Original Article

Outcome of Per-operative Use of Topical Tranexamic Acid for Reduction of Seroma following Mastectomy in BIRDEM General Hospital, Dhaka, Bangladesh

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Abstract

Background: *Formation of a seroma most frequently occurs after mastectomy and axillary surgery. Tranexamic acid is a synthetic antifibrinolytic agent. The role of topical administration of tranexamic acid for reduction of fluid collection in dead space following mastectomy is needed to be evaluated.* ***Objectives:*** *The present study was planned to evaluate the outcome of topical use of tranexamic acid per operatively for reduction of seroma following mastectomy.* ***Materials and method:*** *This prospective observational study was done in BIRDEM General Hospital, Shahbag, Dhaka, Bangladesh, from February 2019 to July 2019. A total of 40 patients of mastectomy were included in the study. Following mastectomy after hemostasis and before wound closure, 1000mg of injection tranexamic acid was sprayed uniformly in the wound (in axilla and under the flaps). Patients were evaluated with complete history, thorough clinical examination and relevant investigations. Collected data were analysed by using SPSS version 23.* ***Results:*** *Out of 40 patients, 9 patients (22.5%) developed seroma and more than two third (66.7%) of which belonged to age group >60 years. Out of which all 9 patients (100%) who were categorized as ASA grade III developed Seroma. Among them, 6 cases developed only seroma and 3 cases had seroma with partial flap necrosis. On 3rd post operative day, all (100%) of the patients in seroma "developed group" had severe pain, whereas only 15(48.4%) in seroma "not developed group" had severe pain. On 5th post operative day, 3(33.0%) patients in seroma "developed group" had severe pain and none in seroma "not developed group". On 14th post operative day, 6(66.7%) patients were found in mild pain in seroma "developed group" and 3(9.7%) in seroma "not developed group", that was statistically significant ($p<0.05$) between two groups. Majority (92.5%) of patients had hospital stay of ≤10 days. The mean hospital stay was found 9.2±1.2 days with range from 8 to 12 days.* ***Conclusion:*** *In conclusion, tranexamic acid is inexpensive. Its cost-effectiveness has been thoroughly documented. Even after operations where bleeding is less common topical application of tranexamic acid may*

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reduce the need for drains and outpatient visits. This simple method has potential for widespread application after surgery.

Keywords: *Mastectomy; Seroma; Tranexamic Acid.*

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Introduction

Ever since mastectomy was first carried out by Halsted in 1882, surgeons have faced several problems such as necrosis of the skin flaps, breakdown of the wound, hematoma, seroma, and infection. Among them, seroma is a common problem in breast surgery.[1] Seroma is defined as collection of serous fluid under the skin flaps or in the axillary dead space following mastectomy and/or axillary dissection and when it is symptomatic, bothersome to the patient, palpable, fluctuant or ballotable, or tense, and requires at least one needle aspiration.[2] Ultrasonography has been used to verify seroma and it is interesting to note that in a study by Jeffrey et al. 92% of patients developed seroma that was detectable by axillary sonography, and 42% required at least one aspiration.[3] Current literatures suggest that the incidence of seroma formation following mastectomy is between 15-81 percent.[4]

The incidence of seroma has been shown to correlate with patient's age, breast size, hypertension, stage of the disease, presence of malignant nodes in the axilla, number of malignant nodes, previous surgical biopsy.[5,6] Early movement of the shoulder during the postoperative period may increase the formation of seroma, although delayed physiotherapy decreases the formation of seroma.[2]

Numerous methods to reduce post-mastectomy seroma formation have been tried with no consistent success.[7,8] Tranexamic acid is the most commonly used medication to prevent fibrinolysis. Tranexamic acid (transaminomethyl cyclohexane carboxylic acid) is a synthetic antifibrinolytic agent. Structurally it resembles aminocaproic acid but is ten times more portent. It acts by blocking the lysine-binding sites on plasminogen, thereby preventing the activation of plasminogen to plasmin. Tranexamic acid also has a direct antiplasmin action, inhibiting fibrin degradation.[9]

In this research, effect of topical Tranexamic acid to reduce seroma formation following mastectomy was evaluated and the immediate post-surgical outcome was assessed. The clinical implementation of the results of this study was to reduce the patient's morbidity by simply ensuring a more resilient way of prevention of seroma in our surgical practice.

