

Original Research Article

Comparison of topical versus intravenous tranexamic acid on blood loss in modified radical mastectomy

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Received: 03 June 2022

Accepted: 02 July 2022

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ABSTRACT

Background: Modified radical mastectomy (MRM) is one of the surgical procedures for breast cancer management. Many complications are associated with wound healing, like hematoma, dehiscence, infection, chronic seroma and skin necrosis. The objective of this study was to compare the mean blood loss in drain output of topical versus intravenous tranexamic acid (TXA) use among patients undergoing modified radical mastectomy.

Methods: This randomized controlled trial was conducted at department of surgery, Holy Family hospital, Rawalpindi from November 2019 to November 2020. 130 patients were randomly divided into two groups. Group A patients received tranexamic acid topically while group B patients received intravenous tranexamic acid during modified radical mastectomy. Drain output and blood loss was recorded after twenty-four hours of the surgery.

Results: Mean age was 51.15 ± 10.33 in group A, while it was 50.58 ± 10.59 in group B. Mean duration of breast cancer among the patients was 11.45 ± 8.70 months. Mean blood loss, 24 hours after MRM was 40.68 ± 20.79 ml in the topical group, while it was 50.83 ± 26.38 ml in the intravenous group ($p=0.016$).

Conclusions: Topical tranexamic acid showed significantly better control on blood loss as compared to intravenous TXA.

Keywords: Modified radical mastectomy, Tranexamic acid, Blood loss

INTRODUCTION

Breast cancer is the leading cause of cancer-related death in women worldwide, with an increasing trend in recent years.

It is reported that approximately 230,480 new cases of invasive breast cancer and 39,520 breast cancer deaths occurred among US women in 2011. Surgery is important for the treatment of early-stage breast cancer.¹

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.²

The most commonly used antifibrinolytic agent is TXA. It is a synthetic analogue of the amino acid lysine. TXA blocks lysine-binding sites on plasminogen molecules and decrease the conversion of plasminogen to plasmin, thereby inhibiting the interaction of plasma fibrin to exerts its antifibrinolytic effect.³ Due to these properties, TXA can enhance haemostasis, potentially reduce blood loss during surgery and therefore, the transfusion requirements. Previous studies have reported satisfactory results with either intravenous or topical administration of TXA in reducing blood loss and transfusion requirement in joint arthroplasty.^{4,5}

However, there is no consensus regarding the administration routes of TXA. Both topical and intravenous TXA are effective in reducing blood loss and

transfusion rates in patients who underwent major surgeries.⁶ There has been much debate and controversy about the optimal regimen of TXA.^{3,7} A trial by Emara et al showed that the mean blood loss was 640±25 ml with intravenous TXA and 625±35 ml, when TXA was applied topically. The difference was statistically insignificant ($p>0.05$).⁸

The published literature reported equal efficacy of both topical and intravenous routes of TXA in controlling blood loss after breast surgery. However, increased dosage of intravenous tranexamic acid (above 2 g) may cause renal impairment, thrombosis and risk of seizures. The topical route though has showed relatively less blood loss and lesser side effects than intravenous TXA due to lower systemic concentrations.

Unfortunately, no local data was available in this regard. The rationale of this study was to compare the effects of topical with intravenous TXA in patients undergoing MRM on mean blood loss and drain output. This will help us determine a more beneficial route for TXA administration in controlling excessive blood loss and prevent blood transfusions and other complications like seroma formation and hematoma.

METHODS

This randomized controlled trial was conducted at the department of surgery, Holy Family Hospital, Rawalpindi from November 2019 to November 2020. Approval for the study was obtained from the Institutional Research Ethical Committee. All patients were kept blinded to the group allocated throughout the study.

One hundred and thirty (130) patients who fulfilled the inclusion criteria were enrolled in this study. Informed written consent was obtained from all patients.

All female breast cancer patients aged 30-70 years, undergoing MRM in general anesthesia, with ASA status I and II were included in the study.

Exclusion criteria included patients with advanced breast cancer and those who received neoadjuvant chemoradiotherapy. All those patients who were on anticoagulants, had a prior history of thromboembolic disease, hypersensitivity to TXA and pregnant women were also excluded.

