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Effects of Goserellin on Serum VEGF, Anti-Endometrial Antibody and Sex Hormone Levels in Patients with Endometriosis

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YM and XY collected the samples. YM and HL analyzed the data. XY and HL conducted the experiments and analyzed the results. All authors discussed the results and wrote the manuscript.

Key words
Goserellin, Endometriosis, Vascular endothelial growth factor, Anti-endometrial antibody, Sex hormone

ABSTRACT

The objective of this study was to explore the effect of goserellin on the levels of serum vascular endothelial growth factor (VEGF), anti-endometrial antibody (EMAb) and sex hormone in patients with endometriosis. Participants in the study, 92 patients with endometriosis admitted from June 2016 to May 2017 to our hospital, randomly were divided into control group and study group (46 cases in each group). The control group was given routine treatment such as medroxyprogesterone acetate tablet, and the study group was given injection of goserellin on the basis of the control group. The changes of serum VEGF, EMAb, CA125 and sex hormones (FSH, LH, E2, P) were compared before and after treatment. Adverse reactions were recorded during the treatment The occurrence and recurrence were followed up for 1 year. After treatment, the total effective rate of the study group was 95.65%, which was significantly higher than the control group of 80.43% ($P < 0.05$). After treatment, the VEGF level in the study group was significantly lower than the control group, and the EMAb, CA125 levels, and EMAb positive rates were significantly higher In the control group, the difference was statistically significant ($P < 0.05$); after treatment, the levels of FSH, LH, E2, and P in the study group were significantly lower than those in the control group ($P < 0.05$); there was no statistically significant difference in the incidence of adverse reactions between the two groups; After a 1-year follow-up, the relapse rate in the study group was 8.69%, which was significantly lower than the control group's 52.17%. It was concluded that Goserellin has a definite clinical effect in the treatment of endometriosis. It can significantly reduce the levels of VEGF, EMAb and CA125 in serum, regulate the level of sex hormone, inhibit the growth of endometriosis, reduce the recurrence rate, and have a high safety.

INTRODUCTION

Endometriosis (EMS) refers to the normal endometrial tissue growing outside the uterus, mostly in the pelvic genitalia and the peritoneum of adjacent organs, forming nodules and masses, resulting in pelvic adhesion, pain, even infertility, which brings serious harm to the physical and mental health of patients. In recent years, the incidence of EMS is increasing (Li *et al*., 2015; Yue and Jin, 2015). At present, laparoscopic surgery is the main clinical treatment, but some studies show that if no drug treatment is used after surgery, the recurrence rate of 2 years after surgery can reach 30.4% (Kong and Guo, 2015). Therefore, to explore the clinical application of drugs after EMS and evaluate the effect of drug treatment after operation is of great significance to reduce the recurrence rate of EMS and promote the rehabilitation of patients.

Goserellin is the most commonly used gonadotropin releasing hormone agonist (GnRHa) in clinical. It has the advantages of long-term, targeting, high bioavailability, termination of administration at any time and fewer side effects, so it is widely used in a variety of hormone dependent diseases (Cao *et al*., 2015). However, the specific efficacy and mechanism of its effect on patients

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with endometriosis have not been clarified.

In this study, 92 patients with endometriosis were divided into control group and study group. Goserellin was used to treat patients with endometriosis, and the effects of it on the levels of serum Vascular Endothelial Growth Factor (VEGF), anti-endometrial antibody and sex hormone were further observed. It is reported as follows.

MATERIALS AND METHODS

General information

From June 2016 to May 2017, 92 patients with endometriosis were selected. Inclusion criteria: (1) patients were in accordance with the relevant diagnostic criteria in the guidelines for the diagnosis and treatment of endometriosis formulated by the obstetrics and Gynecology Department of the Chinese Medical Association (Endometriosis Collaboration Group, 2015), and were definitely diagnosed by color ultrasound, CT, MRI imaging and postoperative pathological tissue biopsy; (2) The age was 20-40 years; (3) The patients who first found endometriosis and did not receive treatment; (4) The patients did not use hormone drugs or contraceptives within half a year; (5) Patients and their families have informed consent and cooperate with the treatment. Exclusion criteria: (1) pregnant women or pregnant women, breast-feeding women; (2) Postoperative pathological results show that EMS and uterine fibroids coexist; (3) Patients with severe heart, liver and kidney dysfunction and adenomyosis; (4) Patients with abnormal organ bleeding and undiagnosed diagnosis; (5) Allergic constitution, especially those allergic to the study drug; (6) Patients with poor compliance. The patients were randomly divided into study group (46 cases) and control group (46 cases), age 20-40 years, average (31.5±7.6) years, course of disease 5-15 years, average (6.5±3.6) years, menstrual cycle 27-32 days, average (29.6±2.7) days, menstrual period 4-7 days, average (5.5±1.2) days; EMT stage, stage I-II 58 cases, stage III-IV 34 cases; pathological location, unilateral ovarian chocolate cyst 49 cases, bilateral ovarian Qiao Qiao There were 16 cases of cleft cyst and 27 cases of mass of utero rectal fossa. There was no significant difference in age, duration and menstrual cycle between the two groups ($P > 0.05$; Table I).

