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EFFECT OF LNG IUCD (MIRENA) VS DIENOGEST IN ADENOMYOSIS: A RANDOMIZED CONTROL TRIAL

Obstetrics & Gynaecology

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ABSTRACT

Background: Adenomyosis, a common gynecological condition in reproductive-aged women, causes dysmenorrhea, menorrhagia, and pelvic pain, significantly affecting quality of life. Hormonal therapies like LNG-IUS and dienogest offer uterus-preserving treatment options. **Objectives:** To compare the clinical efficacy, symptom control, and adverse effect profile of oral dienogest versus levonorgestrel-releasing intrauterine device (LNG-IUS) in the management of adenomyosis. **Methods:** A randomized controlled trial (RCT) was conducted on 100 women diagnosed with adenomyosis. Participants were randomly divided into two groups: oral dienogest (2 mg daily) and LNG-IUS (Mirena), and followed up at 3, 6, and 12 months. VAS scores, PBAC scores, uterine volume, and adverse effects were analyzed. **Results:** Dienogest showed superior reduction in pain and menstrual volume at 6 and 12 months. LNG-IUS was more effective in reducing uterine volume. Irregular bleeding and device expulsion were higher with LNG-IUS. **Conclusion:** Dienogest demonstrated better long-term symptom control and tolerability, making it a favorable conservative option for adenomyosis.

KEYWORDS

Adenomyosis; Dienogest; Levonorgestrel intrauterine device; Dysmenorrhea; Uterine bleeding; Hormonal therapy.

INTRODUCTION

Adenomyosis is defined by the invasion of endometrial glands and stroma into the uterine myometrium, resulting in hypertrophy of adjacent smooth muscle cells and manifesting as diffuse or localized lesions [1–3]. It primarily affects women aged 30–50 years, with incidence reportedly increasing in recent years [4]. Though its etiology is unclear, risk factors include high parity, abortions, endometrial hyperplasia, endometriosis, prior uterine surgeries (e.g., cesarean, curettage), and lifestyle factors such as smoking. MRI classifies adenomyosis into diffuse, focal, and extrinsic types.

Clinically, it presents with dysmenorrhea, menorrhagia, pelvic pain, dyspareunia, and subfertility, significantly impairing quality of life [5]. While hysterectomy offers definitive treatment [6], conservative hormonal options are essential for women wishing to retain fertility or avoid surgery [7].

Common hormonal therapies include oral contraceptives, progestins, and GnRH analogues. Among these, LNG-IUS and dienogest are frequently used for symptomatic relief. LNG-IUS delivers levonorgestrel locally, promoting endometrial atrophy and lesion suppression. However, it may cause irregular bleeding, amenorrhea, backache, expulsion, and is expensive, limiting its use in low-resource settings. Symptoms may recur post-removal [8].

Dienogest, an oral progestin (Visanne), suppresses follicular activity and estradiol levels, thereby reducing inflammation, angiogenesis, and ectopic tissue growth [9]. Long-term use minimizes lesion size [10], nerve density, and pain via inhibition of nerve growth factors [11,12].

Despite its advantages, dienogest remains underused in India due to cost concerns and limited awareness. This study is designed to compare the clinical efficacy and safety of oral dienogest versus LNG-IUS in the conservative treatment of adenomyosis.

MATERIALS AND METHODS

A randomized controlled trial (RCT) was conducted on 100 women clinically and radiologically diagnosed with adenomyosis, presenting with symptoms such as dysmenorrhea, menorrhagia, or infertility. The study was carried out at Rohilkhand Medical College and Hospital, Bareilly, between September 2023 to October 2024, after receiving approval from the Institutional Ethics Committee. Participants aged between 25 and 50 years were enrolled and randomly assigned using a computer-generated random number table into two groups: one receiving oral dienogest (2 mg daily, n = 50) and the other treated with a levonorgestrel-releasing intrauterine device (Mirena, n = 50), inserted during days 3 to 7 of the menstrual cycle.

Women included in the study met diagnostic criteria for adenomyosis and had no contraindications to the study medications. All participants had normal ovarian function, were capable of providing informed consent, and had a uterine cavity suitable for LNG-IUCD placement. Exclusion criteria included recent hormonal therapy use (within 3 months), suspected gynecological malignancy, autoimmune or severe hepatic/renal disease, ovarian dysfunction, or associated pathologies such as endometriosis or adenomyoma. Patients

Group A received dienogest orally starting from the second day of menstruation and continued daily for a period of 12 months. Group B underwent LNG-IUCD (Mirena) insertion during the early proliferative phase of the menstrual cycle and was monitored with the device in situ for the same duration. All patients underwent baseline evaluation followed by assessments at 3, 6, and 12 months. Clinical outcomes were measured using the Visual Analog Scale (VAS) to assess the severity of dysmenorrhea, dyspareunia, and chronic pelvic pain on a scale of 0 to 10. Menstrual blood loss was evaluated using the Pictorial Blood Loss Assessment Chart (PBAC), with scores over 100 indicating significant menorrhagia.

