

Research Article

Analysis of the Clinical Effects of Different Methods for Preventing the Postoperative Recurrence of Ovarian Endometriosis

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Abstract

Objective: This study compared the clinical effects of different methods aimed at preventing the recurrence of ovarian Endometriosis (EMS) cysts following conservative surgery.

Methods: The clinical data of 432 patients with ovarian cysts treated in Luohe Central Hospital from January 2016 to January 2019 were collected. Among them, 402 cases were followed up for two years. The patients were divided into three groups according to the different postoperative methods that were adopted for preventing recurrence as follows: group A (n=126) received Gonadotropin-Releasing Hormone agonist (GnRH-a) only; group B (n=168) received six courses of GnRH-a, combined with short-term oral contraceptive maintenance therapy, for one year after surgery; group C (n=108) did not receive any preventive measures following surgery. By following up on the patients for two years post-surgery, the general condition, focal recurrence rate, dysmenorrhea symptoms relief rate and adverse drug reaction rate of the three groups were compared.

Results: One and two years after surgery, the recurrence rate in groups A and B was significantly lower than in group C, and the difference was statistically significant. ($P=0.018$, $P<0.001$). One year after surgery, the remission rate of dysmenorrhea in groups A and B was significantly higher than in group C ($P=0.035$). Two years after surgery, the remission rate of dysmenorrhea in group B was significantly higher than in groups A and C ($P=0.028$). There was no significant difference in the incidence of adverse drug reactions among the three groups ($P=0.390$).

Conclusion: Treatment with GnRH-a or GnRH-a combined with oral contraceptives after conservative ovarian endometrial cyst surgeries effectively reduced the recurrence rate of EMS. Compared with GnRH-a only, oral contraceptive maintenance therapy effectively inhibited recurrence for an extended time and significantly relieved the symptoms of dysmenorrhea.

Keywords: Endometriosis; Triptorelin; Short-acting oral contraceptive; Recurrence; Therapeutic effect

Introduction

'Endometriosis' (EMS) refers to the growth and infiltration of endometrial tissue, such as glands and/or stroma outside the uterine or uterine cavities with periodic bleeding, causing symptoms that include dysmenorrhea, chronic pelvic pain, dyspareunia and infertility. It occurs commonly in women of childbearing age [1] and is characterised by extensive invasive lesions of various shapes, variable recurrence rates and hormone dependence. Epidemiological studies indicate that the incidence of EMS is as high as 10%-15%. Furthermore, its occurrence is increasing yearly with a trend toward younger women [2].

Ovarian endometrial cysts are the most commonly observed type of EMS. Although EMS is a benign disease, due to its malignant characteristics, e.g. infiltration growth, implantation and recurrence, the present treatment for ovarian EMS is typically surgery and drug therapy [3]. Clinically, conservative surgery is often adopted to clarify the diagnosis and treatment of EMS. Surgery retains the reproductive and endocrine functions as much as possible and can only remove lesions that are visible under laparoscopy. As a result, residual ectopic endometria may not be cleared. Concurrently, conservative surgery cannot make changes to the oestrogen levels in the body. Therefore, the probability of recurrent, residual, or new lesions after surgery is high [4]. According to the existing literature, the recurrence rate among patients with EMS after laparoscopic surgery is as high as 40% to 50% [5]. Accordingly, preventing the postoperative recurrence of EMS is clinically challenging.

Gonadotropin-Releasing Hormone agonist (GnRH-a) drugs have long been the gold standard treatment for EMS. In recent years, however, these drugs were found to have certain limitations in the treatment process; they can also cause adverse reactions, such as menopausal syndrome and bone mineral density reduction. Conversely, short-acting oral contraceptives can alleviate the symptoms of hypoestrogenism and bone mineral density loss in patients with EMS. The present study aimed to analyse and compare the clinical effects of GnRH-a drugs and GnRH-a combined with

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short-acting oral contraceptives for preventing the postoperative recurrence of ovarian EMS cysts and relieving dysmenorrhea symptoms, thereby providing a basis for preventing the recurrence of EMS in the future.

Materials and Methods

Research participants

Patients treated in Luohe Central Hospital from January 2016 to January 2019 who underwent conservative surgery and were confirmed to have had ovarian endometriotic cysts after surgery were selected as the research participants. The Ethics Committee of Luohe Central Hospital approved this study.