Materials and method

This prospective observational study was conducted in the Department of Surgery, BIRDEM General Hospital, Shahbag, Dhaka, Bangladesh, during the period of February 2019 to July 2019. A total of 40 patients suffering from carcinoma of breast undergoing mastectomy were included in the study. Critically ill patients, patients who received neoadjuvant therapy or who were not available to communicate for follow up after 14 days were excluded from the study. In this study, following mastectomy after hemostasis and before wound closure, 10ml (1000mg) of injection Tranexamic acid were loaded in a sterile 10ml syringe and sprayed uniformly in the wound (in axilla and under the flaps). Two negative pressured drains were placed under the flaps (one in axilla and one in chest wall) to remove this fluid postoperatively and the negative pressures in both drains were reduced gradually. Amount of fluids in both drains were measured in 1st, 3rd, 5th and 7th

post-operative day and drains were removed on 7th post-operative day. Patients were discharged accordingly and called for follow up on 14th post-operative day in Surgical Out Patient Department (OPD). Pain score was measured by VAS score in different follow up visits. VAS 0 score detect as no pain, 1-3 score as mild pain, 4-6 score as moderate pain and ≥7 score as severe pain. A data collection sheet was filled with relevant information and investigation and a written informed consent form was added.

Statistical analysis was carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated by frequencies and percentages. Chi square test was done for categorical variables. A probability (p) value of <0.05 ($p<0.05$) was considered statistically significant and $p<0.001$ was considered highly significant.

Results

Out of 40 patients, majority (37.5%) patients belonged to age group of ≤50 years. The mean age was 54.9±9.4 years with range from 40 to 70 years. Seroma developed in 9 patients, among them more than two third (66.7%) patients belonged to age group >60 years. All (100.0%) patients had ASA grade III, which was statistically significant ($p<0.05$) when compared seroma developed and not developed group (Table I). Volume of axillary drain and chest wall drain from 1st to 7th post operative day are presented in Table II. A total of 37 patients were in severe pain whereas 3 patients were in moderate pain. At 3rd post-operative day: mean VAS score was found 6.9±1.5 with range from 4 to 9. A total of 24 patients were in severe pain whereas 16 patients were in moderate pain. At 5th post-operative day: mean VAS score was found 4.4±1.3 with range from 3 to 7. A total of 3 patients were in severe pain whereas 27 patients were in moderate pain and 10 patients were in mild pain. At 7th post-operative day: mean VAS score was found 2.4±1.2 with range from 1 to 5. A total of 6 patients were in moderate pain whereas 34 patients were in mild pain. At discharge, mean VAS score was found 1.2±0.9 with range from 0 to 3. A total of 30 patients were in mild pain whereas 10 patients were in no pain. At 14th post-operative day, mean VAS score was found 0.5±0.9 with range from 0 to 3. A total of 9 patients were in mild pain whereas 31 patients were in no pain (Table III). At 3rd post operative day, 9(100.0%) patients were found to be in severe pain in seroma developed group and 15(48.4%) in seroma not developed group. At 5th post operative day, 3(33.0%) patients were found to be in severe pain in seroma developed group and 0 in seroma not developed group. At 14th post operative day, 6(66.7%) patients were found to be in mild pain in seroma developed group and 3(9.7%) in seroma not developed group, which were statistically significant ($p<0.05$) between two groups (Table IV). Nine (22.5%) patients developed seroma and 31(77.5%) did not develop seroma. Among the seroma developed patients, 6 cases developed seroma only and 3 cases were seroma with partial flap necrosis. In this study majority (92.5%) of patients had hospital stay of ≤10 days. The mean hospital stay was found 9.2±1.2 days with a range from 8 to 12 days.

