

A prospective study on efficacy of levonorgestrel intrauterine system in abnormal uterine bleeding of perimenopausal age group at tertiary care centre

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Abstract

Background: In women with heavy menstrual bleeding who presented to primary care providers, the LNG-IUS was more effective than usual medical treatment in reducing the effect of heavy menstrual bleeding on quality of life. **Aim:** This study was conducted to evaluate the efficacy, acceptability and side effects of LNG-IUS in perimenopausal women with abnormal uterine bleeding. **Methodology:** 50 women with benign cause of abnormal uterine bleeding in perimenopausal age group were selected from 1st December 2017 to 15th October 2018 and followed till 15th October 2019 at Government maternity hospital, Osmania medical college, Hyderabad which is a tertiary care centre. The hospital health board ethics committee approved the trial protocol. Potential recruits were drawn from outpatient department of this hospital. **Results:** Objectively measured menstrual blood loss assessed by PBAC score was significantly reduced after the treatment compared with pre-treatment scores. At 1 month PBAC scores were slightly variable from pre treatment with significance level of p value <0.05. At 3, 6, and 12 months, PBAC scores were significantly lower in women treated with the LNG-IUS (p value <0.001). By the end of 3 months percentage of patients with dysmenorrhea had fallen from 60% pre treatment to 25%, and to 13% by 6 months and 4.5% by 12 months showing a significant improvement in dysmenorrhea. There was irregular spotting in patients after insertion of LNG-IUS because of endometrial atrophy and decreased estrogen support. Initially at 3 months it was 43.7%, gradually fallen to 28.8% by 6 months and 13.6% by 12 months. By 3 months and 12 months post-treatment, there was a significant reduction in the number of days of heavy bleeding (p value <0.001) compared with pre-treatment. Treatment failures were assessed at 1, 3, 6 and 12 months. There are 5 treatment failures included the following: by 15 days, one LNG-IUS had been removed due to pain not relieved with analgesics; by 3 months there was one expulsion of LNG-IUS; by 6 months there are 3 treatment failures, one woman had expulsion of LNG-IUS, 2 women had removed LNG-IUS due to persisting menorrhagia and unscheduled bleeding, by 12 months there were no treatment failures. Quality of life was assessed using the SF-36 at pre treatment and 12 months post insertion. The results suggest that there was a significant increase in quality of life from pre treatment to 12 months post insertion of LNG-IUS with p value <0.001. **Conclusion:** LNG-IUS can be choice of treatment for entire reproductive years and it also helps in smooth transition to menopause. So, hysterectomy should be avoided for inappropriate reasons and femininity must be preserved.

Keywords: LNG-IUS, Menorrhagia, Hysterectomy, Menopause, Menstrual blood.

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Introduction

Heavy menstrual bleeding is defined as prolonged (>7 days) or excessive menstrual blood loss greater than or equal to 80 ml per menstrual cycle. It interferes with women's physical, mental and emotional quality of life and is a frequent problem that affects many perimenopausal women worldwide and is the most important reason for their visit to the outpatient department of gynaecology[1,2]. One in 20 women between 30 to 49 years of age consult with heavy menstrual bleeding. Hormonal treatment with the oral contraceptive pill or the levonorgestrel releasing intra uterine system (LNG-IUS) or non-hormonal treatment with tranexamic acid or non-steroidal anti-inflammatory drugs (NSAID) are advised as treatments of first choice. Nevertheless 77% of the women are not willing to continue their treatment and often end up undergoing other treatment or even surgery[3,4]

Hysterectomy is a definitive solution for the treatment of heavy menstrual bleeding[5], and should be considered the preferred strategy for the treatment of heavy menstrual bleeding based on cost-effectiveness[6]. It is a major surgical procedure and has significant physical complications and social and economic costs[7].

A significant number of women with heavy menstrual bleeding who seek treatment did not benefit from, or did not wish to continue the medical treatment and are keen to preserve their uterus[3,8]. Many women opt for a less invasive treatment even when they are informed of the fact that success is not always assured[9].

LNG-IUS device has also been found to be cost-effective with less side effects and to increase the quality of life (QOL). The QOL of women treated with the LNG-IUS is markedly improved, causing high levels of patient satisfaction. Hence, this study was conducted to evaluate the efficacy, acceptability and side effects of LNG-IUS in perimenopausal women with abnormal uterine bleeding.

