Original Article

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Effect of Topical Application of Tranexamic Acid on Wound Drainage and Seroma Formation after Modified Radical Mastectomy: An Observational Study

Surgery Section

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ABSTRACT

Introduction: Breast cancer is the most common malignancy detected in the female population in Kerala, India. Seroma formation after Modified Radical Mastectomy (MRM) may lead to a delay in recovery, a prolongation of hospital stay, and can also affect treatment by delaying adjuvant therapy and increasing the risk of infection. Topical Tranexamic Acid (TXA) reduces bleeding, wound drainage duration and seroma formation.

Aim: To find the effect of topical application of TXA on wound drainage and seroma formation after MRM.

Materials and Methods: The present prospective observational study was conducted in the Department of General Surgery, Government Medical College, Kottayam, Kerala, India, from February 2022 to January 2023. A total of 150 patients who underwent MRM were randomly selected to receive either TXA or a placebo before wound closure. Two groups were formed: Group-1 (interventional group) received 20 mL of diluted TXA (25 mg/mL), while Group-2 (placebo group) received normal saline. Each group consisted of 75 female patients. They were compared based on drain amount, number of days the drain was in place and seroma formation. Categorical parameters like the number of days the drain was kept, cumulative drain amount, and seroma occurrence were expressed as percentages. Statistical analysis was done with Chi-square test with a p-value <0.05.

Results: The median age of the patients was 50-60 years. On postoperative day 1, the drain amount in Group-1 was 37.3%, while in Group-2, it was 54.7%, with 1.3% of patients in Group-1 and 6.7% in Group-2 having more than 300 mL drained (p-value=0.001). By postoperative day 7, 21.3% of patients in Group-1 had drained less than 50 mL, compared to only 4% in Group-2 (p-value=0.02). The majority of patients in Group-1 had their drains removed in 5-10 days (97.3%), whereas in Group-2, drains were removed in 11-14 days (56%). Seroma formation occurred in 8% of patients in Group-1 and 5.3% in Group-2 (p-value=0.512).

Conclusion: All patients tolerated TXA without any side effects and it effective in lowering the volume and duration of wound drainage following MRM.

Keywords: Breast cancer, Cumulative drain, Drain, Intervention, Placebo

INTRODUCTION

Breast cancer is the most common malignancy detected in the female population in Kerala, India. In 2022, cancer incidence in India was 105.4 per one lakh people, while in Kerala it was 169 per one lakh people. The most commonly performed surgeries for carcinoma of the breast include MRM and breast conservation surgery [1]. MRM allows local control with long-term survival advantages, but its disadvantages include lymphoedema, disfigurement, seroma formation, flap necrosis and emotional impact. Seroma is a collection of serous fluid that occurs after MRM in the dead space of the post-mastectomy skin flap, which can lead to delayed recovery, prolonged hospital stay, and may affect treatment by delaying adjuvant therapy and increasing the risk of infection [2]. Topical TXA, an antifibrinolytic agent, helps control fluid accumulation in the dead space under the skin and axillary fossa [3]. When TXA is applied topically, it results in low systemic concentration and high drug concentration at the site of application, thus, decreasing wound drainage and seroma formation [4-7]. The present study emphasised the effect of topical TXA on drain amount and seroma formation.

MATERIALS AND METHODS

The present prospective observational study was conducted in the Department of General Surgery, Government Medical College Kottayam, Kerala, India, from February 2022 to January 2023. After obtaining approval for the study from the Institutional Review Board (IRB No-8/22) and the ethical committee, patients admitted to the Department of General Surgery for MRM qualifying the inclusion and exclusion criteria were included in the study.

Sample size calculation: The sample size was calculated using the formula $N=(Z)^{2*}p*q/d^2$, where N is the sample size, p is the prevalence according to a previous study [6], q is 100-p, Z is the Type 1 error, d is the allowable clinical error, Z is 1.96 at 95% CI, p is 39%, q is 61%, and d is 20% of p=20/100*39. Therefore, the sample size was calculated to be 150.

Inclusion criteria: Patients with histopathologically proven carcinoma of the breast undergoing MRM in the age group of 18-80 years were included in the study.

Exclusion criteria: Patients who require immediate reconstruction, who were pregnant or breastfeeding, patients with known thromboembolic disease, patients on anticoagulants, myocardial infarction, transient ischaemic attack/ stroke within the last year were excluded from the study. Patients with history of seizure disorder and neoadjuvant chemoradiation were also excluded from the study.

Study Procedure

Patients were divided into two groups, Group-1 and Group-2 using a single-blinding method, where the patient was unaware of whether they were placed in an experimental or control group by drawing lots.

