



Efficacy of Ethanol Sclerotherapy Versus Laparoscopic Excision in the Treatment of Ovarian Endometrioma

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Abstract

Objective The purpose of this study was to examine the recurrence rates of ovarian endometrioma, dysmenorrhea, dyspareunia, and related complications between sclerotherapy and laparoscopic ovarian cystectomy in individuals aged 25 to 38.

Methods Eighty-eight women participated in this retrospective, single-center study between January 2020 and February 2022. Patients received either laparoscopy or sclerotherapy, depending on the opinion of the pertinent physician. In this study, the following parameters were retrospectively analyzed in follow-up visits 2, 6 and 12 months after sclerotherapy and laparoscopy: dysmenorrhea and dyspareunia by visual analog scale, complications following the intervention, and serial pelvic sonograms for endometrioma cyst recurrence. Moreover, serum Anti-Müllerian hormone (AMH) level before and 6 months after sclerotherapy/surgery were analyzed. The collected data were then analyzed using R software.

Results The results demonstrate the efficiency of both sclerotherapy and laparoscopic techniques in reducing endometrioma-related dysmenorrhea and dyspareunia over a 12-month period. There was no statistically significant difference in the occurrence of complications and recurrence rate between these two therapies, and both are equally beneficial. Also, the rate of AMH decline after laparoscopy was higher than sclerotherapy; however there was not a statistically significant change in serum level of AMH in laparoscopy compared to the sclerotherapy after 6 months.

Conclusion Considering all the data, it appears that sclerotherapy, with its lower cost, shorter hospital stay, and quicker return to activities, can be a laparoscopic alternative to endometrioma cyst removal. More studies are required.

Keywords Endometrioma · Sclerotherapy · Laparoscopy · Dysmenorrhea · Dyspareunia

Introduction

Endometriosis is a prevalent disorder that affects around 10 percent of women in the reproductive age group all over the world. During this condition, endometrial tissue is present outside the uterus in places such as the ovaries, peritoneum, and intestines [1]. Chronic pelvic pain and infertility are connected with this condition. The most frequently mentioned symptoms are dysmenorrhea and dyspareunia [2]. Endometriosis patients who also have ovarian endometrioma (OMA) make up 17 to 44% of all patients with endometriosis [3]. According to the updated American Society for Reproductive Medicine (ASRM) classification, OMAs are found in patients with advanced disease stages [4]; nonetheless, their cause and management remain controversial. Regardless of its size, endometrioma can cause ovarian injury by mechanical straining. As it contains inflammatory factors, proteolytic enzymes, and degrading agents, its substance induces metaplasia and fibrosis and lowers the number of cortical-specific

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stromal cells [4, 5]. Despite the considerable frequency of endometriosis, gynecologists have always debated a treatment that could increase fertility, relieve pain, and prevent the disease's recurrence. Laparoscopic cystectomy is the treatment of choice for endometriomas, with documented recurrence rates ranging from 5 to 66.7% [6]. However, the loss of neighboring healthy ovarian tissue by ovarian cystectomy may result in a diminished ovarian reserve [7]. It's also been found that 2.6% of women experience premature ovarian failure and menopause after undergoing bilateral ovarian cystectomy (to remove an endometrioma) [8]. Other less invasive methods must be developed in order to avoid postoperative complications and minimize the impact on fertility. Ethanol sclerotherapy [9] is an alternate method for preserving ovarian reserve. Sclerotherapy with ethanol has been used in various organs for a long (such as thyroid, liver, kidney, and spleen). In 1988, Akamatsu et al. used ethanol to treat endometriomas for the first time [10]. This minimally invasive method removed the cyst by disrupting the epithelial lining of the cyst, resulting in inflammation and fibrosis [11]. Sclerotherapy following aspiration was found to be more effective than aspiration alone in terms of recurrence (8 to 14.9 percent and 83.3 percent, respectively) [12, 13]. The reported recurrence rates following sclerotherapy, after 12 to 24 months of follow-up, vary from 0 to 62.5%, depending on the procedure employed [10, 14, 15]. This conservative approach may be effective in alleviating symptoms while also saving money. Endometriosis is accompanied by dysmenorrhea, dyspareunia, pelvic pain, and infertility. Endometriosis is the most prevalent cause of secondary dysmenorrhea, which has a detrimental influence on an individual's quality of life and productivity. Endometriosis-related dysmenorrhea is treated with anti-inflammatory drugs, GnRH agonists, danazol, and surgery.

