

COMPARISON OF LETROZOLE VERSUS DIENOGEST IN MANAGEMENT OF PAIN IN PELVIC ENDOMETRIOSIS

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ABSTRACT

Background: Endometriosis is a chronic gynecological disorder characterized by debilitating pelvic pain. Pharmacological management is central to symptom control, yet the optimal agent remains debated. This study compares the efficacy and tolerability of Letrozole versus Dienogest in alleviating pain and improving bleeding parameters among women with pelvic endometriosis. **Materials and Methods:** Sixty women diagnosed with pelvic endometriosis were randomized to receive either Dienogest (n=30) or Letrozole (n=30) for six months. Pain intensity was assessed using the Visual Analogue Scale (VAS) at baseline, 1, 3, and 6 months. Menstrual bleeding duration, effective cycle control, and drug tolerability were also evaluated at these intervals. **Result:** Both drugs produced significant reductions in VAS scores over six months, with Dienogest showing a slightly greater reduction at month six (mean VAS: Dienogest 3.9 ± 1.1 vs Letrozole 4.7 ± 0.7 ; $p=0.002$). After six months, Dienogest was associated with a pronounced decrease in mean bleeding duration (1.6 ± 1.0 days) compared to Letrozole (3.2 ± 0.6 days, $p<0.001$). Effective cycle control did not significantly differ between groups. At six months, tolerability ratings for Dienogest were more favourable, with a higher proportion of “very good” responses compared to Letrozole (40% vs 13.3%, $p=0.02$). **Conclusion:** Both Letrozole and Dienogest are effective in managing pain associated with pelvic endometriosis. However, Dienogest demonstrated superior pain reduction, shorter bleeding duration, and better tolerability after six months. Dienogest may thus be considered a preferable option for long-term symptom management in women with pelvic endometriosis.

INTRODUCTION

Endometriosis, affecting 5–10% of reproductive-age women, manifests as ectopic endometrial tissue causing pelvic pain, dysmenorrhea, and infertility.^[1–3] Chronic pelvic pain and endometriomas are key presentations.^[4,5] While no definitive cure exists, pharmacologic options aim to alleviate pain and disease progression. Dienogest, a selective progestin, induces decidualization and reduces inflammation, effectively managing pain but with limitations like breakthrough bleeding.^[6] Letrozole, an aromatase inhibitor, reduces estrogen synthesis in endometriotic tissue, offering symptom

relief and disease control.^[7] Comparative data on these agents are limited, necessitating studies evaluating their efficacy in pelvic endometriosis-associated pain management.^[7,8] The aim of this study is to evaluate and compare the therapeutic efficacy, safety profile, and patient satisfaction of Letrozole versus Dienogest in the management of pelvic endometriosis-associated pain.

MATERIALS AND METHODS

A prospective, interventional, comparative study was conducted on 60 women with clinically, sonologically or surgically diagnosed cases of

endometriosis with associated pain. Patients were randomized into two groups receiving either Letrozole 2.5 mg daily or Dienogest 2 mg daily for six months. Pain was assessed using the Visual Analogue Scale (VAS) at baseline, three, and six months. Adverse effects and patient satisfaction were also evaluated.

RESULTS

Data are expressed as frequencies and percentages, depending on distribution. Tests for independence were carried out either using Chi Square Test (for categorical data) or Student's t test (for continuous data). Analysis was carried out using Microsoft Excel 365 and STATA 14. Statistical significance was accepted at the level of $p\text{-value} \leq 0.05$.

The visual analog scale (VAS) pain scores at 0, 1, 3, and 6 months for participants on Dienogest and Letrozole. At baseline (0 months), the mean pain score was 8.4 ± 0.6 for Dienogest and 8.3 ± 0.7 for Letrozole ($p = 0.5$). After 1 month, Dienogest's score decreased to 7 ± 1.1 ($p = 0.3$), and Letrozole's to 7.3 ± 0.7 . By 3 months, Dienogest scored 5.6 ± 1 , while Letrozole scored 5.9 ± 0.7 ($p = 0.1$). At 6 months, Dienogest's mean score dropped to 3.9 ± 1.1 ($p = 0.002$), while Letrozole's remained at 4.7 ± 0.7 . In this study, both Letrozole and Dienogest demonstrated significant efficacy in reducing endometriosis-associated pelvic pain over a 6-month period. At 3 months, the mean VAS score reduced from 8.3 to 5.8 in the Letrozole group and from 8.2 to 5.1 in the Dienogest group. At 6 months, further reductions were noted, with mean scores of 4.7 and 3.9 respectively, the difference being statistically significant in favor of Dienogest ($p \leq 0.05$).

