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Effects of postoperative medical treatment and expectant treatment on dysmenorrhea after conservative laparoscopic surgery for deep-infiltrating endometriosis accompanied by dysmenorrhea

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Abstract

Objective: To compare the efficacy of postoperative adjuvant treatment (gonadotropin-releasing hormone agonists [GnRHas] and oral contraceptives [OCs]) and expectant treatment in preventing recurrent dysmenorrhea following conservative laparoscopic surgery for deep infiltrating endometriosis (DIE) with dysmenorrhea.

Methods: A prospective cohort study was conducted in Shanghai, China. In total, 147 patients with dysmenorrhea who underwent conservative laparoscopic surgery for DIE were enrolled. Following surgery, patients received either postoperative adjuvant therapy (GnRHa or OCs) for 6 months or expectant treatment according to a shared medical decision-making approach. The primary outcome was the postoperative recurrence of dysmenorrhea. The secondary outcomes included reproductive outcomes and drug-induced side effects.

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Results: The generalized estimating equation analysis illustrated that the visual analog scale for dysmenorrhea was significantly higher in the adjuvant treatment group than in the expectant treatment group. Kaplan–Meier analysis and the log-rank test demonstrated that the cumulative recurrence rate was higher in the expectant treatment group than in the adjuvant treatment group, but no difference was noted between the two hormonal treatments. Similar cumulative 24-month clinical pregnancy rates were observed among the three groups.
Conclusions: Compared with expectant management, postoperative medical treatment more effectively relieved symptoms and prevented the recurrence of dysmenorrhea.

Keywords
Deep endometriosis, dysmenorrhea, gonadotropin-releasing hormone agonist, oral contraceptives, expectant management, fertility, adjuvant treatment

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Introduction

Endometriosis (EM) is a common gynecologic disease that affects up to 10% of women of childbearing age. Deep infiltrating endometriosis (DIE) is the most debilitating form of the disease, and it is associated with various types of pelvic pain, infertility, and obstruction of vital organs.[1,2] According to the current consensus, surgical management is frequently selected for significant impairment of the affected organs in patients with severe EM, including symptomatic DIE,[3,4] and conservative surgery is preferred over radical surgery because most women with EM are of reproductive age. DIE is currently an extremely challenging disease, and even with the complete excision of DIE lesions to reduce pain and enhance fertility, cumulative 5-year recurrence rates of 20% to 40% have been reported.[5] These high recurrence rates in turn affect patient quality of life and increase costs for both the individual and society. Therefore, it is crucial to prevent recurrence after conservative surgery. Accordingly, DIE can be viewed as a chronic disease requiring a long-term management strategy after conservative surgery. However, only a few reports specifically focused on postoperative medications for DIE.

At present, the Generation Data Group guidelines state that for women who are surgically treated for EM, postoperative adjuvant medical treatment should be attempted to reduce treatment failures and symptom recurrence.[6] Both gonadotropin-releasing hormone analogs (GnRHas) and low-dose combined estro-progestins (oral contraceptives [OCs]) have been proposed for this purpose.[6] DIE lesions differ from other EM lesions owing to their histopathologic features and correlation with more severe pelvic pain.[7,8] It must be noted that choosing the most effective postoperative management method is challenging, and treatment should be based on patient history, clinical signs/symptoms, the severity of EM lesions, whether the lesion was completely resected, and fertility requirements. However, evidence-based medicine remains poor in this area because data elucidating the great heterogeneity in the postoperative management of patients with DIE are lacking. We therefore conducted the

present study to focus on the efficacy of adjuvant medical therapy following conservative laparoscopic surgery for DIE in alleviating dysmenorrhea, preventing symptom recurrence, and improving fertility and quality of life. We expect this study to provide appropriate clinical evidence for the postoperative decision-making process for patients with DIE.

