Original Article

Effect of High Dose Intra-Operative Tranexamic Acid Infusion to Reduce Postoperative Bleeding in Cardiac Surgery

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Background: Tranexamic acid (TXA) have been used to reduce blood loss and transfusion in patients undergoing cardiac surgery. The effect to reduce blood loss and transfusion among different doses remains unclear. In addition, higher dose of TXA is associated with increased risk of stroke and postoperative seizure.

Objective: The aim of this retrospective study was to investigate safety and efficacy of high dose TXA infusion in patients undergoing adult cardiac surgery.

Materials and Methods: From November 2016 to January 2018, 127 adult patients were included (41 in TXA group and 86 in control group) and retrospectively reviewed.

Results: Patient characteristics were similar between groups. Chest tube output 680 (360, 1,140) mL vs. 635 (420, 1,020) mL (p = 0.604), re-operation for bleeding 4.88% vs. 3.49% (p = 0.658), and blood transfusion 240 (0, 518) mL vs. 250 (0, 579) mL (p = 0.498) were not significantly different between groups. Subgroup analysis for chest tube output and transfusion in each type of operation was also not different. No hospital death, seizure, and thrombotic complications occurred. Overall postoperative complications were not statistically different between groups.

Conclusion: High dose TXA infusion does not reduce blood loss and transfusion requirement in cardiac surgery; however, incidence of seizure, thrombotic complications, postoperative complications, and mortality are not increased with TXA.

Keywords: Tranexamic acid, Cardiac surgery

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Bleeding and transfusion are common in cardiac surgery. Tranexamic acid (TXA) is an antifibrinolytic agent that has been used to reduce blood loss and transfusion in patients undergoing cardiac surgery[1,2]. Various doses have been described in many studies, however, the effect to reduce blood loss and transfusion among different doses remains unclear[3,4]. Moreover, administration of tranexamic acid is associated with increased risk of stroke and postoperative seizure[5-8]. The aim of this retrospective study was to investigate the safety and efficacy of high dose tranexamic acid infusion in patients undergoing adult cardiac surgery.

Materials and Methods

Patients population and Study design

The present study was single-center retrospective study. The data were collected from hospital database. Inclusion criteria included patients aged 18 years or older undergoing adult cardiac surgery with cardiopulmonary bypass. Type of operation included isolated coronary artery bypass grafting (CABG), isolated valve surgery, combined valve surgery, or concomitant CABG and valve surgery. From November 2016 to January 2018, 127 adult patients were enrolled, 41 cases in the TXA group and 86 cases in the control group (Non-TXA) and retrospectively reviewed. The present study was approved by institutional review board (reference number 016142).

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TXA infusion protocol

In patients with high dose TXA infusion, loading dose of 30 mg/kg of TXA was administered before incision then followed by maintenance dose of 16 mg/kg/hr infusion until finishing skin closure. 2 mg/kg of TXA was also added to the priming of cardiopulmonary bypass.

Outcomes

Primary outcomes included total chest tube output, re-operation for bleeding and blood transfusion in

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postoperative period. Secondary outcomes included thrombotic complications (postoperative myocardial infarction, graft occlusion, deep vein thrombosis, and pulmonary embolism), seizure, and postoperative complications. Postoperative complications were as defined by the Society of Thoracic Surgeons (STS) Adult Cardiac Surgical Database.

Statistical analysis

Continuous data were presented as mean (standard deviation, SD) or median (interquartile range, IQR) and compared by independent sample t-test or the Mann-Whitney U test. Categorical variables were presented as frequency (%) and compared by Chi-square or Fisher exact test. All analyses were calculated using STATA version 14 (Texas, USA). Statistical significance was defined as p-value <0.05.