Methods

The patients in the control group were treated with oral medroxyprogesterone acetate tablets (Zhejiang Xianju Pharmaceutical Co., Ltd., production batch number: 33020715, specification: 2mg * 100 tablets) 30mg/ time, once a day, and Ibuprofen tablets (Harbin renhuang Pharmaceutical Co., Ltd., production batch number: 23021739, specification: 0.2g) 0.1g/time, once a day. On this basis, the study group was injected subcutaneously with astrazeneca UK Limited, production batch No.: 20160314, specification: 3.6mg/piece) 3.6mg/ time, on the anterior abdominal wall, once every 28d since the injection date. Both groups are treated for 6 months continuously. The occurrence of vaginal bleeding, hot flashes, hyperhidrosis and other adverse reactions during the treatment were observed and recorded.

Observation indicators

Before and after the treatment, 5ml of fasting venous blood was taken from the patients in the morning. The serum was separated, and stored at - 20 ℃.

Total effective rate = (cure + effective + effective)/ total cases × 100%

Cure: the clinical symptoms disappear, the pelvic cyst mass disappears, and the infertile patients get pregnant successfully. Significant effect: The clinical symptoms improve significantly, the pelvic mass shrinks by more than 50%, the infertile patients get pregnant successfully. Effective: The clinical symptoms reduce significantly, thepelvic mass shrinks by 30% ~ 50%,

Table I. Comparison of two groups of general data.

Project		Treatment group	Control group
Age (years)	20~40	32.8±7.5	32.4±6.2
Course of disease (year)	5~15	6.2±3.4	6.3±3.6
Menstrual cycle (d)	27~32	29.8±2.4	29.2±2.8
Period (d)	4~7	5.4±1.6	5.5±1.5
EMS staging (example)	Stage I ~ II	28	18
	Stage III ~ IV	30	16
Lesion (example)	Unilateral ovarian chocolate cyst	24	25
	Bilateral ovarian chocolate cysts	9	7
	Uterine rectal fossa mass	13	14

Table II. Comparative analysis of sex hormone levels and adverse reactions before and after treatment.

		Treatment group (n=43)	Control group (n=43)	χ^2	P
FSH (mmol/mL)	Before treatment	8.97±2.83	8.90±2.65	0.152	>0.05
	After treatment	3.85±2.26	5.23±2.39	6.706	<0.05
LH (mmol/mL)	Before treatment	8.87±3.32	8.83±3.12	0.072	>0.05
	After treatment	4.32±2.23	5.73±2.50	2.797	<0.05
E2 (pg/mL)	Before treatment	112.15±12.39	112.63±12.25	0.177	>0.05
	After treatment	76.45±7.92	85.83±8.06	6.600	<0.05
P (nmol/L)	Before treatment	281.65±17.36	287.15±19.50	0.072	>0.05
	After treatment	204.40±18.43	235.35±18.42	2.797	<0.05
Vaginal bleeding		1 (2.17%)	2 (4.34%)	-	-
Hot flashes		3 (6.52%)	2 (4.34%)	-	-
Hyperhidrosis		2 (4.34%)	3 (6.52%)	-	-
Total incidence rate		6 (13.04%)	7 (15.21%)	-	-

and the drug is stopped for 3 months after the symptoms did not aggravate; invalid: clinical symptoms and signs did not change or even worsen. Subjective symptoms = pelvic symptoms score (9 points) + positive signs score (6 points), the higher the score, the more serious the disease.

The levels of VEGF and EMAb were detected by enzyme-linked immunosorbent assay (ELISA). The positive standard of EMAb was OD at 450nm of the serum to be tested / OD at 450nm of the negative control > 2.1.

CA125 level was detected by electro chemilumin escence.

The level of FSH, LH, E2 and progesterone (P) were measured by automatic biochemical immune analyser.

Statistical methods

Spss 19.0 software package was used to carry out statistical analysis on the research data. The measurement data was indicated by $\bar{x}\pm s$. The comparison between groups was indicated by 't' test. The count data was indicated by n%%. The comparison between groups was indicated by χ^2 test, $P < 0.05$, the difference was statistically significant.

RESULTS

The total effective rate of the study group after treatment was 95.65%, and that of the control group was 80.43%. The difference between the two groups was statistically significant ($P < 0.05$).