Each strategy offers benefits and drawbacks that can be utilized based on the patient's situation [16]. The purpose of this retrospective study was to investigate the degree of pain (dysmenorrheal and dyspareunia), the rate of recurrence of OMA, serum AMH level and related complications following sclerotherapy vs. laparoscopic ovarian cystectomy in patients aged 25–38 years.

Materials and Methods

Study Design

The ethical criteria of the institutional committee, as well as the Helsinki Declaration from 1964, were strictly adhered to throughout the entirety of the procedures that were carried out in this study involving human participants. From January 2020 to February 2022, we retrospectively analyzed data from patients aged 25 to 38 years who were treated for

ovarian endometrioma. Patients were included in the study if they met the inclusion criteria listed below; patients between 25 and 38 years of age with primary or recurrent endometrioma who have been diagnosed with endometrioma based on their history, clinical examination, and ultrasound, and who have been treated with either sclerotherapy or laparoscopy based on the opinion of the relevant physician. They participated in the study after receiving informed consent. In every subject, dysmenorrhea was judged to be one of the symptoms. To investigate the impact of the procedures on the ovarian reserve, patients whose serum AMH levels were analyzed before and 6 months after sclerotherapy or surgery were included.

Exclusion criteria include the presence or history of liver, renal, and heart illness, endometrioma cysts smaller than 3 cm and cysts with thick walls, and ultrasound results suggesting malignancy.

One hundred nine patients were first screened. Twenty-one patients were removed based on the aforementioned criteria, leaving 88 patients for this study.

Operation Technique

At Shariati Hospital, sclerotherapy is conducted as an operation in the operating room while the patient is under mild anesthetic and lithotomy position. Following intravaginal lavage with betadine, the patients underwent vaginal ultrasound, and the contents of the cyst were removed with a needle and submitted for cytology analysis. Before adding ethanol as the sclerosing agent, the contents of the cyst were flushed with sterile normal saline, and numerous intracystic saline washes were conducted until the aspirated liquid was entirely clear. Then, 80 percent of the aspirated volume cyst was replaced with 98 percent ethanol, which stayed in the cyst for 15 min before being removed to allow for additional washing with saline until the cyst was entirely dry. After that, seven days of antibiotics were taken orally (Fig. 1).



Fig. 1 Sclerotherapy of a 31-year-old woman with ovarian endometrioma

All laparoscopic cystectomies were conducted by specialists under general anesthesia under video surveillance. Obstetricians followed worldwide guidelines to minimize ovarian injury to healthy tissue[7]. Operative laparoscopies were done through a subumbilical incision (10 mm) and three or four lower abdomen incisions (5 mm). Ovarian cystectomy was performed following a surgical incision at the antimesenteric site of the cyst. A biopsy was performed on the tissue removed after the endometrioma was excised. The ovaries were freed from adhesions after a thorough dissection. When necessary, bipolar electrocauterization was used to stop bleeding (Fig. 2).

Outcome Measures

Following the intervention, the factors examined included dysmenorrhea, dyspareunia, recurrence rate, and complications. After matching both groups (laparoscopy and sclerotherapy) for age and initial OMA size on ultrasonography, these variables were evaluated. Data were gathered by looking over the medical records of patients, as well as descriptions of their operations and conversations with them over the phone. At our facility, all women are monitored in accordance with an internal policy. Before surgery (T1), a standard gynecological examination and transvaginal ultrasound are performed, as well as 2 (T2), 6 (T3), and 12 (T4) months after surgery, and then annually after surgery. This series of pelvic sonograms are performed to assess any cyst recurrence. Moreover, serum AMH level before and 6 months after sclerotherapy/surgery were analyzed to observe the impact on the ovarian reserve. Symptoms of pain are also assessed. During the follow-up appointments, patients were asked if they had experienced dysmenorrhea, pelvic pain, or dyspareunia. The VAS was used to evaluate pre-and post-procedure pain. All significant procedure complications were documented. Endometrioma recurrence was determined using ultrasonography. Ovarian cyst with a thin wall (at least 2 cm in diameter), regular margins,



Fig. 2 Laparoscopy of a 34-year-old woman with ovarian endometrioma

homogeneous low echogenic fluid content with scattered internal echoes, and not resolving after multiple subsequent menstrual cycles were described as recurrent endometrioma.

