

## ROLE OF TETRACYCLINE IN PREVENTION OF POST-MODIFIED RADICAL MASTECTOMY SEROMA; RANDOMIZED CONTROL STUDY

Moamen Mahrous El-Hosseiny, Wesam Mohamed Amr, Hazem Nour Abdellatif, Mohamed Abdallah Zaitoun

1- General Surgery department, Al ahrar Teaching Hospital, Sharkia, Egypt.

2- General Surgery department, Faculty of medicine Zagazig University Hospitals, Sharkia, Egypt.

**Corresponding author:** Moamen Mahrous Mohammad El-Hosseiny

**E-mail** Moamen1189@gmail.com

**Telephone:** 01128790211

### INTRODUCTION:

Breast cancer is the most frequent female cancer with an estimated 2 million new cases were diagnosed worldwide [1].

Nowadays, modified radical mastectomy (MRM) is the principal treatment of breast cancer, provides sufficient tumor clearance, and decrease the local recurrence rate [2].

Seroma is the commonest post-Mastectomy complication. and known as a collection of serous fluid combined with blood, plasma, and lymph fluid under the skin flap. As early sequel after MRM [3-4].

In the current literature incidence of postmastectomy seroma formation ranged from 3% up to 90% [3].

Seroma is the noisiest event for the patient and the surgeon. Seroma formation can lead to patient discomfort, repeated seroma aspirations with the risk of infection, prolonged hospital stay, delayed wound healing, skin flap necrosis, delay in receiving adjuvant therapies and extended hospital stay may be required which increases costs for the patient and healthcare system and higher surgical expenditures [5].

Despite numerous trials of new techniques which have attempted to reduce the incidence of seroma formation, no single method appears to be uniformly effective.

Recently, many researchers developed variable techniques to prevent seroma formation. reduction of dead space was the main principle of these techniques [6]. Variable methods for reduction of dead space were reported; use of suction drain, antibiotics like Tetracycline, adhesive tissue glues as fibrin glue, natural coagulation factors, and Octreotide [7].

Topical sclerotherapy with Tetracycline has long been used successfully in the treatment of malignant pleural effusions to cause obliteration of the pleural space [8]. The first report of Tetracycline sclerotherapy for treating seromas after mastectomy was by Sitzmann et al. [9].

In the current study we evaluate the effectiveness of using Tetracycline and closure of the dead space in reducing seroma after Modified Radical Mastectomy.

### PATIENTS AND METHOD:

We conduct this randomized control study from October 2018 and April 2020 in the general surgery department of Zagazig University Hospitals and Al Ahrar teaching hospital, Zagazig, Egypt.

This study was approved by the Faculty of Medicine Zagazig University Institutional Review Board (IRB). Then we take an informed consent of our participant.

We enrolled and allocated 84 females with breast cancer in two groups; Group A: 42 cases with tetracycline, suction drain, and tight bandage. Group B: 42 cases with mechanical closure of dead space, suction drain, and tight bandage, "without tetracycline".

**Inclusion criteria:** All patients with breast cancer and undergoing modified radical mastectomy. **Exclusion criteria:** Any breast cancer surgery other than modified radical mastectomy and patients who refused the study.

All patients were subjected to Demographic data taking, complete clinical examination, routine preoperative Laboratory investigations, and stander Radiological investigations for breast cancer.

## **Technique:**

Patients in both groups subjected to stander modified radical mastectomy, with minimal use of electrocautery, Limit dissection below the level of the Axillary vein.

Patients in group (A); underwent irrigation of the wound with 2g of dissolved Tetracycline caps in 100 cm saline, Fig (1).

While in group (B); we use Vicryl 1 interrupted sutures (zero) to fix the anterior edge of the latissimus dorsi muscle to the chest wall, anterior to the long thoracic nerve; to close the dead space in the axilla.

Vicryl sutures (zero) at periodic intervals (3 cm apart) are placed from the skin flap to the underlying muscle. Multiple rows were done to close all the space under the skin flap Fig (2). Insertion of a suction drain lateral to axilla Fig (3). Applying tight bandage Fig (4).

## **Postoperative follow-up:**

We followed up all participants daily post-operative till they were discharged and weekly in outpatient clinic for two months after the operation. We used Visual Analog Scale (VAS) pain score to measure post-operative pain [10].

