

**EFFECT OF DIENOGEST AND MEDROXYPROGESTERONE ACETATE (MPA) ON
QUALITY OF LIFE IN ENDOMETRIOSIS: A COMPARATIVE STUDY**¹Dr. Amiya*, ²Dr. Jyoti Kaushal and ³Dr. Savita Rani Singhal¹Resident, Department of Pharmacology, Pt. B. D. Sharma PGIMS, Rohtak, Haryana.²Professor, Department of Pharmacology, Pt. B. D. Sharma PGIMS, Rohtak, Haryana.³Professor and Unit Head, Department of Obstetrics and Gynaecology, Pt. B. D. Sharma PGIMS, Rohtak, Haryana.***Corresponding Author: Dr. Amiya**

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ABSTRACT

Introduction: Endometriosis is common in reproductive women usually between 15 to 49 years age characterized by clinical symptoms like dysmenorrhea, chronic pelvic pain, dyspareunia, dyschezia, irregular uterine bleeding and infertility which can severely affect a woman's quality of life (QOL). This study was done to observe improvement in quality of life after treatment with dienogest versus medroxyprogesterone acetate (MPA) in women with endometriosis. **Materials & Methods:** A prospective, randomized, comparative clinical study was conducted on 60 patients and they were randomly divided in two groups of 30 each to receive either Dienogest 2 mg OD (Group A) or Medroxyprogesterone acetate 10 mg BD (Group B) orally for 12 weeks. Quality of life assessment was done using Endometriosis health profile-30 (EHP-30) Questionnaire. **Results:** At the end of 12 weeks, there was reduction in the scores of all the domains of QOL with both the drugs i.e. pain domain, control & powerlessness domain, emotion domain, social support domain and self-image domain in dienogest group (79.19%, 74.82%, 77.82%, 68.99% and 53.96%) and MPA group (61.86%, 62.58%, 61.30%, 54.48% and 19.03%) respectively as compared to baseline values. On intergroup analysis, dienogest showed statistically significant better response than MPA in reduction of pain & emotional domain ($p=0.004$ & $p=0.012$ respectively). **Conclusion:** Although there was a definite improvement in QOL with both types of treatment in women with endometriosis but on comparing both the groups, dienogest showed more improvement in QOL than MPA especially in pain & emotional domain.

KEYWORDS: Dienogest, medroxyprogesterone acetate, endometriosis, quality of life, endometriosis health profile-30, progestin.

INTRODUCTION

Endometriosis is a common benign and chronic gynaecologic disorder related to the presence of endometrial glands and stroma outside their normal location,^[1] most commonly in the pelvic cavity, including the ovaries, the uterosacral ligaments, and the pouch of Douglas.^[2] It is a relatively common disorder estimated to be experienced by one in ten women during their reproductive years usually between the ages of 15 to 49, which is approximately 176 million women in the world.^[3] The prevalence of pelvic endometriosis is 6–10% in Indian as well as western female population.^[1,4] Symptoms include chronic pelvic pain, dysmenorrhea, dyspareunia, dyschezia, irregular uterine bleeding and infertility in reproductive-age women leading to impairment of quality of life. Dysmenorrhea is the most common symptom in patients with endometriosis.^[1]

Quality of life (QOL) studies show that symptoms of endometriosis impact on many aspects of a woman's life, including work and education, relationships, and social

functioning.^[5,6,7] In a recent international survey, women with endometriosis reported a substantial 38% reduction in work productivity, which was attributable primarily to reduced work effectiveness in the presence of pelvic pain.^[8] Endometriosis also impacts mental health, with one study showing that 87% of the women investigated with endometriosis had depressive symptoms and 88% had anxiety.^[9] Disease specific endometriosis health profile questionnaire (EHP-30) is used to assess the health related QOL in women with Endometriosis.

Clinical interventions in women having endometriosis that influence chronic pelvic pain, dysmenorrhea, dyspareunia or dyschezia would be expected to improve overall QOL. According to major international guidelines, progestines with or without estrogens, should be considered as first line medical therapy for symptomatic endometriosis.^[10] Progestins such as medroxyprogesterone acetate and dienogest have been shown to improve all these somatic problems in patients with endometriosis.^[11-13] There are few studies depicting

impact of these drugs on quality of life.^[14,15] This study was done to assess and compare the effect of these two drugs on quality of life in women with endometriosis.

