

## To study the efficacy of levonorgestrel intrauterine system in heavy menstrual bleeding

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### Abstract:

**Background:** Abnormal uterine bleeding (AUB) is the commonest symptom for which women seek gynaecologist's consultation. The excessive blood loss interferes with woman's social, emotional, physical and material quality of life. Medical treatment is the preferred primary intervention though hysterectomy or endometrial ablation is the treatment of choice when medical treatment is ineffective or unacceptable. The levonorgestrel releasing intrauterine system (IUS) is a nonsurgical, long acting, alternative to the traditional medical and surgical treatments for heavy menstrual bleeding. **Objectives:** To assess the effectiveness of levonorgestrel IUS in heavy menstrual bleeding in terms of decreased menstruation and blood loss and to follow these patients for at least 2 years. **Methods:** A hospital based prospective, observational study was conducted with 35 patients from September 2019 - February 2021, to study the efficacy of levonorgestrel intra-uterine system (LNG - IUS) in the management of heavy menstrual bleeding. LNG-IUS was inserted in post menstrual phase. Follow up was done at 3, 6, 12, 24 months. At each visit blood loss, menstrual pattern and opinion of women for satisfaction was recorded. **Results:** In first 3 months, 13 patients had irregular heavy bleeding and 11 had irregular spotting. 7 achieved normal menstrual cycle and 2 had scanty menstrual flow. During 6 months follow-up, 4 patients had irregular heavy bleeding and 3 had irregular spotting. 5 achieved normal menstrual cycle and 13 had scanty menstrual flow. 4 patients had achieved amenorrhoea, 9 experienced dysmenorrhoea. During 1 year follow-up, 2 patients had irregular spotting and 3 had scanty menstrual flow. 20 patients had achieved amenorrhoea while 1 experienced dysmenorrhoea. During 2 years follow-up, 1 patient had scanty menstrual flow and 9 patients had achieved amenorrhoea. There was significant reduction in the incidence of irregular heavy bleeding, irregular spotting and dysmenorrhoea and significantly higher number of patients achieved amenorrhoea as per chi-square test ( $p < 0.05$ ). **Conclusion:** LNG-IUS is an effective, long acting nonsurgical treatment for women with heavy menstrual bleeding. It can be a good alternative to hysterectomy for heavy menstrual bleeding due to many benign etiologies.

**Keywords:** LNG-IUS, heavy menstrual bleeding, dysmenorrhea.

Abnormal uterine bleeding (AUB) is the commonest symptom for which women seek gynaecologist's consultation. Heavy menstrual bleeding (HMB) is defined as a menstrual blood loss (MBL) of 80 ml or more in research and clinical settings<sup>1, 2</sup>. The National Institute for Health and Care Excellence in the United Kingdom defined HMB as

excessive blood loss that interferes with woman's social, emotional, physical and material quality of life and this can occur alone or in combination with other symptoms and with menstrual blood loss of <80 mL.<sup>3</sup>

International federation of obstetrics and gynaecology (FIGO) has classified the aetiologies of AUB using PALM-COEIN acronym where PALM describes structural issues, COEI describes non-structural issues and N stands for "Not otherwise classified" -

Structural causes: P – Polyp; A – Adenomyosis; L – Leiomyoma; M – Malignancies.

Non-structural causes: C – Coagulopathy; O – Ovulatory; E – Endometrial; I – Iatrogenic.

The causes of heavy menstrual bleeding (HMB) in reproductive are ovulatory disorders, primary endometrial disorders, fibroid, adenomyosis, endometriosis or genital malignancies.<sup>4</sup> Medical treatment including hormonal or nonhormonal oral medications is the preferred primary intervention though hysterectomy or endometrial ablation is the treatment of choice when medical treatment is ineffective or unacceptable. The ACOG suggested that treatment for each woman depends on suspected etiology of bleeding, clinical stability, overall acuity, desired for future fertility and underlying medical problems.<sup>5</sup> The levonorgestrel releasing intrauterine system is a nonsurgical, long acting, alternative to the traditional medical and surgical treatments for heavy menstrual bleeding.<sup>6</sup> Hence the present study was done at our tertiary care centre to assess the efficacy, patient satisfaction and side effects related to the use of LNG-IUS in heavy menstrual bleeding.

