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Original Research Article

Dienogest versus Medroxyprogesterone Acetate for Control of Menstrual Pain with Endometriosis

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Abstract:

Introduction: Endometriosis is a chronic, estrogen-dependent inflammatory conditions that impacts women in their reproductive age, commonly presenting as pelvic pain, dysmenorrhea, dyspareunia, and infertility. Despite different medical and surgical treatments, managing menstrual pain related to endometriosis remains a clinical challenge.

Objectives: The purpose of the study is to compare the effectiveness and safety of the pharmacological intervention by oral Dienogest and Intramuscular depot Medroxyprogesterone acetate for the management of pelvic endometriosis with special reference to reduction of menstrual pain.

Methods: This was an observational, prospective, comparative study of 12 months of women age between18 to 45 years attending Gynaecology OPD at RG Kar Medical College and Hospital, Kolkata. Group A(n=40)- received Tab. Dienogest 2mg orally once daily and Group-B(n=40) received Inj. Depot Medroxy Progesterone Acetate 150mg 3 monthly for 6months. The intensity of pain in VAS was calculated at baseline and after 6months of treatments.

Results: Dienogest significantly reduced menstrual pain (mean score: 2.2250±.8002) compared to MPA (mean score: 3.7750±.9997), with $p<0.0001$. Both drugs showed mild side effects; weight gain was slightly higher in MPA users (12.5%) than in Dienogest users (7.5%).

Conclusion: Dienogest demonstrated better tolerability, fewer adverse effects, and improved patient satisfaction compared to MPA. But DMPA (Medroxyprogesterone Acetate) is a more cost-effective option with quarterly injections. The study suggests Dienogest as a superior first-line therapy for endometriosis-related pain**,** but further long-term research is needed.

Keywords: Dienogest, Menstrual Pain, Efficacy and Endometriosis.

Introduction

Endometriosis-associated pelvic pain affects approximately 6 -10% of women of reproductive age [1]. Other than pelvic pain, women mainly experience dysmenorrhea with cyclical or peri-menstrual symptoms, dyspareunia, dyschezia, fatigue and infertility [2,3]. If no appropriate therapy is applied, it has a progressive course with worsened symptoms [4]. Usually, drugs adopted to treat the chronic pelvic pain are not able to cure women with this problem. Progestins or hormonal contraceptives [5,6] GnRH agonists [7,8] aromatase inhibitors [9], etonogestrel subdermal implant [10], or levonorgestrel-releasing intrauterine devices [11,12] are used to counteract the ovarian estrogenic secretion on the endometrium-like tissue developing outside the uterus [13]. Even if each of these treatments may be effective and pelvic pain usually reappears when women discontinue their usage. Moreover, women affected by chronic pelvic pain should use drugs having a continuous regimen, including hormonal contraceptives [14]. Several women take on-demand non-steroidal anti-inflammatory drugs (NSAIDs) as first line agents to control their pelvic pain [15]. Hormonal treatment is adopted only after a specialist diagnoses endometriosis as the cause of the pelvic pain. It is important to remark that wom-

en are different in their sensitivity to chronic pelvic pain. Thus, the first step in prescribing a drug for chronic pelvic pain is to understand the needs of each subject. Dienogest is a synthetic progestin that is currently used for clinical treatment of endometriosis with a dose of 2 mg daily [16]. Depot medroxyprogesterone acetate a 17-hydroxy derivate progestogen with moderate androgenic activity that is administered intramuscularly as a single 150-mg dose every 3 months, is a well-established and effective long-term treatment option for pelvic pain caused by endometriosis. Although medroxyprogesterone acetate therapy is effective in reducing endometriosis-associated pelvic pain, it is often accompanied by unintentional weight gain, loss of libido, acne and reversible bone loss, which might adversely affect a woman's quality of life and preclude long-term use. [17,18] This study aimed to compare dienogest with medroxyprogesterone acetate for management of endometriosis in terms of menstrual pain, adverse effects, tolerability, and overall satisfaction.

Method

Approval of this hospital based observational, prospective, comparative study was taken from ethical committee of R. G. Kar Medical College and Hospital.

