Effect of Amount & Different Intravenous Tranexamic Acid on Postoperative Bleeding in Patients Undergoing Coronary Artery Bypass Graft (*CABG*)

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Abstract: CABG is one of the most common major surgical procedures. The most important complication is bleeding in CABG under *Cardio pulmonary bypass* (CPB). Tranexamic Acid, an anti-fibrinolytic drug is hydrophilic and a competitive and reversible convert plasminogen to plasmin can be prevented. That can be administered orally or intravenously during certain procedures to reduce bleeding. The most important complication of CABG in patients undergoing Cardio *pulmonary bypass* (CPB) is bleeding, 15 to 20 percent of the consumption of blood products in cardiac surgery patients is about 5% of patients with excessive bleeding due to surgery needs to be re-operation that may increase morbidity and mortality. Various methods to reduce bleeding in CABG surgery around the infusion of blood products and injections of anti-fibrinolytic drugs (Tranexamic acid) are. In this study, treatment with different doses and different methods Tranexamic acid in order to find the minimum effective dose and the injection method in controlling bleeding and reducing the need for transfusion of blood products has been used.

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1. Introduction

The most important complication of CABG in patients undergoing (CPB: *Cardio pulmonary bypass*) is bleeding, 15 to 20 percent of the consumption of blood products in cardiac surgery patients is about 5% of patients with excessive bleeding due to surgery needs to be re-operation that may increase morbidity and mortality. Various methods to reduce bleeding in CABG surgery around the infusion of blood products and injections of anti-fibrinolytic drugs (Tranexamic acid) are.

In this study, treatment with different doses and different methods Tranexamic acid in order to find the minimum effective dose and the injection method in controlling bleeding and reducing the need for transfusion of blood products has been used.

CABG is one of the most common major surgical procedures (1-2) the most important complication is bleeding CABG under CPB (3). Although blood transfusions and blood products to control bleeding after CABG major bleeding is the control and treatment, 15%-20% of the consumption of blood products associated with cardiac surgery (4-11).

Transfusion of blood products in cardiac surgery increases risk the infection and sepsis (6), lung dysfunction, prolonged mechanical ventilation (13), hospital mortality (9) short permanent quality of life after surgery (5).

Tranexamic Acid, an anti-fibrinolytic drug Hydrophilic is a competitive and reversible (8) blocks the conversion of plasminogen to plasmin, which can be administered orally or intravenously during certain procedures to reduce bleeding (2).

Tranexamic acid has been reported that anti-inflammatory effects on its chemical form, and therefore its chemical form in parotid surgery, CABG surgery under general use and hemophilia (1).

Tranexamic acid primarily filtered by the glomeruli, and over 95% of the excreted unchanged in urine is (1) Symptoms seen in the drug include the following:

A. Hypotension in rapid injection. (Faster than 1 CC in minute) intravenously and orally, but not seen.
B. Gastrointestinal symptoms include nausea, vomiting, abdominal pain and diarrhea, which decreased the effective dose, is also lower.
C. Thrombocytopenia, prolonged bleeding time (10).
D. The main risk of Thromboembolism complications of drug inhibition of fibrinolysis, which is a natural defense mechanism against thrombosis formation, is caused (7-12).

Therefore in this study with different doses and different ways to remedy acid Tranexamic find the minimum effective dose and the injection control

bleeding and reduce the need for transfusion of blood products in CABG surgery has been used.

2. Materials and Methods

This study was a randomized clinical trial in 2011 on 70 patients with ASA Class 2-3 age group 50-70 years and due to arteries disease in coronary heart surgery Ahwaz JundiShapur University of Medical Sciences, Golestan Hospital Affiliated to have been a candidate for elective CABG. Divided into blocks and each block of seven patients randomly treated with a combination of fast or slow infusion technique and dose (10-15 & 20mg/kg) were.

Control group not given drug. The numbers of patients in each 10 were in group therapy.

In all groups studied was a heart surgeon, and hepatic and renal disease in patients with no history of ant platelet and anticoagulant drugs at the time of the cut and coagulation tests were normal before surgery. The night before surgery in all patients after surgery, talk to them and explain the procedures for obtaining informed consent from patients has been.

One hour before surgery as premedication to all patients' 0.1 mg/kg morphine is injected into muscle.

5cc/kg surgical bed volume of normal saline solution as *Compensatory* ***volume expansion*** of the volume was injected into the patient, monitoring should include (CV. line-Arterial line-ECG monitoring - Pullsoximetry-) and establish a baseline ABG was sent to patients.

Induction of anesthesia drugs, midazolam, sufentanil, sodium thiopental and atracurium and intubation performed in the same circumstances would do. Patients divided into seven blocks and seven bits in each block, patients randomly treated with a combination of two methods of rapid infusion (over 20 minutes before incision and after Rivers heparin) and slow infusion (over 4 hours during surgery) Tranexamic 10-15-20mg/kg acid with three doses plus 300cc normal saline) were included.