The level of VEGF in the study group was significantly lower than that in the control group. The level of EMAb and the positive rate of EMAb were significantly higher than that in the control group, with a statistically significant difference ($P < 0.05$).

There was no significant difference in serum CA125 level between the two groups before treatment ($P > 0.05$). After treatment, the serum CA125 level of the two groups was significantly lower, and the level of the study group was significantly lower than that of the control group ($P < 0.05$).

After treatment, the water levels of FSH, LH, E2 and P in the two groups were significantly lower than those in the control group ($P < 0.05$). The difference was statistically significant ($P < 0.05$; Table II).

After treatment, the incidence of adverse reactions was 13.04% in the study group and 15.21% in the control group. There was no significant difference between the two groups ($P > 0.05$; Table II).

The two groups were followed up for one year. There were four cases of recurrence in the study group (8.69%) and 24 cases of recurrence in the control group (52.17%). The difference between the two groups was statistically significant ($P < 0.05$).

DISCUSSION

Endometriosis is a common progressive disease in gynecology, which is characterized by chronic pelvic pain, menstrual disorders, dysmenorrhea, coital pain and infertility, with aggressive growth and high recurrence rate (Vercellini *et al*., 2016). The pathogenesis of EMS has not been clear. It has been found that EMS is an estrogen dependent disease, which may be related to metabolism, endocrine state change and genetic factors, and may also be related to ovarian hormone secretion and immune disorders (Montgomery *et al*., 2015). In recent years, GnRHa has been widely used in the treatment of EMS, and the effect is ideal. The representative drug is goserellin, which can reduce the inflammatory response

around the endometriosis focus, reduce the formation of blood vessels, and significantly reduce the endometriosis capsule by inhibiting the secretion of gonadal hormones in the pituitary gland It has good effect on hysteromyoma, endometriosis and prostate cancer (Weng *et al*., 2015). In this study, goserellin was used to treat endometriosis, the results are as follows.

The results of this study showed that the total effective rate of the study group was 95.65% after treatment, which was significantly higher than that of the control group (80.43%), and there was no increase in the incidence of adverse reactions. After one year of follow-up, the recurrence rate of the study group was also significantly lower than that of the control group, which indicated that goserelin could effectively improve the clinical subjective symptoms of EMS patients, reduce the recurrence rate, and have a high safety. The mechanism may be that goserellin can reduce the steroids secreted by the ovary by regulating the secretion function of the pituitary gland, force the patient to amenorrhea, and cause the endometrial lesions to be reduced, so as to alleviate the clinical symptoms. Due to the biological instability of goserellin, its ability to penetrate the intestinal epithelium of human body is poor. Therefore, only parenteral administration such as subcutaneous injection is used (Zhang *et al*., 2017).

VEGF is considered to be one of the most important angiogenic factors. It can stimulate the differentiation and proliferation of endothelial cells, increase the permeability of micro vessels, and promote the formation of endothelial cells and small blood vessels by binding with corresponding receptors. It has been found that the expression of VEGF in EMS patients increased significantly, suggesting that VEGF can promote the formation of new blood vessels in ectopic lesions, and promote the progress of EMS (Zhou and Huang, 2018). The results of this study showed that the VEGF level of the study group was significantly lower than that of the control group after the treatment of goserelin, which confirmed that goserelin can effectively inhibit the growth and development of ectopic vascular endothelial cells, and slow down the progress of EMS. The reason is that goserelin can reduce the endometriosis focus by inhibiting the secretion of estrogen in the body The level of estrogen can block the nutritional support to the ectopic focus, and then reduce the secretion of VEGF, so as to inhibit the growth of ectopic endometrium (Liu and Sanqin, 2017).

In recent years, EMAb, as an autoantibody targeting endometrial antigen, has become a marker antibody of endometriosis. Some studies have shown that endometrium can change the immune system of patients to a certain extent under pathological state, which can induce immunity and produce anti EMAb, and increase the content of EMAb in the body, showing positive expression (Berkkanoglu and Arici, 2015). The results of this study showed that the level of EMAb and the positive rate of EMAb in the study group were significantly higher than those in the control group, which confirmed the significance of EMAb in the diagnosis of endometriosis. It has been found that because the barrier between pathological tissue and blood vessel of EMS patients is destroyed, CA125 enters into the blood in a large amount, resulting in the increase of CA125 content in serum, which further aggravates the extent of infiltration of the focus into the peritoneum (Vercellini *et al*., 2016).

