

■ Orijinal Makale

A retrospective perspective on abnormal uterine bleeding and the PALM-COEIN classification: Experiences of a tertiary center

Anormal uterin kanama ve PALM-COEIN sınıflandırmasına retrospektif bakış açısı: Tersiyer merkezin deneyimleri

Canan Tapkan¹ , Bengü Mutlu Sutcuoglu¹ , Hande Nur Oncu² , Mujde Can Ibanoglu^{*2} 

¹ Department of Gynecology, Ankara Kecioren Training and Research Hospital, Ankara, Turkey

² Department of Gynecology, Ankara Etlik Zubeyde Hanım Women's Health Training and Research Hospital, Ankara, Turkey

Abstract

Background: The Menstrual Disorders Working Group of the International Federation of Gynecology and Obstetrics (FIGO) created a new classification system called "PALM-COEIN" for abnormal uterine bleeding in 2011. The aim of our study is to investigate the new classification system and compare it with the classical terminology for abnormal uterine bleeding.

Materials and Methods: Our study was conducted retrospectively between February 2022 and July 2022 in the gynecology clinic of Kecioren Training and Research Hospital. Premenopausal women without known chronic disease were enrolled in the study. Each patient enrolled in the study was examined based on anatomical structure, physical examination, and pelvic ultrasonography. If necessary, endometrial specimens and hysterectomy material were obtained for histopathologic examination. Possible causes were classified according to the new classification system.

Results: The study included 135 premenopausal women with abnormal uterine bleeding. In general, the patients with bleeding complaints had leiomyoma uteri and polyps according to the classical terminology. They were grouped under the labels of hypermenorrhea, menorrhagia, metrorrhagia, and menometrorrhagia, which were due to various causes, including polyps, adenomyosis, hyperplasia, and iatrogenic causes. According to the classification PALM-COEIN, 35 (25.9%) polyps, 16 (11.8%) adenomyosis, 38 (28.1%) leiomyomas, 4 (2.9%) malignancies and hyperplasia were detected.

Conclusion: The classification of abnormal uterine bleeding is generally inconsistent. The new classification system, created for many reasons, is an important step towards understanding complex situations. Another need is that a widely accepted and known classification system should facilitate communication among clinicians and clarify the review of the target population. It is also clear that the new classification system will improve communication between patients. Widespread use of the system will also reveal new treatment options for abnormal uterine bleeding.

Keywords: Abnormal uterine bleeding; classification; dysfunctional uterine bleeding; menstrual disorders

Öz

Amaç: 2011 yılında Uluslararası Jinekoloji ve Obstetrik Federasyonu'nun (FIGO) Menstrüel Bozukluklar Çalışma Grubu, anormal uterin kanama için "PALM-COEIN" adlı yeni bir sınıflandırma sistemi oluşturdu. Çalışmamızın amacı, anormal uterin kanama için yeni sınıflandırma sistemini araştırmak ve klasik terminoloji ile karşılaştırmaktır.

Gereç ve Yöntem: Çalışmamız Şubat 2022 ile Temmuz 2022 tarihleri arasında Keçiören Eğitim ve Araştırma Hastanesi kadın hastalıkları kliniğinde retrospektif olarak yapılmıştır. Bilinen kronik hastalığı olmayan premenopozal kadınlar çalışmaya dahil edilmiştir. Çalışmaya alınan her hasta fizik muayene ve pelvik ultrasonografi ile değerlendirilmiştir. Gerekirse histerektomi materyali ve endometriyal spesmen histopatolojik inceleme için alındı. Olası nedenler yeni sınıflandırma sistemine göre sınıflandırıldı.

Bulgular: Çalışmaya anormal uterin kanaması olan 135 premenopozal kadın dahil edildi. Kanama şikayeti ile başvuran hastalar; polipler, adenomyozis, hiperplazi ve iyatrojenik nedenler gibi çeşitli nedenlere bağlı hipermenore, menoraji, metroraji ve menometroraji etiketleri altında gruplandırılmıştır. PALM-COEIN sınıflamasına göre 35 (%25,9) polip, 16 (%11,8) adenomyozis, 38 (%28,1) leiomyom, 4 (%2,9) malignite ve hiperplazi tespit edildi.

