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Treatment of abnormal uterine bleeding using levonorgestrel-releasing intrauterine devices: experience from a Turkish tertiary hospital

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Abstract. – OBJECTIVE: We evaluated the efficacy of the levonorgestrel-releasing intrauterine device in treating menorrhagia using a pictorial blood assessment chart.

PATIENTS AND METHODS: We retrospectively examined 822 patients treated with a levonorgestrel-releasing intrauterine device for abnormal uterine bleeding between January 1, 2017, and December 31, 2020, at a Turkish tertiary hospital. A pictorial blood assessment chart was used to determine each patient's blood loss amount, which involves the use of an objective scoring system to determine the amount of bleeding in towels, pads, or tampons. Descriptive statistical values were presented as mean and standard deviation, and paired sample t-tests were used for within-group comparisons of normally distributed parameters. Moreover, in the part of the descriptive statistical analysis, the mean and median values for the non-normally distributed tests were not close to each other, indicating that the data obtained and analyzed in this study had a non-normal distribution.

RESULTS: Of 822 patients, 751 (91.4%) exhibited a significant reduction in menstrual bleeding after device insertion. Moreover, a significant decrease was observed in the pictorial blood assessment chart scores 6 months postoperatively ($p < 0.05$).

CONCLUSIONS: This study revealed that the levonorgestrel-releasing intrauterine device is an easy-to-insert, safe, and effective treatment option for abnormal uterine bleeding (AUB). Furthermore, the pictorial blood assessment chart is a simple and reliable tool for evaluating menstrual blood loss in women before and after the insertion of levonorgestrel-releasing intrauterine devices.

Key Words:
Pictorial blood loss assessment chart, Levonorgestrel-releasing intrauterine device, Treatment of abnormal uterine bleeding.

Introduction

The menstrual cycle is usually between 21 and 35 days[1]. Abnormal uterine bleeding (AUB) is defined as excessive, frequent, or prolonged bleeding by the International Federation of Gynecology and Obstetrics (FIGO). Notably, AUB includes menorrhagia, metrorrhagia, hypermenorrhea, polymenorrhea, and dysfunctional uterine bleeding[2]. FIGO uses the acronym PALM (polyps, adenomyosis, leiomyoma, and malignancy) to refer to the structural causes of AUB and COEIN (coagulopathy, ovulatory dysfunction, endometrial dysfunction, iatrogenic, and non-classifiable) to refer to the nonstructural causes. Treatment options include levonorgestrel-containing intrauterine devices (LNG-IUD), danazol, oral progesterone, oral contraceptives, and anti-fibrinolytic drugs[3]. Approximately 30% of hysterectomies are performed because of AUB[4]. Medical practitioners aim to treat patients using the least invasive techniques that allow patients to resume their activities of daily life as soon as possible[5].

The present study aimed to evaluate the efficacy of LNG-IUD in the treatment of AUB using a pictorial blood assessment chart.

Patients and Methods

In this retrospective study, 822 patients were implanted with an LNG-IUD for the treatment of AUB at the Gynecology and Obstetrics Clinic of Istanbul Kanuni Training and Research Hospital between January 1, 2017, and December 31, 2020. Of these, 9 patients who were unable to attend the follow-up visits were excluded from the analysis, leading to a total sample size of 822 patients. The data were collected at baseline as well as at 3- and 6-month

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follow-up visits after IUD insertion. Moreover, the clinical characteristics of the patients were recorded, including treatment details, parity (number of children delivered), body mass index (BMI), concomitant diseases, previous surgeries, and systemic side effects associated with the IUD. In addition, bleeding characteristics, menstrual cycle duration, and hemoglobin and hematocrit levels were compared before and after IUD placement. Furthermore, all existing vaginal infections were treated. An LNG-IUD (Mirena® Bayer, Whippany, NJ 07981, Leverkusen, Germania) device was inserted in all eligible patients within the first 5 days of their menstrual cycle. None of the patients required local or general anesthesia. Notably, prophylactic antibiotics were not provided. After the device was placed, transvaginal ultrasonography (USG; Mindray DC30, Shenzhen, China) was performed to confirm the correct placement of the device. Moreover, the blood hemoglobin and hematocrit levels were assessed on the same day. The amount of blood loss was measured using the pictorial blood assessment chart (PBAC)[6], which involves the use of an objective scoring system to determine the amount of bleeding in towels, pads, or tampons[7]. For each day of the menstrual period, light spotting or blood clots (1 point), spotting or blood clots exceeding 2.5 cm, moderate spotting (5 points), and complete wet-staining (blood in pad or tampon) were assigned scores. Monthly scores of ≥100 were deemed to indicate >80 mm of bleeding based on this system. Furthermore, bleeding patterns and any side effects were carefully monitored in all patients.