## **Statistical analysis:**

Data collected, coded, and entered using Microsoft Excel software. Data were analyzed by Statistical Package for the Social Sciences (SPSS version 23.0) software. Qualitative data were represented as number and percentage, quantitative continues group represented by mean  $\pm$  SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi-square test (X<sup>2</sup>). Differences between quantitative independent groups by t-test, P-value was set at <0.05 for significant results.

## **RESULTS:**

Table 1 represent study participants Demographic properties. Clinical data and cancer properties were illustrated in table 2 Most of both groups had right-sided breast cancer 25(59.5%) and 23(45.8%) respectively for group A and group B. Grade III represents about two-thirds of both groups 28(67.7%) and 26(61.9%) respectively. Both groups have positive LN affection.

Operative data and outcome were demonstrated in table 3 There was no significant difference between groups regard duration of drain or amount of seroma. The mean duration of drain was (5.96 $\pm$ 1.3) and (5.89 $\pm$ 1.06) days for group A and B respectively. The amount of seroma in group A was (1010.71 $\pm$ 330) ml and in group B was (973.21 $\pm$ 299.2) ml. without significant difference between both groups.

We found significant increase in operative time in group A than group B. Also, group A showed significant higher VAS score than group B.

## **DISCUSSION:**

In this study we evaluate topical administration of Tetracycline in prevention of postoperative seroma. We found No differences between both groups, and no evidence suggest that Tetracycline reduced seroma formation. There was significantly postoperative pain in group A compared to group B.

We found the operative time in tetracycline group significantly longer than group B; we believe that due to using tetracycline solution take extra time. Our results was in line with Khater et al, [11] they found operative time was longer in intervention group than stander group.

Post-operative pain was significantly higher at group A than group B. Topical Tetracycline may be interacted as a foreign body inside the wound and the sclerotic effect of Tetracycline to the tissue increase pain sensation post-operative. VAS was (5.39 $\pm$ 0.62) in group A and (2.39 $\pm$ 0.49) in group B. Study of McCarthy PM et al, [12] agreed with our results they found sclerotic effect of tetracycline caused severe postoperative pain and doesn't affect seroma formation. Rice et al, [13] doesn't agree with our finding they report in their study postoperative pain was almost the same in both groups. Also, no effect of sclerotic agent on seroma formation 1 month postoperatively.

In our study we did not noticed any significant different between both groups as regard to hospital stay.

We found in our study the mean time of drain removal was (5.96  $\pm$  1.31) days in group A and (5.89  $\pm$  1.06) days in group B. and the amount of fluid collected during this period was (1010.71  $\pm$  330.0) ml in group A and (973.21  $\pm$  299.22) ml in group B. without any statistically significant difference between study groups. Our finding supported by Kelley et al, [14] who found that there was no significant difference between groups regard duration of drain or amount of fluid. But Peeters et al,

[15] compared 5 versus 8 days axillary drainage and Gupta et al. [16] compared 3 versus long-term drainage. Both conclude that long-term drainage decreases seroma aspirations trials.

According to current literature incidence of seroma formation post breast surgery was ranged from 3% up to 90% [3].

In current study total cases presented by post MRM seroma in both groups was 15 cases (27.4%); 14 cases in group A (60.9%), and 9 cases in group B (39.1%). Which considered better outcome compared to Nadkarni et al, [17] who reported that the incidence of post-operative seroma (73%) and (35%) in study of Hashemi et al, [18].

The difference in seroma formation in our study groups was statistically insignificant.

Study of Nadkarni et al, [17] showed that suturing of flaps to muscle has obliterate dead space, but has bad cosmetic outcome.

