



# Recovery Rate of Patients with Recurrent Ovarian Endometriomas Using Sclerotherapy with 95% Ethanol

## ARTICLE INFO

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## ABSTRACT

**Aims** Ovarian endometrioma is a prevalent gynecologic disease in women of reproductive age that is accompanied with a number of symptoms and has a high recurrence rate after hormone therapy and surgery. The aim of this study was to evaluate the effectiveness of sclerotherapy with 95% ethanol in patients with recurrent ovarian endometriomas.

**Materials & Methods** In this pre-post clinical trial, 14 patients with infertility and recurrent ovarian endometriomas were examined during a period from December 2012 to December 2013 in Ghadir Mother and Child Hospital affiliated with Shiraz University of Medical Sciences. These subjects had undergone a laparotomy to remove their cysts at least once. They were selected using convenience sampling method. The patients underwent sclerotherapy with 95% ethanol and referred 1, 3, 6, and 12 months after the procedure for their periodic examinations and levels of FSH, AMH, CA125, E2, AFC, mass size, and pelvic pain were measured. The data were analyzed using repeated measures analysis of variance (ANOVA) by SPSS 14 software.

**Findings** While the level of FSH significantly decreased ( $p=0.01$ ), the AMH level began to increase after the treatment ( $p=0.17$ ); however, this increase was not significant. The AFC level increased with the aid of the treatment ( $p=0.002$ ). The mass size and the patients' pain also significantly decreased ( $p<0.05$ ). Four cases of pregnancy happened. In 2 of the patients, the cysts recurred and grew again.

**Conclusion** Sclerotherapy with 95% ethanol can be used as an appropriate alternative therapy in patients with recurrent endometriomas.

**Keywords** Endometrioma; Sclerotherapy; Ethanol

## CITATION LINKS

- [1] Management of ovarian endometrioma
- [2] Coagulation or excision of ovarian endometriomas?
- [3] Management of ovarian endometriomas
- [4] Management of endometriomas in women requiring IVF: to touch or not to touch
- [5] The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis
- [6] Impact of laparoscopic cystectomy on ovarian reserve: serial changes of serum anti-Müllerian hormone levels
- [7] Ten principles for safe surgical treatment of ovarian endometriosis
- [8] The post-operative decline in serum antiMullerian hormone correlates with the bilaterality and severity of endometriosis
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- [10] Repeat transvaginal ultrasound-guided aspiration of ovarian endometrioma in infertile women with endometriosis
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- [13] Ethanol sclerotherapy of ovarian endometrioma: a safe and effective minimal invasive procedure. Preliminary results
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- [15] Aspiration and ethanol sclerotherapy to treat recurrent ovarian endometriomas prior to in vitro fertilization-a pilot study
- [16] Management of transvaginal ultrasound-guided absolute ethanol sclerotherapy for ovarian endometriotic cysts
- [17] Efficacy of ethanol sclerotherapy for ovarian endometriomas
- [18] Effectiveness of ultrasound-guided aspiration and sclerotherapy with 95% ethanol for treatment of recurrent ovarian endometriomas
- [19] Ultrasound-guided aspiration and ethanol sclerotherapy (EST) for treatment of cyst recurrence in patients after previous endometriosis surgery: analysis of influencing factors using a decision tree
- [20] Assessing the efficacy of aspiration and ethanol injection in recurrent endometrioma before IVF cycle: A randomized clinical trial
- [21] Surgery for endometriosis-associated infertility: a pragmatic approach

## Introduction

Ovarian endometrioma is an estrogen-dependent cystic disease with a high recurrence rate in women of reproductive age that one of the most important effects of it is infertility [1]. Endometrioma is treated using a variety of procedures which are all categorized into two groups, i.e. medical treatments and other surgical procedures [2]. Nowadays, it has been proven that medical treatments alone are inadequate [1, 3] and conventional surgical procedures (laparoscopy and laparotomy) reduce ovarian reserve by removing some healthy ovarian tissue during endometrial ablation and decrease the number of oocytes available for the next pregnancy [4-6].

A localized inflammation following a surgery or a vascular injury due to the use of vascular coagulants is another possible complication that decreases the ovarian reserve and damages oocytes [5]. Therefore, using a second surgical procedure for recurrent endometrioma is not accepted by many experts.

