



FOUNDATION FOR
Women & Girls
with Blood Disorders

Gynecologic Treatment for Heavy Menstrual Bleeding

Presented By:

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Vision: All women and girls with blood disorders are correctly diagnosed and optimally treated and managed at every life stage



OBJECTIVES

Heavy menstrual bleeding (HMB) may manifest at menarche or later in life.

In reproductive age women, evaluation of HMB involves anatomic (uterine) and systemic factors (including the possibility of a bleeding disorder).

HMB may manifest over several months or present as acute uterine hemorrhage.

Gynecologic care for these women, therefore, spans decades and impacts decisions for menstrual management and contraception.

A review of strategies and options for managing menses, contraception and acute bleeding episodes will be presented.



FIGO Classification System for Abnormal Uterine Bleeding (AUB)

- 9 categories pertain to general clinical care
- Subclassifications may assist future directions for research or have subspecialty applications
- The term “dysfunctional uterine bleeding (DUB)” should now be abandoned

P = Endometrial or endocervical polyps

A = Adenomyosis

L = Leiomyomata

M = Malignancy (hyperplasia and malignancy)

C = Coagulopathy (includes women with life-long anticoagulation)

O = Ovulatory function

E = Endometrial (hemostasis, inflammation, altered vascularity)

I = Iatrogenic

N = Not yet classified



Estrogen and Progesterone Effects on the Endometrium

ESTROGENS (E)

- rapid regrowth of epithelium and stroma
- stimulate vasospasm of the uterine arteries
- promote platelet aggregation and capillary clotting
- increase fibrinogen and factors V and XI
- increase production of E and P receptors

PROGESTINS (P)

- stabilize endometrial fragility
- inhibit endometrial growth by apoptosis
- stimulate conversion of estradiol to less active estrone
- prevent ovulation and ovarian steroidogenesis
- interrupt endometrial production of E receptors
- lead to atrophic endometrium



Acute versus Chronic Abnormal Uterine Bleeding (AUB)

Acute AUB: “an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to prevent further blood loss”

- usually symptomatic (pallor, dizziness, fatigue, SOB)
- frequently associated with altered hemodynamic status or severe anemia
- could occur in the setting of chronic HMB or AUB

Chronic AUB: “bleeding from the uterine corpus that is abnormal in volume, regularity and/or timing and has been present for the majority of the past 6 months”

- may be urgent but not emergent
- customarily evaluated as an outpatient



Clinical Assessment of HMB

1. Bleeding pattern: quantity, intervals, duration, “menstrual shape”(historical “clues” include clots >1 inch, requiring 2 forms of sanitary protection at a time, changing sanitary supplies <q1 hr., soiling, flow duration >7 d
2. Anemia symptoms: pallor, fatigue, SOB, pica
3. Sexual and reproductive history
4. Other menstrual symptoms: cramps, loose stools, N&V
5. Systemic symptoms suggesting an endocrinopathy, bleeding disorder or autoimmune disorder or chronic medical condition (renal, liver)
6. Medications and supplements (nutritional and medical)
7. Family history- bleeding, gynecologic, medical



Pertinent Physical Exam:

BMI, thyroid, abdomen, skin

Genital exam pertinent to patient age and medical condition

Initial Laboratory Evaluation: Beta HCG

CBC, Hct, Hgb

CMP, Endocrine studies,

Testing for bleeding disorders

Imaging: USG - abdominal or transvaginal (leiomyoma, polyps)

Saline infusion sonography (*AJOG* 1996, *Obstet Gynecol* 2004)

MRI (anomalies, adenomyosis)

Endometrial sampling - exclusion of hyperplasia, malignancy



Acute Uterine Bleeding

1. Intravenous Conjugated Estrogens: 25 mg IV q 4-6 hrs.

- antiemetics recommended
- risk of thrombosis

(*Obstet Gynecol* 1982)

- addition of combined hormone therapy when bleeding lessens or by 24 hrs: A. CHC – oral, patch

(monocyclic 30-35 mcg EE 2-4x/d, or cascading)

B. Progestin only therapy- multi-dose

(MPA 10-20 mg, Norethindrone 5 mg, megestrol acetate 20-60 mg - 1-2x/d)

C. Cyclic E and P (E 2.5 mg x 21-24d, P x 10 d)

(*Obstet Gynecol* 2006; Speroff 2005; others)



Acute Uterine Bleeding

2. Tranexamic Acid - oral or IV, 1-1.5 gm 3-4x/day

- anti-fibrinolytic effect by reversible blocking of lysine binding sites on plasminogen (prevents fibrin degradation)
- risk of thrombosis
- alternative is aminocaproic acid (Amicar) - oral, IV, topical

(ASH 2010)

3. Ddavn (synthetic vasopressin)

- intranasal in measured dose q 12-24 hrs. 150 or 300 mcg
- intravenous 0.3 mcg/kg
- stimulates release of vWF via cyclic-AMP mediated signaling mechanism
- limiting factor is tachyphylaxis
- efficacy / safety alone or with hormonal medications

4. Clotting Factor concentrates-specific for bleeding disorder



Acute Uterine Bleeding

5. Intrauterine Balloon

- 10, or 30 cc Foley catheter- filled with sterile fluid to mild resistance
- outpatient or operative insertion well tolerated
- combined with other medical therapies
- contraindications: retained POC, uterine rupture, purulent infection, uterine malformation(?)
- effective when coagulopathy present

Other considerations: prophylactic antibiotics, endometrial sampling

- remove after 24 hrs.
- monitor for continued blood loss

(JPAG 2003)



Acute Uterine Bleeding

6. Intrauterine Packing (continuous gauze)

- may add 5000 u thrombin in 5 cc sterile saline
- analgesia/ anesthesia for patient comfort
- antibiotic prophylaxis
- remove slowly in 24 hrs.