Materials and methods

Participants

Women between 24 and 44 years old who experienced moderate-to-severe dysmenorrhea for more than 6 months before surgery and who were diagnosed with DIE and underwent conservative laparoscopic surgery within 1 month before enrollment were deemed eligible. Patients were required to be mentally and physically able to describe their symptoms and answer questions. The exclusion criteria were as follows: 1) contraindication to GnRHas, estrogens, or progesterone; 2) pregnancy or lactation; 3) premenopause in women who might reach menopause within 3 years of recruitment; 4) previous surgery for EM or receipt of preoperative hormonal treatment within 6 months of enrollment; and 5) partial resection of ureter, bladder, or intestinal tract tissue during surgery because of mucosal invasion by endometriotic nodules.

Ethics approval

This study was approved by the institutional review board of the International Peace Maternity and Child Health Hospital in Shanghai, China (No. GKLW 2015-34), and written informed consent was obtained from each subject prior to recruitment. Patients were also informed that they had the right to refuse the interview and withdraw from the study at any time.

Diagnostic criteria

The diagnosis of DIE was based on vaginorecto-abdominal examination performed by two surgeons, transvaginal ultrasonography, laparoscopic findings during surgery, and the histologic demonstration of DIE after surgery. The severity of dysmenorrhea was assessed using a 10-point visual analog scale (VAS)[9] as follows: $\geq$7, severe; 4 to 6, moderate; and 1 to 3, mild. Recurrence was defined after surgery as dysmenorrhea with VAS $\geq$ 4. The cumulative clinical pregnancy rate was assessed in subjects within 24 months after surgery.

Procedures

Conservative laparoscopic surgery was performed according to previously described techniques.[10] The conservative techniques included ovarian cystectomy, adhesion lysis, excision of endometriotic lesions, and uterus-sparing surgery. After adhesiolysis, the deep endometriotic implants were dissected, isolated, and then removed. Endometriotic lesions located in the ureters, bladder, rectovaginal septa, and intestinal tract were treated according to the shaving technique, and the surrounding tissue was reinforced with interrupted sutures[11,12] (for patients with rectal wall involvement, the endometriotic implants should be removed using a shaving technique until reaching the normal muscularis layers of the rectum; if endometriosis infiltrates the entire thickness of the vaginal wall through the mucosa, then partial colectomy combined with rectovaginal septum dissection is required). DIE was classified using the procedure specified by the revised American Society for Reproductive Medicine (r-ASRM) guidelines,[13] and the anatomical location of DIE was described according to Chapron.[14]

After conservative surgery for DIE, either drug therapy (GnRHa or OC

group) was administered for 6 months, or patients received no treatment (expectant group) according to an informed and shared medical decision-making approach. Women and physicians considered available information regarding the medical problem in question (the nature of the decision, benefits and risks of the alternatives, uncertainties associated with the decision, an assessment of the patient's understanding of the decision, and the patient's preference) and reached a decision based on mutual agreement.[15] In the GnRHa group, patients were administered 3.75 mg of diphereline via intramuscular injection every 4 weeks after surgery for 6 months. In the OC group, patients took one Yasmin tablet (0.03 mg of ethinyl estradiol combined with 3 mg of drospirenone) every night for 21 days each month starting on the first day of the menstrual period for 6 months after surgery. After postoperative medical or expectant treatment, women who wished to become pregnant were advised to participate in an in vitro fertilization (IVF) protocol if they were older than 35 years, exhibited severe EM (r-ASRM score >70), or if the partner had serious male factor infertility; otherwise, it was recommended that women attempt to become pregnant naturally. IVF was also suggested if patients failed to conceive after 6 months of normal sexual activity.

Data collection and outcome measurement

Baseline characteristics and surgical data were recorded. Patients were scheduled to attend follow-up visits every 3 months for 24 months after surgery. At every visit, each patient was asked to complete a questionnaire regarding the presence and severity of dysmenorrhea (primary outcome) as well as reproductive outcomes and drug side effects (secondary outcomes). In addition, gynecologic or imaging examinations were performed as necessary. Follow-up was discontinued if patients became pregnant and resumed after the end of pregnancy.

