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# Impact of tranexamic acid on bleeding during coronary artery bypass for patients under treatment of low molecular weight heparin

## Koroner arter bypass operasyonlarında düşük molekül ağırlıklı heparin tedavisi gören hastalarda traneksamik asidin kanama üzerine etkileri

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**Abstract**

Aim: Tranexamic acid (TA) is an antifibrinolytic agent that prevents the dissolution of fibrin clot. We investigated the impact of the use of tranexamic acid (TA) on bleeding for patients under treatment of low molecular weight heparin during coronary artery bypass graft (CABG) operations.

Methods: Among 82 patients, 60 patients undergoing CABG with cardiopulmonary bypass (CPB) were enrolled into a case-control study within a six month-period. On the first postoperative day, patients were divided into two groups depending on the intraoperative use of TA. TA was not administered to control group patients (n=30) while those in the study group (n=30) received TA intravenously at a dose of 10 mg/kg. Coagulation variables including complete blood cell count, D-Dimer, fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR) values were collected preoperatively and 24 hours after surgery. Estimated blood loss, loss by drainage, total amounts of packed red blood cell and fresh frozen plasma transfusions were recorded. *P*-value <0.05 was considered statistically significant.

Results: Among 60 patients included in the study, there were 39 and 21 males and females, respectively. The mean age of all patients was 61.6 years. The two groups were similar in terms of use of fresh frozen plasma, age, height, and weight (P=0.268, *P*=0.586, *P*=0.787, *P*=0.641, respectively). The amount of postoperatively transfused packed red blood cells in units were lower in the study group (*P*=0.04). Total mediastinal drainage amounts in the 4$^{th}$, 8$^{th}$, 12$^{th}$ hours and overall were lower in the study group (*P*=0.016, *P*=0.006, *P*=0.013, *P*=0.04, respectively).

Conclusion: TA is a safe drug that reduces postoperative bleeding without side effects in patients using DMAH undergoing CABG operations.

**Keywords:** Coronary bypass surgery, Low molecular weight heparin, Tranexamic acid, Bleeding, Blood products

**Öz**

Amaç: Traneksamik asit (TA), fibrin pıhtısının çözünmesini önleyen antifibrinolitik bir maddedir. Koroner arter bypass greft (KABG) operasyonları sırasında düşük moleküler ağırlıklı heparin tedavisi alan hastalarda TA kullanımının kanama üzerindeki etkisini araştırdık.

Yöntemler: Toplam 82 hastadan, kardiyopulmoner bypass (CPB) ile KABG uygulanan 60 hasta, altı aylık bir dönemde vaka-kontrol bir çalışmaya alındı. Ameliyat sonrası birinci günde, intraoperatif TA kullanımına bağlı olarak hastalar iki gruba ayrıldı. Kontrol grubunda (n=30) TA verilmezken, çalışma grubunda Grup 2'de (n=30) TA intravenöz 10 mg/kg dozda uygulandı. Pıhtılaşma değişkenleri; tam kan hücresi sayımı, D-Dimer, fibrinojen, protrombin zamanı (PT), aktive parsiyel tromboplastin zamanı (aPTT) ve uluslararası normalleştirilmiş oran (INR) değerleri ameliyat öncesi ve ameliyattan 24 saat sonra toplandı. Tahmini kan kaybı, drenaj kaybı, toplam eritrosit süspansiyonu ve taze donmuş plazma hacimleri kaydedildi. *P*-değeri <0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışmaya alınan, 60 hastanın 39'si erkek, 21'i kadın, hastaların yaş ortalaması 61,6/ yıl idi. Hastaların yaş, boy, kilo verileri benzerdi (sırası ile; *P*=0,586, *P*=0,787, *P*=0,641). Postoperatif verilen taze donmuş plazna transfüzyonu iki grupta benzer iken (*P*=0,692), postoperatif verilen eritrosit süspansiyonu ünite miktarı çalışma grubunda daha düşüktü (*P*=0,04). Ameliyat sonrası, 4., 8., 12. ve total mediastinal drenaj miktarları çalışma grubunda daha düşüktü (sırasıyla; *P*=0,016, *P*=0,006, *P*=0,013, *P*=0,04).

Sonuç: TA, CABG operasyonları sırasında DMAH tedavisi alan hastalarda yan etki olmaksızın postoperatif kanamayı azaltan güvenli bir ilaçtır.

