Severe anemia from heavy menstrual bleeding requires heightened attention

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OBJECTIVE: The objective of the study was to analyze the behaviors of women that resulted in menstrually related severe anemia (hemoglobin <5 g/dL) from a single public hospital serving indigent women.

STUDY DESIGN: This was a retrospective cohort study of all women identified as having been treated at Harbor-UCLA Medical Center for excessive menstruation (*International Classification of Diseases*, ninth revision, codes 285.9, 6256.2) and hemoglobin values less than 5 g/dL in the 6 years from 2008 to 2013.

RESULTS: Approvals were obtained from the Human Subjects and Research Committees. This search identified 271 women with those 2 diagnoses; 122 were excluded because their severe anemia had nonmenstrual causes. The remaining 149 women had 168 episodes with hemoglobin levels below 5 g/dL attributed to chronic excessive menstrual bleeding. Mean age was 41 years (range, 19–55 years). Mean body mass index was 28.9 kg/m^2 (range, 18–57 kg/m^2); 58.2% were actively bleeding at presentation, and 90.4% reported chronic excessive blood loss. Two thirds recognized heavy bleeding that had persisted for more than 6 months without seeking help. However, 7.8% described their bleeding as normal, and 40.5% had received at least 1 previous transfusion. Mean nadir hemoglobin was

4.15 g/dL (range, 1.6–4.9 g/dL). Mean corpuscular volume was 62.2 fL (range, 47.7–99.8 fL) and mean corpuscular hemoglobin concentration was 29.2 g/dL (range, 25.7–33.6 g/dL). Nearly a quarter had reactive thrombocytosis, which might have created a hypercoagulable state. Bleeding was ultimately attributed to leiomyoma in 47.9%; cancer was detected in 4.8%. A total of 33.9% were discharged without being offered any therapy to prevent subsequent bleeding; 3.0% declined any medical therapy; 35.1% were lost to follow-up prior to receiving effective therapy; and 26.8% had multiple subsequent transfusions before seeking/receiving definitive treatments.

CONCLUSION: Even when faced with potentially life-threatening anemia because of chronic, excessive menstrual blood loss, some women are not impressed with the serious nature of their problem. Women will benefit from recognizing the health consequences of chronic excessive blood loss. Chronic excessive blood loss should be treated as both an urgent and potentially recurrent problem; physicians should address this clinical concern proactively.

Key words: anemia, heavy menstrual bleeding, reactive thrombocytosis

In the last few years, considerable advances have been made to address heavy menstrual bleeding. There is now a better understanding of its pathophysiology.[1-4] There is more precise terminology[5] and an improved classification system.[6,7] New, effective medical therapies[8-11] and less invasive surgical treatment options have also become available.[12,13]

Heavy menstrual bleeding causes iron deficiency anemia and limits normal activity in two thirds of women with objectively measured blood loss in excess of 80 mL per cycle.[14,15] Women with increased menstrual bleeding experience work loss[16] and are more likely to use health care,[17] resulting in a measurable economic burden.[18] The amount of iron lost per cycle in women with heavy bleeding averages 5–6 times more than in women with average blood loss and results in significant depletion of their iron stores.[19]

Iron deficiency produces important clinical problems, including fatigue, atrophic epithelial changes, oral lesions, dysphagia, nail lesions, and reduced immune response.[20,21] Severe iron deficiency has also been associated with acute ischemic stroke,[22-24] venous stasis, retinopathy,[25] and cerebral sinovenous thrombosis.[26]

Both thrombocytopenia and reactive thrombocytosis have been associated with severe anemia.[27-29] One in 3 US women undergoes a hysterectomy before age 60 years; in half of these women, the primary presenting problem is heavy menstrual bleeding.[30] It is not clear that women themselves reliably recognize that their bleeding is excessive and that it places themselves at risk for such serious health consequences.[31-35]

Among 300,359 women in one large database who were hospitalized with gynecological conditions associated with heavy menstrual bleeding, more than 25% were diagnosed with anemia; nearly one quarter of these women were transfused.[36] Isolated case reports of severe anemia describe the considerable challenges in managing such patients,[37] but

no recent studies have investigated the acute presentations and follow-ups of women with severe anemia because of heavy menstrual bleeding. The frequency with which women are treated for these problems at Harbor-UCLA Medical Center provided an opportunity to report detailed information about women with these problems in the 21st century.

MATERIALS AND METHODS

Consent was obtained to conduct this study from the John R. Wolfe Human Subjects Committee and from the Research Committee of the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center. A waiver for informed consent was granted because no personal identifying information was collected.