In addition, the results of this study showed that the serum CA125 level in the study group was significantly lower than that in the control group after treatment, which further confirmed that goserellin could effectively prevent the progress of EMS, consistent with the results of Wang Jun *et al*. After the treatment, FSH, LH, E2, P levels in the study group were significantly lower than those in the control group at the same time, suggesting that goserellin can effectively improve the level of sex hormones in EMS patients and promote the recovery of the disease. It may be that goserellin can significantly reduce the level of estrogen in the body, and then effectively inhibit the growth of ectopic endometrial lesions, which is consistent with the research results of Zhang Yufang (Yang *et al*., 2018). However, this study also has some limitations, such as a small number of included cases, there may still be individual differences, inadequate mechanism research and so on, we still need to further explore in the future.

CONCLUSIONS

In conclusion, goserelin can effectively improve the clinical symptoms of patients with endometriosis by regulating the levels of VEGF, EMAb and sex hormone, reducing the occurrence of inflammatory reaction, inhibiting the growth of endometriosis, reducing the recurrence rate, and not increasing the incidence of adverse reactions. It is worthy of clinical application.

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Data availability

The data used to support the findings of this study are available from the corresponding author upon request.

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IRB approval

This research was carried out with the approval of Research Guidance Workshop Committee (The First Affiliated Hospital of Guangxi Medical University).

Ethical statement

The study was carried out in compliance withguidelines issued by ethical review board and institutional biosafety committee of Wuming Hospital of Guangxi Medical University. The official letter would be available on fair request to corresponding author.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Berkkanoglu, M., and Arici, A., 2015. Immunology and endometriosis. *Am. J. Rep. Immun.,* **50**: 48-59. https://doi.org/10.1034/j.1600-0897.2003.00042.x

Cao, W., Li, H. and Chu, L., 2015. Clinical efficacy and pregnancy status of conservative surgery combined with goserelin in treating endometriosis. *Chin. Sex. Sci.,* **6**: 45-48.

Endometriosis Collaboration Group of Chinese Medical Association Obstetrics and Gynecology Branch. 2015. Guidelines for the diagnosis and treatment of endometriosis. *Chin. J. Obst. Gynec.,* **3**: 161-169.

Kong, D. and Guo, H., 2015. Research progress on long-term medication to prevent recurrence after conservative surgery for endometriosi. *J. Pract. Obst. Gynecol.*, **31**: 19-22.

Li, Y., Wang, D. and Chen, Y., 2015. Analysis of clinical characteristics and significance of different types of endometrioses. *J. Pract. Obst. Gynecol.*, **31**: 34-36.

Liu, Y. and Sanqin, X.Y., 2017. Clinical significance of serum CA125, EMAb, ENA-78, EPO, and VEGF levels in patients with endometriosis. *Chin. J. Fam. Plan.,* **25**: 479-481.

Montgomery, G.W., Nyholt, D.R. and Zhao, Z.Z., 2015. The search for genes contributing to endometriosis risk. *Hum. Reprod. Update,* **14**: 447-457. https://doi.org/10.1093/humupd/dmn016

Vercellini, P., Crosignani, P.G., Abbiati, A., 2016. The effect of surgery for symptomatic endometriosis: The other side of the story. *Hum. Reprod. Update,* **15**: 177. https://doi.org/10.1093/humupd/dmn062

Vercellini, P., Somigliana, E. and Viganò, P., 2016. Endometriosis: Current therapies and new pharmacological developments. *Drugs*, **69**: 649. https://doi.org/10.2165/00003495-200969060-00002

Wang, J., Li, X. and Yuan, D., 2015. Effects of GnRH-a on serum CA125, EMAB and RANTES in patients with endometriosis. *Prog. Mod. Biomed.*, **15**: 6686-6688.

Weng, Q., Ding, Z.M. and Lv, X.L., 2015. Chinese medicinal plants for advanced endometriosis after conservative surgery: A prospective, multi-center and controlled trial. *Int. J. clin. exp. Med.,* **8**: 11307-11311.

Yang, Y., Gong, H. and Yuan, S., 2018. Clinical study of Xiaojin Wan combined with goserelin in the treatment of endometriosis. *Mod. Med. Clin.,* **9**: 2326-2330.

Yue, J. and Jin, L., 2015. Impact of endometriosis on female fertility and evaluation methods. *J. Pract. Obst. Gynecol.*, **31**: 7-9.

Zhang, L. and Zhong-Xin, W.U., 2017. GnRH-a combined with estrogen reverse therapy in the treatment of severe endometriosis patients for pain and long-term recurrence rate. *J. clin. exp. Med.,* **15**: 25-66.

Zhou, Y. and Huang, Y., 2018. Effect of gonadotropin-releasing hormone agonist on endometriosis and its effect on expression of vascular endothelial growth factor and neutrophil activating peptide 78. *Chin. Mater. China Hlth. Car.,* **2**: 13-19.