

Original Article

Efficacy of goserelin combined with laparoscopic surgery for endometriosis and its effects on ovarian function and oxidative stress

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Abstract: Objective: To investigate the efficacy of goserelin (GOS) combined with laparoscopic surgery (LS) in the treatment of endometriosis (EMS), and its effects on ovarian function and oxidative stress (OS). Methods: A total of 208 patients with EMS were enrolled in this retrospective study. The control group (n=102) received LS alone, while the research group (n=106) received GOS combined with LS. The endpoints included therapeutic efficacy, time to ovulation resumption, time to menstrual recovery, dysmenorrhea, pelvic pain, ovarian function indices [follicle-stimulating hormone (FSH), estradiol (E_2), luteinizing hormone (LH)], inflammatory markers [interleukin (IL)-1 β , IL-6, tumor necrosis factor (TNF)- α], OS indices [reactive oxygen species (ROS), malondialdehyde (MDA), advanced oxidation protein products (AOPP)], adverse reactions, and postoperative recurrence. Subgroup analyses were performed by stratifying patients based on age, ovarian cyst diameter, and American Society for Reproductive Medicine (ASRM) classification. Results: Compared to the control group, the research group showed the following significant differences: (1) The total effective rate was notably higher, and the time to ovulation resumption and menstrual recovery was significantly shorter; (2) Postoperative dysmenorrhea and pelvic pain were evidently relieved, and the postoperative levels of FSH, E_2 , LH, IL-1 β , IL-6, TNF- α , ROS, MDA, and AOPP were statistically lower; (3) The recurrence rates at 6 months and 1 year after surgery were significantly reduced (all $P < 0.05$). There was no significant difference in the overall incidence of adverse reactions between groups ($P > 0.05$). The interactions of age, ovarian cyst diameter, and ASRM classification with therapeutic efficacy were not statistically significant (all $P > 0.05$). Conclusion: On the basis of LS, the addition of GOS is effective for the treatment of EMS, and it exerts positive effects on improving ovarian function and inhibiting OS.

Keywords: Goserelin, laparoscopic surgery, endometriosis, therapeutic effect, oxidative stress, ovarian function

Introduction

Endometriosis (EMS) is a common benign gynecologic lesion, as well as a chronic estrogen-dependent inflammatory disease that can cause dysmenorrhea, chronic pelvic pain, infertility, etc. [1, 2]. Epidemiologic data show that EMS affects 11% of reproductive-aged women, among whom 50-60% of women and adolescent girls with pelvic pain, and 50% of infertile women are affected by this disease [3]. Pathologically, EMS is characterized by the growth of endometrial-like tissue outside the uterus, mainly in the pelvic peritoneum, ovaries, and rectovaginal septa. It not only impairs the fertility of women of childbearing age but also affects their interpersonal relationships,

work efficiency, physical and mental health, and quality of life [4]. Its pathologic mechanism is closely related to oxidative stress (OS), which promotes the excessive secretion of pro-inflammatory molecules and drives the immune system to shift towards a pro-inflammatory state. This in turn damages ovarian reserve function, reduces oocyte quality, further aggravates EMS, and leads to impaired oocyte quality and eutopic endometrium [5, 6].

Laparoscopic surgery (LS) is the standard treatment for women with EMS-related pain or infertility who fail to respond to pharmacotherapy, with the effects of relieving pain and improving fertility [7]. Its therapeutic mechanism is to remove or destroy endometriotic lesions on the

peritoneum, so as to minimize the adverse effects of these lesions on oocyte quality and/or embryo implantation [8]. Compared to open surgery, LS provides a clearer view of lesions, accelerates postoperative recovery, relieves pain, and achieves better cosmetic outcomes [9]. However, it still has some limitations, including difficulty in completely removing deep and micro-endometriotic lesions, high postoperative recurrence risk, and further damage to patients' ovarian function [10].

