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Effect of Implantation and Fixation of Mirena in the Treatment of Adenomyosis and its Influence on Serum Inflammatory Factors

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ABSTRACT

This experiment was carried out to analyze the placement and fixation of Mirena in the treatment of adenomyosis (AM) and its influence on the level of serum inflammatory factors in patients. For this purpose, the subjects of this study were 100 AM patients hospitalized in our hospital from June 2019 to June 2021. They were divided into two groups according to the lottery method (n=50 for each group). The control group was treated with intramuscular triprerelin after the operation, and the observation group was treated with Mirena during the operation. Sex hormone indexes, VAS score, uterine volume, serum inflammatory indexes, the total incidence of adverse reactions, WHOQOL-BREF score and recurrence rate were compared between the two groups. Results showed that in the observation group after treatment E_2VAS score and uterine volume were lower, serum IL-8 and TNF-A were lower, the whoqOL-BREf score was higher, and the recurrence rate (0) was lower than that in the control group (12.00%). The total incidence of adr in the observation group (4.00%) was lower than in the control group (8.00%). Then intraoperative placement of Mirena can effectively regulate sex hormone indexes of AM patients, reduce uterine volume, relieve dysmenorrhea symptoms, reduce the inflammatory response, improve quality of life, and reduce recurrence rate, without obvious adverse reactions.

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Introduction

AM (adenomyosis) of the uterus is a common gynecological disease, mostly in women of childbearing age, with uterine enlargement, abnormal menstruation, and dysmenorrhea as the main symptoms, and severe cases will appear as infertility(1). In recent years, the incidence of AM has increased significantly in China, and the incidence of AM tends to be younger(2). Currently, the clinical treatment of AM is mainly laparoscopic lesions resection. Still, the improvement effect of postoperative dysmenorrhea and other symptoms in some patients is not obvious. There are varying degrees of the inflammatory response, the disease is prone to recurrence, and certain limitations exist (3). Mirena releases levonorgestrel, which inhibits endometrial cell proliferation, improves dysmenorrhea and reduces blood loss(4). Based on this, in order to explore the application effect of Mirena in AM treatment, 100 AM patients hospitalized in our hospital from June 2019 to June 2021 were studied.

Materials and Methods

General Information

The subjects of this study were 100 AM patients hospitalized from June 2019 to June 2021, which the hospital ethics committee had approved. They were divided into two groups by lottery (n=50 for each group). The observation group was 32-60 years old, with an average of (46.52±5.34) years old. The disease course ranged from 1 to 6 years, with an average of (3.52±1.94) years. ASA (American Society of Anesthesiologists) grading: 29 cases grade I, 21 cases grade II; the number of pregnancies ranged from 1 to 6, averaging (3.52±1.64). The average number of times was (2.06±0.41). BMI (body mass index) 25-33kg/m^2, average (29.52±1.44) kg/m^2.Control group: 34-59 years old, average (46.62±5.27) years old; the disease course was 2-5 years, with an average of (3.55±1.91) years. ASA classification: 30 cases were grade I and 20 cases were grade II. The number of pregnancies ranged from 1 to 5, averaging (3.55±1.61). The average number of times was (2.05±0.38).BMI26-33kg/m^2, average (29.59±1.38) kg/m^2.P>0.05 was comparable between the two groups.

Diagnostic criteria: all met the Consensus of Chinese experts on the Diagnosis and treatment of adenomyosis (5).

Inclusion criteria: ① Age >18 years old ②Progressive dysmenorrhea, prolonged menstrual period, increased menstrual volume and other symptoms. ③ASA was classified in grades I-II. ④ Answer the question and be conscious. ⑤ the indications of anesthesia and operation were satisfied. ⑥ The purpose of this study has been informed and the informed consent has been signed.

Exclusion criteria: ① combined with cervicitis, uterine

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fibroids and other gynecological diseases.② Patients with depression, dementia and other diseases.③ Patients who had received symptomatic treatment before enrollment.④ Patients with previous uterine surgery. ⑤ Allergic constitution. ⑥ Anemia, hematopoietic dysfunction. ⑦ People with low immune function.⑧ with cervical cancer and other malignant tumors.⑨ Persons with syphilis, AIDS and other diseases.⑩ Patients with acute or chronic infectious diseases.