The following inclusion criteria were observed: (1) patients aged between 25-40 years; (2) patients who had no fertility requirements in the two preceding years; (3) patients with simple ovarian EMS cysts; (4) patients with an EMS cyst diameter ≥ 4 cm; (5) patients who were able to go to the hospital regularly for follow-up visits up to two years after the surgery; (6) all selected patients were aware of the details of this study and volunteered to participate.

The following exclusion criteria were observed: (1) patients with adenomyosis or other types of EMS; (2) patients who had used GnRH-a or short-acting oral contraceptives in the past; (3) patients with systemic diseases who were not advised to undergo surgery or who had used GnRH-a or short-acting oral contraceptives after surgery was contraindicated; (4) patients with premature ovarian failure or insufficiency.

Grouping

The participants were fully informed of the advantages, disadvantages and risks of various treatment methods before undergoing the postoperative drug treatment. The patients selected their treatment method and were divided into three groups, based on their voluntary participation in the research aimed at preventing recurrence after surgery. Group A was given GnRH-a; group B was given six courses of postoperative GnRH-a, combined with short-acting oral contraceptives for one year; group C was treated without any preventive measures after surgery. The postoperative follow-up time was two years; 402 patients completed regular follow-up visits, and the follow-up completion rate was 93.1%. Among the patients who completed the follow-up, there were 126 patients in group A, 168 in group B and 108 in group C. During the two-year follow-up of the patients, the general conditions of the participants in the three groups, the recurrence of lesions, the relief of dysmenorrhea symptoms and adverse drug reactions after conservative surgery were compared (Figure 1).

Methods

Treatment and management: Patients in group A were given intramuscular injections of 3.75 mg triptorelin acetate (Changchun GenSci Pharmaceutical Co., Ltd.) every 28 days for a total of six doses starting on the first day of menstruation after conservative surgery for ovarian EMS cysts. When using GnRH-a, if the patient had severe perimenopausal symptoms that affected their daily life due to hypoestrogenemia, the patient was given 1.25~2.5 mg/d tibolone (China Resources Zizhu Pharmaceutical Co., Ltd.) as an add-back treatment to alleviate their discomfort. The blood oestradiol levels of patients who had been prescribed add-back therapy were closely monitored to avoid exceeding 40 pg/ml; if necessary, the add-back drugs were reduced or stopped. Patients in group B were given

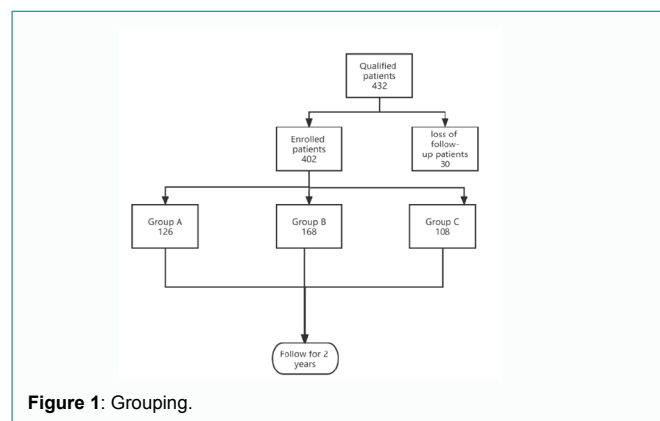


Figure 1: Grouping.

intramuscular injections of 3.75 mg triptorelin acetate (Changchun GenSci Pharmaceutical Co., Ltd.) every 28 days for a total of six doses starting on the first day of menstruation after conservative surgery for ovarian EMS cysts. Subsequently, the patients stopped taking GnRH-a drugs and began taking the Yasmin short-acting oral contraceptive (Bayer Healthcare Co., Ltd.) once menstruation returned. They started the oral contraceptives on the fifth day of each menstrual cycle, one tablet daily for 21 days for 12 menstrual cycles. Patients in group C were not given any treatment. The conservative surgeries for ovarian EMS cysts for all patients in this study were completed by gynaecologists and obstetricians with the title of 'deputy director' or higher who had been performing this type of surgery for more than five years. Before initiating this study, all of the surgeons were given unified guidance and training related to this surgical procedure.