Goserelin (GOS) is a gonadotropin-releasing hormone (GnRH) agonist. Long-term use of GOS can inhibit the secretion of pituitary gonadotropins, reduce serum estradiol (E_2) to postmenopausal levels, and thus induce the atrophy of ectopic endometrial lesions [11]. In addition, GnRH agonists can be used as postoperative adjuvant therapy after laparoscopic eradication of deep infiltrating EMS, which helps relieve pain and prevent postoperative recurrence [12]. Currently, there is insufficient research on the mechanism of GOS combined with LS for the treatment of EMS, particularly regarding its efficacy and effects on ovarian function and OS. This study aims to address this clinical gap by conducting a relevant analysis, so as to provide new insight for the management of EMS.

Patients and methods

General information

A total of 208 patients with EMS treated at the Affiliated Hospital of Southwest Jiaotong University from October 2021 to October 2024 were enrolled in this retrospective study. Among them, 102 patients in the control group received LS alone, and 106 patients in the research group received GOS combined with LS. Ethical approval was obtained from the Ethics Committee of the Affiliated Hospital of Southwest Jiaotong University.

Patient selection criteria

Inclusion criteria: (1) adult patients aged >18 years; (2) initially diagnosed with EMS according to the relevant diagnostic criteria [13]; (3) stage II-IV disease according to the American Society for Reproductive Medicine (ASRM) classification [14]; (4) meeting indications for LS; (5) no allergy to the study drugs; (6) complete clinical data.

Exclusion criteria: (1) acute gynecologic inflammation; (2) impaired vital organ function; (3) primary immunodeficiencies; (4) other gynecological diseases (including polycystic ovary syndrome, adenomyosis, or hydrosalpinx); (5) reproductive system infection or reproductive tract malformations; (6) use of immunosuppressants, anti-infective agents, or other related drugs within the past 3 months; (7) cognitive impairment or abnormal mental status.

Treatment methods

The control group underwent LS, with specific procedures as follows: Patients received general anesthesia by endotracheal intubation and were placed in the Trendelenburg lithotomy position during surgery. A small arc-shaped incision was made under the umbilical margin to establish a pneumoperitoneum (pressure: 12-14 mmHg; 1 mmHg=0.133 kPa). Operating holes were made at the left and right McBurney's points for the placement of laparoscopic and surgical instruments. During the operation, the pelvic cavity was carefully explored by laparoscopy; after lesion localization, adhesive tissue was separated using an electrocoagulation hook. Ovarian endometriotic lesions were directly enucleated; peritoneal lesions were directly resected or cauterized. After thorough hemostasis, routine pelvic irrigation was performed to prevent pelvic adhesions. Subsequently, the pneumoperitoneum was decompressed, and the incision was closed. For infection prevention, patients received routine antibiotic treatment before and after surgery.

The research group received additional GOS treatment on the basis of LS. GOS was subcutaneously implanted on the first day of menstruation, at a dose of 3.6 mg each time, once every 28 days. The postoperative treatment duration for both groups was 6 months.

Outcome measures

Therapeutic efficacy: Efficacy was evaluated according to the following criteria: Cure: no clinical manifestations and no pelvic cysts detected. Markedly effective: no clinical manifestations and significant reduction in pelvic cysts. Effective: clinical manifestations were controlled, but pelvic cyst size did not decrease. Ineffective: clinical manifestations deteriorat-

ed, and pelvic cysts did not shrink. Total effective rate = (number of cured cases + number of markedly effective cases + number of effective cases)/total number of cases × 100%.

Postoperative recovery: The time to ovulation resumption and menstrual recovery was observed in both groups.

Postoperative pain: The intensity of dysmenorrhea and pelvic pain was assessed before treatment and 6 months after treatment using the 10-point Numeric Rating Scale (NRS) [15], with higher scores indicating more severe pain.

