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Clinical study on the treatment of abnormal uterine hemorrhage due to anovulatory disorder with deoxygestrel ethinylestradiol tablets and ethinylestradiol cyproterone tablets

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Abstract. Objective: to compare and analyze the clinical value of oxygestrel ethinylestradiol tablets and ethinylestradiol cycloprogesterone tablets in the treatment of abnormal uterine bleeding in patients with ovulation disorders and their inhibitory effects on sex hormones. Methods: 76 patients with abnormal uterine bleeding due to ovulation disorder admitted from January 2018 to January 2021 were selected as the study subjects, and all patients were randomly divided into the Observation Group and the Control Group, with 38 patients in each group. The patients in the Control Group were treated with Deoxygestrel ethinyl estradiol tablets, and the patients in the Observation Group were treated with ethinyl estradiol cycloprogesterone tablets. The changes of clinical indicators hormone levels, adverse reactions during treatment, and quality of life after treatment were compared between both groups. Results: There was no significant difference in hemoglobin (Hb) level, endometrial thickness, menstrual time and menstrual volume between both groups before treatment (P>0.05). After treatment, the Hb level in both groups increased, while that in the Observation Group was higher than that in the Control Group (P<0.05). The endometrial thickness, menstrual time and menstrual volume decreased, while that in the Observation Group was lower than that in the Control Group (P<0.05); there was no significant difference between both groups in luteinizing hormone (LH), follicle stimulating hormone (FSH) and estradiol (E_2) before treatment (P>0.05). After treatment, the levels of LH, FSH and E_2 in both groups were lower than those in the Control Group (P<0.05); there was no significant difference in the total incidence of adverse reactions between both groups (P>0.05); after treatment, the scores of quality of life in both groups were higher, and the scores in the Observation Group were higher than those in the Control Group (P<0.05). Conclusion: the clinical effect of ethinyl estradiol cycloprogesterone tablets on patients with abnormal uterine bleeding due to ovulation disorder is better than that of oxygestrel ethinyl estradiol tablets, which can reduce the clinical symptoms of patients, inhibit the sex hormones, have lower adverse reactions, and can improve the quality of life of patients.

Keywords. Deoxygestrel ethinylestradiol tablets, Ethinylestradiol cycloprogesterone tablets, Ovulation disorder, Abnormal uterine bleeding, Sex hormones, Quality of life.

Abnormal uterine bleeding is a common disease in women. Some patients are prone to anemia when bleeding for a long time or a large amount of time, and even shock in severe cases. There are many reasons for abnormal uterine bleeding, among which ovulation disorder is a common one, which is mainly caused by hypoluteal function and low ovulation [1]. Patients with abnormal uterine bleeding due to ovulatory disorder usually have prolonged menstruation, excessive menstruation, and menstrual disorder. If treatment is not timely, anemia, infertility, infection, and other serious consequences will be caused, which will have a negative impact on the quality of life of patients. Current treatment methods mainly include surgical treatment and drug conservative treatment. Since surgical treatment will bring some trauma to patients, most patients will choose drug conservative treatment [2]. Deoxygestrel ethinylestradiol tablets and ethinylestradiol cycloprogesterone tablets are commonly used to treat abnormal uterine bleeding in clinical practice. Both drugs have significant therapeutic effects, but there is no definite conclusion on the study of the application of the two drugs to treat abnormal uterine bleeding due to ovulation disorder [3]. Therefore, in order to improve the therapeutic effect of abnormal uterine bleeding due to ovulation disorders, 76 patients with abnormal uterine bleeding due to ovulation disorders admitted in our hospital from January 2018 to January 2021 were selected as the research objects, and the clinical value and the inhibitory effect on sex hormones of desoxygestrel ethinylestradiol tablets and ethinylestradiol cycloproterone tablets for abnormal uterine bleeding in patients with ovulation disorders were compared and analyzed. The specific report is as follows.

