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Clinical Efficacy of Dienogest and Levonorgestrel-Releasing Intrauterine System in the Treatment of Adenomyosis

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Abstract: *Objective:* To compare the clinical efficacy and adverse reactions of dienogest and levonorgestrel-releasing intrauterine system in the treatment of adenomyosis. *Methods:* A total of 60 cases of adenomyosis admitted to Dezhou Women and Children's Hospital from January 2020 to October 2021 were selected and randomly divided into two groups (Group A and Group B), which were initiated on dienogest and levonorgestrel-releasing intrauterine system, respectively. The therapeutic effects and adverse reactions of the two groups were analyzed. *Results:* After 6 months of treatment, the uterine volume in the LNG-IUS group reduced slightly compared with that before treatment, with no statistical significance ($p > 0.05$), while that in the DNG group increased slightly compared with that before treatment, with no statistical significance ($p > 0.05$). After 6 months of treatment, the hemoglobin of patients in both groups increased compared with that before treatment; there was no significant difference in the DNG group ($p > 0.05$), but there was significant difference in the LNG-IUS group ($p < 0.01$). After 6 months of treatment, the VAS scores of the two groups were significantly lower than those before treatment ($p < 0.01$); the serum CA125 level in both groups decreased significantly compared with that before treatment ($p < 0.01$). *Conclusion:* Mirena (levonorgestrel-releasing intrauterine system) has better therapeutic effect on adenomyosis and fewer adverse reactions than deinogest.

Keywords: Adenomyosis; Deinogest; Levonorgestrel-releasing intrauterine system; Clinical efficacy

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1. Introduction

Adenomyosis refers to the invasion and growth of endometrial glands and stroma into the myometrium. The main clinical manifestations include dysmenorrhea, excessive menstruation, gradual enlargement of the uterus, and infertility [1]. As a chronic disease, adenomyosis requires long-term management. Patients have suffered considerable physical and mental damage as a result of the disease's uncertain cause and limited therapeutic options. Although the curative effect of surgery is significant, it causes trauma, complications, and affects the reproductive function of patients. The main treatment for adenomyosis is drug therapy. Non-steroidal anti-inflammatory drugs, levonorgestrel-releasing intrauterine system, compound oral contraceptives, gonadotropin-releasing hormone agonists, oral progesterone drugs, and other drugs are now the principal pharmacological therapies [1,2].

Deinogest (DNG) was listed in China in 2019. It is a fourth-generation synthetic progesterone, and its therapeutic effect on endometriosis is equivalent to that of GnRH agonists [3]. Adenomyosis and endometriosis are associated; hence, deinogest also has a therapeutic effect on adenomyosis. However, it

has limited clinical application and research at present. The efficacy of DNG and LNG-IUS in the treatment of adenomyosis was compared in this study of 60 patients with adenomyosis.

2. Data and methods

2.1.Study population

A total of 60 patients with adenomyosis in Dezhou Women and Children's Hospital from January 2020 to October 2021 were selected as the research subjects. They were divided into two groups: Group A (DNG group) and Group B (LNG-IUS group).

2.2. Inclusion and exclusion criteria

The inclusion criteria were patients who were diagnosed with adenomyosis based on gynecological examination, relevant auxiliary examination, and medical history, as well as patients with uterus length and diameter of less than 10 cm. These patients were requested to sign the informed consent form. The exclusion criteria were patients with uterine malformation, patients with uterine malignant tumor, patients with submucous myoma and hysteromyoma with a diameter greater than 3 cm, patients with liver and kidney dysfunction, patients with a history of drug allergy; patients who have contraindications to DNG and LNG-IUS.

2.3. Study design

Beginning on any day of their menstrual cycle, the patients in Group A received 2 mg of DNG orally every day for 6 months.

About 5-7 days following menstruation, LNG-IUS was implanted in the uterus of the patients in group B. The same professionally trained doctor carried out the procedure for each patient in the group. Following the procedure, they received anti-infectives and were followed up six months later.

2.4. Observation indicators

The observation indicators were hemoglobin, CA125, uterine volume, visual analog scale (VAS) score, and adverse reactions of the two groups before and 6 months after treatment. The uterine size was measured via ultrasound. The VAS score indicated the degree of pain, wherein 0 indicated no pain, while 10 indicated severe pain.

2.5. Statistical analysis

SPSS 26.0 was used for statistical analysis. Chi-square test was performed for counting data comparison, while t-test was performed for measurement data comparison. $p < 0.05$ indicated that the difference was statistically significant.

3. Results

3.1. General data

As shown in **Table 1**, the average age of patients in the DNG group was 36.7 years old, while in the LNG-IUS group, the average age was 36.9 years old. The average course of disease was 3.5 years and 4.3 years in the DNG group and LNG-IUS group, respectively. The average body mass index (BMI) of patients in the DNG group was 22.1 kg/m^2, while in the LNG-IUS group, the average BMI was 22.7 kg/m^2. There was no statistical significance in the comparison of general data between the two groups ($p > 0.05$).

Table 1. Comparison of general data between the two groups of patients

	DNG group	LNG-IUS group	*p*
Age (years)	36.73 ± 5.19	36.93 ± 5.36	0.38
Course of disease (years)	3.50 ± 1.70	4.30 ± 2.38	0.17
BMI (kg/m^2)	22.10 ± 2.45	22.73 ± 2.59	0.34

3.2. Comparison of clinical efficacy

Table 2 shows the uterine volume, hemoglobin level, VAS score, and CA125 level of the two groups. The uterine volume of the DNG group increased slightly after treatment, in which the difference was not statistically significant ($p > 0.05$). After treatment, the uterine volume of the LNG-IUS group was slightly smaller than that before, but there was no statistical significance ($p > 0.05$); the hemoglobin level, VAS score, and CA125 level, on the other hand, significantly improved ($p < 0.05$).

