# COMPARISON OF MEAN BLOOD LOSS WITH AND WITHOUT TOPICAL TRANEXAMIC ACID IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

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## ABSTRACT

**OBJECTIVE:** The objective of the study was to compare mean blood loss with and without topical tranexamic acid in patients undergoing coronary artery bypass grafting.

**METHODS:** It was a randomized controlled trial, conducted at Shaikha Fatima Institute of Nursing and Health Sciences Lahore between May to December 2022. Total 130 patients who underwent coronary artery bypass grafting were included in the study. Randomization was done by assigning even numbers to intervention group and odd numbers to placebo group. A proforma was filled containing demographic information of the participants and blood loss during surgery and transfusion of any blood product. The data was entered and analyzed using the SPSS v25.0.

**RESULTS:** Total 130 patients undergoing coronary artery bypass grafting were studied. Blood loss in each group was measured in milliliters, in intervention group mean blood loss was 366.52ml with a standard deviation of 32.38 and in placebo group mean blood loss was 483.08 with 86.26 standard deviation, difference between the mean blood loss among groups was statistically significant with p-value=0.001 by applying t-test.

**CONCLUSION:** Patients having primary coronary artery bypass grafting lead to a substantial decrease in post-operative blood loss and the need for blood transfusion when tranexamic acid (TXA) was applied topically.

**KEYWORDS:** Coronary Artery Bypass Grafting, Blood Loss, Tranexamic Acid.

## INTRODUCTION

In the United States, around 15 million units of red blood cell transfusions are administered to surgical patients each year. Within the realm of cardiac surgical operations, this accounts for a substantial proportion, ranging from 10% to 15% of the total transfusion volume. The occurrence of perioperative bleeding is a frequently observed complication that is closely linked to the requirement for transfusion and subsequent surgical intervention.[1-2]

These variables have a detrimental influence on post-operative morbidity, mortality, and expenses. The utilisation of cardiopulmonary bypass has been associated with the development of coagulopathy, a condition characterised by abnormal blood clotting and increased risk of bleeding. This phenomenon is believed to occur due to the activation of both the intrinsic and extrinsic coagulation pathways, as well as platelet dysfunction and a systemic inflammatory response.[1-4]

Therefore, it is advisable to implement strategies aimed at preventing perioperative coagulopathy. In order to achieve this objective, anti-fibrinolytic drugs are employed to inhibit the degradation of blood clots mediated by plasmin. Tranexamic acid is a pharmacological drug with anti-fibrinolytic properties, which has demonstrated efficacy in mitigating haemorrhage in the context of major surgical procedures and trauma cases.[5]

Consequently, contemporary clinical practise recommendations advocate for the use of this intervention in several perioperative contexts, notably including heart surgery. Tranexamic acid functions by effectively inhibiting the lysine binding sites of plasminogen, so impeding the activation of plasmin and subsequently limiting the degradation of polymerized fibrin.[5-7]

TXA is commonly employed to improve hemostasis, particularly in cases when bleeding is caused by fibrinolysis. Tranexamic acid has been employed in therapeutic settings for the treatment of menorrhagia, management of trauma-induced bleeding, and prevention of perioperative bleeding linked to orthopaedic and cardiac surgical procedures. Significantly, the use of tranexamic acid is not devoid of deleterious consequences.[8]

TXA has been linked to the occurrence of seizures, as well as concerns regarding potential heightened thromboembolic events, such as stroke. However, it is important to note that these associations have not been substantiated in randomised controlled studies thus far. The occurrence of stroke following heart surgery has been associated with elevated rates of both mortality and morbidity, as well as prolonged stays in the intensive care unit (ICU) and hospital. Furthermore, there has been variation in both the administration method and dosage of tranexamic acid in cardiac surgery trials.[9-12]

Tranexamic acid has the potential to be delivered by oral, topical, and intravenous routes. The most often employed routes of administration in perioperative cardiac operations are topical and intravenous. TXA is further employed in the context of cardiac operations. The study conducted by Shah et al. aimed to assess the effectiveness of topically applied Tranexamic acid in managing postoperative bleeding following open-heart surgery. There was a notable disparity observed in the average amount of postoperative bleeding within a 24-hour period between the two groups. The Tranexamic acid group exhibited a mean bleeding volume of