**Anahtar kelimeler:** Koroner bypass cerrahisi, Düşük molekül ağırlıklı heparin, Traneksamik asit, Kanama, Kan ürünleri

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## Introduction

In cases which the cardiac muscle, also known as myocardium, is not oxygenated due to several reasons (such as an increase in the volume of blood reaching the heart and decrease in heart contractility), ischemic cardiac diseases develop. In this disease, blood flow into cardiac muscle is decreased, which deteriorates the balance of oxygen demand and supply of myocardium. Hypertension, tachycardia, spasm of the coronary arteries or anatomical obstruction, severe hypotension, anemia, aortic stenosis, and regurgitation are among the main causes of myocardial ischemia [1,2].

The first objective of cardiopulmonary bypass (CPB) in open-heart surgery is to ensure systemic homeostasis. This is achieved by establishing systemic perfusion, blood oxygenation, and carbon dioxide elimination. Hemorrhage, which requires immediate reoperation after open-heart surgery, constitutes one of the most severe postoperative complications. Among patients undergoing open-heart surgery, 2-7% require reoperation due to hemorrhage [3-5]. Some of the reasons for not being able to detect a hemorrhagic focus in almost half of the patients who are reoperated include the depletion of hemodilution and coagulation factors, thrombocyte function disorders, decrease in number of thrombocytes, abundance of heparin and protamine, excessive fibrinolysis, complement activation, and common intravascular coagulation. The most frequently seen are thrombocyte function disorders and excessive fibrinolysis [6-8].

The release of plasmin during CPB activates fibrinolysis. The activity of heparin is monitored with activated clotting time (ACT). The normal value of ACT is between 80 and 120 seconds. Antithrombin III is a serine protease inhibitor which inhibits clotting when combined with heparin. The dose of heparin needed for increasing ACT above 480 seconds during CPB is 3.5 mg/kg. 1.3 mg protamine is required to neutralize every 1 mg of heparin administered during CPB. Protamine adheres to heparin, preventing it from forming a complex with antithrombin III, thus retuning thrombin functions and the coagulation cascade to normal [5,8-10].

The hemostatic mechanisms are negatively affected from cardiopulmonary bypass. Increased fibrinolysis, decreased number and function of thrombocytes, dilution of coagulation factors, effect of heparin, residual effects of excessive protamine, and preoperative use of anticoagulant medications such as LMWH, along with the operation, increase the risk of postoperative hemorrhage. Tranexamic acid (TA), a synthetic derivative of the amino acid lysine, is an antifibrinolytic agent. In numerous studies and meta-analyses, this anti-fibrinolytic medication was shown to decrease postoperative hemorrhage [8,11,12].

In the present study, our aim was to investigate whether the use of tranexamic acid (TA) and low molecular weight heparin (DMAH) together may have an impact on bleeding-related parameters in coronary artery bypass graft (CABG) operations.

## Materials and methods

From a total of 82 patients, 60 patients undergoing CABG with cardiopulmonary bypass (CPB) were enrolled into a case-control study within a six month-period. Eleven patients refused to participate in the study. Ethics committee approval was received from Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital Ethics Committee (date and number: 2010.4/02). All included patients and their relatives provided written informed consent forms to participate in the study, which was conducted in accordance with the Helsinki Declaration for human rights preservation.

On the first postoperative day, patients were divided into two groups depending on the use of intraoperative TA. TA was not administered to control group patients (n=30) while those in the study group (n=30) received TA intravenously before CPB at a dose of 10 mg/kg.

The eligibility criteria included patients older than 18 and younger than 80 years, those undergoing elective CABG surgery with CPB, with an American Society of Anesthesiology (ASA) physical status of 2 or 3 and those who received DMAH preoperatively. The CABG operation was planned for patients with severe stenosis in left main coronary artery or unstable angina who would have to undergo two or three vessel operations.

Exclusion criteria included those undergoing repeat cardiac surgery, emergency surgery, patients with preoperative coagulation disorders, preoperative use of coumarin anticoagulants, heparin, or acetylsalicylic acid within 5 days before the operation, preoperative congestive heart failure, a history of severe heart failure (ejection fraction below 30 %), preoperative renal dysfunction (serum creatinine > 1.3 mg/dl), chronic oliguria/anuria requiring dialysis, preoperative hepatic dysfunction (serum aspartate/alanine amino transferase > 40U/L), preoperative electrolyte imbalance, history of pancreatitis or current corticosteroid treatment, and a history of allergy to LMWH or TA.