1. Data and methods

1.1. General information

76 patients with abnormal uterine bleeding due to ovulation disorders admitted in our hospital from January 2018 to January 2021 were selected as the research objects. All patients were randomly divided into the Observation Group and the Control Group according to the ratio of 1:1, with 38 cases in each group. Inclusion criteria: all patients met the diagnostic criteria for abnormal uterine bleeding due to ovulation disorder [4]; no allergy or contraindication to the studied drug; know about this study and sign the consent form. Exclusion criteria: patients with endometrial cancer; those with hysteromyoma or endometrial polyp; abnormal or impaired blood coagulation function; patients with systemic infectious diseases; those who can be pregnant. There was no statistically significant difference in general data between both groups (P>0.05), as shown in Table 1.

1.2. Methods

All patients received routine treatment such as antibiotic, iron supplement and vitamin supplement. Patients in the Control Group were treated with Deoxygestrel ethinylestradiol tablets based on routine treatment, (manufacturer: N.V. Organon; Approval No.: X20000268). Usage: Deoxygestrel ethinylestradiol tablets were taken orally from the fifth day after menstruation, three times a day, two tablets a time. The dosage was changed to 2 tablets twice a day after the bleeding stopped. 3 days after the bleeding stopped, 1 tablet was taken every day. Patients in the Observation Group were treated with ethinylestradiol cycloproterone tablets based on routine treatment (manufacturer: Schering GmbH&Co. Produktions KG; National Drug Approval No.: J2014014), with the same usage as those in the Control Group. Both groups were treated for 3 menstrual cycles.

Table 1. General information of both groups of patients ($\bar{x}$±s, n=38)

Group	Age	Course of Disease (Year)	Bleeding Time (D)
Observation Group	32.21±3.21	4.21±1.24	21.21±2.41
Control Group	32.27±4.26	4.53±1.36	21.47±2.16
Statistical value	0.519	0.464	0.295
P-Value	0.597	0.630	0.745

1.3. Observation index

The changes of hemoglobin (Hb) level, endometrial thickness, menstruation time, menstruation volume and the levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol (E_2) in both groups were observed and recorded before and after treatment for 3 months; the adverse reactions, such as vaginal bleeding, breast pain, dizziness, nausea, etc. of both groups of patients were observed and recorded during the treatment; the quality of life questionnaire (WHOQOL-100) was applied to the patients before and 8 weeks after the operation, which mainly included 6 items: mental health, emotional function, vitality, physiological function, physiological function, and overall health. The full score was 100 points. The higher the patient's score, the better the quality of life [5].

1.4. Statistical methods

The statistics software SPSS 20.0 was used for analyzing the data in the text, and counting data cases was expressed by the number/percentage, χ^2 was inspected; the measurement data was expressed by ($\bar{x}$±s), and *t*-test was adopted; the difference was statistically significant with $P<0.05$.

2. Results

2.1. Changes of clinical indicators of patients in both groups before and after treatment

There was no statistically significant difference in Hb level, endometrial thickness, menstrual time and menstrual volume between both groups before treatment ($P>0.05$). The Hb level of patients in both groups increased after treatment, and the Observation Group was higher than the Control Group ($P<0.05$). The endometrial thickness, menstrual time and menstrual volume decreased, and the Observation Group was lower than the Control Group ($P<0.05$), as shown in Table 2.

Table 2. Changes of clinical indicators of patients in both groups before and after treatment ($\bar{x}$±s, n=38)

Index		Control Group	Observation Group	T-value	P-value
Hb (g/L)	Before treatment	86.32±8.36	86.28±7.23	0.585	0.561
	After treatment	91.71±11.68	116.06±16.44	7.443	0.001
	*t*value	2.313	22.198		
	*P*value	0.023	0.001		
Endometrium thickness (mm)	Before treatment	14.94±2.49	15.12±2.11	0.478	0.633
	After treatment	13.12±1.64	8.59±1.24	7.378	0.001
	t-value	6.661	1.989		
	P-value	0.011	0.049		
Menstrual time (d)	Before treatment	7.57±2.33	7.62±2.05	0.373	0.711
	After treatment	5.64±0.47	4.27±0.38	12.288	0.001
	t-value	4.397	18.881		
	*P*value	0.001	0.001		
Menstruation (ml)	Before treatment	152.85±12.64	153.78±13.52	0.747	0.459
	After treatment	131.28±16.61	56.06±12.34	3.260	0.001
	t-value	2.586	6.380		
	P-Value	0.011	0.001		

