

## **The use of tranexamic acid in revision total hip arthroplasty: A pilot study.**

*Brian J, Chase E, Rosenstein AD. Curr Orthop Prac. 2009; 20:152-6.*

Background: Revision total hip arthroplasty is becoming a more commonly performed procedure as patients are living longer and demanding more active lifestyles. However, these procedures can cause a significant amount of blood loss resulting in transfusions.

Methods: A double-blinded, randomized, controlled clinical trial was done to investigate the use of tranexamic acid in revision hip arthroplasty. Data collected included hemoglobin and hematocrit levels for the first 3 postoperative days, blood loss, allogenic blood transfusions, hospital stay, complications and cost of using tranexamic acid with regards to blood transfusions. A total of 10 patients (5 tranexamic acid and 5 placebo) were enrolled in the study.

Results: The placebo group averaged  $3.6 \pm 2.19$  units of allogenic blood transfusions while the tranexamic acid group averaged  $0.4 \pm 0.89$  units ( $P < 0.03$ ). No significant difference was found in length of hospital stay between the placebo and tranexamic acid groups (4.8 days compared with 5.5 days,  $P = 0.52$ ). No complications were reported. The cost of allogenic blood transfusions was reduced by approximately \$800 per patient ( $P < 0.03$ ) in the tranexamic acid group.

Conclusions: Tranexamic acid is effective in reducing allogenic blood transfusions in revision total hip arthroplasty. This drug is a viable option to minimize the use of allogenic blood transfusions in revision total hip arthroplasty surgeries.

## **Blood conservation with tranexamic acid in total hip arthroplasty: A randomized, double-blind study in 40 primary operations.**

*Benoni G, Fredin H, Knebel R, Nilsson P. Acta Orthop Scand. 2001; 72:442-8.*

We performed a randomized, double-blind study on the effect of tranexamic acid on blood loss and blood transfusions in 40 primary total hip arthroplasties. Tranexamic acid, 10 mg/kg body weight, or placebo, was given intravenously just before the operation. Blood loss during the operation and postoperatively into the drains was recorded, as also were blood hemoglobin concentrations. Ultrasound examination 1 week postoperatively was done to estimate the blood loss due to remaining hematomas. Total (operation + drain) blood loss was 0.76 (95 CI 0.63-0.89) L in the tranexamic acid group as compared to 1.0 (CI 0.81-1.2) L in the placebo group ( $p = 0.03$ ). The number of blood transfusions

during the day of operation was 2 vs. 10 ( $p = 0.07$ ) and the total number during the hospital stay was 5 vs. 13 ( $p = 0.2$ ). 1 patient in each group had a pulmonary embolism.

### **Tranexamic acid reduces blood loss after cementless total hip arthroplasty- prospective randomized study in 40 cases.**

*Yamasaki S, Masuhara K, Fuji T. Int Orthop. 2004; 28:69-73.*

We investigated the effects of tranexamic acid in 40 patients who had received cementless total hip arthroplasty (THA) in a prospective, randomized study. In 20 patients, 1000 mg of whole-body tranexamic acid was administered intravenously 5 min before the operation started. The other 20 patients served as a control group and were operated on without tranexamic acid. Perioperative blood loss was similar in the tranexamic acid group and in the control group. Postoperative blood loss of the tranexamic acid group was significantly less than that of the control group at 2, 4, 6, 8, 10, and 12 h. Regarding time-related changes of postoperative blood loss, significant reduction was observed during the first 2 h after surgery in the tranexamic acid group ( $P < 0.001$ ). After the first 2 h, there was no significant difference between the tranexamic acid group and the control group. Preoperative administration of tranexamic acid decreased postoperative blood loss until 12 h and total bleeding in cementless THA by reduction of blood loss during the first 2 h after surgery.

