Intra-articular injection of tranexamic acid to reduce blood loss after total knee arthroplasty

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ABSTRACT

Purpose. To evaluate the effect of intra-articular tranexamic acid (TXA) on blood loss after total knee arthroplasty (TKA).

Methods. Medical records of 73 men and 93 women (mean age, 68 years) who underwent primary TKA for osteoarthritis and received intra-articular TXA 1500 mg (n=56) or 3000 mg (n=56) or not at all (n=54) were reviewed. Reduction in haemoglobin levels on days 1 and 2 was measured, as were the rates of venous thromboembolism (VTE) and blood transfusion.

Results. Reduction in haemoglobin levels on day 2 was significantly greater in controls (35±11 g/dl) than the 1500 mg TXA group (29±9 g/dl, p=0.005) and the 3000 mg TXA group (23±10 g/dl, p<0.001). The difference between the 2 TXA groups was also significant (p=0.002). There was a dose-dependent effect of TXA on blood loss. The rates of VTE and blood transfusion did not differ significantly between groups.

Conclusion. Intra-articular administration of TXA is effective in reducing blood loss after TKA, without increasing the risk of VTE.

Key words: arthroplasty, replacement, knee; hemorrhage; hemostasis; tranexamic acid

INTRODUCTION

Increased bleeding after total knee arthroplasty (TKA) may necessitate blood transfusion and result in knee joint swelling, knee motion restriction, and delayed recovery. Surgical trauma and the use of a pneumatic tourniquet activate the fibrinolytic system in the first few postoperative hours.1 Ischaemia increases fibrinolysis owing to the proteolytic action of plasmin, which leads to fibrinogen scission. This increases postoperative blood loss and thus the need for blood transfusion. Methods to reduce peri-operative bleeding and the need for blood transfusion include hypotensive anaesthesia, preoperative autologous blood donation, intra-operative blood salvage, and haemodilution.2

Tranexamic acid (TXA) is a synthetic amino acid
that inhibits fibrinolysis by saturating the lysine binding sites of plasminogen, thereby competitively inhibiting plasminogen from binding to fibrin.\textsuperscript{3} At higher concentrations, it is a non-competitive inhibitor of plasmin.\textsuperscript{4} Intravenous administration of TXA reduces blood loss and thus the need for blood transfusion after TKA,\textsuperscript{2,4–9} but there are concerns regarding increased risk of venous thromboembolism (VTE). In animal studies, intravenous TXA at high doses over prolonged periods increases thromboembolic toxicity.\textsuperscript{4} However, the risk of VTE does not increase significantly.\textsuperscript{10–14} To detect a 1\% increase in risk, trials with approximately 5000 patients are needed.\textsuperscript{5} Intra-articular administration of TXA minimises the systemic effects on inducing hypercoagulable states.\textsuperscript{3} We evaluated the effect of intra-articular TXA on blood loss after TKA.

**MATERIALS AND METHODS**

Medical records of a consecutive series of 73 men and 93 women (mean age, 68 years) who underwent primary TKA for osteoarthritis between April 2010 and April 2012 and received intra-articular TXA 1500 mg (n=56) or 3000 mg (n=56) or not at all (n=54) were retrospectively reviewed. Patients with a history of haematological disease, severe cardiorespiratory disease, thromboembolic disease, revision TKA, concurrent removal of hardware, extensive synovectomy, or a lateral patellar retinacular release were excluded, as were those who had taken anticoagulants within 5 days prior to TKA. One patient who sustained an intra-operative medial epicondylar avulsion fracture requiring fixation was also excluded.

All operations were performed under spinal anaesthesia through the medial parapatellar approach by 2 surgeons who specialised in TKA. Cemented posterior stabilised prostheses were used: the Legion Knee System (Smith and Nephew, Memphis [TN], USA) or the NexGen LPS Flex (Zimmer, Warsaw [IN], USA). The patella was resurfaced. A tourniquet was used only for the initial surgical exposure and was deflated later.

When an intramedullary guide was used, a bone plug from resection was inserted into the femoral drill hole before cementing to minimise bleeding from canal instrumentation. The intramedullary canal was not violated when a magnetic resonance imaging (MRI)-based cutting guide was used. 44 and 10 knees in the control group, and 13 and 43 knees in the 3000 mg TXA group were aligned with the MRI-based cutting guide and intramedullary guide, respectively.