This study was conducted by the 2013 revision of the Declaration of Helsinki and was approved by the Ethics Committee of Istanbul Kanuni Sultan Süleyman Training and Research Hospital (KAEK 2021.12.342). The requirement for patient consent for participation and publication was waived owing to the retrospective nature of the study. Written informed consent for treatment was previously obtained from all patients.

Inclusion Criteria

Women aged 18-50 years who experienced heavy menstrual bleeding were included in the present study and provided with the necessary training and information on evaluating their blood loss using PBAC. Moreover, necessary control measures were implemented in the sixth month after IUD insertion to confirm its correct placement for at least three consecutive menstrual cycles with no findings of organic pathology, coagulopathy, pregnancy, malignancy, depression, or pelvic infections.

Exclusion Criteria

Patients who were menopausal, presented with uterine malformations, and had suspected malignancies, a history of depression, endometrial polyps, pelvic infections, and missing file information were excluded from the study. Moreover, those who experienced IUD expulsion during the control measures were excluded. However, it should be noted that even when the device is correctly placed, it can slip out of place or be expelled by the body in the first 6 months[8].

Statistical Analysis

All data analyses were performed using SPSS v. 24.0 software (IBM Corp., Armonk, NY, USA). Data were expressed as mean and standard deviation, and the paired sample *t*-test was used for within-group comparisons of normally distributed parameters. Notably, data analyzed by descriptive statistics had a non-normal distribution. Results were reported with a 95% confidence interval, and *p*-values <0.05 were considered significant.

Results

The demographic and clinical characteristics of the participants are shown in Table I. The mean age of the patients in this study was 41.40 ± 4.98 years, the mean parity was 2.51 ± 1.63, and the mean BMI was 24.32 ± 3.22 kg/m^2. Of the 822 patients, 101 patients had concomitant diseases, including hypertension, diabetes mellitus, and goiter in 30 (3.6%), 31 (3.8%), and 30 (3.6%) patients, respectively. Moreover, 10 (1.2%) patients had more than one chronic disease. Overall, 161 (20.2%) patients had a history of abdominal surgery. No perforations or complications were observed during LNG-IUD insertion in any patient; moreover, none of the patients was pregnant.

The uterine bleeding patterns of the patients are shown in Table II. After IUD insertion, the average number of menstrual days of the patients decreased from 11.66 to 2.95 days (75.1% reduction), and this difference was statistically significant ($p < 0.001$). Figure 1 shows a comparison of the PBAC scores of the participants before and after IUD insertion. The mean PBAC score decreased significantly from 214.11 to 44.80 (79.1%; $p < 0.0001$). The mean menstrual cycle time significantly increased from 24.68 to 27.09 days (9.8%; $p < 0.0001$).

Table I. Demographic and clinical characteristics of the study participants.

Demographic features	Mean ± SD	Range
Age (years)	41.40 ± 4.98	22.00-50.00
Parity (number)	2.51 ± 1.63	0.00-9.00
BMI (kg/m^2)	24.32 ± 3.22 (kg/m^2)	21.00-40.00
Comorbidities, n (%)	101.00 (12.3%)	
Previous surgery, n (%)	166.00 (20.2%)	

BMI: body mass index; SD: Standard deviation.

Table II. Uterine bleeding patterns of the patients included in this study.

