with AUB requiring medical attention can be managed in an outpatient setting.

By contrast, patients with an episode of acute uterine bleeding may require urgent evaluation in an emergency department.

- **Associated symptoms and issues**

AUB is often associated with other symptoms (eg, pelvic pain/pressure, dysmenorrhea) or issues (eg, infertility); the underlying etiology (eg, adenomyosis, uterine fibroid) should be identified to select the optimal treatment approach.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Contraceptive needs and plans for future pregnancy**

Many treatments for AUB also provide contraception.

However, for patients trying to conceive, or those desiring pregnancy in the near future, some treatments (eg, levonorgestrel intrauterine device [IUD], depot medroxyprogesterone acetate [DMPA]) should be avoided.

- **Medical comorbidities**

Some treatments (eg, estrogen-progestin contraceptives) are contraindicated in patients with comorbidities (eg, elevated risk for venous thromboembolic disease and/or arterial thrombotic events

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Patient preferences regarding**

As well as access to, medical versus surgical and short-term versus long-term therapy.

- **Time to menopause**

AUB should resolve when a patient becomes menopausal (which occurs, on average, at the age of 51.5 years), and time to menopause may affect management decisions.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Expectant management may be reasonable for some patients :

- **Not anemic**
- **Do not desire treatment**
- **Approaching menopause**

Such patients require close follow-up (eg, ferritin level every 6 to 12 months for patients with heavy menstrual bleeding (HMB), repeat endometrial assessment for patients at risk for hyperplasia/neoplasia).

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

TREATMENT

Patients with a known primary etiology —

Treatment of certain underlying conditions may correct the AUB or make further treatment more effective.

These include structural lesions (eg, submucosal fibroids, polyps), endocrine (eg, polycystic ovarian syndrome), infectious (eg, chronic endometritis), or bleeding disorders.

Bleeding disorders —

Bleeding disorders typically present as HMB. When possible, treatment of the underlying bleeding diathesis should be initiated prior to initiating medical or surgical therapies for AUB .

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Infection —

AUB in patients with suspected or documented chronic endometritis often resolves following a course of antibiotics.

Endocrine abnormalities —

Endocrine abnormalities (eg, hypothyroidism, hyperprolactinemia) may cause anovulatory bleeding (AUB-O), and treatment often restores regular ovulatory cycles

Treatment of other endocrine abnormalities (eg, polycystic ovarian syndrome) can also help decrease the risk of endometrial hyperplasia or carcinoma .

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Patients without a known etiology —

Patients without a primary etiology also have AUB.

Initial management of such patients typically consists of progestin-based treatments including combination oral contraceptives (OCs) or the 52 mg levonorgestrel-releasing intrauterine device (LNG 52; IUD; Mirena or Liletta).

Alternatives for selected patients include high-dose progestin-only oral or injectable medications,

Nonhormonal therapies,

Minimally invasive surgery,

Hysterectomy; however, surgical options are limited in patients who desire future childbearing.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Preferred approach for most patients —

For most patients with AUB and no known primary etiology:

We suggest estrogen-progestin contraceptives or the LNG 52 as first-line therapy.

Both estrogen-progestin contraceptives and the LNG 52 are effective treatments for AUB, provide effective contraception, are well tolerated, and have a low risk of adverse effects.

The choice between the two methods depends on several factors:

- **Patients with a contraindication to estrogen – For patients with a contraindication to contraceptive doses of estrogen, estrogen-progestin contraceptives are not an option; this includes patients with the following characteristics :**

- **Age ≥35 years and smoking ≥15 cigarettes per day**

- **Multiple risk factors for arterial cardiovascular disease (such as older age, smoking, diabetes, and hypertension).**

Because age and obesity represent independent risk factors for venous thromboembolism (VTE) in our practice, we also avoid estrogen-progestin contraceptives in patients ≥40 years of age with obesity.

he choice between the two methods depends on several factors:

- Hypertension
- VTE
- Known thrombogenic mutations
- Known ischemic heart disease
- History of stroke
- Complicated valvular heart disease (pulmonary hypertension, risk for atrial fibrillation, history of subacute bacterial endocarditis)
- Systemic lupus erythematosus (positive or unknown antiphospholipid antibodies)
- Migraine with aura at any age

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

The LNG 52 is often appropriate for such patients, but medical consultation may be required prior to use.

The LNG 52 results in a low level of systemic progestin absorption and its use has not been associated with an elevated risk of VTE in average-risk patients .

However, there are few data regarding use of the LNG 52 in patients with elevated risk of thrombosis .

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Patient preference –**

For other patients, the choice is often based on patient preference.

