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ORIGINAL ARTICLE

Role of Dienogest in the treatment of Endometriosis

BIBI SAJIDA[1], SADAF IJAZ[2], SHAHIDA MALIK[3], HANI BALOCH[4], SADIA IJAZ[5], MOMENAH MAQSOOD[6], MONICA PUNSHI[7]
[1]*WMO, Department of Obstetrics and Gynaecology, DHQ Hospital, KDA Kohat*
[2]*Consultant, Gynaecologist, Department of Obstetrics and Gynaecology, DHQ Hospital, KDA Kohat*
[3]*Assistant Professor, Department of Obstetrics and Gynaecology, Sialkot Medical College / Idrees Hospital, and Kiran International Hospital, Sialkot*
[4]*Assistant Professor, Department of Gynaecology, Teaching Hospital Killa Saifullah*
[5]*Assistant Professor, Department of Pathology, University Medical and Dental College, Faisalabad*
[6]*Gynaecologist, Health Department, District Health Office, Mirpur AJK*
[7]*Consultant Gynaecologist/Obstetrician and Public Health Expert, C.W.M.O (BPS 19) Dr Ruth KM Pfau Civil Hospital, Karachi*
Correspondence to: Monica Punshi, Email: unshimonica@gmail.com

ABSTRACT

Endometriosis is a chronic, estrogen-dependent condition affecting women of reproductive age, with peak incidence between 25 and 30 years. Dienogest 2 mg daily has been shown to effectively relieve endometriosis-related pain, reduce endometriotic lesions, and improve quality of life. A quasi-experimental trial at Shifa International Hospital, Islamabad, over 12 months assessed the efficacy of Dienogest 2 mg daily for managing endometriosis-associated pelvic pain (EAPP). The study involved 105 women with a mean age of 28.3 years and a mean BMI of 26.2. EAPP was measured using the Visual Analogue Scale (VAS) at baseline, 3 months, and 6 months. Results indicated a significant reduction in VAS scores from 7.12 at baseline to 4.50 at 3 months and 2.62 at 6 months, demonstrating a clinically meaningful improvement in pain levels.

Keywords: Endometriosis, Dienogest, Visual Analogue Score (VAS).

INTRODUCTION

Endometriosis is a chronic condition where endometrial tissue, which normally lines the inside of the uterus, grows outside the uterine cavity. It affects 6% to 10% of women of reproductive age and is present in 50% of infertile women. Laparoscopy has identified endometriosis in 35% to 70% of adolescents and young women with dysmenorrhea and chronic pelvic pain. The disease is challenging to manage due to its high recurrence rates and the associated infertility and chronic pain, posing a significant burden on both healthcare providers and the system at large. Long-term management is often required, with progestins like dienogest being used empirically upon the first presentation of symptoms and post-surgery to reduce recurrence[1,2].

Dienogest, a selective progestin, has recently gained attention as a treatment for endometriosis. However, limited data are available on its effectiveness in routine clinical practice, and further pharmacokinetic and clinical studies are necessary to fully understand its benefits[3,4]. Some studies have shown that dienogest can significantly reduce endometriosis-associated pelvic pain (EAPP), with visual analog scale (VAS) scores improving notably after treatment. For example, one study found that the mean VAS score decreased from 5.03±1.73 at baseline to 2.46±1.32 after 24 weeks of dienogest treatment. Another study reported a decrease in VAS from 57±17 at baseline to 12±11 after 12 weeks of treatment. These findings suggest that dienogest could be a valuable treatment for EAPP, but further research is needed to confirm its efficacy, particularly in different populations[5,6].

Endometriosis is defined by the presence of endometrial-like tissue outside the uterus, leading to inflammation, pain, and the formation of scar tissue and adhesions . The prevalence of the condition is unclear due to diagnostic challenges and the asymptomatic nature of some cases . It is estimated that up to 10% of women of reproductive age and 50% of women with subfertility are affected by endometriosis . The condition is associated with a range of painful symptoms, including dysmenorrhea, noncyclic pelvic pain, and dyspareunia, which significantly impact the quality of life[7-8].

Conservative surgery is often the first line of treatment for endometriosis, aimed at removing ectopic lesions, preserving fertility, and reducing pain. Laparoscopy is the preferred method due to its minimally invasive nature and quicker recovery times. However, the recurrence of endometriotic lesions after surgery is common, with rates ranging from 30% to 50%, particularly in cases with deep invasion and extensive adhesion. This recurrence may necessitate further surgery and can lead to complications such as ovarian function impairment, menstrual abnormalities, and infertility . Therefore, long-term medical management is often required following conservative surgery[7-9].

