

## ORIGINAL ARTICLE

# TETRACYCLINE SCLEROTHERAPY IN TREATING POSTMASTECTOMY SEROMA: A SIMPLE SOLUTION FOR A FREQUENTLY OCCURRING PROBLEM

By

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**Aim:** Seroma is the most common complication occurring after breast surgery. Its management usually involves repeated aspiration and drain insertion. Tetracycline sclerotherapy appeared successful for treating many chronic fluid collections e.g. pleural effusions, hydrocele, liver cysts, renal cysts....etc. The present study aimed to evaluate the efficacy of topical tetracycline (TCN) sclerotherapy in treating postmastectomy seroma.

**Methods:** Forty nine female patients with resistant post mastectomy seroma were enrolled in the study. All patients were subjected to aspiration of the seroma and instillation of 2g tetracycline dissolved in 100 ml sodium chloride 0.9% + 10 ml Lidocaine. After 24 hours, the solution is re-aspirated and a crepe bandage is applied to the chest wall. Each patient is asked to record her pain using the Visual Analogue Scale (VAS). The procedure is repeated in patients who had experienced seroma recollection.

**Results:** Thirty six patients (73.4%) were successfully treated with one sclerotherapy session while nine patients (18.4%) needed two sessions and four patients (8.2%) needed three sessions. The majority of the patients (85.7%) had no complications after the technique.

**Conclusion:** the topical application of tetracycline is effective and feasible method in the management of refractory post mastectomy seroma.

**Keywords:** Breast, lymphocele, seromadesis.

## INTRODUCTION

Breast cancer is the most common cause of cancer deaths among women worldwide. Incidence rates are high in more developed countries, whereas, rates in developing countries and Japan are low but are lately increasing.<sup>(1)</sup> In Egypt, breast cancer is the most common cancer in females constituting 33% of all female cancers.<sup>(2)</sup>

For a long period, surgery was the main line of treatment of breast cancer. Application of new techniques in the treatment of cancer such as radiotherapy, hormonal therapy, and chemotherapy allowed better management of the advanced cases. Although other therapeutic modalities competed with surgery in the treatment of the loco-regional primary tumor, nevertheless, surgery is still the major diagnostic and therapeutic mean, but with

a tendency towards less extensive and rather more conservative interventions.<sup>(1)</sup>

Seroma formation is the most frequent postoperative complication after breast cancer surgery. Its incidence after breast surgery is (15-81%).<sup>(3)</sup> It occurs in most patients after mastectomy and is increasingly being considered as a side effect of surgery rather than a complication, however not all patients are clinically symptomatic.<sup>(4)</sup>

Seroma is defined as a serous fluid collection that develops under skin flaps after mastectomy or in the axillary dead space after axillary dissection (as a consequence of both, lymphatic disruption and oozing of capillary beds).<sup>(5)</sup>

Although seroma is not life threatening, it can lead to significant morbidity e.g. infection, flap necrosis, wound dehiscence, predisposes to sepsis, prolonged recovery period, multiple physician visits and may delay adjuvant therapy. Fluid collection is ideally managed by repeated needle aspiration to seal the skin flaps against chest wall.<sup>(6)</sup>

Several interventions have been reported with the aim of reducing seroma formation including the use of ultrasound scissors in performing lymphadenectomy,<sup>(7)</sup> using fibrin glue,<sup>(8,9)</sup> bovine thrombin application,<sup>(10)</sup> and altering surgical technique to close the dead space.<sup>(11)</sup>

Despite numerous trials of new techniques which have attempted to reduce the incidence of seroma formation, no single method appears to be uniformly effective. Topical sclerotherapy with Tetracycline (TCN) has long been used successfully in the treatment of malignant pleural effusions to cause obliteration of the pleural space.<sup>(12)</sup>

