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Original Research Article

Comparative Efficacy of Levonorgestrel-Releasing Intrauterine System versus Oral Norethisterone in the Management of Idiopathic Menorrhagia: A Prospective Comparative Study

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Abstract

Background: Idiopathic menorrhagia is a prevalent gynecological condition characterized by excessive menstrual blood loss without regular structural or organic pelvic pathology. It severely disrupts systemic quality of life and leads to progressive iron deficiency anemia. Levonorgestrel-releasing intrauterine system (LNG-IUS) and oral cyclical norethisterone represent two distinct standard medical approaches requiring structured comparative verification.

Objective: To evaluate and compare the therapeutic efficacy, safety parameters, and overall patient acceptability of LNG-IUS versus oral norethisterone in women suffering from idiopathic menorrhagia.

Materials and Methods: This prospective comparative study spanned an 18-month duration at the Department of Obstetrics and Gynecology, RIMS, Ranchi. Sixty-four reproductive-age females diagnosed with idiopathic menorrhagia were recruited based on explicit criteria and assigned to two equal intervention groups (n=32 per arm). Group A received the intrauterine insertion of an LNG-IUS (Mirena, 52 mg), while Group B was treated with oral Norethisterone tablets (5 mg three times daily from Day 1 to Day 21 of each cycle) for 6 sequential cycles. Serial clinical follow-ups were carried out at 1, 3, and 6 months. Primary outcomes included change in menstrual blood loss quantified via the Pictorial Blood Assessment Chart (PBAC) scores and hemoglobin (Hb) levels. Secondary indices included transvaginal ultrasound assessment of endometrial thickness, intervention failure rates necessitating hysterectomy, and absolute patient satisfaction scores.

Results: Baseline parameters were homogenous across both cohorts. Pre-treatment mean PBAC scores were statistically similar (LNG-IUS: 470.34±51.00 vs Norethisterone: 478.59±55.93, p=0.540). At the 6-month review, the LNG-IUS cohort exhibited an extensive decline in mean PBAC scores to 54.13±11.42, which was significantly lower than the 139.09±110.76 recorded in the norethisterone group (p<0.001).

Conclusion: The levonorgestrel-releasing intrauterine system offers superior clinical efficacy over oral cyclical norethisterone, providing profound management of menstrual blood loss, higher correction of chronic anemia, minimization of subsequent major hysterectomies, and excellent overall patient satisfaction.

Keywords: Idiopathic Menorrhagia, Heavy Menstrual Bleeding, Levonorgestrel Intrauterine System, Norethisterone, PBAC, Hemoglobin, Hysterectomy.

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Introduction

Menorrhagia, modernly defined as Heavy Menstrual Bleeding (HMB), represents an objective menstrual blood volume loss exceeding 80 mL per cycle or menstrual bleeding extending beyond seven consecutive days. It stands as one of the most widespread complaints encountered within contemporary gynecological practices, accounting for roughly one-third of reproductive-age presentations in hospital outpatient settings. When heavy bleeding occurs on a regular cyclic basis without any evidence of localized structural pelvic abnormalities, systemic coagulation pathway errors, or obvious endocrine disorders, it is classified as idiopathic menorrhagia, indicating a localized endometrial dysfunction under the FIGO PALM COEIN classification infrastructure. The operational burden of idiopathic menorrhagia on female health is immense, manifesting as persistent physical exhaustion, iron deficiency anemia, psychological distress, and marked disruptions in normal social and professional activities. The underlying pathophysiological process often

involves an up regulation of localized endometrial fibrinolytic pathways and imbalances in vascular prostaglandin concentrations. Traditional management relies on various non-surgical pharmaceutical choices, including antifibrinolytic agents, non-steroidal anti-inflammatory drugs (NSAIDs), combined oral contraceptives, and oral progestogens. Norethisterone, a classic synthetic oral progestin, is widely prescribed to medically stabilize hyperplastic endometrium; however, its clinical efficacy is frequently limited by systemic adverse reactions (e.g., fluid retention, headaches, nausea) and sub-optimal long-term patient compliance linked with mandatory daily pill ingestion.

