ORIGINAL ARTICLE

Study of Efficacy and Acceptability of Levonorgestrel-Releasing Intrauterine Device in Heavy Menstrual Bleeding Patients

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ABSTRACT

Objective: To determine the efficacy and acceptability of levonorgestrel-releasing intrauterine device (LNG-IUD) in females with heavy menstrual bleeding (HMB).

Study Design: A Quasi-experimental study design.

Place and Duration of Study: The study was conducted at the Obstetrics and Gynecology Department of Pak Emirates Military Hospital (PEMH) Rawalpindi, Pakistan for a duration of 6 months from November 2022 to April 2023.

Methods: A total of 96 patients accomplishing the selection criteria were enrolled after taking written informed consent after the screening, LNG-IUD was inserted in all participants and patients were followed up till the 6th menstrual cycle and outcomes (like having less bleeding or amenorrhea, improvement in hemoglobin, improvement in doing daily tasks, etc.) were assessed.

Results: The mean age of the females was 38.08±5.83 years. Efficacy of treatment was seen in 64 (66.7%) females, and acceptability was seen in 61 (63.5%) females. In terms of side effects, spotting occurred in 17 (17.7%) patients, amenorrhea in 3 (3.1%) patients, oligomenorrhea in 4 (4.2%) patients, weight gain in 6 (6.3%) patients, breast heaviness in 3 (3.1%) patients, 3(3.1%) females had mood fluctuations and 2 (2.1%) had depression.

Conclusion: For treating females with HMB, LNG-IUD was efficacious in 66.7% of females and acceptable in 63.5% of females.

Keywords: *Heavy Menstrual Bleeding, Intrauterine Device, Levonorgestrel.*

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Introduction

The most typical symptom that prompts women to consult with a gynecologist is abnormal uterine bleeding. Menstruation that occurs at regular cycle intervals but with an excessive flow and length is known as heavy menstrual bleeding (HMB).[1] Iron deficiency anemia is frequently brought on by HMB, which has an impact on women's quality of life (QOL). Women with HMB have a decline in QOL, suffer reduced productivity at work, and use up costly medical resources.[2] It is a sign of numerous underlying conditions, including primary endometrial disorders, fibroid, ovulatory disorders, endometriosis, adenomyosis, or genital malignancies, as recently identified by the Menstrual Disorders Working Group of the International Federation of Gynaecology and Obstetrics previously.[3]

Depending on the cause HMB has previously been treated through different modalities of treatment. The purpose of about 30% of hysterectomies is to

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treat HMB.[4] But since treatment expenses to be kept under control and more women have expressed a desire to maintain their uterus, conservative therapy has become more popular in modern gynecology.[5] Traditional medicinal and surgical treatments for HMB can be replaced with the levonorgestrel releasing intrauterine device (LNG-IUD), a minimally invasive, long-acting option.[6] This device is T-shaped that delivers levonorgestrel at a starting rate of 20 mcg/day during 1st year which decreases for subsequent years for up to 5 years directly into the uterine cavity. The local effects of LNG-IUD are principally responsible for its contraceptive and therapeutic effects. The endometrium suffers the most, becoming atrophic and sluggish with few glands and little mitotic activity. Additionally, it results in a local foreign body reaction that is written off as an increased suppression of endometrial epithelium uniformly because it loses its sensitivity to estradiol produced from the ovaries. This explains why there has been a decrease in menstrual blood loss.[7]

Evaluation of the effectiveness of treatments for HMB has changed from a focus solely on the amount of bleeding to one that includes patient-based outcomes as well, particularly measures of QOL.[8] Patient-based outcome measures are encouraged because they accurately reflect the impact of severe bleeding on women's psychological and physical health.[9] Comparative studies have proven that the levonorgestrel-IUD is superior to other therapies for lowering blood loss in HMB patients.[10]

Little local data is available on the efficacy and acceptability of LNG-IUD among females with HMB as it is relatively a newer modality of treatment and the price of the device is high. However, comparing the total cost of surgery and morbidity associated with surgery might prove this device to be cost-effective too, but this can be a future endeavor for research. For now, the current study aims to determine the efficacy and acceptability of LNG-IUD in females with HMB. This study would enable greater patient counseling, facilitate well-informed decision-making, and lessen the burden of unneeded treatments on patients and the healthcare system. It would also serve to better characterize the relative efficacy of frequently used nonsurgical therapy.