MATERIALS AND METHODS

This was a prospective, open label, randomized, comparative clinical study conducted by the Department of Pharmacology and Obstetrics & Gynaecology, Pt. B. D. Sharma PGIMS, Rohtak on 60 patients. Study was in accordance with the principles of good clinical practice (ICH-GCP) and declaration of Helsinki. An informed consent was obtained from all patients enrolled for the study and the study was done after obtaining the ethical clearance from institutional ethical committee. (IEC/Th/17/pharma03, dated: 5/12/2017). Patients enrolled in the study were randomized with the help of computer generated random numbers to allocate the treatment schedule. 79 patients with symptoms of endometriosis were screened and selected as per the inclusion and exclusion criteria for this study. Out of this, 6 patients did not fulfil the predefined inclusion criteria, 2 patients were excluded as they were not willing to give informed consent and 11 patients were lost in follow up, total 60 patients completed the study (Figure 1).

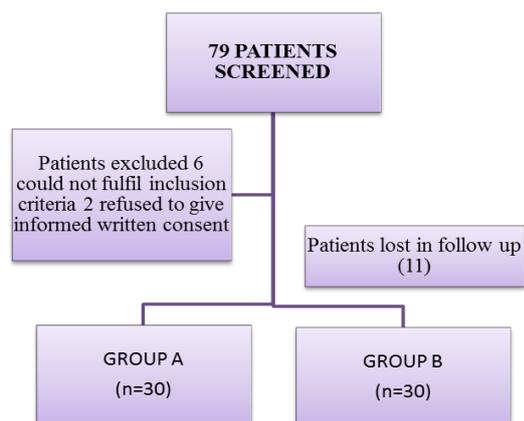


Figure 1: Enrolment of study population.

A total of 60 patients aged 18-40 years were divided in two groups of 30 patients each. The patients were randomly allocated to receive any of two different treatments. All the patients were explained about the study through patient information sheet and informed consent was obtained. The inclusion criteria included females of reproductive age group (18-40 yrs.), diagnosed with endometriosis either by clinical criteria (i.e. definitive presence of nodule in pouch of Douglas or cervix or fixed retroverted uterus) and ultrasonography (thickened and heterogenous endometrium, intracavitary/cul-de-sac fluid) or by laproscopic examination to diagnose and locate pelvic endometriosis and patients who were willing to give a written informed consent. Exclusion criteria were pelvic inflammatory disease, allergy to progestin, contraindications to progestin, neoplastic disease, pregnant and nursing mothers, any history of hormonal agents intake in last 3 months, smokers and alcoholic subjects, inability to

come for regular follow ups. The eligible patients after screening were randomly allocated to two treatment groups. Each study group had 30 patients and received one of the following treatments orally for a period of 12 weeks: Group A received Dienogest 2 mg OD while Group B received Medroxyprogesterone acetate 10 mg BD. Available commercial preparations (same brand) of the drugs were used. During the study, patients were not permitted to take any non-study hormonal drugs.

Before the treatment was initiated, the physical examination was done to check for any chronic illness. Quality of life was assessed by using Endometriosis health profile-30 (EHP-30) Questionnaire at the end of 12 weeks. This questionnaire was developed by Jones et al., in 2001.^[16] It is a 30 items, multi-dimensional, self-report questionnaire developed to specifically address the impact of the disease on the physical, psychological, and social aspects of patient's lives. It comprises 30 questions which consists of five scales (pain, control and powerlessness, emotional well-being, social support and self-image). Items within scales are summed to create a raw score and then each scale is translated into a score ranging from 0 (best health status) to 100 (worst health status). This scaled score is equal to the total of the raw scores of each item in the scale divided by the maximum possible raw score of all the items in the scale, multiplied by 100.

Data was expressed as Mean \pm SEM. Both intragroup and intergroup statistical analyses were done. Intragroup analysis for repeated measures was done using ANOVA while intergroup analysis was done using unpaired t test. A p-value <0.05 was considered as statistically significant.

