COMPARISON OF SYSTEMIC AND LOCAL APPLICATION OF TRANEXAMIC ACID ON BLEEDING AND BLOOD TRANSFUSION NEED IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS

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Abstract: Comparison of the effect of systemic administration and transamine position on bleeding and the need for blood transfusion in patients undergoing coronary artery bypass surgery, goals, comparing the amount of bleeding and blood transfusion in 48 hours after surgery, design by random sampling by blocking, 180 patients will enter this study, How to do after seeking consent, 60 patients will be assigned to the systemic intervention group and 60 patients will be assigned to the intervention group and 60 patients will be in the control group. Entry requirements: All patients undergoing coronary artery bypass graft surgery for the first time. Exclusion criteria in patients with renal failure, anemic patients, patients with low cardiac output, patients with coagulation disorder, and intervention; patients undergoing anesthesia induction of 10 mg / kg of body weight within the regimen Receive a dose of 1 mg of the drug per kg body weight per surgical hour until the end of surgery, after the surgery. In the local group, 1 g of the transamine solution was dissolved in 100 ml of chloride. 0.9% at the end of the surgery in the pericardial cavity of the heart. 60 patients will not receive the drug control group, all of the surgery will be performed by two surgeons under the same anesthetic and bypass procedure, the main outcome of the cerebral hemorrhage 6, 12, 24, 48 hours after surgery, and the rate of blood transfusion in 48 hours. From surgery.

Key word: Local Tranexamic acid, systemic tranexamic acid, coronary artery bypass surgery, bleeding, blood transfusion

Introduction. Despite the recent advances in surgical techniques and post-exposure care, the amount of post-surgical hemorrhage remains around 600-120a0 ml, of which about 25-45% of these cases are fibrinolysis (1, 2). This is while the outflow of blood also exacerbates fibrinolysis (3, 4). Preventive use of fibrinolysis inhibitors (aprotinin and lysine analogues such as aminocaproic acid and transamine) has been common in cardiac surgery to reduce bleeding and the need for transfusion of blood since the 1980s (5). Currently, trancean amine is less expensive and has a higher immunity level than aprotinin, and also 7 to 10 times that of aminocaproic acid, the most commonly used anti-fibrinolytic drug (6-9). This drug, while significantly reducing the concentration of plasminogen, slows down the fibrinolysis process, because although plasmin is still produced, it is inhibited and can not bind to fibrin (10-12). Studies also show anti-inflammatory effects and improve platelet function in patients receiving the drug (15-15). Although systemic use of transamine has been effective in heart surgery and is recommended by the Association of Thoracic Surgeons and the Association of Cardiology Anaesthesiologists, the best way to prescribe it remains to be discussed. (16-18).
According to studies, concerns about the complications observed following systemic administration of the drug, including seizure and thromboembolic complications, have increased (22-19). On the other hand, based on the natural characteristics of the pericardium that prevents the release of substances, topical application of various drugs in the pericardium cavity can increase the desired therapeutic effects of the drug without systemic absorption (1, 23). In the case of transamin, topical administration in the pericardial cavity to avoid systemic complications has had effective results in reducing bleeding (9, 16, 19, 24). Some studies have also reported the need for transfusion of blood products in topical use (5, 9, 19). The topical use of this drug in other cardiovascular and other therapies, including bladder bladder surgery, gynaecologic surgery, oral mouth, and surgeries Otolaryngeal ovary and thrombosis, as well as hemiartheroplasty, have been effective. (25-29).
The aim of this study was to compare the effect of systemic and topical administration of transamineal agents on bleeding and the need for blood transfusion in patients undergoing elective CABG surgery on-pump.

Method

With the approval of the ethics committee of Shiraz University of Medical Sciences and the registration of the IRCT IRCT2013071210311N3 IRCT, this randomized, double blind randomized clinical trial study was conducted on 180 patients with electrocardiogram Who have been undergoing CABG surgery for the first time in the two hospitals of Namazi and Martyr Faghihi from February to August. The primary objective of this study was to determine the amount of bleeding and secondary goals including the measurement of blood transfusion, mechanical ventilation, patient's residence in the ICU, death and thromboembolic complications (early blockage of coronary arteries, stroke, deep vein thrombosis, embolism, seizure), and They were compared in two ways: the administration of systemic and topical transamin. Exit criteria for exclusion criteria were from patients with combined / cadaveric / emergency procedures / haemorrhagic disorders such as hemophilia or platelet counts ≥100,000 / renal failure ≥ 1.5 cr / history of transaminase-peritoneal allergy Cardiac Down (30EF≤) / Anemic (11HB≤) / History of antiplatelet drugs (aspirin / clopidogrel) within 5 days before surgery / history of heparin infusion 24 hours prior to surgery / history of oral anticoagulation (warfarin) and non-inflammatory drugs Non steroid anti inflammatory drugs (steroids) within 3 days before surgery.