Methods

The study was carried out at the Obstetrics and Gynecology Department of Pak Emirates Military Hospital (PEMH) Rawalpindi, Pakistan for a duration of 6 months from November 2022 to April 2023, after taking approval from the Ethical Review Committee of the hospital on dated: 12th July 2022 vide letter no: A/28/209(2)/EC/4726/2022. The study enrolled 96 females who had heavy menstrual bleeding. The sample size of 96 patients was calculated by keeping a 95% confidence level, a 5% margin of error, taking the expected frequency of heavy menstrual bleeding as 6.7%. Non-probability consecutive sampling technique was used.

Inclusion Criteria: The study included healthy, non-pregnant, nulliparous, and parous women between the ages of 18 and 50 who reported regular, heavy menstrual flow for the majority of their periods while not taking hormonal contraception or a copper IUD and had either normal or simple endometrial hyperplasia on biopsy.

Exclusion Criteria: Women with vaginal bleeding associated with cancer, intermenstrual or postcoital bleeding, coagulopathy, medical conditions such as thyroid disruption, and women who were taking anticoagulant medication and had numerous fibroids with a maximum diameter of 3 cm were excluded from the study.

Heavy menstrual bleeding was clinically defined as blood loss greater than or equal to 80 ml per menstrual cycle (measured in terms of the pads soaked per day or by using a measured menstrual cup). The primary outcome measure assessed was the efficacy and acceptability of LNG-IUD. Efficacy was labeled in terms of treatment success. Treatment success was demarcated as menstrual blood loss during IUD treatment less than 80 mL and more than 50% reduction from baseline during the prior 28-day cycle of treatment (cycle 3 or cycle 6). Acceptability was defined in terms of agreement for continuation of treatment after the study period. The secondary outcome measure assessed was the side effects of the treatment.

All participants who fulfilled the selection criteria were enrolled after taking written informed consent. Only those participants were included in the study

who were buying LNG-IUD for their disease condition already and were willing to participate in the study as well. Participants started a screening phase after giving their informed consent, which included evaluating the amount of menstrual blood they lost (measured in terms of no of pads soaked per day or by using a measured menstrual cup) throughout up to three cycles to diagnose severe monthly bleeding and verify their eligibility. Investigators collected demographic data, including race, as needed for regulatory clearance studies at the initial screening visit. In accordance with the entrance requirements, researchers evaluated individuals' medical histories, including the use of any medication, a urine pregnancy test, and blood tests to rule out hormonal or systemic causes of heavy monthly bleeding. Participants underwent pelvic examination and transvaginal ultrasonography was performed on participants who lacked proof of a recent uterine ultrasound examination with normal results to check for exclusionary findings. After that, participants went through an endometrial biopsy, lest a normal biopsy result had been recorded within the previous six months. Participants were given study-specific menstruation products and a paper diary to track daily vaginal bleeding once all evaluations were finished. During all blood-loss assessments, participants were instructed by study staff to only use the menstrual products that were provided to them. Participants brought a large keg that was provided to them and the materials they had collected during menstruation to each screening visit.

Participants were monitored for up to six 28-day cycles before enrollment (IUD placement) took place whenever the investigator was reasonably convinced the participant was not pregnant. The participant was asked to use a barrier device or refrain from engaging in sexual activity for the first seven days if IUD insertion was placed after the first seven days of menstruation in a participant who was not using permanent contraception. Participants were told not to use menstrual cups after getting an IUD and to keep a daily journal until the end of the follow-up. After the levonorgestrel 52-mg IUD was inserted, regular cycles were not anticipated, thus blood-loss assessments (collection of study-specific menstrual products) were carried out over intervals of 28 days during cycles 3 (days 57-84) and 6 (days 141-168) of IUD use. Following the insertion of the IUD and within five days (up to 21 days) of the conclusion of the menstrual product collection, follow-up appointments were planned for four to six weeks. Investigators examined diaries, collected the kegs containing period products (if any blood loss occurred), and administered new menstrual products, if necessary, at each appointment. They also performed a urine pregnancy test and a pelvic exam to confirm the existence of an IUD. Alkaline hematin testing required blood to be drawn in conjunction with menstrual products during the visits following cycles 3 and 6.