The standard anesthesia, surgical and myocardial protection methods were followed for all patients. Before the operation, patients were administered 10 mg diazepam (Deva, Istanbul, Turkey) intramuscularly as premedication. For induction of anesthesia, 0.05 mg/kg midazolam (Dormicum, Deva, Istanbul, Turkey), 8 microgram/kg fentanyl (Fentanyl, Abbot, North Chicago, USA) and 0.1mg/kg pancuronium (Pavulon, Organon, Istanbul, Turkey) were administered intravenously. Fentanyl citrate infusion was maintained at a dose of 1 microgram/kg/hour. During anesthesia maintenance, intravenous pancuronium and midazolam bolus doses were administered. A thermodilution catheter was placed in the internal jugular vein (7.5 F Opticath, Abbot, North Chicago, IL, USA).

After sternotomy and preparation of the left internal thoracic artery pedicle and the ascending aorta, right atrium was cannulated. During CPB, a roller pump (Stöckert, Munich, Germany) and membrane oxygenator (D 708 Simplex Adult Fiber Oxygenator, Dideco, Mirandola, Italy) were used under normothermia. Due to the risk of hypersensitivity and allergic reactions, a test dose of 1 ml intravenous tranexamic acid was applied, followed by TA administration to the study group at a dose of 10mg/kg 10 minutes before the pump as a slow bolus [9,12,15]. The anticoagulation was ensured using heparin (Nevparin Mustafa Nevzat, Istanbul, Turkey) at 300 unit/kg.

Activated clotting timing was monitored with Hemochron 801 device. Anticoagulation was maintained by keeping ACT longer than 400 seconds and administering additional doses of heparin as needed [7-9]. During CPB, the rate of perfusion was ensured with non-pulsatile flow at 2.4 liters/$m^2$/minute and higher. After clamping the ascending aorta, cardiac arrest was achieved via antegrade hyperkalemic blood cardioplegia, which was applied every 20 minutes. After completion of the distal anastomoses, the clamp at the aorta was removed and partial bypass was initiated. The proximal anastomoses were performed by placing clamps collaterally on the aorta. After exiting cardiopulmonary bypass, heparin was neutralized with 1:1-1.3 protamine hydrochloride (Protamine ICN, Onko, İstanbul, Turkey) [7-9]. The operations were performed at 33°C and moderate hypothermia (nasopharyngeal temperature). The room temperature was kept at 20-22°C. Before leaving CPB, patients were heated to 37°C. After placing the clamp on the aorta, 1000 cc cold (4-8°C) blood cardioplegia (25mEq/l potassium) was given with administration of additional doses of 500 cc every 15-20 minutes (antegrade at the root of the aorta and venous grafts and retrograde in main coronary artery disease). The hot blood cardioplegia (36-37°C) was administered before removing the aortic clamp. The operation was completed after placing 2 silicone-coated drains to the mediastinum and one latex drain to the thorax, and by implementing standard hemorrhage control. These drains were removed when the amount of drainage was under a total of 100ml/day. Depending on the electrolyte level, electrolyte replacement solutions were administered when needed during bypass.

After the surgery, packed red blood cell (PRBC) transfusion was considered when hemoglobin level was under 8 g/dL, and hematocrit level was under 25%. Fresh frozen plasma (FFP) was transfused in case of excessive bleeding (>400 mL/h) in the presence of an activated partial thromboplastin time >60 seconds. Platelet concentrates were given if bleeding continued (>400 mL/h) despite normal ACT. Fresh frozen plasma and platelet concentrates were administered in cases of documented postoperative coagulation abnormalities. In case of presence of a hemorrhage disorder (international normalized ratio>1.5, active prothrombin time >60 seconds, thrombocyte count < 80,000/$mm^3$) or in case of suspected postoperative thrombocyte and clotting factor dysfunction, fresh frozen plasma and thrombocyte suspensions were transfused. The decision of re-exploration for hemorrhage was made when 200 ml/h of drainage was documented in two consecutive hours despite measures taken or in case of more than 300 ml/h drainage. Estimated blood loss was defined as the sum of objective losses, e.g., via drainage and swabs plus clinically estimated additional losses. Blood samples were obtained before heparinization, 24 and 48 hours after CPB. Samples for coagulation factor analyses were immediately cooled on ice and plasma was stored at -70°C. The hemoglobin values and platelet count in the whole blood were determined with a Cell-Dyn 610 hematology analyzer (Sequoia-Turner Corp., Mountain View, CA, USA).

