ORIGINAL RESEARCH

Assessment of efficacy and safety of 2 mg and 4 mg Dienogest in endometriosis

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ABSTRACT

Background: Nearly 10% of women of reproductive age suffer with endometriosis, a chronic inflammatory disorder marked by the presence of tissue resembling the endometrium outside the uterus, such as the ovaries and other pelvic structures. The present study was conducted to assess efficacy and safety of 2 mg and 4 mg Dienogest in endometriosis.**Materials & Methods:**50 women aged 20-45 years suffering from endometriosiswere divided into 2 groups of 25 each. Group I received 2 mg Dienogest and group II received 4 mg, Dienogest for 24 weeks. Relief of EAPP was assessed using the visual analogue scale (VAS) score and improvement in quality of life (QoL) was measured.**Results:** The mean age (years) was 27.2 and 27.8, weight (kgs) was 56.4 and 54.3, height (cm) was 148.7 and 149.5, BMI (kg/m2) was 27.2 and 27.9, history of infertility was seen in 9 and 12 and CA125 level (IU/mL) was 91.5 and 96.4 in group I and II respectively. The difference was non- significant (P>0.05). The mean VAS at baseline was 70.4 and 68.5, at 12 weeks was 43.6 and 43.1 and at 24 weeks was 39.7 and 31.6 respectively. Physical health score (QoL) at baseline was 42.7 and 43.8, at 12 weeks was 55.7 and 57.4 and at 24 weeks was 59.2 and 55.1 respectively. The difference was significant (P<0.05). Common adverse events in group I and group II were acne in 2 and 3, decreased libido in 4 and 6, weight gain in 1 and 2 and irregular bleeding in 3 and 5 patients respectively. The difference was significant (P<0.05).**Conclusion:** The best and most successful dose for treating endometriosis is 2 mgDienogest, /day, as it is more tolerable than the 4 mg dose.

Keywords: Dienogest, endometriosis, infertility

INTRODUCTION

Nearly 10% of women of reproductive age suffer with endometriosis, a chronic inflammatory disorder marked by the presence of tissue resembling the endometrium outside the uterus, such as the ovaries and other pelvic structures. Pelvic discomfort, dysmenorrhea, dyspareunia, premenstrual pain, and lower back pain are typical symptoms. There are negative effects on one's social, mental, and physical health from this disorder. The main goal of treatment, in terms of quality of life, is to lessen the agonizing endometriosis symptoms.[1]

Menstrual blood flows backward through the fallopian tubes into the pelvic cavity instead of leaving the body. The endometrial cells then implant and grow outside the uterus.Hormones such as estrogen may transform embryonic cells into endometrial-like cell implants during puberty.After surgeries such as a hysterectomy or C-section, endometrial cells may attach to the surgical incision.[2]Problems with the immune system may make the body unable to recognize and destroy endometrial-like tissue growing outside the uterus.Having a close relative with endometriosis increases the risk.Short menstrual cycles, early menarche, heavy menstrual periods, and low body mass index (BMI) can increase risk.

Although histology of the lesion and laparoscopic examination of the pelvis are usually needed for the diagnosis of endometriosis, new recommendations suggest a non-invasive clinical diagnosis based on clinical symptoms and patient history. There are currently no recommended treatments since they have inferior safety and tolerability, whichlimit their long-termuse.[3]

Dienogest is a selective progestin with a strong local impact on endometrial tissue. It combines the pharmacological qualities of 19-norprogestins and progesterone derivatives in a novel way.[4] By fostering a local progesterone environment, it lessens endometriotic lesions while only slightly decreasing systemic oestrogenic levels. Progestin tolerance is dose-dependent, nevertheless. Regrettably, there aren't enough well-designed studies of long-term Dienogest treatment for endometriosis, particularly in India.[5]The present study was conducted to assess efficacy and safety of 2 mg and 4 mg Dienogest in endometriosis.

MATERIALS & METHODS

The present study was conducted at Department of Gynecological Oncology, IGIMS, Patna, Bihar, India during January 2019 to January 2020.

The present study was conducted on 50 women aged 20-45 years suffering from endometriosis. All were informed regarding the study and their written consent was obtained.