Although it is stated that even if one-tenth of the ovary remains, it will be enough to maintain ovarian and fertility activities, this idea that ablating an ovarian cyst together with the removal or destruction of normal ovarian tissue can reduce the ovarian follicular reserve and fertility is more and more strengthened [7].

Furthermore, there have been cases of ovarian failure in bilateral endometrial cystectomy immediately after a surgery [8, 9].

Another treatment for endometrioma is a simple cystitis aspiration under transvaginal ultrasound. Its recurrence rate is high and there is a need to repeat the treatment multiple times. In general, an aspiration alone is considered an ineffective treatment for endometrioma. However, a repetition of this procedure in recurrent endometriomas is regarded as an alternative approach that is less invasive compared to surgical methods [10, 11]. Therefore, there is a need for finding more effective therapies.

Various studies have shown that combining two methods of aspiration and the use of sclerosing agents can be effective in decreasing the recurrence rate [12-15].

The aim of this study was to evaluate the effectiveness of sclerotherapy with 95% ethanol in patients with recurrent ovarian endometriomas.

## Materials and Methods

In this pre-post clinical trial, 14 patients with infertility and recurrent ovarian endometriomas were examined during a period from December 2012 to December 2013 in Ghadir Mother and Child Hospital affiliated with Shiraz University of Medical Sciences. These subjects had undergone a laparotomy to remove their cysts at least once. They were selected using convenience sampling method. The study was approved by Shiraz University of

Medical Sciences.

Inclusion criteria for the study were as follows:

- 1- Filling out a special informed consent form
- 2- Being diagnosed with endometrioma by a pathologist. While having a history of surgery for endometriomas, they recurred
- 3- Having an FSH (Follicle stimulating hormone) level lower than 10 and an AMH (Anti-Müllerian hormone) level higher than 1
- 4- Being younger than 38 years old

Patients who were unwilling to take part in the study (in each stage), who were virgins, and who had no history of previous cyst endometriosis surgery, and/or those whose pathology of the disease was not available were excluded from the study.

The patients' basic information such as their age, the number of previous surgeries, their infertility type (primary or secondary), and the number of years of infertility were recorded. Moreover, the clinical data of the patients, including abdominal pain and primary site and size of the cyst, i.e. the right side, the left side, and/or both sides, were also collected. Several factors such as FSH, AMH, cancer antigen 125 (CA125), estradiol (E2), antral follicle count (AFC), and the initial size of the cyst before the procedure were measured and recorded.

In addition, the patients completed a questionnaire on pelvic pain resulting from endometriosis before sclerotherapy and in the follow-up courses to assess their pain levels. After the procedure, the patients were admitted to the hospital for a night, treated with intravenous antibiotics (ceftriaxone-gentamicin), and were discharged the next day with an oral antibiotic (cefixime) for 7 to 10 days. The size of the ovarian cyst was also measured and recorded at each stage. Then, the patients underwent transvaginal ultrasound-guided sclerotherapy.

In such a way that using the guided transvaginal ultrasound (Hyundai 2100; UK) with Wallace puncture needles (33cm), their endometrioma cysts were ablated and sent to cytology. Subsequently, the area inside the cyst was washed by normal saline to obtain a clear liquid. Afterward, with a puncture needle, 95% ethanol was injected into the cyst. After 10 minutes, the alcohol was drained and 5cc of it was left in the site. The follow-up examinations and sonographies were respectively carried out 1 month, 3 months, 6 months, and 12 months later. Considering the recurrence of the disease (cysts regrowth) and tests (CA125, AFC, FSH, AMH, and E2), the patients were examined. In the event of pregnancy, the patient's follow up was postponed until after a delivery. The recurrence rate after the procedure was evaluated based on the size of the cyst greater than 2cm in ultrasound.

After the necessary coordination with university and hospital, the patients entered the study and were assessed at regular intervals after the treatment

intervention.

Finally, the data were analyzed using repeated measures analysis of variance (ANOVA). All statistical analyses were performed by SPSS 14 software.

