

PROSPECTIVE OBSERVATIONAL STUDY

Sclerotherapy with Ethanol: An Effective and Safe Alternative to Potentially Complex Surgical Treatment of Recurrent Ovarian Endometrioma

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ABSTRACT

Objective: The aim of this study was to evaluate the efficacy and safety of transvaginal ultrasound guided aspiration of ovarian endometrioma and ethanol sclerotherapy before controlled ovarian hyperstimulation (COH) and intrauterine insemination (IUI) or assisted reproductive technology (ART) in patients with recurrent ovarian endometrioma.

Design: Prospective study.

Setting: Infertility Care and Research Center (ICRC Pvt Ltd.), Dhaka, Bangladesh.

Materials and methods: Fifty-three patients with infertility and recurrent ovarian endometrioma were the target population of this study. Sclerotherapy was performed under sedation (Pethidine) or G/A (propofol) and transvaginal ultrasound guidance. An 16-gauge, double-lumen needle was inserted into the endometrioma and the cyst contents were sequentially aspirated and flushed with sterile saline until the aspirated fluid was clear. Ninety-five percent ethyle alcohol (ethanol) was then instilled into the cyst and kept *in situ*. Ultrasound was performed 6 weeks, 3, 6 and 12 months later to assess the efficacy of treatment. Controlled ovarian hyperstimulation and IUI or ART was performed according to patients' profile and desire.

Main outcome measures: Resolution and recurrence of endometrioma and pregnancy rate.

Results: Thirty-nine patients had unilateral, 14 had bilateral, 36 had single and 17 had more than one cysts. Size of the cysts were 3.5 to 10 cm, average 6.75 ± 1.64 cm. Complete resolution of cyst took place in 42 (79.25%) cases. Eleven patients had persistence and refilling of cyst. Four of them needed reaspiration. No complications developed in any case. Thirty patients (52 cycles) underwent COH and IUI and 5 (16.57%) of them got pregnant. Forty-one patients underwent ART (63 cycles) and 13 (31.71%) got pregnant. Six (11.32) patients developed small cyst <3 cm within 1 year during the course of treatment.

Conclusion: Sclerotherapy with 95% ethanol is a simple, effective and safe alternative to surgical intervention for treatment of recurrent ovarian endometriomas before COH and IUI or ART.

Keywords: Pregnancy rate, Recurrence, Recurrent endometrioma, Resolution, Sclerotherapy.

How to cite this article: Begum MR, Ehsan M, Ehsan N, Santa MSB, Khan F, Sharmin F. Sclerotherapy with Ethanol: An Effective and Safe Alternative to Potentially Complex Surgical Treatment of Recurrent Ovarian Endometrioma. J South Asian Feder Obst Gynae 2015;7(2):97-101.

Source of support: Nil

Conflict of interest: None

Date of received: 25 May 2015

Date of acceptance: 30 June 2015

Date of publication: August 2015

INTRODUCTION

Endometriosis is a common disease among women of reproductive age with a high recurrence rate irrespective of type of treatment. Endometrioma is defined as the formation of a cyst with ectopic endometriotic lining within the ovary. They are associated with advanced stage of endometriosis and increased morbidity. Aim of treatment is: (a) to alleviate symptoms, (b) to improve natural fecundity, (c) to prevent recurrence, (d) in preparation for *in vitro* fertilization (IVF) treatment. Treatment options of ovarian endometriosis are: (a) expectant management, (b) medical treatment and (c) surgery.

Conventional surgical treatment of ovarian endometriosis involves either laparotomy or laparoscopic drainage of the cyst contents with subsequent removal of the cyst wall. Laparoscopic cystectomy to remove ovarian endometriosis is the gold standard treatment. But, there are many arguments in favor and against the surgery. Arguments, in favor of surgery are symptoms will be greatly reduced,¹ improve pregnancy rates (around 50%) after surgical removal of endometrioma²⁻⁵ and is an effective procedure of get rid of cysts. Moreover, surgery reduces the incidence of ovarian carcinoma as number of

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carcinoma was increasing with endometriosis.⁶ Finally, surgical preparation of pelvis of women with endometrioma makes the ovum pick up easier and accessible in IVF cycles. Against the argument is deleterious effect of surgery on ovarian reserve and the higher risk of premature ovarian failure.^{7,8} This deleterious effect is more pronounced in repeat surgery in recurrent cases. In many cases, normal ovarian tissue is inadvertently removed, which may decrease the number of oocytes available for subsequent fertility treatment. This surgical removal of ovarian tissue along with cauterization may further decrease the number of oocytes and reduce ovarian reserve for future fertility.⁹⁻¹¹

A large percentage of the patients have advanced stage of disease and have had multiple previous surgeries. Most of them developed pelvic adhesions due to repeated surgeries. In the presence of pelvic adhesions from previous surgery, fibrosis of endometriotic tissue and gonadotropin-releasing hormone against (GnRHA) induced fibrosis- or in advance stage of disease it is difficult to visualize pelvic structures leading to suboptimal resection and frequent cyst formation, which could further diminish the ovarian reserve even at expert hand. Many patients with recurrent ovarian endometriomas are at increased risk of complications from further surgery. There is potential risk of injury to gut, ureter and bladder where there is dense fibrosis due to previous surgery.

