Abnormal uterine bleeding in premenopausal woman

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Abstract

Background and purpose: Abnormal uterine bleeding (AUB) is defined as bleeding from the uterine corpus that is abnormal in duration, volume, frequency and/or regularity. The prevalence of abnormal uterine bleeding (AUB) is estimated at 11–13% in the general population and increases with age, reaching 24% in those aged 36–40 years.

The objective of this study was to describe abnormal uterine bleeding (AUB) in premenopausal women. And to determine the underlying factors and the potential for long term health consequences, decrease life quality and causes anemia and many other problems therefor valuation of the menstrual cycle should be an additional vital sign to be looked into in any female. Beginning with definition of normal menstrual cycle, evaluation, approach to diagnosis and treatment of AUB will be discussed in this paper.

Outcomes evaluated include the impact of AUB on quality of life and the results of interventions including medical and surgical management of AUB.

One of common treatment is the combined oral contraceptive, which is the effective treatment method to control AUB. Oral contraceptive pills (OCPs) supress endometrial development, re-establishes predictable bleeding patterns, decrease menstrual flow, and lower the risk of iron deficiency anemia.

Keywords: Menorrhagia; abnormal uterine bleeding; heavy menstrual bleeding; hysterectomy.

Introduction:

Menarche usually occurs between the ages of 12-13 years [4,5]. The normal cycle of an adolescent female occurs every 21-45 days with bleeding lasting between two and seven days [6,7,8]. and involve blood loss of up to 80 ml. Chronic loss of ≥80 mL blood is associated with anemia [12]. More than 50% of the total menstrual loss is an endometrial transudate and 30-50% consists of whole blood components [11]. Menstrual cycles are 21-34 days, similar to adults, in 60-80% of adolescents by the third year after menarche [8,9].

Abnormal uterine bleeding is a common condition, with a prevalence of 11–13% in the general population and increases with age, reaching 24% in those aged 36–40 years. The frequency of cycles decreases at higher postmenarchal ages [7]. It negatively affects quality of life and is associated with financial loss, decreased productivity, poor health, and increased use of health care resources.[2–4] In 2011 the International Federation of Gynecology and

Obstetrics convened a working group that produced standardized definitions and classifications for menstrual disorders, which the American College of Obstetricians and Gynecologists subsequently endorsed. The updated terminology pertains only to nonpregnant women of reproductive age, which is the scope of this review.

FIGO defines the etiology of AUB using the acronym PALM-COEIN facilitates classification, with PALM referring to structural etiologies (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia), and COEIN referring to nonstructural etiologies (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified)[4]. Evaluation involves a detailed history and pelvic examination, as well as laboratory testing that include a pregnancy test and complete blood count. Endometrial sampling should be performed in patients 45 years and older, and in younger patients with a significant history of unopposed estrogen exposure[4,5]. Transvaginal ultrasonography is the preferred imaging modality and is indicated if a structural etiology is suspected or if symptoms persist despite appropriate initial treatment. Medical and surgical treatment options are available [2, 4]. Emergency interventions for severe bleeding that causes hemodynamic instability include uterine tamponad, intravenous estrogen, dilation and curettage, and uterine artery embolization. To avoid surgical risks and preserve fertility, medical management is the preferred initial approach for hemodynamically stable patients. Patients with severe bleeding can be treated initially with oral estrogen, high-dose estrogen-progestin oral contraceptives, oral progestins, or intravenous tranexamic acid. The most effective long-term medical treatment for heavy menstrual bleeding is the levonorgestrel-releasing intrauterine system.[4] Other long-term medical treatment options include estrogen-progestin oral contraceptives, oral progestins, oral tranexamic acid, nonsteroidal anti-inflammatory drugs, and depot medroxyprogesterone. Hysterectomy is the definitive treatment. A lower-risk surgical option is endometrial ablation, which performs as well as the levonorgestrel-releasing intrauterine system.[4,6]

The combined oral contraceptive is effective drug for control of AUB.[7] Oral contraceptive pills (OCPs) supress endometrial development, re-establishes predictable bleeding patterns, decrease menstrual flow, and lower the risk of iron deficiency anemia.[7]

Goal:

To describe AUB in premenpausal age and the causes of AUB in this age group and the recommended management.