## Materials and methods

A hospital based prospective, observational study was conducted with 35 patients to study the efficacy of Levonorgestrel Intra-uterine system (IUS) in the management of heavy menstrual bleeding from September 2019 to February 2021 in the department of Obstetrics and Gynaecology, Dr DY Patil Medical College, hospital and research Centre, Pune.

### Inclusion criteria

- All the reproductive age group and perimenopausal women who has excessive menstrual blood loss after excluding endometrial carcinoma.
- Dysmenorrhea.
- Dysfunctional uterine bleeding.
- Adenomyosis.
- Small fibroids.

### Exclusion criteria:

- Postmenopausal status.
- Those whose who intend to conceive over the next 5 years.
- Child birth within one year, abortion within three months, and lactating mothers.
- All the reproductive age group women using any drugs affecting menstrual blood loss.
- All women with the history/current clinical evidence/suspicion of malignancy or chronic systemic illness.
- Evidence of sexually transmitted diseases.
- Women with the congenital anomalies of uterus.

The study was done after permission from institutional ethics committee and review board. A valid informed consent was taken in written from patients or patient's attendant. Patients were counselled about other treatment modalities, and the pros and cons of these modalities were discussed. Once patients were enrolled for study, thorough history and physical examination was done as per proforma. Detailed clinical history of illness, clinical examination of the patients and the treatment history was recorded. All patients have undergone pelvic USG, diagnostic hysteroscopy and endometrial curettage for histopathological examination.

Following investigations were noted -

- Complete hemogram with peripheral blood smear, red cell indices
- Urine routine microscopy
- Plasma blood sugar
- HIV
- HBsAg

- VDRL
- Thyroid function tests
- Pelvic ultrasonography

Pap smear and endometrial biopsy were done to rule out malignancy. LNG-IUS was inserted in post menstrual phase. Follow up was done at 3, 6, 12, 24 months. At each visit blood loss, menstrual pattern and opinion of women for satisfaction was recorded.

Statistical analysis: Quantitative data is presented with the help of mean and standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of fisher test, student 't' test and chi-square test. 'P' value less than 0.05 is taken as significant. Results were graphically represented where deemed necessary. Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 will be used for statistical analysis. Graphical representation will be done in MS Excel 2010.

## Results

Majority of the patients (60%) were in the age group of 41-45 years followed by 20% in the age group of 36-40 years, 14.3% in the age group of 21-30 years and 5.7% in the age group of 31-35 years. The mean age of the patients was  $37.86 \pm 7.77$  years (table 1).

<b>Table 1: Distribution of patients according to age</b>		
<b>Age (Years)</b>	<b>N</b>	<b>%</b>
21-30 years	5	14.3%
31-35 years	2	5.7%
36-40 years	7	20%
41-45 years	21	60%
Total	35	100%
Mean $\pm$ SD	$37.86 \pm 7.77$	

The most common etiology of HMB was ovulatory disorders or endometrial dysfunction (48.6%) followed by endometrial hyperplasia (22.9%), adenomyosis (17.1%) and fibroid (11.4%) (table 2).

<b>Table 2: Distribution of patients according to etiology of HMB</b>		
<b>Etiology of HMB</b>	<b>N</b>	<b>%</b>
Ovulatory/endometrial dysfunction	17	48.6%
Fibroid	4	11.4%
Adenomyosis	6	17.1%
Endometrial hyperplasia	8	22.9%
Total	35	100%