The seven bits of each block as a patient in 300cc normal saline as a placebo was given. Maintenance of anesthesia was in patients with midazolam, atracurium and sufentanil.

Patients transferred to ICU after cardiac surgery, 6-4 hours after surgery, patients were Rivers and X-Tube. All patients with ON PUMP and hypothermia during cardiac surgery were 32 degrees Celsius.

The amount of heparin and protamine sulfate was used based on the same weight. Criteria for measuring the blood volume of postoperative bleeding in patients with chest bottle within 24 hours after the separation time to time is measured and recorded. The amount of blood product transfusions, incidence of side effects, low levels of platelets and coagulation tests within 24 hours after surgery were measured in seven groups, were recorded and compared. Total operative time and pump time were recorded and were compared.

Statistical Software was performed by data processing for quantitative variables are expressed as mean and standard deviation and maximum and minimum data was used. Qualitative variables were used for the percentage and number of P-Value <0.05 was considered significant.

3. Results

Comparison of the bleeding (6 hours) - (6-12 AM) (12-18PM) (18-24 hours) and total time of 24 hours after surgery showed a significant difference between control group and other groups the (P_V=0.0001).

The second significant difference between bleeding 6 hours (6-12 pm) after the dose groups10-15 & 20mg/kg)) method was performed with a slow infusion of 20 mg kg and the infusion was rapid. Within 24 hours after surgery to control bleeding from other groups has had an average 500cc.

Comparison between the control group received blood products and other studies show a significant difference (P_V=0.26).

Injection between groups with different doses and methods of receiving blood products was not significant difference (P_V=0.1).

Groups were studied in 9 patients experienced adverse events (13.88%) and minimal side effects that are not significant in the group with the slow infusion in groups so that the injection of acid Tranexamic 10-15mg/kg and no slow not shown any symptoms.

Total time of operation and on-pump group showed no significant difference (P_V=0.66).

Injection Tranexamic with periodic acid, 15 mg kg and with a slow infusion method in reducing the incidence of adverse bleeding and Transfusion blood products within 24 hours after CABG surgery has the best performance.

To compare the mean age of patients (seven groups) of ANOVA was used with (P_V=0.819) significant differences between age groups was found.

Patients (58.6%) and males (41.4%) were female. The average age of men (58±9.6) the average age of women (59±7.43) the t-test showed no significant difference in age between the sexes (P_V=0.45).

The mean BMI ^{2} in different groups (seven groups) of ANOVA were significant differences between groups in BMI was observed P_V = 0.184.

The mean BMI in the total study population (27.48±4.3) and men (26.78±3.9) and women (28.34±4.7) was.

In this study 64 patients (IHD =91.4%) and 41 patients (MI= 58.6%) patients. Of 36 patients (51.4%) Fc = 3 and 34 (48.6%) FC = 2 have. Of 36 patients (51.4%) patients with HTN and 19 (27.1%) with

diabetes and 21 patients (30%), smoking, and 7 patients (10%), use alcohol, and 11 patients (15.7%) Addictions to Drugs have.

ANOVA to compare the amount of bleeding in the seven groups studied during the first 6 hours postoperatively was used (P_V=0.0001) significant difference in bleeding rate of at least two groups was observed (Table 1).

LSD separation test showed that the control group with other groups had significant bleeding (P_V=0.00001).

ANOVA to compare the amount of bleeding in seven cases reviewed in 6 second (now 6-12) was used after the (P_V=0.0001) were significant, LSD tests showed that the control group with other denotative groups had significant bleeding ($0.04 \geq P_V$).

The second significant difference between the amount of bleeding at 6 h after the injection Tranexamic acid in doses of 20mg/kg dose 10-15& 20mg/kg and slow infusion and rapid infusion was necessary to mention the amount of bleeding in rapid injection of 20mg/kg and the second at 6 h after injection of the groups has been slow (Table 2).

ANOVA to compare the amount of bleeding in seven cases reviewed in the third after 6 hours (12-18 hours) was used with (P_V=0.17) significant difference was observed in at least two groups.

LSD test for significant differences between control group and other groups indicated the bleeding (P_V=0.05). No difference was observed in other groups.

ANOVA to compare the amount of bleeding in seven quarters examined within 6 hours (18-24 hours) after surgery was used with P = 0.025 least significant difference was observed between the denotative LSD test significant differences between control group and other groups showed (P_V=0.05) together with other groups did not differ significantly.

ANOVA to compare the amount of bleeding in seven groups total about 24 hours after surgery was used with (P=0.0001) the least significant difference was observed between the two groups (Table 3).

Disaggregated LSD test showed significant differences between control group and other groups (p =0. 0001).

It operates 24 hours after the bleeding control of bleeding from other groups is 500cc.

ANOVA to compare the action of platelets in the control group and other groups was not significant difference (p = 0.49).