RESULTS

The patients in each group were found to be comparable at the time of their initial visit with regard to baseline characteristics such as age, weight, marital status and other parameters (Table 1).

Table 1: Comparison of Study Population Characteristics.

Variables	Group A (n=30)	Group B (n=30)	'p' value
Age in years	26.03 \pm 1.11	26.9 \pm 1.01	0.564
Weight (Kgs)	54.2 \pm 1.83	54.23 \pm 1.82	0.991
Marital Status			
Married	25	28	-
Unmarried	5	2	
Education			
Literate	26	24	-
Illiterate	4	6	
Age at menarche	11.9 \pm 0.21	12.03 \pm 0.19	0.648
History of drug allergy	0	0	-

- Age and weight are expressed as Mean \pm SEM
- Group A: Dienogest 2 mg OD
- Group B: Medroxyprogesterone acetate 10 mg BD

Quality of life was assessed by using Endometriosis health profile-30 (EHP-30) Questionnaire. Assessment of QOL was divided into five domains i.e. pain, control and powerlessness, emotional well-being, social support and self-image. Each domain score of QOL was recorded in all the patients of either group before drug administration (baseline) and at end of 12 weeks. Table 2 shows the changes in domain scores with the treatment. On intragroup analysis, at the end of 12 weeks there was reduction in the scores of all the domains of QOL i.e. pain domain, control & powerlessness domain, emotion

domain, social support domain and self-image domain with both the drugs. In dienogest group, reduction in scores of these domains was 79.19%, 74.82%, 77.82%, 68.99% and 53.96% respectively as compared to baseline values. In medroxyprogesterone acetate group, reduction in the scores of these domains was 61.86%, 62.58%, 61.30%, 54.48% and 19.03% respectively as compared to baseline values. On intergroup analysis, dienogest showed statistically significant better response than medroxyprogesterone acetate in reduction of pain & emotional domain ($p=0.004$ & $p=0.012$ respectively).

Table 2: Comparison of Changes in Scores of Various Domains of QOL In Both The Groups.

EHP-30 domains		Dienogest (Group A) (n=30)		MPA (Group B) (n=30)		p-value (Intergroup)
		Mean \pm SEM	Reduction from baseline (%)	Mean \pm SEM	Reduction from baseline (%)	
Pain domain	Baseline	50.23 \pm 3.35	-	55.61 \pm 2.73	-	0.218
	12 Weeks	10.45 \pm 2.78**	39.78 (79.19%)	21.21 \pm 2.27**	34.4 (61.86%)	0.004 [#]
Control & powerlessness domain	Baseline	39.72 \pm 4.33	-	40.83 \pm 2.99	-	0.834
	12 Weeks	10 \pm 3.79**	29.72 (74.82%)	15.28 \pm 1.95**	25.55 (62.58%)	0.220
Emotion domain	Baseline	29.44 \pm 2.35	-	31.94 \pm 2.15	-	0.436
	12 Weeks	6.53 \pm 1.68**	22.91 (77.82%)	12.36 \pm 1.47**	19.58 (61.30%)	0.012 [#]
Social support domain	Baseline	29.58 \pm 4.51	-	37.08 \pm 4.75	-	0.257
	12 Weeks	9.17 \pm 3.15**	20.41 (68.99%)	16.88 \pm 3.16**	20.2 (54.48%)	0.089
Self-image domain	Baseline	21.11 \pm 3.41	-	17.5 \pm 2.54	-	0.399
	12 Weeks	9.72 \pm 2.47*	11.39 (53.96%)	14.17 \pm 2.62	3.33 (19.03%)	0.221

- All values are expressed as Mean \pm SEM
- Group A: Dienogest 2 mg OD
- Group B: Medroxyprogesterone acetate 10 mg BD

