

Efficacy of GnRH- α Combined with Mirena in the Treatment of Adenomyosis and its Impact on Ovarian Function

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Abstract: *Objective:* To discuss and analyze the clinical effects and changes of ovarian function after GnRH- α combined with Mirena treatment in patients with adenomyosis. *Methods:* The research subjects in this study were all adenomyosis patients (60 cases) who were admitted to our hospital from January 2020 to June 2022. They were randomly divided into a control group (30 cases, received Mirena treatment) and an observation group (30 cases, received GnRH- α combined with Mirena treatment). The relevant indicators of both groups were compared. *Results:* After treatment, both the observation group and the control group exhibited reduced uterine volume, thinner endometrial thickness, lower VAS score, PBAC score, serum FSH, LH, and E2 levels compared to pre-treatment values. The serum AMH level and various FSFI scores were higher than before treatment, with the observation group showing a more noticeable increase. Additionally, the observation group had a lower incidence of adverse reactions compared to the control group (all $P < 0.05$). *Conclusion:* The application of GnRH- α combined with Mirena in patients with adenomyosis can reduce the amount of menstrual bleeding, reduce the volume of the uterus, relieve pain, promote the recovery of ovarian function, improve the quality of sexual life, and it is safe. Therefore, this method of treatment should be promoted in clinical practice.

Key words: Adenomyosis; Mirena; Gonadotropin-releasing hormone agonist drugs; Ovarian function

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1. Introduction

Adenomyosis is a relatively common gynecological disease. After the onset of the disease, patients often present with abnormally increased menstrual flow and dysmenorrhea. The continuous development can affect their ovarian function, and even cause infertility^[1]. Common treatment methods for this disease include surgery and conservative treatment. Surgical treatment is highly effective, but it cannot preserve the physiological function of the uterus, and some patients may develop resistance. The Mirena IUD is a topical hormonal contraceptive method that can significantly reduce menstrual bleeding and provide long-term effectiveness. However, there is a risk of hair loss, which could potentially affect its effectiveness^[2]. Therefore, there is still a need to develop more comprehensive and effective treatment methods for this disease. Gonadotropin-releasing hormone agonist drugs (GnRH- α) are currently widely used in clinical practice, which can regulate the ovarian function of

patients and improve the therapeutic effect^[3]. In this study, we analyzed the clinical outcomes and changes in ovarian function in patients with adenomyosis who underwent treatment with GnRH- α in combination with Mirena.

2. Materials and methods

2.1. Basic information

The research included 60 adenomyosis patients who were admitted to our hospital between January 2020 and June 2022. These patients were randomly divided into two groups: the control group (30 cases) and the observation group (30 cases).

In the control group, the duration of the disease ranged from 1 to 6 years, with an average of 3.11 ± 0.24 years. The number of pregnancies varied from 1 to 4, with an average of 2.14 ± 0.23 . The patients' ages ranged from 25 to 65 years old, with an average age of 47.89 ± 3.75 years. In the observation group, the duration of the disease ranged from 1 to 5 years, with an average of 3.09 ± 0.23 years. The number of pregnancies varied from 1 to 5, with an average of 2.16 ± 0.25 . The ages of patients ranged from 26 to 65 years, with an average of 47.87 ± 3.73 years. The patients were diagnosed according to *Practical Obstetrics and Gynecology (2nd Edition)*^[4]. Inclusion criteria: those who were married but were not planning to have children in the future, those with abnormal menstrual flow, those with functioning ovaries, etc. Exclusion criteria: those who received other treatments before enrollment, those who were intolerant to treatment-related drugs, those with blood diseases, etc. This study was reviewed and approved by the Medical Ethics Committee of our hospital. All research subjects voluntarily signed relevant consent forms after understanding the research content and the risks involved.

2.2. Methods

The menstrual status of the patient was observed, and levonorgestrel intrauterine system treatment was given 3 days after the menstruation period. The treatment was performed in an aseptic environment. A slider was inserted and pushed until it reached the top of the uterus, and the depth of the uterine cavity was measured after the intrauterine system was completely placed in the tube. The slider was placed at a distance of 1.8 cm from the cervix. After 5 to 10 seconds, the slider was slowly to the bottom of the uterus. The tail extended 2 cm from the cervix, the slider was kept in the body for 6 months. The observation group received a subcutaneous injection of leuprolide acetate microspheres (3.75 mg) (Shanghai Livzon Pharmaceutical Co., Ltd., National Pharmaceutical Approval: H20093852) on the 1st day of menstruation every 4 weeks. After 3 consecutive injections, Mirena rings were placed in accordance with the control group's protocol.