Ovarian function indices: Fasting peripheral venous blood (3 mL) was collected from each patient before surgery and 6 months after surgery, and serum was isolated by centrifugation. Follicle-stimulating hormone (FSH), estradiol (E_2), and luteinizing hormone (LH) levels were measured by radioimmunoassay.

Inflammatory markers: Enzyme-linked immunosorbent assays (ELISAs) were performed to detect serum interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF)- α levels at baseline and 3 months after surgery.

OS indices: Serum reactive oxygen species (ROS), malondialdehyde (MDA), and advanced oxidation protein products (AOPP) levels were quantified using ELISA before and 3 days after surgery.

Adverse events: The occurrence and incidence of postoperative adverse reactions, including transaminase elevation, dizziness and fatigue, gastrointestinal discomfort, and vaginal bleeding, were recorded.

Postoperative recurrence: Patients in both groups were followed up by telephone and outpatient visits to compare the 6-month and 1-year postoperative recurrence rates.

Statistical methods

Measured data with a normal distribution were expressed as mean $\pm$ Standard Deviation (SD). Independent samples t-test and paired t-test were used for inter-group and intra-group (pre- and post-intervention) comparisons, respectively. Measured data with non-normal distribution were expressed as median (interquartile range) [M (P25, P75)]. Mann-Whitney U test and Wilcoxon signed-rank test were used for inter-

group and intra-group comparisons, respectively. For all continuous variables, Shapiro-Wilk test was first performed to test for normality; A P -value >0.05 indicated normal distribution, and a P -value ≤ 0.05 indicated non-normal distribution. Counted data were expressed as cases (percentages) and analyzed by χ^2 test. A binary Logistic regression model (Enter method) was further constructed, with age (continuous variable), ovarian cyst diameter (continuous variable), and ASRM classification (II vs. III-IV) as subgroup variables, and treatment subgroups, subgroup variables, and their interaction terms as covariates. The P -value for interaction was calculated to examine whether subgroup variables acted as effect modifiers for efficacy; a P -value for interaction <0.05 indicated a significant interaction. Hosmer-Lemeshow test was used to assess the goodness-of-fit of the model. All data were imported into SPSS 28.0 for statistical analysis, and a significance level of $P < 0.05$ was adopted.

Results

Patients' general information

There were no significant differences between the two groups in terms of age, disease course, parity, body mass index (BMI), cyst diameter, bilateral cyst status, or ASRM stage (all $P > 0.05$; **Table 1**).

Therapeutic efficacy

In the control group, there were 30 cured cases, 25 markedly effective cases, 22 effective cases, and 25 ineffective cases; in the research group, the corresponding numbers were 39, 32, 26, and 9, respectively. The total effective rate was 91.51% in the research group and 75.49% in the control group, with significant difference ($P = 0.002$; **Table 2**).

Postoperative recovery

Patients in the research group had significantly earlier ovulation resumption and shorter time to menstrual recovery than those in the control group (both $P < 0.001$; **Table 3**).

Postoperative pain

NRS assessment results showed that there were no significant differences in baseline dysmenorrhea and pelvic pain between the two groups (both $P > 0.05$). Both groups showed

Table 1. General data of the two groups of endometriosis patients

Variable	Control group (n=102)	Research group (n=106)	$\chi^2/t/Z$	P
Age (years)	30.81±4.64	30.68±4.93	0.196	0.845
Disease course (years)	3.00 (2.00, 3.00)	3.00 (2.00, 3.00)	-0.558	0.577
Parity (times)	2.00 (1.00, 2.00)	1.50 (1.00, 2.00)	-0.347	0.729
Body mass index (kg/m ²)	22.42±2.12	22.76±2.27	1.115	0.266
Cyst diameter (cm)	3.89±1.02	3.82±0.96	0.510	0.611
Bilateral cysts			0.763	0.382
No	74 (72.55)	71 (66.98)		
Yes	28 (27.45)	35 (33.02)		
ASRM staging			0.269	0.874
II	40 (39.22)	38 (35.85)		
III	39 (38.24)	42 (39.62)		
IV	23 (22.55)	26 (24.53)		

Note: ASRM, American Society for Reproductive Medicine.

