

Efficacy of mifepristone and GnRH-a in patients with endometriosis after operation

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Objective: The effect of mifepristone and GnRH-a on patients with endometriosis after operation. **Methods:** 100 cases of endometriosis treated by laparoscopic surgery in our hospital from May 2017 to October 2019 were divided into GnRH-a group (34 cases), mifepristone group (33 cases) and non-drug group (33 cases) according to the numerical random method, and the treatment effect of the three groups was compared. **Result:** After the drug treatment, the cumulative recurrence rate of non misoprostone group and GnRH-a group was 18.18% and 21.21%, $P > 0.05$ between the two groups, and 33.33% between the two groups, $P < 0.05$. After treatment, FSH, LH and other hormone indexes in mifepristone group were compared with those before treatment ($P > 0.05$), while E2 levels were compared with those before treatment ($P < 0.05$); FSH, LH, E2 levels in GnRH-a group were compared with those before treatment ($P < 0.05$), and those in mifepristone group were compared with those after treatment ($P < 0.05$). After treatment, the complete remission rate of the patients in the non misoprostone group and the GnRH-a group were 51.52% and 55.88%, respectively, $P > 0.05$ for the comparison between the groups, and 36.36% for the comparison between the patients in the non misoprostone group and the GnRH-a group, $P < 0.05$ for the comparison between the two groups. There was no significant difference between the two groups ($P > 0.05$). **Conclusion:** Mifepristone and GnRH-a have good effect on patients with endometriosis after operation. They can effectively reduce the recurrence rate and adverse reactions after EMT.

Key words: Mifepristone; GnRH-a; Endometriosis; Postoperative effect

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In clinic, endometriosis (EMT) mainly refers to a common gynecological disease of women formed by active endometrial cells working outside the endometrium. Most of the patients are women of childbearing age. The occurrence of this disease is invasive¹⁻⁴. Some research results show that the clinical probability of this disease is about 3% - 10% for women of childbearing age, and 25% - 35% for infertile women⁵. EMT is an estrogen dependent disease in clinic. It is still likely to recur after surgical treatment. Therefore, how to effectively reduce postoperative recurrence of surgical patients is also the key point in the treatment process⁶. Nowadays, after the surgical treatment of endometriosis patients, drugs are often

used to consolidate the treatment. In this process, GnRH-a and mifepristone are commonly used drugs. In order to better study which drug has better clinical treatment effect, this paper focuses on mifepristone and G The efficacy of nrh-a in patients with endometriosis after operation was studied as follows:

MATERIALS AND METHODS

General information

100 cases of endometriosis treated by laparoscopic surgery in our hospital from May 2017 to October 2019 were taken as the study objects. The minimum age of the patients was 18 years, the maximum age was 45 years, and the

average age was (30.34 ± 6.35) years; the shortest course of the patients was 4 months, the longest course was 10 years, and the average course of the patients was (4.45 ± 1.42) years. According to the modified endometriosis staging method in the United States, 18 patients were divided into two stages, 49 patients into three stages and 33 patients into four stages, 40 of them were complicated with infertility. 100 patients were randomly divided into GnRH-a group (34 cases), mifepristone group (33 cases) and non-drug group (33 cases). The general data of the three groups were compared. The results showed that there was no statistically significant difference between the component comparison data ($P > 0.05$).

Inclusion and exclusion criteria

Inclusion criteria ⁷: all patients met the EMT diagnostic criteria; had the relevant indications for laparoscopic surgery, and were the first laparoscopic surgery; the complete set of results of sublimation and large routine examination showed normal, and did not take any hormone drugs half a year before the operation.

Exclusion criteria: exclude patients with history of tumor, hypertension, diabetes, heart disease and tuberculosis; patients with GnRH-a or contraindications of mifepristone use.

Method

Operation method. During the operation, all patients need to work out the corresponding operation plan according to the results of laparoscopy. If the organs of patients show clear lesions, they need to be completely removed as much as possible. For the patients with small lesions or the location is not ideal, they can use bipolar direct cauterization and other methods to eliminate the lesions. If the patient is a patient with ovarian endometriosis cyst, the ovarian cyst of the patient needs to be completely removed; if the patient is combined with infertility, the methylene blue liquid test can be carried out; if the patient has salpingostomy and other conditions, the salpingostomy is needed.