We hypothesised that dienogest was superior to medroxyprogesterone acetate in reducing endometriosis-associated menstrual pain. After 6 months of treatment, the mean reduction in pain score was 82% for dienogest [19] and 53% for medroxyprogesterone acetate [20]. A difference of 30% between the study cohortswas considered clinically significant. To have a 80% chance of detecting such a difference at an overall significance level of 0.05

$$\text{Patients per group} = \frac{P1(1-P1) + P2(1-P2)}{(P2-P1)^2} \times f(\alpha\beta) = 37$$

We aimed to recruit 40 patients per group to allow for dropouts. 80 patient was recruited from OPD having endometriosis and menstrual pain between April 2023 to March 2024. Inclusion criteria were age 18-45 years with Regular menstrual cycles and clinical, laparoscopic or histological diagnosis of Endometriosis. Informed consent was obtained. Exclusion criteria were undiagnosed genital bleeding, contraindication of progestin therapy, consulting for infertility. They was divided into two groups according to their preference/ choice. Group A(n=40) will receive Dienogest 2mg orally daily for 6months and group B(n=40) will receive Depot MedroxyProgesterone Acetate 150mg intramuscularly every 3months. Each patient had undergone a thorough medical history, comorbidities, Lower abdominal pain, Dyspareunia, Defecation pain, Nausea, Headache, Pain on internal examinationand was recorded in the proforma. Primary outcome was Reduction of pain score at the end of 6 months therapy measured by the means of a 10 point Visual Analogue Score (VAS Score) consisting of a 10 cm line with 2 end points marked as ‘no pain’ and ‘worst pain ever’. Secondary outcome was Nausea & vomiting, Headache, Bloating/ abdominal cramps, Weight gain, Trouble sleeping, Acne, Menstrual irregularity, Breast pain and tenderness, Mood swing, Dizziness & drowsiness, Reduced libido, Alopecia. Patients of both the groups was evaluated at the beginning of the treatment (t0) after 6 months(t6). For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data were compiled as mean and standard deviation of numerical variables and percentages of category variables. Two-sample t-tests of mean differences included independent samples or unpaired samples. Odd proportions were compared using the Chi-square test or Fischer's exact test as appropriate. Statistical significance in all evaluation defined as $p<0.05$. Adjustment was made to preserve at least 95% confidence intervals for primary and secondary outcomes when needed.

Results

There was no drop out in this study. So, all 40 patients in Group A and 40 patients in Group B continued the study. At baseline two groups were homomgenous as per age, parity, BMI, baseline lower abdominal pain. Dyspareunia, dyschezia, pain on internal examinations. After 6months of treatments the mean VAS score for menstrual pain in the dienogest and medroxyprogesterone acetate groups reduced from 7.45 and 7.5 to 2.22 and 3.77 respectively.

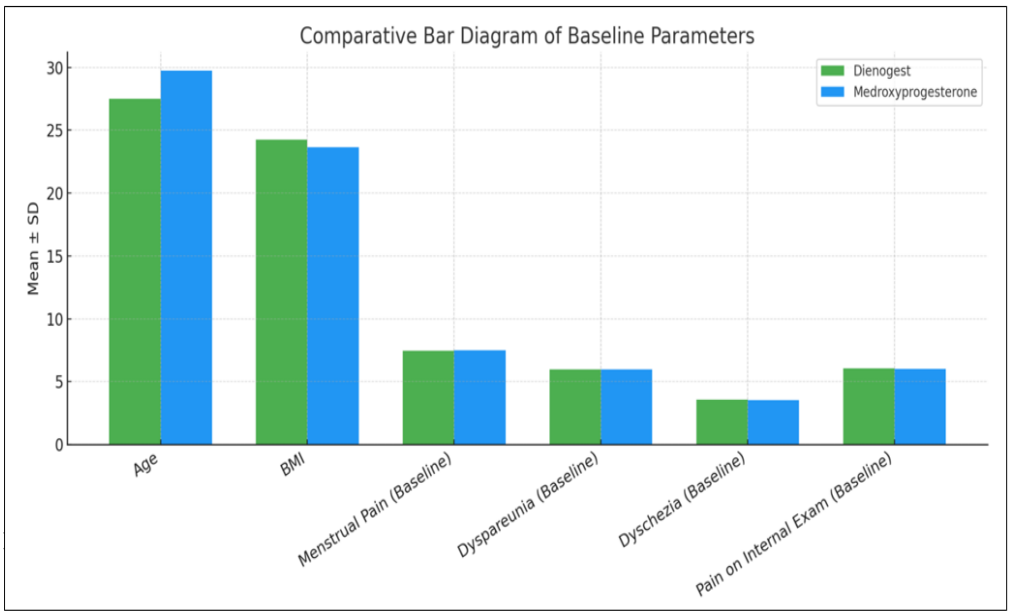

Figure 1: Baseline characteristics between the dienogest and medroxyprogesterone acetate groups

Table 1: Comparison of the dienogest and medroxyprogesterone acetate groups in terms of baseline characteristics, efficacy of treatment.