Patients were randomly assigned to one of the three groups using permutation blocks.
The first group (systemic): 60 patients entered into this group received normal 10 mg / kg 10 transamine in 20 ml of normal saline in 20 minutes after induction and before incision, followed by infusion of 1 mg / kg / hr The drug was taken as a solution in 50 ml normal saline until the end of the treatment. At the end of the surgery and before closing the sternum, 100 ml of normal saline was poured into the surgical area and the pericardial space. After 15 minutes, the casts of the tubes were removed and drainage was performed.

Group II (topical): 60 patients entered this group after induction and before skin incision, similar to the systemic boluses and infusion group, with the difference that only normal saline was used instead of the medication. At the end of the surgery and before closing the sternum, 1 g of transamine was dissolved in 100 ml of normal saline in the surgical area and the pericardial space. After 15 minutes, the clusters of the chest tubes were removed and drainage was performed.
Group III (control): 60 patients entered into this group received both the systemic and topical methods at similar times and the same values as normal saline alone.
According to a study conducted in 1995 on various systemic doses of transamine (from 2.5 mg / kg to 40 mg / kg) (19), the minimum and effective dose of this drug was 10 mg / kg bolus In the next infusion, mg / kg / hr 1 was expressed, as in the topical method, the first result was 1 g of drug (21). These values are used as the minimum effective dose of the drug in two different methods of administration in this study. Pre-prepared solutions, not prescription drugs (anesthetist nurse and scrub nurse), were aware of the contents of the solutions, nor were the nurses of the special department aware of the grouping of patients. Two heart surgeons using the same surgical technique in this study have been used. Anesthesiologists and perfusionists from these two anesthetic management centers and CPB all patients in accordance with a predetermined protocol.
Anesthesia induction was performed using midazolam (0.15 mg / kg), sufentanil (5 μg / kg), pantothenal (3 mg / kg), morphine (0.1 mg / kg) and fulmin (0.15 mg / kg). Propofol is also used to maintain anesthesia. Prior to CPB, 3,000 u / kg of heparin was prescribed and 3 minutes later ACT was investigated, the oxygenator used for CPB, Hepari coated, however, was added to the primer solution to ensure heurinisation of all levels and pathways of about 5000 heparins. The primer solution contains a serum lingerie ringer veiner. Generally, hypothermic cardioplegia is a combination of blood, crystalloid and anti-gradient for cardiopulmonary artery, and the LIMA (Left Internal Mammary Artery) artery and the saphenous vein for the treatment of coronary arteries. Eventually, in order to reverse the effect of heparin, 1 mg of protamine was administered per 100 ui heparin and transferred to the intensive care unit after closure of the patient's chest.
All demographic characteristics of the patients, such as age, sex, BSA, history of underlying diseases (diabetes, hypertension, hyperlipidemia, heart attack, DVT, COPD) were collected at the time of admission. Blood and coagulation tests including pre-operative HB / CR / PT / PTT / INR were recorded immediately after entering ICU and 24 hours after surgery.
All cases were recorded and checked to ensure that the conditions were the same during operation such as duration of surgery, CPB duration, aortic cross-clamping time, number of casts, duration of sternum closure (from the time of injection of protamine to the last skin surgeries) . In ICU, the drainage of chest tubes at 6, 12, and 24 hours after surgery, as well as the length of stay there and the mechanical ventilation time were recorded. Transfusion of blood products to patients is also done according to a protocol that prescribes tuberculosis with HCT 30 and FFP in the case of 1.5 INR in patients with active bleeding and platelet administration with platelet levels below 70,000 and continued. Blood is done (30). In the case of re-implantation, reexploration has been excluded from the study with a sudden increase in drainage of chest tubes (300 ml / hr), or the occurrence of any postoperative complications, including thromboembolic complications and death.
Statistics Analysis
All data were analyzed using R software version 3.3.1. First, Kolmogorov-Smirnov test was used to evaluate the natural distribution of data. In order to determine the intra-group and inter-group differences in the distribution of measured variables, if the data are normal, Repeated measures, ANOVA and, if not normal, Friedman test) And kruskal-wallis test. Chi-square test was used to test the demographic and clinical variables in two groups. . P value <0.05 was considered as a significant level for all statistical analyzes.