Medication. In the course of medication, the patients

in the mifepristone group need to use 25 mg mifepristone (Beijing Zizhu Pharmaceutical Co., Ltd., h10950003) for treatment from 1 W after operation, which needs to be taken for 6 months continuously; the patients in the GnRH-a group need to inject dafelin subcutaneously every 4 W after operation (French Bofu Yipu pharmaceutical, h20140298), with a dose of 3.75 mg , which also needs to be treated continuously. The patients in the non-drug group were not given any medication except operation. During the period, patients in both groups need to have a follow-up visit every month to observe the side effects of drugs and changes in liver function. After the operation, the patients need to reexamine once every 3-6 months to record the clinical symptoms and signs, serum hormones, related gynecological ultrasound, liver and kidney function, bone density and other information. After one-year follow-up, the recurrence rate and pregnancy rate of the two groups were compared.

Observation index and efficacy judgment standard

(1) Observation index. When observing the recurrence of the two groups of patients, the following criteria were used to determine: ① The results of postoperative ultrasound showed that there was a new endometriosis focus; ② The pelvic positive signs disappeared after the operation or returned to the level before the operation; ③ The patients' serum CA decreased and then increased again; ④ There were other diseases. After 3 months, the disease recurred and became more serious. If one of the above ①, ② and ③ is accompanied or not accompanied with ④, we will judge it as recurrence. In addition, we used radioimmunoassay to detect and observe the levels of FSH, LH and E2 before and after treatment.

(2) Efficacy criteria ⁸: if the patient has no clinical symptoms and no pelvic mass is found, it is a complete relief; if the severity of the patient's original symptoms and signs is significantly lower than before, and no obvious positive signs are found in physical examination, it is an improvement.

(3) Adverse reactions. The adverse reactions of the three groups were compared to determine the impact of different treatment plans.

Statistical analysis

SPSS 21.0 was used for statistical analysis. The measurement data of normal distribution are expressed by means of mean \pm standard deviation, t-test and one-way ANOVA, the measurement data of non-normal distribution are expressed by means of median (interquartile interval), Mann Whitney rank sum test, χ^2 test for counting data, and multivariate linear regression analysis for correlation analysis. The mean \pm standard deviation and median were used to represent the data⁹. The difference was statistically significant ($P < 0.05$).

RESULTS

Comparison of recurrence in three groups

There was no significant difference between the two groups ($P > 0.05$); the difference between the two groups was statistically significant ($P < 0.05$). See Table 1 below for details.

Table 1. Comparison of recurrence in three groups						
Group	Number of cases	3 months after operation	6 months after operation	9 months after operation	12 months after operation	1 year cumulative recurrence rate
Femidone	33	1 (3.03)	2 (6.06)	2 (6.06)	1 (3.03)	6 (18.18) *
GnRH-a group	34	1 (2.94)	3 (8.82)	2 (5.88)	1 (2.94)	7 (20.59) *
Untreated group	33	2 (6.06)	3 (9.09)	3 (9.09)	3 (9.09)	11 (33.33)

Note: * compared with the control group ($P < 0.05$)

Comparison of the changes of postoperative hormone use between the two groups

After treatment, the changes of FSH, LH and other hormone indexes in mifepristone group were not statistically significant ($P > 0.05$), but the decrease of E2 level was very significant ($P < 0.05$); the levels of FSH, LH and E2 in GnRH-a group were significantly lower than those in mifepristone group before treatment, and the degree of decrease was significantly lower than that in mifepristone group

after treatment Hormone level $P < 0.05$. See Table 2 below for details.

Table 2.

Comparison of the changes of postoperative hormone use between the two groups

Group	Numb er of cases	FSH (U/L)		LH (U/L)		E2 (ng/L)	
		Before	After	Before	After	Before	After
		treatme nt	treatme nt	treatme nt	treatme nt	treatme nt	treatme nt
Femido ne	33	7.9±1.0	7.5±0.2	6.9±1.2	7.2±1.4	304±21	214±9*
GnRH- a group	34	6.6±1.1	2.4±0.1 ##	7.7±1.0	2.6±0.2 ##	292±9	99±4*#

Note: * compared with untreated group (P < 0.05); compared with mifepristone group (P < 0.05)

Comparison of clinical effects of three groups of patients

After the treatment, the complete remission rate of patients in non misoprostone group and GnRH-a group were 51.52% and 55.88% respectively, and there was no significant difference between the two groups; 36.36% of patients in the two groups were compared with those in the non-drug group, and the difference was statistically significant ($P < 0.05$). See Table 3 below for details.