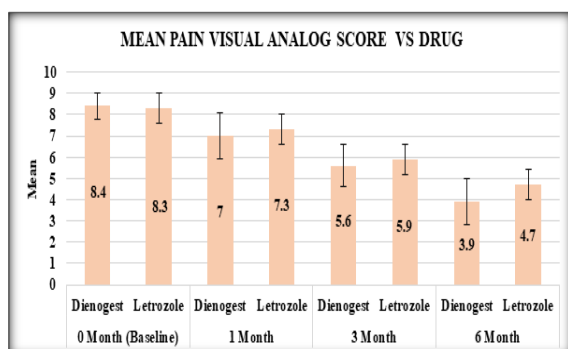


Figure 1: Mean pain visual analog score according to the type of drug.

The mean menstrual bleeding duration reduced markedly in the Dienogest group from 4.6 ± 1.2 days at 1 month to 1.6 ± 1 days at 6 months, compared to 3.2 ± 0.6 days with Letrozole ($p < 0.001$).

Regarding safety, Dienogest maintained a high safety rate (90%) at 6 months versus 83.3% with Letrozole ($p = 0.4$). Side effects varied: Dienogest was associated with more headache (23.3% vs. 0%; $p = 0.005$), while Letrozole caused more hot flushes (13.3% vs. 0%; $p = 0.002$). Other side effects like nausea, dry mouth, and low mood were not significantly different.

Tolerability assessments at 6 months revealed a higher 'very good' rating for Dienogest (40%) compared to Letrozole (13.3%), with this difference being statistically significant ($p = 0.02$). Importantly, there were no withdrawals in either group during the study period.

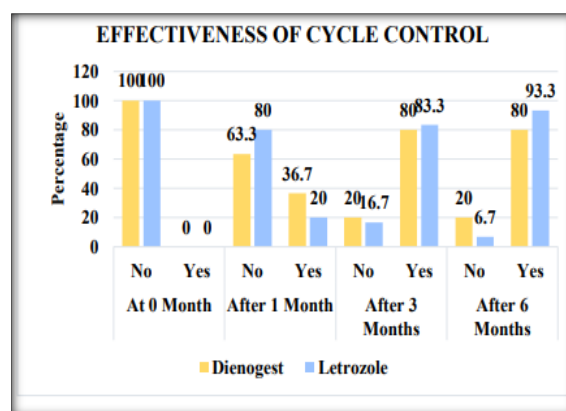


Figure 2: Distribution of participants according to the effectiveness of cycle control and type of drug received

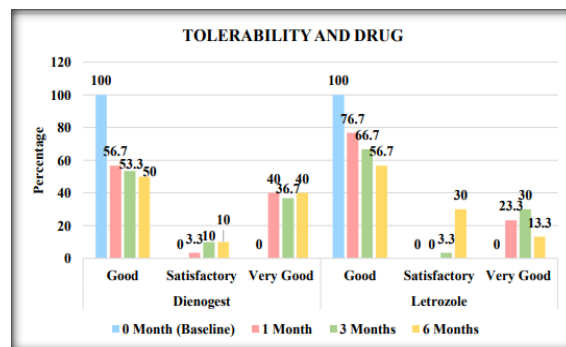


Figure 3: Distribution of participant's tolerability and the drug received

Table 1: Mean \pm SD of pain VAS AT 0, 1, 3 and 6 months in the two groups

VAS	Drug (N=60)	Mean \pm SD	Min	Max	p-value
0 Month (Baseline)	Dienogest (n=30)	8.4 ± 0.6	7	9	0.5
	Letrozole (n=30)	8.3 ± 0.7	7	9	
1 Month	Dienogest (n=30)	7 ± 1.1	4	9	0.3
	Letrozole (n=30)	7.3 ± 0.7	6	8	
3 Month	Dienogest (n=30)	5.6 ± 1	4	8	0.1
	Letrozole (n=30)	5.9 ± 0.7	5	7	
6 Month	Dienogest (n=30)	3.9 ± 1.1	2	6	0.002
	Letrozole (n=30)	4.7 ± 0.7	3	6	

Table 2: mean \pm sd of duration of menstrual bleeding effectiveness of cycle control after 1, 3 and 6 months in the two groups