**Findings**

The mean age of the patients participating in the study was 30.0±0.8 years and the maximum and minimum age of the participants were 28 and 35 years, respectively. Out of the 14 patients who took part in the study, 11 patients (78.6%) had primary infertility and 3 patients (21.4%) had secondary infertility, with an average of 3.0±0.5. years of infertility.

The mean FSH level decreased in comparison to its level obtained before the treatment with sclerotherapy and its reduction was statistically significant (p=0.01; Diagram 1).

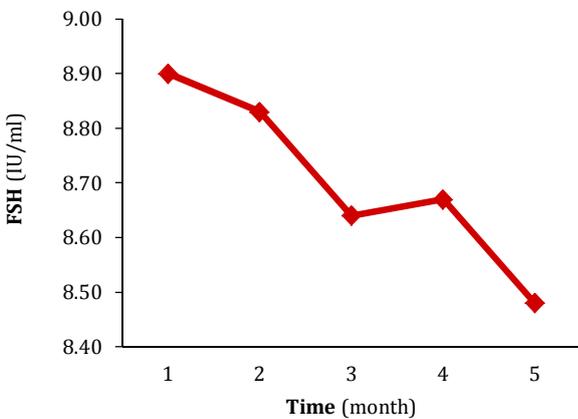
The levels of AMH began to increase after sclerotherapy; however, this increase was not statistically significant (p=0.17; Diagram 2).

The number of anterior ovarian follicles also increased. This increase was statistically significant (p=0.002; Diagram 3).

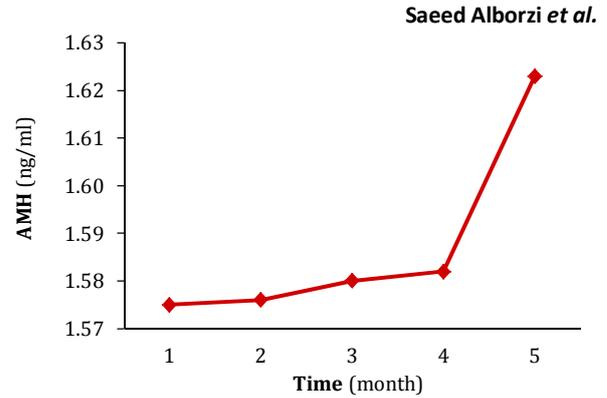
The patients' pelvic pain was decreased after sclerotherapy and this decrease was statistically significant (p=0.01). Reducing pain in the patients was so high that most patients reported that their pain was one out of ten in the third month after sclerotherapy (Diagram 4).

Two other blood factors which were measured in the patients with endometriomas were CA125 and E2, both of which were assessed at the zero time (before the procedure) and at the fifth time (12 months after the procedure). The CA125 and E2 levels did not change a lot during the study and their changes were not statistically significant (Table 1).

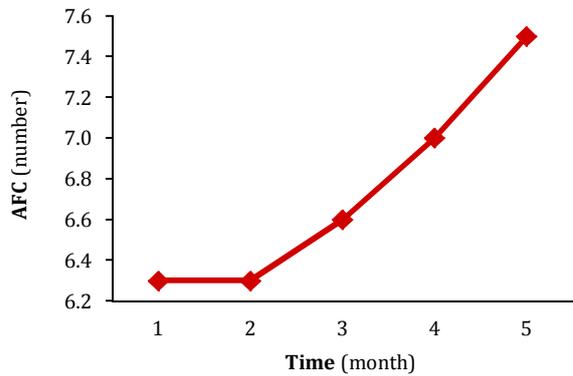
The last factor in was the size of the ovarian endometrioma cyst that was examined by transvaginal ultrasound at the 5th time. The size of the cysts significantly reduced and the obtained data were statistically significant (p=0.001; Diagram 5).