In first 3 months, 13 (37.1%) patients had HMB and 11 (31.4%) patients had irregular spotting. 9 (25.8%) patients achieved normal menstrual cycle and 2 (5.7%) patients had scanty menstrual flow. No patients had achieved amenorrhoea while 9 (25.7%) patients experienced dysmenorrhoea. During 6 months follow-up, 4 (13.3%) patients had HMB and 3 (10%) patients had irregular spotting. 6 (20%) patients achieved normal menstrual cycle and 13 (43.4%) patients had scanty menstrual flow. 4 (13.3%) patients had achieved amenorrhoea while 4 (13.3%) patients experienced dysmenorrhoea. During 1 year follow-up, 2 (8.3%) patients had irregular spotting and 3 (12.5%) patients had scanty menstrual flow. 19 (79.2%) patients had achieved amenorrhoea. No patient had HMB, normal menstrual cycle and dysmenorrhoea. During 2 years follow-up, 1 (10%) patient had scanty menstrual flow and 9 (90%) patients had achieved amenorrhoea. No patient had HMB, irregular spotting, normal menstrual cycle and dysmenorrhoea. There was significant reduction in the incidence of irregular heavy bleeding, irregular spotting and dysmenorrhoea and significantly higher number of patients achieved amenorrhoea as per chi-square test ( $p < 0.05$ ).

<b>Table 3: Distribution of patients according to efficacy of LNG - IUS during follow-up period</b>									
Parameters	3 months (n=35)		6 months (n=30)		1 year (n=24)		2 years (n=10)		P Value
	N	%	N	%	N	%	N	%	
Heavy menstrual bleeding	13	37.1%	4	13.3%	0	-	0	-	<0.05
Irregular spotting	11	31.4%	3	10%	2	8.3%	0	-	
Normal menses	9	25.8%	6	16.7%	0	-	0	-	
Scanty menstrual flow	2	5.7%	13	43.4%	3	12.5%	1	10%	
Amenorrhoea	0	-	4	13.3%	19	79.2%	9	90%	
Total	35	100%	30	100%	24	100%	10	100%	
Dysmenorrhoea	9	25.7%	4	13.3%	0	-	0	-	

## Discussion

A hospital based prospective, observational study was conducted with 35 patients to study the efficacy of levonorgestrel intra-uterine system (IUS) in the management of heavy menstrual bleeding. The distribution of age and the etiology of HMB in our study were comparable to the studies of Singh K et al<sup>7</sup>, Dash S et al<sup>8</sup> and Desai RM et al<sup>9</sup>.

The efficacy of levonorgestrel intra-uterine system and the follow up of patients post insertion at 3 months, 6 months, 1 year, 2 years were also comparable to the studies of Singh K et al<sup>7</sup>, Dash S et al<sup>8</sup> and Desai RM et al<sup>9</sup>. Dash S et al<sup>8</sup> observed 78.6% attained desired MBL after 1-month postinsertion. 89.3% attained desired MBL after 3 months of LNG-IUS insertion. While 6-month postinsertion of LNG-IUS insertion, 90% achieved desired MBL. Desai RM et al<sup>9</sup> observed, 3 (7.5%) women had regular cycles, 24 (60%) had spotting, 5 (12.5%) had infrequent cycles with scanty menstruation, 8 (20%) continued to have HMB after 3 months of LNG-IUS insertion. No women had regular cycles, 13 (32.5%) had spotting, 11 (27.5%) had scanty menstruation, 9 (22.5%) had amenorrhoea and three (7.5%) continued to have HMB, 4 (10%) women expelled LNG-IUS after 6 months. Singh K et al<sup>7</sup> observed, 21% patients achieved normal menstrual cycle in first 3 months, 44.44% had scanty menstrual flow at 6 months. There was significant reduction in pain and bleeding in cases of severe dysmenorrhea, endometriosis and chronic pelvic pain after 6 months. The frequent complaint was irregular heavy bleeding in 37.5% in initial 3 months, at 6 months it reduced to 13.89% and at 1 year follow up it was 0%. The second most complaint was irregular spotting in 32.5% in initial 3 months that persisted at 1 year follow up in 7.4%. There was spontaneous expulsion of device in first 3 menstrual cycles in 4.7% patients. There was continuous irregular heavy bleeding in 2 patients who requested for removal of the device and opted for hysterectomy.