	Before the insertion of a levonorgestrel-releasing intrauterine device			6 months after the insertion of a levonorgestrel-releasing intrauterine device			*p*-value
	Mean ± SD	Min.	Max.	Mean ± SD	Min.	Max.	
The average number of menstrual days	11.66 ± 2.56	8	20	2.95 ± 2.43	0	15	<0.001*
Pictorial blood assessment chart scores	214.11 ± 24.11	180	250	44.80 ± 44.59	10	270	<0.001*
Mean hemoglobin	8.73 ± 1.78	4.2	11.1	11.51 ± 0.79	8.8	13	<0.001*
Mean hematocrit	26.18 ± 5.34	12.6	33.3	34.53 ± 2.39	26.4	39	<0.001*
Mean menstrual cycle duration	27.03 ± 2.46	19	29	24.72 ± 2.68	20	45	<0.001*

PBAC, pictorial blood loss assessment chart; SD, standard deviation. Paired *t*-tests were used to compare the number of menstrual days, PBAC scores, mean menstrual cycle duration, and hemoglobin and hematocrit levels of the patients before and after treatment. The *p*-values for all of these comparisons were below 0.001. *$p < 0.05$.

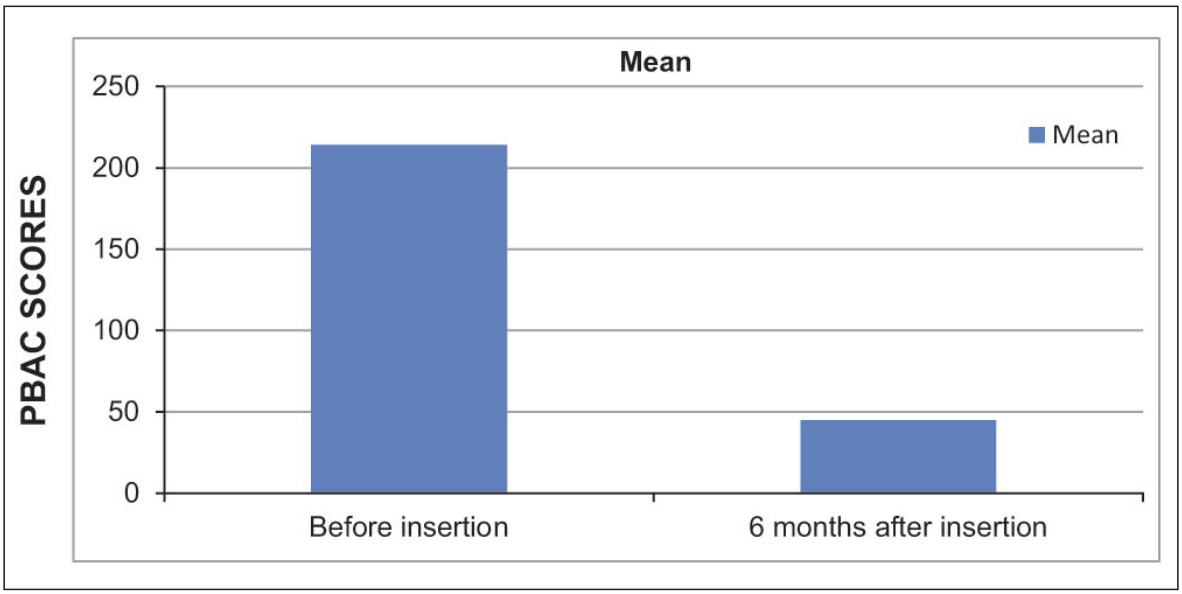

Figure 1. Comparison of the pictorial blood assessment scores of women with abnormal uterine bleeding before and 6 months after levonorgestrel-releasing intrauterine device placement. PBAC, pictorial blood loss assessment chart.
The figure shows the PBAC scores before and 6 months after the insertion of levonorgestrel-releasing intrauterine devices. Notably, LNG-IUD insertion led to a significant decrease in blood loss in women with abnormal uterine bleeding.

Table III. Systemic side effects from levonorgestrel-releasing intrauterine devices for abnormal uterine blood loss.

