

Improve the Quality of Life of Women and Reduce Clinical and Morphological Features of Endometriosis under the Influence of Dienogest Preparation

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Abstract:

Background: the aim of our study was to analyze the effect of dienogest on the endometroidglands in the myometrium. Atransvaginalsonographic morphologic assessment of the effect of the drugs, taking into account its safety, as well as as an assessment of changes in the quality of life of women associated with decreases in the severity symptomsof adenomyosis and endometriosis. **Objectives:** To evaluate the effectiveness of Dienogestin improving quality of life to reduce clinical manifestation of adenomyosis. **Methods:** It is a randomized control study conducted from January 2022 to December 2023 that included women aged 20-50 years,which is diagnosed as adenomyosisby clinical presentation manifested by the presence of pelvic pain,abnormal uterine bleeding, painful, and or heavy menstruation,as well as the presence of anemia andtransvaginalsonography. Patients were divided into 3 groups depending on the name of the drugs that they used. 20 patients of group 1 receivedthe drug “dienogest” at 2 mg/day for 6 months. The second group received the combined oral contraceptive drug, “Marvelon “which contains estrogen and progesterone. The third group included 20patients who received only progesterone “medroxy”10 mg continuously for 6 months. **Result:** After the starting of drugs for 6-12 months bloody discharge from the genital tract in group 1 completely stopped in all 8 women. In group ii, the discharge decreased in 3 women and completely stopped in 6 women. In group iii, the discharge decreased in 3 women and completely stopped in 5 women. pain in

group 1 completely stopped in 5 women out of 6(83.3%) and 2 women decreased pain out of 6 (33.4%) in the second group the pain stopped completely in 6 women out of 10 (58.3%) and decreased in 4 women out of 10 (34.66%). In the third group, pain completely recovered in 6 out of 10 (60%) and decreased in 4 women out of 10 (40%). According to transvaginalsonographic evidence of myometrium with endometroid glands before treatment, group 1 had 12.2 ± 3.8 glands before treatment and $1.4 \pm .8$ after treatment. In the second group, the number of glands before treatment was 10.8 ± 1.4 and after treatment $3.8 \pm .7$ glands.in the third group before treatment, 6.7 ± 2.1 endometroid glands were determined and after treatment 2.7 ± 1.4 glands in the field of view. **Conclusion:** Dienogest is effective in the treatment of endometriosis and reduces both the clinical manifestations of adenomyosis (abnormal uterine bleeding and chronic pelvic pain)and increases hemoglobin levels, together with a decrease in the activity of the endometroid glands in the myometrium. Dienogest is highly selective progesterone against progesterone receptors and hasanti-proliferative activity in isolated human endometrial cells. Given the indicators of the 25- item short-form survey questionnaire, the quality of life in allthe studied groups improved in all parameters, which indicates the effectiveness of the dienogest-containing drugs used.

Keywords: Adenomyosis, medical treatment, pelvic pain, abnormal uterine bleeding, dienogest, marvelon, medroxy.

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Introduction:

Adenomyosis is a common gynecological disease in late reproductive age and pre-menopausal women. It is also found in early reproductive age.¹ The most common symptoms are progressive menorrhagia, dysmenorrhea, chronic pelvic pain, dyspareunia, heavy menstrual bleeding, and abnormal uterine bleeding.² The severity and frequency of symptoms often correlate with the size and depth of the inclusion of the endometrium in the myometrium, which corresponds to the pathology of endometriosis and disease progression.³ As a rule, diffuse spherical enlargement of the uterus is the main sign of adenomyosis, and the size in this case usually does not exceed 12 weeks of

pregnancy. such an increase in the uterus is associated with the reaction of the myometrium to the penetration of the endometrial glands, and the development of hypertrophy of altered myocytes, around the glandular elements.⁴ Adenomyosis diagnosis confirmed by histopathology. However, our study did not include histopathology.

