# *Editorial Commentary:* Tranexamic Acid: Okay, It Reduces the Bleeding, but Are We Sure Topical Use Is Not Harmful to the Cartilage?

Assoc. Prof. Dr. Fatih Karaaslan

**Abstract:** Numerous studies have estimated the role of hemarthrosis and intra-articular drains in anterior cruciate ligament (ACL) reconstructive procedures. Long-standing hemarthrosis and related pain can disrupt rehabilitation and lead to arthrofibrosis. A significant number of orthopaedic surgeons use intra-articular suction drains following arthroscopic ACL reconstruction. Hemarthrosis and pain have undesirable effects on the functional outcomes of ACL reconstruction in the early postoperative period.

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An increasing number of studies on use of tranexamic acid (TXA) for controlling bleeding in orthopaedic surgery have been published over the last decade. TXA has been shown to be effective in orthopaedic surgery, especially total knee and hip arthroplasty and spinal surgery, in minimizing perioperative bleeding. Even though worldwide agreement has not been reached on TXA administration, it is effective in reducing blood loss and the need for transfusion. By decreasing other costs, TXA is cost-effective in specific orthopaedic surgical procedures.[1-8]

The use of TXA to reduce operative and postoperative bleeding and the subsequent need for blood transfusion is well defined for certain orthopaedic procedures, yet it still raises some questions for arthroscopic surgeons.[9,10]

The subject of this commentary is the well-performed study in this issue on reducing hemarthrosis after anterior cruciate ligament reconstruction (ACLR) by Chiang, Chen, Wang, Ma, Chang, Liu, Chen[11] titled "Intra-articular Injection of Tranexamic Acid Reduced Postoperative Hemarthrosis in Arthroscopic Anterior Cruciate Ligament Reconstruction: A Prospective Randomized Study." It is well written, has an important clinical message, and should be of great interest to readers. The authors have considered both postoperative bleeding as well as pain scores. In addition, they studied postoperative clinical scores both with or without use of TXA. Patients were excluded for the following reasons: previous knee procedures on the same side, renal disorder or insufficiency, abnormal coagulation profile, and refusal to participate in the study. The same surgical team performed the same surgical procedure and used a standard postoperative regimen of physiotherapy for all patients. The TXA group patients underwent ACLRs and 10-mL intra-articular injection of TXA after the procedure. Results show that 24 hours after surgery a significant decrease in the amount of drainage in patients receiving the intra-articular injections was observed in the TXA group (56.1 $\pm$ 34.1 mL) versus the control group (80.1 $\pm$ 48 mL; $P < .05$). Also, at day 3 and week 4, significantly reduced pain scores were reported by the TXA group patients. However, at week 4, clinical function scores did not show significant differences between the 2 groups. The authors concluded that intra-articular injection of TXA could be considered as an effective and relatively safe solution to reduce postoperative bleeding and pain in ACLR.[11] However, intra-articular administering of TXA brings some concerns.

Topical administration of TXA may avoid the danger of potentially increased systemic coagulating risk, mainly in patients defined as high risk. Nevertheless, the theory that systemic TXA levels could be reduced is related to TXA administered intravenously. Some studies suggest

*Acibadem University*

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that topically used TXA in doses of 1.5 and 3 g can reach mean plasma values of 4.5 and 8.5 mg/L. Plasma concentrations 1 hour after administration of 10 mg/kg TXA have yielded mean levels of 18 mg/L. Although topically used TXA seems therefore to lead to lower plasma values, one should observe that values between 5 and 10 mg/L are regarded as pharmaceutically active. Thus, at least in theory, topical administration has systemic effects and, possibly, side effects.[12-14]

The risk that a high local level of TXA, once it has been used topically, could cause increasing local complications at the operation site must be carefully considered. Topical use of TXA may offer advantages over intravenous administration with regard to reducing systemic plasma values, but well designed studies are needed to show safety. Meanwhile, the administration of TXA has risen in popularity because of its effectiveness and affordability. However, its risks and benefits need to be continuously evaluated as new data appear, particularly regarding adverse events.

Further studies are required to discover more about the correlation of the effectiveness of TXA with alternative administration procedures, doses, exposure duration, and timing as well as the association of TXA use with functional outcomes. However, we still do not have enough data supporting its use in all joints. There are a few other studies that are concerning with regard to topical use.[15-19] The results reported by McLean et al.[20] suggest that attention must be paid when thinking through exposing articular tissues to TXA at high levels or for exposure times even as short as 1 hour. The method of intra-articular injection or infusion, extended surgical soaking, or tissue saturation, especially in an enclosed joint space, needs to be examined in conjunction with the findings of this study and other studies that demonstrate increasing cell mortality.[20]

I believe it is necessary for studies to focus on determining the chondral and synovial toxic dose limit and exposure time in the joint space, as we well know that the use of TXA may decrease bleeding. I wonder if instead of injection into the joint, diluted TXA in the irrigation fluid may have the same effect with a reduced concern about probable toxic effects. Further studies should add a third group without drains to resolve the uncertainties about the necessity for drain use in ACLR. An analytical and recurrent reconsideration of accessible data is essential to confirm an evidence-based methodology on the suitable administration of TXA. TXA acid may reduce bleeding, but its effect on cartilage requires investigation.

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