Data such as name, age, etc. was recorded. Patients were divided into 2 groups of 25 each. Group I received 2 mg Dienogest and group II received 4 mg, Dienogest for 24 weeks. Relief of EAPP was assessed using the visual analogue scale (VAS) score and improvement in quality of life (QoL) was measured. Treatment-related adverse events were also recorded.Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Assessment of baseline parameters

Parameters	Group I	Group II	P value
Age (years)	27.2	27.8	0.35
Weight (kgs)	56.4	54.3	0.62
Height (cm)	148.7	149.5	0.57
BMI (kg/m^2)	27.2	27.9	0.84
History of infertility	9	12	0.24
CA125 level (IU/mL)	91.5	96.4	0.89

Table I shows that mean age (years) was 27.2 and 27.8, weight (kgs) was 56.4 and 54.3, height (cm) was 148.7 and 149.5, BMI (kg/m2) was 27.2 and 27.9, history of infertility was seen in 9 and 12 and CA125 level (IU/mL) was 91.5 and 96.4 in group I and II respectively. The difference was non- significant (P>0.05).

Table II Assessment of parameters

Parameters	Variable	Group I	Group II	P value
VAS	Baseline	70.4	68.5	0.94
	12 weeks	43.6	43.1	0.73
	24 weeks	39.7	31.6	0.02
Physical health score (QoL)	Baseline	42.7	43.8	0.12
	12 weeks	55.7	57.4	0.05
	24 weeks	59.2	55.1	0.04

Table II, graph I shows that mean VAS at baseline was 70.4 and 68.5, at 12 weeks was 43.6 and 43.1 and at 24 weeks was 39.7 and 31.6 respectively. Physical health score (QoL) at baseline was 42.7 and 43.8, at 12 weeks was 55.7 and 57.4 and at 24 weeks was 59.2 and 55.1respectively. The difference was significant (P<0.05).

Graph IAssessment of parameters

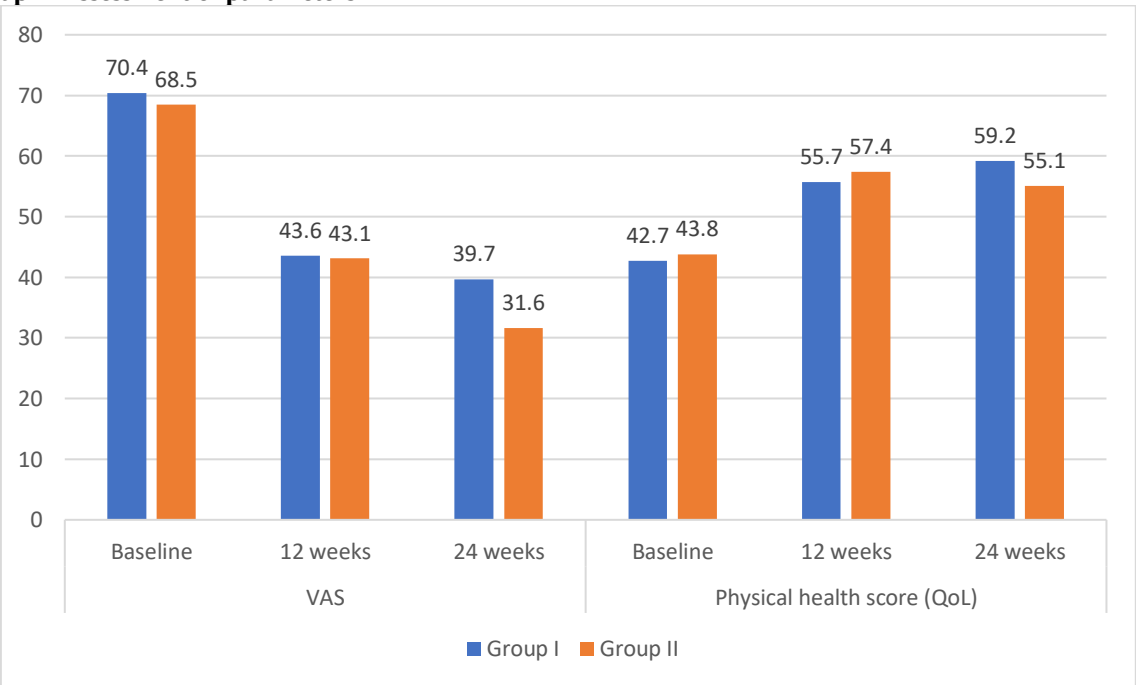

Table III Adverse events

Adverse events	Group I	Group II	P value
Acne	2	3	0.01
Decreased libido	4	6	
Weight gain	1	2	
Irregular bleeding	3	5	

Table III shows that common adverse events in group I and group II were acne in 2 and 3, decreased libido in 4 and 6, weight gain in 1 and 2 and irregular bleeding in 3 and 5 patients respectively. The difference was significant (P<0.05).