Patients may prefer estrogen-progestin contraceptives if they prefer taking a daily oral medication, regular bleeding, or are planning to conceive in the near future.

By contrast, patients may prefer the low maintenance of having an IUD or are willing to tolerate the irregular bleeding that initially accompanies placement of a LNG 52 given the subsequent light bleeding or amenorrhea that often occurs.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

In systematic reviews and a meta-analysis including randomized trials, the LNG 52 reduced menstrual blood loss more than other medical treatments, however, the certainty of this evidence was low .

In one review including patients with HMB, placement of a LNG 52 resulted in a greater reduction in menstrual blood loss (71 to 95 percent reduction) than estrogen-progestin contraceptives (35 to 69 percent reduction) .

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Estrogen-progestin contraceptives —

For many patients with AUB, estrogen-progestin contraceptives are first-line management.

The advantages of estrogen-progestin contraceptives are that:

They typically make bleeding more regular, lighter, and reduce dysmenorrhea

As well as provide contraception.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

The only OC approved by the US Food and Drug Administration (FDA) for treatment of HMB is:

Estradiol and dienogest (Natazia; includes 2 to 3 mg of estradiol valerate [dose varies and is equivalent to 1.5 to 2.25 mg of micronized oral estradiol or <20 mcg of ethinyl estradiol) which has 26 hormonally active tablets per each 28-day pill pack.

In addition to estradiol valerate/dienogest:

There are many other formulations of estrogen-progestin contraceptives that vary by the type, dose, route, and schedule

Estrogen-progestin contraceptives are contraindicated in patients who are at elevated risk for thrombosis.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Levonorgestrel intrauterine device —

For patients with HMB who do not desire pregnancy in the near future, or for those with a contraindication to estrogen

The LNG 52 is often used as first-line management ,and is approved by the FDA for this indication.

Further study is needed to determine the efficacy of other progestin IUDs (eg, 19.5 mg and 13.5 mg LNG devices) in treating HMB .

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Factors specific to treatment of HMB with the LNG 52 include:

- **Reduction of bleeding –**

Most patients using the LNG 52 develop scant bleeding or amenorrhea

Some studies suggest this treatment, compared with other hormonal or nonhormonal treatments, is associated with an improved quality of life

In studies of patients with HMB, within three months of IUD placement, most patients experience spotting

At six months, menstrual suppression is substantially greater, with most patients experiencing amenorrhea or infrequent bleeding; median hemoglobin and ferritin levels also increased from baseline (7.5 and 68.8 percent, respectively).

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Risk of expulsion –**

Expulsion rates are higher in patients using the LNG 52 for treatment of HMB compared with those using the device specifically for contraception (up to 20 versus 10 percent, respectively) .

For patients with adenomyosis, one study reported a 25 percent expulsion rate with the LNG 52 .

Package labeling for the LNG 52 lists congenital or acquired distortion of the endometrial cavity (eg, by fibroids) as a contraindication to placement of this IUD.

Nonetheless, in patients with HMB who wish to avoid surgery or in whom the risk of surgical complications is elevated, use of the LNG 52 may be appropriate in well-counseled patients.

When placing the LNG 52 in patients with a distorted endometrial cavity, some clinicians use abdominal ultrasound guidance to ensure optimal placement.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Patients who cannot or choose not to use a preferred method —

Alternatives include :

other progestin-therapies (eg, high-dose oral progestins, depot medroxyprogesterone acetate [DMPA])

Noncontraceptive doses of estrogen-progestin

Nonhormonal therapies (eg, tranexamic acid, nonsteroidal antiinflammatory drugs [NSAIDs]).

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Patients without a known etiology:**

•For most patients with AUB and no known etiology, we suggest estrogen-progestin contraceptives or the 52 mg levonorgestrel-releasing intrauterine device (LNG 52; IUD).

Both estrogen-progestin contraceptives and the LNG 52 are effective treatments for AUB, provide effective contraception, are well tolerated, and have a low risk of adverse effects.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

For patients with AUB who are at an increased risk of venous or arterial thrombosis (eg, history of venous thromboembolism [VTE], known thrombogenic mutations, ≥35 years-old with concomitant smoking ≥15 cigarettes/day, hypertension), therapy with contraceptive doses of estrogen is contraindicated.

Thus, for such patients we use the LNG 52.

