



Heavy Menstrual Bleeding (HMB) and Anticoagulants

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Introduction: What Is Heavy Menstrual Bleeding?



Heavy menstrual bleeding (HMB, formerly known as menorrhagia) is a common disorder among menstruating women. It refers to bleeding

- Lasting longer than seven days
- Involves more blood flow than is typical during menstruation
- Change the pad every hour for several hours back-to-back
- Blood clots the size of a quarter or even larger
- So heavy that it interferes with physical, emotional, or material quality of life.

HMB is a well-known adverse effect of anticoagulant therapy. As women do not necessarily spontaneously report their menstrual bleeding patterns and physicians may not inquire about them, HMB may be missed during clinic visits, and potentially useful treatment options may therefore not be considered, discussed, and implemented.

HMB – Overview

Dr. Boonyawat and colleagues indicate the following:

- 1) HMB associated with anticoagulant use is common
- 2) Vitamin K antagonists significantly increase the duration of menstruation, flooding, passage of clots, and intermenstrual bleeding
- 3) HMB seems to be more common with direct factor X inhibitors than with warfarin, but may be less common with dabigatran compared with warfarin
- 4) Although direct oral anticoagulants (DOACs) have not been directly compared with one another in clinical trials, prospective real-world data (of mostly rivaroxaban-treated patients) have suggested that HMB may be comparable for all factor Xa inhibitors.
- 5) Lower dose of rivaroxaban (10 mg once daily, compared with 20 mg once daily) leads to less menstrual flow length and intensity.



Incidence of HMB

Heavy Menstrual Bleeding is a common disorder that affects approximately 27–54% of people who menstruate. It is characterized by bleeding lasting longer than 7 days during menstruation.

- Common issue in women in reproductive ages
 - More common in subjects taking Direct Oral Anticoagulants
- Women using rivaroxaban, which is a factor Xa inhibitor, are more likely to experience HMB compared to women using vitamin K antagonists



Causes of HMB



- Thyroid disease.
- **P**oly**C**ystic **O**vary **S**ndrome (PCOS)
- Overweight
- Non-cancerous growths (polyps, fibroids)
- Cancerous growths in uterus (uterine cancer, cervical cancer)
- Infections
- Pregnancy complications
- Medications such as aspirin, hormone replacement therapy, tamoxifen, birth control pills, and anticoagulants

Signs & Symptoms of HMB



- Abdominal pain.
- Periods lasting longer than seven days.
- Passing blood clots that are the size of a quarter or bigger. The blood may appear red, pink, brown, or even rust-like.
- Bleeding through 1 or more tampons or pads each hour for more than two consecutive hours.
- Losing more than 80 milliliters of blood during the period instead of what is typical, 35-40 milliliters.
- Anemia symptoms, like feeling exhausted, tired or short of breath.

Is Heavy Menstrual Bleeding Serious?

Yes, heavy menstrual bleeding can be serious and may result in anemia.

Abnormal vaginal bleeding can complicate direct oral anticoagulant (DOAC) treatment. Data were derived from the AMPLIFY trial.

- A total of 1122 women were treated with apixaban and 1106 received enoxaparin/warfarin.
- A clinically relevant non-major vaginal bleeding occurred in 28 (2.5 %) apixaban and 24 (2.1 %) enoxaparin/warfarin recipients.
- Of all bleeds, 28 of 62 (45 %) and 24 of 120 (20 %) were of vaginal origin in the apixaban and enoxaparin/warfarin group, respectively.
- Premenopausal vaginal bleeds on apixaban were characterized by more prolonged bleeding. Medical treatment was deemed not necessary in 16 (57 %) apixaban and 16 (67 %) enoxaparin/warfarin recipients.
- The severity of clinical presentation and course of the bleeds was mild in 75 % of the cases in both groups.
- Although the absolute number of vaginal bleeding events is comparable between apixaban and enoxaparin/warfarin recipients, the relative occurrence of vaginal bleeds is higher in apixaban-treated women.

Diagnosis of HMB



- History
- Physical exam and a pelvic exam.
- Sonohysterogram (saline–infusion sonography)
- A hysteroscopy
- A blood test to check for signs of anemia, clotting issues, or thyroid disease.
- A Pap smear to study cells from the cervix for changes that may indicate cancer.

Diagnosis of HMB (contd.)



- An endometrial biopsy to check uterine tissue for cancer cells or other irregularities.
- Transvaginal ultrasound to check the appearance of the organs and tissues in your pelvis.
- Magnetic resonance imaging (MRI) to check for abnormal structures inside the uterus when an ultrasound doesn't provide enough information.
- A cervical culture to test for infection, as indicated by the medical history and the results of the physical exam.

Management & Treatment of HMB




- Iron supplements improve iron stores.
- Nonsteroidal Anti-inflammatory Drugs (NSAIDs) such as ibuprofen or aspirin to ease cramps and reduce bleeding.
- Hormone therapy to help balance the amount of estrogen and progesterone
- Hysteroscopy
- Myomectomy
- Uterine artery embolization to restrict the blood flow from fibroids and tumors.

Management & Treatment of HMB (cont.)