Methods

Control group: 3.75mg triprerelin was given an intramuscular injection after surgery, and 3.75mg triprerelin was given an intramuscular injection at the 1st month after surgery, once every 4 weeks on the 3rd day of menstruating.

Observation group: Postoperative 3 d first menstruating, sex, be man month coil treatment, routine preoperative examination of the department of gynaecology, uterus through colour to exceed evaluation of location, size, etc., will be happy man month coil open aseptic packaging, strictly follow the principle of aseptic push the slider to the top, prompted the intrauterine device placed in the tube, probe the uterine cavity depth using the probe, Gently push the applicator to the fundus until it touches the cervix. After the position of the applicator is fixed, continue to drag downward until it is the most generous and slowly release the intrauterine birth control system. After the applicator was gently removed, cut off the tail wire to ensure that the tail wire is visible at 2cm outside the cervix.

Observation indicators and evaluation criteria

Comparison of the two groups: ① Sex hormone index: E was detected by electrochemiluminescence$_2$(estradiol), LH (luteinizing hormone), FSH (follicle stimulating hormone). ② VAS score of dysmenorrhea: 0 for painless, 1-3 for mild, 4-6 for moderate and 7-9 for severe. ③ Uterine volume: Color ultrasound was used to measure the transverse diameter, thickness and long diameter of the uterus, and the transverse diameter × thickness × long diameter ×0.523= uterine volume(6). ④ Serum inflammatory indicators: IL-8 (interleukin-8) and TNF-A (tumor necrosis factor-A) were detected by ELISA. ⑤ Total incidence of adverse reactions: Total incidence of irregular vaginal bleeding, headache, rash and fever were counted. ⑥ WHOQOL-BREF score: including personal belief/religious/spiritual world, environment, society, psychology, independence and physiology, the higher the quality of life, the higher the final score (7). ⑦ Recurrence rate: Follow-up for six months AM recurrence rate was calculated.

Statistical methods

SPSS26.0 software was used to test, and the normally distributed measurement data (sex hormone index, VAS score, uterine volume, serum inflammation index, WHO-qOL-BREf score) were paired with sample T to test the data within the same group, and independent sample T to test the data between different groups, which was represented by "M±S". Counting data (total incidence of adverse reactions and recurrence rate) were tested by Pearson Chi-square test, cell expected frequency <5, continuous correction test, represented by "[N/(%)]", $P < 0.05$, indicating the statistical difference.

Results

Comparison of sex hormone indicators

Observation group E before treatment$_2$, LH, FSH compared with the control group, P>0.05; The observation group was lower than the control group after treatment (P<0.05), as shown in Table 1.

Comparison of VAS score and uterine volume for dysmenorrhea

VAS score and uterine volume of the observation group were compared with those of the control group before treatment (P>0.05). The observation group was lower than the control group after treatment ($P < 0.05$), as shown in Table 2.

Comparison of serum inflammatory indicators

Serum IL-8 and TNF-A in the observation group were compared with the control group before treatment (P>0.05). The observation group was lower than the control group after treatment (P<0.05), as shown in Table 3.

Comparison of total incidence of adverse reactions

The total incidence of adverse reactions in the observation group (4.00%) was compared with that in the control group (8.00%), P>0.05, as shown in Table 4.

Comparison of WHOQol-BREF score

The whoqol-bref score of the observation group was compared with the control group before treatment (P>0.05). The observation group was higher than the control group after treatment, $P < 0.05$, as shown in Table 5.

Comparison of recurrence rates

The recurrence rate of the observation group (0) was

Table 1. Comparison of sex hormone indexes (M±S score).

group	E_2(pmol/L)		LH (mIU/L)		FSH (U/L)	
	BF	AT	BF	AT	BF	AT
Control group (n=50)	356.26 + / - 29.31	326.52 + / - 18.62[a]	7.62 + / - 1.52	7.06 + / - 1.32[a]	9.62 + / - 1.99	8.62 + / - 0.64[a]
Observation group (n=50)	360.04 + / - 28.33	263.31 + / - 10.54[a]	7.59 + / - 1.66	4.92 + / - 0.46[a]	9.59 + / - 1.89	6.26 + / - 0.27[a]
T-value	0.656	20.890	0.094	10.825	0.077	24.024
P-values	0.514	0.000	0.925	0.000	0.939	0.000

Note: Compared with before treatment,[a]*(P < 0.05).* BF (Before the treatment). AT (After treatment).

