Taiwanese Journal of Obstetrics & Gynecology 54 (2015) 483–488

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Review Article

Medical treatment for heavy menstrual bleeding

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ARTICLE INFO

Article history:
Accepted 4 August 2015

Keywords:
antifibrinolytics
heavy menstrual bleeding
HMB
levonorgestrel-releasing intrauterine system
medical treatment

ABSTRACT

Heavy menstrual bleeding, or menorrhagia, is subjectively defined as a "complaint of a large amount of bleeding during menstrual cycles that occurs over several consecutive cycles" and is objectively defined as menstrual blood loss of more than 80 mL per cycle that is associated with an anemia status (defined as a hemoglobin level of <10 g/dL). During their reproductive age, more than 30% of women will complain of or experience a heavy amount of bleeding, which leads to a debilitating health outcome, including significantly reduced health-related quality of life, and a considerable economic burden on the health care system. Although surgical treatment might be the most important definite treatment, especially hysterectomy for those women who have finished bearing children, the uterus is still regarded as the regulator and controller of important physiological functions, a sexual organ, a source of energy and vitality, and a maintainer of youth and attractiveness. This has resulted in a modern trend in which women may reconsider the possibility of organ preservation. For women who wish to retain the uterus, medical treatment may be one of the best alternatives. In this review, recent trends in the management of women with heavy menstrual bleeding are discussed.

Introduction

Heavy menstrual bleeding (HMB), defined as a blood loss of more than 80 mL per cycle and often accompanied with anemia, is a major reason for gynecologic consultations around the world. Women with HMB experience a diminished quality of life and a loss of work productivity, and face high expenses for medical services [1]. Various terms have been used to describe HMB, including menometrorrhagia, metrorrhagia, menorrhagia, and polymenorrhea. The confusing and inconsistently applied nomenclature and the lack of standardized methods for investigation and categorization of the various potential etiologies make it difficult to compare studies performed by different investigators or research groups. Therefore, a universally accepted system of nomenclature and classification seems to be a necessary step in the evolution of collaborative research and evidence-based application of results to clinical practice [1]. In addition, an accurate diagnosis based on a universally accepted system of nomenclature and classification might offer a better understanding of the pathophysiology of HMB, which would help physicians make better decisions regarding the management of women with this condition. After an effective treatment, good control of the patient's symptoms and signs will improve her quality of life [2–4].

To clearly demonstrate HMB, the Menstrual Disorders Working Group of the International Federation of Gynecology and Obstetrics (FIGO) has proposed abandoning the use of one common term, "dysfunctional uterine bleeding" [5]. There are nine main categories, arranged according to the acronym PALM–COEIN (polyp, adenomyosis, leiomyomas, malignancy, hyperplasia–coagulopathy,

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http://dx.doi.org/10.1016/j.tjog.2015.08.001