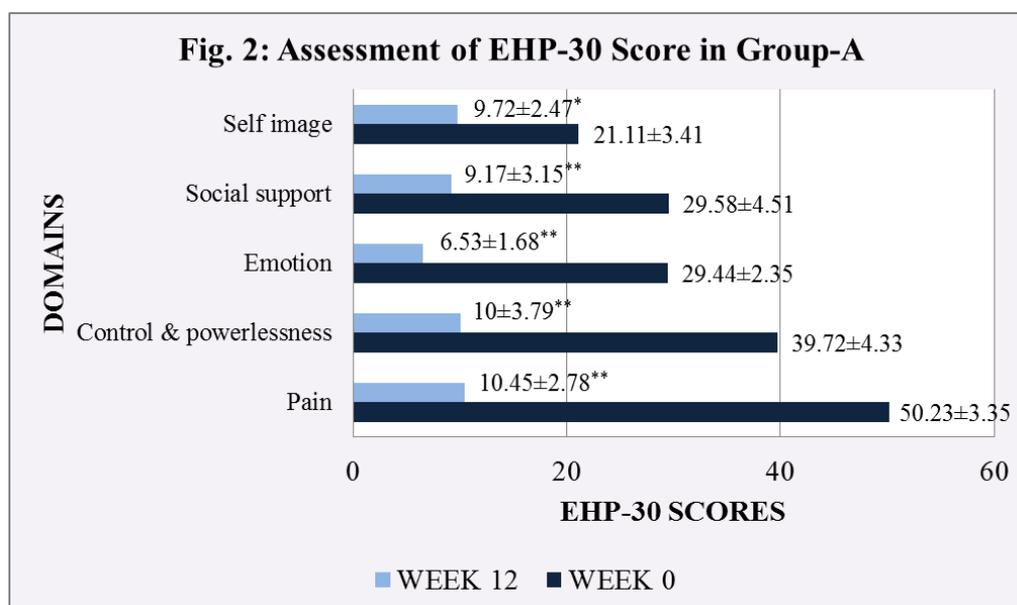
INTRAGROUP ANALYSIS

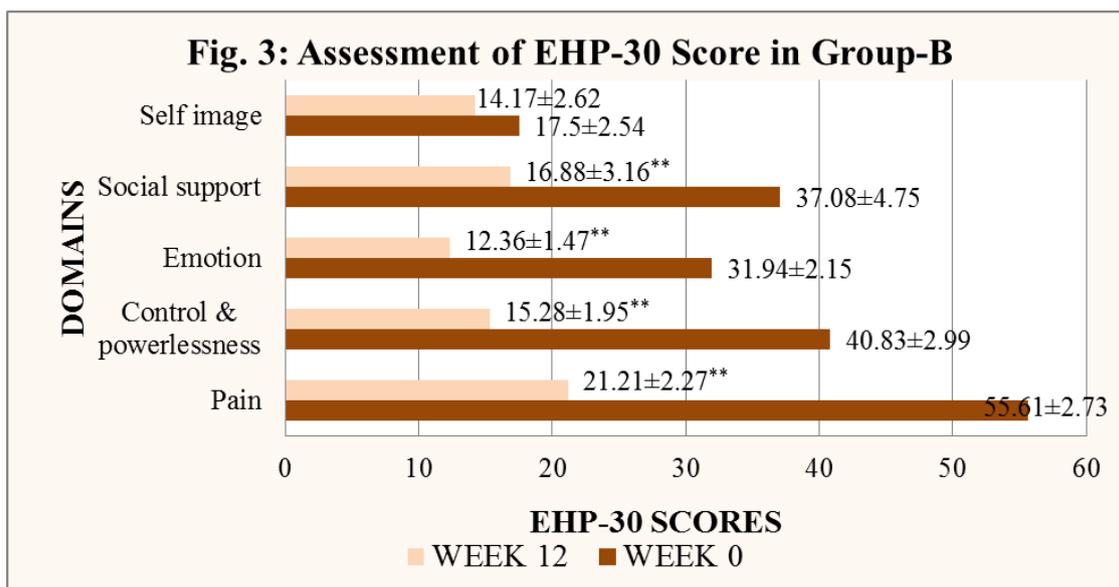
* Comparison of values at end of week 12 with baseline values showing statistically significant difference ($p<0.05$).

