Review Article

Tranexamic Acid in Hip and Knee Arthroplasty

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Abstract

Perioperative blood loss is a significant concern for patients undergoing total joint arthroplasty. A growing body of evidence has shown tranexamic acid (TXA) to be effective in decreasing perioperative blood loss and transfusion requirements in both primary and revision hip and knee arthroplasty. TXA is a synthetic drug that limits blood loss through inhibition of fibrinolysis and clot degradation. Both topical and intravenous administration of TXA, in a variety of dosing regimens, has proven effective. Further investigation is required to determine the optimal dose and dosing regimens; however, evidence exists to recommend an initial intravenous dose be given before beginning the procedure, with at least one additional intravenous dose administered postoperatively. Additionally, topical TXA doses >2 g appear to be more efficacious than lower doses. Finally, relatively few adverse reactions have been reported in arthroplasty patients, and no study to date has demonstrated an increased risk of symptomatic venous thromboembolic events in this patient population.

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In the US, >600,000 total knee arthroplasties (TKAs) and >285,000 total hip arthroplasties (THAs) are performed each year.[1] These procedures frequently have perioperative blood loss >1 L, resulting in a longer hospital stay and delayed rehabilitation, and may be poorly tolerated by patients with comorbidities.[2,3] Perioperative blood loss is often treated with blood transfusion, with reported transfusion rates ranging from 11% to 67%.[4,5] Both autologous and allogeneic blood transfusions result in increased costs, carry the risks of disease transmission and transfusion reaction, and have been associated with increased rates of periprosthetic infection.[6]

Numerous approaches have been used to minimize transfusion requirements, including blood salvage, controlled hypotension, hemodilution, and stimulation of erythropoiesis with epoetin alfa, with varying degrees of success reported along with increased cost. Recently, the use of pharmacologic agents, such as antifibrinolytic tranexamic acid (TXA), to minimize perioperative blood loss associated with total joint arthroplasty (TJA) has been investigated.

TXA is a synthetic drug that limits blood loss through inhibition of fibrinolysis and clot degradation. Surgical trauma is known to cause fibrinolysis, which increases with the use of a pneumatic tourniquet.[7] TXA reversibly saturates the lysine binding site of plasminogen, preventing the interaction of the active protease, plasmin, with the surface-binding site on fibrin. This inhibits the degradation of a fibrin clot by plasmin (Figure 1). TXA is available in intravenous (IV), topical, and oral