**Primary and secondary end points**

As a primary end point, we analyzed and compared the values of hemoglobin, hematocrit, platelet, prothrombin time, activated prothrombin time, and international normalized ratio (INR) between groups. Also, estimated blood loss, the amount of mediastinal drainage, transfused PRBC in unit value, transfused fresh frozen plasma in unit value and coagulation variables before and 24 hours after surgery were compared between groups. Possible side effects related to TA administration intraoperatively were noted and these include hemodynamical changes such as hypotension or hypertension, bradycardia or tachycardia, allergic skin reactions, anaphylactoid reactions, heart rhythm disturbances, or other possible suspected adverse events [13].

**Statistical analysis**

Statistical analyses were performed using SPSS software for Windows version 17.0 (Statistical Package for the Social Sciences Inc., Chicago, IL, USA). Continuous variables were expressed as median or mean values (standard deviation (SD)). Categorical variables were expressed as number and percentages. Demographic characteristics and outcomes of the groups were compared using "independent samples *t*-test" for continuous variables, and 'Chi-square test' and 'Fisher's exact test' for categorical variables. *P*-value <0.05 was considered statistically significant. Repeated measures of two groups were compared with analysis of variance and Kruskal Wallis tests. The sample size was estimated depending on previous data showing that 24-hour postoperative blood loss indicated by chest tube drainage was 250 mL. A minimum sample size of 60 patients (30 per group) was sufficient to detect a 250 mL difference between groups with 90% power at 0.05 significance level [13].

## Results

TA was administered intraoperatively, and group assignments were made on the first postoperative day based on whether they received TA. There were no differences in terms of demographic features, preoperative and postoperative data between the control and TA groups (Table 1). Durations of cardiopulmonary bypass and aortic cross clamp, extubation time, duration of intensive care unit and hospital stay were similar (*P*=0.121, *P*=0.491, *P*=0.380, *P*=0.106, *P*=0.326), along with estimated blood loss (*P*=0.322). While postoperative FFP transfusion was similar in two groups (*P*=0.692), postoperative erythrocyte suspension transfusion was lower in the study group with 1(0-7) units, compared to 2(0-3) units in the control group (*P*=0.04). The postoperative mediastinal drainage was lower in the study group compared to the control group at the $4^{th}$, $8^{th}$, $12^{th}$ $16h^{th}$ hours, and overall (*P*=0.016, *P*=0.006, *P*=0.001, *P*=0.312, *P*=0.004) (Table 2). There was no difference between D-dimer, fibrinogen, INR, hemoglobin and platelet values before and after surgery (*P*=0.728, *P*=0.196, *P*=0.535, *P*=0.632, *P*=0.108, *P*= 0.057, *P*=0.750, *P*=0.293, *P*=0.579, *P*=0.252, respectively) (Table 3). Side effects related to TA administration were not observed intraoperatively. No adverse events related to TA were noted postoperatively.

Table 1: Demographic data and preoperative characteristics of the groups

| Parameters | Control group (n=30) | Study group (n=30) | *P*-value |
|---|---|---|---|
| Mean age (SD) | 60.8 (9.1) | 62.2 (10.2) | 0.586 |
| Gender (M/F) (n %) | 11/19 (37/63) | 10/20 (33/67) | 0.787 |
| Height (cm) | 164.1 (9.6) | 163.2 (9.1) | 0.690 |
| Weight (kg) | 76 (10.9) | 74.7 (11.2) | 0.641 |
| BMI | 28.2 (3.4) | 28.1 (4.2) | 0.936 |
| ASAPS of 2 | 21 (70) | 18 (60) | 0.417 |
| ASAPS of 3 | 9 (30) | 12 (40) | |
| EuroSCORE | 6 (2.8) | 6 (3.2) | 0.571 |
| Preoperative EF (%) | 55.0 (35-65) | 60 (30-65) | 0.804 |
| Number of coronary vessels | 3.0 (1.0-5.0) | 3.0 (1.0-5.0) | 0.881 |
| Preoperative risk factors for CAD | | | |
| Diabetes mellitus | 19 (28.8) | 11 (16.7) | 0.145 |
| Hypertension | 13 (43.3) | 12 (40) | 0.793 |
| COPD | 7 (23) | 8 (27) | 0.697 |
| Use of smoke | 9 (30) | 7 (23) | 0.459 |
| Obesity | 6 (20) | 7 (23) | 0.663 |
| Hypercholesterolemia | 5 (17) | 8 (27) | 0.347 |