Efficacy evaluation and follow-up: The general conditions of the three groups of patients were compared. During the regular follow-up of patients in each group after surgery, clinical symptom inquiries, gynaecological examinations and vaginal ultrasonography were performed every three months for one to two years. The disease recurrence and remission of dysmenorrhea symptoms were recorded, analysed and compared. The clinical efficacy and observation indexes were as follows: (1) the recurrence of EMS: (i) cysts in the unilateral or bilateral ovaries were detected by transvaginal colour Doppler ultrasound three months after surgery, based on the characteristic echo of EMS, which still existed after more than three consecutive menstrual cycles; (ii) the new lesion was confirmed by reoperation, and the pathological results showed that it was an ovarian EMS cyst. Patients who met any of the above conditions, with or without symptoms of related dysmenorrhea or chronic pelvic pain, were defined as having disease recurrence. (2) Relief of dysmenorrhea: after surgery, the symptoms of dysmenorrhea were relieved or had even disappeared [6]. (3) Recurrence of dysmenorrhea: the symptoms of dysmenorrhea were relieved after surgical treatment but worsened to the preoperative level after three months of follow-up visits [6].

Statistical methods

The statistical analysis was completed using the SPSS Statistics 20.0 software program. Qualitative data were described according to the study cases (%). The chi-square (χ^2) test was conducted for comparisons among the groups. The Bonferroni correction method was used for pair wise comparison between the groups. Quantitative data with a normal distribution were described by measurement data. Analysis of variance was conducted for comparison among the three groups, and pair wise comparison was performed using the least significant difference method; $P < 0.05$ indicated a statistically

significant difference.

Results

General conditions

There were no statistical differences in age (32.63 ± 4.41 vs. 33.13 ± 4.56 vs. 32.32 ± 4.25), Body Mass Index (21.91 ± 1.47 vs. 22.03 ± 1.88 vs. 21.81 ± 1.46) and ovarian EMS cyst diameter (79.83 ± 22.79 vs. 78.48 ± 23.80 vs. 82.62 ± 22.20) among the three groups ($P > 0.05$) (Table 1). There were no significant differences in the incidence of preoperative dysmenorrhea, an existing history of EMS, the prevalence of unilateral or bilateral ovarian EMS cysts and EMS stage among the three groups ($P > 0.05$) (Table 2).

Comparison of disease recurrence, dysmenorrhea remission and adverse reaction rates

Among the 402 patients, at one and two years after surgery, the recurrence rates among the three groups were significantly different ($P = 0.018$, $P < 0.001$), and the recurrence rates of groups A and B were significantly lower than those of group C (3.17% vs. 9.26%, 2.38% vs. 9.29%, 4.76% vs. 16.67%, 2.98% vs. 16.67%); this difference was statistically significant ($P < 0.05$). At one and two years after surgery, the difference in the dysmenorrhea remission rates among the three groups was statistically significant ($P = 0.035$, $P = 0.028$). At one year after surgery, the dysmenorrhea remission rates of groups A and B were significantly higher than in group C (90.16% vs. 83.33%, 96.34% vs. 83.33%); this difference was statistically significant ($P < 0.05$). Two years after surgery, the dysmenorrhea remission rates of groups A and C were significantly lower than those of group B (83.61% vs. 95.12%, 81.48%); this difference was statistically significant ($P < 0.05$). There was no significant difference in the incidence of adverse drug reactions among the three groups ($P = 0.390$) (Table 3).

Discussion

Endometriosis is a frequent and commonly occurring disease in women of childbearing age [1]. It is a benign lesion with malignant characteristics that often causes severe dysmenorrhea and chronic pelvic pain, long-term infertility, complex pelvic adhesions and mass formations. Ectopic endometria can invade all parts of the body and can occur in many forms. It is characteristically invasive and has a high recurrence rate after treatment. Studies at home and abroad [7,8] have found that the incidence, recurrence and prognosis of EMS were related to ovarian function. In recent years, with an increasing understanding of EMS in clinical research, the condition's diagnostic rate has increased alongside its incidence rate. Because of its poor treatment effect, EMS is often defined as a 'refractory disease' [9] that seriously affects the health and quality of life of patients. To date, surgical and drug treatments, based on ovarian function inhibition, remain the primary methods for treating EMS [10].