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Aims and objectives

The main objectives of the study are

1. Reduction in menstrual blood loss
2. Improvement in quality of life
3. Patient's satisfaction

among perimenopausal women treated with LNG- IUS for AUB with heavy menstrual bleeding.

Materials and methods

50 women with benign cause of abnormal uterine bleeding in perimenopausal age group were selected from 1st December 2017 to 15th October 2018 and followed till 15th October 2019 at Government maternity hospital , Osmania medical college, Hyderabad which is a tertiary care centre . The hospital health board ethics committee approved the trial protocol. Potential recruits were drawn from outpatient department of this hospital.

Inclusion criteria

Women in perimenopausal age group with Benign causes of menorrhagia like

- ❖ Ovulatory dysfunction / endometrial causes
- ❖ Fibroids less than 3cms size
- ❖ Adenomyosis
- ❖ Idiopathic menorrhagia

Exclusion criteria

- ❖ Ultrasound abnormalities (submucosal fibroids, intramural fibroids greater than 3 cm in diameter, endometrial polyps).
- ❖ Active genital tract infection.
- ❖ Uterine anomalies.

Results and observations

- ❖ Scarred uterus.
- ❖ Laboratory abnormalities (thyroid -stimulating hormone level [TSH] elevated).
- ❖ Adverse endometrial histology.
- ❖ Untreated abnormal cervical cytology.
- ❖ Coagulopathies.

All the women will undergo complete history taking, physical examination and investigations like complete blood picture, blood grouping typing, HIV , HbsAg, serum creatinine, serum urea, serum bilirubin, blood sugar levels, bleeding time clotting time, BMI, pap smear, ultrasonography of abdomen and pelvis, and histopathology of endometrial biopsy.

Patients were counselled regarding altered bleeding pattern and amenorrhea with LNG-IUS, possible side effects and after taking their informed consent, LNG-IUS is inserted in post menstrual phase. Post insertion, patients will be asked to maintain a PBAC (Pictorial Blood loss Assessment Chart). Patients were followed after 1 month, 3 months, 6 months and 1 year post insertion, their menstrual pattern, menstrual symptoms, quality of life (QOL) ¹⁰ as measured by Short Form-36 (SF-36) and side effects were studied and assessed. Women had direct access to the research doctor throughout the study, and if necessary, alternative management options were discussed, selected and arranged. A treatment failure for the LNG-IUS, was confirmed expulsion, completed removal or the initiation of alternative therapy.

Table 1: Age wise Distribution of Patients

AGE CATEGORY			
	Frequency	Present study	Singh et al ¹⁵
<39 years	22	44%	53%
40-44 years	22	44%	34%
45-49 years	6	12%	13%
Total	50	100%	100%

Age Wise Distribution of Patients

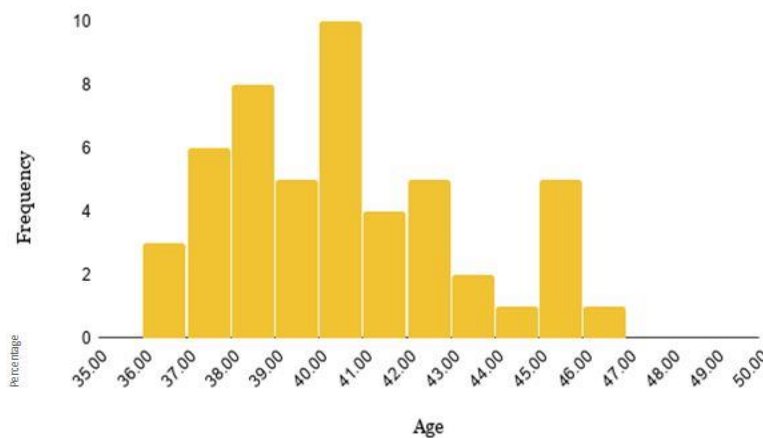


Fig 1: Histogram showing age wise distribution of patients (88% of patients are in between 36 and 44 yrs of age)

Table 2 : BMI wise Distribution of Patients

BMI CATEGORY		
	Frequency	Percentage
<= 24.9	14	28%
25 – 29.9	32	64%
30-35	4	8%
Total	50	100%

64% of the patients are having BMI in the range of 25- 29.9.