340.1±112.4 ml, whereas the placebo group had a mean bleeding volume of 665±187.28 ml ($p<0.001$).[13]

The mitigation of blood loss during and post-coronary artery bypass graft (CABG) surgery is a significant problem within cardiac surgery departments at medical facilities. There exist several methodologies for attaining the objective. The administration of Tranexamic acid through intravenous injection is considered the preferred therapeutic option. Nevertheless, there is a correlation between it and an increased occurrence of thrombotic events in these individuals.

This study aims to assess the efficacy of topical tranexamic acid in lowering post-operative blood loss and the need for blood transfusion in the local Pakistani healthcare context. This study aims to mitigate the burden of illness and death resulting from excessive blood loss. Additionally, the use of intravenous tranexamic acid in patients undergoing coronary artery bypass grafting (CABG) has the potential to alleviate the morbidity and mortality associated with thrombotic events.

## METHODOLOGY

The present investigation was carried out at the Shaikha Fatima Institute of Nursing and Health Sciences in Lahore. After obtaining clearance from the institutional ethics committee, a total of 130 patients who had coronary artery bypass grafting were included in the study. The participants in the study provided written informed permission for their involvement and the utilisation of their data for research purposes. The participants were provided with assurance on the confidentiality of their personal information. Exclusion criteria were patients exhibiting clotting abnormalities, renal failure with a creatinine level over 1.7, documented allergy to tranexamic acid, concurrent use of antiplatelet medications, and administration of heparin within 48 hours before the surgical procedure.

The presence of a medical history of diabetes and hypertension was observed in the patients. The randomization process involved the allocation of patients with even-numbered identifiers to either group A, which received topical tranexamic acid, or group B, which received a placebo. Demographic information of the participants was recorded, encompassing variables such as age and gender. All patients had bypass grafting in accordance with the hospital's established procedure, and normal patient treatment was carried out. In the treatment group, a solution of tranexamic acid was made by dissolving 1 gram of the substance in 100 ml of normal saline. In the placebo group, 100 ml of normal saline was administered.

At the conclusion of the surgical procedure, the solution was administered to the pericardium, mediastinal cavity, and mediastinal ridge. This was done prior to the surgeon suturing the sternum, while the chest tubes were temporarily occluded. Following the transfer of patients to the critical care unit, the chest tube drainages of each patient were assessed on an hourly basis. Additionally, the total blood loss over a 24-hour period, measured in millilitres, was recorded for both groups. The requirements for blood transfusion were same across all patients. Blood transfusion was administered in the form of packed red cells when the hematocrit (HCT) level was below 24% and the haemoglobin (Hb) level was below 8 mg/dL.

The prescription criteria for fresh frozen plasma (FFP) involved a prothrombin time (PT) that exceeded the basic rate by a factor of 1.5, in addition to the presence of disseminated bleeding. On the other hand, the prescription criteria for platelets included the presence of disseminated bleeding and a platelet count below 50,000/$mm^3$. A surgical procedure was conducted many times in order to manage excessive blood loss, namely when the drainage from the chest tubes exceeded 300 mL over a two-hour period. This was done while simultaneously monitoring the patient's coagulation tests to ensure appropriate clotting function.

The data that was gathered was inputted and examined using SPSS version 25.0. The mean and standard deviation were utilised to depict quantitative factors such as age and blood loss. The frequencies and percentages were calculated to represent the qualitative factors, such as gender, diabetes, and hypertension. The mean blood loss was compared between the two groups using an independent samples t-test. The comparison of transfusion need between the two groups was conducted using a Chi-square test. A significance level of $P \leq 0.05$ was deemed to be statistically significant.