This is a retrospective cohort study of all premenopausal women treated at Harbor-UCLA during the 6 years of 2008–2013, with a hemoglobin value of less than 5 g/dL because of heavy menstrual bleeding. A list of potential subjects was developed from the *International Classification of Diseases*, ninth revision, codes for excessive menstruation (285.9, 626.2) and hemoglobin values less than 5 g/dL. The diagnosis of excessive menstruation was made clinically by the woman's gynecologists, based on the patient's description of the duration and/or flow supported by laboratory findings and the absence of any other etiology for her anemia.

Harbor-UCLA Medical Center is part of the Los Angeles Department of Health Services and serves primarily indigent, uninsured minority (predominantly Hispanic) residents. The medical records at Harbor-UCLA are in transition from paper charts to electronic versions. Once the computerized list of names of potential subjects was obtained, electronic records were consulted to verify that the patient's anemia was attributed by her clinician to her menstrual bleeding and to obtain computerized laboratory results.

Individual patient paper charts were reviewed for additional information from any of the written records including the emergency room sheets, nursing notes, and daily notes and follow-up clinic notes. Demographic information, menstrual bleeding records, medical and surgical history, and records at the time of presentation were all collected as were the physical findings, laboratory test results, and discharge treatments provided. Data were entered into Excel and calculations made using standard statistical programs. Statistical significance was set at $P < .05$ when χ^2 comparisons were made.

RESULTS

The computer search identified 271 premenopausal women who experienced severe anemia, (hemoglobin <5 g/dL) and excessive menstrual blood loss; 122 women were excluded because their anemia was not related to heavy menses; the most common nongynecological causes for severe anemia in these women were end-stage renal disease, leukemia, and trauma. Interestingly, the admission notes in these cases did not include any information about menstrual bleeding patterns of the women. Other cases were excluded because the low hemoglobin did not occur at the time that heavy bleeding was noted to be a problem.

After appropriate exclusions were made, the study population included 149 women who experienced 168 episodes of hemoglobin less than 5 g/dL, thought at the time of the presentation to be due only to heavy menstrual bleeding treated at this facility during those years.

Table 1 displays the demographic characteristics of the study population. The mean age at the time of diagnosis was 41.6 years, with a range of 19–55 years; 77% of the women were in their 40s. The gravidity of the study population ranged from 0 to 10, with the mean value of 2. Parity ranged from 0 to 7, with the mean of 1. The majority of the study population was ethnically split between African-American (40%) and Hispanic (44%), with white non-Hispanic, Asian, Pacific Islanders, and others each contributing 1–6% of the population. For women, information about ethnicity was not available.

Many women reported medical comorbidities, but not all the histories were complete. Hypertension was reported in 33 of the admissions, diabetes in 21, thyroid dysfunction in 11, hepatic abnormalities in 6, idiopathic thrombocytopenic purpura in 3, sickle cell trait in 6, thalassemia in 3, and von Willebrand disease in 1 instance.

The menstrual histories provided by women were varied and are displayed in Table 2. At one extreme, 7.8% of women considered their menses to be normal, and 7% were referred to the hospital because of an incidental finding of severe anemia discovered during routine screening elsewhere. At the other extreme, almost 90% reported heavy or prolonged menses; 66% admitted to having heavy bleeding for more than 6 months and another 13% said their problem had existed for 3–6 months. Nearly 40% had previously received blood transfusions. Fewer than 55% of women presented with active bleeding.

The body mass indices averaged 28.9 kg/m^2; 43.8% were obese and 23.8% were overweight. Pelvic examinations were documented on admission in 69.6% of women; 42.9% were found to be actively bleeding.

Most women were admitted to the gynecology service, but a substantial minority of the time (25%), the woman was treated only in the emergency room. One woman was treated for a few days on the gynecology service for her bleeding but was then admitted to the psychiatry service; her total hospitalization lasted 22 days. The mean number of units of packed red blood cells given to each woman was 3.75 U, with a median of 4 U and a range of 0–9 U. Of note, 6% of the women were Jehovah's Witnesses; all but 1 of these women declined transfusions.

Table 3 displays the laboratory findings. The mean hemoglobin was 4.2 g/dL, with a range of 1.6–6.4 g/dL. The lowest hemoglobin for individual women during hospitalization ranged from 1.6 to 4.9 g/dL. Mean corpuscular volume (MCV) was 62.2 fL; 93.4% were abnormally low. Similarly, the mean value for mean corpuscular hemoglobin concentration (MCHC) was 29.2 g/dL; 99.4% were abnormally low.

Ferritin is the most accurate test to identify iron deficiency anemia.[38] It was tested in 56.6% of cases; 86.3% of those values were abnormally low. Coagulation factors were tested in slightly more