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DIAGNOSIS AND PREVENTION OF RECURRENCE OF OVARIAN ENDOMETRIOSIS (OE) AFTER SURGICAL TREATMENT

Saidjalilova D.D., Kuzieva Y.M.
Tashkent medical academy

XULOSA

Maqolada endometrioz bilan bog’liq bepushtlik patogenezida oksidlovchi stressning rolini aniqlashga qaratilgan tuxumdon endometriozi (TE) va bepushtlik bilan kasallangan ayollarni keng qamrovli klinik va biokimyoviy o’rganish natijalari keltirilgan. Laparoskopik va morfologik tekshiruv bilan tasdiqlangan tuxumdon kistasi (ICD-10: N80.1) tashhisi bilan jami 106 nafar bemor tekshirildi. Ularga kista kapsulasi >5,0 sm enukleatsiya bilan laparoskopik sistektomiya o‘tkazildi. DNG olgan ayollarda bir yildan keyin takrorlanish darajasi 2,4% ni tashkil etdi, bu terapiya olmagan ayollarga qaraganda 9,5 baravar kam.

Kalit so’zlar: *tuxumdon endometriozi (TE), bepushtlik, retsidivga qarshi terapiya, jarrohlik davolash, endometrioid tuxumdon kistalari.*

РЕЗЮМЕ

В статье представлены результаты комплексного клинико-биохимического исследования женщин с эндометриозом яичников (ЭЯ) и бесплодием, направленного на выяснение роли оксидативного стресса в патогенезе эндометриоз-ассоциированного бесплодия. Обследовано 106 пациенток с диагнозом «кист яичников» (МКБ-10: N80.1), подтвержденным лапароскопически и морфологическим исследованием, которым была выполнена лапароскопическая цистэктомия с энуклеацией капсулы кисты >5,0 см. Частота рецидивов через год у женщин, получавших ДНГ, составила 2,4%, что в 9,5 раза меньше, чем у женщин, не получавших терапию.

Ключевые слова: *эндометриоз яичников (ЭЯ), бесплодие, противорецидивная терапия, хирургическое лечение, эндометриоидные кисты яичников.*

Endometriosis is a condition characterized by the presence of endometrial stromal and glandular tissue outside the uterine cavity, affecting about 10% of women of reproductive age. It commonly leads to symptoms such as chronic pelvic pain, painful menstruation (dysmenorrhea), and infertility, which can severely impact quality of life [1–4]. Endometriosis lesions are typically classified into three main types: peritoneal, ovarian, and deep infiltrating endometriosis. One of the most frequent forms is ovarian endometriosis, presenting as endometriomas (endometrioid ovarian cysts), which occur in over 55% of women diagnosed with the disease [5]. The pathogenesis of endometriomas is complex, not fully elucidated, and distinct from the development of other benign ovarian tumors.

OBJECTIVE

This study aims to investigate the recurrence rates of ovarian endometriosis following surgical treatment and to evaluate the clinical effectiveness and safety of long-term postoperative oral administration of dienogest (2 mg).

MATERIAL AND METHODS

This prospective comparative study was carried out between June 2021 and March 2024 to evaluate the recurrence rate of ovarian endometriosis (OE) following surgical treatment, and to assess the clinical efficacy and safety of long-term postoperative oral administration of dienogest (DNG) at a dose of 2 mg per day.

The study included 106 women diagnosed with ovarian endometriosis (ICD-10 code: N80.1). Diagnosis was confirmed through laparoscopy and histological examination. All patients underwent laparoscopic cystectomy with complete removal (enucleation) of ovarian cysts larger than 5.0 cm in diameter.

Participants were divided into two subgroups based on their postoperative treatment approach:

- Group 1A (n = 85): These patients received oral dienogest at a dose of 2 mg daily for 6 months after surgery, in accordance with the recommendations of the European Society of Human Reproduction and Embryology (ESHRE).
- Group 1B (n = 21): These patients did not receive any postoperative hormonal therapy, either due to contraindications to hormone use or personal choice (e.g., fear of hormonal side effects).