Table 2. Therapeutic effects of the two groups of endometriosis patients

Variable	Control group (n=102)	Research group (n=106)	χ^2	P
Cured	30 (29.41)	39 (36.79)		
Markedly effective	25 (24.51)	32 (30.19)		
Effective	22 (21.57)	26 (24.53)		
Ineffective	25 (24.51)	9 (8.49)		
Overall efficacy	77 (75.49)	97 (91.51)	9.755	0.002

Table 3. Postoperative recovery of endometriosis patients in the two groups

Variable	Control group (n=102)	Research group (n=106)	t	P
Time to ovulation resumption (d)	15.54±2.73	9.68±2.32	16.704	<0.001
Time to menstrual period recovery (d)	29.36±2.56	25.92±2.63	9.554	<0.001

Table 4. Postoperative pain of endometriosis patients in the two groups

Variable	Control group (n=102)	Research group (n=106)	Z	P
Dysmenorrhea (points; pre-operation)	6.00 (4.00, 7.00)	5.00 (3.00, 7.00)	-1.097	0.272
Dysmenorrhea (points; post-operation)	2.00 (1.00, 3.00)	1.00 (1.00, 2.00)	-3.119	0.002
Pelvic pain (points; pre-operation)	5.00 (3.00, 6.00)	5.00 (4.00, 7.00)	-1.731	0.083
Pelvic pain (points; post-operation)	2.00 (1.00, 3.75)	1.00 (1.00, 2.00)	-4.484	<0.001

relieved dysmenorrhea and pelvic pain after surgery, and the pain intensity in the research group was significantly milder than that in the control group (both $P<0.01$; **Table 4**).

Ovarian function indices

There were no significant differences in baseline FSH, E2, or LH levels between the two groups (all $P>0.05$). Postoperatively, these indices were significantly down-regulated in both groups (all $P<0.01$), and the reduction was significantly more in the research group (all $P<0.05$; **Figure 1**).

Inflammatory markers

There were no significant differences in preoperative IL-1 β , IL-6, or TNF- α levels between the two groups (all $P>0.05$). These indices decreased in both groups after surgery (all $P<0.05$), and the levels in the research group were significantly lower than those of the control group (all $P<0.05$; **Figure 2**).

OS indices

There were no significant differences in preoperative ROS, MDA, or AOPP levels between

Goserelin plus laparoscopic surgery for endometriosis

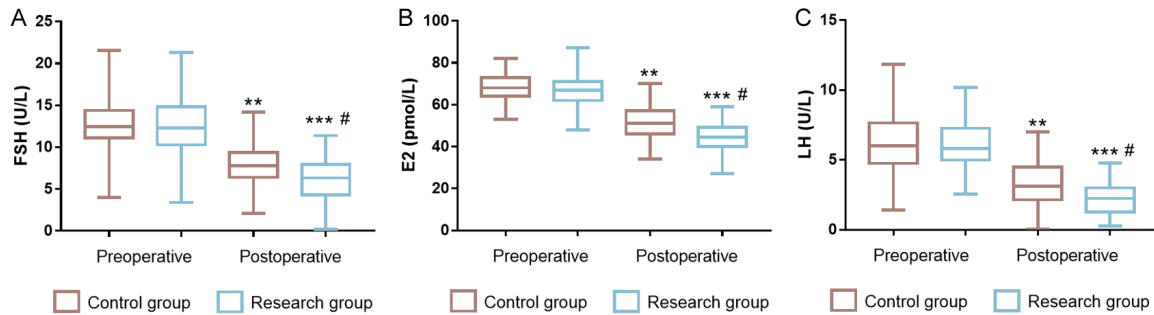


Figure 1. Ovarian function indices of endometriosis (EMS) patients in the two groups. A. Comparison of follicle-stimulating hormone (FSH) levels between the control and research groups before and 6 months after the operation. B. Comparison of estradiol (E_2) levels between the control and research groups before and 6 months after the operation. C. Comparison of luteinizing hormone (LH) levels between the control and research groups before and 6 months after surgery. Note: ** $P < 0.01$, *** $P < 0.001$ vs. preoperative; # $P < 0.05$ vs. control group.