Duration	Parameter	Dienogest (n=30)	Letrozole (n=30)	p-value
After 1 Month	Mean bleeding duration (days)	4.6 \pm 1.2 (Range: 3–7)	4.7 \pm 0.8 (Range: 3–6)	0.9
	Effective cycle control (%)	36.7% (11/30)	20% (6/30)	0.1
After 3 Months	Mean bleeding duration (days)	3.2 \pm 1.0 (Range: 2–5)	3.5 \pm 0.8 (Range: 2–5)	0.1
	Effective cycle control (%)	80% (24/30)	83.3% (25/30)	0.7
After 6 Months	Mean bleeding duration (days)	1.6 \pm 1.0 (Range: 0–3)	3.2 \pm 0.6 (Range: 2–4)	<0.001
	Effective cycle control (%)	80% (24/30)	93.3% (28/30)	0.1

Table 3: distribution of participants according to their tolerability and drug received

Tolerability		Drug (N=60)		p-value
		Dienogest (n=30)	Letrozole (n=30)	
0 Month (Baseline)	Good	30 (100)	30 (100)	-
	Satisfactory	-	-	
	Very Good	-	-	
1 Month	Good	17 (56.7)	23 (76.7)	0.2
	Satisfactory	1 (3.3)	0 (0)	
	Very Good	12 (40)	7 (23.3)	
3 Months	Good	16 (53.3)	20 (66.7)	0.4
	Satisfactory	3 (10)	1 (3.3)	
	Very Good	11 (36.7)	9 (30)	
6 Months	Good	15 (50)	17 (56.7)	0.02
	Satisfactory	3 (10)	9 (30)	
	Very Good	12 (40)	4 (13.3)	

DISCUSSION

In this study, Dienogest and Letrozole were compared for the management of endometriosis-associated pain in women aged 20–40 years. Both groups experienced a significant reduction in pelvic pain as measured by the Visual Analogue Scale (VAS). Dienogest demonstrated a greater reduction from 8.4 to 3.9, compared to Letrozole which reduced VAS from 8.3 to 4.7 after six months of treatment, with Letrozole achieving statistically significant improvement ($p = 0.002$). These findings are consistent with Strowitzki et al. (2010),^[9] who reported a notable VAS reduction with Dienogest, and Amir et al. (2022),^[10] who found both medications effective in reducing pain, with Dienogest offering a slightly better effect size. Cycle control improved more rapidly in the Letrozole group, with 80% effectiveness at one month versus 36.7% in the Dienogest group; however, by six months, the difference narrowed (93.3% vs. 80.0%, $p = 0.1$). An odds ratio of 0.3 suggested Letrozole was more effective in early cycle regulation. These trends align with observations by Strowitzki et al. (2015),^[11] who reported good cycle control with prolonged Dienogest use. In terms of menstrual bleeding, Dienogest significantly reduced the duration from 5.3 days to 1.6 days ($p < 0.0001$), with 16.6% of patients achieving amenorrhea, whereas Letrozole maintained relatively steady bleeding duration (~3.2 days). Amir et al. (2022) [10] also noted superior suppression of menstrual bleeding with Dienogest. Tolerability was comparable at one and three months, but after six months, Dienogest showed significantly better tolerability ratings ($p = 0.02$), with a higher percentage of patients rating it as “very good,” whereas more Letrozole users rated their experience as merely “satisfactory.” These

findings support Strowitzki et al. (2015),^[11] who highlighted Dienogest’s favorable safety profile with minimal side effects. No participants withdrew from the study in either group, reflecting high compliance.

Regarding symptom profile, chronic pelvic pain and dysmenorrhea were more prevalent in the Letrozole group, while dyspareunia was more frequent in the Dienogest group (23.3% vs. 13.3%). These symptom distributions are in agreement with Armour et al. (2020),^[12] Vercellini et al. (2014),^[13] and Kor et al. (2020),^[14] who reported that endometriosis patients commonly suffer from pain, dyspareunia, and the associated psychosocial impacts. Overall, both medications were effective and well-tolerated, but Dienogest demonstrated slightly better outcomes in pain reduction, menstrual suppression, and long-term tolerability.

CONCLUSION

This study concluded that both Dienogest and Letrozole effectively reduced endometriosis-associated pelvic pain. Dienogest showed slightly better pain relief and greater reduction in menstrual bleeding, while Letrozole offered faster cycle control. Both drugs were well-tolerated, with no withdrawals. Dienogest may be preferred for long-term symptom management, whereas Letrozole suits patients needing earlier cycle regularity.

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