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Review Article

The Role of Tranexamic Acid in Reducing Blood Loss Following Total Joint Arthroplasty: A Review Article

Ehsan Fallah[1], Alireza Moharrami[2], Amir Hossein Ahmadi Nouri[3], Mir Mansour Moazen Jamshidi[4], Amir Reza Mafi[2], Seyed Mohammad Javad Mortazavi[5,*]

[1]Knee Surgery Fellowship, Joint Reconstruction Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2] Resident, Joint Reconstruction Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3] General Practitioner, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[4] Hip Surgery Fellowship, Joint Reconstruction Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[5] Professor, Joint Reconstruction Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

[*]Corresponding author: Seyed Mohammad Javad Mortazavi; Joint Reconstruction Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract

Total Joint Arthroplasty (TJA) is a major surgery performed for patients who suffer from severe joint destruction. It is so important to reduce the blood loss in the TJA surgery to decrease the infection rate, falling, and other complications following the surgery. Many methods could reduce blood loss, such as mechanical methods and chemical methods. Tranexamic acid (TXA) is a chemical method to reduce blood loss in surgery. There are numerous methods of administration of TXA in the literature, such as intravenous (IV), intra-articular, and combination of intra-articular and -venous methods. In the present review article, we review the studies that compared the efficacy of each method of the TXA administration.

Keywords: Tranexamic Acid; Postoperative Hemorrhage; Arthroplasty; Knee; Hip

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Background

Total joint arthroplasty (TJA) is a major surgery performed for patients who suffer from severe joint osteoarthritis (hip or knee). Total knee arthroplasty (TKA) is considered by many as the method of choice for the management of end-stage knee degenerative osteoarthritis with a survival rate of 15-20 years (1). In the United States (US), over 2% of the population have undergone total knee or hip joint replacement (2), and almost 1065000 primary TKAs were performed in the year 2020 in the US (3).

One of the most critical complications of TKA, like any other surgery, is perioperative blood loss (PBL). The average PBL in a TKA surgery has been estimated at 1498 ml (4). The blood transfusion following PBL may be associated with an increased hospital stay, delayed wound healing, periprosthetic joint infection (PJI), and increased mortality within 90 days following the TKA surgery (5).

Widespread application of tranexamic acid (TXA) as a method for eliminating the PBL decreases blood transfusion rate from approximately 33% to nearly 2% of TKA cases and reduces the PJI by 50% (5). Its administration also reduces the inpatient hospital cost from 15110$ to 14890$ (6).

There are different methods of TXA administration, including topical, intravenous (IV), intra-articular (IA), oral, and combined IV/IA. The 2019 guideline has emphasized controversy about the best route for TXA administration (7). Some studies have demonstrated that the combined IV/IA method is associated with less PBL in TKA surgery (8-10). In the present study, we aimed to review the role of TXA in TJA. We reviewed the studies about the role of the TXA in TJA from January 2013 to September 2021.

TXA

TXA exerts its antifibrinolytic effect by blocking lysine binding sites on plasminogen molecules, thereby inhibiting the interaction of plasminogen and the heavy chain of plasmin with lysine residues on the surface of fibrin. Although plasmin can still be formed under these circumstances, it is unable to bind to and degrade fibrin.

TXA is 6 to 10 times more potent in terms of binding to plasminogen/plasmin than the other synthetic antifibrinolytic agent ε-aminocaproic acid (EACA). Suppression of fibrinolysis by TXA is manifested in surgical patients by reductions in blood levels of D-dimer, but the drug has no effect on blood coagulation parameters. Concurrent administration of heparin does not influence the activity of TXA.

Maximum plasma concentrations of TXA are attained within 3 hours of an oral dose; the presence of food in the gastrointestinal tract does not affect the pharmacokinetic parameters of the drug. Elimination after IV administration is triexponential, and over 95% of each dose is eliminated as an unchanged drug in the urine. The total cumulative excretion after an IV dose is approximately 90% after 24 hours.

Of the total amount of circulating TXA, 3% is bound to plasminogen. The drug crosses the blood-brain barrier (BBB)and the placenta, but excretion into breast milk is minimal. TXA is not detectable in saliva after systemic (oral) administration, and mouth washing with 5% w/v aqueous solutions of the drug results in plasma drug concentrations below 2 mg/l.

TXA in TJA

TXA, as an antifibrinolytic agent, is used in TKA surgeries in order to reduce the blood loss and transfusion requirement. Different administration methods have been introduced and investigated, but the most efficient

method is still a matter of debate (7).

