

ORIGINAL ARTICLE

EFFECT OF PREOPERATIVE INTRAVENOUS STEROIDS ON SEROMA FORMATION AFTER MODIFIED RADICAL MASTECTOMY

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Background: With the steep increase in breast cancer incidence globally and regionally, there has been a trend toward reducing patient morbidity by meticulous surgical techniques to obviate complications like seroma formation; use to pre-operative steroids seems to be convenient, cost effective and shows promising results in trials. **Methods:** This randomized clinical trial was conducted at Surgical Department of Khyber Teaching Hospital Peshawar, from January 2012 to April 2014 on 65 patients randomly allocated to Group A and Group B using lottery method. Group A underwent MRM+AD in the conventional manner while Group B received a 120 mg of injection Depomedrol intravenously 1 hour before the surgery. The two were compared in terms of total drainage, days of drainage, wound complications and incidence of seroma. Data was entered and analysed using statistical program SPSS-21. **Results:** The mean age in group A was 34.2 ± 10.1 years and B was 32.3 ± 9.1 years. The mean drainage in intervention group was significantly reduced as compared to control group ($755.4 \pm 65\text{ml}$ vs 928.3 ± 102.5). Total drainage days were reduced (6.5 ± 1.6 days vs 10.2 ± 2.2 days) and incidence of seroma was also reduced (A=18.75% vs B=6.06%). However, three patients in group B had wound infection. **Conclusions:** Seroma formation is the most common complication of Mastectomy and among the methods used to reduce its incidence, steroid administration seems to be the most cost effective and shows promising results.

Keywords: Mastectomy; Modified Radical Mastectomy; Methylprednisolone; Seroma Formation

J Ayub Med Coll Abbottabad 2017;29(2):207–10

INTRODUCTION

According to the current statistics shared by International Agency for Research on Cancer (IARC) 2012; the number of new breast cancer cases was 1.7 million and the number of women alive who had been diagnosed with breast cancer in the last five years was 6.3 million. Since 2008, the estimated incidence of breast cancer has increased by more than 20%, while mortality has escalated 14%. Breast cancer is also the most common cause of cancer death among women (522,000 deaths in 2012) and the most frequently diagnosed cancer among women in 140 of 184 countries worldwide. It is the cause of death in every fourth woman.^{1,2}

Moreover, the incidence of breast cancer is on the rise across the globe including Asian countries like Pakistan. Regarding the disease burden of breast cancer in Pakistan, it has been reported as the most common cancer and is claimed to account for 34.6% of total cancer cases in women. Moreover, the incidence of breast cancer in Pakistan is about 2.5 times higher than its neighbouring countries; Iran and India, being the highest incidence of breast cancer for any Asian population, after Jews in Israel.³ Another alarming fact is that in Pakistan, this malignancy is more frequently seen in quite younger age group contrary to the West where it is more common in older women.⁴

Breast cancer management is multi-disciplinary which includes surgical resection, radiotherapy, hormones and chemotherapy where surgery plays the pivotal role. Among the surgical procedures, modified radical mastectomy (MRM) with axillary clearance is the most widely used.⁵ MRM with axillary clearance is performed with curative intent and is associated with very low incidence of long term morbidity and mortality which is usually about 1%. However, seroma formation is the most common peri-operative complication of this surgical procedure which affects almost 35–80% of the patients.⁶

Seroma is defined as a serous fluid collection that develops under the skin flaps during mastectomy or in the axillary dead space after axillary dissection which usually begins to develop on the seventh post op day, reaches a peak on the eighth day and slows continuously until the sixteenth day when it generally resolves. It ends up in prolonged hospitalization and outpatient follow-up, further adding to the miseries of the breast cancer patients and may also delay subsequent adjuvant therapies.⁷

