Effectiveness of Aspiration and Sclerotherapy of Ovarian Cyst: A Comparative Study of Ethanol 95% or Tetracycline Solution versus Simple Aspiration

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Abstract: Objectives: To evaluate the therapeutic yield of aspiration and sclerotherapy of simple ovarian cyst or endometrioma, using tetracycline or ethanol 95%. **Patients & Methods**: The study included 120 multigravida multipara women with average age of 30±4.6 years old. women were randomly allocated into 3 equal groups included (Group A) : Aspiration group assigned to undergo transvaginal ultrasonography guided cyst aspiration without sclerotherapy, (Group T) Tetracycline group assigned to undergo cyst aspiration and instillation of tetracycline 5% solution (5-10 ml) and (Group E) Ethanol group assigned to undergo cyst aspiration and instillation of ethanol 95% in a volume equal to the volume aspirated out of the cyst. Patients were assessed after 3 months for cyst resolution and at 6th and 12th postoperative (PO) months for recurrence; the cyst was considered recurrent if it >4cm in diameter. **Results:** the results indicated that 49 women (40.8%) had simple serous cyst and 71 women (59.2%) had endometrioma. All procedures were conducted uneventfully as one-day procedure. At the end of the 3rd PO month, all cysts showed significant diminution of diameter compared to preoperative diameter. At the 6th PO month, 17 women had recurrent cysts and at the 12th PO month, another 20 patients had recurrent cysts. Collectively, there were 13 recurrent serous cysts and 24 recurrent endometrioma. Aspiration only showed a significantly higher recurrence rate (55%) compared to aspiration and instillation (18.8%), irrespective of the sclerosant used. Moreover, Group A showed significantly higher recurrence rate compared to Group T and Group E, 20% and 17.5%, respectively with non-significantly higher recurrence rate with tetracycline than with ethanol. Morever recurrence rate of endometrioma was significantly higher in Group A compared to Group T and Group E with non-significantly higher recurrence rate of endometrioma in Group T compared to Group E. **Conclusion:** Aspiration and sclerotherapy of ovarian cyst is a safe and effective treatment with a significantly low recurrence rate compared to simple aspiration only. The non-significant difference between the outcome of tetracycline and ethanol sclerotherapy allowed the choice to depend on the surgeon's preference.
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Key words: Ovarian cyst, Aspiration, Ethanol, Tetracycline, Instillation.

1. Introduction

Wider and more liberal use of diagnostic ultrasound in gynaecological clinics has resulted in the detection of adnexal masses in a large number of patients. There has also been an increase in the use of other imaging modalities such at CT and MRI to assess a variety of medical complaints resulting in incidental detection of adnexal tumours **(Nunes *et al.*, 2012)**.

Confirmation and clarification of an adnexal mass is a domain of transvaginal ultrasound. The highest hit ratio is achieved by experienced sonographers relying on a dedicated set of sonomorphologic criteria. However;less experienced may consult validated scores, color Doppler findings and the tumor marker CA125. The assignment to one of the three groups simple cyst, benign tumor and malignant tumor should lead to an adequate procedure control, laparoscopy or laparotomy. Consequently, simple cysts should be treated conservatively avoiding unnecessary surgical interventions **(Bajka, 2011)**.

Laparoscopic treatment of adnexal masses is recommended when all criteria of a benign lesion are present including transvaginal ultrasound demonstrates a mass <5 cm, with liquid or dermoid content, with <3 fine partitions (<3 mm), a thin wall (<3 mm), no vegetations and normal Doppler. Laparoscopy is also indicated for "benign" cysts measuring 5 to 10 cm if laparoscopy is feasible and peroperative exploration is the rule **(Capar *et al.*, 2009; Seckin *et al.*, 2011)**.

Ultrasound guided aspiration of ovarian endometrioma had been tried as an alternative therapeutic modality in patients whose desire to avoid surgery or surgical approach is contraindicated since 1991. Cyst puncture can reduce tumor volume and destruct the cyst wall, alleviate sticking circumstances and enhance the chance of recovery. But simple aspiration without other treatments results in high recurrence rate (28.5 % to 100 %). In order to reduce recurrence after aspiration, ultrasound-guided aspiration with instillation of methotrexate, and

recombinant interleukin-2 has been combined and proven to be effective with reduced recurrence rates, **(Koutlaki *et al.*, 2011; Wang *et al.*, 2013)**.