Figure 1

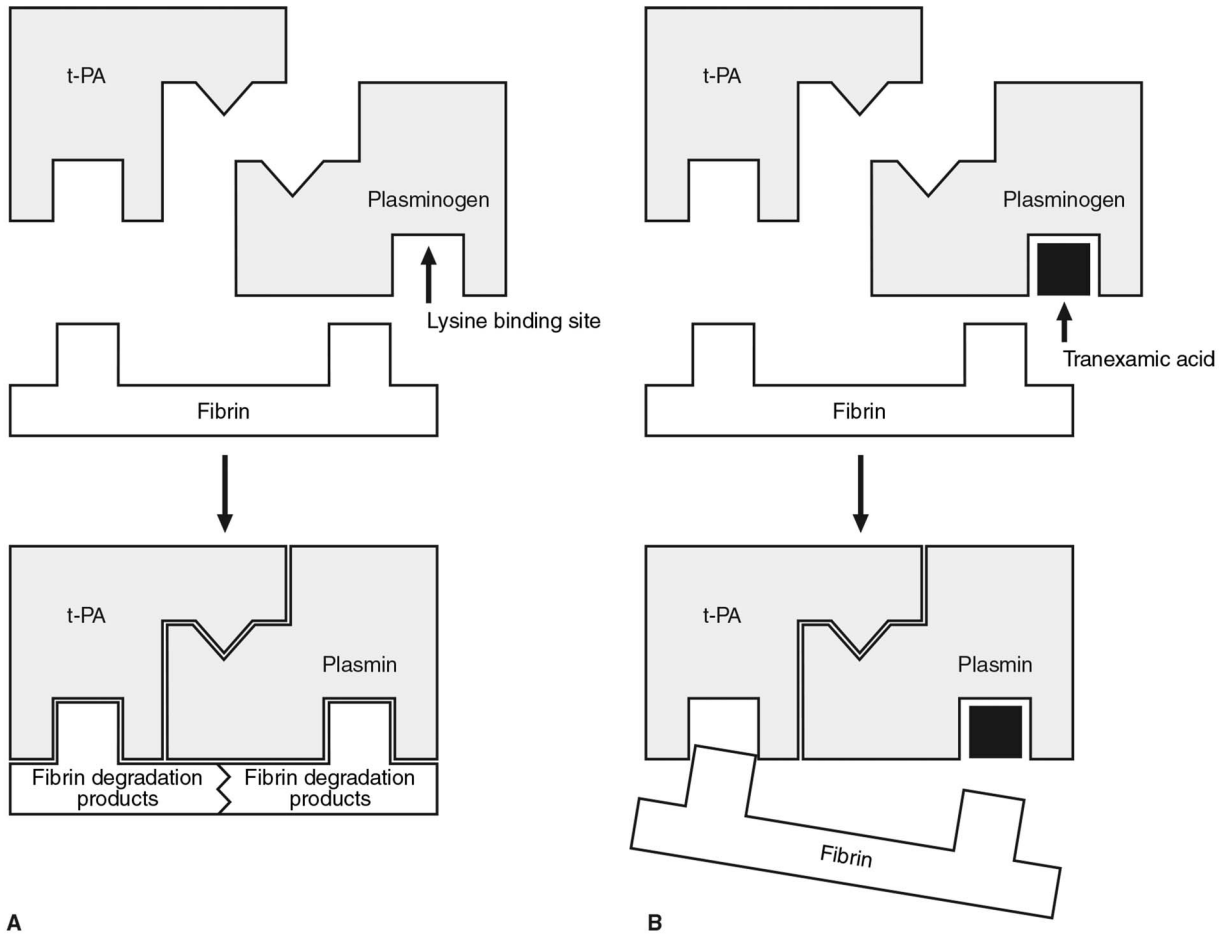

Illustration demonstrating the mechanism of action of tranexamic acid. **A,** Activation of fibrinolysis. **B,** Inhibition of fibrinolysis. The competitive inhibition produced as tranexamic acid binds to plasminogen makes it impossible for plasminogen to bind with fibrin. t-PA = tissue plasminogen activator. (Adapted with permission from Dunn CJ, Goa KL: Tranexamic acid: A review of its use in surgery and other indications. *Drugs* 1999;57:1005-1032.)

forms and has been used widely in many surgical specialties, including cardiac surgery, gynecology, gastrointestinal surgery, and neurosurgery. Typically, doses used in hip and knee arthroplasty (1 to 2 g perioperatively) have been lower than doses for nonarthroplasty cases (ie, 1- to 2-g bolus with 0.4 to 1 g/h for cardiac surgery, 3 to 4 g/d for 4 to 5 days for menstrual bleeding, 4 to 6 g/d for 20 days for subarachnoid hemorrhage).[8] TXA is approved by the FDA for use only in patients with hemophilia to reduce or prevent hemorrhage during and following tooth extraction. Therefore, its use in TKA and THA is off label.

Efficacy in Primary Total Knee Arthroplasty

Numerous studies have shown TXA to be beneficial in reducing the rate of blood loss and the transfusion requirements associated with primary TKA[9-14] (Table 1). A recent meta-analysis of randomized controlled trials on primary TKA demonstrated that, compared with placebo, IV administration of TXA reduced blood loss by 504 mL and decreased the number of units transfused per patient by 1.43 units.[9] In this meta-analysis, 14 of 15 studies used low doses (10 to 50 mg/kg) of TXA, and the remaining study used a high-dose (150 mg/kg) regimen. The authors concluded that TXA is safe and effective for reducing blood loss associated with TKA.

Several recent studies have found that topical application of TXA is also effective. In a randomized study of 101 patients who underwent TKA, patients received either 2.0 g TXA in 75 mL of normal saline or a placebo solution applied for 5 minutes during

Table 1

The Effect of Tranexamic Acid on Blood Loss and Transfusion in Total Knee Arthroplasty