Sample size

A recurrence rate of 31% has been previously reported for dysmenorrhea after conservative laparoscopic surgery combined with postoperative GnRHa treatment for EM,[16] and a difference of 25% in recurrence rates between hormonal and expectant treatment for DIE has been hypothesized.[12] We wished to achieve a statistical power of 90% and detect a difference of 25% in the recurrence rate for dysmenorrhea between the hormonal and expectant groups. With an anticipated dropout rate of 10%, we thereby required 44 patients per group. We used a two-sided alpha level of 0.05 to detect significance.

Statistical analyses

SPSS (version 18; SPSS Inc, Chicago, IL, USA) was used to perform statistical analyses. Categorical variables were analyzed using the chi-squared (χ^2) or Fisher's exact probability test. Continuous variables were compared using a *t*-test and Mann–Whitney's U test for normally and non-normally distributed data, respectively. Longitudinal data were analyzed using a generalized estimating equation (GEE) model to obtain valid standard errors. Kaplan–Meier analysis was used to calculate 24-month cumulative postoperative recurrence rates for dysmenorrhea and 24-month cumulative clinical pregnancy rates among the three groups, and the differences were compared using a log-rank test. Cox proportional hazards multivariate analysis (forward) was also used to adjust for age, body mass index (BMI), duration of disease, previous EM surgery, previous infertility history, preoperative dysmenorrhea VAS score, main operative indication,

DIE anatomical location, concurrent ovarian cysts, concurrent adenomyoma, and postoperative management. The data collected during pregnancy were processed as missing data. For life table analysis, the date of entry for each patient was the date of surgery. The last day of analysis was the date of dysmenorrhea recurrence or the date of the last follow-up visit in patients who remained asymptomatic. For all patients who had no event at the end of the analysis, their data were censored. Two-sided p-values of <0.05 were considered statistically significant.

Results

Participants

Between January 2012 and January 2016, 147 women were found to be eligible; 138 women were allocated to the GnRHa (n = 48), OC (n = 44), and expectant groups (n = 46). One patient in the GnRHa group withdrew because of severe vasomotor symptoms, and four patients were lost to follow-up (one, two, and one patient in the GnRHa, OC, and expectant groups, respectively). Ultimately, 46 women in the GnRHa group, 42 women in the OC group, and 45 women in the expectant group were included in the analysis (Figure 1).

Baseline data

The baseline characteristics of the patients are shown in Table 1. No differences were observed among the three groups regarding age, BMI, duration of disease, gravidity, parity, previous hormonal therapy, infertility history, and preoperative dysmenorrhea severity (VAS). Surgical data are shown in Table 2. Operative indications, intraoperative blood loss, operative time, pelvic EM stage, and the position of DIE lesions were similar among the three groups. Ninety-seven patients (35, 31, and 31 patients in the GnRHa, OC, and expectant groups, respectively) underwent an additional oophorocystectomy, and 10 patients (three, three, and four patients in the GnRHa, OC, and expectant groups, respectively) underwent an additional uterus-sparing operation.

Primary outcomes

Figure 2a shows the postoperative VAS for dysmenorrhea during follow-up in the three groups. Based on the GEE model, the postoperative dysmenorrhea scores of all three groups increased gradually over 15 months of follow-up (all $P < 0.05$, Table 3), However, after 15 months, no time-dependent effects were observed. Furthermore, the VAS for dysmenorrhea was significantly lower in the GnRHa and OC groups than in the expectant group, but there was no statistical difference between the GnRHa and OC groups (Table 3).

Figure 2b illustrates the 24-month cumulative dysmenorrhea recurrence rates among the three groups. During the 24 months after surgery, 23 (17.29%) patients experienced recurrent dysmenorrhea. The cumulative recurrence rate in the expectant group (12/45, 26.67%) was higher than that in the hormonal groups (P= 0 .03), but there was no statistical difference between the two hormonal groups. Of 23 patients with recurrence, six were diagnosed with ovarian cysts (all <5 cm in size) during the follow-up period, but no patients required further surgery. Three patients in the hormonal groups underwent hysterectomy for severe pelvic pain, ovarian malignant tumor, or adenomyoma. Multifactor regression analysis illustrated that concurrent adenomyoma, vaginal DIE, non-postoperative adjuvant treatment, and high preoperative dysmenorrhea VAS were risk factors for dysmenorrhea recurrence (Table 4).

