MASAC Document #286
(Replaces Document #264)

MASAC RECOMMENDATIONS REGARDING DIAGNOSIS AND MANAGEMENT OF INHERITED BLEEDING DISORDERS IN GIRLS AND WOMEN WITH PERSONAL AND FAMILY HISTORY OF BLEEDING

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on March 8, 2024, and endorsed by the NBDF Board of Directors on April 11, 2024.

Background

Inherited bleeding disorders are under-recognized as a cause of excessive uterine bleeding since uterine bleeding is expected during menstruation and with pregnancy. Approximately 40% of those who menstruate report heavy bleeding and at least half of those may have an inherited bleeding disorder, including 1% of the population who have subnormal von Willebrand levels.[1,2] As many as 50% of girls and women who are carriers for hemophilia A or B have factor VIII or IX levels below 50% and are at risk for bleeding symptoms or heavy bleeding related to menstruation or pregnancy.[3] Additionally, while low factor levels are generally associated with a higher risk of bleeding problems, abnormal bleeding symptoms may occur with normal factor levels in up to 70% of genetic carriers of hemophilia.[2,3]

Implications

Establishing a diagnosis of an inherited bleeding disorder has important implications for prevention and management of bleeding, to improve quality of life and mental health, and facilitates obtaining recommendations for invasive procedures, pregnancy and delivery management, and family planning and testing. Additionally, screening for bleeding symptoms, even in the absence of a diagnosed bleeding disorder improves diagnosis and treatment of iron deficiency and may decrease the stigma of heavy menstrual bleeding.

Screening for bleeding symptoms

With such a large proportion of the population reporting heavy menstrual bleeding and obstetric hemorrhage events, it can be difficult to know who should undergo screening for an inherited bleeding disorder. Fortunately, several screening tools are available to patients and providers to aid with assessment of bleeding amount and indications for diagnostic testing or re-testing.

Screening using these tools should be widely disseminated and used by the following groups:

- Pediatricians and primary health care providers of adolescents who menstruate.
- Obstetrician gynecologists and other clinicians who care for patients during pregnancy.
- Hematologists and staff at Hemophilia Treatment Centers who care for families of patients with inherited bleeding disorders.

Heavy menstrual bleeding (HMB)

In clinical practice, HMB is defined subjectively as excessive menstrual loss, which interferes with physical, social, emotional, and/or material quality of life. In terms of blood loss, HMB is

defined as a measured menstrual blood loss of >80 mL per menstrual episode, obtained in research laboratory settings. Use of simple indirect methods such as detailed menstrual history or a pictorial blood loss assessment chart (PBAC) provide a semi-quantitative assessment of the blood loss and its severity and monitor response to treatment. A PBAC score >100 points per cycle is considered HMB. Other elements of menstruation have been included in screening tools; including menstrual episode duration ≥8 days, number/type of menstrual products used, nighttime overflow, and formation of large menstrual fluid clots. All those with HMB should undergo a basic diagnostic workup for bleeding disorder, even after initiating successful menstrual treatment. Screening tools incorporating bleeding symptoms can help identify patients at highest risk.

Obstetric or postpartum hemorrhage (PPH)

Excessive bleeding can occur at the conclusion of a pregnancy of any duration, with miscarriage, induced abortion, or birth at any gestation. The amount of bleeding that is considered normal varies by gestational size from 50 mL to 500 mL or up to 1000 mL at the time of cesarean delivery. Many contributing factors can lead to obstetric hemorrhage, including retained gestational tissue, abnormal placentation, infection, prolonged labor, coagulopathy unrelated to an inherited bleeding disorder, and surgical vascular bleeding. Generally, only severe (>2L) or unexplained PPH in the setting of a positive bleeding history should prompt a diagnostic workup.

Bleeding Symptoms (see https://www.betteryouknow.org/i-want-to-know-for-women)

- History of bruising or prolonged bleeding >10 minutes from cuts
    - Bruises larger than 1 cm in diameter, especially in the proximal upper and lower extremities, as well as trunk and back
- History of mucosal bleeding
    - Epistaxis lasting >10 minutes or at least 5/year.
- History of post-operative bleeding including bleeding >3 hr after dental extraction
- History of iron deficiency
- History of severe or unexplained postpartum hemorrhage
- History of heavy menstrual bleeding (HMB)
    - Perceived heavy menses affecting quality of life
    - Lasting ≥8 days.
    - Consistently soaks through 1 or more menstrual protection item every 2 hours on multiple days.
    - Requires use of ≥1 menstrual protection item at a time.
    - Requires changing menstrual protection during the night.
    - Associated with repeat passing of blood clots.
    - Pictorial Bleeding Assessment Chart (PBAC) score >100.