** Comparison of values at end of week 12 with baseline values showing statistically highly significant difference ($p<0.001$).

INTERGROUP ANALYSIS

[#] Comparison of values between Group A and B showing statistically significant difference ($p<0.05$)





DISCUSSION

Endometriosis is a common benign and chronic gynaecologic disorder related to the presence of endometrial glands and stroma outside their normal location,^[1] most commonly in the pelvic cavity. The disease often begins in adolescence, but is most often recognized after years of dysmenorrhea.^[2] Although the pathogenesis of endometriosis is complex but is still thought to be principally associated with attachment and implantation of endometrial glands and stroma on the peritoneum from retrograde menstruation.^[17] Specific organ involvement in endometriosis may result in pain or physiologic dysfunction of those organs, such as tenesmus around the menstrual cycle, diarrhoea or constipation, cramping and dyschezia in cases of bowel involvement or dysuria and hematuria in cases of bladder involvement.^[18]

Endometriosis women suffer from marked reductions in quality-of-life, impaired emotional well-being. WHO defined Quality of life as “the concept of an individual of his status in life in relation to the culture and the system of values in which he lives, and in relation to the goals, standards and needs”.^[19] The definition comprises six large areas, namely physical health, emotional status, level of independence, social relations, environmental characteristics and spiritual needs. In 1990, Spilker described the assessment of quality of life by means of three interrelated parameters: global assessment of wellbeing, comprehensive domains (e.g., physical, psychological or social domains) and the individual components of each domain.^[20] These components classified the multidimensional character of quality of life. In the present study assessment of QOL was divided into five domains i.e. (pain, control and powerlessness, emotional well-being, social support, and self-image) on the basis of validated questionnaire given by Jones et al.^[16]

Although exact similar studies were not available in which similar treatment groups were compared for observing the effects on QOL using EHP-30. However after literature search, we could get the study in which effect of dienogest on QOL was observed using EHP-30. In a study done by Morotti et al^[21], after 24 weeks of treatment, quality-of-life was assessed in 25 endometriosis patients who were not satisfied with norethisterone acetate treatment for 6 months & subsequently given dienogest (2 mg/day). Assessment was done using EHP-30 questionnaire after the treatment. During this treatment decrease in several domains of EHP-30 (pain, control and powerlessness, self-image) was observed with respect to baseline. There was also an overall improvement in QOL (54.10±6.73) with dienogest. The findings of our study are quite similar to the above mentioned study as there was an improvement in pain, control and powerlessness, self-image domains of EHP-30. In addition emotional domain & social support domain were also assessed and found to be improved in our study. However, the exact comparison is not possible. The reason could be that they evaluated the effect at the end of 24 weeks whereas it was at the end of 12 weeks in our study.

In a study done by Kennedy S et al^[15], which was a randomized, evaluator-blinded, multicenter study, comparing 6 months treatment with Depot Medroxyprogesterone Acetate (DMPA) and leuprolide acetate (LA) on quality of life in endometriosis in patients with endometriosis-associated pain. After 6 months of treatment, there was a substantial effect on the pain dimension (1.67), powerlessness (1.32) and emotional well-being (0.91). Smaller effect was found for the social support (0.76), self-image (0.54) domains, but all indicated positive improvement. The findings of our study are quite similar to the above mentioned study as there was an improvement in all domains of EHP-30 in both the studies. But exact comparison is not possible as they used DMPA in their study whereas it was oral

MPA in our study. Moreover intergroup comparison is not possible as they compared with leuprolide acetate whereas it was compared with dienogest in our study.

CONCLUSION

Both treatment groups i.e. Dienogest and Medoxyprogesterone acetate (MPA) showed improved quality of life in patients suffering from endometriosis. On comparing the above mentioned treatment groups, dienogest showed more improvement in quality of life than MPA especially in pain & emotional domain. Hence, in our study dienogest was found to be the better treatment option for endometriosis patients.

However, more studies observing the effect of treatment on QOL would be beneficial in order to provide guidance in making clinical decision to prescribing physicians. In addition, further studies are required to explore the impact of endometriosis upon QOL and the effect of drugs improving the QOL.

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