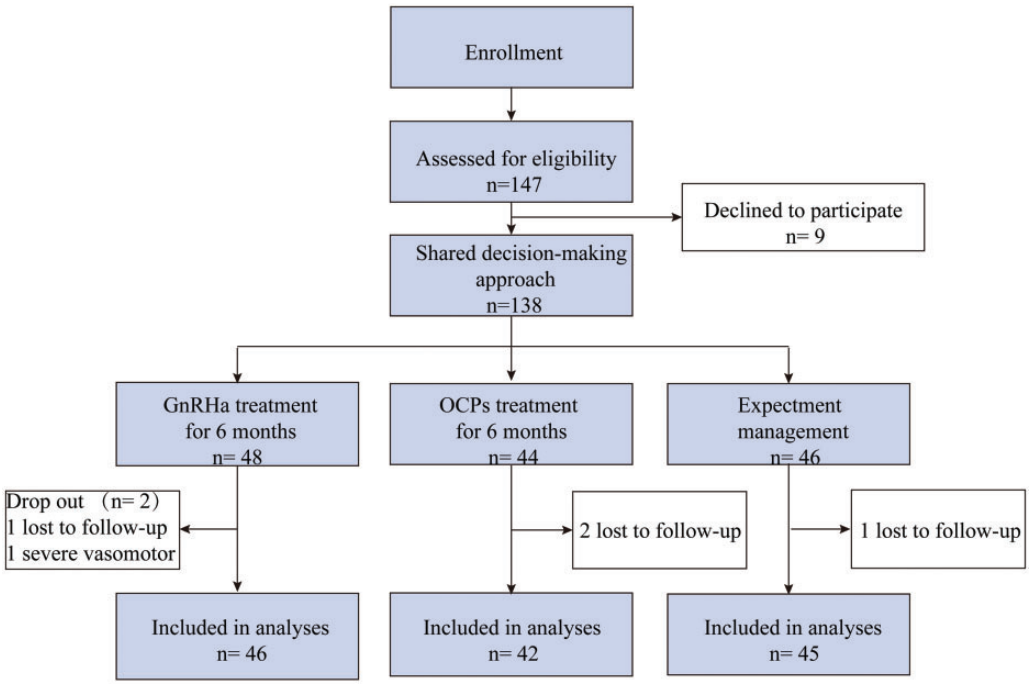

Figure 1. Flow chart.

Table 1. Baseline characteristics of the three groups.

Variables	GnRHa group (n = 46)	OC group (n = 42)	Expectant group (n = 45)
Age[a] (years)	33.96 ± 5.23	34.79 ± 5.00	34.56 ± 4.89
BMI[a] (kg/m^2)	21.57 ± 2.65	21.98 ± 2.35	21.91 ± 3.07
Duration of disease[a,b] (years)	6.71 ± 5.48	6.14 ± 5.31	6.44 ± 6.01
Gravidity[a]	1.07 ± 1.14	1.12 ±1.09	0.95 ±1.07
Parity[a]	0.57 ± 0.62	0.57 ±0.63	0.6 ± 0.62
Previous hormone therapy[c] (n, %)	9 (19.57)	9 (21.43)	9 (20)
GnRHa	3 (6.52)	4 (9.52)	5 (11.11)
OC	4 (8.70)	5 (11.90)	3 (6.67)
GnRHa + OC	1 (2.17)	1 (2.38)	0 (0.00)
GnRHa + LNG-IUS	1 (2.17)	0 (0.00)	1 (2.22)
Previous infertility history (n, %)	15 (32.61)	13 (30.95)	16 (35.56)
Preoperative VAS[a,d]	6.63 ± 1.91	6.62 ± 1.97	6.78 ± 2.17

GnRHa, gonadotropin-releasing hormone agonist; OC, oral contraceptive; BMI, body max index; LNG-IUS, levonorgestrel-releasing intrauterine system, VAS, visual analog scale.