Patients in both groups were monitored for 12 months following surgery to observe recurrence rates and evaluate the effectiveness of the anti-relapse treatment.

RESULTS

The effectiveness of postoperative management was evaluated based on the recurrence rate of ovarian endometriosis 12 months after surgery. Recurrence was determined by control transvaginal ultrasound examination.

Pain symptoms were assessed using the Numeric Rating Scale (NRS), where patients rated their pain on a scale from 0 (no pain) to 10 (unbearable pain). This method allowed for a standardized assessment of the intensity of chronic pelvic pain (CPP), dysmenorrhea, and dyspareunia.

Additionally, pain was also measured using the Visual Analog Scale (VAS) to quantify the severity of dyspareunia, dysmenorrhea, and CPP. Assessments were

carried out immediately after surgery and repeated at 3 and 6 months post-treatment to monitor the change in pain intensity over time.

To evaluate the inflammatory response and potential biochemical indicators of disease activity, serum levels of proinflammatory cytokines and CA-125 were measured in all patients. The specific markers included interleukin-17 (IL-17), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and CA-125. These blood tests were conducted at baseline (postoperative) and at follow-up intervals to detect any correlation between inflammatory activity and clinical outcomes.

Recurrence of endometrioma was defined as the detection of a new cystic lesion with typical characteristics on transvaginal pelvic ultrasound during the 12-month follow-up. Endometriomas were identified by their typical sonographic features–hypoechoic, homogeneous, and partly solid cystic ovarian masses.

Treatment outcomes were analyzed and compared between the study groups using the chi-square (χ^2) test and analysis of variance (ANOVA), depending on the type of data. A p-value less than 0.01 was considered statistically significant, while p-values greater than 0.05 were regarded as not significant.

For categorical variables with expected frequencies below 10, comparisons were made using Fisher's exact test. All data were processed and analyzed using SPSS software, version 11.0.1 for Windows (SPSS Inc., USA).

The analysis of clinical and historical (anamnestic) data among women with ovarian endometriosis showed no statistically significant differences between the groups in terms of age, body mass index (BMI), age at menarche, and parity. There was also no significant difference in the distribution of unilateral versus bilateral endometriomas between the groups (Table 1).

Table 1

Clinical and demographic characteristics of patients in Group 1A and Group 1B

Indicator	Group 1A (n = 85)	Group 1B (n = 21)	p-value
Age (years, M ± m)	32,2±9,7	33,5±8,9	>0,05
BMI (kg/m², M ± m)	22,3±4,1	23,5±3,9	>0,05
Age at menarche (years, M ± m)	12,6±2,0	13,1±1,71	>0,05
Parity (M±m)	0,36±0,78	0,29±0,62	>0,05
Unilateral endometrioma (n/%)	57 / 69,5	16 / 72,7	-
Bilateral endometrioma, (n/%)	25 / 30,5	15 / 27,3	-

Conducting a survey on VAS scales of patients with EO before surgery also showed unreliably significant differences between the groups (Table 2). The severity of pain syndrome did not differ statistically significantly between the two groups.

Table 2

Results of the survey on the scales of patients with EO before surgery

Indicator	Group 1A (n = 85)	Group 1B (n = 21)	p-value
Average pain intensity (NRS, M ± m)	4,58±3,3	4,43±2,7	>0,05
Chronic pelvic pain intensity (VAS, M ± m)	35,2±5,6	36,4±6,1	>0,05
Dyspareunia intensity (VAS, M ± m)	28,4±7,7	29,3±8,9	>0,05
Dysmenorrhea intensity (VAS, M ± m)	27,4±11,5	26,6±9,1	>0,05

Following surgical treatment, all patients were monitored at 3 and 6 months after initiation of therapy. Pain intensity was assessed using the NRS and VAS scales for chronic pelvic pain (CPP), dyspareunia, and dysmenorrhea (see Table 3).