Results

Patient demographics

Patient characteristics were similar between groups, including age 64.29±9.45 years vs. 63.71±10.48 years (p = 0.762), body surface area (BSA) 1.695±0.19 m^2 vs. 1.692±0.21 m^2 (p = 0.932), Male gender 58.54% vs. 66.28% (p = 0.396), Serum creatinine 0.93 (0.72, 2.10) mg/dL vs. 1.09 (0.88, 2.21) mg/dL (p = 0.432), comorbidities and type of operation. Baseline patient characteristics are summarized in Table 1.

Postoperative outcomes

Chest tube output 680 (360, 1,140) mL vs. 635 (420, 1,020) mL (p = 0.604), re-operation for bleeding 4.88% vs. 3.49% (p = 0.658), and blood transfusion 240 (0, 518) mL vs. 250 (0, 579) mL (p = 0.498) were not significantly different between groups. Subgroup analysis for chest tube output and transfusion in each type of operation was also not different. Chest tube output and blood transfusion were summarized in Table 2. No hospital death, seizure, and thrombotic complications occurred. Overall postoperative complications were not statistically different between groups. Complications were summarized in Table 3.

Discussion

The present study suggested that high dose TXA infusion does not reduce chest tube output, blood transfusion, and re-operation for bleeding compared to non-treatment group. High dose TXA infusion does not increase incidence of seizure, thrombotic complications, postoperative complications, and mortality.

Excessive blood loss and blood transfusion are common in patients undergoing cardiac surgery. Re-operation for bleeding and massive transfusion are subsequently major complication in patients with life-threatening bleeding and associated with poor outcomes after cardiac surgery[9,10]. Effect of TXA to reduce blood loss and transfusion in cardiac surgery has been consistently reported in many studies[3,4,7,11],

Table 1. Patient characteristics

Variable	TXA (n = 41)	No TXA (n = 86)	p-value
Age (year), mean ± SD	64.29±9.45	63.71±10.48	0.762
BSA (m^2), mean ± SD	1.695±0.19	1.692±0.21	0.932
Gender, n(%)			
Male	24 (58.54)	57 (66.28)	0.396
Female	17 (41.46)	29 (33.72)	
Creatinine, median (IQR)	0.93 (0.72, 2.10)	1.09 (0.88, 2.21)	0.432
Underlying, n(%)			
Diabetes	19 (46.34)	37 (43.02)	0.725
Hyperlipidemia	29 (70.73)	55 (63.95)	0.450
Hypertension	34 (82.93)	67 (77.91)	0.512
Chronic kidney disease	7 (17.07)	17 (19.77)	0.717
Hemodialysis	3 (42.86)	9 (64.29)	0.397
Chronic obstructive pulmonary disease	2 (4.88)	1 (1.16)	0.244
Cirrhosis	0	1 (1.16)	0.999
Atrial fibrillation	7 (17.07)	15 (17.14)	0.959
Prior stroke	4 (9.76)	6 (6.98)	0.726
Operation, n (%)			
CABG	25 (60.98)	47 (54.65)	0.501
Aortic valve surgery + CABG	2 (4.88)	7 (8.14)	0.717
Mitral valve surgery + CABG	5 (12.20)	4 (4.65)	0.147
Aortic valve surgery	1 (2.44)	10 (11.63)	0.103
Mitral valve surgery	5 (12.20)	15 (17.44)	0.448
AVR + MVR	3 (7.32)	2 (2.33)	0.327
AVR + MVR + CABG	0	1 (1.16)	0.999

TXA = Tranexamic acid; CABG = Coronary bypass grafting; AVR = Aortic valve replacement; MVR = Mitral valve replacement; BSA = Body surface area