Currently, dienogest containing preparations is dienogest. It is characterized by high bioavailability and has a pronounced progestin effect, due to its high selectivity to the progesterone receptor. It is reported that it is one of the progestogens with the strongest effect on the endometrium.⁵ Its half-life is 9-10 hours, and kidneys excrete it by approximately 90%. The therapeutic dose of dienogest for the treatment of endometriosis, and adenomyosis is 2mg per day, providing a blood level of 10.7mol/l. Although the dienogest in the blood after oral administration is very low, the symptoms of endometriosis are reduced.⁶ our study aimed to study the effect of dienogest on the endometriotic glands in the myometrium, a sonological assessment of the effect of the drugs, and also an assessment of changes in the quality of life of women associated with a decrease in the severity of symptoms of the manifestation of adenomyosis.^{7,8}

Damage to the myometrial junction caused by adenomyosis leads to the displacement of the endometrium into the surrounding myometrium, where the myometrial cells proliferate and undergo metaplasia, which leads to a thickening in the junction of the endometrium and the myometrium.^{9,10} Against the background of taking hormonal preparation containing dienogest, degradation, and atrophy of the endometroid glands in myometrium is determined.¹¹ Using dienogest, a pronounced clinical effect is determined, manifested in a decrease in the symptoms of endometriosis, the frequency of dysmenorrhea, chronic pelvic pain and other sign also reduced. In addition, the volume of menstrual blood loss decreases and, as a result, the incidence of anemia in patients with adenomyosis decreases.^{12,13}

Methods:

A randomized control study was conducted from January 2022 to December 2023 based on the Ibn Sina Superspecialist Hospital's gynecology department in Dhaka. The study included women aged 20-50 years who are manifested in the presence of pelvic

pain, abnormal uterine bleeding, painful and or heavy menstruation, as well as the presence of anemia. All patients were divided into three groups, and each group contained 20 patients. Before starting drugs transvaginal sonography was done for all. Then they were prescribed dienogest for the first group, for the second group combined oral contraceptive pill, and third group medroxy progesterone. Drugs prescribed for 6 months. The inclusion criteria were chronic pelvic pain, anemia, infertility, and sonographic evidence of adenomyosis. The exclusion criteria were patients with liver, kidney, autoimmune diseases, coagulopathies, endometrioid cysts, or receiving hormone therapy were also excluded.

The study included 60 patients whose age was 20-50 years, while ultrasonographic diagnostic criteria for these patients included the enlarged uterus, anteroposterior asymmetry of the myometrium, poorly defined areas in the myometrium, the heterogeneous texture of the myometrium, small cystic areas in the myometrium. Randomization was carried out by dividing patients into three groups depending on the name of the drugs that they used. 20 patients of group 1 received the drugs dienogest at 2 mg /day for 6 months. In the second group, 20 patients received the oral contraceptive pill marvelon containing 2 mg estradiol valerate +3 mg dienogest. The third group included 20 patients who received medroxy progesterone continuously for 6 months. The phase of the menstrual cycle was determined by the last menstrual period in patients. After hormonal therapy for 6 months, the patients included in the study underwent repeat transvaginal sonography to see the sonographic morphological changes in the presence of the drugs. In addition, life quality assessment indicators were evaluated (reduction in pelvic pain, decrease in menstrual blood loss resulting increase in hemoglobin level)

Result:

Each parameter is presented as mean \pm standard deviation or median 25 (75%) depending on the data distribution. Clinical characters were compared using a student's t-test for the difference between the two groups. It was analyzed using the nonparametric Mann-Whitney U test; a value of $p < 0.05$ was considered statistically significant. According to the study parameters of hemoglobin level in gram per liter, mild chronic iron deficiency anemia due to an

increased volume of menstrual blood loss was detected in group one in 6 out of 20 patients, (33.3%), with a hemoglobin index of 96 ± 4.8 gm /l, second group 8 out of 20 patients (40.6%) with 98 ± 5.3 g/l and the third group 5 out of 20 patients (25%) with 98.8 ± 5.1 g/l. this study included patients only iron deficiency anemia. After starting the treatment in three groups for 6 months the hemoglobin index increased in group I by 22.6 ± 3.4 g/l, in group II hemoglobin increased by 23.5 ± 2.6 g/l and in group III hemoglobin increased by 17.2 ± 2.8 g/l. After appointment of drugs for 6 months, bloody discharge from the genital tract in group I completely stopped in all 8 women in group II, the discharge decreased in four women and completely stopped in 8 women, and in group III, the discharge decreased in 3 women and completely stopped in 7 women. Pain in the group stopped in 4 out of 6 (66.66%) and decreased in 2 women (33.34%). In the second group, the pain stopped completely in 6 women out of 10 women (60%) and decreased in 4 women (40%), in group III pain disappeared 5 out of 10 women (50%). Figure 1 shows the sonographic features of adenomyosis before treatment. Figure II shows the uterus after the dienogest used for 6 months of therapy