Systemic side effects	n = 208 n (%)
Amenorrhea/oligomenorrhea	48 (5.3)
Abdominal pain/groin pain	33 (4.01)
Weight gain	28 (3.40)
Mood changes	24 (2.92)
Abdominal bloating	18 (2.19)
Breast tenderness/mastalgia	16 (1.95)
Skin disorders/edema/acne	14 (1.70)
Headaches	14 (1.70)
Nausea	13 (1.60)

The mean baseline hemoglobin level was 8.73 g/dL, and the baseline hematocrit level was 26.2%. At the end of the sixth month, the mean hemoglobin was 11.51 g/dL, whereas the mean hematocrit was 34.5%. Notably, the increases in the hemoglobin and hematocrit levels of 2.78 g/dL (31.8%) and 8.4% (31.9%), respectively, were both statistically significant ($p < 0.0001$). Overall, 617 (75.06%) patients were diagnosed with anemia and received antianemia treatment. In contrast, the remaining 205 (24.94%) did not require any antianemia agents.

Bleeding volume did not improve in 55 (6.7%) patients. Of these, 24 (2.9%) patients experienced bleeding because LNG-IUD was expelled from the uterus. In total, 71 (8.6%) patients discontinued their IUD treatment; of these, 55 (6.7%) patients underwent subsequent hysterectomies. The remaining 16 (2.1%) patients were treated with a combination of tranexamic acid, oral progesterone, and endometrial ablation therapy. Of all participants, 751 (91.4%) patients were treated with LNG-IUDs. Overall, 208 (25.3%) patients experienced side effects due to LNG-IUD. Of these, 16 (1.9%) experienced severe side effects, whereas 192 (23.4%) experienced mild side effects. In total, 33 (4.0%), 48 (5.8%), 28 (3.4%), 24 (2.92%), 18 (2.2%), 14 (1.7%), 16 (2.0%), 14 (1.7%), and 13 (1.6%) patients experienced abdominal/groin pain, amenorrhea/oligomenorrhea, weight gain, mood changes, abdominal bloating, acne/skin disorders, breast tenderness/mastalgia, headaches, and nausea, respectively. In particular, the most common reasons for discontinuing treatment were amenorrhea/oligomenorrhea, abdominal/groin pain, and weight gain. The systemic side effects caused by LNG-IUD are shown in Table III.

Discussion

Findings and Interpretation

LNG-IUDs are simple-to-use, safe, effective, and well-tolerated as AUB treatment. Similarly, PBAC is a simple, valid, and reliable tool for evaluating the volume of menstrual blood loss in women with AUB. It can be used both before and after LNG-IUD insertion. In the present study, we found that IUD insertion significantly lowered the PBAC score. As LNG-IUDs are less invasive and have fewer side effects, they are a better treatment option than endometrial ablation or hysterectomy. Moreover, they preserve fertility, have reversible effects, and are cost-effective. Although they are contraindicated in patients with depression, they can be safely used in patients with concomitant diseases and those who have undergone previous abdominal surgery. Furthermore, LNG-IUDs preserve the uterine condition of patients with AUB.

Results in the Context of What is Known

AUB (menorrhagia) is a common condition among women of childbearing age. It is subjectively defined as heavy, frequent, or long menstrual bleeding and objectively as total menstrual blood loss of >80 mL per month[9]. However, the measurement of menstrual blood loss is difficult and error-prone. PBAC is a simple non-laboratory technique for unbiased AUB diagnosis based on self-recorded patient scores; in addition, it is a functional tool for assessing other types of blood loss. The sensitivity and specificity of this method have been reported[10,11] to be 86% and 89% respectively. A crucial aspect of this study was to investigate the use of PBAC to assess the efficacy of LNG-IUD for AUB. A previous study[12] reported a 79% and 93% decrease in blood loss, respectively, as assessed by PBAC scores at 3 and 6 months after device placement. In the current study, the mean percentage decrease in bleeding at 6 months after IUD placement was 88%.

We also observed a significant decrease in the number of menstrual days, a significant increase in the mean cycle duration, and significant increases in the mean hemoglobin and hematocrit values. Only 8.6% of the patients in our study had failed LNG-IUD treatment, whereas 91.4% of the patients underwent a successful treatment, reducing their blood loss. Furthermore, only 55 (6.69%) patients underwent a hysterectomy, indicating that LNG-IUDs are an effective alternative treatment to hysterectomy. This finding is also consistent with the findings of a previous study[13].