Intra-Articular TXA

Intra-articular injection of TXA has been investigated in many studies. TXA administration may be in two stages of surgery, mainly about the time of tourniquet release or wound closure. It may also be injected in different doses ranging from 1 to 3 grams. When TXA was used in the topical route, a study has found that combined use of intra-articular injection (IAI) and periarticular injection (PAI) of TXA can significantly reduce the total blood loss (TBL) and the need for blood transfusion without delaying wound healing or increasing the risk of deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE) (8).

Intravenous TXA

Intravenous TXA can be administered in different doses and stages. Studies suggest doses ranging from 10 to 20 mg/kg and pre-operatively, intra-operatively, post-operatively, or in combination. In a study, Oztas et al. used 1-hour slow infusion (11).

Intra- Articular and– Venous Combination of TXA

The combination of intravenous and intra-articular TXA administration is non-inferior to the administration of each one alone (12).

Using TXA and Chemoprophylaxis Anticoagulants

While the options include aspirin, warfarin, rivaroxaban, and compression, a study found that there is no difference in PBL when different types of anticoagulants (including apixaban, enoxaparin sodium, nadroparin calcium, rivaroxaban) are used with TXA administration (13).

Discussion

Following the literature review, we reviewed 36 studies that compared the methods of TXA injection, as seen in table 1 (8-12, 14-43).

The intravenous TXA can be admitted in different doses and stages. This method could help reduce blood loss following the surgery. Many studies compared the effect of intravenous TXA with other methods. In our evaluation of the studies, just 4 studies recognized that the intravenous method had more potent than other methods (14, 23, 24, 31).

The intra-articular TXA can be administered in different doses and stages. This method could reduce blood loss with topical effect. In the literature, this method is more potent than the IV method in most studies. In our literature evaluation, 9 studies revealed that the IA method had a more potent effect in reducing blood loss following TJA (8, 11, 15, 17, 20, 26, 41, 44).

Table 1. The characteristics of the reviewed studies used tranexamic acid (TXA) in TJA from 2013 to 2021