The LNG 52 results in a low level of systemic progestin absorption and its use has not been associated with an elevated risk of VTE in average-risk patients.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **For patients who cannot or choose not to use a preferred method (ie, estrogen-progestin contraceptives, LNG 52):**

Reasonable alternatives may include treatment with other progestin-only therapies :

Depot medroxyprogesterone acetate [DMPA]

Noncontraceptive estrogen-progestin formulations

Nonhormonal therapies (eg, tranexamic acid, nonsteroidal antiinflammatory drugs [NSAIDs]), or surgery. Medical consultation is helpful to determine thrombotic risk with these treatments.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **For patients with AUB who are trying to conceive or planning a pregnancy in the near future:**

We suggest oral progestin therapy rather than other medical therapies .

DMPA is not an option for such patients as its contraceptive effect persists for long periods of time; similarly, use of the LNG 52 may not be desirable or cost-effective.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

- **Nonsteroidal antiinflammatory drugs –**

NSAIDs used to treat HMB include ibuprofen, naproxen, and mefenamic acid; they reduce the volume of menstrual blood loss by causing a decline in the rate of prostaglandin (PGE2 and PGF2 alpha) synthesis in the endometrium, leading to vasoconstriction and reduced bleeding .

NSAIDs are not typically used to treat patients with AUB-O.

Abnormal uterine bleeding in nonpregnant reproductive-age patients: Management

Advantages of NSAIDs include:

- **Do not increase risk of thrombosis**
- **Low risk of adverse effects**
- **Reduce rates of dysmenorrhea**
- **Low cost and often available over the counter**
- **Do not need to be taken daily**

When used for treatment of HMB, NSAIDs are prescribed to start on the first day of bleeding and should be continued for four or five days or until menstruation ceases.

Surgical Management of Abnormal Uterine Bleeding

DR.Z . BOUZARI

The indications for surgery for women with AUB

include :

failure to respond to medical therapy

inability to utilize medical therapies (i.e. side effects, contraindications)

significant anemia

impact on quality of life

concomitant uterine pathology (large uterine fibroids, endometrial hyperplasia).

Surgical options for managing AUB depend on several factors including:

the patient's expectations and uterine pathology

Surgical options include

Dilation and uterine curettage

Hysteroscopic polypectomy

Endometrial ablation

Myomectomy

Hysterectomy

- **Surgery is usually a second-line treatment of HMB.**
- **Endometrial resection/ablation (EA/ER) to remove or ablate the endometrium is less invasive than hysterectomy.**
- **Hysterectomy is the definitive treatment and can be via open (laparotomy) approach, or via minimally invasive approaches (vaginally or laparoscopically).**

Dilation and curettage (D & C)

Dilation and curettage (D & C) is rarely required as a diagnostic or treatment tool in adolescents.

It should be reserved for the rare patient who continues to bleed heavily despite adequate hormonal therapy or who is unable to take estrogen.

If D & C is performed in adolescents, care must be taken to prevent Asherman syndrome (scarring of the endometrial lining).

Dilatation and curettage

except possibly in cases of severe acute bleeding refractory to medical therapy, should be relegated to a diagnostic technique when endometrial sampling or hysteroscopic evaluation is not possible

HYSTEROSCOPY VERSUS ENDOMETRIAL ABLATION

Hysteroscopy refers to the direct visualization of the endometrial canal, with the goal of diagnosis or management.

Polypectomy, directed biopsy, and myomectomy may all be conducted using this intervention

Endometrial Ablation

Method	Advantages	Disadvantages
Cryoablation	Not completely blind Less pain than methods using heat energy Requires minimal or no anesthesia	No outcomes data for women with intracavitary lesions
Thermal balloon ablation	First global technique approved for use Easy to learn	Not recommended for women with an abnormal uterine cavity (anomaly, enlarged, polyps, myomas, adhesions)
Hydrothermal ablation	Circulating hot water contacts all endometrial surfaces, regardless of shape Direct visualization of uterine cavity	Not recommended for women with a uterus >10 cm Requires 8 mm hysteroscope Hot water stimulates pain Risk for burns to vagina and perineum
Bipolar radiofrequency ablation	Short procedure time Easy to perform Requires no endometrial pretreatment	Not recommended for women with an enlarged or abnormal uterine cavity
Microwave ablation	Applicable in women with large cavity or small myomas (<3 cm)	Requires pretreatment ultrasonography to document minimum 1 cm myometrial thickness in all areas Contraindicated for women with previous transmural myomectomy or classical cesarean section

Endometrial ablation (EA)

Endometrial ablation is a minimally invasive surgical option for heavy menstrual bleeding.

It may be considered in women who have :

Failed medical treatment

Have completed childbearing

May not be candidates for major surgery

EA is a procedure designed for women as a alternative to hysterectomy, or, perhaps, medical therapy, when future fertility is no longer desired.