Multiple studies evaluated the effectiveness of ethanol 95% or tetracycline as sclerotherapy after cyst evacuation in multiple organs; **Egilmez *et al.* (2007)** documented that ethanol sclerotherapy under CT guidance is a successful and safe procedure and it can be used for the treatment of simple renal cysts. Moreover **Kilinc *et al.* (2008)** reported success rate of 85.7% with tetracycline sclerotherapy group of simple renal cysts. **Fabrizzi *et al.* (2009)** found aspiration and tetracycline hydrochloride solution (5%) injection into the cystic cavity in hepatic cysts resulted in total collapse and deflation of the cyst leaving a hyperechoic linear scar on US examination at 1 year. **Vergès *et al.* (2011)** reported that non-US-guided ethanol sclerotherapy is a safe and "easy-to-use" procedure to treat benign thyroid cysts effectively.

The current prospective study aimed to evaluate the therapeutic yield of aspiration and sclerotherapy of ovarian cyst or endometrioma, using tetracycline or ethanol 95% in comparison to simple aspiration alone.

2. Patients and Methods

The study was conducted at Department of Obstetric & Gynecology, Benha University Hospital and private practice settings since june 2011 till May 2013. After approval of the study protocol and obtaining patients' written fully informed consent, all women with ovarian cyst detected on routine gynecological examination were recruited in the study irrespective of patients' age. Patients were eligible for inclusion in study if they had cystic ovarian masse(s) on ultrasonography with a diameter larger than 4 cm, a well defined cystic wall and not more than 2 thin septa. Patients with free fluid in pouch of Douglas, history of malignant neoplasm, or recurrent cyst or showed multiple septa were excluded from the study.

One hundred twenty women were divided, using sealed envelops, into 3 equal groups: Aspiration only group (Group A) included patient assigned to undergo transvaginal ultrasonography guided cyst aspiration without sclerotherapy and was considered as the control group. Tetracycline group (Group T) included patients assigned to undergo transvaginal ultrasonography guided cyst aspiration and instillation of tetracycline 5% solution in a dose of 5-10 ml. Ethanol group (Group E) included patients assigned to undergo transvaginal ultrasonography guided cyst aspiration and instillation of ethanol 95% in a volume equal to the volume aspirated out of the cyst. All women were pre-medicated with midazolam(0.05 mg/kg), 2 minutes thereafter, anathesia was induced by a bolus of remifentanel (1 ug/kg) followed by propofol (1-2 mg/kg) and vecuronium was given in dose of 1 mg/kg to facilitate tracheal intubation followed by maintenance doses of 10-20 mg. Anathesia was maintained by isoflurane 1-2 %.

An 18-gauge, single-lumen needle was inserted into the cyst or the endometrioma, and the cyst contents were sequentially aspirated and flushed with sterile saline until the aspirated fluid was clear. Then the sclerosant fluid was injected and retained in the cyst. Then, saline was injected into the cul-de-sac to dilute any tetracycline or ethanol that may have leaked and the fluid was then removed. An ultrasound examination was performed in the 3rd month for assessment of cyst resolution and at 6th and 12th months after therapy to cheek for recurrence; a cyst to be considered recurrent if it was > 4 cm in diameter.

All procedures were received declophenac sodium (3mg ampule) as rescue postoperative analgesia. All women were managed as one day procedure and were discharged after being fully – recovered and can move independently.All women were advised to attend the follow –up visit regularly at the outpatient clinic.

Statistical analysis obtained data were presented as mean± SD, ranges, numbers and ratios. results were analyzed using wilcoxon; ranked test for unrelated data (Z-test)and Chi-square test (X^2 test).statistical analysis was conducted using the SPSS(version 15,2006) for windows statistical package.p value < 0.05 was considered statistically significant.

3. Results

The study included 120 women with mean age of 30±4.6;and 21-38 years. All enrolled women were multigravida with mean gravidity rate of 2±0.7; range: 1-3 pregnancies and mean parity rate of 1.7±0.7; range: 0-3 para. Seven women were of average weight with BMI <25 kg/m^2; 79 women were overweight with BMI in range of 25-30 kg/m^2 and 34 women were obese with BMI>30 kg/m^2. There was non-significant (p>0.05) difference between studied groups as regards enrolment data, (Table 1).

Forty-nine women (40.8%) had simple serous cyst with a mean diameter of 12±1.7; range: 9-15 cm, while 71 women (59.2%) had endometrioma with a mean diameter of 34.3±8.9 mm; range: 15-56 cm. There was non-significant (p>0.05) difference between the studied groups as regards the frequency of simple cysts and endometrioma and as the mean cyst diameter, (Table 2, Fig. 1).