Statistical Analysis

First, the Shapiro-test was run on all variables to ensure that the data were normal. To examine dysmenorrhea and dyspareunia at intervals of 2, 6, and 12 months, repeated measures (ANOVA test) were utilized, and the Chi-square test was used for comparing recurrence and complication variables. To compare the pre- and post-procedural serum AMH level the paired/unpaired t-test was used. It was presented as means \pm SD (standard deviation). Also, $p < 0.05$ was considered as significant level. R software was used to analyze the collected data. The sample size was estimated for each of the project's objectives separately, and a maximum sample size of roughly 42 people was determined for this project. The initial values are set in accordance with the clinical specialist's recommendations.

Results

In general, in this study, 88 patients with a mean age of 32 years (range 25–38 years) were investigated in two groups: laparoscopic intervention and sclerotherapy (44 patients in each group). No significant differences were found in the average of age, BMI and AMH differences between the two groups. In the laparoscopic group, the average size of endometrioma cysts was 65 mm, and in the sclerotherapy group, it was 68 mm; this difference was not statistically significant (Table 1). Tables 2 and 3 provide descriptive data on dysmenorrhea and dyspareunia in laparoscopic and sclerotherapy procedures. Both approaches demonstrate significant changes between time points t1, t2 / t1, t3/ t1, and t4, indicating that the intervention is highly effective in lowering pain (t1-before intervention, t2-2 months after intervention, t3-6 months after intervention, t4-12 months after intervention). In both groups, changes in t2, t3/t2, t4, and t3, t4 were not statistically significant. Based on these findings, it can be concluded that the results were stable during the follow-up and that there were no statistically significant differences between the two groups in terms of pain reduction (dysmenorrhea and dyspareunia); therefore, each intervention was effective in reducing patient pain. There was no significant difference in the serum AMH level before and 6 months after sclerotherapy ($p = 0.761$), but a significant reduction in the serum AMH level was observed in the laparoscopy group (0.027) after 6 months. Additionally, there was a statistically significant change in serum level of AMH in laparoscopy compared to the sclerotherapy ($p = 0.003$)(Table 4). Sclerotherapy and laparoscopic operation both had a recurrence

Table 1 General characteristics of study participants

Variables	Mean \pm SD sclerotherapy (n = 44)	Mean \pm SD laparoscopy (n = 44)	P
Age(years)	31.84 \pm 5.74	32.36 \pm 4.16	0.745
BMI(kg/m ²) (Baseline)	23.24 \pm 1.59	24.12 \pm 1.67	0.802
AMH(ng/ml) (Baseline)	1.14 \pm 1.53	1.46 \pm 1.07	0.137
Median size of endometrioma (mm)	68 \pm 13.53	65.07 \pm 11.37	0.677
<i>Localization</i>			
Bilateral	21(47.7%)	17(38.6%)	0.112
Right	9 (19.1%)	12(27.2%)	0.09
Left	14(31.8%)	15(34%)	0.385

P Based on unpaired *t*-test

AMH Anti-Müllerian hormone, BMI Body mass index

Table 2 Descriptive data on dysmenorrhea and dyspareunia in sclerotherapy procedures

Variables		Mean \pm SD sclerotherapy (n = 44)	P ^a	p ^b
Dysmenorrhea	T1	8.48 \pm 1.69	*	ns
	T2	2.46 \pm 2.56	0.003	0.123
	T3	3.27 \pm 2.90	0.018	0.201
	T4	3.59 \pm 2.93	0.009	0.439
Dyspareunia	T1	7.84 \pm 1.41	* 0.007	ns
	T2	1.93 \pm 2.34	0.006	0.095
	T3	3.18 \pm 2.91	0.021	0.111
	T4	3.93 \pm 2.67		0.27

P^a Based on compared T2, T3 and T4 with T1, respectively

p^b Based on compared T2, T3 and T4 together

*Statistically significant, ns None significant, t1-before intervention, t2-2 months after intervention, t3-6 months after intervention, t4-12 months after intervention

Table 3 Descriptive data on dysmenorrhea and dyspareunia in laparoscopic procedure

Variables		Mean \pm SD laparoscopy (n = 44)	P ^a	p ^b
Dysmenorrhea	T1	8.57 \pm 1.44	*	ns
	T2	2.04 \pm 1.90	0.001	0.089
	T3	2.75 \pm 2.19	0.005	0.317
	T4	3.09 \pm 2.52	0.019	0.184
Dyspareunia	T1	8.20 \pm 1.21	* 0.007	ns
	T2	1.39 \pm 1.94	0.023	0.256
	T3	2.73 \pm 2.77	0.036	0.325
	T4	3.43 \pm 2.73		0.107