Study (Design)	Dosing Regimen	No. of Patients	Mean Total Blood Loss (mL)	Mean Units Transfused per Patient
Yang et al[9] (Meta-analysis of RCT)	IV, range, 10–50 mg/kg	406	757	0.94
	PL	431	1,271	2.46
Georgiadis et al[10] (RCT)	Topical 2 g/75 mL NS	50	940	0.0
	PL	51	1,293	0.16
Panteli et al[11] (Meta-analysis of RCT)	Topical (variable dosing)	125	736	0.05
	PL	132	1,012	0.14
MacGillivray et al[12] (RCT)	IV 10 mg/kg intra and post	20	678	0.4
	IV 15 mg/kg intra and post	20	462	0.9
	PL	20	918	0.95
Tanaka et al[13] (RCT)	IV 20 mg/kg pre	24	776	0.5
	IV 20 mg/kg intra	22	896	1.0
	IV 10 mg/kg pre and intra	27	528	0.05
	PL	26	1,470	2
Benon and Fredin[14] (RCT)	IV 10 mg/kg intra and post	43	730	0.27
	PL	43	1,410	0.93

intra = intraoperative, IV = intravenous, NS = normal saline, PL = placebo, post = postoperative, pre = preoperative, RCT = randomized controlled trial

cement hardening.[10] Total blood loss was significantly lower in the TXA group than in the placebo group (940 mL versus 1,293 mL). Chimento et al[15] retrospectively reviewed 683 TKA cases and compared the cases performed without TXA (n = 373) with those performed with topical application of a 3-g dose of TXA in 100 mL of normal saline (n = 310) following cementing. The TXA group had substantially higher postoperative hemoglobin levels, lower transfusion rates, and shorter hospital stays. Mutsuzaki and Ikeda[16] retrospectively reviewed 140 patients who underwent noncemented TKA. Seventy patients received a 1-g retrograde injection of TXA through the drain after closure, with subsequent clamping of the drain for 1 hour, and the remaining patients were the control group. The TXA group had a lower transfusion rate and significantly less total blood loss than did the control group (633 mL versus 1,276 mL). In a meta-analysis of the use of TXA in TKA, Panteli et al[11] found that the use of topical TXA led to significant decreases in drain output (mean difference, −268 mL), total blood loss (mean difference, −220 mL), hemoglobin loss (mean difference, −0.94 g/dL), and the risk of transfusion (risk ratio = 0.47; confidence interval = 0.26 to 0.84). The authors also found that doses >2 g had a greater effect than did lower doses on reducing transfusion requirements.

Two recent studies have compared IV and topical administration of TXA. Huang et al[17] compared the efficacy of a combined IV and topical regimen of TXA (1.5 g IV and 1.5 g topical) with that of a single 3-g dose of TXA administered intravenously. Both dosing regimens had similar effects on reducing blood loss and transfusion requirements. Sarzaeem et al[18] compared the efficacy of three administration routes for TXA. A 1.5-g dose of TXA was administered intravenously at wound closure, a 3-g dose of topical TXA was applied at wound closure, and a 1.5-g dose of topical TXA was injected through the drain after closure. IV administration of TXA was found to be the most effective in limiting overall hemoglobin loss and the number of units required for transfusion, whereas TXA injected through the drain was most effective in decreasing postoperative drainage. These studies suggest that combined IV and topical TXA regimens warrant further investigation.

Although the use of IV and topical TXA in TKA has been studied extensively, three studies found that the use of oral TXA is also beneficial. In a study of oral versus IV administration of TXA used in patients undergoing primary TKA and THA, Irwin et al[19] compared 2,698 patients treated with 15 mg/kg of IV TXA before induction with 302 patients treated with 25 mg/kg oral TXA and found that the transfusion requirement was lower in the oral

Table 2

The Effect of Tranexamic Acid on Blood Loss and Transfusion in Total Hip Arthroplasty

Study (Design)	Dosing Regimen	No. of Patients	Mean Total Blood Loss (mL)	Mean Units Transfused per Patient
Niskanen et al[22] (RCT)	IV 10 mg/kg pre and post	19	792	0.52
	PL	20	1,102	0.9
Zhou et al[23] (Meta-analysis of RCT)	IV (variable dosing)	168	1,196	NR
	PL	194	1,470	NR
Yue et al[24] (RCT)	Topical 3 g/150 mL NS intra	52	945	0.1
	PL	51	1,255	0.48
Johansson et al[25] (RCT)	IV 15 mg/kg pre	47	969	0.36
	PL	53	1,324	1.07

intra = intraoperative, IV = intravenous, NR = not reported, NS = normal saline, PL = placebo, post = postoperative, pre = preoperative, RCT = randomized controlled trial

TXA group (odds ratio, 0.48), and the safety profile of oral TXA was similar to that of IV TXA. In a double-blind randomized study of 53 patients who received oral TXA before TKA, Alipour et al[20] found that a 1-g oral dose of TXA given 2 hours before surgery and every 6 hours postoperatively for 18 hours led to substantially less blood loss compared with that of control subjects (364 mL versus 588 mL) at 24 hours postoperatively. Zohar et al[21] found similar success with oral TXA in a prospective, randomized, single-blind study of 80 patients. Patients who received a 1-g oral dose of TXA 1 hour before surgery and a redose postoperatively every 6 hours for 18 hours had substantially lower allogeneic blood transfusion rates than did control subjects. Additionally, the oral regimen was as effective as an IV regimen and a combined IV and oral regimen.