Table 2. Comparison of VAS score and uterine volume for dysmenorrhea (M±S).

group	VAS score for dysmenorrhea (score)		Uterine volume $(cm)^3$)	
	BF	AT	BF	AT
Control group (n=50)	6.95 + / - 1.32	3.95 + / - 0.52[a]	276.16 + / - 28.62	184.26 + / - 13.05[a]
Observation group (n=50)	6.99 + / - 1.29	1.05 + / - 0.11[a]	277.01 + / - 27.95	131.06 + / - 9.34[a]
T-value	0.153	38.581	0.150	23.441
P-values	0.879	0.000	0.881	0.000

Note: Compared with before treatment,[a]*(P < 0.05).* BF (Before the treatment). AT (After treatment).

Table 3. Comparison of serum inflammatory indicators (M±S).

group	IL - 8 (pg/mL)		TNF - a (pg/mL)	
	BF	AT	BF	AT
Control group (n=50)	201.62 + / - 15.33	152.62 + / - 9.21[a]	91.62 + / - 6.05	64.62 + / - 4.05[a]
Observation group (n=50)	202.59 + / - 16.34	68.62 + / - 1.34[a]	92.01 + / - 6.11	38.62 + / - 1.34[a]
T value	0.306	63.820	0.321	43.097
P values	0.760	0.000	0.749	0.000

Note: Compared with before treatment,[a]*(P < 0.05).* BF (Before the treatment). AT (After treatment).

Table 4. Comparison of total incidence of adverse reactions [N/(%)].

group	Irregular vaginal bleeding	Have a headache	The rash	fever	Total incidence of adverse reactions
Control group (n=50)	3 (6.00)	1 (2.00)	0 (0.00)	0 (0.00)	4 (8.00)
Observation group (n=50)	0 (0.00)	0 (0.00)	1 (2.00)	1 (2.00)	2 (4.00)
χ^2value	--	--	--	--	0.177
P values	--	--	--	--	0.674

Table 5. Comparison of WHOQOL-BREF score (M±S score).

group	Personal belief/ religion/spiritual world		The environment		social		psychological		independent		The physiological	
	BF	AT	BF	AT	BF	AT	BF	AT	BF	AT	BF	AT
Control (n=50)	12.52 + / - 2.61	16.82 + / - 3.62[a]	10.26 + / - 1.11	13.62 + / - 1.84[a]	12.62 + / - 2.32	15.62 + / - 3.55[a]	8.62 + / - 0.34	11.62 + / - 1.34[a]	12.62 + / - 1.02	15.62 + / - 1.84[a]	10.26 + / - 0.64	13.85 + / - 1.95[a]
Observation (n=50)	12.55 + / - 2.59	20.52 + / - 3.95[a]	10.33 + / - 1.16	16.82 + / - 2.84[a]	12.59 + / - 2.41	19.52 + / - 4.14[a]	8.59 + / - 0.41	14.52 + / - 2.05[a]	12.77 + / - 1.06	18.62 + / - 2.95[a]	10.33 + / - 0.59	16.82 + / - 2.57[a]
T value	0.058	4.883	0.308	6.687	0.063	5.057	0.398	8.373	0.721	6.101	0.569	6.510
P values	0.954	0.000	0.759	0.000	0.950	0.000	0.691	0.000	0.473	0.000	0.571	0.000

Note: Compared with before treatment,[a]*(P < 0.05).* BF (Before the treatment). AT (After treatment).

Table 6. Comparison of recurrence Rates [N/(%)].

group	recurrence	No recurrence,
Control group (n=50)	6 (12.00)	44 (88.00)
Observation group (n=50)	0 (0.00)	50 (100.00)
χ^2value	4.433	
P values	0.035	

lower than that of the control group (12.00%) (P < 0.05), as shown in Table 6.