The development of the Levonorgestrel-Releasing Intrauterine System (LNG-IUS) represents a key advancement in uterus-preserving gynaecological therapies. It consists of a flexible T-shaped plastic frame carrying a reservoir that releases a continuous low dose of levonorgestrel (~20 μg per day) directly into the endometrial cavity. This localized delivery pattern maintains exceptionally low systemic drug exposure while generating strong, stable mucosal decidualization and subsequent glandular atrophy. This prospective study was explicitly designed to evaluate and directly compare the long-term clinical performance, hematological status, endometrial adjustments, and consumer acceptability of the LNG-IUS against the standard oral cyclical norethisterone regimen in an active institutional cohort.

Aims and Objectives

Aim of the Study: To compare the clinical efficacy, safety profiles, and patient acceptability of the levonorgestrel-releasing intrauterine system (LNG-IUS) versus the oral norethisterone regimen in women diagnosed with idiopathic menorrhagia

Primary Objective: To measure and analyze the longitudinal reduction in excessive menstrual blood loss using the Pictorial Blood Assessment Chart (PBAC) index after the administration of LNG-IUS versus oral cyclical norethisterone.

Secondary Objectives:

- To measure post-treatment changes in systemic hemoglobin (Hb) values and ultrasound-derived endometrial thickness across both groups.
- To calculate the absolute rate of surgical treatment failures requiring definitive abdominal hysterectomy.
- To evaluate patient satisfaction levels via a standardized follow-up review framework.

Materials and Methods

Study Design: A prospective, open-label, comparative clinical study.

Study Duration: Conducted over an active clinical span of 18 months.

Study Centre: Department of Obstetrics and Gynecology, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India.

Study Population: Reproductive-age women presenting with verified symptoms of heavy menstrual bleeding without structural organic pelvic pathology.

Sample Size: A final active sample size of 64 patients was maintained, partitioned equally into two comparative intervention arms of 32 subjects each.

Sample Size Formula: The calculation was executed based on the power-bound comparative equation:

$$N = \frac{2 \times [Z(1-\alpha/2) + Z(1-\beta)]2 \times [P1(1-P1) + P2(1-P2)]}{(P1 - P2)2}$$

Where confidence interval coefficient $Z(1-\alpha/2) = 1.96$ (allowable alpha error $\alpha=5\%$), study power factor $Z(1-\beta) = 0.80$ (power=80%), and expected treatment response proportions $P1 = 0.90$ (LNG-IUS) and $P2 = 0.55$ (Norethisterone). This yielded $N = 32$ per group.

Inclusion Criteria:

1. Pelvic ultrasound confirming a structurally normal or symmetrically enlarged uterus up to a 6-week gestational size due to uniform adenomyosis.
2. Patient within active reproductive age.
3. Normal cervical cytological Pap smear screening.
4. Expressed willingness to stick to follow-up timelines.

Exclusion Criteria:

1. Active Pelvic Inflammatory Disease (PID) or lower tract reproductive infection.
2. Established coagulation pathway defects or bleeding disorders.
3. Uncorrected clinical hypothyroidism or hyperthyroidism.
4. Identifiable structural organic causes of bleeding (e.g., submucosal leiomyoma, endometrial polyps, atypical neoplastic hyperplasia).
5. Known absolute hypersensitivity to progestogen therapies.

Intervention Plan: Enrolled patients were assigned to two arms. Group A (n=32) underwent intrauterine insertion of the LNG-IUS (Mirena

system) at the end of their menstrual phase. Group B (n=32) was initiated on oral synthetic Norethisterone tablets at a dosage of 5 mg three times daily administered in a cyclical fashion from Day 1 through Day 21 of each cycle for 6 consecutive cycles. Baseline evaluations included full blood counts, metabolic panels, pictorial charting parameters, and initial sonographic tracking. Serial follow-up reviews were executed at 1 month, 3 months, and 6 months intervals.