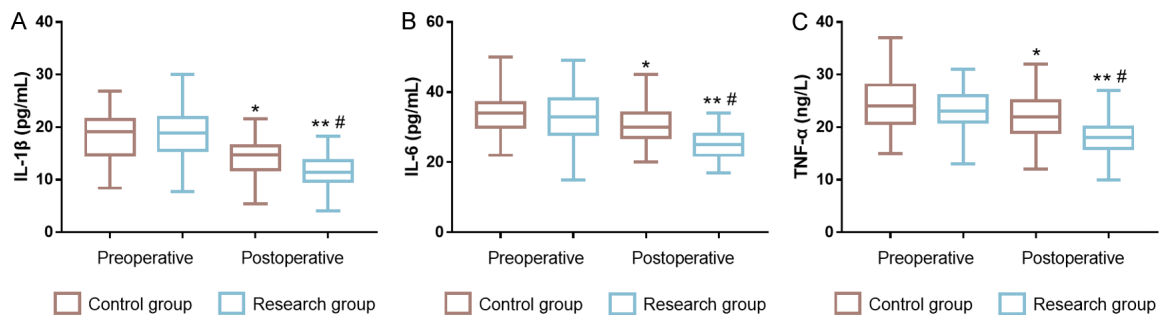


Figure 2. Inflammatory markers of endometriosis (EMS) patients in the two groups. A. Comparison of interleukin (IL)-1 β levels between the control and research groups before and 3 months after the operation. B. Comparison of IL-6 levels between the control and research groups before and 3 months after the operation. C. Comparison of tumor necrosis factor (TNF)- α levels between the control and research groups before and 3 months after the operation. Note: ** $P < 0.01$, *** $P < 0.001$ vs. preoperative; # $P < 0.05$ vs. control group.

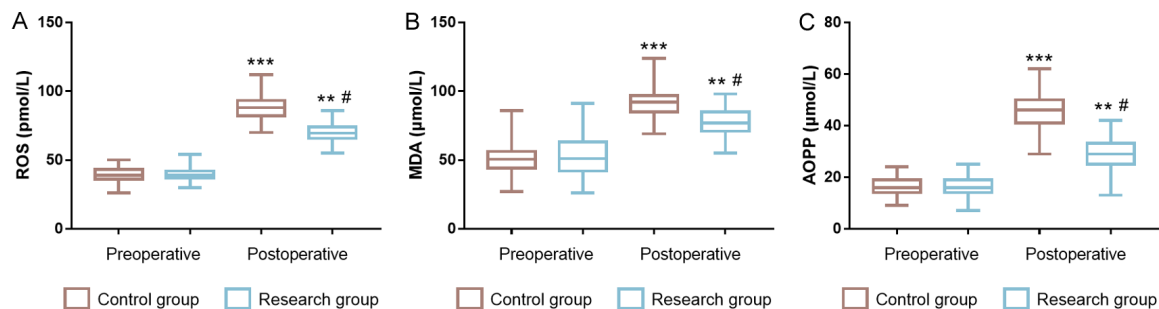


Figure 3. Oxidative stress of endometriosis (EMS) patients in the two groups. A. The changing trend in reactive oxygen species (ROS) levels in the control and research groups (preoperative vs. postoperative day 3) and inter-group differences. B. The changing trend in malondialdehyde (MDA) levels in the control and research groups (preoperative vs. postoperative day 3) and inter-group differences. C. The changing trend in advanced oxidation protein products (AOPP) levels in the control and research groups (preoperative vs. postoperative day 3) and inter-group differences. Note: ** $P < 0.01$, *** $P < 0.001$ vs. preoperative; # $P < 0.05$ vs. control group.

the two groups (all $P > 0.05$). The above indicators in both groups increased significantly following the operation ($P < 0.01$), with levels lower in the research group than in the control group ($P < 0.05$; **Figure 3**).