[a]Data are shown as the mean ± SD.

[b]Duration of disease refers to the period starting from the date of diagnosis to that of recruitment.

[c]Previous GnRHa or OC therapy for >1 month.

[d]The degree of baseline dysmenorrhea was evaluated by the preoperative VAS (0, no pain, 10, severe pain).

Table 2. Intraoperative parameters of the three groups.

Variables	GnRHa group (n = 46)	OC group (n = 42)	Expectant group (n = 45)
Main operative indication[a]			
Pain	26 (56.52)	24 (57.14)	24 (53.33)
Infertility	10 (21.74)	8 (19.05)	10 (22.22)
Ovarian cyst	10 (21.74)	10 (23.81)	11 (24.44)
Intraoperative blood loss (mL)	163.91 ± 142.12	158.93 ± 147.88	170.22 ± 142.96
Operative time (minutes)	160.65 ± 52.68	160.48 ± 71.73	165.33 ± 70.47
r-ASRM stage of pelvic EM[b]			
Stage II	6 (13.04)	5 (11.90)	8 (17.78)
Stage III	15 (32.61)	15 (35.71)	14 (31.11)
Stage IV	25 (54.35)	22 (52.38)	26 (57.78)
DIE anatomical location[c] (main lesion) (N, %)			
Uterosacral ligament	20 (43.48)	21 (50.00)	24 (53.33)
Vagina	11 (23.91)	9 (21.73)	9 (20.00)
Bladder	3 (6.52)	3 (7.14)	2 (4.44)
Intestine	10 (21.74)	8 (19.05)	8 (17.78)
Ureter	2 (4.35)	1 (2.38)	2 (4.44)
Combine with ovarian cyst			
Unilateral cyst	21 (45.65)	17 (40.48)	19 (42.22)
Bilateral cyst	19 (41.30)	17 (40.48)	17 (37.78)
Combined with adenomyosis	6 (13.04)	6 (14.29)	7 (15.55)
Combined with adenomyomectomy	3 (6.52)	3 (7.14)	4 (9.52)

GnRHa, gonadotropin-releasing hormone agonist; OC, oral contraceptive; EM, endometriosis; DIE, deep infiltrating endometriosis; r-ASRM, revised American Society for Reproductive Medicine.

[a]GnRHa group: 18 patients had two indications; OC group: two patients had three indications, and 16 patients had two indications. Expectant group: two patients had three indications, and 16 patients had two indications.

[b]The r-ASRM stage was based on the revised American Society for Reproductive Medicine (1997).[13]

[c]The DIE anatomical location was used as described by Chapron.[14]

Secondary outcomes

Of the 133 women, 61 patients (45.9%) desired to conceive (21, 18, and 22 patients in the GnRHa, OC, and expectant groups, respectively), Of these patients, 25 patients (nine, eight, and seven patients in the GnRHa, OC, and expectant groups, respectively) underwent an IVF protocol after surgical-medical treatment because of their advanced age, severe EM, or male factor infertility in their partners, and 14 patients (four, four, and six patients in the GnRHa, OC, and expectant groups, respectively) underwent IVF because they failed to become pregnant naturally. The overall 24-month cumulative clinical pregnancy rate was 59.02% (36/61), and no statistical differences were observed among the three groups (Figure 2c). The recurrence rate of dysmenorrhea was comparable between women who wished to conceive (13.11%) and those who did not wish to conceive (20.83%). The overall cumulative 24-month live birth rate was 41.98% (25/61), and the rates were comparable among the groups.