Uterine volume and endometrial thickness were measured by transvaginal ultrasonography using the standard formula: 0.52 × length × width × anteroposterior diameter, with scans scheduled 3 to 7 days after menstruation for standardization. Adverse effects, particularly irregular bleeding, vaginal discharge, and any device-related complications, were recorded during routine follow-up throughout the study period.

All statistical analyses were conducted using SPSS version 26.0. Quantitative variables were expressed as mean ± standard deviation and compared using independent t-tests or repeated measures ANOVA as appropriate. Qualitative data were analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically significant for all comparisons.

RESULTS

Our study enrolled 100 women with adenomyosis, evenly divided between the dienogest and LNG-IUS groups. The majority aged between 31–40 years (58%), and a similar age distribution in both treatment groups. Most participants were multiparous (Parity 1–2, 65%), belonged to the middle socioeconomic class (62%), and resided in urban areas (70%). Educationally, over half had primary or secondary education (55%), while 36% were graduates. The majority were homemakers (73%) and married (96%), ensuring a relatively homogenous socio-demographic profile across both groups, which supports comparability and minimizes baseline confounding, as shown in Table 1.

Table 1: Socio-Demographic Profile of Study Participants (n = 100)

Parameter	Category	Group A (Dienogest)	Group B (LNG IUCD)	Total (n = 100)
Age Group (years)	25–30	10 (20.0%)	8 (16.0%)	18 (18.0%)
	31–40	28 (56.0%)	30 (60.0%)	58 (58.0%)
	41–50	12 (24.0%)	12 (24.0%)	24 (24.0%)
Parity	Nulliparous	8 (16.0%)	7 (14.0%)	15 (15.0%)
	Parity 1–2	32 (64.0%)	33 (66.0%)	65 (65.0%)
	≥ 3	10 (20.0%)	10 (20.0%)	20 (20.0%)
Socioeconomic Status (Kuppuswamy Scale)	Upper	6 (12.0%)	5 (10.0%)	11 (11.0%)
	Middle	30 (60.0%)	32 (64.0%)	62 (62.0%)
	Lower	14 (28.0%)	13 (26.0%)	27 (27.0%)
Residence	Urban	36 (72.0%)	34 (68.0%)	70 (70.0%)
	Rural	14 (28.0%)	16 (32.0%)	30 (30.0%)
Education Level	Illiterate	4 (8.0%)	5 (10.0%)	9 (9.0%)
	Primary/Secondary	28 (56.0%)	27 (54.0%)	55 (55.0%)
	Graduate and above	18 (36.0%)	18 (36.0%)	36 (36.0%)
Occupation	Homemaker	38 (76.0%)	35 (70.0%)	73 (73.0%)
	Employed	10 (20.0%)	13 (26.0%)	23 (23.0%)
	Others	2 (4.0%)	2 (4.0%)	4 (4.0%)
Marital Status	Married	49 (98.0%)	47 (94.0%)	96 (96.0%)
	Others	1 (2.0%)	3 (6.0%)	4 (4.0%)

Both dienogest and LNG-IUS significantly reduced dysmenorrhea, pelvic pain, and menstrual volume over 12 months. However, dienogest demonstrated a more consistent and greater reduction in all parameters, especially at 6 and 12 months, indicating superior long-term symptom control in adenomyosis patients, as shown in Table 2.

Table 2: VAS Scores and Menstrual Volume Before and After Treatment

Parameter	Dienogest (n=50)	LNG-IUS (n=50)
Baseline Dysmenorrhea	8.76 ± 0.97	8.89 ± 0.99
3 Months Dysmenorrhea	5.30 ± 1.05	6.10 ± 0.97
6 Months Dysmenorrhea	3.20 ± 0.90	4.50 ± 1.00
12 Months Dysmenorrhea	2.60 ± 0.95	4.30 ± 0.92
Baseline Pelvic Pain	5.20 ± 0.86	5.40 ± 1.06
3 Months Pelvic Pain	2.90 ± 0.85	4.20 ± 0.82
6 Months Pelvic Pain	1.80 ± 0.75	2.70 ± 0.71
12 Months Pelvic Pain	1.40 ± 0.66	2.60 ± 0.89
Baseline Menstrual Volume	172 ± 40	172 ± 36
3 Months Volume	80 ± 14	81 ± 17
6 Months Volume	49 ± 17	71 ± 24
12 Months Volume	48 ± 15	70 ± 23

LNG-IUS led to a marked reduction in uterine volume over 12 months, whereas dienogest showed minimal change. Both treatments resulted in a comparable decrease in endometrial thickness, suggesting equal efficacy in suppressing endometrial growth, as shown in Table 3.

Table 3: Uterine Volume And Endometrial Thickness

Parameter	Dienogest (n=50)	LNG-IUS (n=50)
Baseline Uterine Volume (cm^3)	138 ± 48	126 ± 56
12 Months Uterine Volume (cm^3)	135 ± 45	87 ± 43
Baseline Endometrial Thickness(mm)	6.1 ± 1.9	6.0 ± 2.4
12 Months Endometrial Thickness(mm)	3.4 ± 1.0	3.3 ± 0.8

Irregular vaginal bleeding was more frequently prolonged in the LNG-IUS group, with 24% of patients experiencing bleeding beyond 6 months. In contrast, the majority of dienogest users had bleeding limited to the first 3 months, indicating better bleeding tolerability, as shown in Table 4.