In Group 1A (n = 85), which received postoperative hormonal therapy with dienogest (2 mg/day), a marked improvement in pain symptoms was observed. After 3 months of treatment, pain scores decreased by an average of 2.5 times across all scales (NRS, VAS for dyspareunia, dysmenorrhea, and CPP), indicating a reduction from moderate to mild pain. Continued therapy for 6 months resulted in further improvement, with pain scores reduced by approximately 5 times compared to baseline levels–reflecting either mild symptoms or complete resolution of pain.

In contrast, Group 1B (n = 21), which did not receive any postoperative hormonal therapy, demonstrated an opposite trend. No significant reduction in pain levels was observed during follow-up. In some patients, symptoms of dyspareunia, dysmenorrhea, and CPP persisted or even worsened over time, underscoring the clinical benefit of anti-relapse hormonal therapy in managing postoperative endometriosis symptoms.

In parallel with clinical studies, we conducted a study of inflammation markers IL-17, IL-6, TNF, as well as the concentration of CA-125 in the blood plasma of patients over time. When using DNG in the postoperative period, a decrease in proinflammatory cytokines was observed after 6 months: IL-17 - by 1.8 times, IL-6 - by 1.5 times and TNF - by 1.48 times ($p<0.001$). Whereas, the results in patients in group 1B did not show statistically significant changes in the concentrations of the studied markers during the 12-month observation period.

Table 3

Dynamics of regression of pelvic pain in women with ovarian cystitis in the postoperative period, depending on management (M±m)

Survey scales	1A group (n=85)			1B group (n=21)			P
	Before therapy	3 months of therapy	6 months of therapy	Before therapy	3 months of therapy	6 months of therapy	
Pain intensity according to the NRS scale	4,58±3,3	1,25±0,4	0,63±0,6	4,43±2,7	4,9±3,1	5,56±1,4	<0,001
Average chronic pelvic pain intensity on the VAS scale	35,2±5,6	7,26±2,1	4,32±4,3	36,4±6,1	44,4±5,8	56,4±3,7	<0,001
Average pain intensity on the VAS scale, dyspareunia	28,4±7,7	8,73±0,6	3,31±2,5	29,3±8,9	35,8±7,6	44,08±12,0	<0,001
Average pain intensity on the VAS scale, dysmenorrhea	27,4±11,5	13,18±4,3	5,56±3,7	26,6±9,1	37,4±6,8	52,34±13,1	<0,001

In addition to improvements in pain symptoms, a significant reduction in serum CA-125 levels was observed in Group 1A (patients receiving dienogest therapy). After 6 months of treatment, CA-125 concentrations decreased on average 3.2-fold compared to pre-treatment values, a change that was statistically significant ($p < 0.05$). In contrast, Group 1B (patients who did not receive anti-relapse hormonal therapy) showed no significant change in CA-125 levels over the same follow-up period ($p > 0.05$), indicating the absence of a biochemical response in the absence of postoperative medical treatment.

At the end of the study, we assessed the incidence of recurrence of ovarian cancer using transvaginal echography. The recurrence rate one year after surgical treatment in the group of women receiving DNG was 2.4% (n=2). Whereas, in the group of women who did not receive DNG therapy after surgery, the recurrence rate was 22.7% (n=5), which is 9.5 times more frequent.

CONCLUSIONS

1.The use of DNG (2 mg) for 6 months after surgical treatment of ovarian endometriosis has proven to be highly effective in the treatment of pelvic pain: a 3.6-fold decrease in the severity of pain after 3 months of therapy with complete relief of pelvic pain after 6 months of therapy (according to NRS); a 3.3-fold decrease in the severity of dyspareunia (according to VAS) after 3 months with its greater relief after 6 months; a 2.1-fold decrease in the severity of dysmenorrhea after 3 months and 4.9-fold decrease after 6 months of therapy, relative to the indicators before the start of therapy.

2 The recurrence rate after one year in women who received DNG was 2.4%, 9.5 times less than in women who did not receive therapy.

3 When using DNG in the postoperative period, a decrease in proinflammatory cytokines was observed after 6 months: IL-17 - by 1.8 times, IL-6 - by 1.5 times and TNF - by 1.48 times ($p < 0.001$) and a decrease in the concentration of the CA-125 marker by 3.2 times compared to before the start of therapy ($p < 0.05$).

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