Side effect data are presented in Table 5. Amenorrhea was more common in the GnRHa group than in the other two groups ($P < 0.001$). However, no significant differences were observed between the hormonal groups regarding the incidence of

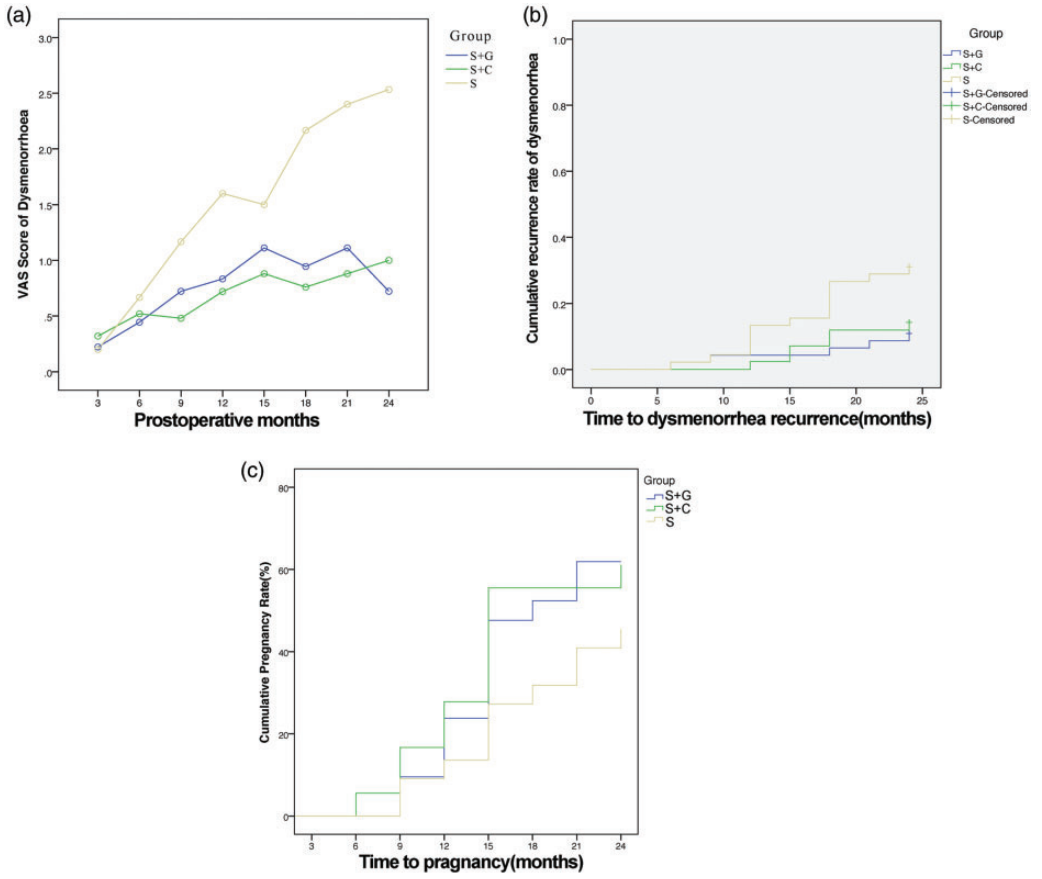

Figure 2. Statistical analyses for postoperative symptoms among the three groups. (a) VAS of dysmenorrhea in postoperative follow-up visits among the three groups. (b) Kaplan–Meier analysis and log-rank test for the 24-month cumulative postoperative dysmenorrhea recurrence rate. The cumulative recurrence rate was higher in the expectant group than in the two therapeutic regimens groups ($\chi^2 = 7.20$, $P = 0.03$), but the rate was not significantly different between the GnRHa and OC groups ($\chi^2 = 0.22$, $P = 0.64$). (c) Kaplan–Meier analysis and log-rank test for 24-month cumulative postoperative pregnancy rates. There were no statistically significant differences among the three groups among the 61 women who wished to conceive ($\chi^2 = 2.23$; $P = 0.33$).
VAS, visual analog scale; GnRHa, gonadotropin-releasing hormone agonist; OC, oral contraceptive.

vasomotor symptoms, irregular bleeding, headache, bloating, nausea, decreased libido, or weight gain. The side effects were generally well tolerated, excluding one woman in the GnRHa group who withdrew because of severe vasomotor symptoms.