There are various techniques in research and practice reported to prevent or diminish seroma formation, but no single method has been shown to be constantly and reliably effective. These methods include external compression dressing,

immobilization of the arm, excessive use of the electric scalpel compared to ligature of the lymphatic branches, fibrin glue application, number of drains and the type of suction (high or low pressure) applied. It is proposed that thorough attention applied to techniques of the surgery itself; to reduce the leakage from dissected vessels and lymphatics and to obliterate the dead space may reduce the incidence of seroma formation.⁸ Use of electro cautery, ultrasonic dissection, harmonic or laser scalpel and other techniques like drains, sealants and sclerotherapy may also be used but their usefulness and cost-effectiveness are debatable.⁹ Surgical technique of obliterating dead space using flap fixation or quilting has been introduced with promising results.¹⁰⁻¹² Some drugs have also been used which have shown efficacy in reducing seroma fluid for example beta-glucan.¹³

In a controlled pilot study by Okholm, it was tested whether a single dose of glucocorticoid (methyl prednisolonsuccinate) given intravenously 1.5 hours preoperatively was effective against seroma formation after mastectomy and axillary dissection. The drainage volume during the first two postoperative days, total seroma volume during days 1-5 and the number of seroma punctures were reduced, but not significantly. The number of seroma punctures and the seroma volume was half that of the control group during the first 69 days postoperatively. There were no differences in wound healing time or rate of infectious complications between the group.¹²

As it is proven by literature that seroma formation is by far the most common complication after mastectomy leading to increased morbidity, psychological trauma, increased length and cost of treatment and flap fixation is a promising method for preventing seroma formation. The aim of the study is to ascertain the benefits of flap fixation in reducing the incidence of post mastectomy seroma and associated complications. This will not only provide enhanced recovery and satisfaction to patients undergoing mastectomy but also reduce hospital stay, cost of treatment and use of antibiotics.

MATERIAL AND METHODS

This randomized clinical trial was conducted at Surgical Department of Khyber Teaching Hospital Peshawar, Pakistan from January 2012 to April 2014 on 65 patients. Patients who presented with symptoms of Breast Cancer were evaluated by taking history, examination; radiological workup and biopsy to confirm the diagnosis. Those patients who presented with 1st, 2nd and 3rd stage of breast cancer was included in the study. Those with stage 4,

recurrent disease, bleeding disorders or hypertensive were excluded from the study.

The patients were randomly allocated into Group A and Group B. Randomization was performed using lottery method. The patients in Group A underwent MRM+AD in the conventional manner while those in Group B received a 120 mg of injection Depomedrol intravenously 1 hour before the surgery. A closed suction drain was placed in both groups and was removed when it drained <30 ml/24 hours.

The total drainage was recorded in millilitres; the number of days of drainage was also recorded. Some patients were discharged once drain was nil while others were sent home with drain and they were followed up on 10th post-operative day at the time of stitches removal and any wound complication (infection, necrosis, dehiscence etc.) as well as to exclude Seroma formation.

Seroma was defined as clinically palpable collection of serous fluid, documented by needle aspiration and confirmed by ultrasound as an anechoic collection on the seventh post op day, it was graded according to the Common Terminology Criteria for Adverse Events v3.0 as; Grade 1: Asymptomatic; Grade 2: Symptomatic (medical intervention or simple aspiration indicated); Grade 3: Symptomatic (interventional radiology or operative intervention indicated).¹²

All information was recorded on pre-designed *pro forma*. Patients were explained about the two procedures and then informed consent was taken about inclusion in the trial. The protocol was approved by the hospital ethics committee

Data was entered and analysed using statistical program SPSS-21. Qualitative data (frequencies and percentages) such as Seroma formation, grade of seroma, wound complications were presented as n (%) and chi square test was applied to compare the proportion between groups A and B. Numerical variables like age, total drainage and duration of drainage were presented as Mean±SD. All the data was calculated on 95% confidence interval. Independent *t*-test was applied to calculate difference between means and a *p*-value <0.05 was considered as statistically significant level for all comparisons.

RESULTS

In the study period 80 patients fulfilled the inclusion criteria; 10 patients were not included because they refused to give consent while another 15 patients were lost during follow up thus a total of 65 patients were included in the study and randomized such that 32 patients were in Group A and 33 patients in Group B.