Results
The three groups included in this study were comparable in terms of preliminary demographic data and risk factors (including underlying diseases) (Table 1).

Table 1. Patients Demographics and Cardiac Risk Factors.

Parameters	Control Group (n=59)	IV Group (n=57)	Top Group (n=59)	P-Value
Age(y)	59.76±10.31*	62.57±8.58	62.05±10.23	0.157
Sex (males/females%)	59.3/40.7	49.1/50.9	45.8/54.2	0.307

Weight(kg)	67.15±10.93	66.26±11.75	66.25±11.20	0.775
BSA(m²)	1.72±0.14	1.68±0.15	1.66±0.16	0.136
EF(%)	51.27±6.66	49.21±7.66	51.01±6.68	0.265
DM(%)	23(39)	20(35.1)	29(49.2)	0.273
HTN(%)	38(64.4)	36(63.2)	35(59.3)	0.853
HLP(%)	23(39)	31(54.4)	31(52.5)	0.199
COPD(%)	11(18.6)	8(14)	9(15.3)	0.815
MI(%)	11(18.6)	18(31.6)	12(20.3)	0.213

*Mean±Standard Deviation
Abbreviations; BSA: body surface area, EF: ejection fraction, DM: diabetes mellitus, HTN: hypertension, HLP: hyperlipidemia, COPD: chronic obstructive pulmonary disease, MI: myocardial infarction

Also, the comparison of surgical parameters including the number of casts, the use of the LIMA artery, the duration of operation, the duration of the aortic aberration and cross-clamping, as well as the duration of sternum closure (from the beginning of the injection of protamine to the last skin surgeries), showed that three groups In the operating room, the conditions were the same and there was no significant difference between the three groups (Table 2).

Table 2. Intra-0perative Data.

Parameters	Control Group (n=59)	IV Group (n=57)	Top Group (n=59)	P-Value
Number of Grafts (no)	2.94±0.70*	2.89±0.58	2.71±0.67	0.095
Use of LIMA (% used)	89.8	89.5	88.1	0.953
Surgical time (min)	135.93±16.30	133.15±17.46	133.72±14.87	0.669
Cross-clamp (min)	31.45±9.44	28.98±6.6	29.23±8.34	0.325
CPB (min)	50.47±10.41	51.40±9.15	49.57±10.95	0.341
Sternal-closure Time (min)	38.30±10.97	35.35±9.25	34.40±7.99	0.111

*Mean±Standard Deviation
Abbreviations; LIMA: left intenal mammary artery, CPB: cardiopulmonary bypass.

Measured laboratory parameters included hemoglobin, creatinine, prothrombin time, partial thromboplastin time, international normalized ratio.

Before surgery, immediately after entering the ICU, and the day after operation, in Table 3, the comparison was made between the three groups except PTT factor (P = 0.008) and INR (P = 0.017)

Table 3. Hematologic Measures in Time1(Pre-operative), Time2(Immediately Post-operative), Time3(Post-operative Day 1).

Parameters	Control Group (n=59)	IV Group (n=57)	Top Group (n=59)	P-Value

HB(g/dl) Time1 Time2 Time3	13.06±1.9* 10.5± 2.8 11.1± 1.05	13.05±1.1 10.8± 1.3 11.45± 1.1	12.40±1.8 10.3± 1.4 11.05± 1.1	0.06 0.65 0.24
Cr(mg/dl) Time1 Time2 Time3	1.08± 0.2 1.0± 0.2 1.18± 0.37	1.05± 0.1 0.94± 0.2 1.15± 0.26	1.04± 0.2 1.16± 0.39 1.16± 0.39	0.47 0.42 0.82
PT(s) Time1 Time2 Time3	12.9± 0.7 14.02± 0.6 15.16± 1.2	13.2± 0.7 13.9± 0.7 15.53± 1.27	13.09± 0.8 13.8± 0.6 15.24 ±1.56	0.10 0.79 0.11
PTT(s) Time1 Time2 Time3	31.4± 5.2 36.2± 4.02 47.9± 22.1	33.1± 4.2 34.1± 3.8 46.3 ±24.1	32.8± 5.9 35.3± 4.1 44.8± 22.4	0.20 0.008** 0.32
INR Time1 Time2 Time3	1.09± 0.1 1.32± 0.15 1.33± 0.15	1.12± 0.1 1.39± 0.14 1.34± 0.16	1.54± 0.3 1.41± 0.13 1.31± 0.16	0.45 0.017*** 0.68

