

## Effect of Intraoperative Wound Irrigation with Topical Phenytoin on Postoperative Seroma Formation after Modified Radical Mastectomy

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### ABSTRACT

**Background:** Modified radical mastectomy (MRM), as a surgical treatment in breast cancer patients, may lead to important complications with significant morbidities including seroma formation. **Objective:** This study aimed to determine the effect of wound irrigation with topical phenytoin on postoperative seroma formation after modified radical mastectomy.

**Patients and methods:** This is a double-blinded randomized clinical trial study, which was carried out in Zagazig University Hospital during a period of 6 months. It included 60 patients who were candidates for modified radical mastectomy (MRM). All patients were subjected to demographic data taking, clinical and chemical examination, clinical evaluation, radiological evaluation, Lab. Investigations.

**Results:** Average daily breast drainage (in milliliters) of drains according to their location and day of evaluation: Group A (Phenytoin) in day 5 drained a mean of 24.62 with SD of 32.79, in day 7 mean of drainage was 28.89 and SD was 18.33, in days 8 to 10 mean of drainage was 32 and SD was 10.95, and in days 11 to 13 mean of drainage was 15 and SD was 7.07. Group B (Control): day 5 group drained a mean of 35.88 with SD of 12.93, in day 7 mean of drainage was 28.18 and SD was 12.68, in days 8 to 10 mean of drainage was 21.43 and SD was 11.07, in days 11 to 13 only one patient in control group had breast drain after 11<sup>th</sup> postoperative day drainage was 50 and in days 14 to 16 drainage was 20. **Conclusion:** Topical irrigation of the surgery site with phenytoin was effective in reducing axillary surgical wound drainage.

**Keywords:** Breast surgery, MRM, Seroma.

### INTRODUCTION

Modified radical mastectomy (MRM) is defined as complete removal of the breast and the underlying fascia along with the removal of level I and II axillary lymph nodes. Although this procedure has been replaced by conservative breast surgery in most patients with early stage breast cancer, it is still the treatment of choice in patients diagnosed with more advanced disease. In contrast to its therapeutic benefits, MRM may lead to important complications with significant morbidities. Lymphedema and compromised range of motion of the shoulder are known complications that can be quite troublesome<sup>(1,2)</sup>.

Seroma formation is the most common complication after breast cancer surgery. Seroma formation is a relatively common complication in MRM, which may occur on early postoperative days. It is probably secondary to the disruption of lymphatic vessels during surgery that leads to the accumulation of lymphatic fluid beneath the skin<sup>(3,4)</sup>.

It may cause patient discomfort, requires repeated aspirations, and is a potential source of wound infection, as well<sup>(5)</sup>.

The incidence of seroma has been reported to vary from 15 to 55 percent in different studies<sup>(6,7)</sup>.

Adopting measures to prevent seroma formation helps to reduce morbidity and improve postoperative wellbeing of the patients. Placing drains in the axilla is

widely used and has been shown to have considerable effects on reducing seroma formation<sup>(8,9)</sup>.

Other methods like using fibrin glue, topical phenytoin, and quilting sutures have been applied to reduce seroma formation, as well. The efficacy of these methods is controversial and yet must be determined<sup>(10,11)</sup>.

The effect of phenytoin on wound healing has been investigated in several studies and evidence suggests that phenytoin can accelerate the healing process<sup>(12,13)</sup>. In this study, we used topical phenytoin during the MRM procedure to evaluate its impact on breast and axillary wound drainage and seroma formation.

### PATIENTS AND METHODS

This study is a double-blinded randomized clinical trial carried out at the General Surgery outpatient clinic of Zagazig University Hospital during a period of 6 months.

#### Sample size:

Assuming the total number that met the inclusion and exclusion criteria would be included in the study. During the study period (6 months), 10 cases/ month, 60 cases (30 cases in each group) were included as a comprehensive sample.



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**Ethical considerations:**

An approval of the study was obtained from Zagazig University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Inclusion criteria:** The patients with pathologically confirmed breast cancer were enrolled in the study. The patients were candidates for MRM based on the disease stage.

**Exclusion criteria:** The patients with a previous diagnosis of epilepsy, history of convulsive attacks, history of head trauma and cardiac arrhythmia were not eligible for enrollment (To prevent of any possibility of interaction between phenytoin and the medications or the course of these cases).

All patients were subjected to demographic data taking, clinical and chemical examination, clinical evaluation, radiological evaluation, Lab. Investigations, follow up. In addition to demographic data, postoperative variables including daily drainage of breast and axillary drains, drain removal days, and possible complications including seroma formation and their management were recorded.

**The patients were randomly assigned to two groups:**

Group A: (30 cases) received topical phenytoin 1% solution (at a dose of 4 mg/kg for each patient) for irrigation of the wound at the end of the procedure while MRM. Group B: (30 cases) (control group) underwent irrigation of the wound with the normal saline solution.

**Outcome measurement:**

All pre- and postoperative data were collected using a form prepared by the researchers. Preoperative data including age, body mass index (BMI), histologic type of the breast cancer, history of previous breast and/or axillary surgery, and history of neoadjuvant therapy (and number of neoadjuvant sessions) were all recorded. Postoperative variables included daily drainage of the breast and axillary drains, drain removal days, and complications including seroma and their management.