Efficacy in Primary Total Hip Arthroplasty

Similar to TKA, several reports have demonstrated substantially lower rates of blood loss and transfusion requirements associated with the use of TXA during THA[22-25] (Table 2). In a study of 21 patients who underwent staged, bilateral non-cemented THA, patients received a single 1-g IV dose of TXA before skin incision on one hip and no TXA before the surgery on the second hip.[26] Intraoperative blood loss was found to be similar between these groups, but total blood loss was substantially lower in the TXA group than in the control group (1,349 mL versus 1,646 mL) at all time points. Additionally, hemoglobin levels in the TXA group were substantially higher than those in the control group at postoperative days 1, 7, and 14. No thromboembolic complications were noted. Rajesparan et al[27] reported similar results in a study of 73 patients undergoing THA. Thirty-six patients received a single 1-g bolus of TXA before skin incision and the remaining patients did not receive TXA. Although intraoperative blood loss was not affected by TXA, early postoperative and total blood loss were substantially lower. The mean maximum percentage decrease in hematocrit was 16.7% lower in the TXA group (P = 0.004), and the transfusion requirement was significantly lower in this group, as well. All patients underwent postoperative venography, with one deep vein thrombosis (DVT) noted in the TXA group and two noted in the control group.

Niskanen and Korkala[22] investigated the use of TXA in cemented THA in a randomized, double-blind study of 39 patients. In the experimental group, a 10-mg/kg bolus of TXA was administered before surgery, with two additional 10-mg/kg boluses administered at 8-hour intervals. The control group received corresponding doses of saline. Total blood loss was significantly lower in the TXA group than in the control group (792 mL versus 1,102 mL; P = 0.03). No thromboembolic complications were noted.

In a randomized controlled trial of 66 patients who underwent cemented THA, McConnell et al[28] compared the reduction in blood loss associated with the use of TXA or fibrin spray. The TXA group received a 10-mg/kg IV bolus before surgery, the second group received 10 mL of fibrin spray during surgery, and the control group did not receive TXA or fibrin spray. Blood loss was substantially reduced in both the TXA and fibrin spray groups compared with the control group.

Two meta-analyses have investigated the use of TXA in primary THA, with positive findings reported. Gill and Rosenstein[29] examined 13 randomized controlled trials and found that the use of IV TXA in various doses substantially reduced intraoperative and total blood loss, but they found no corresponding decrease in the units of blood transfused. However, these studies lacked standard transfusion thresholds, limiting the interpretation of the results. The authors found no significant differences between the TXA and control groups with regard to DVT or pulmonary embolism (PE). Zhou et al[23] analyzed 19 randomized control trials that used various doses of IV TXA in THA. Compared with the control group, there were marked reductions in total, intraoperative, postoperative, and hidden blood loss in the TXA group. In addition, fewer patients who received TXA required blood transfusion, and there was no difference between the groups with regard to the incidence of DVT or PE.

Although the literature on the use of IV TXA in THA is more robust than that for topical and oral TXA, multiple studies have demonstrated the positive effects of topical and oral TXA. In a recent retrospective study of 388 THAs, Chang et al[30] found that there was a smaller decrease in hemoglobin (1.87 g/dL) and decreased transfusion rates (17% versus 35%) in the topical TXA group than in control subjects. In a randomized double-blind controlled trial by Yue et al,[24] 52 patients received a 3-g dose of topical TXA, and 51 patients received the same dose of saline. The TXA group had a lower transfusion rate than did the control group (5.7% versus 22.4%), with no difference in thromboembolic complications reported. Only one study has evaluated the use of oral TXA in primary THA. Irwin et al[19] found that oral TXA was more effective than IV TXA in reducing the risk of transfusion (odds ratio, 0.48) in a study of both primary TKA and THA.