*Mean±Standard Deviation
Abbreviation; HB: hemoglobin, CR: creatinine, PT: prothrombin time, PTT: partial thrombpplastin time, INR:international normalized ratio.
**(Local-Systemic p=0.002)
***(Local-control p=0.030) ,(Local-systemic p=0.007)

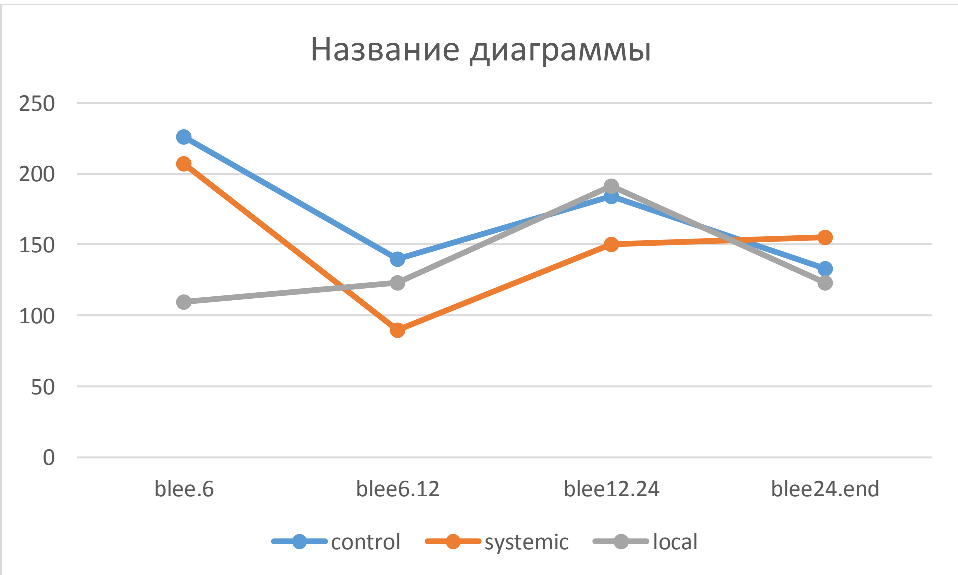

Fig 1. Pos-op Blood Loss/Time Interval

At the second time of measurement, there is no significant difference between the groups .The amount of postoperative bleeding is shown in Fig. 1, which shows that the average drainage of the chest tubes in the first 6 hours immediately after surgery (which is a golden age) is between the three control groups (227.26 ± 187.16) and the systemic (207.01 ± 180.63) and localized (109.32 ± 104.00) had a significant significant difference (p = 0.0001), At the same time, the

results of the comparison between the groups indicated that the bleeding in the local group was lower not only compared to the control group (p = 0.0001), but even less than the systemic group (p = 0.002). In the follow-up drainage study, at 6 hours after surgery (12 hours), the mean of bleeding in the control groups (139.83 ± 122.39) and systemic (89.47 ± 63.20) and topical (122.88 ± 85.76) groups was statistically significant (p <0.001). p = 0.039). Compared with the control group (p = 0.027) and compared with the patients in the topical group (p = 0.027), they had less bleeding than the patients who received systemic transamine in the first 6 hours. After 12 hours of surgery, there was a decrease in the rate of bleeding between the groups, so that at the time (12-24 hours), the mean of bleeding in the control group (183.89 ± 154.37) and systemic (150.00 ± 116.49) and topical (191.52 ± 118.23) showed no significant difference (p = 0.106). From the second day (24-end), the mean of bleeding in the control group (133.65 ± 97.64), systemic (155.26 ± 161.93), and localized (91.59 ± 122.88) were the mean of the previous time, with a decrease in the amount of bleeding in There was no significant difference between the two intervention groups as compared to the control group (p = 0.669).
The results of the study of cumulative bleeding during the first 24 hours after surgery and general bleeding (from the beginning to the exit of the chest tubes) indicate that the rate of bleeding in the patients receiving topical transaminazole has significantly decreased compared with those receiving placebo (Respectively 0.011 p = and 0.010 p =). Also, although the rate of cumulative hemorrhage in patients receiving intra-erythropoietin transamine was always lower than that of placebo recipients, this difference was significant only at the end of the first day (p = 0.030) and not in total (p = 0.067) . In comparison with the two intervention groups, the results indicated that the effect of topical administration of the drug on the reduction of cumulative bleeding was higher in the first 24 hours (p = 0.73) and in total (p = 0.47) than in the systemic administration, The statistical significance was not significant (Fig. 2)