7. Uterine curettage

- allows removal of clots and exclusion of abnormal endometrial pathology
- often ineffective without concurrent medical therapy

8. Uterine artery embolization (UAE)

- first choice if a uterine A-V malformation
- uncertain safety of pregnancy after this procedure

(AJOG 2015)

9. Endometrial Ablation

- not recommended for women desiring future pregnancy
- limits future evaluation of the endometrial cavity



Heavy Menstrual Bleeding (HMB)

ORAL MEDICATIONS

1. Cyclic E + P: conjugated E 2.5 mg qid 21-25 d followed by oral P for 10 days (MPA, Norethindrone)
2. Combined OCPS: Monophasic 30-35 mcg EE 2-4x/d x5d or cascading
 - after 5 d begin one tablet daily
 - small series of transdermal patches
 - Estradiol valerate and Dienogest/estradiol valerate (Natazia)-combined OCP approved by FDA for control of HMB (March 2012)

Estrogens – prevent FSH secretion and development of a dominant follicle, provide endometrial stability and growth and enhance progestational effects

Progestins – prevent LH surge and ovulation and create an atrophic endometrial lining



Heavy Menstrual Bleeding (HMB)

3. Oral Progestins - cyclic or continuous- most beneficial with a thickened endometrium
 - A. Medroxyprogesterone acetate (MPA) 10-20 mg BID
 - B. Megestrol acetate 20-60 mg BID
 - C. Norethindrone 5 mg 1-2/ d

(Obstet Gynecol 2006)

4. Gonadotropin-releasing hormone agonists
 - expect initial FSH and LH surge which can cause transient increased bleeding
 - expect decreased bleeding volume in about a week
 - new uses in combination with aromatase inhibitor or GnRH antagonists



Chronic Heavy Menstrual Bleeding - Treatment Options

Combined contraceptives - oral or transdermal (patch or ring)
- cyclic, extended or noncyclic

Progestins - oral or injectable (IM, SQ DMPA)
- cyclic or continuous

Tranexamic acid - 650 mg TID x3-5 d.

NSAIDS – Meclofenamic acid 100 mg tid x 5 d
– Ibuprofen 600-800 mg q 6-8 hrs. x 5 d

Levonorgestrel - releasing intrauterine system (LNG-IUS)

Other options - GnRH agonist (*Clin Exp Obstet Gynecol* 1995)
3.75 IM q mo or 11.25 mg IM q 3 mos.
(*J Obstet Gynecol* 1987)

Danazol 160-400 mg po daily - side effects unacceptable



Levonorgestrel-Releasing Intrauterine System

- Releases 20 mcg levonorgestrel/ day
- Consistent hormone release x 5 years
- Investigations in progress to extend use to 6 years
- May be used for 7 years in menopausal women for hormone treatment
- Excellent reduction in blood loss and contraceptive efficacy
- Efficacious in women with bleeding disorders (*BJOG* 2004)
- May require additional therapies for breakthrough bleeding (estradiol, doxycycline low dose, NSAID)



Management of HMB in Women With Bleeding Disorders

- LNG-IUS
- Continuous (noncyclic) contraceptive regimens - oral or transdermal
- Progestins - continuous - oral, injectable
- Tranexaminic acid
- DDAVP - mainly for women with VWD
- GnRH agonist
- Danazol - androgenic side effects



Anticoagulation and Hormone Therapy

- CDC review of this topic - *Contraception* 2009
 - 6 articles met inclusion criteria
 - NO complications were reported with any hormone therapy

Findings:

1. DMPA decreases recurrent hemorrhagic cysts in women on anticoagulants (small case series n=13)
2. LNG-IUS resulted in decreased bleeding (14/17)
3. Single pharmacologic study reported no evidence of interaction between warfarin and OCPs

US Medical Eligibility Criteria acknowledges possible different risk / benefit ratio for women using a hormonal contraceptive for “therapy” versus “contraception” alone (CDC *MMWR* 2010)



- No published trials with clinical outcomes assessing risk of recurrent VTE in women using both hormonal contraceptives and anticoagulants for VTE
- Risks should decrease greatly since anticoagulants in pregnant women are effective in reducing recurrent VTE risk
- ISTH Guidelines recommend discontinuation of hormonal medications before discontinuation of anticoagulants and discuss effective contraceptive alternatives
- For some women the benefits may out weigh the risks of hormone therapy
(J Thromb Haemost 2012)
- Extended management options for women requiring long-term anticoagulation:
 - LNG-IUS, oral or depo progestins, GnRH agonists (bone density monitoring)

Thank you Gracias Merci



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