ORIGINAL ARTICLE: ENDOMETRIOSIS

Sclerotherapy in the management of ovarian endometrioma: systematic review and meta-analysis

Aviad Cohen, M.D.,[a] Benny Almog, M.D.,[b] and Togas Tulandi, M.D., M.H.C.M.[a]

[a] Department of Obstetrics and Gynecology, McGill University, Montreal, Quebec, Canada; and [b] Department of Obstetrics and Gynecology, Lis Maternity Hospital, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Objective: To evaluate the efficacy of sclerotherapy for ovarian endometrioma on the risk of recurrence, clinical symptoms, and reproductive function.
Design: Systematic review and meta-analysis.
Setting: Not applicable.
Patient(s): Patients who underwent sclerotherapy of ovarian endometrioma.
Intervention(s): An electronic-based search with the use of Pubmed, Embase, Ovid Medline, Google Scholar, Clinicaltrials.gov, and the Cochrane Central Register of Controlled Trials.
Main Outcome Measure(s): Recurrence rate, symptoms relief, fertility outcome, and adverse events.
Result(s): Eighteen studies were included in our review. The overall recurrence rates of endometrioma after sclerotherapy ranged from 0 to 62.5%. The risk of recurrence was significantly higher in women who were treated by means of ethanol washing than by means of ethanol retention. The number of oocytes retrieved was higher after endometrioma sclerotherapy compared with laparoscopic cystectomy, but clinical pregnancy rates were similar. There was no difference in the number of oocytes retrieved and the clinical pregnancy rates between the sclerotherapy-treated group with and the untreated group.
Conclusion(s): Sclerotherapy for ovarian endometrioma may be considered in symptomatic women who plan to conceive. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: Endometrioma, sclerotherapy, aspiration, fertility, ovarian cystectomy

Discuss: You can discuss this article with its authors and with other ASRM members at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/16657-23881

Endometriosis is a common gynecologic condition affecting 6%–10% of reproductive-age women. It is defined as the presence of endometrial glands and stroma outside the uterine cavity, commonly found in the ovary and on the peritoneum. It can be superficial or deep (1). Ovarian endometriomas are ovarian cysts that are lined with endometrial tissue and contain fluid that arises from accumulation of menstrual debris. They are found in 17%–44% of women with endometriosis (2). Theories regarding the origin of ovarian endometrioma include invagination of the ovarian cortex with menstrual debris arising from bleeding endometrial implants and epithelial inclusions from the ovarian surface that invaginate and undergo metaplasia into endometrial tissue (3). The clinical manifestations of endometriosis include pelvic pain and infertility, and the estimated prevalence of endometriosis among women with infertility, pelvic pain, or both is 35%–50% (4).

The pathophysiology of endometrioma-related infertility in women with endometriosis remains unclear. Suggested theories include not only distortion of tubo-ovarian anatomy, but also damage to the affected ovary. It seems that the cyst contains cellular damage–mediating factors, inflammatory molecules, and proteolytic enzymes that will eventually result in fibrosis, reduction of cortex-specific stromal cells, smooth muscle cell metaplasia, and a vascularization defect that will later be accompanied by follicular loss (2).

The conventional treatment of ovarian endometrioma has been surgery, and the most common surgical method is laparoscopic cystectomy. It is associated with reduced recurrence of the endometrioma and pain symptoms. Furthermore, compared with drainage of the endometrioma with or without the ablation of the pseudocapsule, excision of the endometrioma tends to be associated with a higher pregnancy rate or better outcome (5).

However, ovarian cystectomy can lead to decreased ovarian reserve (6, 7). This is due to removal of healthy

Received February 16, 2017; revised and accepted May 9, 2017.
A.C. has nothing to disclose. B.A. has nothing to disclose. T.T. is an advisor for Abbvie, Allergan, and Genzyme.
Reprint requests: Aviad Cohen, M.D., McGill University Health Center, 1001 Decarie Boulevard, Montreal, QC H4A 3J1, Canada (E-mail: co.aviad@gmail.com).

Fertility and Sterility® Vol. ■, No. ■, ■ 2017 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2017.05.015

ovarian tissue adjacent to the cyst wall, especially when there is no cleavage plane between the endometrioma and the ovarian tissue. Another reason is excessive coagulation to the ovary for hemostasis (7). As a result, increased amounts of gonadotropins are needed to attain follicle development (8). These findings have led to a shift of opinion toward a more conservative approach in the treatment of endometrioma. As a result, the European Society of Human Reproduction and Embryology guideline from 2013 suggested that surgery before assisted reproductive technology (ART) treatment should be considered only in women with endometriomas of >3 cm and only to improve endometriosis-associated pain or the accessibility of follicles (9). Moreover, clinicians are advised to consult with women undergoing surgery regarding the risks of reduced ovarian function after surgery.