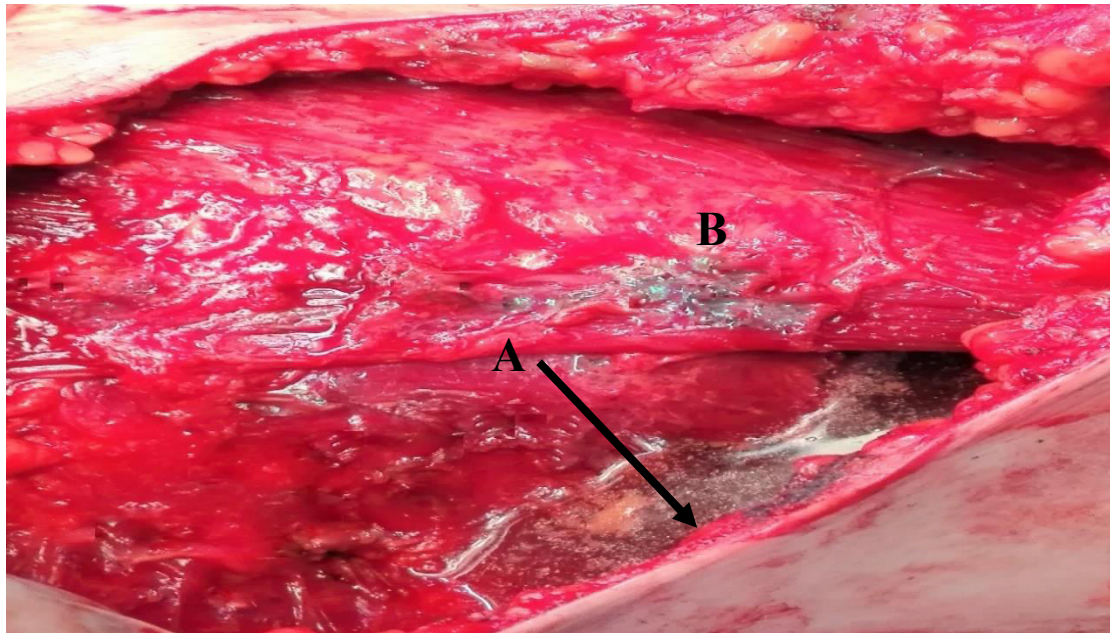
Therefore, we can limit the incidence of post-mastectomy seroma by using of closed-suction drains until their output is less than 30 to 50 ml for 2 consecutive days [19]. Suturing of skin flaps to the underlying muscle reduce "dead space" recent study suggests this technique to reduce the incidence of seroma formation [21]. These two methods, in combine with ligation of axillary lymphatics, are the most important factors in preventing post MRM seroma.

**DISCLOSURE:** no conflict of interest

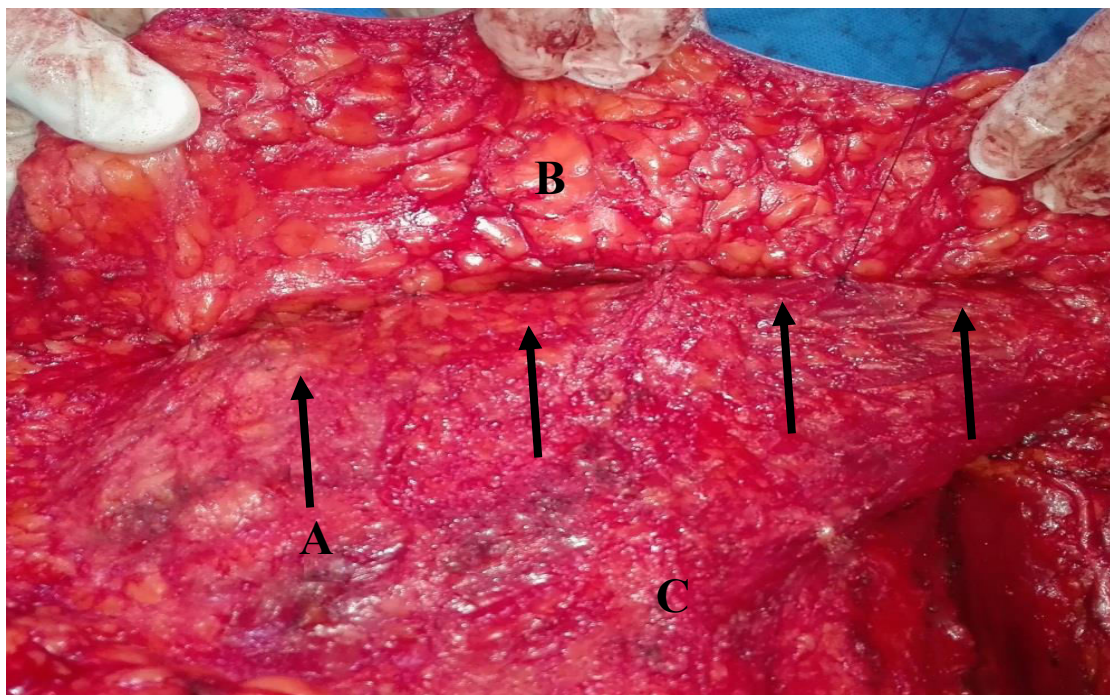
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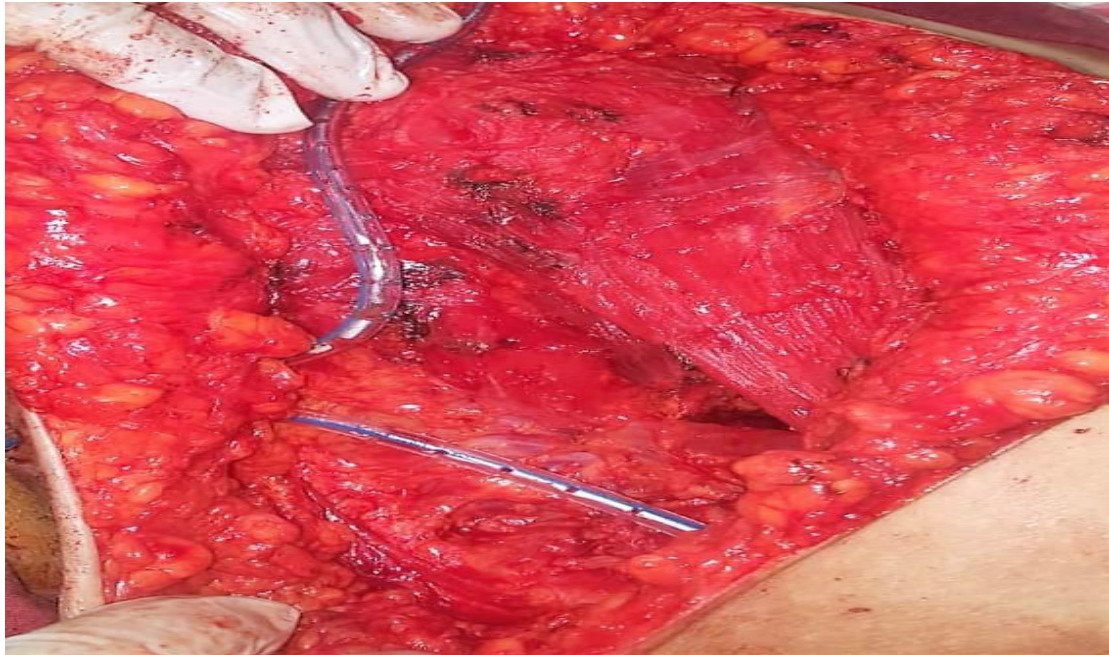
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**Figure (1):** Shows (a): Irrigation with Tetracycline (2gm+100cm saline) and (b): Pectoralis major muscle.