Parameters	Dienogest (Mean ± SD)	Medroxyprogesterone (Mean ± SD)	P-value
Age	27.50 ± 5.25	29.75 ± 5.47	0.0643
BMI	24.26 ± 5.45	23.66 ± 4.13	0.5852
Menstrual Pain (Baseline)	7.45 ± 0.90	7.50 ± 0.88	0.8025
Menstrual Pain (After 6 months)	2.23 ± 0.80	3.78 ± 1.00	<0.0001
Dyspareunia (Baseline)	6.00 ± 1.22	6.00 ± 1.15	<0.0001
Dyspareunia (After 6 months)	1.08 ± 0.76	1.88 ± 0.85	<0.0001
Dyschezia (Baseline)	3.58 ± 1.01	3.55 ± 1.04	0.9133
Dyschezia (After 6 months)	1.08 ± 0.76	2.13 ± 0.76	<0.0001
Pain on Internal Examination (Baseline)	6.05 ± 1.18	6.03 ± 1.19	0.9248
Pain on Internal Examination (After 6 months)	1.15 ± 0.80	1.80 ± 0.88	0.0009

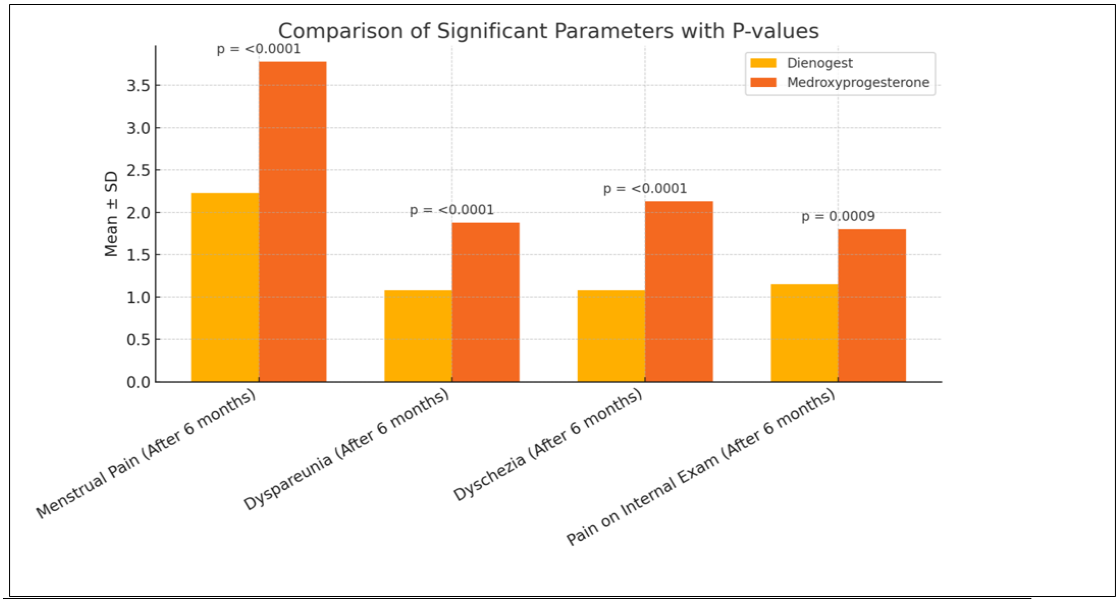

Figure 2: Comparison of the dienogest and medroxyprogesterone acetate groups in terms of efficacy of treatment.

Minor side effects were observed in both the groups but, no major side effects were seen. None of the participant left during the treatments.

Table 2: Comparison of the dienogest and medroxyprogesterone acetate groups in terms of side effects during treatment.

Side Effects	Dienogest (n, %)	Medroxyprogesterone (n, %)
Headache	6 (15%)	4 (10%)
Nausea	5 (12%)	3 (8%)
Breast Tenderness	7 (18%)	6 (14%)
Mood Swings	4 (10%)	5 (12%)
Weight Gain	8 (20%)	10 (25%)
Irregular Bleeding/Spotting	12 (30%)	11 (28%)