Sonuç: Anormal uterin kanamanın sınıflandırılması genellikle tutarsızdır. Birçok nedenden dolayı oluşturulan yeni sınıflandırma sistemi, karmaşık durumları anlamak için önemli bir adımdır. Diğer bir ihtiyaç ise, yaygın olarak kabul edilen ve bilinen bir sınıflandırma sisteminin klinisyenler arasındaki iletişimi kolaylaştırması ve hedef popülasyonun gözden geçirilmesini netleştirmesidir. Yeni sınıflandırma sisteminin hastalar arasındaki iletişimi iyileştireceği de açıktır. Sistemin yaygın kullanımı anormal uterin kanamalar için de yeni tedavi seçeneklerini ortaya çıkaracaktır.

Anahtar Kelimeler: Anormal uterin kanama; sınıflandırma; disfonksiyonel uterin kanama; menstrüel düzensizlik

1. Introduction

Abnormal uterine bleeding (AUB) is usually defined as an abnormality in the pattern, quantity, frequency, or duration of the menstrual cycle (1,2). Abnormal uterine bleeding can be classified as acute or chronic. Acute AUB means a severe episode. It is a severe uterine bleeding episode that may require immediate intervention to prevent hemodynamic instability (3). Abnormal uterine bleeding that persists over a 6-month period is called chronic AUB (3). It occurs in about 10 to 35 percent of women during their fertile years (4). Chronic heavy or persistent uterine bleeding can cause anemia, interfere with daily activities and require emergency medical care. Patients are also at increased risk for uterine cancer (5).

The causes of AUB are multifactorial, and the causes are usually common. The Menstrual Disorders Working Group of the International Federation of Gynecology and Obstetrics (FIGO) has presented a classification system and revised terminology (2). This new classification system was intended to avoid inadequate coverage or confusion of the terms menorrhagia, menometrorrhagia, polymenorrhea, oligomenorrhea, etc. previously used to describe AUB (6). This system classified the etiologies of AUB as "associated with structural abnormalities of the uterus" and "not associated with structural abnormalities of the uterus." Under these main headings, AUB is categorized according to the abbreviation PALM-COEIN: Polyp, Adenomyosis, Leiomyoma, Malignancy and Hyperplasia, Coagulopathy, Ovulatory Disorder, Endometrial, Iatrogenic,

and Not Otherwise Classified (2). Determining the etiology of uterine bleeding is critical to select the most appropriate and effective treatment strategies for individual patients. The overall inconsistency of the classification used to define AUB was cited as the primary reason for the creation of this FIGO approved classification system. Another requirement for the use of a new, widely accepted, and well-known classification system is to facilitate communication between clinicians, researchers, and also patients. This system can clarify the terms and target populations to be used in clinical trials. The widespread adoption of the PALM-COEIN system will pave the way for the development of new treatments and research into AUB. For this reason, we wanted to find out how the relationship between the common definitions and the terms used in the new classification can be explained with our data.

2. Material and Methods

This descriptive cross-sectional study was conducted between February 2022 and July 2022 in the gynecology clinic of Keçiören Training and Research Hospital in Ankara. The study was planned as a retrospective study and the study protocol was approved by the Institutional Review Board (2/22/2012#2012-KAEK-15/2463). The study included 135 premenopausal women of reproductive age (25-45 years) who presented to the outpatient clinic with complaints of abnormal uterine bleeding characterized by unpredictable, irregular, excessive duration, abnormal volume, and/or abnormal menstrual frequency, and intermenstrual bleeding. An anatomic