Table 2. Chest tube output and blood transfusion

Variable	TXA (n = 41)	No TXA (n = 86)	*p*-value
Chest tube output (mL), median (IQR)	680 (360, 1,140)	635 (420, 1,020)	0.604
CABG	680 (480, 1,100)	700 (440, 1,000)	0.929
Aortic valve surgery + CABG	705 (480, 930)	650 (400, 1,250)	0.769
Mitral valve surgery + CABG	1,120 (360, 1,340)	550 (210, 4,155)	0.806
Aortic valve surgery	360 (360, 360)	310 (280, 410)	0.751
Mitral valve surgery	440 (320, 1,160)	880 (500, 1,200)	0.274
AVR + MVR	1,360 (470, 1,380)	1,310 (1,020, 1,600)	0.563
AVR + MVR + CABG	-	630	-
Total blood transfusion (mL), median (IQR)	240 (0, 518)	250 (0, 579)	0.498
CABG	269 (243, 678)	520 (378, 760)	0.135
Aortic valve surgery + CABG	1,010 (1,010, 1,010)	935 (509.5, 1,431)	0.999
Mitral valve surgery + CABG	1,459 (500, 1,810)	1,550 (510, 1,584)	0.827
Aortic valve surgery	-	264.5 (220, 1,102)	-
Mitral valve surgery	518 (287, 1,144)	826.5 (822, 842)	0.301
AVR + MVR	549 (252, 723)	541 (240, 842)	0.999
AVR + MVR + CABG	-	1,303	-
Transfusion requirement (n, %)	22 (53.66)	49 (56.98)	0.725

Table 3. Complications

Variable	TXA (n = 41)	No TXA (n = 86)	*p*-value
Complication, n (%)			
Seizure	0	0	-
Thrombotic complications	0	0	-
Renal failure	0	0	-
Prolonged ventilation ≥24 hr	1 (2.44)	2 (2.33)	0.999
Stroke	1 (2.44)	2 (2.33)	0.999
Re-operation for bleeding	2 (4.88)	3 (3.49)	0.658

however, most of these studies usually report with only certain operation to compare the effect of TXA, for example, coronary bypass surgery. Unfortunately, blood loss and transfusion in our study were not significantly different between groups. This finding may have resulted from a small sample size and including more complex operations in the study, such as combine valve surgery, and concomitant coronary bypass surgery with valve surgery. Although subgroup analysis was also not different, this issue requires a larger randomized study to make a robust conclusion.

TXA was associated with an increased risk of neurological complications including seizure after cardiac surgery in previous study. An increased risk of seizure is also related with higher dose of TXA[7,8]. Differently, the present study demonstrated no difference in postoperative seizure. In fact, no seizure occurred in the present study. Because the incidence of seizure was very low (0.7 to 1.4%)[3,7] and postoperative seizure is not associated with poor outcomes[7], this issue also needs a larger randomized study to investigate this adverse neurological complication.

Some studies have shown that TXA reduces cerebral blood flow and increases the risk of cerebral infarction[5,6]. Postoperative complications, especially stroke were not significantly increased with TXA in the present study. Thrombotic complications and other postoperative complications, such as renal failure, and prolonged intubation more than 24 hours were also similar. This finding suggested that high dose TXA is safe and can be used without an increased risk of postoperative and thrombotic complications. Similar results were also observed in other studies[3,4,7].

Limitation

This study has several limitations, non-randomized, Retrospective basis, small sample size being the main weak points. Although patient characteristics were comparable, the inherent biases from study design and confounding factors from non-randomized, small sample size were inevitably existed. Conduction of a large randomized trial is required for further investigation of safety and efficacy of high dose TXA infusion in cardiac surgery.

Conclusion

High dose TXA infusion does not reduce blood loss and transfusion requirement in cardiac surgery; however, incidence of seizure, thrombotic complications, postoperative complications, and mortality are not increased with TXA.

What is already known on this topic?

The optimal dose of tranexamic acid to reduce blood loss and transfusion in cardiac surgery remains unclear. Incidence of seizure is related to higher dose of tranexamic acid.

What this study adds?

High dose tranexamic acid can be safely used without an increased risk of seizure, thrombotic and postoperative complications.

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Potential conflicts of interest

The authors declare no conflict of interest.

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