Discussion

Although studies have revealed that postoperative adjuvant medical treatment after surgery can reduce symptom recurrence in patients with EM,[6] the effectiveness of postoperative medical treatment after surgery in

Table 3. Parameter estimation of postoperative VAS for dysmenorrhea during follow-up visits in the three groups based on the generalized estimation equation model.

Parameters	Standard error	95% Wald confidence interval		p value
		Upper limit	Lower limit	
Intercept	0.28	1.33	2.43	0.00[a]
Paired comparison between groups				
GnRHa versus expectant	0.27	−1.33	−0.29	<0.001
OC versus expectant	0.26	−1.24	−0.23	<0.001
GnRHa versus OC	0.23	−0.51	0.37	0.75
Paired comparison between months				
6 versus 3	0.06	0.19	0.44	0.00[a]
9 versus 6	0.06	0.01	0.34	0.01
12 versus 9	0.10	0.12	0.50	0.01
15 versus 12	0.09	0.03	0.02	0.04
18 versus 15	0.14	−0.05	0.49	0.12
21 versus 18	0.12	−0.15	0.33	0.47
24 versus 21	0.14	−0.45	0.11	0.24

VAS, visual analog scale; GnRHa, gonadotropin-releasing hormone agonist; OC, oral contraceptive.
Dependent variable: VAS
Model: (intercept), group, postoperative month.
[a]The parameter was redundant, and thus, it was set at 0.

Table 4. Multivariate analysis of the factors of recurrence of preoperative dysmenorrhea.

Variable	B	Standard error	Wald	p value	Hazard ratio	95% confidence interval	
Concurrent adenomyoma	1.28	0.44	8.44	<0.001	3.59	1.52	8.52
Vaginal DIE	1.06	0.42	6.30	0.01	2.87	1.26	6.54
Non-postoperative adjuvant treatment	1.25	0.54	5.43	0.02	3.50	1.22	10.01
Preoperative dysmenorrhea VAS score	0.22	0.11	3.87	0.05	1.24	1.00	1.52

DIE, deep infiltrating endometriosis; VAS, visual analog scale; Wald, Wald statistic.

Table 5. Side effects of postoperative hormone therapy in the GnRHa and OC groups.

Variables	GnRHa group (n, %) (n = 46)	OC group (n, %) (n = 42)
Amenorrhea	19 (41.30)[a]	4 (9.52)
Irregular bleeding	6 (13.04)	6 (14.29)
Bloating or swelling	3 (6.52)	4 (9.52)
Nausea	2 (4.35)	3 (7.14)
Weight gain	1 (2.17)	4 (9.52)
Decreased libido	3 (6.52)	2 (4.76)
Vasomotor symptoms	6 (13.04)	1 (2.38)
Headache	2 (4.35)	4 (9.52)

GnRHa, gonadotropin-releasing hormone agonist; OC, oral contraceptive.
[a]Amenorrhea was more frequently observed in the GnRHa group than in the OC group ($P < 0.001$).

patients with DIE remains under debate in China. The results of the current study illustrated that postoperative medical treatment (GnRHa or OC therapy) protected against the recurrence of dysmenorrhea. Furthermore, concurrent adenomyoma, vaginal DIE, non-postoperative adjuvant treatment, and high preoperative dysmenorrhea VAS were closely associated with the recurrence of dysmenorrhea.

Pain is the most prevalent clinical manifestation of DIE,[17] and the severe pelvic pain of patients with DIE might be attributed to its rich innervation[8] and inflammatory nature.[18] GnRHas inhibit the growth of ectopic endometrium, decrease inflammation and vascularization, and induce apoptosis in tissues derived from women with EM,[19,20] whereas OCs suppress ovarian activity, inhibit the production of gonadal estrogen, and reduce EM-associated inflammation and the excessive growth of nerve fibers.[21] The recurrence of pain does not mean the recurrence of lesions, and rates of recurrence were higher when using the resurgence of pain as the definition of relapse rather than surgical findings.[22,23] In our series, the overall symptom recurrence rate was 17.29%. Although all patients with recurrence had a relapse of pain, few DIE masses were detected via imaging or pathologic examination after a second laparoscopic surgery. This may be related to the short follow-up period (24 months) and small sample size of the present study. It is interesting to note over the first 15 months after surgery, the dysmenorrhea score increased commensurately over time (in months), but beyond 15 months, the dysmenorrhea score did not increase, which reminds us that the first 15 months after conservative surgery for DIE is the key period for preventing recurrence and that postoperative adjuvant therapy may be more effective when used at later times.