**Statistical analysis:**

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ( $\chi^2$ ) was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean  $\pm$  SD (Standard deviation). Independent samples t-test

was used to compare between two independent groups of normally distributed variables (parametric data). P value  $<$  0.05 was considered significant.

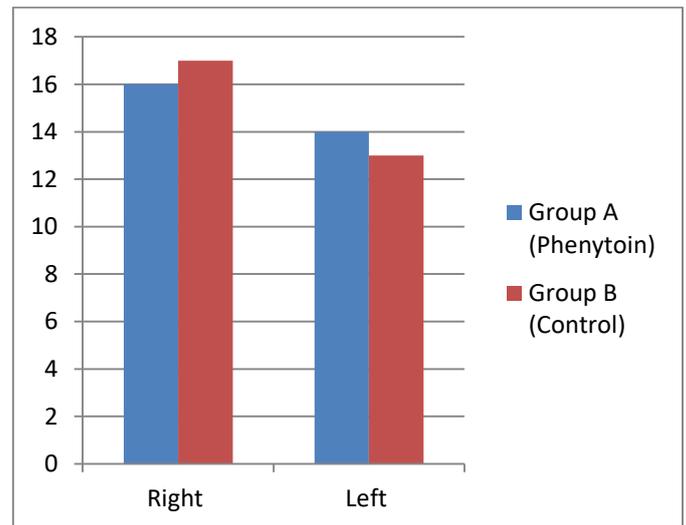
**RESULTS**

The demographic data of the studied group are shown in table 1.

**Table (1):** Demographic data of the studied patients

Characteristics	No. of patients (%)
Age: mean $\pm$ SD [range] (years)	53.30 $\pm$ 11.5
BMI	25.52 $\pm$ 4.87
Occupation	Housewives, workers, nursery, butchery and plowing fields
Address	Egypt, Sharqia

In Group A (Phenytoin) subjects having right side breast were little more than those having left side breast cancer. Group B (Control) showed the same pattern as regard laterality (Figure 1).



**Figure (1):** Shows side of breast cancer in both groups.

**Table 2; According to Days of Evaluation in Axillary Drain** Mean of drainage was higher in group B than group A in day 7, 8-10 and 11-13 (Table 2).

**Table (2):** Average daily Axillary drainage (in milliliters) of drains according to their location and day of evaluation

Day of Evaluation in Axillary Drain	Group A (Phenytoin)	Group B (Control)	P-value
5	65.92 $\pm$ 35.57	64.57 $\pm$ 19.75	0.234
7	43.24 $\pm$ 30.28	73.93 $\pm$ 25.80	$<$ 0.001
8-10	33.00 $\pm$ 15.76	65.76 $\pm$ 41.07	$<$ 0.001
11-13	21.67 $\pm$ 6.26	42.00 $\pm$ 23.22	$<$ 0.001
14-16		29.73 $\pm$ 13.00	

Group A (Phenytoin) day 5 group drained significantly less than group B (Table 3).

**Table (3):** Average daily breast drainage (in milliliters) of drains according to their location and day of evaluation

Day of Evaluation in Breast Drain	Group A (Phenytoin)	Group B (Control)	P-value
5	23.23±33.81	39.03±13.03	0.042
7	27.98±13.34	29.1±13.01	0.903
8-10	31.4±11.95	22.03±12.1	0.133
11-13	15.55±6.87	45.62 *	0.154
14-16		23*	

\* Only one patient in control group had breast drain after 11<sup>th</sup> postoperative day

The detected edema and congestion are shown in table 4. The difference was significant between both groups.

**Table (4):** Detected edema and congestion

	Group A (Phenytoin)	Group B (Control)	P-value
	Detected Cases		
Edema	3 (10%)	10 (33.33%)	0.05
Congestion	4 (13.33%)	13 (43.33%)	0.001

There was insignificant difference between both groups as regard seroma formation and number of seroma aspiration (Table 5)

**Table (5):** Postoperative seroma formation

	Group A (Phenytoin)	Group B (Control)	P-value
Seroma formation			
Yes	3 (10%)	5 (16.67%)	0.693
No	27 (90%)	25 (83.33%)	
Number of seroma aspirations			
0	27 (90%)	25 (83.33%)	0.226
1	2 (6.67%)	0	
2	1 (3.33%)	3 (10%)	
3	0	2 (6.67%)	

**DISCUSSION**

In this study participants' age ranged from 50-78 years with a mean value of 53.30±11.5 years. BMI mean was 26.52 and SD was 4.87.

As for side of breast cancer, in Group A (Phenytoin) 16 (53.33%) subjects showed right side breast cancer and 14 (46.67) subjects showed left side breast cancer. In Group B (Control) 17 (56.67%) subjects showed right side breast cancer and 13 (43.33%) subjects showed left side breast cancer. In

**Tang et al.** (14) Screening, location of the tumor was: Left (55.6%) right (36.2%) and bilateral (8.1%). In **Putt et al.** (15) screening, location of the tumor was left (49%) bilateral (8%).