Each patient was randomly assigned to one of two groups by lottery method. The envelope was opened in the operation theatre by the postgraduate resident prior to induction of general anesthesia for MRM to indicate which patient is to receive tranexamic acid topically (group A) or intravenously (group B).

For group A patients, 20 ml of 0.9% normal saline (NS) was given as an intravenous bolus prior to skin incision, followed by normal saline infusion at the rate of 80

ml/hour till the end of surgery. Prior to wound closure, 1500 mg of TXA in 100 ml of 0.9% NS was poured in the surgical field and left for five minutes before suction.

In group B, patients received intravenous TXA at a dose of 10 mg/kg in 20 ml of normal saline as a bolus prior to skin incision, followed by an infusion of 5 mg/kg/hour as 500 mg TXA in 250 ml normal saline at the rate of 80 ml/hour till the end of surgery. Prior to wound closure, 100 ml of 0.9% NS was poured in the surgical field and left for five minutes before suction. All surgeries were performed by a single surgical team. TXA injections were purchased from a single vendor.

Two drains (flap and axillary) were placed at the wound site. After the surgery, patients were shifted to post-surgical wards. Patient demographics, risk factors, details of the procedure and any adverse event was recorded on a predesigned performa. All the possible confounding variables were taken into consideration and bias removed by randomization.

Post-MRM blood loss, as evident by drain output was the primary outcome. During the first 24 hours after surgery, patients were closely observed, and total blood loss and drain output in 24 hours was recorded.

SPSS software (SPSS Version 25) was used for data analysis. Descriptive statistics were calculated for both qualitative and quantitative variables. Mean±SD was calculated for age, duration of carcinoma and mean blood loss in drain. Independent sample t test was employed to analyze mean blood loss between the two study groups. Data was stratified for age and duration of carcinoma. Independent sample t test was applied after the stratification. Qualitative variables were presented through tables and figure. P value of <0.05 was considered statistically significant.

RESULTS

A total of 130 patients were enrolled in the study. The study population was in the age group of 30 to 70 years (mean age 50.87±10.42 years). This is shown in Figure 1. Mean age was 51.15±10.33 in the topical group, while it was 50.58±10.59 in the intravenous group.

Table 1: Characteristics of the patients.

Characteristics	Topical TXA (n=65)	Intravenous TXA (n=65)
Age (years)	51.15±10.33	50.58±10.59
Duration of breast carcinoma	10.65±8.67	12.25±8.72

The mean duration of breast carcinoma among the patients was 11.45±8.70 months (range 1-50 months). In the topical group, it was calculated to be 10.65±8.67 months, whereas it was 12.25±8.72 months in the

intravenous group. Patient characteristics are shown in Table 1.

Twenty-four hours following MRM for breast cancer, the mean blood loss was found to be 45.75 ± 24.20 ml in all patients (range 10-95 ml). Mean blood loss in drain was 40.68 ± 20.79 ml in the topical TXA group, while it was 50.83 ± 26.38 ml in the intravenous group. This difference

in mean values of blood loss was statistically significant ($p=0.016$). This is shown in Table 2. Mean blood loss was stratified according to age and duration of breast carcinoma in both study groups. The difference between the two groups was found to statistically significant in age group less than 50 years ($p=0.002$) and breast carcinoma duration of less than 20 months ($p=0.007$), as shown in Table 3.

Table 2: Mean blood loss 24 hours after MRM in both groups.

Treatment group	N	Mean	Std. deviation	P value
Topical	65	40.68	20.79	0.016
Intravenous	65	50.83	26.38	

Table 3: Comparison of blood loss between study groups stratified by age and duration of breast carcinoma.

Blood loss		Study groups		P value
		Topical TXA	Intravenous TXA	
Age (years)	≤ 50	37.31 ± 20.57	56.08 ± 28.49	0.002
	> 50	44.86 ± 20.65	44.31 ± 22.27	0.922
Duration of carcinoma (months)	≤ 20	38.76 ± 20.90	51.67 ± 27.60	0.007
	> 20	50.09 ± 18.26	46.73 ± 19.82	0.683