Participants had the option to keep their IUDs or have them removed by a research investigator after the six-cycle treatment period unless doing so was medically contraindicated. To check for any IUD- or IUD removal-related adverse events, all study participants who underwent IUD removal were contacted 7–10 days later.

The data was analyzed through Statistical Package for Social Sciences (SPSS) version 25.0. Quantitative data such as age, BMI, and amount of blood loss was presented as mean and standard deviation. Qualitative data such as parity, efficacy, acceptability, and side effects of the treatment were presented as frequency and percentages. Data for efficacy was stratified concerning age, BMI, and parity, and a post-stratification chi-square test was applied and a *P*-value of ≤0.05 was considered significant. Paired sample t-test was used to compare mean blood loss at baseline and the end of the study period i.e. after treatment for 6 cycles and a *P* value of ≤0.05 was considered as significant.

Result

A total of 96 patients were enrolled. The mean age of the females was 38.08±5.83 years. The mean BMI of the participants was 27.28±3.28 Kg/m^2, the mean blood loss at baseline was 152.72±22.24 ml, and after 6 cycles were 80.26±14.96 and this difference between the mean amount of blood loss at baseline and after 6 menstrual cycles was statistically significant i.e. *P* <0.001. (Table-1).

There were 11 (11.5%) females of age group 20 to 30 years, 54 (56.2%) females of age 31 to 40 years and

Table-1: Mean of Quantitative Variables (n=96)		
Variables	**Mean±Standard deviation**	***P*-value**
Age (in year)	38.08±5.83	-
BMI (in kg/m^2)	27.28±3.28	-
Blood loss at baseline (in ml)	152.72±22.24	< 0.001
Blood loss after 6 cycles (in ml)	80.26±14.96	

31 (32.3%) females of 41 to 50 years. BMI was normal in 31 (32.2%) females, 42 (43.8%) patients were overweight and 23 (24%) females were obese. In terms of parity, 20 (20.8%) were nulliparous and 76 (79.2%) females were parous. Efficacy of treatment was seen in 64 (66.7%) females, and acceptability was seen in 61 (63.5%) females. In terms of side effects, spotting was reported by 17 (17.7%) patients, amenorrhea was reported by 3 (3.1%) patients, oligomenorrhea occurred in 4 (4.2%) patients, weight gain was reported by 6 (6.3%) patients, breast heaviness occurred in 3 (3.1%) patients, 3 (3.1%) females had mood fluctuations and 2 (2.1%) had depression, measured in terms new onset low mood or irritability after starting the use of device. (Table-2).

Table-2: Frequency of Qualitative Variables	
Variables	**Frequency (%)**
Age group	
20 to 30 years	11 (11.5%)
31 to 40 years	54 (56.2%)
41 to 50 years	31 (32.3%)
BMI	
Normal BMI	31 (32.2%)
Overweight	42 (43.8%)
Obese	23 (24%)
Parity	
Nulliparous	20 (20.8%)
Parous	76 (79.2%)
Efficacy of treatment	
Yes	64 (66.7%)
No	32 (33.3%)
Acceptability	
Yes	61 (63.5%)
No	35 (36.5%)
Side effects	
No Side Effects	58 (60.4%)
Spotting	17 (17.7%)
Amenorrhea	3 (3.1%)
Oligomenorrhea	4 (4.2%)
Weight Gain	6 (6.3%)
Breast Heaviness	3 (3.1%)
Mood Fluctuations	3 (3.1%)
Depression	2 (2.1%)

Stratification of efficacy with respect to age, BMI, and parity is shown in Table-3.