2.2. Comparative analysis of hormone level changes in both groups of patients before and after treatment

There was no significant difference in LH, FSH and E_2 before treatment between both groups ($P>0.05$). The levels of

LH, FSH and E_2 in both groups decreased after treatment, and the levels in the Observation Group were lower than those in the Control Group (P<0.05), as shown in Table 3.

Table 3. Comparative analysis of hormone level changes between both groups before and after treatment ($\bar{x}\pm$ s, n=38)

Group	LH (U/L)				FSH (U/L)				E_2 (pmol/L)			
	Before treatment	After treatment	T-Value	P-Value	Before treatment	After treatment	T-Value	P-Value	Before treatment	After treatment	T-Value	P-Value
Control Group	13.32 ± 3.36	10.87 ± 1.68	2.114	0.040	13.58 ± 1.15	12.32 ± 4.78	2.491	0.014	483.94 ± 61.49	425.59 ± 55.24	1.989	0.049
Observation Group	13.28 ± 3.23	9.06 ± 1.44	22.198	0.001	13.36 ± 1.52	10.34 ± 1.31	16.899	0.001	485.32 ± 64.11	236.12 ± 41.64	6.661	0.011
T-value			0.585	4.480			0.182	17.365			0.478	7.378
P-value			0.561	0.001			0.856	0.001			0.633	0.001

2.3. Comparison and analysis of adverse reactions of both groups of patients

There was no significant difference in the total incidence of adverse reactions between both groups (χ^2=5.905, P=0.015 > 0.05), as shown in Table 4.

Table 4. Comparison and analysis of adverse reactions between both groups of patients (n=38)

Group	Vaginal Bleeding (Example)	Breast Tenderness (Example)	Dizzy (Example)	Nausea (Example)	Total [Example (%)]
Observation Group	0	1	1	2	4(10.53)
Control Group	1	2	1	3	7(18.42)

2.4. Comparative analysis of the quality of life of both groups of patients after treatment

After treatment, the quality of life scores of patients in both groups increased, and the scores in the Observation Group were higher than those in the Control Group (P<0.05), as shown in Table 5.

Table 5. Comparison of life quality scores ($\bar{x}\pm$ s, score, n=38)

Group	Quality of Life Score		T-Value	P-Value
	Before treatment	After treatment		
Observation Group	65.68±13.21	84.27±15.26	24.029	0.001
Control Group	65.47±13.02	76.00±12.34	21.134	0.001
T-Value	0.323	25.563		
P-Value	0.747	0.001		

3. Discussion

According to the pathogenic factors, abnormal uterine bleeding can be divided into two types: the presence of changes in uterine structure and the absence of changes in uterine structure. Abnormal uterine bleeding due to ovulation disorders belongs to the absence of changes in uterine structure. According to data statistics [6], abnormal uterine bleeding due to ovulation disorders accounts for more than 58% of all abnormal uterine bleeding, which is an important factor of abnormal uterine bleeding at present. Clinically, the patients with abnormal uterine bleeding due to ovulation disorders mainly focus on controlling the amount of bleeding, improving anemia, and adjusting menstruation. Therefore, the intrauterine contraceptive system, short acting contraceptives, progesterone and estrogen are often used for treatment, but there is no specific unified treatment standard. Deoxygestrel ethinylestradiol tablets, also known as oxygestrel ethinylestradiol tablets, are mainly composed of ethinylestradiol and oxygestrel, which belong to estrogen and progesterone respectively. Together, they can supplement the estrogen and progesterone in the patient's body, so as to achieve the effect of hemostasis. However, the treatment cycle of drugs is relatively long, and may damage the immune system. Therefore, more and more clinical scholars recommend that patients with abnormal uterine bleeding due to ovulation disorder should be treated with ethinylestradiol cycloproterone tablets. Ethinylestradiol cycloproprogesterone tablets are the third generation of steroid oral contraceptives. The main components are cycloproprogesterone acetate and estrogen, which can promote the transformation of endometrial secretory phase and play a hemostatic effect. It has been found [7] that ethinylestradiol cycloproprogesterone tablets can inhibit the secretion of ovarian estrogen and gonadotropin to achieve hemostatic effect. Therefore, the therapeutic effects of Deoxygestrel ethinylestradiol tablets and ethinylestradiol cycloproterone tablets were compared in this article, hoping to provide reference for the treatment of abnormal uterine bleeding due to ovulation disorders.