In a systematic review, younger age and higher BMI were identified as risk factors for DIE recurrence,[24] which was contrary to the findings in our study. It was interesting to observe that a higher preoperative VAS increased the risk of dysmenorrhea recurrence, indicating that a greater severity of preoperative dysmenorrhea increases the likelihood of relapse after surgery. In addition, concurrent adenomyoma was also a risk factor for DIE recurrence after surgery, which might be attributable to the absence of intraoperative treatment of adenomyoma (which can also cause dysmenorrhea). Vaginal DIE is also more likely to manifest dysmenorrhea recurrence than other types of DIE. Although the specific reasons for this remain unclear, one reason may be the high density of nerve fibers in vaginal endometriotic nodules.[25]

Previous reports illustrated that pregnancy rates reached 45% to 58% after the excision of lesions in patients with DIE and infertility,[26,27] which is comparable with the pregnancy rate in our study (59.02%). The European Society of Human Reproduction and Embryology suggested that 3 to 6 months of GnRHa treatment before medically assisted reproductive technologies may be beneficial.[6,28] However, the magnitude of the improvement is likely low, and the available evidence is of poor quality. Consistent with previous results, we did not identify a statistical difference in the cumulative pregnancy and live birth rates between the two postoperative adjuvant treatment subgroups and the expectant group. However, because of the small sample size of our study, for patients who wish to become pregnant after DIE surgery, additional clinical studies are needed to assess whether drug adjuvant therapy is warranted.

The main limitations of our study were the shared decision-making approach and the lack of randomization between medical and expectant management, leading to a lower level of clinical evidence for the study. Because there were no clear

guidelines on whether postoperative medical treatment after DIE could reduce recurrence prior to this study, it was difficult to conduct a randomized controlled study for ethical reasons. From the perspective of feasibility, the shared decision-making approach implemented in this study is more feasible. Nevertheless, the baseline characteristics of the study groups did not differ significantly, thus limiting bias of the final findings of our investigation. Another limitation was the use of postoperative medication only for 6 months with only a 2-year follow-up period. In addition, we used OCs cyclically and not continuously. According to the 2015 guidelines for the diagnosis and treatment of EM in China, cyclic or continuous OC treatment for at least 6 months is recommended. Considering the minimal side effects of OCs, we selected cyclic OC treatment for 6 months. Furthermore, this study only investigated dysmenorrhea, and it did not evaluate other pain symptoms related to DIE (e.g., dyspareunia, chronic pelvic pain, pain at the time of ovulation). This limitation must be improved in future research. At present, we advocate for long-term management after conservative DIE surgery and recommend that future studies focus on clinical randomized controlled trials using different drugs with few side effects, strategies to improve compliance, different durations of treatment, long-term follow-up, and larger sample sizes to clarify the efficacy of surgical-medical treatment for DIE.

Conclusions

This prospective study comprehensively demonstrated that postoperative GnRHa and OC treatment effectively prevented the recurrence of dysmenorrhea symptoms after conservative laparoscopic surgery for DIE. Therefore, we recommend conventional medications after conservative surgery.

Author contributions

Jian Zhang conceived of the study and participated in its design, as well as supervised the study and critically revised the manuscript. Qian Zhu, Jue Ma, and Xiaoya Zhao were responsible for collecting data and writing the manuscript. Guiling Liang participated in revision of the manuscript. Jing Zhai contributed to statistical analysis. All authors substantially contributed to the revision of the manuscript.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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