Recurrent EMS denotes the condition where, following surgery or standardised drug treatment, the clinical symptoms are initially eliminated or relieved; subsequently, however, after a period of follow-up, the clinical symptoms reappear and return to the level of aggravation before treatment, or the lesions reappear. Regardless of how thorough the initial surgical treatment had been to remove the lesions, the recurrence rates of EMS after two years remain as high as 21.5%, and the cumulative recurrence rate within five years after surgery is as high as 50%. The recurrence and reoperation for EMS will aggravate pain symptoms, reduce fertility and act as a serious burden on patients' financial means and quality of life [11]. The high-risk factors of EMS recurrence are closely related to the clinical stage, lesion location, age, surgical methods and levels, postoperative treatment methods and follow-up time [10]. Therefore, the initial surgical treatment of EMS should be thorough

Table 1: Comparison of general conditions before surgery among the three groups of patients.

Group	Age (years)	BMI (kg/m ²)	Diameter of ovarian endometriosis cyst (mm)
Group A (n=126)	32.63 ± 4.41	21.91 ± 1.47	79.83 ± 22.79
Group B (n=168)	33.13 ± 4.56	22.03 ± 1.88	78.48 ± 23.80
Group C (n=108)	32.32 ± 4.25	21.81 ± 1.46	82.62 ± 22.20
F	1.141	0.601	1.064
P	0.32	0.549	0.346

Table 2: Comparison of preoperative clinical characteristics of three groups of patients [n (%)].

Group	Occurrence of preoperative dysmenorrhea	Past history of endometriosis	Unilateral or bilateral ovarian diseases of ovarian endometriosis cyst		Stage of endometriosis			
			Unilateral	Bilateral	Stage I	Stage II	Stage III	Stage IV
Group A (n=126)	61 (48.41)	4 (3.17)	85 (67.46)	41 (32.54)	2 (1.59)	6 (4.76)	74 (58.73)	44 (34.92)
Group B (n=168)	83 (49.40)	7 (4.17)	130 (77.38)	38 (22.62)	4 (2.38)	13 (7.74)	94 (55.95)	57 (33.93)
Group C (n=108)	53 (49.07)	1 (0.93)	77 (71.30)	31 (28.70)	1 (0.93)	7 (6.48)	56 (51.85)	44 (40.74)
χ^2	0.029	2.407	3.699			3.220		
P	0.986	0.3	0.157			0.781		

Note: The staging of endometriosis is divided into stages I-IV according to the modified endometriosis stage (γ -AFS) standard revised by the American Fertility Society in 1985.

Table 3: Comparison of disease recurrence rate, dysmenorrhea remission rate and adverse reaction rate among three groups of patients [n (%)].

Group	Disease recurrence rate		Dysmenorrhea remission rate		Incidence of adverse drug reactions
	1 year after surgery	2 years after surgery	1 year after surgery	2 years after surgery	
Group A (n=126)	4 (3.17) ^a	6 (4.76) ^a	55 (90.16) ^a	51 (83.61) ^a	2 (1.59) ^a
Group B (n=168)	4 (2.38) ^a	5 (2.98) ^a	79 (96.34) ^a	78 (95.12) ^b	3 (1.79) ^a
Group C (n=108)	10 (9.26) ^b	18 (16.67) ^b	45 (83.33) ^b	44 (81.48) ^a	0 (0.00) ^a
χ^2	8	20.056	6.688	7.127	1.883
P	0.018	<0.001	0.035	0.028	0.39

Note: Bonferroni correction method was used for comparison, there was a statistical difference between a or b or c and the groups with different superscripts ($P < 0.05$), a, b or a, c represented no statistical difference between the two groups ($P > 0.05$).

in terms of consolidating the effect of surgical treatment and reducing postoperative pain and lesion recurrence, aspects that are essential for preventing EMS recurrence postoperatively. The three problematic areas of 'pain', 'infertility', and 'recurrence' in the treatment of EMS have perplexed the majority of front-line clinicians. At present, few studies have been conducted on the treatment methods for preventing EMS recurrence and its treatment after recurrence. Therefore, effectively treating EMS, controlling the condition's activity, reducing and delaying recurrence and realising the long-term management of chronic diseases is particularly important [12].