Efficacy in Revision Total Hip and Knee Arthroplasty

Few studies have examined the use of TXA in revision arthroplasty. However, these studies are limited by their retrospective design, small patient numbers, and the heterogeneity of the procedure. Nonetheless, the available reports found that the use of TXA was associated with reduced blood loss and decreased transfusion rates. This is consistent with numerous reports of the use of TXA in primary TJA.[31-33]

In a case-control study of 40 patients treated with a variety of revision THA procedures, the use of TXA and blood salvage markedly reduced both the number of patients who required transfusion and the total amount of blood transfused compared with the control group.[31] Noordin et al[32] also reported that use of TXA resulted in a decreased number of blood transfusions in a retrospective review of 159 patients who underwent revision THA.

In a retrospective study, Smit et al[33] examined the use of TXA in various revision TKAs. The authors found that a single intraoperative dose of TXA before tourniquet release reduced hemoglobin loss, transfusion rates, and the volume transfused. The transfusion rates were substantially lower in revision of both components and stage one of a two-stage revision to manage infection, with a trend toward reduced transfusion rates in the second stage of the procedure. For an isolated insert exchange, no difference was found in the rate of transfusion with the use of TXA.

Dosage and Timing of Intravenous Administration

In the literature, extensive variability exists with regard to dosage, timing of TXA administration, and the number of doses required. Additional heterogeneity exists among study designs, and small patient numbers further limit many studies. As a result, drawing clear conclusions regarding appropriate IV dosage and timing of administration are difficult, but some general conclusions can be made.

In many published reports on the use of IV TXA in TJA, doses ranged from 10 to 20 mg/kg, and several studies have used a standardized dose of 1 g. Other studies have examined the use of TXA bolus followed by intraoperative infusion, although this dosing regimen is not well described in the orthopaedic literature.[34] Few studies have compared the effects of different doses of TXA. In a recent prospective randomized controlled study, the use of a 1-g IV dose of TXA was compared with a weight-based dose of 20 mg/kg administered before tourniquet release in primary TKA.[35] Compared with the control group, both TXA groups showed a substantial improvement in blood loss, but there was no difference in efficacy between the two experimental groups. Another study examined the use of TXA in bilateral TKA, with one dose given before the tourniquet release and a repeat dose administered 3 hours later.[12] No significant difference was found between a 10-mg/kg dose and a 15-mg/kg dose with regard to transfusion volume. Thus, the authors concluded that the lower dose was equally effective in reducing the transfusion requirement. In a meta-analysis of the use of TXA in various surgical procedures, including cardiac, orthopaedic, obstetric and gynecologic, head and neck, breast

cancer, and hepatic and urologic surgery, the doses used varied from 5.5 to 300 mg/kg.[36] The authors reported a poor dose-response relationship between TXA dose and blood loss and found that a total dose of 1 g, or approximately 14 mg/kg was sufficient for most adults. It should be noted that there was substantial heterogeneity among the studies included in the meta-analysis, no evaluation of redosing was performed, and blood loss alone may be a suboptimal outcome measure. In contrast, another meta-analysis on the use of TXA in TKA indicated that a total combined dose of >4 g of TXA may be associated with reduced transfusion rates.[37] However, the authors indicated that the small number of patients in the included studies and their heterogeneity require further investigation. Rajesparan et al[27] examined the effect of IV TXA on blood loss in THA and found that a total IV dose >1 g may be beneficial in reducing blood loss. The authors used a standard 1-g IV dose at induction for patients undergoing primary THA and reported a negative correlation between the dose per kg of TXA and total blood loss in women. This correlation did not extend to men; however, the number of patients in the study was limited.

The timing of the IV TXA dose appears to play a role in its effect on blood loss in patients undergoing TJA. Tanaka et al[13] reported that, in patients who underwent TKA, mean postoperative hemoglobin levels were higher and mean apparent and calculated blood loss measurements were lower if the TXA was given 10 minutes preoperatively as opposed to 10 minutes before tourniquet deflation, although these differences did not achieve statistical significance. In a study of patients who underwent noncemented primary THA with a variety of dosing regimens, Imai et al[38] reported that an IV TXA dose administered 10 minutes before surgery rather than 10 minutes before closure substantially reduced intraoperative blood loss. Furthermore, in groups that received a preoperative TXA dose, estimated actual blood loss, drain output, hemoglobin reduction on postoperative day 1, and maximum hemoglobin reduction were all substantially lower than in the control group. Postoperative blood loss was also lower in the group that received a preoperative dose and a second dose 6 hours later than in the group that received a dose 10 minutes before closure and another dose 6 hours later.