Table-I: Comparison of the scoring parameters of the quality of life of the structure question 25 before and after treatment in the dienogest comparison group 1

Grade scale	Group 1 before treatment	Group 1 after treatment
Dysmenorrhea	$72.4 \pm 2.6^*$	82.4 ± 4.2
Menorrhagia	$70.2 \pm 3.6^*$	$90.5 \pm 2.1^*$
Dyspareunia	$71.2 \pm 5.2^{**}$	$84.5 \pm 1.9^*$
Chronic pelvic pain	$60.1 \pm 4.8^{**}$	$80.2 \pm 3.8^*$
General Health	$61.6 \pm 6.4^{**}$	$83.5 \pm 5.1^{**}$

*p<0.01, **p<0.05

Table-II: Comparison of the scoring parameters of the quality of life scales of the questionnaire before and after treatment in Marvelon comparison group II

Grading scales	Group II before treatment	Group II after treatment
Dysmenorrhea	$60.1 \pm 2.6^*$	$71 \pm 2.1^*$
Menorrhagia	$62.2 \pm 3.3^*$	$72 \pm 3.1^*$
Dyspareunia	$64 \pm 3.2^*$	$74 \pm 2.6^*$
Chronic pelvic pain	$54 \pm 8.2^{**}$	$64 \pm 3.9^*$
General Health	$52 \pm 5.6^{**}$	$64 \pm 5.7^{**}$

*p<0.01, **p<0.05

Table-III: Comparison of the scoring parameters of the quality of life scales of the questionnaire before and after treatment in medroxy progesterone comparison group III

Grading scales	Group III before treatment	Group III after treatment
Dysmenorrhea	$74 \pm 3.1^*$	$82.3 \pm 2.1^*$
Menorrhagia	$64 \pm 3.2^*$	$70 \pm 3.2^*$
Dyspareunia	$70 \pm 3.4^*$	$70 \pm 4.4^*$
Chronic pelvic pain	$62 \pm 6.4^{**}$	$70 \pm 4.7^*$
General health	$68 \pm 7.2^{**}$	$70 \pm 2.2^*$

*p<0.01, **p<0.05

Table-IV: Comparison of social functioning between 3 groups before and after treatment.

Social functioning	Group I before treatment	Group I after treatment	Group II before treatment	Group II after treatment	Group III before treatment	Group III after treatment
Disturbance in education	62.3 ± 2.4	$84.5 \pm 5.6^{**}$	$54 \pm 6.2^{**}$	$73 \pm 1.4^{**}$	$58 \pm 3.9^*$	$72.1 \pm 1.9^*$
Disturbance in performing job	$60.2 \pm 4.3^{**}$	$80.1 \pm 3.8^*$	$54 \pm 6.2^{**}$	$73 \pm 1.4^*$	$57.1 \pm 3.1^*$	$68.3 \pm 1.2^*$
Disturbance in performing house hold work	$61.3 \pm 6.4^{**}$	$83.5 \pm 5.1^{**}$	$58.2 \pm 3.2^*$	$71.1 \pm 6.5^{**}$	$60.3 \pm 3.5^*$	$70.6 \pm 1.2^*$

Table-V: Comparison of mental health between 3 groups before and after treatment

Mental health	Group I before treatment	Group I after treatment	Group II before treatment	Group II after treatment	Group III before treatment	Group III after treatment
depression	$66.7 \pm 4.7^*$	86.3 ± 1.2	$64 \pm 4.8^{**}$	74 ± 3.2	$64 \pm 3.1^*$	$73 \pm 5.4^{**}$
anxiety	$70.1 \pm 4.1^*$	$85.1 \pm 2.1^*$	$68.3 \pm 2.3^*$	$73.2 \pm 3.1^*$	65 ± 1.2	71.2 ± 1.3

Table-VI: Comparison of hemoglobin index increases between 3 groups before and after treatment.