At present, the primary means of preventing recurrence remains postoperative medication. Commonly used drugs in this context include oral high-efficiency progesterone, short-acting oral contraceptives, GnRH-a drugs and levonorgestrel intrauterine sustained-release systems [13]. Among these, short-acting oral contraceptives are the initial hormonal drugs used to prevent the recurrence of EMS after surgery. These drugs reduce oestrogen levels through the hypothalamic-pituitary-ovarian axis and inhibit endometrial growth and atrophy, thereby preventing the recurrence of EMS lesions [14]. A synthetic decapeptide compound, GnRH-a has the same effect as natural GnRH in the body and promotes the release of luteinizing hormone and follicle-stimulating hormone from the pituitary gland. Its biological activity on GnRH receptors is up to 100-times higher than natural GnRH. It has a long half-life, good stability and promotes the reduction of gonadotropin secretion by the pituitary gland, thereby significantly reducing the levels of ovarian hormones, particularly oestrogen, which will lead to the observable degradation of ectopic endometria. In this instance, temporary menopause will occur, causing the lesions to shrink, degenerate or absorb, thereby preventing their recurrence [15].

Although GnRH-a drugs have achieved good results in the clinical treatment of EMS in recent years, their application time remains limited. Their long-term use will not only cause various menopausal symptoms but will also lead to a series of adverse reactions such as decreased bone density; accordingly, they cannot achieve the long-term continuous control of EMS lesions. Additionally, related studies found that the application of GnRH-a drugs after EMS surgery had a limited effect on relieving dysmenorrhea in patients [16]. The present study compared and analysed the clinical effects of different methods to prevent the postoperative recurrence of ovarian EMS cysts and relieve dysmenorrhea symptoms, specifically, the application of GnRH-a drugs, combined with short-acting oral contraceptives after six courses of treatment, to achieve the long-term maintenance and management of patients with EMS. The clinical effects of focus recurrence and dysmenorrhea were followed up and summarised to provide a basis for treatment focused on preventing the recurrence of EMS in the future.

The results of this study showed that, for preventing disease recurrence, GnRH-a was prescribed for six months after conservative surgery for ovarian EMS. Compared with no preventive measures after surgery, the recurrence rate was effectively reduced and the difference was statistically significant ($P < 0.05$). Two follow-up visits after surgery showed that the recurrence rates among patients who used GnRH-a drugs for six courses post-operatively, combined with short-acting oral contraceptives, were slightly lower than for patients who only used GnRH-a drugs to prevent EMS recurrence.

In terms of dysmenorrhea relief, one year after conservative surgery, 179 cases of postoperative dysmenorrhea symptoms

were relieved, and the total remission rate was 90.86% (179/197). Two years after conservative surgery, 173 cases of postoperative dysmenorrhea symptoms were relieved, and the total remission rate was 87.82% (173/197). During follow-up visits, one and two years after conservative surgery for ovarian EMS cysts, the remission rate of dysmenorrhea in patients treated with GnRH-a drugs for six courses of treatment, combined with short-acting oral contraceptives, was found to be significantly higher than in patients who did not take any preventive measures, or who used GnRH-a drugs only to prevent the recurrence of EMS. The difference was statistically significant ($P < 0.05$), and this result was similar to those of other studies [17,18]. Short-acting oral contraceptives can inhibit the growth of eutopic and ectopic endometria, reduce the secretion of inflammatory factors and inhibit the synthesis of prostaglandins from alleviating dysmenorrhea. The long-term oral administration of GnRH-a drugs, combined with short-acting oral contraceptives after conservative EMS surgery, can effectively inhibit the recurrence of EMS lesions and also plays a role in maintenance treatment; it can realize the purpose of long-term treatment and management, i.e. effectively prevent the recurrence of lesions and significantly alleviate dysmenorrhea symptoms [19,20].

In this study, the participants were followed up for two years. The results showed that GnRH-a or GnRH-a combined with oral contraceptives after conservative surgery for ovarian EMS cysts could effectively reduce the recurrence rate of the disease. Compared with GnRH-a only, the maintenance treatment of postoperative GnRH-a drugs combined with oral contraceptives achieved the long-term and continuous control of disease recurrence and, concurrently, alleviated dysmenorrhea.

This study has some limitations. Due to the relatively short follow-up time, the postoperative application of GnRH-a drugs combined with short-acting oral contraceptives requires further long-term follow-up observation. Accordingly, it was not possible to observe the long-term efficacy of surgical treatment for ovarian EMS followed by conservative treatment using three different drug therapies. Further large-scale, multi-centre, randomised controlled studies and clinical observations are thus needed to confirm the results of the present research.