According to days of evaluation in axillary drain in Group A (Phenytoin) in day 5 drained a mean of 65.92 with SD of 35.57, in day 7 mean of drainage was 43.24 and SD was 30.28, in days 8 to 10 mean of drainage was 33 and SD was 15.76, and in days 11 to 13 mean of drainage was 21.67 and SD was 6.26. Group B (Control) day 5 group drained a mean of 64.57 with SD of 19.75, in day 7 mean of drainage was 73.93 and SD was 25.80, in days 8 to 10 mean of drainage was 65.76 and SD was 41.07, in days 11 to 13 mean of drainage was 42 and SD was 23.22 and in days 14 to 16 mean of drainage was 29.73 and SD was 13.

In **Elyasinia et al.** (16) according to days of evaluation in axillary drain in Group A (Phenytoin) day 5 group drained a mean of 60.93 with SD of 30.57, in day 7 mean of drainage was 44.24 and SD was 33.29, in days 8 to 10 mean of drainage was 30 and SD was 13.76, and in days 11 to 13 mean of drainage was 22.67 and SD was 6.86. Group B (Control) in day 5 drained a mean of 67.57 with SD of 18.75, in day 7 mean of drainage was 75.83 and SD was 27.80, in days 8 to 10 mean of drainage was 62.76 and SD was 39.07, in days 11 to 13 mean of drainage was 45 and SD was 29.22, and in days 14 to 16 mean of drainage was 27.73 and SD was 13.48.

In an old study **Parikh et al.** (17) early drain removal following modified radical mastectomy was at mean of total 340.92 ml after 3 days and total of 589.49 ml after 6 days. In **Kabbash et al.** (18) early drain removal in ml was at mean of 6.56 with SD of 2.4, in last 3 days was 155.67 with SD of 90.8 and drained fluid last day was 35.22 with SD of 10.5.

Average daily breast drainage (in milliliters) of drains according to their location and day of evaluation. Group A (Phenytoin) in day 5 drained a mean of 23.23 with SD of 33.81, in day 7 mean of drainage was 27.89 and SD was 13.34, in days 8 to 10 mean of drainage was 31.4 and SD was 11.95, and in days 11 to 13 mean of drainage was 15.55 and SD was 6.87. Group B (Control) day 5 group drained a mean of 39.03 with SD of 13.03, in day 7 mean of drainage was 29.1 and SD was 13.01, in days 8 to 10 mean of drainage was 22.03 and SD was 12.01, and in days 11 to 13 only one patient in control group had breast drain after 11<sup>th</sup> postoperative day drainage was 45.62 and in days 14 to 16 drainage was 23.

In **Elyasinia et al.** (16) average daily breast drainage (in milliliters) of drains according to their location and day of evaluation: Group A (Phenytoin) in day 5 drained a mean of 24.62 with SD of 32.79, in day 7 mean of drainage was 28.89 and SD was 18.33, in days 8 to 10 mean of drainage was 32 and SD was 10.95, and in days 11 to 13 mean of drainage was 15 and SD was 7.07. Group B (Control) in day 5 drained a mean of 35.88 with SD of 12.93, in day 7 mean of drainage was 28.18

and SD was 12.68, in days 8 to 10 mean of drainage was 21.43 and SD was 11.07, and in days 11 to 13 only one patient in control group had breast drain after 11<sup>th</sup> postoperative day drainage was 50 and in days 14 to 16 drainage was 20.

According to edema and congestion. In Group A (Phenytoin) edema was detected in 3 (10%) cases and congestion in 4 (13.33%) cases. In Group B (Control) edema was detected in 10 (33.33%) cases and congestion in 13 (43.33%) cases. In Group A (Phenytoin) seroma was detected in 3 (10%) and in Group B (Control) seroma was detected in 5 (16.67%).

In **Elyasinia et al.**<sup>(16)</sup> in Group A (Phenytoin) seroma was detected in 7.1% and in Group B (Control) seroma was detected in 9.5%. **Rhodes et al.**<sup>(19)</sup> has reported that topical phenytoin increases granulation tissue formation and decreases wound discharge in trophic leprosy ulcers and improves the healing of decubitus ulcers. **El-Nahas et al.**<sup>(20)</sup> reported the positive impact of phenytoin in treating neuropathic diabetic ulcers. **Shaw et al.**<sup>(13)</sup> published a systematic review that summarized fourteen studies on the effect of phenytoin in healing of diabetic and chronic wounds. They suggested that phenytoin might have a positive effect on wound healing.

Studies evaluating the effect of topical phenytoin on the reduction of seroma formation after mastectomy or axillary dissection are scarce in the literature. **Eser et al.**<sup>(21)</sup> evaluated the effect of topical phenytoin on seroma formation after mastectomy and axillary dissection in mice. They found that topical phenytoin reduced the seroma volume after surgery. They also reported that fibrosis was significantly increased and angiogenesis was reduced following topical phenytoin application.

## CONCLUSION

Topical irrigation of the surgery site with phenytoin was effective in reducing axillary surgical wound drainage.

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**Conflict of interest:** Nil.

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