In the last decade, there have been several reports of less invasive alternative treatment of ovarian endometrioma to avoid surgical complications and to preserve ovarian reserve. Transvaginal ultrasound guided aspiration of ovarian endometriomas was first proposed in 1991^{12,13} for patients who decline surgery or in whom surgery was contraindicated. But they have reported varying rates of recurrence (up to 85%) after simple aspiration. To reduce recurrence investigators used *in situ* injection of a sclerosing agents like tetracycline,¹⁴ methotrexate,¹⁵ recombinant interleukin-2¹⁶ or ethanol^{17,18} following aspiration. Most of them reported that using sclerosing agent is effective at reducing the recurrence rate. Ethanol instillation into the cyst cavity for more than 10 minutes was most effective at reducing the recurrence rate. The aim of this study was to investigate the efficacy of ultrasound guided transvaginal aspiration and sclerotherapy with 95% ethanol for the treatment of recurrent ovarian endometrioma.

MATERIALS AND METHODS

This prospective study was conducted in Infertility Care and Research Centre (ICRC), Dhaka, Bangladesh,

between January 2005 and December 2013. Fifty-three infertile patients having chocolate cysts with history of laparotomy or laparoscopy or both for endometriosis were the target population for this study. Endometrioma was diagnosed by transvaginal sonography (TVS). Cyst with diameter >3 cm was defined as recurrent endometrioma and was recruited for this study. Both unilateral, bilateral, single and multiple cysts were included. With all aseptic precaution TVS-guided cyst aspiration and instillation of ethanol was done under sedation (pathedine) or G/A (propofol). A 16-gauge double lumen ovum pick up (OPU) needle was inserted into the endometrioma and the cyst contents were sequentially aspirated and flushed with normal saline until the aspirated fluid was clear. Ethanol amounting 75% of aspirated fluid was instilled and removed. Then 5 to 10 ml ethanol re-instilled and kept in situ. All cyst aspirates were examined cytopathologically. Patients were kept under GnRHA or oral contraceptive pill (OCP) for 8 to 12 weeks. Ultrasound was performed at 6 weeks, 3, 6, 9 and 12 months to assess the efficacy of treatment. Patients were eligible for fertility treatment 12 weeks after the sclerotherapy or earlier if the endometrioma was completely resolved. Controlled ovarian hyperstimulation and IUI or ART was performed according to patients' tubal factor, ovarian reserve and desire during this period. Ovarian reserve was tested by basal follicle stimulating hormone (FSH) till 2011 as anti-Müllerian hormone (AMH) was not available at that time. Afterwards both FSH and AMH were tested to assess ovarian reserve. The tests were repeated after 3 months of the procedure. Outcome measures were resolution of cyst and pregnancy rates. As we did the procedure for treatment purpose and not solely for research, we did not sought for ethical permission.

RESULTS

Mean age of the patients was 32.28 ± 2.17 years. Thirty-nine patients had cyst in one ovary and 14 patients had bilateral cysts. Number of cysts in each patient were 1 to 3. In 36 cases, there was single cyst and in 17 cases, there were more than one cyst. Average size of the cyst was 6.75 ± 1.64 cm ranging from 3.5 to 10 cm (Table 1).

In 42 (79.25%) cases, cysts regressed completely. In 11 (20.75%) cases, cysts refilled but 7 of them regressed spontaneously and 4 (7.55%) needed reaspiration. Aspirated fluid was thin and straw colored. Twenty-three patients were recruited for ART and 30 for IUI. Among 30 IUI cases, 5 got pregnant out of 52 cycles (15×1 , 8×2 , 7×3 cycles). Eighteen of failed IUI cases subsequently did ART. So, total 41 (23 + 18) patients did ART. Among

Table 1: Characteristics of the patients with sclerotherapy

Patients characteristics	Mean \pm SD	Range
Age (years)	32.28 \pm 2.17	28-37
Cyst size (cm)	6.75 \pm 1.64	3.5-10
Number of cyst	1.34 \pm .68	1-3
	N	Percentage
Unilateral	39	73.58
Bilateral	14	26.42
Single cyst	36	67.92
More than one cyst	17	32.07

41 cases, 13 (31.71%) got pregnant out of 63 cycles (21 \times 1, 20 \times 2 cycles) (Table 2). Six patients developed cyst during course of treatment within 1 year, though size was less than 3 cm.