Author Contributions

(I) Conception and design: J Li, X Fu; (II) Administrative support: J Lv, R Li; (III) Provision of study materials or patients: J Li, G Chu; (IV) Collection and assembly of data: J Li, G Chu; (V) Data analysis and interpretation: J Li, G Chu; (VI) Manuscript writing: All authors; (VII) Final approval of the manuscript: All authors.

References

- Scutiero G, Iannone P, Bernardi G, Bonaccorsi G, Spadaro S, Volta CA, et al. Oxidative Stress and Endometriosis: A Systematic Review of the Literature. *Oxid Med Cell Longev*. 2017;2017:7265238.
- Shafir AL, Farland LV, Shah DK, Harris HR, Kvaskoff M, Zondervan K, et al. Risk for and consequences of endometriosis: A critical epidemiologic review. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:1-15.
- Roberta G, Antonino P, Gloria C, Salvatore S, Pasquale DF, Nicola C, et al. Gonadotrophin-releasing hormone analogue or dienogest plus estradiol valerate to prevent pain recurrence after laparoscopic surgery for endometriosis: a multi-center randomized trial. *Acta Obstet Gynecol Scand*. 2015;94(6):637-45.
- Li XY, Chao XP, Leng JH, Zhang W, Zhang JJ, Dai Y, et al. Risk factors for postoperative recurrence of ovarian endometriosis: long-term follow-up of 358 women. *J Ovarian Res*. 2019;12(1):79.

5. Bendifallah S, Vesale E, Daraï E, Thomassin-Naggara I, Bazot M, Tuech JJ, et al. Recurrence after Surgery for Colorectal Endometriosis: A Systematic Review and Meta-analysis. *J Minim Invasive Gynecol.* 2020;27(2):441-51.e2.
6. Zhang G. Study on the curative effect and recurrence of dysmenorrhea after ultrasonic ablation of adenomyosis. Hebei Medical University. 2020.
7. Sanchez AM, Vanni VS, Bartiromo L, Papaleo E, Zilberberg E, Candiani M, et al. Is the oocyte quality affected by endometriosis? A review of the literature. *J Ovarian Res.* 2017;10(1):43.
8. Zhou Y, Wu YX, Jin ZJ. Research progress on the pathogenesis of endometriosis. *Int J Obs Gynecol.* 2017;44(01):103-7.
9. Sun WW, Yu B, Liu Y, Zhao RH. Long-term management concepts and management principles of endometriosis. *Chinese Journal of Health Management.* 2019(03):2624.
10. Luna RMA, Chalif JN, Falcone T. Clinical management of endometriosis. *Minerva Ginecol.* 2020;72(2):106-18.
11. Dunselman GAJ, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, Bie BD, et al. ESHRE guideline: management of women with endometriosis. *Hum Reprod.* 2014;29(3):400-12.
12. Nezhat C, Vang N, Tanaka PP, Nezhat C. Optimal Management of Endometriosis and Pain. *Obstet Gynecol.* 2019;134(4):834-9.
13. Muñoz-Hernando L, Muñoz-Gonzalez Jose L, Alvarez-Conejo C, Tejerizo-García A, Lopez-Gonzalez G, Villegas-Muñoz E, et al. Endometriosis: alternative methods of medical treatment. *Int J Womens Health.* 2015;7:595-603.
14. Rolla E. Endometriosis: advances and controversies in classification, pathogenesis, diagnosis, and treatment. *F1000Res.* 2019;8:F1000.
15. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases. 2012.
16. Koga K, Takamura M, Fujii T, Osuga Y. Prevention of the recurrence of symptom and lesions after conservative surgery for endometriosis. *Fertil Steril.* 2015;104(4):793-801.
17. Qiao HF, Liu YL, Lu XY, Yu C, Liu MH. Clinical efficacy of changes in the administration of gonadotropin-releasing hormone analogs on severe ovarian endometriosis. *Chinese Journal of Clinicians (Electronic Edition).* 2016;10(21):3190-4.
18. Zhang L, Liu XQ. Treatment strategies for endometriosis-related infertility. *J Reprod Med.* 2018;27(08):804-8.
19. Charles C, Louis M, Bruno B, Santulli P. Rethinking mechanisms, diagnosis and management of endometriosis. *Nat Rev Endocrinol.* 2019;15(11):666-82.
20. Zhou YF. The necessity of long-term management of patients with endometriosis. *Chinese J Obs Gynecol.* 2017;(3):145-6.