2.3. Observation indicators

(i) A color Doppler ultrasonic diagnostic system (Guangdong Jizhun 20172231168, model: P70T) was used to measure the uterine volume and endometrial thickness. The degree of pain was scored with reference to the Visual Analogue Scale (VAS), which ranged from 0–10 points^[5], the higher the score, the higher the degree of pain. The menstrual fluid volume was evaluated based on the Blood Volume Graphic Analysis Score (PBAC)^[6], and > 80 points indicated excessive menstrual flow. (ii) About 3 mL of venous blood was collected from the patients before and after treatment. After drawing the patient's blood, the serum centrifuged at a speed 2800 r/min for 10 min, and the levels of serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E_2) and anti-Müllerian hormone (AMH) of the patients were detected through the enzyme-linked immunosorbent assay. (iii) The quality of sexual life of the patients was evaluated by the Female Sexual Function Index (FSFI)^[7], with each item ranging from 0–6 points (sexual desire, orgasm, sexual excitement,

vaginal lubrication, etc.), and the worse the quality of sexual life, the lower the score. (iii) The occurrence of adverse reactions such as abdominal pain, irregular bleeding, and skin rash during treatment were recorded.

2.4. Statistical methods

A *t*-test was used to compare the measurement data of both groups and is expressed in the form of mean \pm standard deviation. A χ^2 test was used to compare the count data and is expressed in the form of *n* (%). All data were analyzed using SPSS 20.0, and *P* < 0.05 indicates statistical significance.

3. Results

3.1. Uterine volume, endometrial thickness, VAS score, PBAC score

The uterine volume, endometrial thickness, VAS score, and PBAC score of the two groups are shown in **Table 1**. The results demonstrated that following treatment, the uterine volume and endometrial thickness decreased, and the VAS and PBAC scores were lower compared to before treatment in both groups. However, these changes were more prominent in the observation group, and the differences in the data were statistically significant (*P* < 0.05) when compared to the control group.

Table 1. Comparison of uterine volume, endometrial thickness, VAS score, and PBAC score between the two groups before and after treatment (mean \pm standard deviation)

Group	Number of cases	Uterine volume (m ³)		Endometrial thickness (mm)		VAS score (points)		PBAC score (points)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	30	156.75 \pm 8.15	105.71 \pm 6.29*	9.14 \pm 1.01	6.84 \pm 0.27*	7.46 \pm 1.04	2.77 \pm 0.64*	144.11 \pm 9.25	66.97 \pm 5.51*
Observation group	30	156.73 \pm 8.17	82.92 \pm 4.20*	9.12 \pm 1.02	5.16 \pm 0.12*	7.44 \pm 1.02	1.05 \pm 0.22*	144.13 \pm 9.23	56.01 \pm 5.27*
<i>t</i>		0.009	16.504	0.076	31.143	0.075	13.921	0.008	7.873
<i>P</i>		> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

Note: **P* < 0.05 compared to before treatment

3.2. Sex hormone levels

Table 2 shows the results related to the levels of sex hormones in the two groups. The findings indicate that after treatment, the serum levels of FSH, LH, and E₂ in both groups decreased, while the serum AMH levels increased compared to pre-treatment levels. The changes in the hormone levels of patients in the observation group were more pronounced compared to the control group, with statistical significance (*P* < 0.05).

Table 2. Comparison of sex hormone levels before and after treatment in the two groups (mean \pm standard deviation)

Group	Number of cases	FSH (IU/L)		LH (IU/L)		E ₂ (pmol/L)		AMH (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	30	74.81 \pm 6.66	42.73 \pm 4.49*	42.51 \pm 8.44	31.13 \pm 6.41*	66.11 \pm 3.12	48.51 \pm 6.11*	3.11 \pm 0.25	4.47 \pm 0.31*
Observation group	30	74.82 \pm 6.68	40.20 \pm 3.35*	42.50 \pm 8.42	18.15 \pm 4.20*	66.09 \pm 3.14	40.03 \pm 4.04*	3.13 \pm 0.23	4.01 \pm 0.24*
<i>t</i>		0.006	2.474	0.005	9.277	0.025	6.341	0.322	6.427
<i>P</i>		> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

Note: **P* < 0.05 compared to before treatment

3.3. Quality of sexual life

Table 3 shows the results of the parameters related to the quality of sexual life of both groups. The results showed that the FSFI scores of the observation group and the control group after treatment were higher than those before treatment, with observation group having higher scores than the control group. The differences between the data of both groups after treatment were significant ($P < 0.05$).