Group-1 (Intervention arm): TXA was diluted to a volume sufficient to maintain a fairly large wound surface. Two 10 mL syringes containing 25 mg/mL TXA were topically instilled to ensure a sufficiently high

concentration. Twenty milliliters moistens about 1500 cm^2. It was prepared by diluting one ampoule of TXA in 15 mL of normal saline, so the prepared solution contains 20 mL of 25 mg/mL TXA. In all patients, a continuous vacuum suction drain with an 800 mL capacity reservoir was used. A suction drain was placed in the surgical bed, and occlusive dressings were placed over the surgical wounds. Drains were placed in surgical wounds during the operation, and the amount of blood on the drain was measured in mL [6].

Group-2 (Placebo arm): Two 10 mL syringes containing 10 mL NS were applied topically to the mastectomy cavity for 15 minutes before wound closure. Parameters measured were:

1. Drain production in the first 24 hours (since bleeding may contribute to drainage in the first 24 hours, it is recorded separately).
2. Drain production up to drain removal-cumulative volume (time frame: three weeks).
3. In patients with seroma, aspiration was done, and the volume was measured.
4. Number of days the drain was kept.

The drain was subsequently removed when wound drainage was less than 50 mL/24 hours for three consecutive days. Local postoperative complications (necrosis of the breast skin flap, seroma, haematoma, and infection of the surgical wound) were also observed for all patients, wherein the only complication that occurred among the study population was seroma. All patients were followed-up until the drain was removed.

STATISTICAL ANALYSIS

The data obtained were entered into an Microsoft Excel sheet and analysed using Statistical Package for the Social Sciences (SPSS) software version 16.0 with a Chi-square test.

RESULTS

The median age of the patients was 50-60 years. There was no significant difference in the age group between both groups [Table/Fig-1]. On postoperative day 1, the drain amount in Group-1 was 37.3%, while in Group-2, it was 54.7%, with 1.3% of patients in Group-1 and 6.7% in Group-2 having more than 300 mL drained (p-value=0.001). By postoperative day 7, 21.3% of patients in Group-1 had drained less than 50 mL, compared to only 4% in Group-2 (p-value=0.02). The majority of patients in Group-1 had their drains removed in 5-10 days (97.3%), whereas in Group-2, drains were removed in 11-14 days (56%). Seroma formation occurred in 8% of patients in Group-1 and 5.3% in Group-2 (p-value=0.512). The amount of wound drainage was significantly lower in the study group compared with the control group in each volume range (p-value <0.005) [Table/Fig-2]. Six (8%) patients in the study group had seroma formation after the removal of drains compared with 4 (5.3%) patients in the control group [Table/Fig-3].

Single aspiration was used to treat each patient with seroma development in the study group and the control groups. The amount of seroma in the intervention group was in the range of 150-200 mL for about 50% of patients and in the control group in the range of 200-250 mL for about 75% of patients [Table/Fig-4]. Considering the total number of days the drain was kept, it was 5-10 days (97.3%) in Group-1, whereas Group-2 had their drain removed in 11-14 days (56%) [Table/Fig-5].

DISCUSSION

Breast cancer is the most common cancer in women and the second leading cause of cancer-related death in women worldwide [7]. Perioperative bleeding has always been an important determinant in the care of surgical patients. One of the main effects of surgery is the increased activity of local fibrinolytic factors and enhanced

Patient group		Age (years)					Total	χ^2	p-value
		30-40	41-50	51-60	61-70	71-80			
Group-1	n	5	18	32	13	7	75	3.12	0.537
	%	6.7	24.0	42.7	17.3	9.3	100.0		
Group-2	n	6	20	22	17	10	75		
	%	8.0	26.7	29.3	22.7	13.3	100.0		
Total	n	11	38	54	30	17	150		
	%	7.3	25.3	36.0	20.0	11.3	100.0		

[Table/Fig-1]: Age ranges.

Patient group		Cumulative drain (mL)					Total	χ^2	p-value
		600-800	800-1000	1000-1200	1200-1400	1400-1600			
Group-1	n	10	12	52	1	0	75	85.26	0.001*
	%	13.3	16.0	69.3	1.3	0	100.0		
Group-2	n	1	1	26	45	2	75		
	%	1.3	1.3	34.7	60.0	2.7	100.0		
Total	n	11	13	78	46	2	150		
	%	7.3	8.7	52.0	30.7	1.3	100.0		

[Table/Fig-2]: Cumulative drain.
*The p-value <0.05 was considered statistically significant

Patient group		Seroma formation		Total	χ^2	p-value
		Absent	Present			
Group-1	n	69	6	75	0.431	0.511
	%	92.0	8.0	100.0		
Group-2	n	71	4	75		
	%	94.7	5.3	100.0		
Total	n	140	10	150		
	%	93.3	6.7	100.0		

[Table/Fig-3]: Seroma formation.