Literature review:

Reproductive capability in a young woman begins at the point of menarche, which is the beginning of cyclic uterine bleeding in the anatomically and physiologically normal female. Menarche marks the beginning of an important stage in a young woman's physiological reproductive maturation and development[12]. Even before the onset of this entirely natural but potentially disturbing function, a young woman's early psychological reactions to menstruation , and probably also her life long view, can be influenced by the accuracy of her

information and the degree of empathy with which this knowledge has been conveyed to her.[12]

Many women conclude that any departure from their personal menstrual experience is abnormal, and they will seek treatment for these departures[7,12]. Conversely, some women accept or ignore even significant variations in their menstrual function, sometimes to the extent that serious health impairment occurs (severe iron deficiency anemia).[7,12]

Menarche usually occurs between the ages of 12-13 years [4,5]. The normal cycle of an adolescent female occurs every 21-45 days with bleeding lasting between two and seven days [6,7,8]. The frequency of cycles decreases at higher postmenarchal ages [7]. Menstrual cycles are 21-34 days, similar to adults, in 60-80% of adolescents by the third year after menarche [8,9]. The average blood loss during a normal menstrual cycle is 30-40 mL, requiring the use of 3-6 pads or tampons per day or 10-15 soaked pads or tampons per cycle [10]. More than 50% of the total menstrual loss is an endometrial transudate and 30-50% consists of whole blood components [11]. Chronic loss of ≥80 mL blood is associated with anemia [12].

Abnormal uterine bleeding is a symptom, not a diagnosis; the term is used to describe bleeding that falls outside population-based 5th to 95th percentiles for menstrual regularity, frequency, duration, and volume [7] Abnormal bleeding is considered chronic when it has occurred for most of the previous six months, or acute when an episode of heavy bleeding warrants immediate intervention.[5]

Here are some terms uses to diagnose the type of AUB:

Polymenorrhea: a menstrual cycle interval of less than 21 days.[4]

Causes: It is seen predominantly during adolescence, preceding menopause. [12]

Amenorrhea: the absence of menstrual bleeding for 3 months.[12]

Oligomenorrhea: the absence of menstrual bleeding for 37 days.[4] The causes are obesity, age related, endocrine disorder[12]

Metrorrhagia: a period of menstrual bleeding longer than 7days, or interval bleeding. [4, 12]

Menorrhagia: excessive menstrual bleeding the causes are some of underlying pathology_ organic or functional. [12, 4]

Postmenopausal bleeding: uterine bleeding occurring more than 12months after the last menstrual period of a menopausal woman. [7]

Break through bleeding: intermenstrual bleeding that is the result of exogenous hormones.[12]

Differential Diagnosis: Although the uterus is often the source, any part of the female reproductive tract can result in vaginal bleeding. Women may also mistake bleeding from nongynecologic sites (e.g., bladder, urethra, perineum, and anus) as vaginal bleeding. The prevalence of conditions that cause abnormal bleeding varies according to age. For example,

anovulation is more common in adolescents and perimenopausal women, whereas the prevalence of structural lesions and malignancy increases with age.[8]

The most common causes of abnormal uterine bleeding are described with the acronym PALM-COEIN.[5] The etiologies in the PALM group (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia) are structural and can be imaged or biopsied. The etiologies in the COEIN group (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified) are nonstructural. These etiologies are not mutually exclusive, and patients may have more than one cause. [12]

TABLE 1

Common causes of Abnormal Uterine Bleeding [8]