### **Tranexamic acid reduces postoperative blood loss in cementless total hip arthroplasty.**

*Yamasaki S, Masuhara K, Fuji T. J Bone Joint Surg Am. 2005; 87:766-70.*

**BACKGROUND:** Tranexamic acid, an inhibitor of fibrinolysis that blocks the lysine-binding site of plasminogen to fibrin, has been reported to reduce intraoperative and postoperative blood loss in patients undergoing total hip arthroplasty with cement. However, there have been few reports describing the effects of tranexamic acid on blood loss during and following total hip arthroplasty without cement.

**METHODS:** We investigated the effects of tranexamic acid in twenty-one patients who underwent staged bilateral total hip arthroplasty without cement for the treatment of osteoarthritis of the hip. The average interval between the two procedures was 16 +/- 16 months. On one side, 1000 mg of tranexamic acid was administered intravenously five minutes before the skin incision. On the other side, tranexamic acid was not administered.

Baseline hemoglobin and hematocrit values were obtained three weeks before each arthroplasty. The volume of postoperative blood loss was recorded at two-hour intervals for the first twelve hours and then again at twenty-four hours, and the values were compared between the two groups.

**RESULTS:** The total intraoperative blood loss in the tranexamic acid group (607 +/- 298 mL) was similar to that in the control group (633 +/- 220 mL). The postoperative blood loss in the tranexamic acid group was significantly lower than that in the control group at all time-points during the first twenty-four hours ( $p < 0.001$  for all comparisons). The greatest reduction in blood loss was observed during the first four hours after surgery in the tranexamic acid group ( $p < 0.01$ ).

**CONCLUSIONS:** In patients undergoing total hip arthroplasty without cement, preoperative administration of tranexamic acid is associated with decreased postoperative blood loss during the first twenty-four hours, especially during the first four hours after surgery.

### **Low risk of thromboembolic complications with tranexamic acid after primary total hip and knee arthroplasty**

*Gillette BP, DeSimone LJ, Trousdale RT, Pagnano MW, Sierra RJ.: Clin Orthop Relat Res. 2013 Jan; 471(1):150-4. Source: Department of Orthopedic Surgery, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA.*

**BACKGROUND:** The use of antifibrinolytic medications in hip and knee arthroplasty reduces intraoperative blood loss and decreases transfusion rates postoperatively. Tranexamic acid (TXA) specifically has not been associated with increased thromboembolic (TE) complications, but concerns remain about the risk of symptomatic TE events, particularly when less aggressive chemical prophylaxis methods such as aspirin alone are chosen.

**QUESTIONS/PURPOSES:** We determined whether the rate of symptomatic TE events differed among patients given intraoperative TXA when three different postoperative prophylactic regimens were used after primary THA and TKA.

**METHODS:** We retrospectively reviewed 2046 patients who underwent primary THA or TKA and received TXA from 2007 to 2009. The three chemical regimens included aspirin alone, warfarin (target international normalized ratio, 1.8-2.2), and dalteparin. Primary outcome measures were venous TE events, including symptomatic deep vein thrombosis (DVT) and pulmonary embolism (PE), and arterioocclusive events, including myocardial

infarction and cerebrovascular accident. Patients judged to be at high risk for TE due to recent cardiac stent placement or strong personal/family history of TE disease were excluded.

RESULTS: For aspirin, warfarin, and dalteparin, the rates of symptomatic DVT (0.35%, 0.15%, and 0.52%, respectively) and nonfatal PE were similar (0.17%, 0.43%, and 0.26%, respectively). There were no fatal PE. Among the three groups, we found no difference in the rates of symptomatic DVT or PE with or without stratification by ASA score.

CONCLUSIONS: A low complication rate was seen when using TXA as a blood conservation modality during primary THA and TKA with less aggressive thromboprophylactic regimens such as aspirin alone and dose-adjusted warfarin.

