

# Heavy Menstrual Bleeding: A Hematology Perspective- A Short Review



Shivani Sharma and Ruchika Sharma\*

Blood Center of Wisconsin, Milwaukee, USA

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\*Corresponding author: Ruchika Sharma, Blood Center of Wisconsin, Milwaukee, USA, Email: Ruchika.Sharma@BCW.edu

## Abstract

Heavy menstrual bleeding or menorrhagia is a major problem in adolescence affecting health related quality of life and morbidity. A number is patients with heavy menstrual bleeding may have underlying bleeding disorders. In this review we will briefly describe prevalence of bleeding disorders, bleeding history evaluation, laboratory evaluation of bleeding disorders and management of heavy menstrual bleeding from a hematology perspective.

**Keywords:** Heavy menstrual bleeding; Bleeding disorders; Iron deficiency anemia

**Abbreviations:** HMB: Heavy Menstrual Bleeding; PBAC: Pictorial Blood Assessment Chart; BAT: Bleeding Assessment Tool; PT: Prothrombin Time; INR: International Normalized Ratio; ISTH: International Society on Thrombosis and Hemostasis; aPTT: activated Partial Thromboplastin Time; VWF: von Willebrand Factor; PAI-1: Plasminogen Activator Inhibitor-1; aPCC: activated Prothrombin Complex

## Introduction

Heavy menstrual bleeding (HMB) is defined as heavy bleeding that lasts more than 7 days, causing >80ml blood loss per menses or a subjective complaint of increased menstrual blood flow that negatively affects well-being and quality of life [1]. The term menorrhagia is used interchangeably with HMB. Heavy menstrual bleeding may impact physical, psychological and social well-being. HMB may be associated with impaired quality of life, anemia, blood transfusion requirements, hospitalizations, higher unemployment and absence from work and school [1,2].

## Causes of Heavy Menstrual Bleeding

Anovulatory bleeding and bleeding disorder are most common causes of HMB in adolescent girls followed by bleeding due to anticoagulant therapy. This review will focus on bleeding disorders causing HMB. Up to of 20% of women with HMB may have an underlying bleeding disorder [3].

## Bleeding Disorders Causing Heavy Menstrual Bleeding

Bleeding disorders may present as HMB for the first time. In patients with HMB, the overall prevalence of von Willebrand disease has been reported to be about 13% and rare bleeding disorders (including deficiencies of factors II, V, X, XI and XIII) to

be 1-4 % [3]. Idiopathic thrombocytopenia is also known to be a cause of HMB and the prevalence of platelet function defects has been reported to be anywhere between 1-47% due to diagnostic challenges. The prevalence of HMB in symptomatic hemophilia carriers has been underestimated but reported to be about 1-4%.

## Assessment of Bleeding History

As HMB is a clinical diagnosis a thorough history and physical exam are essential to evaluate these patients. Menorrhagia specific tools including the Phillip's Menorrhagia score and the Pictorial Blood Assessment Chart (PBAC) have been utilized to objectively diagnose heavy menstrual bleeding. The PBAC comprises of a chart that patients complete indicating the type and degree of change of protection during menses resulting in a score, and a score  $\geq 100$  per cycle is considered suggestive of heavy menstrual bleeding with a sensitivity and specificity ranging from 58 to 98 % and 7.5 to 97 % respectively [4]. The Phillip's menorrhagia score comprises four questions specific to menorrhagia (including prolonged cycles, reported flooding, soaking through protection, history of anemia and bleeding and personal or family history of bleeding symptoms) [5]. There are a number of bleeding specific scores that have been utilized to quantify bleeding symptoms. The most widely

used score that was established by the International Society on Thrombosis and Hemostasis (ISTH) in 2010 is the ISTH Bleeding Assessment Tool (BAT). This tool includes specific questions on epistaxis, cutaneous bleeding, bleeding from minor wounds, hematuria, gastrointestinal bleeding, oral cavity bleeding, bleeding after surgery, post-partum bleeding, muscle hematoma, hemarthrosis and central nervous system bleeding [6]. Physical exam should include assessment for ecchymosis, bleeding stigmata, physical features that may be associated with congenital bleeding disorders and a Beighton score to evaluate for hypermobility disorders such as Ehlers Danlos syndrome (EDS) which is a collagen disorder also associated with heavy menstrual bleeding [7].

## Laboratory Evaluation of Bleeding Disorders

Patients who present for an initial evaluation for HMB should have a first-line bleeding evaluation performed. This would include a complete blood count looking for thrombocytopenia or bone marrow disorders; iron studies including a ferritin to screen for iron deficiency, a basic prothrombin time and international normalized ratio (PT/INR), activated partial thromboplastin time (aPTT) to screen for coagulation factor deficiencies except for factor XIII; evaluation for von Willebrand disease (including von Willebrand factor (VWF) antigen, VWF ristocetin cofactor binding activity, VWF multimer analysis and Factor VIII clotting activity); and a thrombin time or fibrinogen level to look for quantitative as well as qualitative fibrinogen defects. In patients with a family history of Hemophilia a factor VIII and IX activity should also be obtained as some aPTT assays are not as sensitive to mild deficiencies of these which can be seen in symptomatic carriers [8].

Further investigations may be directed by patient's symptomatology and laboratory studies. These may include testing for specific platelet function disorders, assessing factor XIII deficiency and evaluating for rare disorders such as plasminogen activator inhibitor-1 (PAI-1) deficiency. Platelet function disorders may be assessed by platelet aggregation studies (evaluation for Glanzmann thrombasthenia, Bernard Soulier syndrome, other release defects and receptor defects) and platelet electron microscopy studies (evaluation for granule defects such as dense granule deficiency in Hermansky-Pudlak syndrome and alpha granule deficiency in Gray Platelet Syndrome). Supplemental studies may include platelet glycoprotein expression studies and genetic testing for specific evaluation of the bleeding diatheses [8]. Evaluation for EDS may include genetic testing for collagen mutations, however EDS is a clinical diagnosis and an evaluation by a geneticist may be warranted.

## Management from a Hematology Perspective

The most commonly used first-line treatment method is combined oral contraceptives in both patients with or without

underlying bleeding disorders. Alevonorgestrel intrauterine device is a reasonable alternative first line therapy to offer patients with compliance concerns. In patients with underlying bleeding disorders specific therapies should be utilized. These include VWF/FVIII concentrates, platelet transfusions, desmopressin and anti-fibrinolytics (such as aminocaproic acid and tranexamic acid). Surgical treatments are used in some women with refractory bleeding [9].

For HMB in patients on anticoagulation, anticoagulation reversal should not be delayed. In case of life-threatening bleeding in these women considerations may include activated prothrombin complex concentrate (aPCC) rather than fresh frozen plasma or Vitamin K. Other treatment options include mechanical approaches. Anti-fibrinolytics and desmopressin must be used with caution as these may increase the risk for thrombosis in these patients.

Menstruating women are at high risk of iron deficiency with or without anemia. Iron deficiency is most commonly treated with oral iron which may cause gastrointestinal side effects in 70% patients [10]. Other options include enteric coated oral iron formulations, polysaccharide formulations as well as intravenous iron (such as iron sucrose, iron carboxymaltose and iron dextran) which is a good alternative in severe deficiency and non-compliant patients.

## Conclusion

Heavy menstrual bleeding may be indicative of an underlying bleeding disorder in about 20% cases and a high index of suspicion is required for these cases. Fatigue is a very common symptom of iron deficiency and appropriate screening is essential for early diagnosis and treatment. Treatment options for heavy menstrual bleeding with or without bleeding disorders include hormonal and non-hormonal therapies.

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