Study	Intravenous (IV)	Intra-articular (IA)	Thromboprophylaxis	Preferred
Jules-Elysee et al. (24)	1 g TXA × two doses; POPO	3 g TXA × one dose; before tourniquet release	Unclear	IV>IA
Laoruengthana et al. (26)	10 mg/kg TXA × one dose; IO	15 mg/kg TXA × one dose; before closure	LMWH/warfarin	IA>IV
Maniar et al. (45)	10 mg/kg TXA × two doses (bilateral); IO 10 mg/kg TXA × three doses; POIOPO	3 g TXA × two doses(bilateral); after cemented	LMWH Ankle pumping exercise Compression stocking	
Abdel et al. (14)	1 g TXA × one dose; PEO	3 g TXA × one dose; after cemented	Aspirin/warfarin	IV>IA
Ahmed et al. (17)	1.5 g TXA × one dose; PTO	1.5 g TXA × one dose; during the closure	Unclear	IA>IV
Maniar et al. (45)	1 g TXA × one dose; PEO	1 g TXA × one dose; after closure	Unclear	IA>IV
George et al. (12)	10 mg/kg TXA × two doses; POPO	1.5 g TXA × one dose; before closure	LMWH/aspirin	Neutral
Subramanyam et al. (37)	10 mg/kg TXA × one dose; PEO	1.5 g TXA × one dose; after closure	Aspirin Calf pump	Neutral
Wei et al. (42)	10 mg/kg TXA × one dose; PEO	1 g TXA × one dose; before tourniquet release	LMWH	Neutral
Goyal et al. (23)	1 g TXA × three doses; IO/PTO/PTO	3 g TXA × one dose; after closure	LMWH/aspirin Compression stocking	Neutral
Goyal et al. (23)	10 mg/kg TXA × two doses; POPO	3 g TXA × one dose; after cemented	Unclear	IV>IA
Zhang et al. (8, 46)	20 mg/kg TXA × one dose; PEO	3 g TXA × one dose; after closure	Rivaroxaban	IA>IV
Prakash et al. (31)	10 mg/kg TXA × three doses; POIOPO	3 g TXA × one dose; before closure	LMWH Calf pump	IV>IA
Song et al. (34)	10 mg/kg TXA × three doses; POIOPO	1.5 g TXA × one dose; after closure	LMWH in high-risk patient	Neutral
Stowers et al. (36)	1 g TXA × one dose; IO	1 g TXA × one dose; after closure	Aspirin	Neutral
Ugurlu et al. (39)	20 mg/kg TXA × one dose; PEO	3 g TXA × one dose; after closure	LMWH Compression stocking	Neutral
Wang et al. (40, 41)	1 g TXA × one dose; IO	1 g TXA × one dose; before closure	LMWH/rivaroxaban Elastic bandage	IA>IV
Zekcer et al. (43)	20 mg/kg TXA × one dose; unclear	1.5 g TXA × one dose; before tourniquet release	LMWH Compression stocking	Neutral
Aggarwal et al. (15)	15 mg/kg TXA × two-dose; IOPO	15 mg/kg TXA × one dose; before closure	Aspirin	IA>IV
Chen et al. (18, 19)	1.5 g TXA × one dose; IO	1.5 g TXA × one dose; after cemented	LMWH Calf pumps	Neutral
Drosos et al. (21)	1 g TXA × one dose; PEO	1 g TXA × one dose; before closure	LMWH Compression stocking	Neutral
Keyhani et al. (25)	0.5 g TXA × one dose; IO	1.5 g TXA × two doses; before/after closure	LMWH	Neutral
May et al. (27)	1 g TXA × two doses; POPO	2 g TXA × one dose; after closure	LMWH Sequential compression	Neutral
May et al. (27)	0.75 mg TXA × one dose; IO	0.75 mg × one dose; before tourniquet release	Ankle pumping exercise Early ambulation	Neutral
Tzatzairis et al. (38)	1 g TXA × one dose; PEO	1 g TXA × one dose; after closure	LMWH Compression stocking	Neutral
Aguilera et al. (16)	1 g TXA × two doses; POIO	1 g TXA × one dose; after cemented	LMWH	Neutral
Digas et al. (20)	15 mg/kg TXA × one dose; IO	2 g TXA × one dose; after closure	Tinzaparin	IA>IV
Oztas et al. (11)	15 mg/kg TXA × two doses; POPO 10 mg/kg TXA × one dose; 1-h infusion	2 g TXA × one dose; before tourniquet release	LMWH	IA>IV
Gomez-Barrena et al. (22)	15 mg/kg TXA × two doses; IOPO	3 g TXA × one dose; before + after closure	LMWH	Neutral
Patel et al. (30)	10 mg/kg TXA × one dose; IO	2 g TXA × one dose; before tourniquet release	LMWH	Neutral
Sarzaeem et al. (32)	1.5 g TXA × one dose; PTO	1.5 g TXA × one dose; before closure 1.5 g TXA × one dose; after closure	Unclear	Neutral
Soni et al. (35)	10 mg/kg TXA × three doses; POIOPO	3 g TXA × one dose; before tourniquet release	LMWH Ankle pumping exercise	Neutral
Seo et al. (33)	1.5 g TXA × one dose; PTO 10 mg/kg TXA × one dose; IO	1.5 g TXA × one dose; during the closure	Unclear	IA>IV
Maniar et al. (45)	10 mg/kg TXA × two doses; IOPO 10 mg/kg TXA × two doses; POIO 10 mg/kg TXA × three doses; POIOPO	3 g TXA × one dose; before tourniquet release	LMWH Ankle pumping exercise Compression stocking	Neutral
Mortazavi et al. (28)	15 mg/kg TXA × one dose; PEO	15 mg/kg TXA × one dose; after closure	Aspirin	Neutral
Bagheri et al. (29)	15 mg/kg TXA ×one dose; PEO	15 mg/kg TXA × one dose; after closure	Aspirin	Combination is better

IO: Intraoperative dose; IOPO: Intra- and postoperative doses; PEO: Preoperative dose; POIO: Pre- and intra-operative doses; POIOPO: All three doses; POPO: Pre- and postoperative doses; PTO: Postoperative dose; TXA: Tranexamic acid.

In most studies and clinical trials, the IA and IV methods of TXA did not have any significant differences in reducing blood loss. There are so many studies that have compared these two methods of administration of TXA, and they confirmed that there are not any significant differences between the methods (12, 16, 18, 21-23, 25, 27, 28, 30, 32, 34, 36, 37, 39, 42, 43, 45).

There are few studies about the role of the combination of IV and IA TXA in reducing blood loss. However, the studies confirmed that this method is more potent than other methods (8, 29, 34). However, there was an attitude that the combined TXA could increase the chance of venous thromboembolism (VTE) and needs more potent chemoprophylaxis such as low-molecular-weight heparins (LMWHs) or warfarin. However, in the studies by Mortazavi et al. (28) and Bagheri et al. (29), they confirmed that the use of aspirin is enough as a VTE chemoprophylaxis following TJA using TXA in any method.

Conclusion

In conclusion, the TXA is a safe method in reducing blood loss following TJA. The recent studies confirmed that using any methods of TXA in TJA surgery is effective in avoiding blood loss. However, the combination IV and IA and the IA methods were more potent than IV alone.

Conflict of Interest

The authors declare no conflict of interest in this study.

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