### **Tranexamic acid and thrombosis.**

*[No authors listed] Prescrire Int. 2013 Jul;22(140):182-3.*

Tranexamic acid is an antifibrinolytic drug. It therefore reduces bleeding but, in certain situations, it may expose patients to a risk of thrombosis. It is used for the treatment of various types of bleeding, including menorrhagia, haematuria, certain surgical procedures and trauma. Its harm-benefit balance is favourable in certain situations associated with serious bleeding. The harm-benefit balance is different in minor bleeding: the expected benefits are smaller because the condition is not serious, and the risk of thromboembolism may be higher without the haemodilution associated with severe bleeding. Various drug regulatory agencies have received reports of thrombotic events attributed to tranexamic acid. In a case-control study using data from the British General Practice Research Database, women taking tranexamic acid had a 3-fold higher risk of developing deep vein thrombosis. There was a wide 95% confidence interval, ranging from 0.7 to 15.8; thus, a major increase in the risk of thrombosis cannot be ruled out. Only one comparative randomised trial assessed thrombotic events in 53 women receiving tranexamic acid for menorrhagia; too few patients were studied to determine the risk. Clinical trials conducted in serious haemorrhage or in patients undergoing surgery with a high risk of bleeding have not shown an increased risk of thrombosis with tranexamic acid. In practice, as of early 2013, the harm-benefit balance of tranexamic acid is favourable in severe traumatic bleeding. But when bleeding is not life-threatening, the thrombotic risk is too poorly documented to justify exposing patients to a plausible and inadequately evaluated risk.

## **The frequency of thrombotic events among adults given antifibrinolytic drugs for spontaneous bleeding: systematic review and meta-analysis of observational studies and randomized trials.**

*Ross J, Al-Shahi Salman R: Curr Drug Saf. 2012 Feb;7(1):44-54. Source: Division of Clinical Neurosciences, Centre for Clinical Brain Sciences, University of Edinburgh, UK.*

**AIMS:** The antifibrinolytic drug tranexamic acid (TXA) improves survival after trauma. Antifibrinolytic drugs may also improve outcome after spontaneous bleeding, so we conducted a systematic review of the frequency of thrombotic events associated with their use after spontaneous bleeding, to help design future randomized controlled trials.

**METHODS:** We sought trials or observational studies of  $\geq 20$  adults involving any antifibrinolytic drug (TXA, epsilonaminocaproic acid (EACA) or aprotinin) for spontaneous (non-traumatic, non-surgical/iatrogenic), non-haemophilic bleeding. We searched the Cochrane Central Register of Controlled Trials, OVID Medline from 1966, EMBASE from 1980, and the bibliographies of relevant articles in October 2009. We meta-analysed proportions of patients with thrombotic events, using a random effects model.

**RESULTS:** We found 57 studies involving 5,049 patients, 3,616 (72%) of whom had spontaneous subarachnoid haemorrhage. 3,414 (68%) patients received TXA-based treatment and 1,635 (32%) received EACA. The frequencies of limb ischaemia and myocardial infarction were  $<1\%$  for TXA and EACA. The frequency of deep vein thrombosis or pulmonary embolism was 1.9% (95% confidence interval (CI) 1.1 to 2.9) for TXA and 3.0% (95% CI 1.8 to 4.6) for EACA. The occurrence of cerebral infarction was restricted to studies of subarachnoid haemorrhage when compared to other indications, both for TXA (9.7% [95% CI 5.5 to 14.8] versus 0% [95% CI 0 to 0.5]) and for EACA (7.7% [95% CI 1.8 to 17.4] versus 0% [95% CI 0 to 2.1]).

**CONCLUSIONS:** Thrombotic events have occurred infrequently with antifibrinolytic drugs after spontaneous bleeding apart from subarachnoid haemorrhage, so further exploration of their safety and efficacy after spontaneous bleeding is justified in randomized trials.