The value of redosing TXA is more apparent than is the dose required for optimal benefit. A meta-analysis of 18 randomized controlled trials that included 1,094 patients who underwent primary TKA indicated that redosing of IV TXA may reduce the need for transfusion.[39] Similarly, Iwai et al[40] found that postoperative blood loss was reduced in patients who underwent TKA when TXA was redosed after 3 hours versus administration of a single dose alone. Tanaka et al[13] evaluated a variety of timing and redosing regimens in patients undergoing TKA. They found that, compared with a single dose of TXA alone, redosing resulted in reduced apparent and calculated blood loss as well as higher minimum hemoglobin levels postoperatively. In another study of the use of TXA in TKA, the authors examined different TXA doses, time measurements, and methods of administration. Compared with the control group and the group that received a single intraoperative dose of TXA, the use of repeated doses (ie, preoperative/intraoperative and preoperative/intraoperative/postoperative) was shown to be more effective in reducing total blood loss.[41] The three-dose regimen (ie, 10 mg/kg given preoperatively, intraoperatively, and postoperatively) resulted in a significant reduction in drain loss compared with a single intraoperative dose. In contrast, Lin et al[42] found no benefit with regard to mean total blood loss or transfusion rates in primary minimally invasive TKA when a preoperative dose of TXA was given in addition to a standard dose given at tourniquet deflation. Although few data exist regarding TXA redosing in revision surgery, the associated decrease in both blood loss and the length of surgery, along with the encouraging results reported for standard TJA, supports redosing TXA in the revision setting. It is important to note that, even with redosing regimens (some as long as 5 days postoperatively), no evidence of increased risk for venous thromboembolism (VTE) has been shown.[14,40,43] Administration of additional doses 24 hours after surgery is of questionable benefit, however.[44]

Given the available evidence, an IV TXA dose of 10 to 20 mg/kg is reasonable for most patients undergoing primary or revision TJA. This range has been shown to be effective in reducing blood loss and transfusion requirements.[12,27,34,35] Furthermore, with regard to timing, convincing evidence exists for the use of an initial dose given before the beginning of the procedure, with at least one repeated dose. This recommendation is also consistent with published pharmacokinetics, which indicate that a single TXA dose of 10 mg/kg should maintain plasma concentration of 10 to 15 ng/mL (ie, the estimated level required for fibrinolysis suppression) for 3 to 4 hours in an otherwise healthy person.[45] Based on this evidence, at our institutions, a standard 1-g IV dose of TXA is given before incision or tourniquet inflation with an additional 1-g IV dose given at closure. This appears to be sufficiently effective and obviates the need for weight-based calculations. Additional large studies will be needed

to further refine the ideal dosing and timing of IV TXA.

Cost Analysis

Several studies have shown TXA to be a significant cost-saving measure secondary to reduced transfusion-related expenses; it has also proven to be more cost-effective than other transfusion-preventing interventions (eg, fibrin spray).[14,25,27,28,31,46,47] The amount saved varies by institution and depends on the costs of transfusion, the pharmacy costs associated with TXA, and the regimen used. In one study, the use of IV TXA increased pharmacy costs by a mean of $140 per patient, but this was offset by a reduction in transfusion rates from 21.6% to 8.9%, which led to a direct hospital cost savings of $879, on average.[48] In a similar study, topical TXA reduced blood bank costs and helped to offset increased pharmacy costs, with an overall reduced direct cost to the hospital, resulting in approximately $1,500 of savings per patient.[9] Transfusions have been linked to increased complications, such as infection, in patients who underwent THA and TKA.[6] Therefore, additional cost savings may be realized by avoiding complications, although this value is difficult to study and quantify.