Patient group		Amount of seroma				Total	χ^2	p-value
		100-150 mL	150-200 mL	200-250 mL	250-300 mL			
Group-1	n	2	3	1	0	6	8.96	0.030*
	%	33.3	50	16.7	0	100.0		
Group-2	n	0	0	3	1	4		
	%	0	0	75	25	100.0		
Total	n	2	3	4	1	10		
	%	20.0	30.0	40.0	10.0	100.0		

[Table/Fig-4]: Amount of seroma.
*The p-value <0.05 was considered statistically significant

Patient group		Total no. of days drain kept		Total	χ^2	p-value
		5-10	11-14			
Group-1	n	73	2	75	60.20	0.001*
	%	97.3	2.7	100.0		
Group-2	n	33	42	75		
	%	44.0	56.0	100.0		
Total	n	106	44	150		
	%	70.7	29.3	100.0		

[Table/Fig-5]: Number of days the drain kept.
*The p-value <0.05 was considered statistically significant

coagulability. Haemostasis is achieved with catecholamine-mediated platelet function, along with an increase in the level of coagulation factors and decreased function of coagulation inhibitors [8].

The TXA is a synthetic antifibrinolytic drug [9]. It has been extensively used in different disciplines of surgery for reducing perioperative blood loss, the need for blood transfusions, and haematoma formation. Still, the route of administration of TXA and its effective dose need to be standardised [10]. In-vitro, a minimum concentration of 5-10 µg/mL is needed to inhibit fibrinolysis [11,12].

The safety profile and efficacy of topical administration of TXA were still unclear in the literature [9,10]. Systemic administration of TXA was associated with reduced mean drain output volume in patients who underwent MRM [13]. The concentration of TXA needed for topical action is not well understood. Patients undergoing cardiac and Orthopaedic surgery have been studied for the administration of a bolus containing 1-3 grams of TXA diluted in 100 milliliters of saline (concentration 10-30 mg/mL) [5,14,15]. In contrast, epistaxis has been treated with sponges moistened with undiluted TXA for intravenous use (100 mg/mL) [16]. The concentration used in this study is 25 mg/mL, which is still sufficiently diluted to generate a volume that is adequate to moisten a sizable surface area. There is no much research that has been published where the application method was similar to the moistening used in the present study.

The use of drains after reduction mammoplasty has little scientific evidence, but is nevertheless common [17]. At the time of the study, the departmental routine was to use drains until fluid production was below 50 mL per 24 hours for three consecutive days. The present study suggests that topical TXA reduces drain fluid production after MRM to below this cut-off value in almost all patients and may obviate the need for a prolonged drain.

None of the patients in both groups had either flap necrosis or haematoma. In the present study, 8% of patients in which TXA was instilled had seroma formation compared to 5.3% in Group-2. One probable explanation is that the patient received a single dose of TXA, which decreased drain output in the early postoperative phase.

However, when the drug's impact was discontinued, seroma production increased, and by then, the drains had been removed [17]. Similar significant results were obtained in the studies conducted by Ausen K et al., who demonstrated the beneficial effects of topical TXA in reducing the mean drain output in MRM patients (p-value=0.026, p-value=0.038) [6]. Once topical TXA was administered at a dose of 25 mg/dL, another randomised controlled trial by Eldesouky MS et al., discovered that it was beneficial in decreasing the amount of drain output. These also had significant results, with a p-value of <0.005 (798.06±107.3 mL vs 1067.1±188.6 mL) [3]. Conversely, a trial carried out by Emara W et al., found a statistically negligible difference. His research shows that when TXA was supplied intravenously, the mean blood loss was 640±25 mL, however, when it was applied topically, the mean blood loss was 625±35 mL (p-value >0.05) [18].

The overall reduction in drain fluid production after the administration of topical TXA here accords with previously published studies [19-22]. Wherein it was performed in patients undergoing total knee arthroplasty, hip and knee replacement, and the outcome of all of them was measured in terms of the range of blood transfusion required. It was a cost-effective modality, thereby reducing bleeding, the need for further blood transfusions, and preventing reoperation due to haemorrhage.

In the present study, the authors were able to identify that topical TXA was effective in decreasing drain production, thereby producing a positive impact on patient outcomes, and the postoperative period was uneventful in the majority.

Limitation(s)

Findings cannot be generalised as the study was conducted in a single centre.

CONCLUSION(S)

Bleeding during MRM is inevitable, and blood transfusion is often required when there is excessive blood loss. Due to this reason, surgeons and anaesthetists have always employed a wide variety of techniques to reduce blood loss. TXA is useful in decreasing the quantity and amount of wound drainage following MRM without affecting the rate of seroma formation. It was tolerated by all patients without any side-effects.

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