Management of excessive menstrual bleeding in women with hemostatic disorders

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Because there are many important considerations for managing excessive menstrual bleeding in women who have systemic disorders of hemostasis, a multidisciplinary approach is the best model for care. Specific attention to effective treatments is highlighted, but few studies have been performed in this population. (Fertil Steril® 2005; 84:1352–9. ©2005 by American Society for Reproductive Medicine.)

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Excessive menstrual bleeding (EMB) is a common gynecologic problem, comprising 12% of all gynecology referrals (1). The contributory etiology may be local or systemic, but a specific cause is identified in fewer than 50% of affected women (2). Known disorders of hemostasis, in particular von Willebrand disease (VWD), have been long recognized to be associated with heavy menstruation. However, the magnitude of these disorders as a possible cause for idiopathic EMB has been underestimated. Testing for disorders of hemostasis is rarely done, and too often clinicians regard it as unnecessary.

Recently, there have been international efforts to assess the prevalence of these disorders in women with EMB. As discussed within the prevalence section by Lukes et al. (3), there are four landmark articles that estimate between 11–20% of females with menorrhagia have VWD. A comprehensive systematic review by Kadir et al. that evaluated the prevalence of VWD, the most common of the bleeding disorders, in women with EMB examined 11 studies (4–14), comprising a total of 988 women. There were 131 women diagnosed with VWD, with an overall prevalence of 13.2% (95% CI, 11.2–15.5%). There is now little doubt that disorders of hemostasis or bleeding disorders can be the underlying cause in a small but significant group of women with EMB across the world.

Testing all women who present with EMB is neither feasible nor necessary. The International Society for Thrombosis and Hemostasis menorrhagia working group has produced recommendations to guide clinicians in patient selection for referral and hemostasis screening (15). Also see the article by Kouides et al. (16).

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GYNECOLOGIC INVESTIGATIONS FOR EMB IN WOMEN WITH DISORDERS OF HEMOSTASIS

Once the diagnosis of a bleeding disorder has been established, what gynecologic investigations are necessary for assessment of these women? In women with inherited bleeding disorders, EMB is likely to be due to an underlying problem of hemostasis, but it may be multifactorial, so other causes must be considered. Individuals must be appropriately assessed in each case, and exclusion of malignancy is important in women older than 35 years of age.

As reviewed by the Royal College of Obstetricians and Gynecologists, there are many guidelines for what investigations should be used for women with EMB (17) (Table 1). Most of these investigations have *not* been assessed for coagulation disorders related to menorrhagia. For clinical practice, the results of general menorrhagia patients can be extrapolated. However, the risk of bleeding complications and need for blood products must always be assessed before performing any invasive investigation such as hysteroscopy.

The Role of Multidisciplinary Clinics

Menorrhagia and bleeding disorders have a major impact on women's health and quality of life. A multidisciplinary clinic specifically set up within the network of hemophilia treatment centers (HTCs) is ideal for comprehensive care. This ensures capable on-site performance of hemostasis testing, which is important given the frequent misdiagnosis of patients with von Willebrand factor deficiency when analyses are made off-site (18). Treatment in a comprehensive clinic also can avoid communication problems between professionals, ensure clear management plans and competent completion of a DDAVP (desmopressin acetate) trial, and address the psychosocial complications of menorrhagia related to bleeding disorders.

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TABLE 1

Summary of levels of evidence of investigations for menorrhagia.

Investigation	Level of evidence in menorrhagia in general	Level of evidence in menorrhagia with bleeding disorders
Pictorial blood assessment chart	C, in favor	C, in favor
Full blood count	B, in favor	B, in favor
Thyroid function test	C, in favor, only when clinically indicated	C, in favor
Other endocrine tests	B, against	(data unavailable)
Pelvic ultrasound	B, in favor	(data unavailable)
Endometrial biopsy	C, in favor, only if persistent	(data unavailable)
Hysteroscopy + endometrial biopsy	A, in favor, only when abnormal pelvic scan	(data unavailable)
Dilation and curettage	B, in favor	(data unavailable)

A. Evidence based on at least one randomized, controlled trial as a part of literature of overall good quality and consistency addressing the specific recommendation.
B. Evidence based on well-controlled clinical studies but no randomized clinical trials.
C. Evidence based on expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality.

Kadir. Hemostasis and menstruation: management. Fertil Steril 2005.

Preliminary data from Kirtava et al. (19) of the Hematologic Disease Branch of the U.S. Centers for Disease Control and Prevention (CDC) supports the beneficial role of HTCs. Of women with VWD who were registered at HTCs in the United States, 95% (71 out of 75) reported a strong positive opinion and satisfaction with their care at the HTC (19).

Similar positive findings have been found among patients of the multidisciplinary Katharine Dormandy Haemophilia Centre of the Royal Free Hospital in London. Patients and professionals report high satisfaction, with potentially fewer patient visits to the hospital. The clinic is staffed by hemophilia specialists, obstetricians, gynecologists, hemophilia nurse specialists, and family counselors and/or therapists, and other professionals are brought into the treatment when necessary. In particular, the presence of the family therapist is viewed favorably by most the women patients and is regarded as helpful for coming to terms and coping with their health and its related problems. Similar clinics have worked well at other sites within the United States, such as the Mary M. Gooley Hemophilia Treatment Center (Rochester, NY) and the Women's Hemostasis and Thrombosis Clinic at the Duke University Medical Center (Durham, NC).

THERAPEUTIC MANAGEMENT FOR EMB

Tranexamic Acid

Tranexamic acid is an antifibrinolytic agent, decreasing fibrinolysis in the uterus by inhibiting the conversion of plasminogen to plasmin. As noted by the systematic review of Lethaby et al. (20), two trials of antifibrinolytic therapy have shown a significant reduction in mean menstrual blood loss (94 mL; 95% CI, 36.5–151.4 mL) compared with placebo (21, 22). Tranexamic acid was also superior to nonsteroidal anti-inflammatory drugs (NSAIDs), with 53% to 54% and 20% to 24% reductions in menstrual loss, respectively (23, 24). However, tranexamic acid treatment has resulted in no differences in the duration of menstruation (23) or women's perception of their menstrual loss (21, 23). Although the side effects of tranexamic acid included nausea, headache, and dizziness, 77% of the women were happy to continue the treatment (23). There has been some concern about thrombotic complications, although a recent study showed no increased risk of thrombosis in women (25). Tranexamic acid is effective and safe, and is now considered to be a first-line therapy for women with menorrhagia who do not require contraception or who prefer nonhormonal treatment (26).

In women with bleeding disorders, tranexamic acid has been widely used (orally, intravenously, or topically alone or as an adjuvant therapy) in the prevention and management of oral cavity bleeding, epistaxis, gastrointestinal bleeding, and menorrhagia. However, there is a lack of objective data on the efficacy of this treatment for reduction of menstrual loss in this population.

At the Royal Free College, tranexamic acid was successful as a first-line therapy for reducing menstrual loss in 40% of 37 women with menorrhagia and bleeding disorders (unpublished data). Menstrual bleeding was measured with the pictorial blood assessment chart (PBAC), and success was defined as a PBAC score of 100 or less. Typically, tranexamic acid is given three or four times a day, as its bioavailability is approximately 35%; however, this increased dosing frequency may reduce patient compliance. There has been a recent report on successful use of a single high-dose therapy (tranexamic acid at a dose of 4 g orally) in three type 2A and