- Endometrial ablation
 - A procedure that destroys all or part of the lining of your uterus.
- Hysterectomy
 - Surgery that removes uterus and prevents from having periods or getting pregnant.
- In some cases, a switch to a different anticoagulant can be considered or a reduced-dosed DOAC can be used (apixaban 2.5 mg twice daily or rivaroxaban 10 mg once daily)



HMB and anticoagulant use (cont.)

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- Abnormal uterine bleeding (AUB) is frequent after initiation of anticoagulant therapy for acute symptomatic VTE
 - Compared to Vitamin K Antagonists, rivaroxaban was associated with prolonged menstrual bleeding
 - More medical interventions and adaptation of anticoagulant treatment for AUB.
 - Most cases can be treated conservatively, but patients with severe bleeding complications should be assessed for underlying anatomical abnormalities, which require surgical treatment.
 - This data can guide proactive discussion with patients starting anticoagulant therapy.
 - Approximately two thirds of all women reported HMB after initiation of anticoagulant therapy
 - Patients using rivaroxaban were more likely to experience prolonged (> 8 days) bleeding

HMB and anticoagulant use (cont.)

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- Real-world data (mostly rivaroxaban-treated patients) have suggested that HMB may be comparable for all factor Xa inhibitors.
 - The lower dose of rivaroxaban (10 mg once daily, as used in the Einstein Choice trial, compared with 20 mg once daily) leads to less menstrual flow length and intensity.
 - Patients on rivaroxaban reported an unscheduled contact with a physician for AUB than patients using VKAs (41% vs. 25%, $P = 0.096$)
 - Also reported increased need for menorrhagia-related medical or surgical intervention and had more adaptations of anticoagulant therapy
 - Tranexamic acid can also be used, which prevents the breakdown of clots

Conclusions



HMB is a common issue which causes a significant negative effect on the quality of life and the patient's mental well being. HMB is usually caused by factors such as thyroid disease, PCOS, and anticoagulant use, including the use of rivaroxaban. Effective management of HMB includes lifestyle changes, medications adjustments, and medical procedures. The management of HMB can greatly improve the physical, mental, and emotional well being of those affected.

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References

<https://my.clevelandclinic.org/health/diseases/17734-menorrhagia-heavy-menstrual-bleeding>


<https://ashpublications.org/thehematologist/article/doi/10.1182/hem.V15.3.8467/462983/Management-of-Heavy-Menstrual-Bleeding-on>

<https://www.mayoclinic.org/diseases-conditions/menorrhagia/symptoms-causes/syc-20352829>

1. Beyer-Westendorf J, Michalski F, Tittl L, et al. Vaginal bleeding and heavy menstrual bleeding during direct oral anti-Xa inhibitor therapy. *Thromb Haemost.* 2016;115:1234-1236.

<https://www.ncbi.nlm.nih.gov/pubmed/26917484>

References (cont.)




2. Boonyawat K, Lensing A, Prins M, et al. Menstrual bleeding patterns in women treated with rivaroxaban: Data from the EINSTEIN CHOICE trial. Abstract at ISTH meeting, Berlin, July 8–13, 2017. Abstract PB 1191. <https://onlinelibrary.wiley.com/doi/pdf/10.1002/rth2.12012>

3. Brekelmans MP, Scheres LJ, Bleker SM, et al. Abnormal vaginal bleeding in women with venous thromboembolism treated with apixaban or warfarin. *Thromb Haemost.* 2017;117:809–815. <https://www.ncbi.nlm.nih.gov/pubmed/28180233>

4. Bryk AH, Piróg M, Plens K, et al. Heavy menstrual bleeding in women treated with rivaroxaban and vitamin K antagonists and the risk of recurrent venous thromboembolism. *Vascul Pharmacol.* 2016;87:242–247. <https://www.ncbi.nlm.nih.gov/pubmed/27865826>

References (cont.)




5. De Crem N, Peerlinck K, Vanassche T, et al. Abnormal uterine bleeding in VTE patients treated with rivaroxaban compared to vitamin K antagonists. *Thromb Res.* 2015;136:749–753.
<https://www.ncbi.nlm.nih.gov/pubmed/26272306>

6. Ferreira M, Barsam S, Patel JP, et al. Heavy menstrual bleeding on rivaroxaban. *Br J Haematol.* 2016;173:314–315.
<https://www.ncbi.nlm.nih.gov/pubmed/26212626>

7. Klok FA, Schreiber K, Stach K, et al. Oral contraception and menstrual bleeding during treatment of venous thromboembolism: Expert opinion versus current practice: combined results of a systematic review, expert panel opinion and an international survey. *Thromb Res.* 2017;153:101–107. <https://www.ncbi.nlm.nih.gov/pubmed/28376343>

References (cont.)



8. Martinelli I, Lensing AW, Middeldorp S, et al. Recurrent venous thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use. *Blood*. 2016;127:1417–1425.
<http://www.bloodjournal.org/content/127/11/1417.long?sso-checked=true>

9. Myers B, and Webster A: Heavy menstrual bleeding on rivaroxaban – comparison with apixaban. *Br J Haematol*. 2017;176:833–835.
<https://www.ncbi.nlm.nih.gov/pubmed/26970315>

Speaker Parts

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