## RESULTS

Total 130 subjects were randomly divided into two groups, 65 received intervention (tranexamic acid) and 65 were controls (placebo). In intervention group, 34(52.3%) were males and 31(47.7%) were female, among these 26(40.0%) were <50 years, 30(46.2%) were 50-70 years and 9(13.8%) were ≥70 years of age.

In placebo group 48(73.8%) participants were males and 17(26.2%) were females. Age of 22(33.8%) of subjects was <50 years, 37(56.9%) was 50-70 years and 6(9.2%) was ≥70 years. Out of 65 cases 29(44.6%) were diabetics and 46(70.8%) were hypertensive. Among 65 controls 48(73.8%) were diabetics and 55(84.6%) were hypertensive.

Blood loss in each group was measured in milliliters, in intervention group mean blood loss was 366.52ml with a standard deviation of 32.38 and in placebo group mean blood loss was 483.08 with 86.26 standard deviation, difference between the mean blood loss among groups was statistically significant with p-value=0.001.

In tranexamic acid group 26(40.0%) patients needed transfusion of blood products, while in placebo group 39(60.0%) needed blood transfusion, significant difference between these proportions (p=0.022) was found when compared by applying chi-square test.

**Table-1: Distribution of demographic characteristics among groups (n=130: Tranexamic acid=65, Placebo=65)**

| Demographic Characteristics | Tranexamic acid n (%) | Placebo n (%) |
|---|---|---|
| **Gender** | | |
| • **Male** | 34 (52.3) | 48 (73.8) |
| • **Female** | 31 (47.7) | 17 (26.2) |
| **Age** | | |
| • **<50 years** | 26 (40.0) | 22 (33.8) |
| • **50-70 years** | 30 (46.2) | 37 (56.9) |
| • **≥70 years** | 9 (13.8) | 6 (9.2) |
| **Total** | 65(100.0) | 65(100.0) |

**Table-2: Medical history among the groups (n=130: tranexamic acid=65, placebo=65)**

| | Tranexamic acid n (%) | Placebo n (%) |
|---|---|---|
| **Diabetes** | | |
| • **Yes** | 29(44.6) | 48(73.8) |
| • **No** | 36(55.4) | 17(26.2) |
| **Hypertension** | | |
| • **Yes** | 46(70.8) | 55(84.6) |
| • **No** | 19(29.2) | 10(15.4) |
| **Total** | 65(100.0) | 65(100.0) |

**Table-3: Comparison of blood loss among groups (n=130: tranexamic acid=65, placebo=65)**

| Groups | Blood loss(ml) | | p-value |
|---|---|---|---|
| | Mean | SD | |
| **Tranexamic acid** | 366.52 | 32.38 | 0.001 |
| **Placebo** | 483.08 | 86.26 | |

**Table-4: Need for blood transfusion among groups (n=130: tranexamic acid=65, placebo=65)**

| Groups | Need for transfusion of any blood product | | p-value |
|---|---|---|---|
| | Yes<br>n (%) | No<br>n (%) | |
| Tranexamic acid | 26(40.0) | 40(61.5) | 0.022 |
| Placebo | 39(60.0) | 25(38.5) | |
| **Total** | 65(100.0) | 65(100.0) | |

## DISCUSSION

Multiple clinical trials have demonstrated the efficacy of intravenous administration of tranexamic acid (TXA) in reducing postoperative bleeding and the need for transfusions in both primary coronary artery bypass grafting (CABG) and re-operative cardiac surgery. TXA is a pharmacological agent of synthetic origin that functions by binding to the lysine-binding sites of plasmin and plasminogen, hence exerting its anti-fibrinolytic effects. During open-heart surgery with cardiopulmonary bypass, the circulation of blood involves its exposure to extracorporeal or non-endothelial surfaces. This interaction triggers the activation of several

cellular and humoral pathways, such as the coagulation, complement, and fibrinolytic pathways.[14-15]