P^a Based on compared T2, T3 and T4 with T1, respectively

p^b Based on compared T2, T3 and T4 together

*Statistically significant, ns None significant, t1-before intervention, t2-2 months after intervention, t3-6 months after intervention, t4-12 months after intervention

Table 4 Serum AMH concentration after laparoscopy versus sclerotherapy

Variables	Mean \pm SD sclerotherapy (n = 44)	Mean \pm SD laparoscopy (n = 44)	P ^a
Baseline	1.14 \pm 1.53	1.46 \pm 1.07	0.137
After 6 months	1.0 \pm 0.99	0.87 \pm 1.23	0.092
Difference	-0.14 \pm 0.85	-0.59 \pm 0.61	0.003*
P ^b	0.761	0.027*	

*Statistically significant ($p < 0.05$)

P^a Based on unpaired *t*-test

P^b Based on paired *t*-test

rate of 11.36 and 15.9%, respectively. Intra- and inter-group comparisons of laparoscopic and sclerotherapy recurrence rates indicate no statistically significant differences ($p < 0.05$, $p = 0.82$, respectively). The laparoscopic intervention has not been associated with any complications, but 2.27% of sclerotherapy interventions have been associated with complications. Comparing the two groups, the rate of complications is not statistically significant, and complications are comparable in both groups ($p = 0.322$) (Table 5).

Discussion

OMA affects 17–44% of women with endometriosis and is a devastating condition [3]. Endometrioma and endometriosis pain recurrence is associated with a number of clinical and surgical variables. Evidence suggests that ectopic endometrial cells can thrive in a peritoneal milieu that is activated by immune cells, adherent molecules, extracellular matrix metalloproteinase, and proinflammatory cytokines [17]. Laparoscopic stripping is common for cysts that are symptomatic or big [18]. Recurrence rates two years after resection range from 6 to 30% [19, 20]. Ovarian reserve is reduced by laparoscopic surgery [21]. Additional minimally invasive

Table 5 Comparison of recurrence rate and complication between sclerotherapy and laparoscopy during 12 months

Variables	Mean \pm SD sclerotherapy ($n = 44$)	Mean \pm SD laparoscopy ($n = 44$)	<i>P</i>
Recurrence rate (%)	5/44(11.36)	7/44 (15.9%)	0.82
Complication (%)	1/44 (2.27) (ovarian abscess)	0/44	0.322

P Based on unpaired *t*-test

techniques are required to reduce postoperative complications and reproductive loss. Medical treatments have shown to be ineffectual [22, 23]. An alternative technique for conserving ovarian reserve is ethanol sclerotherapy [9]. This conservative approach may help alleviate symptoms while also saving money.

Sclerotherapy and laparoscopic intervention were compared in terms of discomfort (dysmenorrhea and dyspareunia), recurrence rate, and complications in endometriotic women following 2, 6, and 12 months. Moreover, serum AMH level before and 6 months after sclerotherapy/laparoscopy were analyzed to observe the impact on the ovarian reserve. All of our patients were classified as stage III or IV ASRM due to the existence of OMA of more than 3 cm. The findings of our study revealed that there was a significant reduction in dysmenorrhea and dyspareunia in both groups, and the related complications were not significantly different in either group; also, the recurrence rate was not significantly in the sclerotherapy group when compared to the laparoscopy group. Additionally, the rate of AMH decline after laparoscopy was higher than sclerotherapy; also, there was a statistically significant change in serum level of AMH in laparoscopy compared to the sclerotherapy after 6 months. The overall endometrioma recurrence rate following sclerotherapy varies from 0 to 62.5% [9]. Based on the length of the follow-up, the recurrence rate in the sclerotherapy method was dramatically different: 0–20% after six months of follow-up to 11–28.6% after sixteen to twenty months [24–27]. Women who were treated with ethanol washing had a considerably higher incidence of recurrence than those who were treated with ethanol retention [9]. When the ethanol was left for < 10 min, the recurrence rate was 62.5%, but only 9.1% when it was left for more than 10 min [12]. In the current study, ethanol was removed after 15 min because ethanol retention permits efflux of ethanol into the abdominal cavity, which increases postoperative abdominal pain and promotes peritoneal adhesions. Our 11.36 percent recurrence rate following sclerotherapy was comparable to other data. The literature reports 12% recurrence after 10 months [28], 14.9% after 6 months [12], and 11.1% after 16 months [26]. Different studies' recurrence findings are connected to inclusion criteria (cyst size and number), procedure, and follow-up period. Within 1–6 years following endometrioma excision, recurrence rates were observed to range between 7.31 percent and 32% [29, 30]. Researchers