Adverse reactions

In the control group, 1 case had transaminase elevation, 5 cases had dizziness and fatigue, 4 cases had gastrointestinal discomfort, and 6

Table 5. Adverse events of endometriosis (EMS) patients in the two groups

Variable	Control group (n=102)	Research group (n=106)	χ^2	P
Transaminase elevation	1 (0.98)	1 (0.94)		>0.999
Dizziness and fatigue	5 (4.90)	5 (4.72)	0.004	0.950
Gastrointestinal discomfort	4 (3.92)	3 (2.83)		0.717
Vaginal bleeding	6 (5.88)	4 (3.77)		0.532
Total	16 (15.69)	13 (12.26)	0.507	0.476

Table 6. Postoperative recurrence of endometriosis (EMS) patients in the two groups

Variable	Control group (n=102)	Research group (n=106)	χ^2	P
6 months post-operation	15 (14.71)	6 (5.66)	4.686	0.030
1 year post-operation	25 (24.51)	8 (7.55)	11.205	<0.001

Table 7. Subgroup analysis

Subgroup variable	B	SE	Wald	P	OR	95% CI
Age (continuous variable)						
Group	-5.520	3.482	2.514	0.113	0.004	0.000-3.683
Age	-0.068	0.138	0.245	0.620	0.934	0.713-1.224
Age × Group	0.130	0.104	1.551	0.213	1.138	0.928-1.396
Cyst diameter (continuous variable)						
Group	-1.645	1.730	0.904	0.342	0.193	0.006-5.733
Cyst diameter	-0.022	0.578	0.001	0.970	0.978	0.315-3.034
Cyst diameter × Group	0.101	0.425	0.057	0.812	1.106	0.481-2.543
ASRM classification (dichotomized)						
Group	-2.642	1.074	6.055	0.014	0.071	0.009-0.584
ASRM classification	-2.122	1.428	2.207	0.137	0.120	0.007-1.969
ASRM classification × Group	1.859	1.177	2.492	0.114	6.416	0.638-64.488

Note: ASRM, American Society for Reproductive Medicine.

cases had vaginal bleeding, with an overall incidence of 15.69%. In the research group, 1 case had transaminase elevation, 5 cases had dizziness and fatigue, 3 cases had gastrointestinal discomfort, and 4 cases had vaginal bleeding, with an overall incidence of 12.26%. There were no significant differences in individual adverse reactions or overall incidence between the two groups (all $P > 0.05$; **Table 5**).

Postoperative recurrence

Compared to the control group, the research group had significantly lower 6-month and 1-year postoperative recurrence rates ($P < 0.05$; **Table 6**).

Subgroup analyses based on age, ovarian cyst diameter, and ASRM classification

Age and cyst diameter (continuous variables), as well as ASRM classification (dichotomized

into II vs. III-IV), were included in the binary Logistic regression model (Enter method). Hosmer-Lemeshow test showed that the model fitted well ($P > 0.05$). The P -values for interaction of all subgroup variables were greater than 0.05, indicating that the efficacy of the combined therapy was consistent across different age groups, ovarian cyst diameters, and ASRM classifications. Age, ovarian cyst diameter, and ASRM classification had no significant association with therapeutic efficacy, nor did they act as significant effect modifiers for efficacy (**Table 7**).