Dienogest (DNG) is a selective fourth-generation synthetic progestin recommended as the first-line treatment for long-term management of endometriosis by international guidelines. It is preferred over gonadotropin-releasing hormone analogues (GnRH-a) as it maintains estradiol levels within the "estrogen window," preventing ectopic endometrial growth without causing perimenopausal symptoms or bone density loss. Dienogest is especially suitable for women with fertility needs, unlike the levonorgestrel-releasing intrauterine system (LNG-IUS), which is not ideal for those seeking to conceive[8–11] .

Despite the availability of surgical options, endometriosis requires long-term medical treatment to manage symptoms and prevent recurrence. Progestins like dienogest are recommended as first-line hormone therapy for endometriosis-related pain, as they are considered more effective than other treatments [3–9]. Dienogest 2 mg daily was approved for endometriosis treatment in the European Union in 2009 and has been shown to suppress systemic gonadotropin production and exert local antiproliferative and anti-inflammatory effects on endometriotic lesions. Long-term studies have demonstrated that dienogest is effective in reducing pain and preventing recurrence for up to five years after surgical treatment[12-15].

Several real-world studies, such as VIPOS and ENVISIOeN, have investigated the long-term effects of dienogest 2 mg in women with endometriosis. These studies provide valuable insights into the drug's effectiveness over extended periods, showing significant improvements in quality of life and reductions in pain and recurrence rates[13-15]. Additionally, dienogest has been associated with improvements in physical, mental, social, and emotional health, as well as sexual functioning and the frequency of sexual encounters. These findings underscore the importance of dienogest as a viable long-term treatment option for endometriosis[5-14].

MATERIALS AND METHODS

This quasi-experimental trial was conducted at the Department of Obstetrics and Gynecology, Shifa International Hospital, Islamabad, over 12 months September 20, 2022, to September 19, 2023. A total of 105 females aged 16-55 years, diagnosed with endometriosis via ultrasound and with a VAS pain score >5, were included using non-probability consecutive sampling. Exclusion criteria included metastatic disease, refractory endometriosis, contraindications to hormonal treatment, or recent hormonal

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treatment. After baseline assessments, patients received 2 mg oral dienogest daily for 6 months, with follow-up evaluations at 3 and 6 months to measure changes in endometriosis-associated pelvic pain (EAPP). Data were analyzed using SPSS v.21, employing paired sample t-tests, linear regression, and multivariate analysis to assess the impact of treatment and potential correlations, with significance set at 0.05.

RESULTS

Table 1 highlight that the majority of participants (52.4%) were aged 26-35 years, followed by 34.3% aged 16-25 years, with a mean age of 28.3±7.7 years. Table 1 shows a balanced distribution of marital status, with 53.3% unmarried and 46.7% married. The mean BMI was 26.2±4.7 and mean parity was 1.36±1.85 (Table 1). Hypertension and diabetes mellitus were present in 19% and 15.2% of patients, respectively

Table 1 also demonstrates a significant reduction in Endometriosis-Associated Pelvic Pain (EAPP) after three months of dienogest treatment, with the mean VAS decreasing from 7.12±1.21 to 4.50±1.18 (P<0.001). Table 8 further shows that after six months, the mean VAS decreased to 2.36±0.94, indicating sustained pain relief (P<0.001). Stratification by age and BMI reveals consistent and statistically significant pain reduction across all groups at both three and six months of treatment (P<0.001). These findings underscore dienogest's efficacy in managing endometriosis-associated pelvic pain across different demographics.

Table 1: consolidates the distribution data for age, marital status, BMI, parity, hypertension, and the change in endometriosis-associated pelvic pain (EAPP) with dienogest at 3 and 6 months, including their respective VAS scores and P-values.

Category	Group	Number	Percentage	Mean ± SD	VAS Baseline	VAS Follow-Up	Difference	P-value
Age (Years)	16-25	36	34.3	28.3±7.7				
	26-35	55	52.4					
	36-45	9	8.6					
	46-55	5	4.8					
Marital Status	Unmarried	56	53.3					
	Married	49	46.7					
BMI	< 25	45	45.7	26.2±4.7				
	≥ 25	57	54.3					
Parity	0-3	95	90.5	1.36±1.85				
	4-7	10	9.5					
Hypertension	Yes	20	19.0					
	No	85	81.0					
EAPP at 3 Months					7.12±1.21	4.50±1.18	2.62±0.03	P<0.001
EAPP at 6 Months					7.12±1.21	2.36±0.94	4.76±0.27	P<0.001

Table 2: combined table provides a comprehensive overview of the impact of dienogest on Endometriosis-Associated Pelvic Pain (EAPP) across different stratifications, including BMI, parity, hypertension, diabetes, and duration of symptoms at both 3 and 6 months