The results of this study showed that there was no significant difference between both groups in hemoglobin (Hb) level, endometrial thickness, menstrual time and menstrual volume before treatment (P>0.05). After treatment, the Hb level of patients in both groups increased, the Observation Group was higher than the Control Group (P<0.05), the endometrial thickness, menstrual time and menstrual volume decreased, and the Observation Group was lower than the Control Group (P<0.05), the application of ethinylestradiol cycloproprogesterone tablets can alleviate the clinical symptoms of patients. This is because it can promote the shedding of endometrium and obtain good hemostatic effect

although there is a certain amount of estrogen in the body of patients with abnormal uterine bleeding due to ovulation disorder. Some studies have found that [8], the use of ethinylestradiol cyclopropro gesterone tablets in the treatment of perimenopausal patients with abnormal uterine bleeding can significantly reduce the amount and time of menstruation, which is consistent with the results of this study; Before treatment, there was no significant difference between both groups in luteinizing hormone (LH), follicle stimulating hormone (FSH) and estradiol (E_2) ($P>0.05$). After treatment, the levels of LH, FSH and E_2 in both groups were lower, and the Observation Group was lower than the Control Group ($P<0.05$). This proved that ethinylestradiol cycloproterone tablets could inhibit the sex hormones. This is because the pituitary secretion of gonadotropin in patients with ovulatory disorder and abnormal uterine bleeding is out of balance, leading to the decrease of the secretion function of the hypothalamus, pituitary and ovary, affecting the ovary and causing ovulation disorder. Through the treatment of ethinylestradiol cyclopropro gesterone tablets, the level of cyclopropro gesterone acetate and estrogen in the patient's body can be supplemented, the endocrine can be adjusted, and the level of sex hormone can be improved; there was no significant difference in the total incidence of adverse reactions between both groups of patients ($P>0.05$). Some studies found that [9], the drug safety was high and the adverse reactions were few during the application of ethinyl estradiol cyclopropro gesterone tablets and deoxypregnant ethinyl estradiol tablets. Only ethinyl estradiol cyclopropro gesterone tablets may have a small amount of gastrointestinal adverse reactions during the administration, but both were within the acceptable range, consistent with the results of this study; after treatment, the scores of quality of life in both groups were higher, and the scores in the Observation Group were higher than those in the Control Group ($P<0.05$). This proves that the application of ethinylestradiol cyclopropro gesterone tablets can improve the quality of life of patients. This is because the treatment of ethinylestradiol cyclopropro gesterone tablets can reduce the amount and time of menstruation of patients on the basis of effective hemostasis, thereby reducing the incidence of anemia and improving the quality of life of patients. At present, most of the drug treatment studies on abnormal uterine bleeding due to ovulation disorder are the analysis of the treatment effect, and few studies analyze the impact of patients' quality of life, which is also the innovation of this study.

To sum up, the clinical effect of using ethinyl estradiol cyclopropro gesterone tablets to treat patients with abnormal uterine bleeding due to ovulation disorder is better than that of oxygestrel ethinyl estradiol tablets, which can reduce the clinical symptoms of patients, inhibit sex hormones, have fewer adverse reactions, and promote the quality of life of patients. However, this study may have some limitations due to the small sample size, so it is necessary to increase the sample size for continuous and in-depth research in subsequent studies.

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