Table 3 : No. of Days Bleeding wise Distribution (Pre-Treatment)

DAYS OF BLEEDING			
Days	Frequency	Present study	Dash et al
<= 7 days	17	34%	59%
8-10 days	25	50%	30%
>= 11 days	8	16%	11%
Total	50	100%	100%

50% of the patients bleed for 8 to 10 days per menstrual cycle

Table 4: Table Showing Histopathology of Endometrium

ENDOMETRIAL HISTOPATHOLOGY			
	Frequency	Present study	Jayanthi et al
Proliferative Endometrium	29	58%	60%
Secretory Phase	11	22%	25.7%
Simple Hyperplasia	6	12%	2.8%
Disordered	4	8%	
Total	50	100%	

58% patients have proliferative endometrium on endometrial histopathology.

Table 5: Etiology wise Distribution of patients

Etiology	Frequency	Present study	Singh et al ¹⁵
Ovulatory/Endometrial dysfunction	40	80%	76.2%
Adenomyosis	6	12%	9.5%
Leiomyoma	4	8%	14.3%
Total	50	100%	100%

80% of patients have ovulatory/endometrial dysfunction.

Table6: Distribution of Patients based on Endometrial Thickness (Pre-Treatment)

ENDOMETRIAL THICKNESS		
	Frequency	Percentage
<= 10 mm	28	56%
11 – 15 mm	13	26%
16 – 20 mm	6	12%
> 20 mm	3	6%
Total	50	100%

56% of the patients have endometrial thickness <=10mm

Table 7: Hemoglobin Levels at Pre-treatment and 12 months Post-treatment

Hemoglobin %	Mean	StandardDeviation	t	p
Pre-Treatment	9.1	1.1054	8.3	< 0.001
At 12 Months	10.9	0.6950		

There is significant (p<0.001) improvement in haemoglobin levels at 12 months after insertion compared to before treatment.

Table 8: Table Showing no. of Women with Amenorrhea at 1 month , 3 months,6 months and 12 months of Treatment

AMENORRHEA			
	Frequency	Present study	Singh et al ¹⁵
At 1 month	0	0%	0%
At 3 months	1	2%	0%
At 6 months	6	13%	14%
At 12 months	27	61%	81.5%

61% women among cases had amenorrhea by 12 months after insertion of LNG-IUS

Table 9: Treatment failure at 1 month, 3 months, 6 months and 12 months of Treatment

TREATMENT FAILURE		
	Frequency	Percentage
At 1 month	1	20%
At 3 months	1	20%
At 6 months	3	60%
At 12 months	0	0%
Total	5	100%

60% treatment failure are at 6 months after treatment.

Table 10 : Table showing dysmenorrhea at 3 months , 6monthsand 12 months of Treatment

DYSMENORRHEA		
	Frequency	Percentage
Pre-Treatment (N =50)	30	60%
At 3 months (N = 48)	12	25%
At 6 months (N = 45)	6	13%
At 12 months (N =44)	2	4.5%

There is signification fall in no. of patients with dysmenorrhea by the end of 12th month of insertion

Table 11 :Irregular Spotting

	Frequency	Percentage
At 3 Months (N = 48)	21	43.7%
At 6 Months (N = 45)	13	28.8%
At 12 Months (N =44)	6	13.6%

Irregular spotting was decreased significantly to 15 % at 12 months from 52% at 3 months.