Table-1: Categorization of patients

	Group A n=32	Group B n=33
AGE (years)	34.2±10.1	32.3±9.1
Tumour stage I	15 (46.9%)	16 (48.5%)
II	13 (40.62%)	12 (36.4%)
III	4 (12.5%)	5 (15.2%)
Simple mastectomy	10 (31.25%)	12 (36.4%)
MRM	04 (12.5%)	05 (15.2%)
MRM+AD	18 (56.25%)	16 (48.5%)

Table-2: Outcome of steroid use in group B vs no steroid use in group A

	Group A	Group B	p-value
Total drainage (ml)	928.3±102.5	755.4±65	<0.005*
Duration of drainage (days)	10.2±2.2	6.5±1.6	<0.005*
Seroma formation	6 (18.75%)	2 (6.06%)	
Grade 1	3 (9.37%)	1 (3.03%)	
Grade 2	2 (6.25%)	1 (3.03%)	
Grade 3	1 (3.12%)	Zero	
Wound status			
Healed	30 (93.75%)	30 (90.9%)	
Necrosis	1 (3.12%)	Zero	
Dehiscence	Zero	Zero	
Infection	1 (3.12%)	3 (9.09%)	

*Significant.

DISCUSSION

Seroma formation is by far the most common complication following breast surgery and the abundance of literature regarding various methods of its prevention is evidence enough that no single method/drug or protocol is fully effective in its prevention.

Although still under research the pathogenesis of seroma formation has been associated with several precipitating factors. Once dissection occurs, a dead space is created which is filled with serous fluid. This fluid then alters composition in the days following surgery. At first it resembles lymph with blood clots, indicating broken lymph and blood vessels due to the dissection. A few days later it transforms into an exudate, as the body reacts to the acute inflammatory condition following surgery. As the patient resumes moving her arm, lymphatic and blood vessels which are damaged by the dissection start oozing blood and lymph, which adds to the seroma. Therefore, the pathophysiology for seroma formation seems to be multifactorial with surgery as its trigger.¹⁴⁻¹⁷

Steroids being anti-inflammatory drugs are thus an ideal candidate to be studied in preventing seroma formation which is patho-physiologically speaking; an inflammatory process.

Axelsson studied local injection of methylprednisolonacetate versus saline in the mastectomy cavity at the time of drain removal¹⁸ while Taghizadeh *et al* studied patients who underwent latissimus dorsi reconstruction after mastectomy by randomizing them to either

triamcinolone or saline in the cavity at the initial seroma puncture. Qvamme G carried out a double-blind randomized controlled intervention study of a single dose of 80 mg methylprednisolone versus saline on seroma formation after mastectomy.¹⁹ The authors observed a statistically significant reduction in the number of punctures, total seroma volume and the duration of seroma production.²⁰

Turel *et al* applied the same technique on a rat model by injecting 30 mg/kg methylprednisolone sodium succinate into the potential space beneath the skin flaps following Mastectomy and axillary lymph node dissection after 7th day of mastectomy, the seroma volumes were noted. He concluded that although methylprednisolone was effective in preventing the seroma but due to the high risk of wound infection it should not be generally applied.²¹

In our study, we found that injecting 120 mg of Depomedrol i/v one hour before surgery was a convenient mode of application, which helped decrease the average drain output and also decreased the days for which drainage was needed. This intervention also reduced the total incidence of seromas on 7th post op day as compared to the non-intervention group (i.e., 18% vs 6%). The only fact that needs consideration is the slightly higher incidence of wound infection (3% vs 9%) with steroid administration; this can be overcome with appropriate pre-operative antibiotics at intervention and post operatively. Reduction in total drainage days adds to patient comfort as well as reduces the demand for analgesia moreover the drain itself is also a source of infection.

CONCLUSION

Since Seroma formation is the most common complication of Mastectomy and among the methods used to reduce its incidence, steroid administration seems to be the most cost effective and shows promising results. Its routine use in every case is recommended under good antibiotic cover and wound care.

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Received: 11 December, 2015

Revised: 19 December, 2016

Accepted: 28 February, 2017

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