Discussion

This study found that Goserelin (GOS) combined with laparoscopic surgery (LS) significantly improved the therapeutic efficacy in EMS patients (91.51% vs. 75.49%). This may be because GOS has a similar effect to hypothalamic gonadotropin-releasing hormone, which

can reduce the stimulation of estrogen on post-operative microlesions and inhibit the secretion of sex hormones by the pituitary gland, thereby enhancing therapeutic efficacy [16]. Consistent with our findings, Song et al. [17] reported that GOS combined with LS was superior to LS alone for the treatment of EMS in terms of efficacy.

Additionally, the time to ovulation resumption and menstrual recovery was further shortened by GOS intervention. This may be because GOS can reversibly restore the function of the hypothalamus-pituitary-ovary axis after treatment discontinuation, normalize the periodic fluctuation of hormone levels, and promote the improvement of the pelvic microenvironment, thus accelerating the recovery of ovulation and menstruation [18]. Furthermore, the addition of GOS after LS effectively relieved dysmenorrhea and pelvic pain, which is consistent with the findings reported by Vercellini et al. [19].

FSH, E₂, and LH levels were measured to assess ovarian function. The measurement was conducted 6 months after surgery to determine the final state of ovarian function inhibition and the overall therapeutic effect after the completion of the entire treatment cycle. We found that supplementary GOS therapy further significantly reduced FSH, E₂, and LH levels, suggesting that GOS has an additional inhibitory effect on ovarian function. Chen et al. conducted a meta-analysis on the application of GOS in EMS patients, and the results showed that GOS can effectively improve the condition, suppress FSH, E₂, and LH levels, relieve pain [20], and reduce recurrence risk, which is consistent with our results.

Inflammation was assessed by measuring IL-1 β , IL-6, and TNF- α levels. To eliminate the interference of surgery (a strong confounder), the assessment was conducted 3 months after surgery. We found that GOS had a more significant inhibitory effect on inflammation in EMS patients. EMS patients have been noted to have immune abnormalities and dysfunction in peritoneal fluid, manifested as a significant increase in pro-inflammatory factors (e.g., IL-6, TNF- α) and a significant decrease in anti-inflammatory cytokines or interferon- γ [21]. A study showed that the anti-inflammatory mechanism of GOS may be partly related to its direct interaction with local GnRH receptors [22]. Mohammed et al. [23] reported that GOS sig-

nificantly reduced serum levels of inflammatory cytokines in the treatment of uterine leiomyoma, which supports our observations.

ROS, MDA, and AOPP levels were detected to assess OS. The measurement was conducted on the 3rd postoperative day (the peak period of acute oxidative damage related to surgical trauma) to verify the independent antioxidant effect of GOS. We found that GOS had a more prominent inhibitory effect on OS in EMS patients. This may be attributed to ischemia-reperfusion injury and increased intra-abdominal pressure caused by pneumoperitoneum during LS, which in turn induces OS, specifically manifested as a short-term abnormal increase in oxidative markers such as ROS, MDA, and AOPP after surgery [24]. However, there are few reports on the effect of GOS on OS in EMS, and the specific mechanism needs further clarification through basic experiments.

Regarding safety, GOS-assisted LS in EMS patients did not increase the risk of overall adverse reactions (transaminase elevation, dizziness and fatigue, gastrointestinal discomfort, and vaginal bleeding). This may be related to the high bioavailability, weak protein-binding ability, and short half-life of GOS, which result in a low possibility of accumulation in the body and thus ensure safety [25]. When used preoperatively in patients with symptomatic uterine fibroids, GOS also shows good safety and tolerability [26], which is similar to the results of this study.