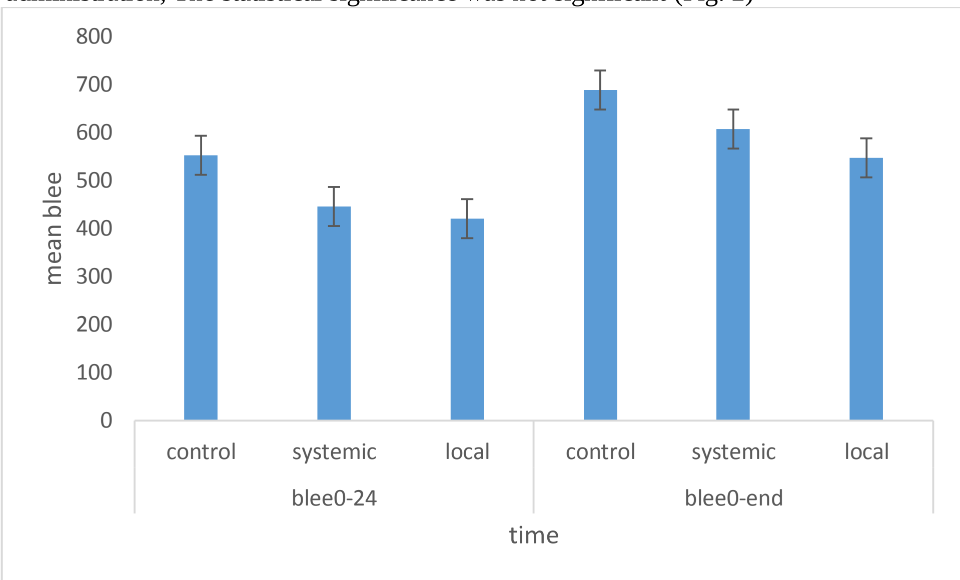

Fig 2. Post –op Blood Loss/24 hours and total.

0-24: control(median of 552.88±294.38), systemic(median of 446.49±257.71), local(median of 421.18±222.87)
0-end: control(median of 688.98±317.18), systemic(median of 607.01±337.59f), local(median of 547.45±246.25)

According to the results of this study, using the protocol used for blood transfusion and blood products, on average 48 hours after coronary artery bypass graft surgery, approximately one unit per injection was given to each patient, although this value was in The two groups of drugs were less than the control group, but there was no significant difference between the two groups. No quantities of platelet products were used in any of the patients in the 3 groups of comparison and did not differ significantly in the consumption of FFP (Table 4).

Table 4. Post-operative Blood Product Transfusion.

Parameters	Control Group (n=59)	IV Group (n=57)	Top Group (n=59)	P-Value
P.R.C	1.169±1.1*	0.80±0.8	0.89±0.8	1.41
FFP	0.84±0.3	0.52±0.2	0.84±0.4	0.88
PLT	0	0	0	-

*Mean±Standard Deviation
Abbreviation: P.R.C, packed red cell; FFP, fresh frozen plasma; PLT, platelet

On the examination of conditions and postoperative complications such asIntubation time (hours), ICU stay (day), MI, CVA, DVT, Seizure, Reexploration, Mortality

It seems that the average time of mechanical ventilation (intubation time) was lower in the two intervention groups than the control group, but in the end, the three groups did not have a significant difference in mechanical ventilation and ICU stay. It should also be noted that the most complications observed belong to the patients in the systemic group, resulting in a patient receiving DVT, one after Reexploration and another patient due to the death of the study.