Women who select EA should anticipate a relatively low risk procedure that will likely reduce their HMB to normal levels or less

Endometrial ablation (EA)

Includes a spectrum of procedures performed with or without hysteroscopic direction

Designed to destroy the endometrium for the treatment of the symptom of heavy menstrual bleeding (HMB) secondary to a spectrum of causes

But most commonly those that are endometrial in origin (AUB-E) or ovulatory disorders (AUB-O).

Endometrial ablation (EA)

Two methods of endometrial ablation may be offered at the present time.

The first method involves hysteroscopic resection and/or ablation.

Previously termed "**first generation**" endometrial ablation, hysteroscopic guided endometrial ablation has a significant number of years of reported experience and effective results.

Endometrial ablation (EA)

Resectoscopic endometrial ablation (REA)

Nonresectoscopic EA or NREA

Endometrial ablation (EA)

Non-hysteroscopic techniques, or “second generation” technologies

Heated balloon

Radiofrequency bipolar technology

Microwave device

These vary in type of energy used, time required, and outcomes.

Non-hysteroscopic techniques

Comparisons of the varying technologies have been difficult because of the large number of competing options available.

The main limitation of most non-hysteroscopic devices is their inability to treat uterine pathologies such as polyps and submucosal fibroids.

Large or very small uterine cavities may also be contraindicated in some technologies

Endometrial ablation (EA)

Risks of endometrial ablation techniques include uterine perforation, infection, hemorrhage, and bowel or bladder injury.

Post ablation syndrome is a condition associated with concomitant or previous tubal ligation and ablation and is a condition of hematometra resulting in cyclical pain with or without hematosalpinx.

Risks specific to hysteroscopic techniques include fluid overload, especially with the use of hypotonic solutions (ex. 1.5% glycine), and resulting hyponatremia and its sequelae.

Endometrial ablation (EA)

Comparisons of hysteroscopic and non-hysteroscopic endometrial ablation techniques

Demonstrate similar patient satisfaction, with the main difference being risks of the procedure.

Women undergoing non-hysteroscopic procedures were less likely to have fluid overload, uterine perforation, cervical lacerations, and hematometra than women undergoing hysteroscopic ablation.

In addition to patient safety, the non-hysteroscopic techniques require less time (average 15 minutes less) but do have more equipment problems.

Endometrial ablation (EA)

A number of randomized controlled trials have been performed comparing endometrial ablative techniques to hysterectomy.

While an overall patient satisfaction rate of > 90% is reported for most types of endometrial ablation, up to 30% of women will require hysterectomy within 4 years.

However, hysterectomy is related to more risks for the patient and therefore a less invasive option, such as ablation, would offer the patient quicker recovery and a lower risk of complications.

Endometrial ablation (EA)

When compared with the progestin intrauterine system, ablation appears to have similar efficacy for bleeding control in women with menorrhagia and an otherwise normal uterine cavity.

Endometrial ablation (EA)

CLINICAL TIPS

Key points for counselling women planned for endometrial ablation:

1. **Confirm childbearing is complete**
2. **Require form of contraception**
3. **Rule out underlying uterine pathology (i.e. hyperplasia or malignancy)**
4. **Clearly outline expectations (patient satisfaction, not amenorrhea)**
5. **Discuss the risk of requiring a hysterectomy in the future**

Endometrial ablation (EA)

CLINICAL TIPS

Several non-hysteroscopic ablation techniques are currently available.

Balloon, microwave, and radiofrequency ablation devices have a large reported clinical experience.

One of the main advantages of these techniques is their successful implementation in a surgical suite or clinic setting, which avoids the use of operating room resources and general anaesthetic.

Endometrial ablation (EA)

Non-hysteroscopic ablation techniques offer similar patient satisfaction results with fewer risks of complication and less anaesthetic requirement than traditional hysteroscopic ablation

Endometrial Ablation

Indications: another option for the management of unexplained heavy menstrual bleeding when medical treatments are rejected, unsuccessful, or poorly tolerated. an effective treatment for women with acute or prolonged bleeding who are hemodynamically stable when medical treatment fails or is contraindicated.

Preoperative evaluation: examination of the uterine cavity by saline sonography or office hysteroscopy to exclude focal lesions such as polyps and myomas that can be resected and to identify women not having a normally shaped uterine cavity.

Endometrial ablation is not a sterilization procedure.

Not recommended : for women at increased risk for endometrial cancer (obesity, diabetes, hypertension, smoking, family history, chronic anovulation)

Complications: hematometra, cervical stenosis, and uterine perforation.


Thanks for your attention