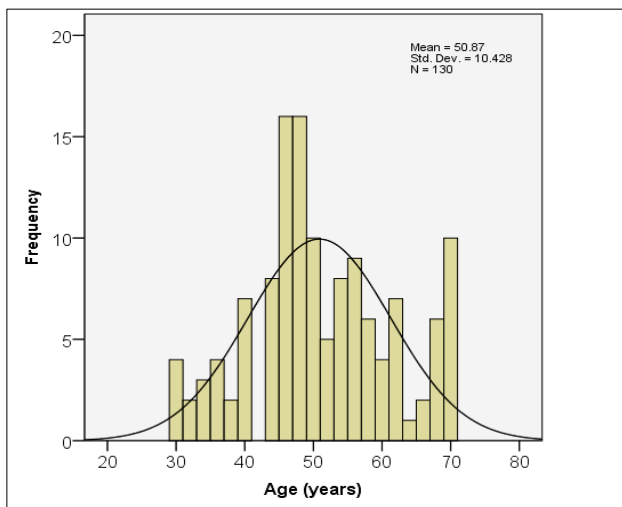


Figure 1: Age distribution of the patients.

DISCUSSION

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 coagulability.⁸ Hemostasis is achieved with catecholamine mediated platelet function, along with an increase in the level of coagulation factors and decreased function of coagulation inhibitors.⁹

TXA is a synthetic antifibrinolytic drug. It has been extensively used in different disciplines of surgery for reducing perioperative blood loss, the need for blood

transfusions and hematoma formation.¹⁰ Still, the route of administration of TXA and its effective dose needs to be standardized.

TXA was used intravenously to minimize peri-operative bleeding and the need for blood transfusions in previous research. Some researchers also investigated the effect of using TXA topically on the surgical site in favor to get the benefits of reduced loss of blood and improved hemostasis while avoiding the hypercoagulation effects of tranexamic acid, once administered systemically.^{11,12} The safety profile and efficacy of topical administration of TXA was still unclear in the literature.¹³

Systemic administration of TXA was associated with reduced mean drain output volume in patients who underwent MRM. A trial conducted in Egypt by Albatanony et al found reduced drain output in patients who received intravenous tranexamic acid as compared to placebo (1229.3 ± 196.8 ml versus 1696.5 ± 182.1 ml, $p < 0.001$).¹⁴ Similar results were obtained in a study by Knight et al who concluded a significant beneficial impact of systemic tranexamic acid on mean postoperative drainage volume reduction ($p < 0.001$).¹⁵

The effects of topical TXA in reducing postoperative blood loss after MRM were also studied in literature. One of the aims was to minimize the side effects associated with systemic administration of TXA. With regards to mean blood loss (drain output), our study found it to be 40.68 ± 20.79 ml in patients who received topical TXA as compared to 50.83 ± 26.38 ml, when the drug was given through the intravenous route. This difference between the two groups was found to be statistically significant

($p=0.016$). Similar significant results were obtained in the studies conducted by Ausen et al who demonstrated the beneficial effects of topical TXA in reducing the mean drain output in MRM patients ($p=0.026$, $p=0.038$).^{16,17}

Another randomized controlled trial conducted by Eldesouky et al also found that topical TXA was beneficial in reducing the amount of drain output, when given in the dose of 25 mg/ml. These results were also significant, with a p value of <0.005 (798.06 ± 107.3 versus 1067.1 ± 188.6 ml).¹⁸ On the other hand, statistically insignificant difference was noted in a trial conducted by Emara et al. According to his study, mean blood loss was 640 ± 25 ml with intravenous TXA administration, while 625 ± 35 ml blood loss was noted with topically administered TXA ($p>0.05$).⁸

A meta-analysis published in 2021 concluded that topically administered TXA was effective in reducing the need for blood transfusion, without causing any significant side effects in patients undergoing surgery.¹²

We proposed that topical administration of 15 mg/ml of TXA before wound closure in patients undergoing MRM was a simple, safe, feasible and effective prophylactic measure with minimal adverse effects. It was a cost-effective modality, thereby reducing bleeding, the need for further blood transfusions and prevent reoperation due to hemorrhage. Further multi-center studies should be done with a larger sample size to further explore the safety and efficacy of topical use.

CONCLUSION

Topical administration of TXA in modified radical mastectomy results in significant control of postoperative blood loss as compared to intravenous TXA.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Nawaz S, Shafique MS, Khadija G, Fatima S, Nayab S, Khan JS. Comparison of topical versus intravenous tranexamic acid on blood loss in modified radical mastectomy. *Int Surg J* 2022;9:1416-20.