Furthermore, GOS-assisted LS in EMS was found to have a significant preventive effect on 6-month and 1-year postoperative recurrence. Although LS can effectively remove pelvic lesions in EMS patients and restore the normal anatomic structure of the pelvic cavity, it cannot completely eliminate deep and atypical lesions. These incompletely removed lesions can form new lesions under estrogen stimulation, leading to a higher recurrence rate [27, 28]. The addition of GOS on the basis of LS helps induce drug-induced menopause in patients, inhibit the proliferation of residual lesions, and accelerate their atrophy and necrosis, thereby effectively preventing EMS recurrence [29]. Soysal et al. [30] reported that although GOS alone has high efficacy in reducing estrogen levels and relieving symptoms in post-surgical EMS patients, its combination

with anastrozole achieves more complete endocrine blockade, further prolonging the pain-free interval (2.4 months vs. 1.7 months) and significantly reducing the 24-month recurrence rate (35.0% vs. 7.5%), which complements the results of this study.

Finally, patients were stratified by age, ovarian cyst diameter, and ASRM classification for subgroup analyses. None of these factors exerted a significant modifying effect on the therapeutic efficacy of the combined treatment regimen, indicating that the therapeutic advantages of the combined treatment over surgical treatment alone are not affected by differences in the above characteristics.

Based on the above findings, this study proposes the following guidance for clinical practice: From the perspective of individualized medication courses, the conventional course of GOS for EMS treatment is subcutaneous injection of 3.6 mg every 28 days, with a total treatment course not exceeding 6 months. For patients with severe postoperative pain, those with advanced ASRM stages (II-IV), or those with high-risk recurrence factors, the combination of add-back therapy (daily administration of estrogen and progesterone preparations) can be considered during GnRH-a treatment to reduce bone mineral density loss and enhance symptom control [31]. In terms of postoperative monitoring planning, risk stratification-based monitoring and recurrence warning strategies are required, since EMS is a chronic disease that requires long-term management. Studies have shown that bilateral cysts, high ASRM stages, and increased postoperative TNF- α levels are risk factors for recurrence in EMS patients after laparoscopic conservative surgery, while older age and postoperative adjuvant drug therapy are protective factors [32]. Based on this, bilateral cysts, advanced ASRM stages (III-IV), postoperative TNF- α elevation, younger age, and no postoperative adjuvant medication can be used as early warning signals for recurrence. For patients with the above high-risk factors, follow-ups and reexaminations should be conducted every 3 to 6 months in the first 2 postoperative years, including gynecological B-ultrasound, serum carbohydrate antigen 125 testing, and symptom evaluation (NRS-based dysmenorrhea and pelvic pain assessment), to minimize the risk of postoperative recurrence.

There were several limitations in this study that need to be noted: First, selection bias caused by single-center samples and non-random grouping, as well as confounders such as surgeon's experience and postoperative adjuvant drugs, may have affected the results. To improve the robustness of research conclusions, large-scale, multi-center validation studies should be conducted, using randomization and propensity score matching to balance confounders between groups. Second, dynamic changes in ovarian function, inflammatory, and oxidative stress indices at multiple time points were not analyzed. In subsequent studies, multiple time points can be set for dynamic monitoring to more comprehensively assess the changing trends of various indicators during treatment, so as to clarify the temporal regulatory mechanism of GOS on pelvic injury and endocrine suppression. Third, this study only compared the overall efficacy of the two groups, without conducting subgroup analyses based on ASRM staging, cyst size, age, and other factors. Therefore, it was impossible to clarify the differences in clinical benefits among patients with different disease subgroups using this combined therapy. Given that subgroup analysis requires a large sample size to obtain reliable statistical conclusions, subsequent verification could be carried out by expanding the sample size and conducting stratified analyses using multi-center data.

In conclusion, GOS combined with LS for EMS significantly improved therapeutic efficacy, promoted ovulation resumption, accelerate menstrual recovery, and relieved dysmenorrhea and pelvic pain. It also effectively inhibited ovarian function, inflammation, and OS, without increasing the incidence of overall adverse reactions. Moreover, the combined therapy helped reduce the recurrence rate at 6 months and 1 year after surgery. In addition, GOS combined with LS showed no significant differential benefits for populations with different disease risks (age, ovarian cyst diameter, and ASRM stage).

Disclosure of conflict of interest

None.

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