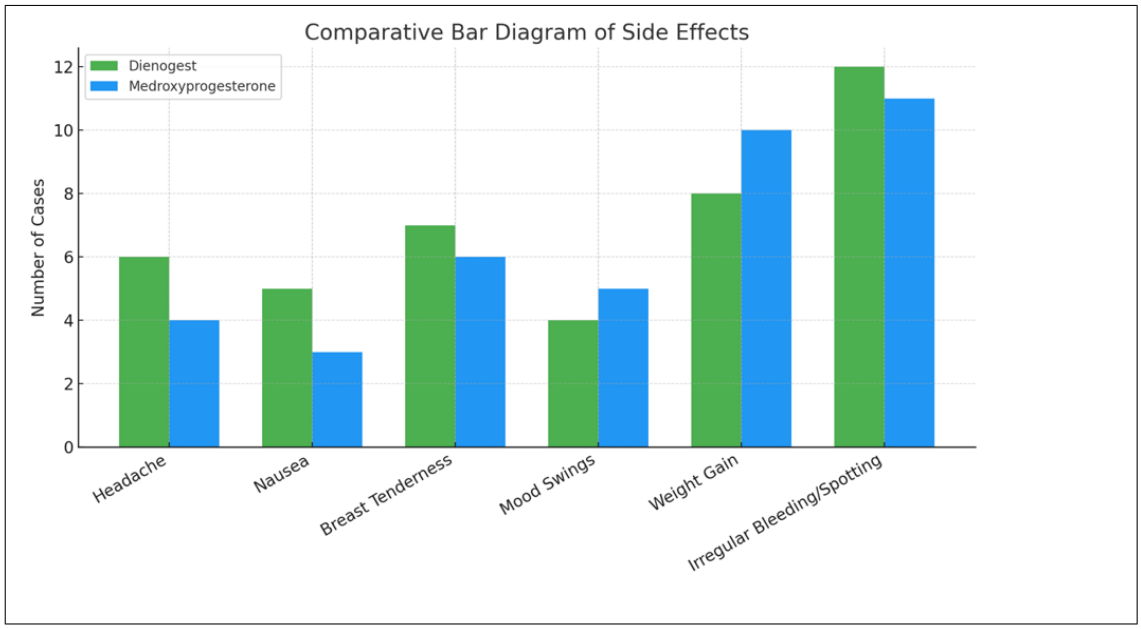

Figure 3: Comparison of the dienogest and medroxyprogesterone acetate groups in terms of side effects duringtreatment.

Discussion

The findings of this study demonstrate that both dienogest and medroxyprogesterone acetate (MPA) are effectively,in reducing menstrual pain associated with endometriosis, but dienogest appears to offer superior pain relief. After six months of treatment, the mean reduction in menstrual pain scores was significantly greater in the dienogest group compared to the MPA group (2.23 vs. 3.78 on the VAS scale, $p < 0.0001$). This aligns with previous research indicating that dienogest, a selective progesterone receptor modulator, effectively suppresses endometriotic lesions and associated pain by inducing decidualization and atrophy of ectopic endometrial tissue (Köhler et al., 2010) [21]. The pronounced pain reduction with dienogest may also be attributed to its anti-inflammatory properties, which mitigate the production of prostaglandins and cytokines involved in pain pathogenesis (Harada et al., 2010) [16]. Secondary outcomes, including dyspareunia, dyschezia, and pain on internal examination, also showed significant improvements in both groups, with dienogest consistently outperforming MPA. For instance, dyspareunia scores decreased from 6.0 to 1.08 in the dienogest group compared to 1.88 in the MPA group ($p < 0.0001$). These results corroborate studies by Strowitzki et al. (2010), who reported similar efficacy of dienogest in alleviating endometriosis-related pain [19]. The superior performance of dienogest may be due to its continuous oral administration, ensuring stable hormonal suppression, whereas MPA's intramuscular delivery could lead to fluctuating drug levels.

Both treatments were well-tolerated, with no statistically significant differences in adverse effects such as headache, weight gain, or menstrual irregularities. However, dienogest had a marginally lower incidence of side effects, such as weight gain (7.5% vs. 12.5%) and menstrual irregularities (10% vs. 15%), though these differences were not statistically significant ($p > 0.05$). This favorable tolerability profile is consistent with long-term studies highlighting dienogest's suitability for extended use (Momocda et al., 2009) [22]. Notably, MPA was associated with a higher discontinuation rate due to

side effects, which may impact adherence in clinical practice.

The study's limitations include its single-center design and relatively small sample size (n = 80), which may limit generalizability. Additionally, the short follow-up period (6 months) precludes assessment of long-term outcomes, such as recurrence rates or bone mineral density changes, particularly relevant for MPA. Future multicenter studies with larger cohorts and extended follow-up are needed to validate these findings and explore the comparative long-term safety of these therapies.

Conclusions:

In treating symptomatic endometriosis, especially in control of menstrual pain Dienogest is potentially more effective than medroxyprogesterone acetate, with comparable tolerability.

These findings support its use as a first-line hormonal therapy, particularly for patients prioritizing pain relief. But, medroxyprogesterone acetate is a cost effective option as it is supplied free of cost by government of India as a contraceptive. However, individualized treatment plans should consider patient preferences, cost, and accessibility to optimize outcomes in endometriosis care.

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