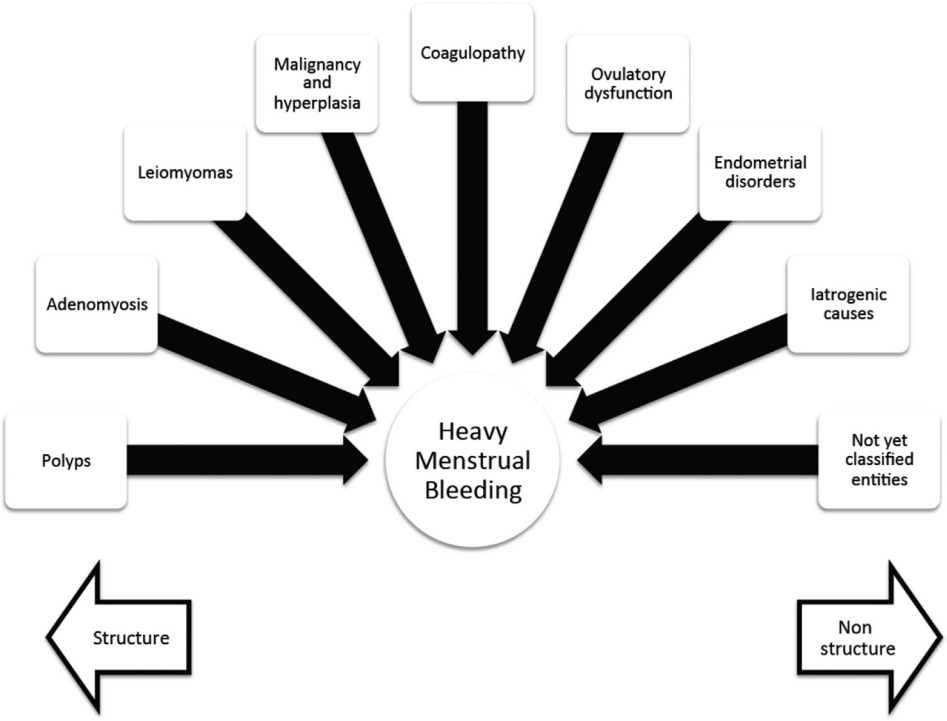

Figure 1. PALM–COEIN (polyp, adenomyosis, leiomyomas, malignancy, hyperplasia- coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic causes and not-yet-classified entities) system for heavy menstrual bleeding.

ovulatory dysfunction, endometrial disorders, iatrogenic causes and not-yet-classified entities) (Figure 1). The PALM categories include polyp, adenomyosis, leiomyomas, and malignancy and hyperplasia [5]. In general, the components of PALM are structural etiologies, which can be measured visually because they can be evaluated by clinical examination, imaging techniques, or histopathology [6]. It is difficult to define a COEIN status by imaging or histopathology, since COEIN is related to nonstructural entities [6], including coagulopathy, ovulatory dysfunction [7], endometrial disorders by exclusion of other identifiable abnormalities in women of reproductive age; , iatrogenic causes, such as insertion of an intrauterine system [8] or medicine directly impacting the endometrium [9], interfering with blood coagulation mechanisms (warfarin, heparin, and low-molecular-weight heparin) [10], and influencing the systemic control of ovulation, and not-yet-classified entities, including chronic endometritis [11], arteriovenous malformation [12], myometrial hypertrophy, and possible future entities.

The primary classification system reflects only the presence (1) or absence (0) [5,6], and cannot totally show the severity of diseases. Therefore, a secondary classification system may be needed in some subgroups. For example, leiomyomas involving the endometrial cavity [submucosal (SM)] need to be distinguished from others (O) because SM lesions are most likely to contribute to the genesis of HMB [5]. Tertiary subclassification of leiomyoma types requires the clinicians to determine the relationship between the leiomyomas and the endometrium, myometrium, and serosa [13]. SM types are 0 (pedunculated intracavitary), 1 (<50% intramural), and 2 (≥50% intramural), and the others are 3 (contracts endometrium, 100% intramural), 4 (intramural), 5 (subserosal ≥50% intramural), 6 (subserosal <50% intramural), 7 (subserosal pedunculated), and 8 (includes cervical or parasitic and other lesions not related to the myometrium) [14].

The PALM–COEIN system not only allows clinicians and researchers to identify and classify women with HMB in a systematic manner, but also provides reliable information for research purposes and for epidemiological and prevalence studies in different settings [15]. This classification is useful for patient-tailored therapy, especially for differential stages of women's reproductive years and for different patterns of HMB [15]. It is important to keep in mind that many of these causes of HMB can be asymptomatic, and that HMB itself might be the first symptom or the only symptom presented by patients [16,17].

Strategy to evaluate women with HMB

Measuring menstrual blood loss accurately is impractical because of the complexity of the techniques [15]. Therefore, HMB could be defined as “excess menstrual blood loss interfering with women's physical, emotional, social and material quality of life.” HMB can occur alone or in combination with other symptoms. Normal limits of menstruation in women include: (1) a menstrual period frequency ranging from 24 days to 38 days; (2) duration of blood flow ranging from 4 days to 8 days; and (3) the volume of monthly blood flow ranging from 5 mL to 80 mL [6]. The cause of HMB can be clearly separated from structural and nonstructural problems. Therefore, all women with HMB should be treated in as diligent and comprehensive a fashion as is practicable, given the clinical situation and the available resources [5]. That is to say, we need to establish necessary parameters to achieve an accurate diagnosis and treatment for women with HMB (Figure 2).

Clinicians should perform a careful evaluation of a woman of reproductive age with HMB, to ensure that the bleeding is not related to an undiagnosed pregnancy and is emanating from the cervical os, rather than from another location [5]. The bleeding should be confirmed, in the absence of any other identifiable source [18]. In addition, a structured history, including the age of the woman, regularity of menstrual cycles and accompanying menstruation problems (for example, dysmenorrhea), beginning and frequency of HMB, symptoms or signs of a tendency to bleed, bruises, epistaxis, and a family history, should be taken and