A solution of 100 ml of 0.2\% ropivacaine with adrenaline and 80 mg triamcinolone acetonide was infiltrated into the posterior capsule, collateral ligaments, and synovium. A further 60 to 100 ml of 0.2\% ropivacaine was infiltrated in the extensor mechanism and skin, depending on the weight of the patient.

A 16 gauge epidural catheter was inserted into the knee joint via the lateral gutter prior to wound closure. TXA was then infiltrated into the joint through the catheter and a compression dressing applied. Another dose of analgesia consisting of 50 ml of 0.2\% ropivacaine and 30 mg of ketorolac was injected through the intra-articular catheter into the knee joint the following day. The intra-articular catheter was then removed. Surgical drains were not used.

For VTE prophylaxis, all patients received bilateral intermittent pneumatic calf compressors, thromboembolic deterrent stockings, and subcutaneous injection of enoxaparin (40 mg daily) or oral administration of aspirin (100 mg daily) according to the surgeon’s preference. More patients received aspirin than enoxaparin in all groups, particularly in the control group. Thus, less blood loss was expected in the control group.\textsuperscript{15} Mobilisation was allowed within 24 hours. Spiral computed tomography pulmonary angiogram was performed when pulmonary embolism was suspected.

Reduction in haemoglobin levels on days 1 and 2 was measured, as were the rates of VTE and blood transfusion. Patients with haemoglobin levels of <80g/dl or having symptoms of acute anaemia underwent blood transfusion at the surgeon’s discretion. Separate unpaired Student’s $t$-tests with Bonferroni correction were used to compare between-group differences. A $p$ value of 0.016 (0.05/3) was considered statistically significant.

**RESULTS**

Reduction in haemoglobin levels on day 2 was significantly greater in controls (35±11 g/dl) than the 1500 mg TXA group (29±9 g/dl, $p=0.005$, $t$ test) and the 3000 mg TXA group (23±10 g/dl, $p<0.001$, $t$ test). The difference between the 2 TXA groups was also significant ($p=0.002$, $t$ test) [Table]. There was a dose-dependent effect of TXA on blood loss. Respectively of the 3 groups, 2, 2, and one patients received 4, 3, and 2 units of blood.

One patient in each group developed deep vein thrombosis. One patient in the 3000 mg TXA group developed a non-fatal pulmonary embolus, which
was managed with 6 months of coumadin therapy. One patient in the control group and 2 patients in the 1500 mg TXA group had superficial wound infection, which was treated with intravenous antibiotics. One patient with a history of unstable diabetes mellitus in the 3000 mg TXA group developed a deep wound infection and underwent a 2-stage revision arthroplasty.

**DISCUSSION**

Intravenous TXA reduces blood loss by nearly 30% and the need for blood transfusion by 53%. In our study, respectively in the 1500 mg and 3000 mg TXA groups, the decreases in blood loss were 16% and 32% and decreases in the need for blood transfusion were 25% and 50%. Intra-articular administration of TXA may reduce the risk of systemic absorption.

Topical application of 1500 mg or 3000 mg TXA for 5 minutes after cementing, followed by suctioning of excess solution prior to wound closure reduces blood loss by 20 to 25%; the efficacy between the 2 groups does not differ significantly. Plasma levels after topical application of TXA are approximately 70% less than those after intravenous TXA of equivalent dose. There is no increase in the VTE risk owing to the subtherapeutic plasma levels of TXA.

This study had some limitations. It was a retrospective study and thus there may have been selection bias and confounders. Patients were not routinely scanned for VTE; hence, patients with asymptomatic deep vein thrombosis or pulmonary embolism would not have been detected. This study was statistically underpowered to evaluate for any differences in VTE or blood transfusion requirements between groups. More patients received aspirin than enoxaparin for VTE prophylaxis in all groups, particularly in the control group. Thus, less blood loss was expected in the control group. The use of different cutting guides may have had a confounding effect.

**CONCLUSION**

Intra-articular administration of TXA is effective in reducing blood loss after TKA, without increasing the risk of VTE.

**DISCLOSURE**

No conflicts of interest were declared by the authors.

**REFERENCES**