

## THE EFFECT OF INJECTION METHYLPREDNISOLONE IN REDUCING POST MASTECTOMY SEROMA: A RANDOMIZED CONTROLLED STUDY

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### Abstract

**Background:** Breast cancer accounts for 25% of all female cancers diagnosed globally. However, there is a significant global disparity in incidence and mortality across continents and countries. The objective is to study the efficacy of injection methylprednisolone in reducing seroma formation following modified radical mastectomy. **Materials and Methods:** 60 patients with a diagnosis of carcinoma breast undergoing modified radical mastectomy were distributed in test and control group. Patients were randomized alternately in both the groups. Patients in test group were administered injection methylprednisolone bolus intravenously 125mg before induction. Drain output was assessed at POD 1,2,3 in both the groups. In both groups the drain was removed if 24hour drain output was less than 30ml. Follow up seroma volume was assessed up to POD-10 and if present aspiration was done and aspirated seroma volume was assessed. **Result:** Seroma formation following the use of injection methylprednisolone in test group was less and subsequently the total drain output was also reduced in the test group when compared to control group owing to the fact that the drain was removed early in the test group. **Conclusion:** As seroma formation is the most common entity following MRM, use of injection methylprednisolone 125mg intravenously before induction can be used as adjunct to reduce seroma formation and shows promising results.

## INTRODUCTION

Breast cancer is the leading cause of cancer death in women around the world.<sup>[1]</sup> Despite the fact that more women are surviving breast cancer due to increased awareness, screening programmes, and better treatments, there are still significant differences in incidence and mortality both globally and within nations.<sup>[2]</sup> A small percentage of breast cancers are caused by known genetic mutations. The majority of breast cancers are classified as "sporadic," and they are linked to a variety of risk factors, some of which are potentially modifiable. Female breast cancer has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases. It is the fifth leading cause of cancer mortality worldwide, with 685,000 deaths. Among women, breast cancer accounts for 1 in 4 cancer cases and 1 in 6 cancer deaths, ranking first for incidence in the vast majority of countries.<sup>[3]</sup>

Globocan reports indicated an increase in breast cancer globally, and Globocan 2018 estimated that in 2018 a total of 2.1 million new breast cancer cases and 6,26,679 deaths due to breast cancer took place globally.<sup>[4]</sup> These were 11.6% of all cancer combined and 6.5% of all deaths.<sup>[3]</sup>

Several factors, including the patient's age, BMI, associated systemic diseases such as hypertension and diabetes, tumor stage, electrocautery use, the extent of axillary dissection, the weight of the specimen, closure techniques, time of starting shoulder exercise, duration, and suction drains, and drain output, have been implicated as predisposing factors for the formation. However, strong evidence for each of these factors is lacking, and thus our understanding of seroma formation is limited.

The inflammatory response caused by wound healing is most likely the cause of seroma formation. Several factors in the seroma fluid have been found to support the theory. These include high levels of IgG, leucocytes, granulocytes, proteinases, proteinase inhibitors, and various cytokines (tPA, uPA, uPAR, PAI-1, PAI-2, IL-6, or IL) Inhibiting

the inflammatory response may reduce seroma formation and possibly improve quality of life after mastectomy. Steroids, for example, inhibit the inflammatory response by inhibiting cytokine function.<sup>[5]</sup>

With this background, we conducted a randomized controlled study of the effect of injection methylprednisolone 125mg iv before induction in a patient undergoing modified radical mastectomy.

## MATERIALS AND METHODS

This randomized controlled study was conducted on patients admitted in the inpatient department of General Surgery in Karnataka Institute of Medical Sciences, Hubli with the diagnosis of carcinoma breast who underwent primary modified radical mastectomy and those who received neoadjuvant chemotherapy followed by modified radical mastectomy during the study period from December 2019 to January 2022. Institutional ethical committee clearance was obtained before the starting of present study

**Methods of collection of data:** All patients who were admitted under the Department of General Surgery in Karnataka Institute of Medical Sciences, Hubli with the diagnosis of carcinoma breast and underwent Modified Radical Mastectomy during the study period from December 2019 to January 2022 satisfying the inclusion criteria were enrolled for the study. Patient details were documented including history and clinical examination (Sex, Age, BP, BMI, Stage of the disease). Patients were randomized alternatively in both test and control groups. All the patients in the Test group undergoing modified radical mastectomy received injection methylprednisolone 125mg bolus intravenously before induction. Postoperatively total drain output is recorded and the drain removal day is noted. The patients are followed up till POD-10 and the seroma if present is aspirated and total seroma volume is recorded.