Dash S et al<sup>8</sup> prospective observational study reported 92% of the cases achieved desired MBL at 1-year postinsertion of LNG-IUS. Although spotting, inter menstrual bleeding per vagina were problem initially for few, after 1 year of insertion none of them were having these problems. Oligomenorrhea/ amenorrhea was present in 19 cases at 1 year. Desai RM et al<sup>9</sup> showed at 12 months of insertion of LNG-IUS, none had regular cycles, 13 (32.5%) had spotting, 11 (27.5%) had infrequent cycles with scanty menstruation, 9 (22.5%) had amenorrhoea. 4 (10%) expelled LNG-IUS in 6 months of insertion, 2 LNG-IUS were removed due to persistent HMB and one removed due to misplacement in cervical canal. Singh K et al<sup>7</sup> observed after 1 year of use 81.5% achieved amenorrhoea whereas 11.1% had regular scanty bleeding. All the patients with severe dysmenorrhea and endometriosis were relieved of their symptoms. Irregular spotting was found in 32.5% women after 3 months which decreased to 7.4% by the end of one year and within 3 months 5% women expelled device. Another 5.5% women had requested to remove the device because of heavy bleeding even after three months.

The levonorgestrel intrauterine system which was initially introduced as IUCD has been used recently for treatment of HMB. Delivery of intrauterine progestin is effective way to give local treatment and skip systemic side effects. It is now emerged as an alternative method to treat AUB<sup>10</sup>. According to the ACOG (American College of Obstetricians and Gynaecologists), the LNG-IUS appears to reduce menstrual blood loss significantly in women with HMB. The actions of levonorgestrel on cervix and endometrium make LNG-IUS effective contraceptive and minimally invasive long-term treatment option for menorrhagia<sup>11</sup>.

Lockhat FB et al<sup>12</sup> study on efficacy, side-effects and continuation rates in women with symptomatic endometriosis undergoing treatment with an intra-uterine administered progestogen (levonorgestrel) found significant improvement in severity and frequency of pain and menstrual symptoms in 85% of patients. Kriplani A et al<sup>13</sup> study on efficacy, acceptability and side effects of the levonorgestrel intrauterine system reported HMB was cured in 77.7% patients at 3 months and in all patients were cured at 36 months and the common side effect is menstrual spotting for a few months after insertion. Yazbeck C et al<sup>14</sup> in a multicenter study on levonorgestrel-releasing intrauterine system in the treatment of dysfunctional uterine bleeding observed 86.1% women with dysfunctional uterine bleeding were very satisfied with the treatment with LNG-IUS as an alternative to hysterectomy. Bofill Rodriguez M et al<sup>15</sup> in a cochrane database determined the effectiveness, acceptability and safety of progestogen-releasing intrauterine devices in reducing HMB reported LNG-IUS results in huge reduction in blood loss during menstruation from baseline in women with HMB compared to other medical treatment. It results in better quality of life, higher satisfaction with treatment and lower withdrawal from treatment at 2 years.

Health quality ontario systematic review<sup>16</sup> comparing LNG-IUS with usual medical therapy in HMB reported LNG-IUS improved quality of life and reduced menstrual blood loss better than usual medical therapy. There was no evidence of a significant difference in these outcomes compared with the improvements offered by endometrial ablation or hysterectomy. Mild hormonal side effects were the most commonly reported. Garg S et al<sup>17</sup> study on non-surgical lifeline for abnormal uterine bleeding reported patients with adenomyosis who had dysmenorrhea had significant reduction in pain post LNG-IUS insertion. By the end of 6 months 56.6% women had no pain and by the end of one year 76.6% women had no pain.

## Conclusion

LNG-IUS is a safe, effective and acceptable mode of treatment of heavy menstrual bleeding. It can be a good alternative to hysterectomy for heavy menstrual bleeding due to many benign etiologies. It is associated with lesser side effects and LNG-IUS can be choice of treatment for entire reproductive years. It also helps in smooth transition to menopause. There was a significant decrease in the number of bleeding days and decrease continued with increasing duration of treatment. LNG-IUS is a better option for women requiring treatment for HMB. LNG-IUS is an effective, long acting nonsurgical treatment for women with HMB.

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