Table 2. Comparison of clinical efficacy before and after treatment in the two groups

	DNG group		*p*	LNG-IUS group		*p*
	Before treatment	6 months after treatment		Before treatment	6 months after treatment	
Uterine volume (cm^3)	138.93 ± 11.12	140.43 ± 12.03	0.62	140.37 ± 10.20	135.57 ± 9.08	0.06
Hemoglobin (g/L)	111.60 ± 11.70	117.00 ± 11.10	0.07	111.07 ± 14.46	125.37 ± 7.33	< 0.01
VAS score (point)	6.63 ± 2.40	1.90 ± 1.19	< 0.01	6.27 ± 1.96	0.90 ± 0.80	< 0.01
CA125 (U/mL)	66.90 ± 17.34	38.10 ± 8.26	< 0.01	73.60 ± 15.74	34.30 ± 4.04	< 0.01

3.3. Comparison of adverse reactions

As shown in **Table 3**, the proportion of abnormal uterine bleeding in the DNG group was significantly higher than that in LNG-IUS group, accounting for 66.7%, whereas the incidence of abnormal uterine bleeding in the LNG-IUS group accounted for 30.0%. The incidence of headache, weight gain, and depression in the DNG group was 6.7%, respectively; the incidence of breast discomfort accounted for 20.0%, and the incidence of nausea, sleep disorders, and acne was 3.3%, respectively. The incidence of weight gain and acne in the LNG-IUS group accounted for 3.3%, while the incidence of breast discomfort and contraceptive device displacement accounted for 6.7%.

Table 3. Proportion of adverse reactions in the two groups

	DNG group (30)		LNG-IUS group (30)	
	n	%	n	%
Headache	2	6,67	0	0.00
Weight gain	2	6.67	1	3.33
Depression	2	6.67	0	0.00
Abnormal uterine bleeding	20	66.70	9	30.00
Breast discomfort	6	20.00	2	6.67
Nausea	1	3.33	0	0.00
Sleep disorders	1	3.33	0	0.00
Acne	1	3.33	1	3.33
IUD displacement	–	–	2	6.67

4. Discussion

Deinogest is a synthetic progesterone. It is the only progesterone with the characteristics of 19 carbon nortestosterone derivatives and progesterone derivatives at the same time. It has high endometrial activity, in which its activity is 13-24 times that of other types of progesterone. The rationale behind DNG's long-term use in the treatment of endometriosis is that it shrinks the ectopic endometrium by creating an endocrine milieu in the body that has low estrogen and high progesterone [4,5]. The pathogeneses of adenomyosis and endometriosis are similar, which is why they respond similarly to therapy. Levonorgestrel-releasing intrauterine system is an effective approach for treating adenomyosis. It releases levonorgestrel into the uterus at a rate of 20 ug per day for up to five years, creating a high-level progesterone environment in the uterine cavity, reducing the size of the ectopic endometrium, lowering the regulation of estrogen receptors and glands in the interstitial cells of the focus, acting as progesterone in antagonizing endometrial hyperplasia, thinning the endometrium, shrinking the glands, reducing the focus, improving clinical symptoms, and achieving the purpose of treating adenomyosis [6,7].

The uterine volume of patients with adenomyosis is often larger than that of normal uterus. This study showed that the uterine volume of patients with adenomyosis did not improve after 6 months of DNG treatment, which is similar to other research [8,9]. According to foreign studies, although the uterine volume and adenomyosis lesions exhibited declining tendencies after 24 weeks of DNG treatment, the difference was not statistically significant [10]. It is clear that DNG has a limited role in reducing the focus and uterine volume of patients with adenomyosis. In this study, six months after LNG-IUS was implanted in the patients, their uterine volume reduced to a certain extent, which is similar to the results reported in previous studies [11,12]. It is evident that LNG-IUS is more effective in reducing uterine volume.

After receiving DNG and LNG-IUS for six months, the VAS score of patients in this study decreased significantly. In a study, Arisa Takeuchi and several researchers showed that DNG can reduce the expression of nerve growth factor and the density of nerve fibers in patients with adenomyosis [13]. It is evident that DNG and LNG-IUS have good therapeutic effects on dysmenorrhea caused by adenomyosis and endometriosis. At present, CA125 is considered as an important marker for ovarian tumor detection in clinical practice. Individuals with adenomyosis have high serum levels of CA125. Therefore, it is of great significance to reduce the level of CA125 in these patients. This study showed that the level of CA125 in both groups decreased significantly after treatment ($p < 0.01$).

In this study, patients who were treated with DNG for six months did not show any improvement in anemia, and during the treatment, 66.7% of patients experienced abnormal uterine bleeding. According to a study, DNG should only be used in patients with hemoglobin levels over 110 g/L and is not recommended in patients with severe abnormal uterine bleeding or anemia [14]. In the LNG-IUS group, the hemoglobin increased significantly after six months of treatment, and the number of patients with irregular uterine bleeding was significantly less than that of the DNG group. It is evident that LNG-IUS is more suitable for patients with adenomyosis complicated with anemia, which is consistent with Qu Jinhua's research findings [15].

In conclusion, while both approaches can successfully treat adenomyosis, LNG-IUS offers more overt benefits and less adverse effects than DNG. However, the sample size of this study was small, and there was not much time for observation. Hence, future discussions can be made by increasing the sample size and observation time, so as to provide further evidence for drug selection in the treatment of adenomyosis.

Disclosure statement

The authors declare no conflict of interest.

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