ORGANIC	*HEMATOLOGIC, ENDOCRINE & OTHERS*	*NON MENSTRUAL BLEEDING*
• Uterine fibroid • Endometriosis • Adenomysis • Endometrial polyps • IUCD • Adnexal pathology • Ovarian neoplasm	• Platelet deficiency • Leukemia • ITP • Von Willebrand disease • Thyroid dysfunction • PCOS • Arteriovenous malformation	Foreign body Urethral caruncle Genital malignancy Miscarriage bleeding

TABLE 2

Classification of Abnormal Uterine Bleeding (FIGO-2011)[8]

STRUCTURAL CAUSES(PALM)	*NONSTRUCTURAL CAUSES(COEIN)*
• Polyp • Adenomysis • Leiomyoma • IUCD • Malignancy and hyperplasia	• Platelet deficiency • Coagulopathy • Ovulatory dysfunction • Endometrial • Iatrogenic • Not yet identified

American college of obstetrics and gynaecologists (ACOG) FIGO-2011)

Diagnostic Evaluation: For all women, the evaluation of excessive and abnormal menses includes a through medical and gynecologic history, the exclusion of pregnancy, the consideration of possible malignancy, and a careful gynecologic examination. [(1)] The focus of initial evaluation of a patient with AUB is to determine whether the bleeding is acute and causing hemodynamic instability, through careful history taking, physical examination, laboratory testing and radiologic imaging. [(1)]

History should include; menstrual history (age of menarche, regularity, duration, number of pads/tampons per day), sexual history, past medical history (systemic illness, current/recent medication), systemic review (symptoms associated with systemic causes of AUB such as obesity, PCOS, hypothyroidism, hyperprolactinemia, hypothalamic or adrenal disorder) and family history (coagulopathy, hormone sensitive cancers). A history of heavy menses since menarche, surgery related bleeding, bleeding associated with dental work, bruising or epistaxis with a frequency of at least once per month, frequent gum bleeding and bleeding symptoms in the family point to an underlying bleeding disorder (2).

A description of the bleeding pattern should be elicited, including frequency, duration, regularity, and volume[(8)]. Heavy menstrual bleeding is defined as more than 80 mL of total blood loss, but quantitative assessment is impractical in routine clinical practice. Historical clues such as passing blood clots or changing pads/tampons at least hourly suggest heavy menstrual bleeding[(1).] A history of postcoital bleeding may indicate cervicitis, ectropion, or, rarely, cervical cancer, whereas abdominopelvic pain may suggest infection, structural lesions, or endometriosis[(7)].

Clinicians may underestimate the prevalence of coagulopathies among patients with abnormal uterine bleeding.[2] These conditions should be considered in women with a family history of abnormal bleeding or a personal history of heavy menstrual bleeding since menarche, or symptoms such as frequent bruising, bleeding gums, epistaxis, postpartum hemorrhage, or bleeding with surgical and dental procedures.[2]

Once hemodynamic stability is established, vital signs should be checked and systematic physical examination should be completed. An examination of the pelvis, including speculum and bimanual examinations, is an important aspect of the evaluation of abnormal uterine bleeding [(1)]. Care should be taken to examine all potential bleeding sites, including the urethra, perineum, and anus. Cervical cancer screening should be performed if it is not up to date. Pelvic ultrasonography provides non-invasive information about genital tract structural lesions. It also gives additional information about endometrial thickness and PCOS. [(2)]

All patients with abnormal uterine bleeding should be evaluated for pregnancy with a urine or serum human chorionic gonadotropin test, and for anemia and thrombocytopenia with a complete blood count.[(6)] Thyroid function should be evaluated in patients with signs or symptoms of thyroid disease, and chlamydia testing should be considered.[(1)] Additional hormonal tests (e.g., prolactin, androgens, estrogen) are indicated only if history or examination findings suggest a specific hormonal cause.[(6,8)] The platelet count, prothrombin

time, and partial thromboplastin time can be initial screening tests when a bleeding disorder is suspected, but results may be normal in women with von Willebrand disease or other bleeding disorders.(7) Diagnosing a bleeding disorder typically requires additional testing, often in consultation with a hematologist.[7]