Among the patients in the 3 groups, only one CVA case was reported that belonged to the local group and was excluded, and also in the control group, a case of death, which led to the deletion of this patient from the study. No cases of MI and seizure have been reported among all patients (Table 5).

Table 5. Post-operative Data and Complications

Parameters	Control Group (n=59)	IV Group (n=57)	Top Group (n=59)	P-Value
ICU stay (day)	1.28±0.6*	1.38±0.7	1.37±0.74	0.81
Intubation time (hours)	13.54±7.6	12.64±6.4	12.67±5.8	0.80
MI (No of patients)	0	0	0	
CVA (No of patients)	0	0	1	
DVT (No of patients)	0	1	0	
Seizure (No of patients)	0	0	0	
Reexploration (No of patients)	0	1	0	
Mortality (No of patients)	1	1	0	

*Mean±Standard Deviation

Discussion & Conclusion

On-pump heart surgery is associated with more coagulation disorders than other surgeries. Fibrinolysis has been reported as the cause of 25-45% of post-surgical hemorrhage. (2) Outward circulation also leads to a significant increase in fibrinolysis, which is indicated by increasing the concentration of plasmin and FDP (Fibrin degradation product) and These two factors have both adverse effects on platelet function (4). On the other hand, reopening of the chest after bleeding can be an independent and potent factor for the occurrence of unpleasant outcomes following heart surgery, including risk factors such as age, low BMI, non-elective patients, and more than 5 anastomosis numbers. (31, 32). As a result of these factors, the rate of blood transfusion in the heart surgery is 30% to 70% more than other surgeries, which itself has many effects. (23, 33, 34) Previous studies in the evaluation of intra-regimen use of transamine Postoperative bleeding and need for blood transfusions.

Also, some investigations have investigated the effect of topical transamine in the surgical field on the rate of hemorrhage and hemostasis, as well as the avoidance of systemic thromboembolic complications. According to our study, systemic administration of 10 mg / kg of transamine medication and infusion of 1 mg / kg / hr to the end of operation in elective patients undergoing coronary artery bypass grafting is effective in reducing postoperative bleeding, especially at a time interval of 12-12 hours. Horrow, in its protocol, expresses at least 10 mg / kg of systemic transaminase systemic effects in heart surgery and infusion of 1 mg / kg / hr to 12 hours postoperatively. According to the results of this study, these values of the drug significantly reduced the amount of bleeding Within 12 hours of cardiac surgery, the systemic dose in our study is also derived from this study and our results confirm this. (35).

It should be noted that when comparing higher doses of transamine (20, 50, and 100 mg / kg), there was no difference in the amount of bleeding during operation and 24 hours after surgery (12, 36). Therefore, it can be said that higher doses do not necessarily have a greater effect on the reduction of bleeding. It should be noted that the differences in the type of operations and the removal or inclusion of high risk patients may be influenced by the systemic administration of the drug, while the pharmacokinetic effects of intravenous administration of this drug are also strongly influenced by CPB (16, 37) Also, our findings suggest that the rate of bleeding in patients receiving 1 g of topical transaminazole in the pericardial cavity during the first 6 hours after surgery was not only comparable to placebo recipients, but even compared to patients receiving systemic transamine Also, it has fallen further. This rapid reduction in the amount of early post-op infection has led to a significantly lower left ventricular hemorrhage rate, even though there is less effect on subsequent periods of time. According to these results and the study of De Bonis, which showed that no drug was absorbed into the blood by laboratory tests of blood, it can be argued that the drug in the pericardium has an anti-

fibrinolytic effect and localized fibrinolysis control can also reduce the rate of postoperative drainage Effectively reduce (9).
On the other hand, regarding the role of CPB, although the fibrinolysis exacerbation is a complication, the results show that the use of 1 g of topical transaminazole in CABG patients by off-pump with a significant reduction in bleeding during the first 24 hours after surgery (24). Thus, it can be argued that obtaining similar results in the local application of the same values of transamine in CABG patients both on-pump and off-pump can confirm the greater role of fibrinolysis activity in the pericardium compared to systemic fibrinolysis. The results of topical use of transamine in our study and other studies indicate that not only in CABG but also in other cardiac injuries, this drug can be effective in reducing postoperative bleeding, as well as in topical administration of transamine to aprotinin Is effective in reducing the amount of bleeding after heart surgery and is economically feasible (1, 38) in clinical interventions recently evaluated by the effect of topical transaminomal lacquer versus pericardial lavage with normal saline , There was no difference in the rate of bleeding 12 hours after the operation (18).