SD: Standard deviation, M/F: male/female, n %: number percentage, BMI: body mass index, ASAPS: American Society of Anesthesiologists Physical Status, EF: ejection fraction, CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease

Table 2: The intraoperative and postoperative parameters and comparisons between the two groups

| Parameters | Control group (wo/TA) (n=30) | Study group (TA) (n=30) | *P*-value |
|---|---|---|---|
| CPB* (minute) | 90 (45.0-204.0) | 87.5 (36.0-193.0) | 0.121 |
| ACC* (minute) | 54.50(28.0-140.0) | 51.50(20.0-151.0) | 0.491 |
| Postoperative EF* (%) | 50.0(40.0-65.0) | 50.0(40.0-65.0) | 0.491 |
| Extubation time (hours) | 8.0(3.0-17.0) | 10(4.0-29.0) | 0.380 |
| Intensive care unit stay (day) | 2.0(1.0-9.0) | 2.0(1.0-12.0) | 0.106 |
| Hospital stay (days) | 9.13 (3.45) | 8.97 (3.65)" | 0.326 |
| Estimated blood loss (ml) | 1100 (700-1350) | 1250 (750-1450) | 0.322 |
| Postoperative 24 hour blood transfusion (units) | 2(0-6) | 1(0-7) | 0.040* |
| Postoperative 24 hour FFP transfusion (units) | 2(0-3) | 2(0-3) | 0.692 |
| 0-4h drainage amount (ml) | 175 (50-500) | 150 (0-500) | 0.016* |
| 4-8h drainage amount (ml) | 200 (50-1250) | 150 (50-1250) | 0.006* |
| 8-12h drainage amount (ml) | 125 (0-450) | 100 (0-500) | 0.001* |
| 12-16 h drainage amount (ml) | 100(0-350) | 100(0-350) | 0.312 |
| Total drainage (ml) | 725(200-1500) | 550(50-1500) | 0.040* |

*$P<0.05$ statistical significance, n,%: number, percentage; ACC: aortic cross-clamp time; CPB: cardiopulmonary bypass time; EF: ejection fraction; FFP: fresh frozen plasma; NS: not significant

Table 3: The comparison of hemostasis related parameters between groups

| Parameters | Control group (wo/TA) (n=30) | Study group (TA) (n=30) | *P*-value |
|---|---|---|---|
| D-dimer (preop) (ng/mL) | 0.49(0.20) | 0.55(0.26) | 0.728 |
| D-dimer (postop. day 1-24h) (ng/mL) | 1.87(0.76) | 2.43(1,44) | 0.196 |
| Fibrinogen (preop) (mg/mL) | 343.4(82.3) | 330.2(82.5) | 0.535 |
| Fibrinogen (postop. day 1-24h) (mg/mL) | 394.8(108.1) | 387.34(108.0) | 0.632 |
| INR (preop) | 1.20(1.0-1.7) | 1.24(1,0-1.9) | 0.108 |
| INR (postop. day 1-24h) | 1.26(1.1-1.7) | 1.29(1.1-1.90) | 0.057 |
| Hemoglobin (mg/dL) (preop) | 13.1(10.8-15.5) | 12.8(8.0-16.3) | 0.750 |
| Hemoglobin (mg/dL) (postop. day 1-24h) | 10.3(7.3-12.3) | 10.4(7.1-13.2) | 0.293 |
| Platelet count (preop) ($x10^9$/L) | 269(142-589) | 246(132-487) | 0.579 |
| Platelet count (postop. day 1-24h) ($x10^9$/L) | 150.5(97-325) | 168(99-453) | 0.252 |

*$P<0.05$ statistical significance, INR: International normalized ratio, Hgb: Hemoglobin

## Discussion

Nowadays, many physiological changes related to cardiopulmonary bypass occur during CABG surgery, which include depletion of hemodilution and coagulation factors, decrease in the number of thrombocytes, thrombocyte dysfunction, and hemorrhage due to severe fibrinolysis. Excessive hemorrhage is observed after CABG operation in 11% of the patients. Within 24 hours after the surgery, 3-5% of the patients experience blood loss more than 2 liters and the incidence of reoperation due to hemorrhage between 4 and 5%. Bleeding depends on the deterioration of physiological mechanisms postoperatively in more than 50% of the patients [14,15]. Mortality increases by 3-4 times together with the re-exploration, the reasons for which include higher incidence of renal failure, higher need for mechanic ventilation support and higher incidence of sepsis, and increase in hospital stay [15,16]. The increase in the postoperative need for blood and blood product transfusion also increases the complication risk and negatively affects the patient's quality of life. Moreover, it prolongs hospitalization and ICU stay durations and increases hospital costs [4-6].