Discussion

AM is a benign lesion, mainly characterized by ectopic glandular tissue and endometrium in the myometrium of the uterus, which is manifested as increased menstrual volume and dysmenorrhea, causing serious adverse effects on the physical and mental health of patients(8). People over 40 years old have a high incidence of AM, and nearly 70% of AM patients have obvious clinical symptoms. AM is one of the important causes of female infertility(9-10). Laparoscopic resection of lesions is the main method for the current clinical treatment of AM. Although it can effectively relieve dysmenorrhea and other symptoms, some patients suffer from incomplete intraoperative resection of lesions, surgical damage to the endometrium, and the surgical effect is affected. There are varying degrees of inflammatory reaction after surgery, and the disease easily relapses (11-12). Therefore, during the treatment of AM patients with laparoscopic lesion resection, adjuvant drug

therapy should be used to consolidate the surgical effect further, inhibit the release of inflammatory factors, reduce the recurrence rate and improve the prognosis of patients.

Tnf-a has a variety of biological activities, mainly produced by lymphocytes and mononuclear macrophages. When the body is injured or infected, serum TNF-A concentration will significantly increase.Il-8 can enhance immune response, induce neovascularization, chemotactic neutrophils, and stimulate interstitial cell proliferation(13-14). Clinical studies have shown that the serum levels of TNF-A and IL-8 in AM patients are significantly higher than those in healthy people. This may be related to the stronger activity of peripheral blood monocytes in AM patients.In AM patients, due to the activation of TNF-A, NF-RB can be activated, local IL-8 overexpression can be induced, neovascularization of lesions can be promoted, and ectopic endometrial implantation and adhesion can be accelerated(15). Therefore, in the treatment of AM, how to inhibit the release of TNF-A and IL-8 is of great significance in improving the prognosis of patients. This study showed that: after treatment, the observation group E_2, LH, FSH, VAS score, uterine volume, serum IL-8 and TNF-A were all lower than those in the control group, whoqOL-BREF score in the observation group was higher than that in the control group after treatment, and recurrence rate in the observation group (0) was lower than that in the control group (12.00%), $P < 0.05$. The total incidence of adr in the observation group (4.00%) was compared with the control group (8.00%), $P>0.05$. The results showed that intraoperative Mirena was effective in the treatment of AM. The analysis is as follows: Mirena ring is a small, soft T-shaped plastic frame. When placed in the uterine cavity, it can release low-dose levonorgestrel slowly and steadily, improve the concentration of local levonorgestrel in the endometrium, effectively inhibit the synthesis of estrogen receptors in the endometrium, and enhance the antagonistic effect of endometrium hyperplasia(16-18). Progesterone, estrogen receptors in the endometrium, reduce the endometrium's response to circulating E_2Can enhance the antagonistic effect of endometrial hyperplasia, relieve dysmenorrhea and other symptoms, reduce the amount of bleeding, shorten the duration of bleeding symptoms(19). The mechanism by which Mirena relieves dysmenorrhea, reduces menstrual volume, and reduces uterine volume is related to the following: The main component of Mirena is levonorgestrel. When placed in the uterine cavity, it will directly affect the lesion, promote endometrial degeneration and atrophy, thicket the capillary wall, promote capillary thrombosis, dilate veins, increase uterine artery resistance, shorten the bleeding time and reduce the amount of bleeding. Levonorgestrel can also reduce the activity of estrogen and glandular receptors in the mesenchymal cells, block the effect of estrogen, and promote the degeneration and atrophy of ectopic lesions. Mirena placement can also effectively prevent intrauterine infection, control menstrual volume, and avoid aggravated inflammatory responses due to disease recurrence. Although Mirena can reduce menstrual volume, the effect of Mirena placement, after all, does not affect E_2Level and ovarian function.In addition, it is important to note that month LeHuan belongs to the intrauterine device, for patients with bulky uterine AM, do not apply, but due to large AM uterine volume in patients with common, therefore, AM patients before month LeHuan placed man, should be GnRH - a treatment for 3 months, uterine volume as possible, help stabilize the fixed synthetic, Reduce the emergence rate of Mirena after implantation.In FanXiaoFan(20)The uterine volume of group B treated with Mirena was (72.63±12.45) cm after treatment^{3}It was lower than that of group A treated with triprerelin (86.28±13.67) cm^3, $P < 0.05$, which was close to the results of this study, confirming that Mirena can effectively reduce the uterine volume in the treatment of AM, and the effect is accurate.

In conclusion, the simultaneous placement of Mirena in treating AM patients with laparoscopic lesion resection can effectively reduce inflammatory response and pain, regulate sex hormones, improve the quality of life, and reduce the recurrence rate. In addition, no obvious adverse reactions occurred in the patients, and the overall safety of the treatment plan is relatively high.

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