In explaining the results, it can be noted that all patients in the study received 2 grams of systemic transamin (1 gram before skin incision and 1 gram after CPB), while in contrast to our protocol, which was administered topically for 15 minutes In the space of the pericardium and then suctioned, in this study, topical use of the drug was only effective for one minute and was used only for lavage. Therefore, our recommendation for topical use of transamine in the pericardium is to give at least 15 minutes to the medication. In our study, for the first time, two systemic and topical administrations of transamine (with a minimum effective dose) were compared in cardiac surgery. According to our results, the study of the amount of bleeding by time intervals shows that in the first 6 hours after surgery, the topical effect of the drug and in the 6 hours after the operation had a systemic effect of the drug on the opposite method, and the maximum effect of both methods of administration of the drug up to 24 The hour will be after the operation. Perhaps the cause of this difference is related to the continuation of systemic systemic infusion until the end of the operation and the administration of topical doses at the end of the procedure, as well as the short acting effect of the drug due to lack of absorption in the systemic circulation.
In order to achieve the second goal of this study on the rate of blood transfusion, we should say that according to our results and other studies, the systemic dose of transamine has no role in the rate of blood transfusion and blood products. In the event of higher systemic doses, the results are also variable (contradictory). (17, 36). Although the larger sample size in the studies seems to be relevant to the study of this factor (39). Unlike De Bonis, who for the first time reported a decrease in blood transfusion requirements for topical use of 1 g of transamine in cardiac surgery (9), Our study results suggest that although the average number of injected blood units in these patients has decreased, this effect is not significant. This difference in the results of the effect of transamine on blood transfusion can have many causes, including the difference in blood transfusion protocols and even the lack of compliance by the specialist staff, the initial hematological status of patients, as well as the difference in sample size and elimination Or the entry of overweight patients will be effective in the study.
In addition, it should be noted that although drainage of chest tubes is a risk factor for blood transfusion, studies show that it is not necessarily a high rate of drainage predicting blood transfusion (29). It should also be noted that, according to our study, the mechanical ventilation and residence time of patients in the icu section are not affected by local and systemic transamin injection. Since the average duration of sternum closure (from the beginning of protamine to the closure of sternum skin) in both groups of medication has been less controlled, it can be said that this time can be an important predictive factor in the estimation of the bleeding status of patients after cardiac surgery. Despite concerns about the risk of developing tamponade over topical use of medication, there is no evidence that the administration of transamin in the pericardium can increase the risk of developing tamponade.
The occurrence of DVT in the patient receiving systemic administration of the drug (with a minimum dose) suggests that the complications of thromboembolic treatment should be avoided. Disturbing results The recent study of systemic systemic doses of transamine (mg / kg) (24) suggests a doubling in the incidence of seizure and mortality in these patients. However, the mechanical ventilation and residence time in ICU has also decreased in these patients (20). However, since this study was conducted in all types of cardiac surgeries, it should be noted that differences in surgical techniques, high risk of embolic events, and exacerbation of inflammatory response due to prolonged CPB in complicated and open heart surgery have had an impact on these outcomes. They are What is always recommended is that the benefits of systemic administration of anti-fibrinolytic drugs should be weighed against its side effects. In general, topical use of 1 g of transamine medication as well as systemic use of 10 mg / kg and infusion of 1 mg / kg / hr up to the end of the operation reduces bleeding to 24 hours following CPB coronary artery bypass graft surgery. Topical use of 1 g of transamine medication may be effective in reducing esrly post-op period bleeding without complications such as tamponade, renal dysfunction and thromboembolic events. Also, although both blood pressure ($P < 0.001$) was reduced with both drug administration methods, it was not statistically significant. Since this comparison between the two methods of prescribing transaminase has not been studied in any cardiac surgery study, more studies are needed with a larger sample size in order to achieve conclusive results.

Limitations
The use of cardiac surgeons with a completely similar technique and the collaboration of anesthesiologists, perfusionists and ICU nurses in complying with the protocols has been one of the limitations of this study. Also, the inability to

check the blood of patients receiving topical transamineal medication was not allowed to comment on the absorption or systemic absorption of this drug in this study.

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