Table 12 : Menstrual Symptoms, PBAC Score, QOL (SF 36) atPre-treatment ,1month;Pre-Treatment, 3 months Pre-Treatment, 6 Months ;Pre-Treatment, 12 months

		N	Mean	Standard Deviation	T	P
No. of days of Heavy Bleeding	Pre-Treatment	48	4.33	1.22	-8.42	< 0.001
	At 3 Months	48	2.1	1.37		
	Pre-Treatment	44	4.27	2	-14	< 0.001
	At 12 Months	44	0.02	0.15		
PBAC	Pre-Treatment	49	427.57	86.6	-3.35	< 0.05
	At 1 Month	49	370	83.43		
	Pre-Treatment	48	428.68	87.1	-18.4	< 0.001
	At 3 Months	48	132.06	69.3		
	Pre-Treatment	45	420.95	78.48	-29.7	< 0.001
	At 6 Months	45	52.73	27.37		
	Pre - Treatment	44	422.75	78.45	-34.6	<0.001
At 12 Months	44	8.27	12.04			
QOL	Pre-Treatment	44	60.5	8.5	14.5	< 0.001
	At 12 Months	44	84.4	6.86		

No. of days of heavy bleeding, PBAC scores and QOL values shows P value less than <0.001 showing significant change in them.

Discussion

Between 1stDecember 2018 till 15th October 2019, patients were screened. Among them 50 patients who were diagnosed to have AUB selected after exclusion criteria and are willing for LNG-IUS treatment and further followed up till one year.

Objectively measured menstrual blood loss assessed by PBAC score was significantly reduced after the treatment compared with pre-treatment scores. At 1 month PBAC scores were slightly variable from pre treatment with significance level of p value <0.05. At 3, 6, and 12 months, PBAC scores were significantly lower in women treated with the LNG-IUS (p value <0.001).

By the end of 3 months percentage of patients with dysmenorrhea had fallen from 60 % pre treatment to 25%, and to 13 % by 6 months and 4.5% by 12 months showing a significant improvement in dysmenorrhea.

There was irregular spotting in patients after insertion of LNG -IUS because of endometrial atrophy and decreased estrogen support. Initially at 3 months it was 43.7%, gradually fallen to 28.8% by 6 months and 13.6% by 12 months.

By 3 months and 12 months post-treatment, there was a significant reduction in the number of days of heavy bleeding (p value <0.001) compared with pre- treatment.

Treatment failures were assessed at 1, 3, 6 and 12 months. There are 5 treatment failures included the following: by 15 days , one LNG-IUS had been removed due to pain not relieved with analgesics; by 3 months there was one expulsion of LNG-IUS ; by 6 months there are 3 treatment failures , one woman had expulsion of LNG-IUS , 2 women had removed LNG-IUS due to persisting menorrhagia and unscheduled bleeding, by 12 months there were no treatment failures.

Of the 5 treatment failures 3 had underwent hysterectomy, 1 was placed on cyclic progesterone therapy and another one on estrogen progesterone pills. One patient had lost follow up after 6 months.

1 patient had amenorrhea by 3rd month, 5 other patients had complete amenorrhea by 6 months of treatment and 21 other patients had amenorrhea by 12 months of treatment; corresponds to 2% of total cases by 3 months, 13% of total cases by 6 months and 61 % of total cases by 12 months.

The results showed significant improvement of anemia i.e., increase in the hemoglobin values from pre treatment and by 12 months significant P value < 0.001

Quality of life was assessed using the SF-36 at pre treatment and 12 months post insertion. The results suggest that there was a significant increase in quality of life from pre treatment to 12 months post insertion of LNG-IUS with p value < 0.001.

There were no serious complications treatment group. This was probably because the treatment was done under strict aseptic precautions and by trained personnel.

There were no cases of uterine perforation, lost threads and post insertion abnormal vaginal discharge and none of them had side effects of progesterone like acne, weight gain, breast tenderness.

The Cochrane data base suggested that the levonorgestrel releasing intrauterine system results in a significant reduction in baseline menstrual blood loss in heavy menstrual bleeding. According to the ACOG the LNG-IUS appears to reduce menstrual blood loss significantly in women with HMB.

Surgery especially hysterectomy while remaining a definitive cure, has significant risk factors. Anatomical, urological, sexual, psychological, emotional sequelae and cost factors are definite drawbacks.

In a study, Garg et al [11], has shown results of 93.3% of patients had significant decrease in blood loss and 76.6% had a significant decrease in pain analysed on visual analog scale and there was significant improvement in symptoms along with significant decrease in cost with LNG-IUS insertion with psychological satisfaction of conserving the uterus. The study described LNG-IUS as a non surgical lifeline for AUB due to its cost effectiveness and psychological and symptomatic relief achieved in woman compared with those who underwent hysterectomy.