Table 3. Comparison of clinical effects of three groups of patients			
Group	Number of cases	Complete remission	Symptom improvement
Femidone	33	17 (51.52)	10 (30.30)
GnRH-a group	34	19 (55.88)	9 (26.47)
Untreated group	33	12 (36.36)	10 (30.30)

Comparison of adverse reactions in patients treated with the two groups

The incidence of reverse addition, abnormal liver function, abnormal bone density, and irregular uterine bleeding in the two groups of patients treated with drugs was compared. The incidence was low. There was no statistically significant difference in the comparison data between the groups $P > 0.05$. See Table 4 below for details.

Table 4.

Comparison of adverse reactions between the two groups

Group	Number of cases	Reverse addition	Abnormal liver function	Abnormal bone mineral density	Irregular uterine bleeding
Femidone	33	0	1	1	1
GnRH-a group	34	0	2	1	1

DISCUSSION

Because of many factors such as the size and location of endometriosis focus and the limitations of clinical operation on endometriosis, the patients with this disease cannot be completely cleared of its tiny focus, and the clinical recurrence often occurs after the surgical treatment of this kind of patients. Therefore, the clinical treatment of endometriosis patients After surgical treatment, most of the patients will use postoperative drugs to consolidate the treatment effect, with the help of drugs to promote the necrosis and atrophy of these residual lesions, so as to effectively prevent or delay the recurrence of the disease ¹⁰. Many research findings show that the reason why endometriosis can be controlled by drug means is that the drug has the function of inhibiting pituitary, ovary and so on, which makes the endometrium shrink and amenorrhea, and finally the ectopic focus will be necrotic and absorbed ¹¹.

GnRH-a can effectively reduce the risk of postoperative complications in patients with endometriosis. However, some adverse reactions of GnRH-a in the course of use are mainly due to the decrease of estrogen level. If it is used for a long time, it is likely to reduce the bone density of patients and eventually lead to pathological fracture ¹². For this reason, when the clinical recommendation is used, its continuous time should not be more than 6 months, plus the high price of this drug, so it has not been widely used in the primary hospitals. Some scholars think that the efficacy of GnRH-a is worthy of affirmation. Considering its safety, tolerance and economic benefits, it can be used as the second-line treatment plan for endometriosis. If there is no effect after using

contraceptive and progesterone, GnRH-a can be used ¹³⁻¹⁵. There is a close relationship between endometriosis and progesterone receptor, and mifepristone, as a progesterone antagonist, has been widely used in the treatment of EMT patients. It has been reported that long-term low-dose mifepristone treatment of endometriosis patients can effectively alleviate the clinical symptoms of patients, at the same time, it can make patients with endometriosis focus necrosis, atrophy, reduce the recurrence rate of patients' disease, and there is no adverse reactions in the use process. In the course of this study, mifepristone and GnRH-a have better improvement effect on the patients with endometriosis surgery. When they are used in the postoperative treatment, they can effectively reduce the postoperative recurrence rate. The results show that the cumulative recurrence rate of non-mifepristone group and GnRH-a group is 18.18% and 21.21% one year after the operation, and the comparison between the groups is $p > 0.05$; The difference between the two groups was 33.33% ($P < 0.05$). This result shows that mifepristone and GnRH-a have a high promotion effect in reducing the recurrence rate of endometriosis, and can effectively improve the hormone level of patients and improve the complete remission rate of patients. In addition, there was no significant difference between the two groups ($P > 0.05$). This result shows that mifepristone and GnRH-a are also safe in the use process, can effectively reduce the occurrence of adverse reactions, and have high safety, which is worthy of application.

CONCLUSION

To sum up, mifepristone and GnRH-a have good effect on patients with endometriosis after operation, can effectively reduce the recurrence rate after EMT operation, reduce the incidence of adverse reactions, it is worth popularizing.

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