Data Analysis: Collected data were processed via Microsoft Excel and exported into SPSS Software version 25. Qualitative elements were presented using counts and percentages, evaluated with the Chi-Square test. Continuous variables were expressed as Mean ± Standard Deviation (SD), evaluated using independent t-tests for inter-group indices and paired t-tests for continuous internal adjustments. P values less than 0.05 were acknowledged as statistically significant.

Results

A total of 64 participants successfully completed the study protocol. Baseline demographic and clinical parameters across both intervention bands were well-balanced, providing a clear basis for objective treatment tracking.

Table 1: Baseline Demographic Characteristics of Study Participant

Demographic Variable	LNG-IUS Group (n=32)	Norethisterone Group (n=32)	Statistical p-value
Mean Age (years ± SD)	39.34 ± 4.06	36.78 ± 2.18	0.003 (Significant)
Rural Residence [n (%)]	6 (18.75%)	8 (25.00%)	0.762 (Non-Significant)
Urban Residence [n (%)]	26 (81.25%)	24 (75.00%)	0.762 (Non-Significant)
Occupational Status: Homemakers [n (%)]	30 (93.75%)	31 (96.88%)	0.554 (Non-Significant)
Multiparity (≥2 births) [n (%)]	30 (93.75%)	31 (96.88%)	0.681 (Non-Significant)

Discussion of Table 1: Table 1 displays the demographic characteristics of the two treatment groups. The mean age in the LNG-IUS group was higher (39.34±4.06 years) than the Norethisterone cohort (36.78±2.18 years, p=0.003). For place of residence, the Chi-square analysis of the categorical residence variable yielded a uniform p-value of 0.762 for both rural and urban rows, demonstrating no significant environmental imbalance.

Substantive similarity was also observed in occupational configuration (p=0.554) and parity distribution (p=0.681), with over 93% being multiparous homemakers.

Table 2: Baseline Clinical Parameters and Primary Symptoms

Clinical Variable	LNG-IUS Group (n=32)	Norethisterone Group (n=32)	Statistical p-value
Heavy Menstrual Bleeding alone [n (%)]	13 (40.63%)	17 (53.13%)	0.604 (Non-Significant)
Prolonged Menstrual Bleeding alone [n (%)]	4 (12.50%)	3 (9.38%)	
Combined Heavy & Prolonged Flow [n (%)]	15 (46.88%)	12 (37.50%)	
Associated Lower Abdominal Pain: Yes [n (%)]	8 (25.00%)	5 (15.63%)	0.534 (Non-Significant)
Uterus normal size on ultrasound [n (%)]	18 (56.25%)	16 (50.00%)	0.719 (Non-Significant)
Uterus 6-week gestational size [n (%)]	14 (43.75%)	16 (50.00%)	
Pre-Treatment Blood Transfusion required [n (%)]	3 (9.38%)	6 (18.75%)	0.472 (Non-Significant)

Discussion of Table 2: Table 2 outlines the primary baseline clinical symptoms and sonographic findings.

The groups were highly balanced with respect to chief complaints (p=0.604), history of pelvic cramping pain (p=0.534), and ultrasound-documented uterine dimension distribution (p=0.719). Baseline severe anemia requiring corrective pre-treatment blood transfusion was present in 9.38% of the Mirena cohort and 18.75% of the Norethisterone cohort, which was not statistically divergent (p=0.472).

Table 3: Comparison of Mean Endometrial Thickness (mm) Before and After Treatment

Endometrial Thickness Timeline	LNG-IUS Group (Mean ± SD)	Norethisterone Group (Mean ± SD)	Inter-Group p-value#
Pre-Treatment Endometrial Size (mm)	8.33 ± 2.03	8.64 ± 1.95	0.528 (Non-Significant)
Post-Treatment Endometrial Size (mm)	5.12 ± 0.94	7.17 ± 1.69	<0.001 (Highly Significant)
Intra-Group Comparison p-value*	**<0.001**	**<0.001**	—

Discussion of Table 3: Table 3 displays changes in mucosal lining thickness measured via ultrasound. Before initiation, there was no notable difference between the groups (8.33 mm vs 8.64 mm, p=0.528). Post-treatment analysis revealed that while both modalities achieved a significant reduction (p<0.001 via paired t-tests*), the

localized delivery of levonorgestrel produced a significantly more profound thinning effect (5.12±0.94 mm) than oral norethisterone (7.17±1.69 mm, inter-group p<0.001#).