Group	Number of patients	Hb index before treatment	Hb index increases after treatment
Group 1	6(34.3%)	96 ± 4.8 gm /l	22.6 ± 3.4 g/l
Group II	8(40.6%)	98 ± 5.3 g/l	23.5 ± 2.6 g/l
Group III	5(25%)	98.8 ± 5.1 g/l	17.2 ± 2.8 g/l

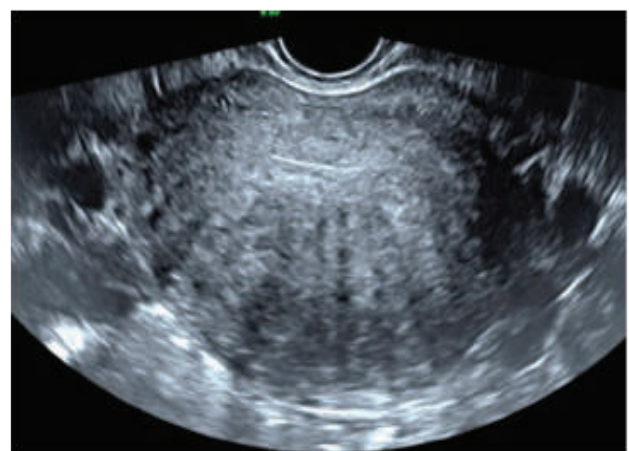


Figure-1: Adenomyotic changes in ultrasonography

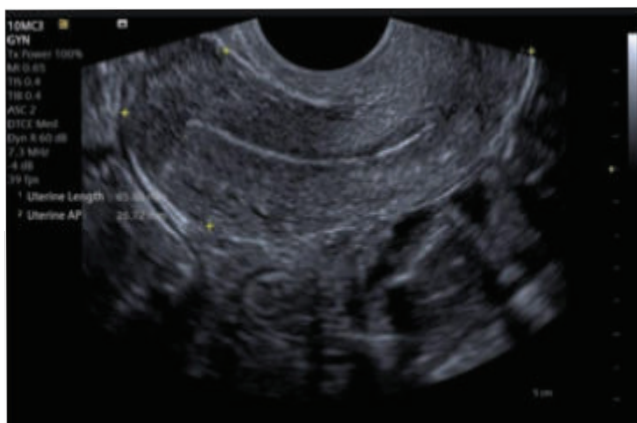


Figure-2: Normal findings of uterus in ultrasonography.

Discussion:

This randomized controlled trial compared the number and severity of endometrial glands in the myometrium in women with adenomyosis after 6 months of treatment with dienogest and in women before treatment. The results showed that dienogest-containing preparations statistically significantly reduced the number and activity of the glandular structure of the ectopic endometrium. This suggests that progestin has a direct effect on the endometrioid glands in addition to its systemic effect, and thus may contribute to their atrophy.¹¹

Dienogest is effective in the treatment of endometriosis and reduces both the clinical manifestations of adenomyosis (abnormal uterine bleeding and chronic pelvic pain) and laboratory blood counts, increasing hemoglobin levels, together with a decrease in the activity of the endometrioid glands in myometrium.⁵ Dienogest is a highly selective progestogen against progesterone receptors and has antiproliferative activity in isolated human endometrial cells. The quality of life in all the studied groups improved in all parameters, indicating the effectiveness of the drug.⁷ To date, a significant amount of data has accumulated confirming the clinical efficacy of dienogest in the treatment of endometriosis.¹⁵ In addition, against the background of prolonged dienogest therapy, the likelihood of recurrence of adenomyosis is significantly reduced.

In our study, each study group had the same number of participants, and the cohort had homogenous features. We sought to investigate the effects of progestogen on the endometrioid glands and the clinical manifestations of endometriosis. However, further studies in the field of proliferation or apoptosis of the endometrioid glands are still needed.

To date, a dienogest, both independently and as a progestogen component of combined oral contraceptives, has proven to be a highly effective treatment for the main symptoms of adenomyosis and relapse after stopping treatment. It is similar in the another study.¹⁴ So dienogest allows us to recommend them for the purpose of long term therapy of adenomyosis.

Conclusion:

Dienogest is effective in the treatment of endometriosis and adenomyosis. It reduces both the clinical manifestation of adenomyosis (abnormal uterine bleeding, chronic pelvic pain.) and increases hemoglobin levels, together with a decrease in the activity of the endometrioid glands in the myometrium. Dienogest is highly selective progesterone against progesterone receptors and has anti-proliferative activity in isolated human endometrial cells. Given the indicators of the 25-item short form survey questionnaire, the quality of life in all studied groups improved in all parameters, which indicates the effectiveness of the dienogest containing drugs used.

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