Pearson correlation coefficient for assessment of the relationship between platelet levels and hemorrhage were studied in patients with (r=-0.11) relationship was not significant (P =0.33).

ANOVA to compare the means of blood products received were used after surgery in patients with (P=0.026) was a significant difference between the denotative LSD test between the control group and other groups showed significant (P_V=0.03).

Injection between the two groups, significant differences were observed in relation to blood transfusion (P_V <0.1).

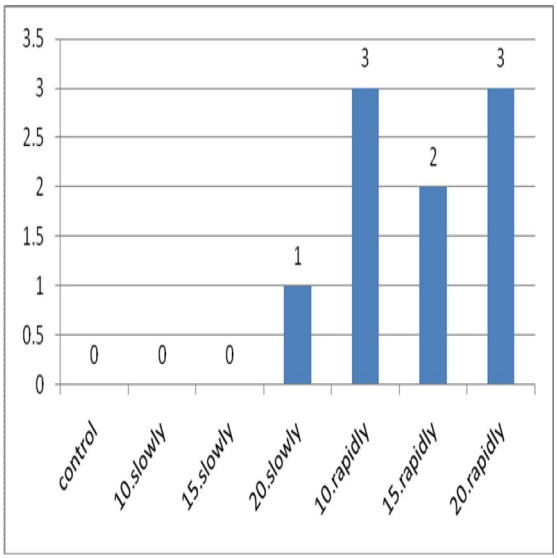

Fig 1. Side effects of slow and fast injection

Side effects

In all patients studied (control group and other groups) 9 people (13.88%) experienced side effects were statistically significant, but the reviews are not in control any side effects not observed in patients in groups of injecting drug Groups with fewer side effects than slow injection was administered as a rapid injection groups 10-15mg/kg and slow infusion methods were not any side effects (Fig 1).

The slow infusion of intravenous injection Tranexamic acid method can be side effects to remove.

The ANOVA comparing the average for the entire time and operate the pump that was used in the study groups (P =0.66) differed significantly between the groups during the entire operation and the pump was not investigated.

Comparison of creatinine and BUN values for repeat test before and after surgery in the groups studied were significant differences between pre and postoperative creatinine and BUN were observed in the groups studied (P =0.001) between the groups but The difference was not significant (P =0. 8).

In our study (paper) no symptoms of Thromboembolism Tranexamic acid injection showed have-not death (mortality) to the time of our follow-up (patients discharged from the hospital) did not happen.

Table 1. ANOVA to compare the amount of bleeding in the seven groups studied during the first 6 hours after surgery

6hrs

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
control	10	395.00	220.668	69.781	237.14	552.86	250	1000
10mg-IV-Slowly	10	146.00	119.648	37.836	60.41	231.59	40	410
15mg-IV-Slowly	10	100.80	59.719	18.885	58.08	143.52	30	230
20mg-IV-Slowly	10	173.00	90.068	28.482	108.57	237.43	0	290
10mg-IV-Rapidly	10	89.50	67.101	21.219	41.50	137.50	0	200
15mg-IV-Rapidly	10	77.00	52.079	16.469	39.74	114.26	0	150
20mg-IV-Rapidly	10	85.00	57.446	18.166	43.91	126.09	0	180
Total	70	152.33	148.836	17.789	116.84	187.82	0	1000

Table 2. ANOVA to compare the amount of bleeding in the seven groups studied during the secondary 6 hours after surgery

6-12hrs

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
control	10	198.50	88.884	28.107	134.92	262.08	80	420
10mg-IV-Slowly	10	57.50	41.982	13.276	27.47	87.53	0	120
15mg-IV-Slowly	10	40.70	31.805	10.058	17.95	63.45	0	100
20mg-IV-Slowly	10	50.00	43.461	13.744	18.91	81.09	0	150
10mg-IV-Rapidly	10	85.00	43.970	13.904	53.55	116.45	0	150
15mg-IV-Rapidly	10	67.50	79.626	25.180	10.54	124.46	0	270
20mg-IV-Rapidly	10	135.50	109.860	34.741	56.91	214.09	10	360
Total	70	90.67	84.333	10.080	70.56	110.78	0	420

Table 3. ANOVA to compare the amount of bleeding in the seven groups studied during the fourth 6 hours after surgery

24hrs

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
control	10	860.00	404.997	128.071	570.28	1149.72	520	1900
10mg-IV-Slowly	10	281.00	141.457	44.733	179.81	382.19	140	600
15mg-IV-Slowly	10	273.80	173.900	54.992	149.40	398.20	85	680
20mg-IV-Slowly	10	332.50	118.539	37.485	247.70	417.30	100	450
10mg-IV-Rapidly	10	293.50	98.094	31.020	223.33	363.67	140	450
15mg-IV-Rapidly	10	304.00	155.863	49.288	192.50	415.50	120	620
20mg-IV-Rapidly	10	315.90	140.283	44.361	215.55	416.25	140	560
Total	70	380.10	275.794	32.964	314.34	445.86	85	1900

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