Because older age is an important risk factor for endometrial cancer, all patients with abnormal uterine bleeding who are 45 years or older should undergo endometrial sampling.[12] Younger women should undergo sampling if they have a history of unopposed estrogen exposure, if medical management fails, or if bleeding symptoms persist.[6] Office-based endometrial biopsy is the preferred approach, with hysteroscopic dilation and curettage reserved for instances in which office sampling fails, is inadequate, or cannot be performed.[5] Blind sampling may miss focal lesions, so hysteroscopic dilation and curettage should be performed if symptoms persist despite normal biopsy results.[14]

Indications for pelvic imaging include abnormalities palpated on bimanual examination or symptoms that persist despite initial treatment.(6) Transvaginal ultrasonography is the first-line approach for most patients, although saline infusion sonohysterography (the infusion of sterile saline into the endometrial cavity while transvaginal ultrasonography is performed) is better at detecting intracavitary lesions.(1) Routine use of magnetic resonance imaging is discouraged but can be considered if sonographic imaging is inadequate.[6]

Management

Attention should be directed to establishing a cause of abnormal uterine bleeding. In most cases, medical therapy is effective in managing abnormal bleeding and should be attempted before surgical management.(1)

Medical management with either combined hormonal contraceptives or progestins is the preferred therapy of anovulatory bleeding in women of reproductive age.(1)

Multiple factors should be considered when choosing among treatment options for abnormal uterine bleeding, (9) including the cause of the bleeding, fertility and contraceptive preferences, medical comorbidities, adverse effects, cost, and relative effectiveness. If the underlying cause of bleeding can be identified and treated, symptoms may resolve without the need for additional intervention. Anemia is an indication for treatment, as is bleeding that negatively affects the patient's quality of life. Because exposure to unopposed estrogen increases the risk of endometrial cancer, treatment of anovulatory abnormal uterine bleeding involves inducing ovulatory cycles or administering supplemental progesterone to antagonize estrogen's proliferative effect on the endometrium.

Woman with AUB with age ≥ 45 years should have endometrial biopsy as an initial step of management(7).

TABLE 4

Treatment Options for Medical Management of Abnormal Uterine Bleeding

DRUG	*SUGGESTED DOSAGE*	*NOTES*
Acute bleeding		
Conjugated equine estrogen	Hemodynamically unstable: 25 mg intravenously every 4 to 6 hours for up to 24 hours	Follow treatment with a progestin to provoke withdrawal bleeding; do not use in patients at increased risk of thrombosis
	Hemodynamically stable: 2.5 mg orally every 6 hours for 21 days	
Estrogen-progestin oral contraceptives	1 monophasic pill containing 35 mcg of ethinyl estradiol orally 3 times daily for 7 days	Other regimens also effective; do not use in patients at increased risk of thrombosis
Progestins	Norethindrone, 5 mg orally 3 times daily for 7 days	Other high-dose oral progestins are also effective
Tranexamic acid	10 mg per kg intravenously every 8 hours or 20 to 25 mg per kg orally every 8 hours	Faster onset if given intravenously; do not use in patients at increased risk of thrombosis
Chronic bleeding		
Depot medroxyprogesterone (Depo-Provera)	150 mg intramuscularly or 104 mg subcutaneously every 13 weeks	Unscheduled bleeding is a common initial adverse effect, but one-half of patients become amenorrheic after 12 months of use