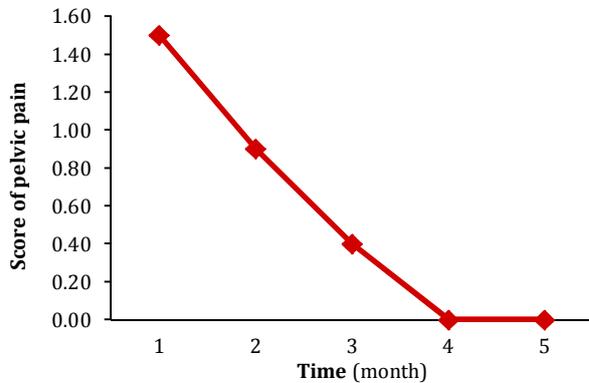
**Diagram 1)** The mean changes in the patients' FSH levels during measurement times



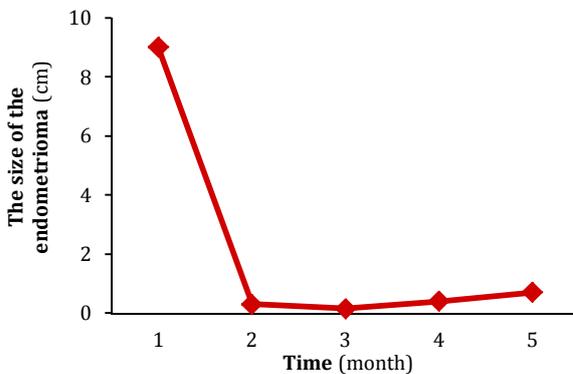
**Diagram 2)** The mean changes in the patients' AMH levels during measurement times



**Diagram 3)** The mean changes in the patients' AFC levels during measurement times



**Diagram 4)** The mean changes in the patients' pelvic pain during measurement times



**Diagram 5)** The mean changes in the size of endometriomas in the patients during measurement times

**Table 1)** Means and standard deviations of the variables under study in the patients with endometriomas before and after the intervention

Before the intervention	First month	Third month	Sixth month	Twelfth month	P.value
<b>FSH (IU/ml)</b> 8.90±0.76	8.83±0.83	8.64±0.90	8.67±0.89	8.48±0.85	0.01
<b>AMH (ng/ml)</b> 1.57±0.33	1.57±0.32	1.58±0.30	1.58±0.29	1.62±0.27	0.17
<b>AFC (Number)</b> 6.28±1.20	6.28±1.32	6.57±1.45	7.00±1.46	7.50±1.60	0.002
<b>CA125 (U/ml)</b> 10.10±4.65	-	-	-	9.21±4.06	0.2
<b>E2 (pg/ml)</b> 72.62±45.87	-	-	-	76.64±41.51	0.6
<b>Size of the Endometrioma (cm)</b> 9.25±7.19	1.08±0.51	0.57±0.21	1.21±0.46	70.71±1.85	0.001
<b>Score of pelvic pain</b> 2.02±1.50	1.20±0.92	0.49±0.35	0.00	0.00	0.01

Out of the 14 patients who participated in the study and referred for follow-up healthcare measures, 4 patients (28.5%) were pregnant. Among these patients, 3 cases of pregnancy occurred spontaneously and the other pregnancy occurred by embryo freezing and receiving an IVF two months after sclerotherapy. In 2 patients, the growth and recurrence of the cysts were observed (14.3%). Furthermore, there was a case of pelvic abscess one week after the procedure. This patient was again hospitalized with symptoms of fever and abdominal pain and underwent an IV AB therapy. After a week, due to lack of response to antibiotic therapy, the abscess was drained using a guided ultrasound.

## Discussion

In this study, the effect of sclerotherapy with 95% ethanol on the treatment of patients with recurrent ovarian endometriomas was investigated. It was indicated that the use of sclerotherapy improved factors associated with the ovarian activity, such as decreasing the level of FSH and increasing the level of AMH and antral follicle count. Moreover, the pain levels of patients significantly reduced. Furthermore, except for one case of a pelvic abscess, no serious complications such as peritonitis, intestinal peritonitis, and internal bleeding were observed and sclerotherapy was well tolerated by the patients.

In line with the results obtained from the current study, there are other studies with different evaluations. In a study conducted by García-Tejedor *et al.*, after 17 months, the recurrence rate was reported to be 12% and no serious complications were observed [13].

A study carried out by Ikuta *et al.* which examined injecting ethanol into cysts for 5 minutes and then aspirating it showed that the recurrence rate was 11.1% [16]. This is while in a study conducted by Yazbeck *et al.*, ethanol was injected for 10 minutes and the recurrence rate was 12.9% in the 10 months after sclerotherapy [14]. Zhu *et al.* suggested that monthly injections of ethanol can reduce the

recurrence rate from 91.5% to 27.9% over a 2-year period [10]. The recurrence rate in a study carried out by Noma and Yoshida was 14.9% [17].