The first report of TCN sclerotherapy for treating seromas after mastectomy was in 1983 by Sitzmann and his colleagues,<sup>(13)</sup> who instilled 2 g of TCN in 150 ml of 0.9% NaCl following aspiration of seromas in 5 patients. All patients had a marked decrease in the size of seromas within 48 hrs. In the same year Nichter and his team,<sup>(14)</sup> demonstrated efficacy of TCN in 4 patients with persistent postoperative seromas. Numerous reports described the use of TCN sclerotherapy in a diverse range of conditions. TCN was used in the past for the treatment of malignant pleural effusions,<sup>(12)</sup> hydroceles of the testes,<sup>(15)</sup> endometrial cysts,<sup>(16)</sup> hepatic cysts,<sup>(17)</sup> pericardial effusions,<sup>(18)</sup> and even the gallbladder lumen.<sup>(19)</sup>

## PATIENTS AND METHODS

Following research committee approval and informed patient consent, our study was designed as prospective research that was carried on female patients presented with postmastectomy seroma at surgery outpatient clinic, Suez Canal University Hospital in the period between December 2007 and July 2008. All patients fulfilling the following inclusion criteria were enrolled in the study:

1. All females with resistant postmastectomy seroma.
2. Any type of mastectomy operations (modified radical mastectomy, radical mastectomy, simple mastectomy and breast conservative technique).
3. Any amount of seroma.
4. Any time of presentation (post operatively).

Patients with the following criteria were excluded from the study:

1. Pregnant or lactating females
2. Known sensitivity to TCN.

3. Patients prepared for reconstructive surgery.
4. Chronic medical illness (diabetes mellitus, end stage renal disease and chronic liver disease).

Forty nine patients were eligible for the study. All patients were reviewed to evaluate the method, timing, and outcome of TCN sclerotherapy. Indication for sclerotherapy was based on recurrent seroma despite of three consecutive sessions of aspiration and crepe bandaging. All sclerotherapy sessions were conducted in the one-day operative room using local anaesthesia. The technique involves inserting wide bore canula (14 or 16 gauge) to aspirate seroma fluid which is calculated and recorded for every patient (Fig. 1). Then, instillation of 2g of TCN in 100 ml of 0.9% of NaCl + 10 ml Lidocaine was done. The instilled amount remains in the cavity for 24 hours after which it is aspirated and a crepe bandage is applied to the chest wall. Pain is recorded according the Visual Analogue Scale (VAS) which was classified as mild (1-4), moderate (5-6) and severe (7-10).



*Fig 1. Aspiration of seroma*

VAS is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patients mark on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring the millimeters from the left hand end of the line to the point that the patient marks.<sup>(20)</sup>

All Patients were followed up every 2 weeks for the development of complications like fever, infection and flap necrosis. Patients, who experienced seroma recollection, were subjected to reaspiration of the collected seroma, recording its amount and TCN sclerotherapy. The subsequent sclerotherapy sessions were performed using the same volume and concentration of previously used formula. The sessions

were repeated till the seroma disappeared.

Data were collected through history of the surgical operations, clinical examination of the wound and seroma cavity, investigations like ultrasound to measure the precise size of the seroma and all details about sclerotherapy sessions for every patient. Data were analyzed by Statistical Package for Social Science (SPSS) version 13.0. Quantitative data were expressed as mean and stander deviation (SD), and qualitative data were expressed as number & percentage of the total. Student t test was used to test the significance of the difference between quantitative variable while chi square test was used for qualitative variables.

## RESULTS

The study was conducted on 49 female patients with mean age 48.5±7.7 years. Modified radical mastectomy was the most frequent operation done to the patients (71.4%), while the frequencies of simple mastectomy and breast conservative technique operations were 18.4% and 10.2% respectively. The amount of aspirated seroma was significantly high in the modified radical mastectomy operations rather than other types of operations (chi square test, P<0.05). The relation between the type of the operation and the aspirated fluid in the first session is illustrated in Table 1.

Thirty seven patients (75.5%) presented as early as ≤ 4 weeks postoperatively, while 12 patients (24.5%) presented late (> 4 weeks), with the mean time of presentation 3.3±0.9 weeks. Thirty six patients (73.4%) had only one instillation, 9 patients (18.4%) had 2 instillations, and 4 patients had 3 instillations (8.2%), with the mean of 1.3±0.6 instillations. Table 2 correlates between amount of aspirated fluid in the first session and number of aspiration/injections.