## **Tranexamic acid reduces early post-operative blood loss after total knee arthroplasty: a prospective randomised controlled trial of 29 patients.**

*Orpen NM, Little C, Walker G, Crawford EJ: Knee. 2006 Mar;13(2):106-10. Epub 2006 Feb 17. Department of Orthopaedics, Northampton General Hospital, Northampton NN1 5BD, UK.*

**INTRODUCTION:** Extensive blood loss related to knee arthroplasty is quite normal and many patients require blood transfusions. Surgery and the use of pneumatic tourniquets lead to an increase in the activity of the fibrinolytic system, which in turn may accentuate the blood loss. Drugs that inhibit the fibrinolytic system may thus be used to reduce blood loss. Tranexamic acid (TA) acts by binding to one of the enzymes at the start of the coagulation cascade, so inhibiting the fibrinolytic system. A concern is that this inhibition may have the side effect of increasing thromboembolic disease, a common complication of joint replacement surgery. We aimed to confirm the reductions in blood loss and to assess the impact of TA usage on clinical and sub-clinical DVT.

**METHOD:** We performed a prospective, randomised, double blind, controlled trial, using patients due to undergo primary unilateral total knee arthroplasty. Patients were randomised to receive either 15 mg/kg of tranexamic acid or a similar volume of normal saline at the time of cementing of the prosthesis. Perioperative blood loss was recorded and patients were screened for DVT with duplex ultrasound assessment of both legs on the fifth post-operative day.

**RESULTS:** A statistically significant ( $p=0.006$ ) decrease in blood loss in the early post-operative period was noted in the group receiving tranexamic acid. This was not associated with a significant difference in total blood loss ( $p=0.55$ ) or in transfusion requirements. There was no evidence of DVT in either group on duplex ultrasound screening of the lower limbs.

**INTERPRETATION:** One injection of 15 mg/kg of tranexamic given at the time of cementing the prosthesis in total knee arthroplasty, before deflation of the tourniquet, significantly decreases the amount of blood loss in the early post-operative period. The treatment was not associated with an increase in thromboembolic complications.

### **Effectiveness of tranexamic acid in routine performance of total knee replacement surgery.**

*Camarasa Godoy MA, Serra-Prat M, Palomera Fanegas E: Rev Esp Anesthesiol Reanim. 2008 Feb;55(2):75-80. Servicio de Anestesiología, Reanimación y Clínica del Dolor, Hospital de Matar, Barcelona.*

**OBJETIVES:** To evaluate the effectiveness of treatment with tranexamic acid, compared to absence of antifibrinolytic treatment, in reducing transfusion rates and the number of units of packed red blood cells required in patients undergoing total knee replacement surgery.

**MATERIAL AND METHODS:** We reviewed the medical records of all patients who underwent total knee replacement surgery in a general hospital in 2006. Information was recorded on treatment with tranexamic acid, use of other antifibrinolytic drugs, hemoglobin and hematocrit levels before surgery and 3 days after surgery, patients requiring transfusions, units of packed red blood cells administered, and whether or not drains were clamped within 4 hours. Complications attributable to tranexamic acid (thromboembolic or systemic complications) and preoperative treatment with erythropoietin were also recorded.

**RESULTS:** Data for 166 patients were analyzed. Of these, 120 (72.3%) received tranexamic acid, 15 (9%) received epsilon-aminocaproic acid, and 31 (18.7%) received no antifibrinolytic treatment. Transfusions were given to 17 patients, of whom 6 (5.0%) had received tranexamic acid, 2 (13.3%) had received epsilon-aminocaproic acid, and 9 (29.0%) had received no antifibrinolytic treatment. The mean numbers of packed red blood cell units transfused in each group were as follows: 0.075 in the tranexamic acid group, 0.200 in the epsilon-aminocaproic acid group, and 0.645 in the group with no antifibrinolytic treatment ( $P < .001$ ). The mean decrease in hemoglobin levels 5 days after surgery was 3.04 g/dL in the tranexamic acid group, 3.55 g/dL in the epsilon-aminocaproic acid group and 3.76 g/dL in the group with no antifibrinolytic treatment ( $P < .001$ ).

**CONCLUSIONS:** Tranexamic acid is effective in reducing the percentage of patients requiring transfusions and in the number of units of packed red blood cells required in total knee replacement surgery. No complications attributable to this treatment were found.