In another study performed by Hsieh *et al.*, 108 patients with recurrent endometriosis with a size greater than 3cm underwent sclerotherapy with 95% ethanol after aspiration of the contents of cysts. The first group of these patients consisted of 78 subjects who had ethanol in their cysts for 10 minutes and the second group consisted of 30 patients who kept ethanol in their cysts. Based on the results of this study, within one year after the treatment, the recurrence rate in the second group was significantly lower than the first group (13.3 versus 32.1). The antral follicle count (AFC) increased and the levels of pain in the patients in both groups decreased. No noticeable change was found at CA125 level. This study concluded that sclerotherapy with 95% ethanol was effective in treating ovarian endometriosis and keeping ethanol in cysts responded better than ethanol irrigation [18]. In the current study, ethanol remained in the site for 10 minutes and the recurrence rate was 14.3%.

Chang *et al.* also found that the recovery rate after sclerotherapy in cases where ethanol remained or not removed for up to 10 minutes was more than that in patients in whom ethanol was removed immediately (47.0% vs 28.7%). Additionally, the recovery rate directly related to lower and smaller size of a cyst and lower levels of CA125. In their study that conducted on 196 patients who underwent sclerotherapy, the size of the cysts and the degree of pain decreased significantly and the AFC levels increased. Furthermore, recurrences were seen in 23% of the patients [19]. This difference in the recurrence rate, compared with the present study, can be due to the greater number of patients in their study.

A study carried out by Aflatonian *et al.* examined the effect of ethanol injection into recurrent endometrioma cysts before the start of IVF cycles. In this study, 20 patients were treated by sclerotherapy with ethanol and after three months,

they were monitored for performing an IVF. The other group, the control group, underwent an IVF without having sclerotherapy and some parameters, including pregnancy rate, IVF success rate, and recurrence rate, were compared in the two groups. The results showed that there was no difference in the demographic characteristics of the patients in the two groups. The mean size of the mass before the treatment was  $41.45 \pm 15.9$  cm and the recurrence rate was 20% after 20 months. The FSH level decreased after the treatment; however, this decrease was not statistically significant. The pregnancy rate was 33.3% in the sclerotherapy group and 15% in the control group. Although the results proved an improvement in the function of the ovary after sclerotherapy, the differences were not statistically significant [20].

According to a study done by Vercellini *et al.*, the incidence of post-laparotomy pregnancy in patients with endometriomas was reported to be 15 to 67% [21]. The pregnancy rate in the current study performed by sclerotherapy was 28.5%.

The size of the cyst is a very important factor associated with the recurrence of endometrioma mass. Based on various previously carried out studies, after sclerotherapy with ethanol, the mass size decreased in most cases [13, 14, 19].

One of the strengths of the present study was the design of the study. This was a clinical trial (quasi-experimental) which compared the patients before and after the intervention. Comparing each patient with herself eliminates a large group of confounding variables which can somehow pave the way for having more precise results. At the same time, a small sample size and a lack of control group were among the limitations of this study. It is recommended that a study is conducted with a control group, a larger number of samples, and a longer duration.

## Conclusion

Sclerotherapy with 95% ethanol can be used as an appropriate alternative therapy in patients with recurrent endometriomas.

**Acknowledgments:** This study was derived from a Ph.D. dissertation titled "Evaluation of the recovery rate of patients with recurrent ovarian endometriomas using sclerotherapy with 95% ethanol from 2012 to 2013 at Ghadir Mother and Children Hospital affiliated with Shiraz University of Medical Sciences" approved on 12 August 2012 under the following code: 91-1-1-4360.

**Ethical Permission:** This study was approved by IR.SUMS.REC.1391.4360 code.

**Conflicts of Interests:** Authors declare no conflict of interests.

**Authors Contribution:** Ahmadbeigi M. (First author), Introduction author/ Methodologist/

Original researcher/ Statistical analyst/ Discussion author (60%); Alborzi S. (Second author), Original researcher (20%); Namavar Jahromi B. (Third author), Original researcher (20%)

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