As regards chemo and radiotherapy, none of the patients had history of previous radiation to the affected side while 5 patients (10%) had received neoadjuvant chemotherapy. Twelve patients had received

postoperative chemotherapy; half of them had seroma before starting chemotherapy sessions and the other half developed seroma during their sessions.

In the first session; the amount of aspirated fluid was <100cc in 10 patients (20.4%), 100-150cc in 22 patients (44.9%), and >150cc in 17 patients (34.7%). In the second session; the amount of aspirated fluid was <100cc in 10 patients (76.9%), 100-150cc in 3 patients (23.1%), and no patients had >150cc. In the third session; the amount of aspirated fluid was <100cc in 3 patients (75%), 100-150cc in one patient (25%), and no patients had >150cc Table 3. The mean aspiration volume across all patients in the first session was 120.9±3.6 ml while it was 100.0±25.2 ml and 75.0±35.4 ml in the second and third sessions respectively. The amount of aspirated seroma was significantly decrease in the second and third session compared with the first one (t-test, P = 0.006, P = 0.003 respectively).

The majority of the patients had no pain during or/and after instillation (91.8% & 89.8% of the patients respectively), the rest of the patients experienced mild to moderate pain and no patients had severe pain during or/and after instillation (as assessed by the Visual Analogue Scale) Table 4. The majority of the patients had no complications after instillation (85.7%), 3 patients (6.1%) suffered from low grade fever and 4 patients (8.2%) had infections in the wound site. Five out of the seven patients (71.4%) who experienced complications were treated in the outpatient clinic by broad spectrum antibiotics and antipyretics while two patients needed hospitalization for treatment with intravenous antibiotics. All the seven patients who experienced complications were subjected to multiple aspiration/injection sessions (4 patients had two sessions while 3 patients had three sessions). Complications developed in (53.8%) of patients who underwent multiple aspiration/injection sessions while no patient (0%) developed complications in the single aspiration/injection group; it was significantly high in patients who underwent multiple aspiration/injection sessions (Chi square test, P = 0.001).

**Table 1. The relation between the type of the operation and the aspirated fluid in the first session.**

Amount/ cc	Type of operation		
	Modified radical mastectomy	Simple mastectomy	Breast conserving therapy
<100 (n=10)	6	2	2
100-150 (n=22)	13	6	3
>150 (n=17)	16	1	0
Total	35	9	5

(X<sup>2</sup> = 6.7 p-value = 0.03).

**Table 2. Correlation between amount of aspirated fluid in the first session and number of aspiration/injections.**

Amount/ cc	Number of instillations		
	One	Two	Three
<100 (n=10)	9	1	0
100-150 (n=22)	16	4	2
>150 (n=17)	11	4	2
Total	36	9	4

( $\chi^2 = 2.3$  p-value > 0.05).

**Table 3. Amount of aspirated fluid in different sessions of injections.**

Aspirate fluid	1st session of injection (n=49)	2nd session of injection (n=13)	3rd session of injection (n=4)
< 100 n (%)	10 (20.4%)	10 (76.9%)	3 (75%)
100 - 150 n (%)	22 (44.9%)	3 (23.1%)	1 (25%)
> 150 n (%)	17 (34.7%)	0 (0%)	0 (0%)
Mean $\pm$ SD	120.9 $\pm$ 3.6	100 $\pm$ 25.2 * (p-value = 0.006)	75 $\pm$ 35.4 * (p-value = 0.003)
Range	60 - 200	70 - 130	50 - 110

\* Statistically significant difference versus 1st session value (t-test, p-value < 0.05).