Table 4: Comparison of Mean Hemoglobin (Hb) Levels (g/dL) at Different Intervals

Evaluation Interval	LNG-IUS Group (Mean ± SD)	Norethisterone Group (Mean ± SD)	Statistical p-value
Pre-Treatment Baseline Hb	8.47 ± 0.88	7.95 ± 0.82	0.018 (Significant)
Follow-up at 1 Month	9.09 ± 0.74	8.36 ± 0.61	<0.001 (Highly Significant)
Follow-up at 3 Months	9.60 ± 0.86	8.60 ± 0.56	<0.001 (Highly Significant)
Follow-up at 6 Months	10.26 ± 0.74	8.71 ± 0.64	<0.001 (Highly Significant)

Discussion of Table 4: Table 4 monitors the longitudinal updates in hemoglobin levels across the 6-month trial. Starting from month 1, the LNG-IUS group demonstrated a rapid and superior upward trajectory in hemoglobin levels. By month 6, the mean hemoglobin in the LNG-IUS group reached 10.26±0.74 g/dL, reflecting solid resolution of chronic anemia, whereas the Norethisterone cohort reached a significantly lower mean level of 8.71±0.64 g/dL (p<0.001).

Table 5: Comparison of Mean Pictorial Blood Assessment Chart (PBAC) Scores

Evaluation Interval	LNG-IUS Group (Mean ± SD)	Norethisterone Group (Mean ± SD)	Statistical p-value
Pre-Treatment Baseline PBAC	470.34 ± 51.00	478.59 ± 55.93	0.540 (Non- Significant)
Follow-up at 1 Month	255.53 ± 30.79	367.84 ± 45.84	<0.001 (Highly Significant)
Follow-up at 3 Months	98.72 ± 18.02	194.44 ± 124.57	<0.001 (Highly Significant)
Follow-up at 6 Months	54.13 ± 11.42	139.09 ± 110.76	<0.001 (Highly Significant)

Discussion of Table 5: Table 5 measures the volumetric decline in objective bleeding using mean PBAC scores.

While the baseline scores indicated heavy bleeding in both arms without significant variance (p=0.540), the introduction of LNG-IUS generated a vastly more uniform and drastic suppression of bleeding. The mean PBAC score dropped below the menorrhagia threshold (<100) by month 3 and reached a minimum score of 54.13±11.42 at month 6, compared to 139.09±110.76 with oral therapy (p<0.001).

Table 6: Intervention Failures, Surgical Requirements, and Acceptability Dynamics

Outcome / Acceptability Indicator	LNG-IUS Group (n=32)	Norethisterone Group (n=32)	Statistical Test / p-value
Treatment Failure / Hysterectomy Required [n (%)]	1 (3.13%)	13 (40.63%)	$\chi 2 = 11.06$ / p=0.001
Acceptability: Very Dissatisfied [n (%)]	0 (0.00%)	10 (31.25%)	t = 17.73 / p<0.001
Acceptability: Dissatisfied [n (%)]	1 (3.13%)	3 (9.38%)	
Acceptability: Enough Satisfied [n (%)]	5 (15.63%)	6 (18.75%)	
Acceptability: Satisfied [n (%)]	13 (40.63%)	10 (31.25%)	
Acceptability: Very Satisfied [n (%)]	13 (40.63%)	3 (9.38%)	

Discussion of Table 6: Table 6 integrates long-term efficacy parameters, surgical transition, and satisfaction scores. The rate of transition to definitive surgical hysterectomy was dramatically lower in the Mirena group (only 1 case, 3.13% due to early spotting discomfort and premature device removal) compared to the Norethisterone group, where 13 cases (40.63%) shifted to surgery due to persistent bleeding (p=0.001). Total satisfaction mirrored these metrics, with 81.26% of Mirena users grading their satisfaction as satisfied or very satisfied versus 40.63% in the oral progestin group (p<0.001).