structure, physical examination, and pelvic ultrasonography were performed in each patient. If necessary, endometrial specimens and hysterectomy specimens were obtained for histopathological examination. Possible causes were classified according to the new classification system. Women with bleeding attributable to cervical causes were excluded from the study. The category “coagulopathy” was assigned to all cases with multiple coagulation disorders. In the classification of PALM-COEIN, definitions other than organic pathologies were evaluated under the title “others”. An iatrogenic grouping was also made. The “iatrogenic” category was characterized by the use of hormones or steroids. “Ovulatory dysfunction” was defined as a condition manifested by a combination of unpredictable bleeding timing and variable bleeding volume (2). Hypermenorrhea was defined as excessive menstrual bleeding, wetting more than one tampon or pad in an hour; menorrhagia was defined as a condition in which prolonged menstruation is accompanied by heavy bleeding; metrorrhagia was defined as increased menstrual flow for more than 7 days that occurs irregularly during the cycle; and menometrorrhagia was defined as heavy, prolonged, and irregular bleeding.

Statistical analysis

SPSS 22 (SPSS Inc. Chicago, IL) was used for statistical analysis. The distribution of parameters was tested for normality using the Kruskal-Wallis test. Descriptive statistics were expressed as mean \pm standard deviation (SD), minimum and maximum values, number (n), and percentage (%).

3. Results

The study involved 135 women who complained of abnormal uterine bleeding. Patients complaining of abnormal uterine bleeding were categorized according to classical terminology

and examined under the designations hypermenorrhea, menorrhagia, metrorrhagia, and menometrorrhagia. Pathologic final samples with these complaints were then examined, and an attempt was made to explain the bleeding patterns based on the PALM-COEIN classification for cause. The mean age of the patients was 42.6 years, the mean body mass index (BMI) was 30.5 kg/m², and the mean number of births was 2.75. Routine ultrasonography revealed a mean thickness of the endometrium of 11.4 mm. Polyps occurred in hypermenorrhea, menorrhagia, metrorrhagia, and menometrorrhagia in different cases; 60% of polyps occurred in hypermenorrhea, 2.8% in menorrhagia, 11.4% in metrorrhagia, and 25.7% of polyps in menometrorrhagia. Of the adenomyosis, 62.5% occurred in hypermenorrhea, 12.5% in menorrhagia, 6.2% in metrorrhagia, and 18.7% in menometrorrhagia. Menometrorrhagia occurred in 39.4% of leiomyomas. Among malignancies, menometrorrhagia occurred most frequently (n=3, 75.0%). In the cases categorized according to the PALM-COEIN classification system, there were 35 (25.9%) polyps, 16 (11.8%) adenomyosis, 38 (28.1%) leiomyomas, 4 (2.9%) malignancies, and hyperplasia (Table 1).

4. Discussion

This study was conducted to identify the causes of AUB based on the PALM-COEIN classification and to compare the clinical and histopathological features to determine the final etiology for appropriate treatment of AUB. Identification of the probable etiology is the most important milestone for effective treatment of AUB. Treatment modalities vary depending on the patient, physician experience, cause of bleeding, and response to drug therapy. The common interpretation of the results of numerous clinical studies on the epidemiology, etiology, treatment, and prognosis of AUB is complicated by the lack of uniformity in

Table 1. Comparison of cases according to classic terminology and the PALM-COEIN system

PALM-COEIN system	Hypermenorrhea	Menorrhagia	Metrorrhagia	Menometrorrhagia
P (Polyp) n=35	21 (60.0%)	1 (2.8%)	4(11.4%)	9 (25.7%)
A (Adenomyosis) n=16	10 (62.5%)	2 (12.5%)	1 (6.2%)	3 (18.7%)
L (Leiomyoma uteri) n=38	14 (36.8%)	5 (13.1%)	4 (10.5%)	15 (39.4%)
M (Malignancy) n= 4	-	1(25.0%)	-	3(75.0%)
O (Others) n=31	3 (9.6%)	1(3.2%)	2 (6.4%)	25 (80.6%)
I (Iatrogenic) n=11	3 (27.2%)	5 (45.4%)	1 (9.0%)	2 (18.1%)

classification (7). Dysfunctional uterine bleeding is defined as irregular uterine bleeding that occurs without identifiable pelvic pathology, general medical illness, or pregnancy. “Dysfunctional uterine bleeding (DUB)” is now a redundant term for women (8).