To preserve the ovarian reserve, nonsurgical management of ovarian endometrioma, including expectant management, aspiration, or sclerotherapy, has been advocated (9, 10). A promising technique for reducing the high recurrence rate associated with aspiration is sclerotherapy (10). It consists of injecting a sclerosing agent into the cyst cavity, which can be either removed ("washing") or retained within the cyst (in situ retention). Its mechanism of action is thought to be a disruption of the cyst epithelial lining with subsequent inflammation and fibrosis, that will eventually result in obliteration of the cyst (11). Sclerotherapy has been shown to be effective and cost-effective for women with ovarian endometrioma or benign ovarian cyst (12). However, it has not been widely used.

The purpose of the present systematic review and meta-analysis was to evaluate the efficacy of sclerotherapy for ovarian endometrioma in terms of the risk of recurrence, clinical symptoms, and reproductive function.

MATERIALS AND METHODS

Search Strategy

We performed an electronic-based search with the use of Pubmed, Embase, Ovid Medline, Google Scholar, Clinicaltrials.gov, and the Cochrane Central Register of Controlled Trials. The following medical subject headings (Mesh) terms and their combinations were used: ultrasound-guided aspiration, ovarian cyst, endometrioma, sclerotherapy, tetracycline sclerotherapy, ethanol sclerotherapy, and methotrexate sclerotherapy. The search was limited to trials in humans and published in the English language up to December 2016. We manually searched the reference lists of identified studies.

Selection Criteria

We included all randomized controlled studies, cohort studies, and case-control studies of endometrial cyst sclerotherapy (ethanol, methotrexate, or tetracycline) and evaluated the recurrence rate, symptom relief, fertility outcome, and adverse events. Review articles and case reports were excluded. The studies were selected and evaluated by two authors (A.C. and T.T.) independently. The third author (B.A.) resolved any discrepancy.

Data Presentation

The review was performed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines (Supplemental Fig. 1; Supplemental Figs. 1–3 and Supplemental Tables 1 and 2 are available online at www.fertstert.org). Articles and published abstracts were analyzed and the following characteristics were obtained: study design, year of publication, number of patients, type of intervention, and treatment outcomes. Methodologic quality assessment of nonrandomized studies for potential risk of bias was reported with the use of the Newcastle-Ottawa Scale for observational studies (Supplemental Table 1). Randomized controlled trials were assessed with the use of the Cochrane Collaboration's tool for assessment of risk of bias (Supplemental Table 2).

Statistical Analysis

The meta-analysis was performed with the use of Review Manager Software (Revman v. 5.3; Cochrane Collaboration). In the absence of statistically significant heterogeneity (i.e., $I^2 = 0–25\%$), the fixed-effects method was used. The Mantel-Haenszel method was used to estimate the pooled risk ratio with 95% confidence intervals (CIs). All statistical assessments were two sided, and a P value of $<.05$ was considered to indicate statistical significance.

RESULTS

Literature Identification

The electronic search generated 634 records; we excluded 605 by screening their titles and abstracts. Twenty-nine studies met the inclusion criteria and were selected for full article assessment. An additional 11 studies were excluded for the following reasons: study design (two case reports), four review articles, one nonhuman study, one double publication, and three that did not meet the outcome measures. Finally, therefore, 18 studies were included in the present review. Supplemental Tables 1 and 2 show study characteristics and risk of bias (13–30).

Reported Interventions during Endometrioma Sclerotherapy

The substances used for sclerotherapy were ethanol (13 studies), tetracycline (two studies), and methotrexate (three studies). Sclerotherapy was performed transvaginally (13 studies), transabdominally (one study), or both (three studies). In women who were treated with the use of ethanol sclerotherapy, 11 studies used the ethanol "washing" technique (ethanol was instilled for 0–15 minutes and then removed) (13,15,16, 20, 21 24, 26, 28, 29), and in four studies the ethanol was left in situ (14, 17, 19, 22). The volume of ethanol instillation ranged from 50% to 100% of the initial aspirated cyst volume. In women who were treated with the use of methotrexate or tetracycline, the sclerosing agent was left in situ. Methotrexate sclerotherapy was performed with the use of 30 mg methotrexate diluted in 3 mL normal saline solution (28, 23, 27), and tetracycline sclerotherapy