Table I: Association between seroma with age and ASA grading (N=40)

	Seroma				p value
	Developed (n=9)		Not developed (n=31)		
	n	%	n	%	
Age group (years)					
<50	0	0.0	15	48.4	
51-60	3	33.3	9	29.0	0.001
>60	6	66.7	7	22.6	
ASA grading					
Grade I	0	0.0	9	29.0	
Grade II	0	0.0	22	71.0	0.001
Grade III	9	100.0	0	0.0	

p value reached from Chi square test

Table II: Axillary drain and chest wall drain in different follow up (N=40)

	Axillary drain (CC)		Chest wall drain (CC)	
	Mean±SD	Range (min-max)	Mean±SD	Range (min-max)
At 1st post operative day	30.7±5.4	20.0-40.0	26.0±5.9	15.0-35.0
At 3rd post operative day	21.0±6.2	10.0-35.0	14.4±4.3	5.0-20.0
At 5th post operative day	12.0±6.3	5.0-30.0	6.6±5.7	0.0-20.0
At 7th post operative day	5.2±8.2	0.0-30.0	2.5±5.7	0.0-20.0

Table III: VAS score in different follow up (N=40)

VAS score	Severe pain (score e 7) (No. of pt.)	Moderate pain (score 4-6) (No. of pt.)	Mild Pain (score 1-3) (No. of pt)	No pain (score 0) (No. of pt.)	Mean ±SD	Range (min-max)
At 1st post-operative day	37	3	0	0	8.9±1.1	6-10
At 3rd post-operative day	24	16	0	0	6.9±1.5	4-9
At 5th post-operative day	3	27	10	0	4.4±1.3	3-7
At 7th post-operative day	0	6	34	0	2.4±1.2	1-5
At discharge	0	0	30	10	1.2±0.9	0-3
At 14th post-operative day	0	0	9	31	0.5±0.9	0-3

Table IV: Association between seroma with VAS score (N=40)

VAS score	Seroma				p value
	Developed (n=9)		Not developed (n=31)		
	n	%	n	%	
At 1st post operative day					
Moderate (4-6 score)	0	0.0	3	9.7	0.331
Severe (e 7 score)	9	100.0	28	90.3	
At 3rd post operative day					
Moderate (4-6 score)	0	0.0	16	51.6	0.005
Severe (e 7 score)	9	100.0	15	48.4	
At 5th post operative day					
Mild (1-3 score)	0	0.0	10	32.3	
Moderate (4-6 score)	6	66.7	21	67.7	0.001
Severe (e 7 score)	3	33.3	0	0.0	
At 7th post operative day					
Mild (1-3 score)	6	66.7	28	90.3	0.080
Moderate (4-6 score)	3	33.3	3	9.7	
At discharge					
None (0 score)	0	0.0	10	32.3	0.052
Mild (1-3 score)	9	100.0	21	67.7	
At 14th post operative day					
None (0 score)	3	33.3	28	90.3	0.001
Mild (1-3 score)	6	66.7	3	9.7	

p value reached from chi square test

Discussion

Seroma formation is the most frequent complication of modified radical mastectomy (MRM). The exact etiology of seroma formation remains controversial but certain factors like extent of mastectomy, extent of lymph node dissection and methods of surgical dissection influence the amount and duration of seroma formation. Several interventions have been reported with the aim to reduce seroma formation. Controlling seroma formation by inhibiting the fibrinolytic action of plasmin system in serum and lymph has shown promising results.[9] This study was carried out with an aim evaluate the outcome of topical use of tranexamic acid per operatively for reduction of seroma following mastectomy.