Subjectively measured menstrual symptoms included dysmenorrhea irregular spotting, the number of days of heavy bleeding.

The Eclipse trial, a UK – based multicentric RCT, featured the use of LNG-IUS in primary care against standard treatment for menorrhagia. The results were published in 2013 in The New England Journal Medicine (NEJM) and provided strong evidence that QOL improved with LNG-IUS more than with usual medical methods of treatment. The accompanying editorial in NEJM also said that the results demonstrated that the LNG-IUS should be considered first line of therapy for HMB [12].

In the Cochrane database systematic review 2015, comparisons were made with placebo, oral medicine, endometrial destruction techniques and hysterectomy, the findings showed that QOL and reduction in HMB were more with the LNG-IUS. High quality evidence showed that reduction in HMB was not as successful as with hysterectomy George Joy Eralii [13] evaluated the effectiveness of LNG-IUS in treating HMB in a retrospective observational study (2016) of Indian women. The comparison with usual medical treatment methods showed higher satisfaction rates over the course of 2 years with 36% discontinuation rates due to the lack of effectiveness and irregular bleeding. Six percent resorted to hysterectomy in both groups, proving that LNG-IUS remains the first choice in our population, as assessed by the impact of bleeding on the women's QOL.

Pontis et al [14] in a systematic review of medical treatment of adenomyosis published in July 2016 spanning a period of 25 years (1990- 2015) concluded that LNG-IUS is the most promising medical therapy available with a low profile of adverse effects.

Singh et al [15] from Patna, India, in a 2 year prospective study on 42 patients once again proved that LNG-IUS is an acceptable, highly efficient method of reducing menstrual blood loss in women with HMB and a good alternative to hysterectomy.

Dhamangaonkar [16] et al showed 91.4 % improvement in satisfaction rate (QOL), significant decrease in HMB, dysmenorrhea and 7.8 % rise in HB levels

Nayar et al 2017 concluded the LNG-IUS has been used as a substitute for hysterectomy in AUB-PALM ranging from polyp, adenomyosis, endometriosis, endometrial hyperplasia to fibroid uterus as well as in non structural causes of AUB i.e. AUB-COEIN [17]

The largest randomised study to date comparing hysterectomy with LNG-IUS has recently reported 5 years of follow up. Among 119 women randomised to LNG-IUS, 50 (42%) eventually underwent hysterectomy, so LNG-IUS is clearly not a completely effective treatment for menorrhagia. Despite this relatively high proportion of women eventually requesting hysterectomy, satisfaction rates were similar in both groups and the discounted direct and indirect costs associated with the LNG-IUS remained significantly lower than those associated with hysterectomy.

Lockhat et al [18] found significant improvement (P < 0.05) in severity and frequency of pain and menstrual symptoms in 85% of patients. In a study by Garg et al there was a significant reduction in the dysmenorrhea associated with adenomyosis after LNG-IUS insertion and pain reduced further with duration of treatment. 56.6% women had no pain at the end of six months and 76.6% women had no pain at 1 year post LNG-IUS. In present study also all patients with severe dysmenorrhea and adenomyosis were relieved of their symptoms.

In a study by Tariq [19] et al 38% women experienced vaginal spotting at the end of 3 months, however, at the end of one year it reduced to 3.5% and spontaneous expulsion of device was noticed in 8.8% women within 3 months. In present study 43.7% patients had irregular spotting after 3 months which reduced to 13.6% at the end of 12 months. 5% patients had expelled LNG-IUS spontaneously. In present study there was expulsion in 4% of patients.

Conclusion

LNG-IUS is a safe, effective and acceptable mode of treatment of heavy menstrual bleeding in peri menopausal women. It can be a good alternative to hysterectomy for heavy menstrual bleeding due to many benign etiologies. This study has shown that the LNG-IUS results in a significantly lower objectively measured blood loss and over 12 months of follow up, the treatment is associated with high levels of patient satisfaction and quality of life with significant improvement in menstrual symptoms. It is associated with lesser side effects. LNG-IUS can be choice of treatment for entire reproductive years and it also helps in smooth transition to menopause. So, hysterectomy should be avoided for inappropriate reasons and femininity must be preserved.

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