In our study seroma is defined as collection of serous fluid after mastectomy on POD-10 after the drain removal (<50 ml on POD-3) which requires aspiration.

### Sample Size Estimation

$$N = \left[ \frac{z\alpha + z\beta}{C} \right]^2 + 3$$

As various other studies have shown variable correlation value, therefore “r” value has been taken as means of all the variables.

Correlation coefficient “r”-0.4

Where Z $\alpha$ - 1.960 at 95% confidence interval

Z $\beta$ - 0.842 at 95% confidence interval

C- 0.5\*ln[(1+r)/(1-r)]

Z $\alpha$  is the standard deviation for  $\alpha$

Z $\beta$  is the standard deviation for  $\beta$

“r” is the expected correlation coefficient.

Therefore, the sample size corresponds to 57 rounded up to 60.

In our study, I have taken 62 cases.

### Inclusion Criteria

- All patients of Carcinoma Breast undergoing Modified Radical Mastectomy.
- Patients with carcinoma breast who received neoadjuvant chemotherapy followed by Modified Radical Mastectomy.

### Exclusion Criteria

- Patients with Diabetes mellitus
- Patients treated with glucocorticoids within 1 month before surgery
- Patients unwilling for study
- Carcinoma Breast Patients who didn't undergo surgery

**Statistical Analysis:** Data were entered into a Microsoft Excel datasheet and analyzed by using SPSS software version 22 (IBM SPSS Statistics, Somers NY, USA) Data was represented in the form of proportions and frequencies.

## RESULTS

The average age cases of carcinoma breast were >45 years. The mean age group in the test group was 48.1% and in the control group was 47.9%. The average BMI in the test group was 23.6 and in the control group was 24.1 in our study. In our study, the seroma was present in 18 patients with a mean BMI of 25 and the seroma was absent in 44 patients with a mean BMI of 23.4 which was statistically significant. In our study, the patients receiving neoadjuvant therapy were 17(54.8%) with 4 in the test group and 13 in the control group.

**Table 1: Comparison of neoadjuvant therapy and seroma in the study population**

| Neoadjuvant therapy | Seroma-Present |      | Seroma-Absent |      |
|---------------------|----------------|------|---------------|------|
|                     | N              | %    | N             | %    |
| No                  | 13             | 28.9 | 32            | 71.1 |
| Yes                 | 5              | 29.4 | 12            | 70.6 |
| Total               | 18             | 29.0 | 44            | 71.0 |

Chi square p value=0.96 (Not significant)

Out of 62 patients, a total of 18 patients developed seroma with maximum occurrence seen in Stage T3 with 29.6%.

**Table 2: Comparison of tumour stage and seroma**

| Tumour stage | Seroma-Present |      | Seroma-Absent |      |
|--------------|----------------|------|---------------|------|
|              | N              | %    | N             | %    |
| T2           | 6              | 26.1 | 17            | 73.9 |
| T3           | 8              | 29.6 | 19            | 70.4 |
| T4b          | 4              | 33.3 | 8             | 66.7 |
| Total        | 18             | 29.0 | 44            | 71.0 |

Chi square p value=0.9 (Not significant)

Lymph node ratio is a ratio between the number of positive lymph nodes divided by the total number of lymph nodes excised. In our study LN ratio of 0.22 was observed in the test group and 0.26 in the control group. In our study, of a total of 62 patients, 18 patients developed seroma including both the groups. A mean lymph node ratio of 0.21 was present in the seroma group and 0.25 in the non-seroma group which was statistically insignificant.

**Table 3: Comparison of LNR and seroma in the study population**

| Seroma  | Number | Mean | SD   | p-value |
|---------|--------|------|------|---------|
| Present | 18     | 0.21 | 0.32 | 0.6     |
| Absent  | 44     | 0.25 | 0.31 |         |

Independent t-test, p value-not significant

In our study, patients were classified from Stage IIA to Stage IIIB of TNM staging with maximum occurrence seen in Stage IIB at 35.5% in both groups.