DRUG	*SUGGESTED DOSAGE*	*NOTES*
Estrogen-progestin oral contraceptives	1 monophasic pill containing 35 mcg of ethinyl estradiol daily	Other routes (transdermal patch, intravaginal ring) are likely also effective; regimens with no or fewer hormone-free intervals may be more effective
Levonorgestrel	52-mg (20-mcg-per-day) intrauterine device (Mirena)	Effectiveness data are based primarily on trials involving the 20-mcg-per-day device; effect on bleeding suppression may wane before contraceptive effectiveness expires
Nonsteroidal anti-inflammatory drugs	Naproxen, 500 mg orally 2 times daily	Other oral nonsteroidal anti-inflammatory drugs are also effective; administer only while patient is bleeding; do not use in patients with coagulopathy
Progestins	Norethindrone, 2.5 to 5 mg orally once daily	Other oral progestins are also effective; administration during only the luteal phase is significantly less effective for treating heavy bleeding
Tranexamic acid (Lysteda)	1,000 to 1,500 mg orally 3 times daily	Faster onset if given intravenously; do not use in patients at increased risk of thrombosis

Note: The 2016 U.S. medical eligibility criteria for contraceptive use, published by the Centers for Disease Control and Prevention (https://www.cdc.gov/mmwr/volumes/65/rr/rr6503a1.htm), can be referenced to guide the use of the hormonal treatments listed in this table.

Most bleeding problems, including anovulatory bleeding , can be managed nonsurgically.[1] Occasionally, abnormal uterine bleeding is of sufficient quantity or duration that emergent attention is required. For hemodynamically unstable patients, uterine tamponade using a Foley catheter or gauze packing can achieve rapid but temporary control of blood loss.[9] Further emergency interventions for hemodynamically unstable patients include intravenous estrogen, dilation and curettage, uterine artery embolization, and, rarely, hysterectomy. Medical therapy (e.g., oral estrogen, combined oral contraceptives, oral progestins, intravenous tranexamic acid) is usually adequate for treating hemodynamically stable patients with severe bleeding.[6]

A wider range of medical and surgical options are available for treatment of nonemergent uterine bleeding *(Table 3)*. To avoid surgical risks and preserve fertility, medical management is the first-line approach for most patients.[4] Among medical therapies, the hormonal management of abnormal bleeding can frequently control excessive or irregular bleeding.[1] Treatment with 20-mcg-per-day formulation of the levonorgestrel-releasing intrauterine system (Mirena) is most effective for decreasing heavy menstrual bleeding (71% to 95% reduction in blood loss) and is as effective as hysterectomy when quality-adjusted life years are considered.[10] Estrogen-progestin oral contraceptives are effective (35% to 69% reduction) and can also be used to regulate bleeding in patients with ovulatory dysfunction.[7] Continuous dosing of oral progestins is another effective hormonal treatment option (87% reduction), but long-term patient satisfaction is low.[1] Two effective, well-tolerated, nonhormonal choices are antifibrinolytics, such as oral tranexamic acid is effective in reducing menstrual blood loss (Lysteda; 26% to 54% reduction) and nonsteroidal anti-inflammatory drugs decreases menstrual flow (30% to 50% reduction).[10] Both are taken only when the patient is bleeding, and tranexamic acid has the added benefit of being safe while the patient is attempting to conceive.[14]

Hysterectomy is the definitive and most effective treatment for abnormal uterine bleeding, and it yields a high level of patient satisfaction.[12] A less invasive, lower-risk surgical option is endometrial ablation, which is as effective as the levonorgestrel-releasing intrauterine system.[8] A variety of ablative techniques are available, and all are equivalent in terms of bleeding outcomes and patient satisfaction.[2] Myomectomy and uterine artery embolization are treatment options for leiomyomas, and endometrial polyps can be treated with polypectomy.[13] Except for myomectomy and polypectomy, surgical interventions for abnormal uterine bleeding are contraindicated in patients who wish to preserve fertility.[15]

Conclusions

Abnormal uterine bleeding is a common and sometimes debilitating condition in women of reproductive age. Standardization of related terminology, a systematic approach to diagnosis and investigation, and a step-wise approach to intervention is necessary. Treatment commencing with medical therapeutic modalities followed by the least invasive surgical modalities achieving results satisfactory to the patient is the ultimate goal of all therapeutic interventions.

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