At the end of the 3rd month after aspiration, all cysts showed significant (p<0.05) diminution of diameter compared to preoperative diameter, (Fig. 2) and all cysts receded in size to the range of 1-3 cm. The estimated diameter of cyst at the 3rd month insignificantly (p>0.05) large size in group A compared to that estimated in the other groups, irrespective of the type of the cyst, (Table 3).

Table (1): Patients enrolment data

			Group A	Group T	Group E	Total
Age (years)	Strata	<25	6 (15%)	4 (10%)	4 (10%)	14 (11.7%)
		25-30	19 (47.5%)	16 (40%)	20 (50%)	55 (45.8%)
		>30-35	15 (37.5%)	15 (37.5%)	9 (22.5%)	39 (32.5%)
		>35	0	5 (12.5%)	7 (17.5%)	12 (10%)
	Total		29.3±4 (23-35)	30.5±5 (21-38)	30.3±4.7 (24-38)	30±4.6 (21-38)
Body built data	Weight (kg)		79.9±4.3 (71-93)	81.6±4.9 (74-90)	80±5.1 (74-89)	80.5±4.8 (71-93)
	Height (cm)		167.5±4.4 (159-180)	169±5.7 (157-180)	167.3±2.2 (159-171)	167.9±4.4 (157-180)
	BMI strata	<25	2 (5%)	5 (12.5%)	0	7 (5.9%)
		25-30	31 (77.5%)	20 (50%)	28 (70%)	79 (65.8%)
		>30-35	7 (17.5%)	15 (37.5%)	12 (30%)	34 (28.3%)
	BMI total		28.5±1.9 (24.8-32.9)	28.7±3 (23.2-34)	28.6±1.8 (26.2-32)	28.6±2.3 (23.2-34)
Obstetric data	Gravidity		2±0.7 (1-3)	1.8±0.7 (1-3)	2.1±0.6 (1-3)	2±0.7 (1-3)
	Parity		1.5±0.7 (0-3)	1.6±0.6 (1-3)	2±0.7 (1-3)	1.7±0.7 (0-3)

Data are presented as numbers & mean±SD; percentages & ranges are in parenthesis

Table (2): Patients' distribution according to type of ovarian cyst

		Group A	Group T	Group E	Total
Serous	Number	19 (47.5%)	17 (42.5%)	13 (32.5%)	49 (40.8%)
	Diameter	11.7±1.9 (9-15)	12±1.1 (10-14)	12.2±2.2 (9-15)	12±1.7 (9-15)
Endometrioma	Number	21 (52.5%)	23 (57.5%)	27 (67.5%)	71 (59.2%)
	Diameter	35.1±8.9 (20-49)	37.3±9.5 (21-56)	31.3±7.6 (15-43)	34.4±8.9 (15-56)

Data are presented as numbers & mean±SD; percentages & ranges are in parenthesis

Table (3): Postoperative cyst diameter estimated at the 3rd postoperative month compared to preoperative diameter

		Group A	Group T	Group E	Total
Serous	Pre	11.7±1.9 (9-15)	12±1.1 (10-14)	12.2±2.2 (9-15)	12±1.7 (9-15)
	PO	2.16±0.7 (1-3)	1.94±0.75 (1-3)	1.85±0.55 (1-3)	2±0.68 (1-3)
Endometrioma	Pre	35.1±8.9 (20-49)	37.3±9.5 (21-56)	31.3±7.6 (15-43)	34.4±8.9 (15-56)
	PO	2.5±0.51 (2-3)	2±0.74 (1-3)	2.15±0.66 (1-3)	2.21±0.67 (1-3)

Data are presented as mean±SD; ranges are in parenthesis

At the 6th month of follow-up, 17 patients had recurrent cysts; 12 of them in group A, 3 in group T and 2 in group E. Only 4 patients had recurrent serous cyst and 13 patients had recurrent endometrioma. At the 12th month of follow-up, another 20 patients had recurrent cysts; 10 in group A and 5 in each of groups T and E. Nine patients had recurrent serous cysts and 11 had recurrent endometrioma. Collectively, there were 13 recurrent serous cysts and 24 recurrent endometrioma, (Table 4).