**Table 4: Comparison of TNM staging across the study groups**

| TNM stage | Test |      | Control |      |
|-----------|------|------|---------|------|
|           | N    | %    | N       | %    |
| IIA       | 9    | 29   | 5       | 16.1 |
| IIB       | 11   | 35.5 | 11      | 35.5 |
| IIIA      | 4    | 12.9 | 10      | 32.3 |
| IIIB      | 7    | 22.6 | 5       | 16.1 |
| Total     | 31   | 100  | 31      | 100  |

Chi square p value=0.25 (Not significant)

Molecular subtypes of breast cancer patients are based on the hormonal receptor (ER, PR, HER2-Neu, Ki-67) and are classified as Luminal A, Luminal B, Her 2 Enriched, Basal Like. In our study, most of the patients belong to BASAL LIKE at 74.2%.

There is a significant difference in the drain removal days between the test and control groups. The post-operative drain removal within 5 days in the test group is 77.4% compared to the control group 16.1%.

Out of 31 patients in the test group 9 patients(29%) had seroma volume less than 50ml in 48 hrs compared to the control group 2 patients(6.5%) which was statistically significant.

The mean Total drain output in the test group is 386.1ml compared to the control group's 644.5ml which is statistically significant.

**Table 5: Comparison of total drain output between the study groups**

| Groups  | Number | Mean  | SD    | p-value |
|---------|--------|-------|-------|---------|
| Test    | 31     | 386.1 | 350.2 | 0.02    |
| Control | 31     | 644.5 | 467.0 |         |

Independent t-test, p-value- Significant

**Table 6: Comparison of aspirated seroma between the study groups**

| Groups  | Number | Mean | SD   | p-value |
|---------|--------|------|------|---------|
| Test    | 7      | 70   | 11.5 | 0.01    |
| Control | 11     | 88.2 | 15.4 |         |

Independent t-test, p value-Significant

Of the total 62 patients in the study, 31 patients in the test group only 7 patients(70%) required intervention in form of seroma aspiration when compared to the control group of 11 patients(88.2%).

**Table 7: Seroma aspiration among various studies**

| Studies         | p-value |
|-----------------|---------|
| G Qvamme et al  | 0.001   |
| S Vijayalakshmi | 0.007   |
| Shyamsundar     | 0.015   |
| Our study       | 0.01    |

The drain output at 48hr less than 50ml is seen with a mean lymph node ratio of 0.26 and drain output at 48hr more than 50ml is seen with a mean lymph node ratio of 0.24 which is statistically insignificant. Of the total 62 patients in the study, 31 patients in the test group only 7 patients(70%) required intervention in form of seroma aspiration when compared to the control group of 11 patients(88.2%).

## DISCUSSION

In our study, the mean age group of carcinoma breast patients in the test group was 48.1% and in the control group was 47.9% which was comparable with the other studies.<sup>[5-7]</sup>

In our study, there was an association of mean BMI with seroma formation with a high BMI value higher the incidence of seroma formation (p-value 0.02) which was comparable with other studies.<sup>[6]</sup>

In our study, the mean total drain output in the intervention group was 386.1ml when compared to the control group 644.5ml which was statistically significant and comparable with other studies.<sup>[7-9]</sup>

In our study, the drain output of <50 ml in 48hrs (POD-2) was 29% in the test group compared to 6.5% in control which was comparable with S Vijayalakshmi et al study 18% vs 6%.<sup>[5]</sup>

In our study, drain removal within 5 days was observed in 77.4% of patients in the test group when compared to the control group 16.1% which was comparable with other studies.<sup>[7,8]</sup>

In our study, out of 31 patients in the test group, 7 patients had seroma and requires aspiration with a mean of 70% compared to the control group where 11 patients had seroma which require aspiration with a mean of 88.2% which was comparable with other studies.<sup>[5,9,10]</sup>

## CONCLUSION

We conclude from our study that, among the techniques employed to lower seroma incidence, injecting methylprednisolone appears to be the most cost-effective and exhibits promising effects.

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