Table 4: Irregular Vaginal Bleeding

Duration	Dienogest (n=50)	LNG-IUS (n=50)
None	4 (8.0%)	2 (4.0%)
0–3 months	34 (68.0%)	23 (46.0%)
4–6 months	8 (16.0%)	13 (26.0%)
Over 6 months	4 (8.0%)	12 (24.0%)

The overall adverse effect profile was similar between both groups, except for a significantly higher rate of device dislodgement (22%) in the LNG-IUS group. Dienogest was free from device-related issues, reinforcing its suitability in patients requiring non-invasive long-term therapy, as shown in Table 5.

Table 5: Adverse Events

Adverse Event	Dienogest (n=50)	LNG-IUS (n=50)
Breast tenderness	10 (20.0%)	7 (14.0%)
Weight gain	24 (48.0%)	26 (52.0%)
Hot flashes & night sweats	3 (6.0%)	4 (8.0%)
Headache & insomnia	6 (12.0%)	5 (10.0%)
Vaginitis	2 (4.0%)	4 (8.0%)
Back pain	3 (6.0%)	9 (18.0%)
Device dislodgement	0 (0.0%)	11 (22.0%)

DISCUSSION

Our study enrolled 100 women with clinically and radiologically diagnosed adenomyosis, with the highest representation in the 31–40 years age group (58%), followed by 41–50 years (24%). This age distribution aligns with the findings of Ota et al. (2021), who also reported that adenomyosis predominantly affects women in their reproductive age, particularly between 30–50 years [2]. Most participants in our study were multiparous (Parity 1–2: 65%), a known risk factor for adenomyosis, which is consistent with trends noted by Yang et al. (2022), who found a similar association between high parity and adenomyosis prevalence [1]. Additionally, the majority of patients in our study were urban residents (70%) and belonged to middle socioeconomic status (62%), reflecting accessibility to tertiary care services. Both treatment groups showed significant improvement in dysmenorrhea, pelvic pain, and menstrual volume, indicating the efficacy of hormonal therapy in symptom control. However, dienogest demonstrated a more sustained and consistent reduction across all parameters, especially at 6 and 12 months. These findings are consistent with those of Park et al. (2016), who observed long-term symptom relief and good tolerability with dienogest in endometriosis patients [13]. Similar conclusions were drawn by Yang et al. (2022), who found dienogest more effective than LNG-IUS in improving clinical symptoms and reducing relapse rates in adenomyosis, supporting its superior efficacy in long-term management [1]. In terms of uterine volume, LNG-IUS resulted in a more significant reduction compared to dienogest, which showed only minimal change after one year. This is attributed to LNG-IUS's localized delivery of levonorgestrel, which induces myometrial remodeling. This observation aligns with the work of Wang and Zhu (2021), who emphasized the benefits of local hormonal action in reducing uterine bulk in patients with adenomyosis [14]. Despite this, both groups showed similar reductions in endometrial thickness, indicating that both treatments effectively suppress endometrial proliferation. Irregular vaginal bleeding, a common adverse effect of hormonal therapy, was more prolonged and frequent in the LNG-IUS group, with 24% of patients experiencing persistent bleeding beyond six months. In contrast, most dienogest users experienced transient bleeding limited to the first three months. These findings are consistent with the ENVISIOeN study by Techatraisak et al. (2019), which reported better menstrual control and patient satisfaction with dienogest during long-term use [15]. Regarding safety, both treatments were well tolerated, with similar rates of systemic side effects such as breast tenderness and weight gain. However, device-related complications such as expulsion were noted exclusively in the LNG-IUS group (22%), an issue not observed with dienogest. This reinforces dienogest's advantage for patients seeking non-invasive, reversible medical management without the risk of mechanical complications.

Limitations

The limitations of the study include its single-center setting, modest sample size, and relatively short follow-up period of 12 months. Lack of blinding and randomization may introduce bias. Additionally, fertility-related outcomes and quality-of-life scores were not assessed, limiting broader evaluation of treatment impact beyond symptom control. Multicentric, longer-term studies are warranted.

Strengths

The strengths of the study include its randomized controlled trial (RCT), clearly defined inclusion criteria, and standardized follow-up intervals. The use of validated assessment tools such as VAS and PBAC ensured objective evaluation of symptom improvement. Direct head-to-head comparison of two widely used treatments enhances the clinical relevance and applicability of the findings in routine gynecological practice.

CONCLUSION

We concluded that dienogest offers superior long-term symptom relief, better bleeding control, and higher tolerability compared to LNG-IUS in the conservative treatment of adenomyosis. While both therapies were effective, dienogest's non-invasive nature and absence of device-related complications make it a favorable option for women seeking fertility-preserving, long-term medical management.

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