Table (4): Postoperative recurrence rate as judged by ultrasonography at 6th and 12th month PO

			Group A	Group T	Group E	Total
Serous	Resolved		13 (32.5%)	13 (32.5%)	10 (25%)	36 (30%)
	Recurrent	6th month	3 (7.5%)	1 (2.5%)	0	4 (3.3%)
		12th month	3 (7.5%)	3 (7.5%)	3 (7.5%)	9 (7.5%)
Endometrioma	Resolved		5 (12.5%)	19 (47.5%)	23 (57.5%)	47 (39.2%)
	Recurrent	6th month	9 (22.5%)	2 (5%)	2 (5%)	13 (10.8%)
		12th month	7 (17.5%)	2 (5%)	2 (5%)	11 (9.2%)

Data in parenthesis are the percentages

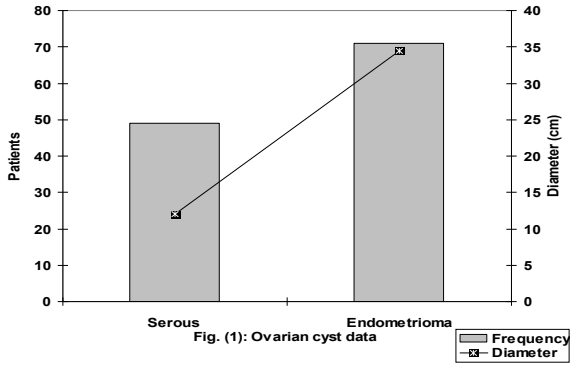

Fig. (1): Ovarian cyst data

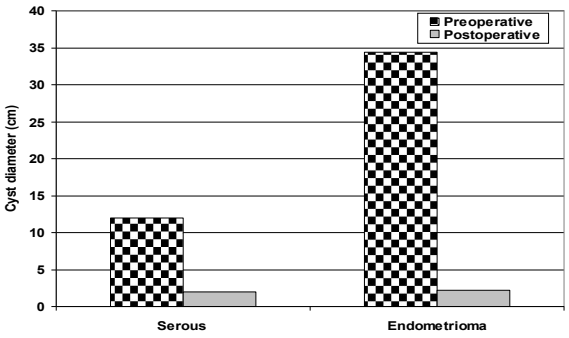

Fig. (2): Postoperative cyst diameter compared to preoperative diameter categorized according to type of cyst

Considering outcome as the 12th month recurrence rate; aspiration only (Group A) showed a significantly (X^2=20.16, p<0.001) higher collective recurrence rate 55% compared to aspiration and instillation (18.8%), irrespective of the sclerosant used. Moreover, Group A showed significantly higher recurrence rate compared to Group T (X^2=18.21, p <0.001) and Group E (X^2=24.92, p<0.001) whose had aspiration and instillation of tetracycline (20%) and ethanol (17.5%), respectively with non-significantly (X^2=0.317, p >0.05) higher recurrence rate with tetracycline than with ethanol, (Fig. 3).

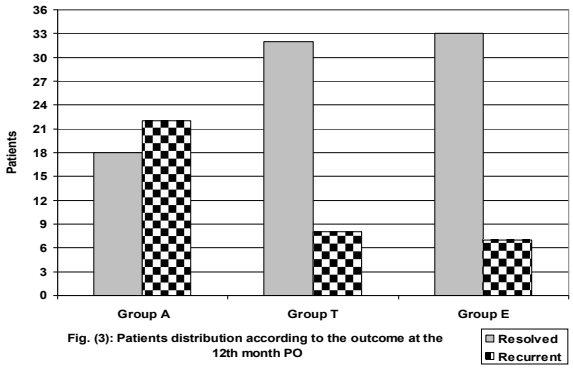

Fig. (3): Patients distribution according to the outcome at the 12th month PO

Differentially according to the type of the cyst; recurrence rate of simple cyst was non-significantly higher in Group A compared to Group T (X^2=1.833, p >0.05) and Group E (X^2=1.674, p >0.05) with non-significantly (X^2=0.915, p >0.05) higher recurrence rate in Group T compared to Group E. On the other hand, recurrence rate of endometrioma was significantly higher in Group A compared to Group T (X^2=43.23, p <0.001) and Group E (X^2=47.45, p <0.001) with non-significantly (X^2=0.497, p >0.05) higher recurrence rate of endometrioma in Group T compared to Group E, (Fig. 4).