**Table 4. Severity of pain as measured by visual analogue scale (VAS) among the studied patients during and after instillation of TCN.**

Severity of pain	During instillation of TCN (n=49)	After instillation of TCN (n=49)	p-value
No (VAS = 0) n (%)	45 (91.8%)	44 (89.8%)	p-value > 0.05 (not statistically significant)
Mild (VAS = 1 - 4) n (%)	2 (4.1%)	4 (8.2%)	
Moderate (VAS = 5 - 6) n (%)	2 (4.1%)	1 (2%)	
Severe (VAS = 7 - 10) n (%)	0 (0%)	0 (0%)	

## DISCUSSION

Postmastectomy seroma can pose a significant and time-consuming problem to the surgeon and often resulting in repeated out-patient attendance and aspiration.<sup>(21)</sup> Treatment usually involves needle aspiration or drain replacement. The rare patient requires return to the operating room for excision of the seroma capsule, which is referred to as a capsulectomy.<sup>(22)</sup>

The use of sclerosant in the management of seroma is not new. Various agents have been investigated, including marine mussel proteins and the Gram-positive anaerobe *Corynebacterium parvum* in rat models.<sup>(23)</sup> In humans, seromadesis has been reported with erythromycin,<sup>(24)</sup> povidone iodine,<sup>(22)</sup> talc<sup>(25)</sup> and hypertonic saline.<sup>(26)</sup> The most commonly reported sclerosant in the literature is tetracycline, and there are reports that found it useful<sup>(13,14,27)</sup> and those that did not.<sup>(28,29)</sup>

Tetracycline sclerotherapy can be administered in two ways. The first is to administer it topically to the chest wall and skin flaps prior to skin closure.<sup>(28)</sup> while the second is to aspirate seroma postoperatively and instill tetracycline after its dilution in 0.9% NaCl.<sup>(13)</sup> The present study aimed to evaluate the efficacy of topical TCN sclerotherapy when used in the second way in treating post-mastectomy seroma.

The results of the current work revealed that the topical use of TCN is highly efficient in treating post-operative seroma as most of the patients (73.4%) responded well to this technique from the first session. This result agrees with that obtained by Sitzmann and his colleagues,<sup>(13)</sup> who treated five patients with seromas following mastectomy and axillary clearance by aspiration and instillation of a sclerosant solution containing tetracycline. He reported that all seromas had resolved promptly without infection, flap necrosis or recurrence. The same was also reported by Nichter and his team,<sup>(14)</sup> who used the previous technique on only 4 patients, he stated that tetracycline sclerotherapy provides a rational non-operative alternative treatment and a rapid resolution of persistent seromas as it is simple and without major complications. However, these two studies are carried on a small sample of patients.

Widgerow et al,<sup>(27)</sup> performed another study on a larger population (69 patients) and he demonstrated the efficacy of tetracycline in tissue adhesion. However, this study was carried in diverse clinical situations involving non-healing wounds and seroma-prone areas.

On the other hand, Rice and his associates,<sup>(28)</sup> performed a prospective, randomized, trial to examine the effect of intraoperatively administered topical TCN on the occurrence of postoperative mastectomy seromas. Thirty-two women were randomized to the control arm (normal saline) and 30 women to the TCN arm. In the treatment group, TCN solution (1g TCN in 100cc 0.9% NaCl) was

administered topically to the chest wall and skin flaps prior to skin closure. The control group received an equal volume of normal saline. Patients were monitored for the development of postoperative wound seroma every 2 weeks. There were no significant differences between groups regarding total volume of closed suction drainage. Seroma formation 2 weeks postoperatively was greater in the TCN group than the control group (53% vs. 22%,  $P = 0.01$ ). There were no differences between groups regarding the degree of postoperative pain, wound infection, or seroma formation 1 month postoperatively. They concluded that topical TCN is not effective at preventing post-mastectomy wound seromas.

The results of our study disagree with that of the previous study in which TCN was instilled intraoperatively and in a lower concentration (1g TCN in 100cc 0.9% NaCl) which may be low to produce proper reaction that enhance tissue adhesion. Also the researchers performed the technique once with no trials for further sessions.

McCarthy et al,<sup>(29)</sup> designed a randomized controlled trial to study the effect of topical tetracycline on patients with post-mastectomy seroma. The trial was aborted as he found that tetracycline was painful and not effective. In the present study, we avoid the development of severe pain by adding 10 cc Lidocaine to the used formula.

We suggest that post operative tetracycline sclerotherapy is a feasible treatment for refractory seroma after mastectomy. It is effective and without serious complications.

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