In addition to reduced transfusion costs, other factors related to transfusion and elevated postoperative hemoglobin levels may provide real economic benefits. These benefits include improved endurance and activity tolerance, better attendance at physical therapy associated with reduced need for transfusion, shorter hospital stay, discharging patients to home rather than to skilled nursing facilities, and decreased readmission rates. Retrospective reviews have shown that, following the introduction of TXA protocols, the length of hospital stay was reduced by as much as 1 day for THA and 1.2 days for TKA.[49,50] Another study reported shorter hospital stays following TKA associated with the use of TXA, but no difference was found in the rates of discharge to home versus discharge to a skilled nursing or rehabilitation facility.[15] One study did report a 9.3% increase in the rate of discharge to home after the institution of a TXA protocol.[46] In addition, a randomized controlled trial on the use of topical TXA in THA and TKA showed a trend toward reduced 30-day readmissions.[51]

Tranexamic Acid in High Risk Patients

Patients considered to be at high risk for VTE events, such as those with a history of stroke or VTE and those with cardiac stents, have generally been excluded in studies of TXA because of concern that it may increase the risk of VTE events. Therefore, evaluating the safety and efficacy of TXA in this population is difficult. One retrospective study examined 1,102 patients with an American Society of Anesthesiologists score of III or IV who underwent TKA or THA (1,131 primary procedures). Of these patients, 402 were considered high risk and 240 received TXA.[52] Patients were considered high risk if they had one or more thromboembolic risk factors, including prior DVT, PE, myocardial infraction, cerebrovascular accident, coronary artery stent placement, coronary artery bypass graft, or a prothrombotic condition (eg, Factor V Leiden deficiency, protein C deficiency, antiphospholipid syndrome). The authors found that high-risk patients had no increased risk for symptomatic VTE within 30 days of surgery when IV TXA was used. However, the study was underpowered, making it difficult to draw firm conclusions regarding the use of TXA in high-risk patients. Many have advocated the use of topical TXA in this population because there appears to be no increased risk of PE or DVT.[53]

Tranexamic Acid and VTE Prophylaxis

The use of a broad spectrum of postoperative VTE chemoprophylaxis has been described. Currently, no evidence exists to suggest that one chemoprophylactic agent used in conjunction with TXA influences the risk of VTE following TJA. A single retrospective study of patients undergoing THA or TKA (with high-risk patients excluded), found similar rates of symptomatic DVT and nonfatal PE in patients taking aspirin, warfarin, and dalteparin.[54] Of note, the study was adequately powered to assess for differences in symptomatic DVT, but not PE.

Contraindications, Cautions, and Complications

Aside from allergy/hypersensitivity, active thromboembolic disease, and seizure disorder, there are currently no clear contraindications to the use of TXA in TJA. TXA is able to cross the blood-brain barrier and has the potential to induce seizures secondary to its interaction with glycine receptors.[55] An increased incidence of postoperative seizures in patients undergoing cardiac surgery and in patients with renal dysfunction has been reported with high doses of TXA (50 mg/kg). In the arthroplasty literature, no reports of seizures exist, but the use of topical TXA in lieu of IV TXA may be reasonable in patients with known seizure disorders.

Impaired color vision and visual disturbances also have been reported with the use of TXA. Therefore, impaired color vision is a relative contraindication to allow for monitoring of potential toxicity. Given the relatively low doses and timing of administration, this complication is potentially less of a concern with the use of TXA in arthroplasty surgery.

TXA is cleared renally; therefore, adjustments should be made for patients with compromised renal function, but this does not preclude its safe use. Reports of patients with seizure activity attributed to TXA administration have generally been associated with higher doses and renal dysfunction, leading to medication accumulation.

With regard to the potential complications associated with the use of TXA in TJA, studies have predominantly focused on VTE events. Several studies have used routine postoperative screening in the form of ultrasonography, whole body CT, ventilation-perfusion scan, and venography.[13,15,27,38] These studies report no increased risk of VTE, but they are limited by the low number of patients, may be underpowered, and have the potential for type II error (ie, the failure to reject a false null hypothesis). Multiple meta-analyses have examined whether an increased risk of VTE associated with the use of TXA exists, and none has found an increased risk of VTE, infection, or adverse outcome.[11,37,39,56-57]

Summary

Numerous randomized studies and meta-analyses have shown TXA to be a cost-effective method of reducing perioperative blood loss and transfusions in both primary and revision THA and TKA. Both topical and IV routes of administration, with a variety of dosing regimens, have proven effective. Moreover, relatively few adverse reactions have been reported in the arthroplasty literature, and no link to increased thromboembolic episodes has been demonstrated.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 6, 9-12, 14, 17, 18, 20, 21-23, 25, 27-29, 34-39, 41-43, 56, and 57 are level I studies. References 4, 13, 26, and 40 are level II studies. References 19, 30-33, 44, 47-50, 53, and 54 are level III studies. References 2, 3, 5, 7, 15, 16, 46, and 52 are level IV studies.

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