The European Society of Contraception and Reproductive Health recently stated[14] that LNG-IUD should not be used as a first-line treatment for patients with depression. However, it can be safely used in patients with concomitant hypertension, diabetes, and thyroid disorders[15]. Notably, LNG-IUDs were used and successfully tolerated by 101 (12.28%) patients with these concomitant diseases. LNG-IUDs improve reproductive function by reducing uterine bleeding[16]. Moreover, they can aid patients with AUB to preserve a healthy uterus[17]. Currently, in second and third-tier hospitals, hormonal intrauterine devices are used for therapeutic rather than contraceptive purposes. In Istanbul, Turkey, most intrauterine device placements are performed in primary care settings. Compared with copper IUDs, the insertion of LNG-IUDs requires no additional skills or equipment and can be performed in primary care settings, allowing patients to receive rapid and effective treatment[18]. The causes of total or partial IUD expulsion may be heavy menstruation, groin pain, or a large uterus. No consensus has been reached on LNG-IUD expulsion rates, which have been reported to range from 7%[19] to 7.5%[20]. In our study, IUD removal was performed in 24 (2.91%) patients.

Notably, LNG-IUDs outperform antifibrinolytics, oral progesterone, and birth control pills in the treatment of AUB[21]. Compared with other pharmacological treatments for menorrhagia, LNG-IUD is safer and more effective[22].

Although the daily dose of levonorgestrel is low and plasma progestin concentrations do not peak, side effects associated with hormone administration can occur. Acne, device rejection, breast tenderness, and dyspareunia have been commonly reported[23]. In the present study, the most common side effects were amenorrhea, abdominal/groin pain, flatulence, weight gain, mastalgia, and headache. Both LNG-IUD and endometrial ablation were shown to be effective in reducing AUB after 1 year of follow-up[24]. However, endometrial ablation requires endoscopic skills and special equipment, which reduces the patient's reproductive capacity.

Clinical and Research Implications

LNG-IUD is a straightforward, safe, effective, and well-tolerated treatment option for AUB. PBAC is a simple, valid, and reliable tool to measure menstrual blood loss in women with AUB, and it can be used both before and after LNG-IUD insertion. The results of this study could contribute to the development of alternative treatment options for AUB.

Before indicating hysterectomy in patients with AUB, LNG-IUD should be offered to patients as an alternative. However, more studies are needed to verify the relevance of the results of this single-center study based on national and international treatment guidelines.

Strengths and Limitations

The data in this study were meticulously collected, and the sample size was larger than that in previous studies[25,26]. To the best of our knowledge, our study results apply to a larger population of women with AUB. Moreover, this research offers insights into the development of alternative treatment options for AUB. The main limitation of this study was that it was a short-term descriptive retrospective study conducted in a single Turkish tertiary care hospital.

Conclusions

IUD placement significantly decreased bleeding in patients with AUB. LNG-IUDs are an easy-to-insert, safe, effective, and well-tolerated treatment for AUB. They also help preserve fertility, have reversible effects, are cost-effective, and are less invasive compared with surgical methods, such as endometrial ablation and hysterectomy. Although contraindicated in patients with depression, they can be safely used for patients with other concomitant diseases or a history of abdominal surgery. Furthermore, PBAC is a simple, valid, and reliable tool for evaluating menstrual blood loss.

Ethics Approval

This study was conducted by the 2013 revision of the Declaration of Helsinki and was approved by the Ethics Committee of Istanbul Kanuni Sultan Süleyman Training and Research Hospital (KAEK 2021.12.342).

Informed Consent

The requirement for patient consent for participation and publication was waived owing to the retrospective nature of the study. Written informed consent for treatment was previously obtained from all patients.

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Conflict of Interests

The authors have no competing interests to declare.

Authors' Contributions
Study concept and design: AB; data collection and drafting of the manuscript: AB and OU; review and final approval of the article: AB and OU.

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