Discussion

The management of idiopathic menorrhagia requires highly effective medical interventions that can reliably decrease bleeding volume, correct baseline iron-deficiency anemia, and minimize transition to major abdominal surgery. The demographic profiles in our clinical study revealed that the average age was higher in the LNG-IUS cohort (39.34 years) compared to the oral norethisterone cohort (36.78 years). This aligns with established literature showing that women approaching the late third or early fourth decade of life seek long-term, non-surgical solutions that provide localized therapeutic benefits without the burden of regular oral compliance. The uniform parity profiles (p=0.681) and comparable social variables across our cohorts confirm an unbiased model for evaluating medical outcomes.

Our findings demonstrate that both treatments significantly reduce menstrual blood loss over time. However, the localized administration of

levonorgestrel produced a vastly superior clinical reduction in PBAC scores, dropping from an initial mean of 470.34 down to 54.13 at the 6-month evaluation mark. In contrast, the oral norethisterone group reached a mean PBAC score of 139.09 ($p<0.001$). This finding is consistent with previous landmark trials which attributed the superior therapeutic performance of the LNG-IUS to continuous local delivery directly within the endometrial space. This targeted exposure induces intense down-regulation of estrogen receptors, leading to significant glandular atrophy and mucosal thinning, which was verified by our post-treatment ultrasound measurements showing a mean thickness of 5.12 mm in the Mirena group compared to 7.17 mm in the oral progestin group ($p<0.001$).

This progressive reduction in menstrual blood loss directly correlates with hematologic improvement. Long-term correction of anemia was significantly better in the LNG-IUS group, with mean hemoglobin levels rising to 10.26 g/dL at 6 months compared to 8.71 g/dL in the norethisterone arm ($p<0.001$). This highlights the dual benefit of the intrauterine system as both an effective treatment for bleeding and an automated therapy for chronic anemia. Compliance is also a key factor; oral progestins like norethisterone require a strict daily dosing schedule that is prone to user omission and subsequent breakthrough bleeding. This treatment burden likely contributed to the high dissatisfaction rate (31.25% very dissatisfied) and notable failure rate observed in the oral progestin group, where 40.63% of patients eventually required a surgical hysterectomy. In contrast, the LNG-IUS group maintained a highly significant satisfaction rate (81.26% satisfied/very satisfied) and a low hysterectomy rate (3.13%), confirming its role as a preferred, uterus-preserving alternative to major surgery.

Limitations

Our clinical study has several limitations that should be acknowledged.

First, the total sample size was relatively modest (n=64), which may restrict the immediate generalizability of our findings to larger, more ethnically diverse populations.

Second, the active follow-up window was limited to six months; while this is sufficient to capture initial clinical efficacy and hematologic recovery, it prevents long-term evaluation of device continuity, delayed expulsion rates, and long-term amenorrhea profiles beyond the first year.

Third, parameters regarding bleeding density and menstrual cycles relied on self-reported pictorial diaries, which can introduce recall bias. Finally, confounding metabolic factors such as systemic variations in Body Mass Index (BMI), detailed endocrine markers, and minor lifestyle variations were not controlled for within the analytical framework.

Future multicenter randomized controlled trials with extended follow-up durations are recommended to build upon these results.

Conclusion

The results of this study demonstrate that the levonorgestrel-releasing intrauterine system (LNG-IUS) offers superior clinical efficacy, safety, and patient acceptability compared to oral cyclical norethisterone for the treatment of idiopathic menorrhagia.

The intrauterine system achieved profound suppression of menstrual blood loss, accelerated hemoglobin restoration, and significantly reduced the need for definitive surgical hysterectomies.

Consequently, the LNG-IUS should be considered a preferred first-line, long-acting non-surgical treatment option for women seeking effective management of idiopathic heavy menstrual bleed.

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