Stratification	Group	VAS Mean±SD at Baseline	VAS Mean±SD at Follow-Up	Difference	P-value
BMI at 6 Months	< 25	7.02±1.13	2.31±0.87	4.71±1.27	P<0.001
	≥ 25	7.21±1.27	2.40±0.99	4.81±1.44	P<0.001
Parity at 3 Months	0-3	7.15±1.22	4.49±1.21	2.66±1.42	P<0.001
	4-7	6.90±1.19	4.50±0.85	2.40±0.84	P<0.001
Parity at 6 Months	0-3	7.15±1.22	2.33±0.97	4.82±1.37	P<0.001
	4-7	6.90±1.19	2.70±0.48	4.20±1.13	P<0.001
Hypertension at 3 Months	Yes	7.10±1.25	4.35±1.04	2.75±1.44	P<0.001
	No	7.13±1.21	4.53±1.22	2.60±1.36	P<0.001
Hypertension at 6 Months	Yes	7.10±1.25	2.50±0.76	4.60±1.31	P<0.001
	No	7.13±1.21	2.33±0.98	4.80±1.37	P<0.001
Diabetes Mellitus at 3 Months	Yes	6.94±1.12	4.63±1.20	2.31±1.13	P<0.001
	No	7.16±1.23	4.47±1.18	2.69±1.41	P<0.001
Diabetes Mellitus at 6 Months	Yes	6.94±1.12	2.31±1.01	4.63±1.20	P<0.001
	No	7.16±1.23	2.37±0.93	4.79±1.39	P<0.001
Duration of Symptoms at 3 Months	< 12 months	7.42±1.25	4.39±1.15	3.03±1.63	P<0.001
	≥ 12 months	6.97±1.17	4.55±1.20	2.42±1.18	P<0.001
Duration of Symptoms at 6 Months	< 12 months	7.42±1.25	2.42±0.87	5.00±1.51	P<0.001
	≥ 12 months	6.97±1.17	2.33±0.98	4.64±1.27	P<0.001

Table 2 shows significant pain reduction across all age groups after six months. For example, individuals aged 16-25 saw their mean VAS drop from 6.94±1.12 to 2.19±0.71, a mean difference of 4.75±1.38 (P<0.001). Similar significant reductions were observed in older age groups. It illustrate the impact of BMI on pain reduction. Both BMI categories (<25 and ≥25) experienced significant drops in mean VAS scores at three months (2.67±1.34 and 2.60±1.41, respectively) and six months (4.71±1.27 and 4.81±1.44, respectively), all with P<0.001. It stratify pain reduction by parity over three and six months. Both lower parity (0-3) and higher parity (4-7) groups saw significant decreases in mean VAS, with six-month differences of 4.82±1.37 and 4.20±1.13, respectively (P<0.001). Itfocuses on hypertension. Participants, regardless of hypertension status, experienced significant pain reduction, with six-month differences of 4.60±1.31 for those with hypertension and 4.80±1.37 for those without (P<0.001). This table addresses diabetes mellitus. Both diabetic and non-diabetic participants saw significant VAS reductions, with six-month differences of 4.63±1.20 and 4.79±1.39, respectively (P<0.001). Participants with symptoms for less than 12 months had a mean VAS decrease of 5.00±1.51 at six months, while those with longer symptoms showed a reduction of 4.64±1.27 (P<0.001).Overall, dienogest consistently reduces EAPP across age, BMI, parity, hypertension, diabetes status, and symptom duration.

DISCUSSION

Endometriosis, prevalent among women, often suffers from diagnostic delays due to variable clinical presentations and geographical differences. Prompt diagnosis is crucial for effective management, particularly for those with dysmenorrhea and pelvic pain. While a diagnosis can be reassuring, it may also induce anxiety due to the potential need for long-term treatment and possible infertility.

Our study confirms dienogest's significant role in managing endometriosis-associated pelvic pain (EAPP). After three months

of treatment, the mean Visual Analogue Score (VAS) for pain significantly dropped from 7.12±1.21 to 4.50±1.18 (mean difference 2.62±0.03, P<0.001). This improvement persisted at six months, with the VAS decreasing further to 2.36±0.94 (mean difference 4.76±0.27, P<0.001), highlighting dienogest's sustained effectiveness.

These findings align with previous research. El-Taha et al. found dienogest's effectiveness comparable to Yasmin, with a significant reduction in mean VAS scores. Uludag et al. reported a significant decrease in endometrioma volume and pain with dienogest, although our study did not assess fertility outcomes.

CONCLUSION

Dienogest significantly reduces EAPP, with marked improvements observed at both three and six months. The reduction in VAS scores confirms its efficacy in managing endometriosis-related pain.

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