ANTICOAGULANTS IN HEAVY MENSTRUAL BLEEDING

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Abstract

Heavy menstrual bleeding (HMB) is a common but often overlooked side effect of anticoagulant (AC) therapy in premenopausal women. This review draws on existing literature, including findings from the EINSTEIN CHOICE Study, to examine the relationship between AC use and HMB. Direct oral anticoagulants (DOACs), such as rivaroxaban, have been associated with increased menstrual bleeding, although lower doses may reduce this risk. Similarly, vitamin K antagonists (VKAs) have shown high rates of HMB among users. Clinical recommendations emphasize the importance of taking a thorough menstrual history, avoiding unnecessary interruption of anticoagulation, and considering supportive therapies to manage symptoms. Overall, HMB in women receiving ACs warrants greater clinical attention, including appropriate patient counseling and individualized care.

Background

HMB is an underrecognized yet common complication in women receiving AC therapy. Anticoagulants, specifically DOACs and VKAs, are essential for preventing blood clots but can unintentionally worsen menstrual bleeding.

Normal menstrual parameters:

- Cycle length: 24-38 days.
- Duration of bleeding: 4.5-8 days.
- Blood loss: 5-80 mL per cycle.

Heavy menstrual bleeding:

- Periods lasting more than 7 days.
- Changing pads or tampons every 2 hours or less.
- Passing clots larger than 1 inch (quarter-sized).

Causes and Mechanisms

- How can ACs contribute to heavy menstrual bleeding?
  ACs interfere with the normal blood clotting process during menstruation, making it harder for the body to control endometrial bleeding.
  Some ACs, such as rivaroxaban, may have a greater impact than others, and other factors, such as dose and duration, also play a role.
- Factor Xa inhibitor DOACS work by directly reducing thrombin generation. This targeted inhibition prevents the formation of fibrin clots, which helps to reduce the risk of stroke, DVT, and PE without the need for frequent monitoring.
- VKAs work by inhibiting the enzyme vitamin K epoxide reductase, which is essential for the activation of factors II, VII, IX, and X. The Ability for clot formation decreases, preventing thromboembolic events.
- Heparin works by enhancing the activity of antithrombin III, a natural inhibitor of clotting factors. This prevents the formation and growth of blood clots, making it effective for anticoagulation in conditions such as DVT or PE.

Purpose

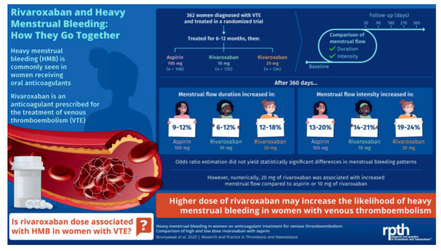
To review the incidence of HMB with different ACs. The aim was to explore clinical studies and real-world data evaluating how often HMB occurs in women who take DOACs and VKAs, including comparisons between different drug classes and dosages.

Methods

Literature Review Considering:

- The EINSTEIN CHOICE Study (Figure 1): This was a randomized control trial to compare the efficacy and safety of two doses (10 mg vs 20 mg) of rivaroxaban vs aspirin for extended prevention of recurrent VTE. The study confirmed that both doses of rivaroxaban reduced the risk of VTE recurrence compared to aspirin.
- Menstrual bleeding data was a secondary outcome.
- DOAC Studies: review of observational cohorts and trials reporting bleeding patterns in women.
- VKA Studies: older studies documenting HMB prevalence with warfarin.

The EINSTEIN CHOICE Study (Figure 1)



Results

DOACs:
Rivaroxaban:

- Higher rates of bleeding than apixaban or dabigatran.
- HMB incidence: 20-27%.
- A 10 mg dose of rivaroxaban associated with reduced menstrual flow length and intensity compared to 20 mg dose.
- Treated women more frequently needed a medical or surgical intervention to reduce abnormal uterine bleeding than those treated with a VKA.

Warfarin and similar agents:

- Observational studies show HMB incidence of 22-65%.
- Wide range due to varying study designs and differing definitions of HMB
- According to an ASH study, patients on warfarin had the highest prevalence of heavy menstrual bleeding. Rivaroxaban was the next highest.

Low Molecular Weight Heparin :

- There is limited data, but it generally lower rates more than DOAC's and VKA's.

Clinical Management

Do:

- Take a detailed menstrual history.
- Consider dose-reduced extended prophylaxis in eligible patients.
- Use a QOL based approach ("How does this condition or treatment impact the way someone actually lives and feels?").
- Counsel patients not to stop AC without medical discussion.
- Consider PADS assessment:
  1. Are periods heavier or more painful since starting AC?
  2. Are they replacing pads/tampons more frequently?
  3. Did they recently stop hormonal therapy?
  4. Send labs and consider supportive therapies or consults as needed.

Don't:

- Stop combined hormonal contraceptives in patients on AC.
- Hold AC for menstruation without careful risk-benefit assessment.

Recommended Treatments

First-line options:

- Levonorgestrel intrauterine system or IUD
  - A hormone releasing IUD that delivers levonorgestrel directly into the endometrium.
  - Reduces menstrual blood loss by up to 90% within 6 months.
  - Ideal for long term control of HMB for women using ACs.
- Tranexamic acid (during menstrual flow; ensure no contraindications)
  - An antifibrinolytic agent.
  - Taken orally during menstruation.
  - Prevents breakdown of fibrin clots, helping to reduce menstrual blood loss.
  - Can reduce bleeding by 30-60%.
  - For short term HMB management.
- High-dose progestin-only therapy
  - Stabilizes endometrial lining and suppresses ovulation.
- Combined hormonal contraceptives (if not contraindicated)
  - Examples are oral contraceptive pills, patches, and vaginal rings.

Conclusions

- HMB is common among premenopausal women on anticoagulants.
- Premenopausal women should be informed about potential menstrual changes before starting AC therapy.
- Management decisions (e.g. holding anticoagulation) depends on individual thrombotic risk and bleeding severity.