DISCUSSION

Nearly 10% of women of reproductive age suffer with endometriosis, a chronic inflammatory disorder marked by the presence of tissue resembling the endometrium outside the uterus, such as the ovaries and other pelvic structures.[6] Pelvic discomfort, dysmenorrhea, dyspareunia, premenstrual pain, and lower back pain are typical symptoms.[7] This illness has a negative effect on one's social, emotional, and physical health. Reducing the uncomfortable symptoms related to endometriosis is the main goal of treatment in terms of quality of life.[8]Although histology of the lesion and laparoscopic examination of the pelvis are usually needed for the diagnosis of endometriosis, new recommendations suggest a non-invasive clinical diagnosis based on clinical symptoms and patient history.[9] The present study was conducted to assess efficacy and safety of 2 mg and 4 mg Dienogest in endometriosis.

We found that mean age (years) was 27.2 and 27.8, weight (kgs) was 56.4 and 54.3, height (cm) was 148.7 and 149.5, BMI (kg/m2) was 27.2 and 27.9, history of infertility was seen in 9 and 12 and CA125 level (IU/mL) was 91.5 and 96.4 in group I and II respectively. Biswas et al[10]compared the efficacy and safety of Dienogest at doses of 2 mg and 4 mg/day orally in the treatment of endometriosis. The absolute reduction in pelvic pain VAS score was 39.71±8.60 at 24 weeks from the initial score of 70.88 (Mean VAS score before treatment with Dienogest) in Group A, compared to 34.80±6.45 from 69.34 (Mean VAS score before treatment with Dienogest) in Group B (p=0.0001). The difference in mean VAS at 24 weeks between the two groups was statistically significant (p=0.0002). At 24 weeks, 18 (24.66%) patients in Group A experienced an irregular bleeding pattern compared to 27 (40.30%) in Group B, with spotting being the most common issue. Adverse effects such as weight gain, acne, alopecia, depression, and decreased libido were observed in both groups, but they were more pronounced in the 4 mg group.

We found that mean VAS at baseline was 70.4 and 68.5, at 12 weekswas 43.6 and 43.1 and at 24 weeks was 39.7 and 31.6 respectively. Physical health score (QoL) at baseline was 42.7 and 43.8, at 12 weeks was 55.7 and 57.4 and at 24 weeks was 59.2 and 55.1 respectively. Momoeda et al[11] in this study, 187 patients diagnosed with endometriosis were enrolled and randomized to three groups, and were administered orally with 1, 2, or 4 mg/day of dienogest for 24 weeks. The proportion of patients assessed as improved in global efficacy resulted in 63.8%, 66.7%, or 73.2% with 1, 2, or 4mg/day group, respectively; no statistically significant dose-response relationship was found. The proportion of patients assessed as tolerable in global safety resulted in 85.2%, 95.0%, or 82.3%, respectively; also no significance was found there. The most common adverse event was genital bleeding which was observed at almost the same frequency and severity in the three groups, however the bleeding was well tolerated in all the groups. Serum estradiol levels were not changed in 1 mg/day group, but decreased significantly in 2 and 4 mg/day groups. In addition, the mean estradiol level in the 2 mg/day group (37.4 pg/mL) was within recommended levels (30 to 50 pg/mL) of the "Therapeutic window" theory for efficacy and safety in the medical treatment of endometriosis, whereas below the window in the 4mg/day group (26.2pg/mL). Conclusions All dienogest doses (1, 2, or 4 mg/day) showed high efficacy and tolerability. Dienogest at a dose of 2 mg/day is thought to be suitable for the treatment of endometriosis.

We observed that common adverse events in group I and group II were acne in 2 and 3, decreased libido in 4 and 6, weight gain in 1 and 2 and irregular bleeding in 3 and 5 patients respectively.Schindler et al[12]demonstrated that dienogest 2 mg daily effectively alleviates the painful symptoms of endometriosis, reduces endometriotic lesions, and improves indices of quality of life. Dienogest showed a favorable safety and tolerability profile in these studies, with predictable adverse effects, high rates of patient compliance, and low withdrawal rates.

The shortcoming of the study is small sample size.

CONCLUSION

Authors found that the best and most successful dose for treating endometriosis is 2 mgDienogest, /day, as it is more tolerable than the 4 mg dose.

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