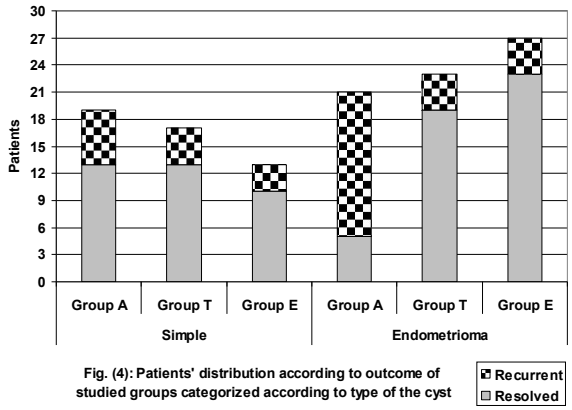

Fig. (4): Patients' distribution according to outcome of studied groups categorized according to type of the cyst

4. Discussion

The management of ovarian cyst is still a challenge to gynecologists due to the inherent character of these cysts; the recurrence which imposes its burden on the psychological status of patients and so affects their quality of life and endanger their fertility especially in case of endometrioma. The current study aimed to determine the frequency of 12-months recurrence rate of aspiration and instillation of sclerosant material in comparison to simple aspiration.

Collectively, aspiration only showed a significantly higher recurrence rate (55%) compared to aspiration and instillation (18.8%), irrespective of the sclerosant used. These findings indicated the success of the decision to use sclerotherapy as an adjuvant therapeutic line to aspiration for the management of ovarian cyst. However, such effect was more pronounced with endometrioma, which hampers patients' fertility, where recurrence rate of endometrioma was significantly higher in patients received aspiration only compared to patients received combined aspiration and sclerosant instillation.

In line with the obtained results, **Noma & Yoshida (2001)** reported a recurrence rate of 14.9% after more than 6 months follow-up after aspiration and ethanol instillation. **Koike *et al.* (2002)** also reported an ovarian cyst recurrence rate of 13.3% in

women who had endometrioma after ethanol instillation. **Messalli *et al.* (2003)** reported that ultrasound-guided alcoholic sclerotherapy of the endometriotic ovarian cysts is effective and safe with a recurrence rate of 10% after a mean follow-up period of about 20 months and concluded that this procedure could be indicated in patients refusing standard surgical therapy.

In the same concern, **Hsieh *et al.* (2009)** found the 1-year recurrence rate was significantly lower in patients who had aspiration and ethanol instillation of endometrioma versus aspiration alone; 32.1% vs. 13.3%, respectively. **Yazbeck *et al.* (2009), Kumbak & Sahin, (2010)** and **Yazbeck *et al.* (2012)** investigated the efficacy of ethanol sclerotherapy (EST) for recurrent endometriotic cysts, before ovarian stimulation in infertile patients with an adequate ovarian status and found that ovarian cysts recurred in 12.9% of cases; at a mean time of 10 months after EST, ovarian reserve and ovarian response to stimulation were better in the EST group than in the control group with consequently higher clinical and cumulative pregnancy rates in EST group than the control group, and concluded that ethanol sclerotherapy may be a good alternative to surgical management of recurrent endometriotic cysts before assisted reproductive treatment.

Wang *et al.* (2011) tried to determine the effectiveness of ultrasound-guided interventional therapy in the treatment of postoperative recurrent chocolate cysts using simple aspiration in one group of patients and ethanol instillation in the other group and found that the chocolate cyst cure rate was significantly higher in the ethanol retention group (96%), while no case was cured in the first group (saline washing) and concluded that ultrasound-guided injection and 95% ethanol retention are an effective therapy for the treatment of postoperative recurrent chocolate cysts

The current study reported a non-significantly lower recurrence rate with ethanol versus tetracycline solution instillation; 17.5% vs. 20%; a finding indicating the efficacy of both modalities as a form of sclerotherapy after cyst aspiration. In line with these data; **Fisch & Sher (2004)** reported complete resolution in 75% of patients at follow-up examination and repeat aspiration of watery fluid was required in 25% of patients before resolution with repeat tetracycline treatment was needed in 6% of patients, but only 2% of patients did not ultimately respond and concluded that sclerotherapy with 5% tetracycline is a simple and effective alternative to surgical intervention for treatment of endometriomas before IVF.

Kars *et al.* (2012) and **Thummalakunta & Panditi (2012)** investigated the value of tetracycline sclerotherapy for management of recurrent or persisting non-neoplastic ovarian cysts in comparison to the aspiration without sclerotherapy and reported a 12-months recurrence rates of 14.6% with tetracycline and 50% in aspiration without sclerotherapy and based on the recurrence rates, suggested transvaginal aspiration together with tetracycline sclerotherapy rather than only simple transvaginal aspiration as the management of non-neoplastic ovarian cysts.

It could be concluded that aspiration and sclerotherapy of ovarian cyst, irrespective of type of sclerosant used, is a safe and effective treatment with a significantly low recurrence rate compared to simple aspiration only. The non-significant difference between the outcome of tetracycline and ethanol sclerotherapy allowed the choice to depend on the surgeon.

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