Present study observed that more than two third (66.7%) patients who developed seroma belonged to age group >60 years, which was statistically significant ($p<0.05$) when compared to not developed group. Loo and Chow[10] reported that patients older than 45 years old had a statistically significant higher chance of developing seroma than younger patients.

All (100.0%) patients developing seroma were of ASA grade III, which was statistically significant ($p<0.05$). Some studies have demonstrated ASA classification as a predictor for perioperative complications.[11,12] In the series, patients classified as ASA 2 or 3 accounted for almost 70% of the entire sample. In contrast to observations from other studies[11,12], the ASA classification did not demonstrate a significant correlation with the incidence of complications. At this point, we believe that this aspect should not contraindicate reconstruction, although one should take additional care in patients with a higher surgical risk.

In our study, the overall reduction in drain fluid production was about 40 per cent after topical administration of tranexamic acid which accords with previously published studies, which

consistently reported a reduction in transfusion need and measurable bleeding of between 30 and 40 per cent after both intravenous and topical tranexamic acid administration.[13-15] There is little information on the concentration of tranexamic acid needed for topical effect. Instillation of a bolus of 1-3 g tranexamic acid diluted in 100 ml saline (concentration 10-30 mg/ml) has been studied in patients undergoing cardiac and orthopaedic surgery, whereas epistaxis has been treated with sponges moistened with undiluted tranexamic acid for intravenous use (100 mg/ml).[13-17] Elbalshy et al.[7] reported that if it is believed that the largest potential dead space is the empty axillary apex after axillary dissection or indeed that seroma formation is contributed significantly to by disruption of axillary lymphatics, it means that closure of this space may prove useful. A few studies introduced the concept of axillary padding to reduce drainage volumes after axillary surgery. The axillae were padded with nearby tissue, and outcomes in terms of seroma formation were excellent. However, a study carried out a limited axillary dissection, and were carried out on patients undergoing breast conservation.[18]

In this study, mean VAS score was 8.9±1.1 at 1st, 6.9±1.5 at 3rd, 4.4±1.3 at 5th, 2.4±1.2 at 7th, 1.2±0.9 at discharge and 0.5±0.9 at 14th post operative day. A study conducted by Ausen et al.[19] found pain scores were similar in breasts treated with tranexamic acid on the day of surgery.

In present study 9(22.5%) patients developed seroma Out of 9 seroma developed patients, 6 patients had developed only seroma and 3 patients had developed seroma with partial flap necrosis. Eldesouky et al.[20] reported that 12.3% patients in their study had seroma formation after removal of drains. Several other studies reported similar findings.[4,8-10] Many previous studies have demonstrated that postoperative drainage fails to prevent seroma formation; the incidence of seroma requiring aspiration ranges from 15 to 83 per cent following drain removal.[21,22]

Ausen et al.[19] reported that there were no significant differences in postoperative pain scores or complications. The study done by Oertli et al.[23] showed that perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer had no significant effect on seroma but decreased it.

In this study, majority (92.5%) of patients had hospital stay of ≤10 days. The mean hospital stay was found 9.2±1.2 days with range from 8 to 12 days. Gumuş et al.[24] observed the mean length of hospital stay for breast cancer surgery was 6.18±3.08. The average hospital stay in the United Kingdom is 7 days for breast surgery.[25] Holcombe et al.[26] reported in a series of patients undergoing axillary dissection, a lower seroma rate in the early discharge with drain in situ group (18%), compared to a standard treatment group (34%) and a reduction in median hospital stay of 5 days.

Several limitations exist to the present study, short period of time, small sample size, randomization was not done. Therefore, selection bias in this study can't be fully eliminated.

Conclusion

Tranexamic acid is inexpensive. Its cost-effectiveness has been thoroughly documented. Even after operations where bleeding is less common topical application of tranexamic acid may reduce the need for drains and outpatient visits. This simple method has potential for widespread application after surgery. Further studies can be undertaken by including large number of patients.

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