**Figure (2):** Showed (a): Suturing the skin flap to the underlying muscle to close the dead space, (b): Skin flap and (c): Pectoralis major muscle.



**Figure (3):** Shows suction drain in the axilla and under skin flap.



**Figure (4):** Shows tight bandage after operation.

**Table 1. Demographic characters:**

		Group A	Group B
		Mean± SD	Mean± SD
Age (Years)		56.32 ± 8.28	52.7 ± 10.34
BMI		28.5± 1.8	29.1± 1.5
Menopausal Status	Pre-Menopause	7(16.7)	11(26.2)
	Post-Menopause	35(83.3)	31(73.8)

**Table 2. Clinical and cancer data:**

		GROUP		X <sup>2</sup>	P
		Group A	Group B		
Side	Bilateral	3 (7.2%)	2(4.7%)	0.56	0.75
	Left	14 (33.3%)	17(40.5%)		
	Right	25(59.5%)	23(45.8%)		
BIRAD	IV	18(42.9%)	18(42.9%)	0	1
	V	24(57.1%)	24(57.1%)		
GRADE	II	14(33.3%)	16(38.1%)	0.31	0.57
	III	28(67.7%)	26(61.9%)		
LN	+VE	42(100%)	42(100%)	0	1

**Table 3. Operative and postoperative data:**

	Group A	Group B	P-Value	
	Mean± SD	Mean± SD		
Operative time (Min)	133± 11.7	115± 8.3	9**	<b>0.001</b>
VAS	5.39 ± 0.62	2.39 ± 0.49	19.7* *	<b>0.0</b>
Hospital stays (Days)	2.35 ± 0.71	2.01 ± 0.12	2.2**	0.3
Drain duration (Days)	5.96 ± 1.31	5.89 ± 1.06	0.2**	0.82
Drainage amount (ml)	1010.71 ± 330	973.21 ± 299.2	0.4*	0.68
Seroma	14(33.3%)	9(21.4%)	0.82	0.36

\*\* for t-test and \* for Chi-square test