These interactions result in the occurrence of hyperfibrinolysis. Post-operative bleeding is a direct and deleterious outcome that can arise from hyperfibrinolysis. The occurrence of fibrinolysis during cardiopulmonary bypass (CPB) is indicated by elevated levels of plasmin and Fibrinogen Degradation Product (FDP). Both plasmin and FDP exhibit inhibitory effects on platelet function, resulting in postoperative bleeding as a consequence of the hemostatic dysfunction induced by extra-corporeal circulation.[16]

Thrombocytopenia, depletion of clotting factors, and extensive administration of heparin result in a notable increase in fibrinolysis, in addition to the extracorporeal cardiopulmonary bypass (CPB) circuit, which contributes to non-surgical bleeding. Cardiac surgery performed with the assistance of a cardiopulmonary bypass machine results in widespread microvascular haemorrhage, commonly referred to as non-surgical bleeding, as it cannot be resolved with surgical interventions. Approximately 50% of individuals undergoing heart surgery and then requiring reoperation owing to postoperative bleeding are discovered to have non-surgical bleeding.[17-18]

The use of anti-fibrinolytic medications by topical application is a practical approach implemented in open-heart operations with the aim of reducing non-surgical blood loss. This is achieved by suppressing the process of fibrinolysis, hence decreasing the requirement for blood transfusions. Lysine analogues have emerged as a prominent alternative in cardiac surgery due to their comparable efficacy, enhanced safety profile, and improved cost-effectiveness in comparison to Aprotinin, Tranexamic acid, and epsilon-Aminocaproic acid.[19-20]

The introduction of anti-fibrinolytic medicines to the pericardial cavity following cardiac surgery has been shown to effectively decrease postoperative non-surgical bleeding by impeding the process of fibrinolysis. The pericardium functions as an inherent barrier, exhibiting no discernible absorption of topical Tranexamic acid into the bloodstream, hence mitigating the occurrence of any undesired systemic adverse effects.[17,21]

In order to mitigate postoperative bleeding, topical administration of anti-fibrinolytic drugs has been employed within the pericardial cavity.[22] This study aimed to measure the amount of blood loss in millilitres in two groups: the intervention group and the placebo group. The intervention group had a mean blood loss of 366.52ml, with a standard deviation of 32.38. On the other hand, the placebo group had a mean blood loss of 483.08ml, with a standard deviation of 86.26. The difference in mean blood loss between the two groups was found to be statistically significant, with a p-value of 0.001.

The decrease in blood loss primarily takes place within the first three hours following the surgical procedure. It is posited that the observed phenomenon might be attributed to the prompt hemostatic impact facilitated by the use of topical tranexamic acid (TXA). There is a suggestion that a regional fibrinolytic condition continues to exist following the closure of the thoracic cavity, which subsequently plays a role in the blood loss seen after surgery.

The administration of tranexamic acid (TXA) into the thoracic cavity prior to the completion of the median sternotomy procedure has the potential to eliminate plasminogen from the fibrin surface of blood clots, thereby impeding the breakdown of fibrin caused by plasmin. Therefore, it is possible that this intervention might impede the dissolution of preexisting blood clots and promote the cessation of bleeding by maintaining their structural integrity.[23]

The results presented in our study revealed a statistically significant decrease in blood loss within the therapy group within the first three hours post-operation. However, this reduction

in blood loss was not shown to be statistically significant throughout the subsequent 21-hour period. It is probable that the concentration of TXA utilised in this particular study, which was 1%, did not effectively inhibit local fibrinolysis for a duration beyond 3 to 4 hours. It is hypothesised that administering a higher dosage of TXA, such as a 5% solution, may result in an extended duration of the drug's hemostatic efficacy.

It is acknowledged that in the present trial, the overall decrease in blood loss seen in the TA group, in comparison to the placebo group, was less than 100 mL. Consequently, this reduction may be considered rather modest, but statistically significant. Nevertheless, it is important to note that the definition of severe bleeding in this context is characterised by a cumulative chest drainage volume above 700 to 800 mL. It is worth emphasising that the majority of patients included in this study experienced minimal bleeding.

