

The Safety Of Tranexamic Acid In Total Joint Arthroplasty

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ABSTRACT

TXA (Tranexamic acid) can be used to reduce blood loss in total joint arthroplasties. Due to the correlation between acute anemia occurring after total joint arthroplasties and postoperative morbidity/mortality rates, many studies were focused on different modalities to minimize blood loss. TXA can be administered by different routes: intravenous, topical, oral or a combination of these. The effective dose and administration technique of TXA is still controversial. Safety of TXA in clinical practice has been debated for a long time. TXA does not increase symptomatic or asymptomatic DVT (Deep vein thrombosis) risk. The safety of TXA is still unclarified in high-risk and comorbid patients. Prospective studies to establish stronger recommendations are necessary.

Key words: Safety of tranexamic acid; Total joint arthroplasty; Blood transfusion

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EDITORIAL

TXA (Tranexamic acid) is a synthetic derivative of lysine that blocks binding of fibrin to plasminogen. TXA prevents degradation of fibrin clots. TXA can be used to reduce blood loss in total joint arthroplasties. Due to the correlation between acute anemia occurring after total joint arthroplasties and postoperative morbidity/mortality rates, many studies were focused on different modalities to minimize blood loss^[1]. Increased load of transfusions are related with high postoperative infection, prolonged recovery period, increasing morbidity and mortality rates^[2].

TXA can be administered by different routes: intravenous, topical, oral or a combination of these. Optimal route of administration is still debated. Low doses of TXA can be sufficient for stabilization of clot and inhibition of fibrinolysis at the target site. DVT (Deep vein thrombosis), PE (Pulmonary embolism) and other thromboembolic events that might be caused by TXA. Topical administration has a better safety profile compared to IV (Intravenous) administration; moreover, topical administration reduces joint swelling, shortens wound healing and enables rapid rehabilitation^[3]. Oral administration is cost effective than intravenous or topical routes. Hyperfibrinolysis continues 18-24 hours after surgery but the effective blood concentration of TXA continues only 6 hours. Although, single dose of TXA is not sufficient for adequate antifibrinolysis after surgical procedures^[4]. Safety of IV TXA in high risk patients with cardiovascular comorbidities and history of venous thromboembolic events is still unclarified. The safety of TXA in high risk patients should be determined with level 1 controlled randomized multicenter studies^[5].

Effects of TXA on blood loss, Hb (Hemoglobin), PT (Prothrombin time), aPTT (Activated partial thromboplastin time), D-dimer and thromboembolic events (DVT and PE) were evaluated in Retrospective and prospective studies of TXA usage in THA (Total Hip Arthroplasty) and TKA (Total Knee Arthroplasty).

Kagoma *et al* determined VTE (Venous Thromboemboly) risk by

imaging methods such as US (Ultrasonography), venography and ventilation-perfusion scintigraphy. TXA usage reduced blood loss in both THA and TKA, also VTE risk didn't increase. Warnings about the safety of erythropoietic stimulating agents have increased concerns^[6]. Fillingham *et al* concluded in their meta-analysis that TXA significantly reduced blood loss and transfusion risk regardless of route of administration. Higher and/or multiple doses were not proven to be more effective^[2]. Maniar *et al* reported that TXA-administered groups had lower amount of postoperative drainage and total blood loss. Only clinically suspected patients were screened by Doppler US but none of them had DVT^[7]. In a prospective study of TXA the reduction of hemoglobin in IV application was lower than topical application in postoperative arthroplasty patients. There were not any thromboembolic complications^[8].

In a prospective cohort study Yamaguchi *et al* investigated the effects of TXA at different doses. When the levels of blood loss from postoperative drains were compared, there was not any significant difference between 1 or 2 grams of TXA groups. Higher amount of blood loss was determined in amikacin-saline solution group compared to 1 or 2 grams of TXA groups. DVT were not detected, but D-dimer levels were found to be increased postoperatively^[9].

Wong *et al* evaluated patients with venous Doppler US to identify asymptomatic DVT cases. 3 grams of topical TXA was administered to 34 patients, 1.5 grams of topical TXA to 31 patients and normal saline solution to 35 patients. A significant decrease of blood loss was observed in both of TXA groups, when compared with placebo group; The difference between 1.5 and 3 grams groups was not statistically significant. DVT was detected in 4 patients with no clinical symptoms. One of those patients was in placebo group, two were in 1.5 grams of TXA group and the other was in 3 grams group^[10].

Barrachina *et al* evaluated 113 patients on the postoperative 3rd and 21st days by using bilateral Doppler US imaging. On 3rd day, 4 patients had DVT and one of them had PE. On 21st day, 3 patients had DVT. Calculation of the blood loss revealed that TXA-administered group had lower blood loss levels than control group in postoperative 3rd day. There was not any significant difference between one dose and two doses of TXA groups. In all groups, D-dimer levels were increased in 1st and 6th hours, but D-dimer levels were higher in control group than TXA groups^[11].

Liu *et al* showed that low or high doses of TXA raised D-dimer, aPTT and PT levels minimally in comparison with the control group. Lower increase of D-dimer values in TXA groups than the control group was explained by the antifibrinolytic effect of TXA^[12]. In another study investigating the effect of TXA on D-dimer values, lower levels of D-dimer was recorded IA (Intraarticular) administration of TXA with combined IV than only-IV or only-IA treatment^[13]. A meta-analysis study revealed that TXA had no a major effect on PT and aPTT levels^[14].

Hourlier *et al* evaluated 164 patients with Doppler US on 7th day and none of them had DVT after TXA application^[15]. 117 patients underwent THA were evaluated with CT (Computerized tomography) on the 7th day by Imai *et al* Patients were randomly distributed into 5 groups. No significant difference was detected for VTE between groups of different TXA application ways^[16].

In another study investigating the effects of multiple doses of TXA, an inverse correlation was observed between increased doses and amount of blood loss. There was significantly lower increase in D-dimer and IL-6 levels with 4 or 5 doses of TXA in the postoperative 24th and 36th hours in comparison with the patients treated with 3 doses of TXA. DVT was not detected in any of the patients with bilateral Doppler US after 2nd week and 3rd month^[2].

Zeng *et al* compared single-dose IV TXA with combined topical and IV administration of TXA in their randomized controlled trial including 150 patients. All patients were evaluated with bilateral Doppler US. The combined IV and topical TXA group presented less blood loss, lower reduction of hemoglobin level and lower blood transfusion. 5 patients had DVT, but no significant difference was detected between the groups^[3].

Safety of TXA on high risk patients with severe comorbidity is not obvious. Whiting *et al* revealed there was no increased risk of thromboembolic events in highly comorbid patients while using TXA^[17]. Fillingham *et al* investigated the safety of TXA in meta-analysis study, Fillingham *et al* evaluated 78 high level randomized controlled trials and revealed that TXA did not increase the risk of thromboembolism, but, limited number of high risk patients limits the strength of the study^[18].

Safety of TXA in clinical practice has been debated for a long time. TXA does not increase symptomatic or asymptomatic DVT risk. TXA can be used to reduce blood loss and transfusion in total joint arthroplasties. The effective dose and administration technique of TXA is still controversial. TXA increases D-dimer less than placebo. The safety of TXA is still unclarified in high-risk and comorbid patients. Prospective studies to establish stronger recommendations are necessary.

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