Women previously classified in this category actually fall into the FIGO categories of various combinations of coagulopathies, ovulatory disorders, or endometrial pathologies and are considered “unrelated to the uterus” (8). Polyps are defined by a combination of ultrasound (including saline infusion sonography) and hysteroscopic imaging with or without histopathology (9). Although most polyps are asymptomatic, the percentage of polyps in AUB varies from 3.7% to 65% (10). In this study, polyps were found in 27.4% of women with AUB, leading to AUB. It is also important to exclude a polyp-looking endometrium, as this appearance may be a variant of a normal, estrogen-affected endometrium. Diagnostic criteria for adenomyosis have traditionally been based on histopathologic assessment of the depth of “endometrial” tissue in the endometrium, particularly in hysterectomy specimens (11). This feature is a factor that severely limits the need to diagnose adenomyosis. In this system, diagnostic criteria based on both sonography and magnetic resonance imaging (MRI) were used (12). The adenomyosis rate in our study was 11.8%. This rate is comparable to the rate reported in the literature. Most leiomyomas (fibroids) are asymptomatic and are often not considered a cause of AUB (13). Leiomyomas are classified into a subclassification system that includes submucous and other leiomyomas and provides a common language for clinicians leading to appropriate treatment (14). Leiomyomas are the most common cause of AUB in the literature. Leiomyomas can be divided into submucosal (L- SM) and other (L-O) subclasses depending on their location (15). Submucosal fibroids are thought to disrupt the uterine cavity and are more likely to cause heavy menstrual bleeding (HMB). In our study, leiomyoma uteri was the most common cause.

Endometrial hyperplasia, i.e. abnormal proliferation of the uterine glands, is a serious cause of AUB and endometrial cancer (16). Obesity has been shown to be a major cause of AUB. Lifetime exposure to estrogen through peripheral aromatization of adrenal androgens increases the incidence of polyps, leiomyomas, and endometrial cancer in obese women (relative risk 3-10%) (13). In the present study, the mean BMI of the patients was in the obese category. Therefore, caution should be exercised in obese women with regard to AUB. Most bleeding is due to exogenous hormone therapy or drugs

that affect hormones. Medications such as anticonvulsants, hormonal steroids, and antipsychotics can cause hormonal imbalances that can lead to AUB (17). An intrauterine device (IUD) can cause low-grade endometritis leading to AUB (10). According to recent studies, iatrogenic causes account for 1.56 % of AUB. In our study, cases were classified based on the positive results of endometrial specimens, hysterectomy specimens (if possible), ultrasound findings, and laboratory results. Endometrial samples do not exclude possible adenomyosis or uterine fibroid. There may be one or more causes, and it is not possible to determine the exact cause of AUB without performing the same diagnostic tests in all cases (hysterectomy specimens, coagulation parameters, imaging, and a detailed medication and medical history). These are the weaknesses of our study.

It is expected that the use of the PALM-COEIN system will help to eliminate confusion about the etiology of AUB and this diagnosis will allow more effective communication with other health professionals, which in turn will lead to better treatment management. In conclusion, further studies are needed to clarify the causes of AUB in the system PALM-COEIN. This analysis will allow us to better understand the classification of etiologic factors in order to develop appropriate management strategies for the treatment of AUD.

Yazar katkısı

Araştırma fikri ve tasarımı:CT, MCI; veri toplama: BMS ve CT; sonuçların analizi ve yorumlanması: CT, HNO, BMS ve MC; araştırma metnini hazırlama: MCI. Tüm yazarlar araştırma sonuçlarını gözden geçirdi ve araştırmanın son halini onayladı.

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Author contribution

Study conception and design: CT,MCI; data collection: BMS, CT; analysis and interpretation of results: CT, HNO, BMS ve MC; draft manuscript preparation: MCI. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the University of Health Sciences, Ankara Atatürk Sanatorium Training and Research Hospital Clinical Research Ethics Committee (Protocol no. 2012-KAEK-15-2463/22.02.2022).

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Conflict of interest

The authors declare that there is no conflict of interest.

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