from the universities of Seoul [31] and China [17] found that post-cystectomy endometrioma recurrence was more common in patients with more advanced stages of the disease and in those who were younger at the time of surgery, with rates ranging from 22.5% in patients aged 30 to 39 to 17.7% in those aged 31 to 40. The recurrence rate of 15.9 percent after laparoscopy was in line with other studies reporting a range of 15 to 30 percent recurrence rates [19, 20].

Preliminary investigations found that surgery due to ovarian injury, will result in a decrease in AMH, which serves as a prognostic indicator for ovarian reserve [21, 32]. In the meta-analysis conducted by Somigliana et al., nine out of eleven papers analysed demonstrated a statistically significant decrease in serum AMH level following surgical intervention [33]. This was consistent with previous recent studies showing a drop of roughly 2 points in concentration of AMH [34]. Researches have shown that ethanol sclerotherapy is an effective treatment for ovarian endometriomas and retains ovarian function well [35]. After six months, laparoscopy had a lower basal AMH concentration than sclerotherapy in our research. It should be noted that the drop in postoperative serum AMH levels may be a temporary phenomenon, as some studies have reported that levels have rebounded over time [36]. However, there is some controversy over the possibility of AMH concentrations recovering. In contrast to our study, Jose M. Martinez-Garcia et al. have reported that both alcohol sclerotherapy and surgery groups, had low basal AMH concentrations [34]. This discrepancy might have been due to the surgical technique used and number of patients included.

The results of our study indicate the effectiveness of both sclerotherapy and laparoscopic methods in reducing dysmenorrhea and dyspareunia due to endometrioma over a period of 12 months. Similarly, researchers found that catheter-directed ethanol sclerotherapy reduced pain and CA125 levels in women with endometriosis while having no negative effects on ovarian reserve [37]. In our research, patients reported a decrease in pain scores for dysmenorrhea. In the field of complication occurrence, no major complications were recorded in the laparoscopic group, but there was a case of ovarian abscess in the sclerotherapy group, which was treated with antibiotics and emptied under ultrasound guidance. There was no significant difference in major complications between the two groups.

According to a retrospective analysis by Miranda and Carvajal [38], laparoscopy-related complications were documented in 17 out of 2140 patients (or 0.79%), while major complications were reported in 10 out of 2140 patients (or 0.46%). Complications may arise as a result of endometriosis adhesions. In another research, the surgical group had one significant complication (Clavien-Dindo IIIb), while the sclerotherapy group had none [15]. This discrepancy may be due to our limited sample size and follow-up duration. In the Alborzi study, no participants had major complications [39]. Also, there were no major complications associated with the surgery in the study of Amparo; however, there were five minor complications recorded [14]. Similarly, Ja Ho Kee, in his study, mentioned two minor complications due to surgery, while no complications were observed in sclerotherapy [40].

Conclusion

Given the above findings, as well as the fact that the reduction of dysmenorrhea and dyspareunia was significant in both groups and the rate of complications and recurrence rate in both groups was not significant, it appears that the sclerotherapy method, with its lower cost, shorter hospital stay, and faster return of the patient to activity, can be used as a laparoscopic alternative in the treatment of endometrioma.

Because endometriosis may advance over time, the follow-up evaluation duration may be a drawback of this study. Consequently, a longer follow-up period yields more precise data. In addition, by establishing a prospective study with bigger sample size, we can judge and compare these two treatments more accurately (laparoscopy and sclerotherapy).

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Authors' Contributions AN developed the idea for the project. The study was designed by AN and AA, and MA, and SM collected data and performed the data analysis and takes full responsibility for the integrity of the data. MJ drafted the manuscript. The final version has been approved by all authors.

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Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Consent for Publication Not applicable.

Ethics Approval and Consent to Participate The Ethics Committee of Tehran University of Medical Sciences approved this retrospective study, and the ethical approval code was IR.TUMS.MEDICINE.

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