With this information in mind, MASAC recommends the following:

Diagnostic evaluation[4]

1. The differential diagnosis in anyone with excessive uterine bleeding should include von Willebrand Disease (VWD) and other inherited bleeding disorders as well as connective tissue and hypermobility disorders.

2. Ideally, diagnostic testing should occur in the absence of anemia, active bleeding, pregnancy, or inflammatory states.
3. Initial testing and evaluation should include the following:
    - CBC
    - Coagulation factors (PT, PTT, fibrinogen)
    - VWD panel: factor VIII activity, VWF activity, VWF antigen
    - Additionally, ferritin should be obtained to assess for iron deficiency.
    - Beighton score (see https://www.physio-pedia.com/Beighton_score)
4. Any provider can initiate screening or testing, but ruling out and confirmation of the diagnosis should be performed in consultation with a hematologist, particularly in the setting of bleeding symptoms and family history of bleeding disorder.
5. Labs should be drawn on-site at a reference laboratory that specializes in coagulation testing to avoid delays in processing that could alter results.[5] [see also MASAC document #262]
6. Re-testing is appropriate if the VWF levels are normal but <100% or to confirm the diagnosis.[6,7]
7. If initial testing is negative in the setting of positive screening for bleeding symptoms, then additional evaluation should be considered for platelet function disorders, other factor deficiencies, fibrinolytic disorders, and connective tissue and hypermobility disorders.
8. In the setting of a family history of inherited bleeding disorder, screening for the relevant factor activity level should be performed as soon as feasible and prior to any planned surgical procedure regardless of age. Additionally, screening, and initial diagnostic testing should be performed if indicated by bleeding symptoms.
9. Those with chronic heavy menstrual bleeding should be regularly evaluated and treated for iron deficiency if ferritin <30 ng/ml even if hemoglobin is within normal limits.[8,9]

Role of the HTC in access to care

All those with inherited bleeding disorders should have access to care within a Hemophilia Treatment Center or other clinical program with expertise in bleeding disorders. HTCs should take an active role in ensuring access to culturally competent care, including in population screening and referral and facilitation of diagnostic testing and ongoing management with inter-disciplinary collaboration. Additionally, HTCs should take an active role in advocating for financial access to off-label medications and access to a full range of options for evidence-based reproductive healthcare, including contraception, gender-affirming hormone therapy, induced abortion, and fertility treatments. HTCs should advocate for removing barriers to optimal care, including improving geographic access to obstetric care. [see also MASAC document #269]

- Those with excessive uterine bleeding should be managed ideally within a multidisciplinary clinic with a hematologist and gynecologist.
- Optimal care should include access to an adolescent health expert (age-dependent), social worker, physical therapist, and nutritionist.
- People with inherited bleeding disorders should have access to genetic counseling and testing for diagnostic purposes and family testing and planning.
- All those with inherited bleeding disorders should have access to appropriate evidence-based treatment options, including antifibrinolytics, hormone therapy, DDAVP, factor replacement products when clinically indicated, and iron supplementation therapies.

Management

- All patients should have an individualized treatment and emergency plan depending on their diagnosis, bleeding, and co-morbidities.
- All patients should have a perioperative management plan for any invasive procedures.
- All pregnant patients should have a pregnancy and obstetric management plan. [See MASAC Document #265]
- Heavy menstrual bleeding should be managed through a multidisciplinary approach informed by patient preferences and frequently requires multiple concomitant therapies to achieve treatment goals (e.g. hormonal therapies plus antifibrinolytics).

Education and research recommendations

There have been significant strides in improved awareness of uterine bleeding symptoms by both the public and clinicians. Nonetheless, we recommend a continued national outreach and education program. Public health education should include primary and secondary health education objectives related to heavy menstrual bleeding and iron deficiency. Medical education objectives targeted to health care professionals (e.g. pediatricians, hematologists/oncologists, internists, OB/GYN, family practitioners, emergency department personnel and dentists as well as advanced practice clinicians in these fields), should include screening tools.

- National public health outreach, including educational objectives.
- Medical education objectives and dissemination.
- Create and support multidisciplinary hematology/gynecology and hematology/obstetric clinics to streamline care in coordination with Hemophilia Treatment Centers.
- NBDF should continue to work with NHLBI, the American Thrombosis and Hemostasis Network (ATHN), the Foundation for Women and Girls^{+} with Blood Disorders, the International Society of Hemostasis and Thrombosis and CDC to develop a national research agenda on women's bleeding disorders.

References

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