The potential concealment of the hemostatic effectiveness of this pharmacological agent may have been facilitated by the limited occurrence of bleeding. The occurrence of postoperative haemorrhage was attributed to the combination of careful surgical hemostasis and the comparatively low susceptibility to bleeding within our patient cohort. A potential outcome of utilising topical tranexamic acid (TA) in the context of surgical interventions with an elevated risk of bleeding is a heightened reduction in blood loss. This impact may be particularly pronounced in operations that are characterised by extended durations and increased complexity.

The present study's inability to observe a decrease in allogenic transfusions, despite a statistically significant reduction in blood loss, may be attributed to various factors, including minimal postoperative bleeding overall, strict criteria for transfusion, and an inadequate sample size to detect a modest effect. In cases when surgical blood loss is already reduced,

the potential positive impact of the medicine on blood product consumption is expected to be limited, especially when transfusion practises adhere to rigorous norms.[24]

The affordability of tranexamic acid (TXA) presents an appealing aspect, nevertheless, in order to establish its complete justification, it is necessary to see a decrease in blood loss that is subsequently accompanied by a reduction in the necessity for transfusion. This study found a statistically significant difference in the mean blood loss across groups, as shown by a p-value of 0.00. The methodologies employed in this study exhibited similarities and yielded identical outcomes to the research conducted by Baric et al., which ultimately determined that the application of topical Tranexamic acid is efficacious in mitigating postoperative haemorrhaging subsequent to heart surgery.[17]

The findings of their research demonstrated a statistically significant decrease in the anticipated average post-24-hour bleeding volume among patients administered topical Tranexamic acid at a dosage of 525 ml, as compared to the placebo group with a volume of 833 ml. Nevertheless, the trial conducted by the researchers consisted of a sample size of roughly 300 patients. In addition to the Tranexamic acid and placebo groups, one of the groups was administered topical Aprotinin. De Bonis et al. were the pioneers in conducting a randomised experiment, wherein they arrived at the conclusion that the use of topical Tranexamic acid leads to a reduction in the average amount of postoperative bleeding following heart surgery.[25]

The findings of their investigation indicated that the average amount of bleeding after a 24-hour period was 485 ml in the group administered with Tranexamic acid, whereas the placebo group exhibited a mean bleeding volume of 641 ml. The study exclusively included individuals who were having coronary artery bypass grafting with the assistance of cardiopulmonary bypass. The intervention was administering a single gramme of Tranexamic

acid solution diluted in 100 ml. The researchers further shown that the application of Tranexamic acid in the pericardial cavity is not only safe, but it also does not result in systemic absorption following topical administration.[25]

The current study noticed that within the tranexamic acid group, 26 patients (40.0%) required blood product transfusion. In contrast, within the placebo group, 39 patients (60.0%) required blood transfusion. A significant difference in proportions (p=0.022) was identified when comparing these groups using a chi-square test. Fawzy et al. (year) similarly observed a substantial reduction in platelet transfusion among the TXA group, aligning with the findings of our study that demonstrated a greater incidence of platelet transfusion in the placebo group. Additionally, it should be noted that the duration of hospitalisation in the critical care unit was comparatively longer among individuals in the placebo group.[26]

The utilisation of topical tranexamic acid (TXA) under general anaesthesia with controlled hypotension (GABC) resulted in a notable decrease in post-operative bleeding, packed cell volume, platelet transfusion, and fresh frozen plasma (FFP) requirements subsequent to surgical procedures. Moreover, it did not provide any substantial impact on the rates of reoperation or death.[27]

The primary constraint of this study pertains to the limited size of the sample. Moreover, there is a dearth of data pertaining to the concentrations of haemoglobin and hematocrit before and after surgical procedures. Currently, there is a lack of published data about the estimate of tranexamic acid (TXA) absorption in blood. There is currently a lack of recorded evidence pertaining to the impact of topical use of tranexamic acid (TXA) on post-operative mortality and thrombotic events.

## CONCLUSION

The administration of tranexamic acid (TXA) topically in patients who are having primary coronary artery bypass grafting has been found to result in a notable decrease in postoperative blood loss and the need for blood transfusion, without introducing any additional danger to the patient.

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