Table 3. Comparison of FSFI scores between the two groups before and after treatment (mean \pm standard deviation, points)

Group	Number of cases	Sexual desire		Orgasm		Sexual excitement		Vaginal lubrication	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	30	1.31 \pm 0.61	2.43 \pm 0.33*	1.85 \pm 0.34	3.14 \pm 0.41*	1.47 \pm 0.13	2.53 \pm 0.61*	1.27 \pm 0.16	3.40 \pm 0.51*
Observation group	30	1.30 \pm 0.63	4.37 \pm 0.47*	1.83 \pm 0.32	4.37 \pm 0.62*	1.49 \pm 0.15	4.38 \pm 1.02*	1.25 \pm 0.18	5.02 \pm 0.46*
<i>t</i>		0.602	18.503	0.235	9.064	0.552	8.526	0.455	12.919
<i>P</i>		> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

Note: * $P < 0.05$ compared to before treatment

3.4. Adverse reactions

Table 4 shows the results related to the occurrence of adverse reactions in both groups. The total incidence of adverse reactions in the observation group was lower than that of the control group, and the difference was significant ($P < 0.05$).

Table 4. Comparison of adverse reactions between the two groups during treatment (*n* [%])

Group	Number of cases, <i>n</i>	Stomachache	Irregular bleeding	Rashes	Total incidence
Control group	30	2 (6.67)	4 (13.33)	3 (10.00)	9 (30.00)
Observation group	30	1 (3.33)	0 (0.00)	1 (3.33)	2 (6.67)
χ^2					5.455
<i>P</i>					< 0.05

Note: * $P < 0.05$ compared to before treatment

4. Discussion

Adenomyosis affects patients' daily life, ovarian function and quality of sexual life to varying degrees. At present, the Mirena birth control ring is a commonly used contraceptive method. It has a significant curative effect, but there is a certain risk of dislocation and hair loss, and the effect of a single application is relatively limited. Therefore, relevant treatment plans should be formulated depending on the patient's condition^[8].

Leuprolide is a kind of GnRH- α commonly used in clinical practice. Although it has a high affinity for gonadotropin-releasing hormone receptors, it can significantly promote the body's gonadal hormones, promote the atrophy and apoptosis of endometriotic lesions in patients in a short period of time. Besides, it reduces the amount of bleeding while reducing the volume of the uterus and plays an auxiliary role in the fixation of IUDs, which in turn reduces the rate of disengagement and cause less pain^[9]. The results of this study revealed that the observation group exhibited a larger decrease in uterine volume and thinner endometrial thickness compared to the control group after treatment. Additionally, the VAS and PBAC scores in the observation group were lower

than those in the control group. These findings suggest that the combined treatment of GnRH- α and Mirena in adenomyosis patients can effectively decrease menstrual bleeding, reduce uterine volume, and alleviate pain. These outcomes are consistent with the research conducted by Zhu *et al* ^[10].

FSH, LH, E₂, and AMH are all important indicators reflecting the body's sex hormone levels, and they are also the main indicators of the ovarian function ^[11]. Patients with adenomyosis may experience varying degrees of ovarian function decline. Besides, the level of sex hormones may become disordered, which may affect quality of the patient's sexual life. Leuprolide can significantly inhibit the progesterone in the myometrium, reduce the sensitivity of peptidase decomposition, and shorten the release time of pituitary luteinizing hormone while inhibiting the secretion of sex hormones in the body, thereby regulating ovarian function, which is conducive to improving the clinical symptoms of patients and improving the quality of their sexual life ^[12]. In addition, GnRH- α combined with Mirena treatment can increase the local drug concentration while regulating the body's sex hormones, which can effectively reduce the risk of irregular bleeding and abdominal pain ^[13,14]. The results of this study showed that after treatment, the serum FSH, LH, and E2 levels in the observation group were lower than those of the control group, whereas the serum AMH levels and FSFI scores were higher than those of the control group.

5. Conclusion

In summary, the application of GnRH- α combined with Mirena in patients with adenomyosis can reduce menstrual bleeding, reduce uterine volume, relieve pain, promote the recovery of ovarian function, improve the quality of sexual life, and it is safe. Therefore, this method of treatment should be popularized in clinical practice.

Disclosure statement

The author declares no conflict of interest,

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