Table-3: Stratification of efficacy with respect to age, BMI, and parity (n=96)

Variables	Efficacy		*P*-value
	Yes	No	
Age group			
20 to 30 years	7 (7.3%)	4 (4.2%)	
31 to 40 years	37 (38.5%)	17 (17.7%)	0.908
41 to 50 years	20 (20.8%)	11 (11.5%)	
BMI			
Normal BMI	21 (21.9%)	10 (10.4%)	
Overweight	29 (30.2%)	13 (13.5%)	0.790
Obese	14 (14.6%)	9 (9.4%)	
Parity			
Nulliparous	12 (12.5%)	8 (8.3%)	0.477
Parous	52 (54.2%)	24 (25%)	

Discussion

The current study findings revealed that the LNG-IUD was efficacious in 66.7% of females with HMB and was acceptable to 63.5% of females. While the commonest side effects are spotting (17.7%), weight gain (6.3%), and oligomenorrhea (4.2%). The mean amount of blood loss following treatment was significantly less compared to that calculated at baseline. Treatment was more efficacious in females of age 31 to 40 years, who were parous and had a BMI in the overweight category.

HMB is common among women of all ages, however, it is more prevalent among women over the age of 40.[11,12] This is mostly explained by the higher frequency of uterine pathology during the perimenopausal years, such as fibroids and polyps.[13] The LNG-IUD offers potential therapeutic advantages in different clinical settings, such as menorrhagia symptomatic fibroids, etc., and this is a well-known and documented fact.[14] But initially, it frequently causes menstruation irregularities, which may prevent clinicians from using it.[15]

Our study results showed that LNG-IUD had a higher efficacy and acceptability among patients with HMB. Tariq et al. revealed that among females with HMB, LNG-IUD was found to be effective in 50.9% of females.[16] A study by Creinin et al. revealed that LNG-IUD was successful in 81.8% of females with HMB in terms of reducing the amount of blood and was found to have good acceptability among all study participants.[17] Habib et al. revealed that LNG-IUD was efficacious in 88.1% of females with HMB and was not acceptable to 7% of females because of side effects.[18] Kriplani et al. revealed LNG-IUD to be efficacious in 77.7%.[19] These findings support our study findings that LNG-IUD is highly effective and acceptable among females with HMB.

In terms of side effects, Creinin et al. revealed that the commonest side effect was cramping or bleeding in 5.7% followed by expulsion in 4.8%.[17] Tariq et al. revealed that the commonest side effect experienced by females who had LNG-IUD was spotting in 42%, followed by oligomenorrhea in 19% and amenorrhea in 10%.[16] Habib et al. revealed that the commonly reported side effects were spotting in 25%, amenorrhea in 6%, oligomenorrhea in 42%, weight gain in 14%, breast pain, and heaviness in 7%, mood changes not including depression in 7% and depression in 7%.[18] These study findings support our study findings that spotting is the commonest side effect experienced by females using LNG-IUD followed by menstrual disturbances and weight gain.

In the context of the Pakistani population's high prevalence of HMB and illiteracy, there is a need for education on simple, efficient medical treatments like LNG-IUD which is efficacious, safe, and can be placed in an outdoor setting as an outdoor procedure. Although, the cost of the device is high as compared to morbidity, hospital stay, and cost of surgery it will seem a cost-effective option as well.

There were certain limitations of the study. The results of this study cannot be generalized because it was a single-center study with a small sample size.

Secondly, the long-term complications were not assessed in the patients i.e. beyond 6 cycles of menstruation. Lastly, a comparison with other available options was not done, therefore, the superior efficacy of LNG-IUD over other available options cannot be commented on.

Conclusion

The current study concluded that for treating females with HMB, LNG-IUD was efficacious in 66.7% of females and acceptable in 63.5% of females, and was associated with a lower rate of side effects. The efficacy of treatment was unaffected by age, BMI, and parity status. Our study findings propose the use of LNG-IUD in females with HMB to increase patient satisfaction and reduce further morbidity. Future studies must be carried out on a larger sample to validate the findings of the current study.

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Conflict of Interest: The authors declare no conflict of interest

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Authors Contribution

RK: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing and proofreading

FSK: Idea conception, study designing, data analysis, results and interpretation, manuscript writing and proofreading

TY: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing and proofreading

RK: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing and proofreading

FM: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing and proofreading

MM: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing and proofreading