DISCUSSION

Surgery should still be considered the first line therapy for most cases of endometriosis. Simple drainage or coagulation of endometriosis without removal of its capsule leads to recurrence up to 85%. For few cases, surgeons should think twice before choosing repeat and potentially complex surgical intervention. Not only there is risk of injuries of gut and surrounding structures but also there is risk of iatrogenic ovarian failure. Extensive adhesiolysis, removal of cyst walls and cauterization reduces ovarian reserve tremendously even may leads to ovarian failure. Many investigators have investigated preoperative and postoperative AMH concentrations and found decreased levels of AMH after surgery.¹⁹⁻²⁶ Tsolakidis et al shown 25.64% reduction of AMH after laparoscopic cystectomy.²⁶ In our experience, we also found 44% increment of FSH and 40% decrement of AMH after cystectomy (unpublished data). Moreover, we found some endometriotic patients who underwent surgeries twice having bilateral cystectomy and in spite of young age ART cycles had to be canceled for not developing eggs. For these cases, less invasive aspiration and sclerotherapy to avoid recurrence and to preserve oocyte pool is a good alternative. In this series, we did FSH for all cases before aspiration and 3 months after the procedure but could not do the AMH testing for all cases as it was not available till 2011. So, we did not put it in the table but found no significant changes before and after the procedure. It indicates that ovarian reserve does not go down after cyst aspiration and sclerotherapy in comparison to cystectomy.

Sclerotherapy was originally used to treat tubercular pneumonitis and is currently used by medical oncologists to treat malignant pleural effusion. In 1991, Aboulghar et al and Dicker et al reported alternative therapeutic modality of TVS guided aspiration of ovarian endometrioma without any sclerotherapy, which was

Table 2: Outcome of sclerotherapy

Outcome	N	Percentage
Cyst		
Resolution of cyst	42	79.25
Refilling of cyst	11	20.75
Reaspiration of cyst	4	7.55
Recurrence within 1 year <3 cm	6	11.32
Pregnancy		
IUI	30	56.60
Pregnancy (5/30, 52 cycles)	5	16.67
ART	41	77.36
Pregnancy (13/41, 63 cycles)	13	31.71

associated with high recurrence rate.^{12,13} In 1993, Aboulghar et al reported the efficacy of tetracycline to resolute cyst completely and used as a means of avoiding surgery in patients with endometrioma.¹⁴ These findings were supported by the work of others.^{27,28} Sclerotherapy with 5% tetracycline before IVF can achieve a resolution rate 75% and pregnancy rate 57%.²⁹ Many other authors^{18,30-32} proved the efficacy and safety of ethanol as sclerotherapy in ovarian endometrioma.

In our series, we also found satisfactory result (79.25% complete resolution) after aspiration and ethanol sclerotherapy. In 11 cases, complete resolution was not observed in 1st monitoring at 6 weeks. Four needed reaspiration and thin dark straw colored fluid came out suggested inflammatory fluid. Others regressed gradually. Six (11.32%) patients developed small <3 cm cysts within 1 year during the process of stimulation. It is not sure whether the cysts were refilling of existing one or appearance of new one. Noma and Yoshida and Hsieh et al reported recurrence rate 14.9% and 26.9% respectively in 12 months follow-up period.^{18,32} No one developed serious postoperative complications in our series, however, mild abdominal cramping reported immediately following the procedure in a few cases. Okagaki et al performed laparoscopy in four cases after ethanol sclerotherapy to assess post procedural effect and found severe and unusual adhesions surrounding the ovaries.³³ Adhesion is the characteristics of endometriosis, so, it is difficult to conclude whether the adhesion was due to leakage of ethanol or due to endometriosis itself? We observed our cases during cesarean section and found flimsy adhesions around ovaries and behind the uterus, which is same as found in other endometriotic cases. Chang et al evaluate the efficacy of cyst aspiration and ethanol instillation in a series of 196 patients and found it effective. They concluded that ultrasound-guided sclerotherapy with 95% ethanol retention is an effective alternative therapy for recurrent ovarian endometrioma, in particular in selected patient groups.³⁴

Cystectomy should still be considered the first line of therapy for most cases of endometrioma. In a few potentially complex cases, it becomes very difficult and dangerous to do surgery. For them less invasive aspiration with sclerotherapy is a good alternative, which is safe and effective.

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