The use of TA in the treatment of common microvascular hemorrhage seen after coronary artery bypass operations is getting gradually more popular [11,12,15]. The anti-fibrinolytic effect of tranexamic acid occurs after the reversible blockage of the lysine-binding zones on the plasminogen molecules. There still is no consensus in the literature on the dose of TA and there are various protocols (50, 100 and 150 mg/kg). The implementation times also vary (before, after and both before and after CPB) [17]. In another study, 32ºC systemic hypothermia instead of 28ºC enabled the increase in effectiveness of tranexamic acid and decrease in doses [18]. In another study, it was determined that TA was administered intravenously at the dose of 50mg/kg following protamine and heparin neutralization after CPB [21]. In our study, 10mg/kg TA was given intravenously before CPB in the TA group and the results were compared to those of controls. We determined that in patients who used LMWH until the day before surgery and had CABG, postoperative hemorrhage and the amount of blood transfusion statistically significantly decreased. In another study, patients to undergo coronary artery bypass surgery and using aspirin (acetylsalicylic acid) until the operation were given 30mg/kg TA [20]. In some of the studies, TA was administered as bolus before the anesthesia induction [21,22]. In this study, TA was administered intravenously in a single dose bolus just before CPB. Despite the differences in TA practices, it was shown that postoperative hemorrhage and the amount of blood erythrocyte suspension transfusion decreased in a comparable manner.

The risk of thromboembolic event development and thrombus formation are significant adverse effects related with the use of TA. While using TA, complications secondary to thrombus formation in coronary arteries, such as ischemic events, pulmonary thromboembolism, cerebrovascular events, myocardial infarction, and deep vein thrombosis may develop [23,24]. No complication related with the thrombus formation and thromboembolism was observed in our study and some of the previous studies [19,25]. This is because complete systemic heparinization during open heart surgery prevents the formation of thrombotic complications of TA. Coagulation returns to the normal only 12 hours after cardiopulmonary bypass, but TA's plasma half-life is 80 minutes [10,17]. It was reported that the postoperative seizures might be seen in recent periods [26]. In this study, it was remarkable that no seizures were observed in any of the 30 patients. This result is similar to those obtained in other studies [19,25]. However, it was also reported that these results were achieved when using TA doses higher than 50 mg/kg [19,26].

In the study performed by Wong et al. [27], heart surgery patients with high transfusion risk were divided into two groups and the effects of aprotinin and TA were examined. No

difference was observed between these patients in terms of the use of blood and blood products and loss of blood. Although it is stated that the aprotinin is an expensive medication, it is now not in use because of its adverse effects [7,8]. In the present study, we observed that fibrinogen was maintained at similar levels with the preoperative values in both groups, and that it remained at the similar levels to the preoperative values in the TA group. Moreover, although D-dimer, one of the breakdown products of fibrin significantly increased on the first postoperative day in both groups, its increase was at a lower level in TA group. In a study conducted by Chauhan et al. [28], TA was compared to aminocaproic acid in cardiac surgery cases. Similar to the results of the present study, the coagulation test results showed that fibrinogen was protected better and the fibrin breakdown products were at lower levels. In numerous studies and meta-analyses, this anti-fibrinolytic medication was shown to reduce postoperative hemorrhage [8,10,17]. In this study, postoperative hemorrhage decreased in patients using TA and the fibrin breakdown products were found to be at low levels.

**Limitations**

This study was conducted in a small group of patients, and a double-blinded study design was not employed, which may have reduced bias. There is need for randomized controlled studies in larger groups.

**Conclusions**

In CABG operations with high risk of bleeding due to the preoperative use of low molecular weight heparin (DMAH), a statistically significant decrease in the amount of postoperative bleeding and the amount of transfused blood was detected in a group of patients receiving TA intraoperatively. Side effects related to TA administration were not observed. TA is a safe drug that reduces postoperative bleeding in patients using DMAH undergoing CABG operations.

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