Print ISSN 1110-208X.

Online ISSN 2357-0016

Original article

Effect of Tranexamic Acid Local Injection in Anterior Cruciate Ligament Reconstruction on Blood Loss

Mohamed S. Shawky, Ali M. Elmasry, Abdelsamie M. Halawa

Department of Orthopaedic Surgery, Faculty of Medicine Benha University, Egypt.

Corresponding to: Ali M. Elmasry, Department of, Orthopaedic Surgery, Faculty of Medicine, Benha University, Egypt.

Email:

alielmasry48@gmail.com

Received:

Accepted:

Abstract

Background: Hemarthrosis after anterior cruciate ligament (ACL) reconstruction procedures can delay rehabilitation and have toxic effects on the cartilage and synovium. The use of TXA in arthroscopic procedures has become a topic of novel study, as use may decrease the frequency of postoperative hemarthrosis . **Methods:** Our study was conducted on fifty patients (48 males and 2 females). The age varied between 16 and 50 years with a mean age of (22-35 years). The patients were randomized into two groups, Patients in the TXA group (n =25) underwent ACLR and a 10-mL intraarticular injection of TXA after the procedure & Patients in the control group (n = 25) only ACLR without TXA injections. **Results:** the decrease in drainage volume was less in the TXA group than in the Control group. Also, the amount of drainage was significantly reduced in TXA patients who underwent different meniscal procedures. decrease in Hb level was less in TXA group than in the Control group. patients receiving intra-articular injections of TXA showed a significant decrease in mean hemarthrosis grade within the first 2 weeks (TXA group, 0.24±0.47, and control group, 1.52±0.49. **Conclusion:** intra-articular injection of TXA could be considered an effective, efficient, and reproducible method for reducing blood loss and hemarthrosis, with the potential to reduce patient discomfort after arthroscopic ACL reconstruction (ACLR).

Key Words: Tranexamic acid, injection anterior cruciate ligament, reconstruction.

Introduction

Anterior cruciate ligament injury is a common athletic injury and one of the most commonly treated conditions of the knee. [1] the number of anterior cruciate ligament reconstructions (ACLRs) is increasing. Although ACLR is considered a relatively safe and minimally invasive procedure, it is not without potential complications. In a cross-sectional study by Salzler et al.,9%of ACLR patients had reported complications postoperative.[2]

The most common complications were pain (6.7%) and tension hemarthrosis requiring arthrocentesis (4.4%) Hemarthrosis creates many adverse joint effects including increased susceptibility to infection, potential toxic effects to the cartilage, possible subsequent synovitis, and increased scar formation with delayed rehabilitation. [3]

Hemarthrosis after anterior cruciate ligament (ACL) reconstruction procedures can delay rehabilitation and have toxic effects on the cartilage and synovium. Tranexamic acid is widely used in adult reconstruction procedures; however, its use in ACL reconstruction is a novel topic of study. [4]

Tranexamic acid (TXA) is a lysine-based inhibitor of plasminogen— the inactive precursor of plasmin, a potent serine protease involved in the dissolution of fibrin blood clots—that effectively stabilizes formed hemostatic clots and decreases perioperative bleeding. [5]

More recently, however, the use of TXA in arthroscopic procedures has become a topic of novel study, as use may decrease the frequency of postoperative hemarthrosis. This complication has been reported in up to 60% of arthroscopic knee procedures, causing increased postoperative pain and swelling, decreased range of motion (ROM), and higher patient pain scores. While the use of intravenous (IV) TXA for arthroscopic procedures has shown promising results in promoting early function and pain relief, the body of literature delineating its safety profile and effectiveness in arthroscopy, particularly sports medicine procedures, is scant. [4]

The aim of This study was To evaluate the hemostatic effect of local injection of tranexamic acid in patients undergoing anterior cruciate ligament reconstructions on blood loss.

Methods

This prospective randomized study conducted on fifty patients (48 males and 2 females), the age varied between 16 and 50 years with a mean age of (22-35 years) between February 2021 and April 2022. This study was done at Benha University, El Helmia Military and Maadi military hospitals. Upon securing approval from the Institutional Ethical Committee of the Faculty of Medicine BenhaUniversity and obtaining informed consent from each patient.

Inclusion criteria:

- skeletally mature patients with ACLRs
- age above 16 years

- skeletally mature patients with ACLRs with medial and lateral menisceal tear that will be treated by meniscectomy or menisceal repair
- Patient with postoperative drain

Exclusion criteria:

- Previous knee procedures on the same side.
- Age younger than 16 years old.
- Renal disorder or insufficiency.
- Abnormal coagulation profile.
- Known hypersensitivity to tranexamic acid.
- History of known thromboembolic disease within 6 months (ie. DVT, PE).
- Blood transfusion within 3 days' pre-operative.
- Refusal to participate in this study.
- History of any acquired disturbances of color vision.
- Participation in another clinical trial involving pharmaceutical drugs.
- patients with a history of seizures

Demographic data:

Age: Ranged from 18 to 41 years, the average age 24.36±6.96 as regard control group, and ranged from 20 to 50 years, the average age 28.68±6.81 as regard tranexamic acid (TXA) group.

Sex distribution: There were 25 (100%) males and zero (0%) females in the control group and 23 (92%) males and 2 (8%) females in the tranexamic acid (TXA) group.

Clinical data:

Affected Side: 12 cases were Right-sided and 13 cases were Left-sided in the control group while 10 cases were Right-sided and 15 cases were Left-sided in the tranexamic acid group.

Associated Injury :13 cases were torn ACL alone and 12 cases were torn ACL plus meniscal injury in the tranexamic acid group control group while 14 cases were torn ACL alone and 11 cases were torn ACL plus meniscal injury in the tranexamic acid control group.

Surgical Technique:

All patients enrolled in this study were operated by a senior surgeon. Spinal anesthesia was administered in all patients, and a pneumatic tourniquet was routinely used and was not released until skin closure. Surgery was performed using a standard two portal techniques with anterolateral (AL) and anteromedial (AM) portals. The autologous hamstring tendons were harvested and prepared, in brief, through a 3-cm incision over the medial proximal tibia, the semitendinosus and gracilis tendons were harvested from the distal insertion. The tendons were quadrupled and whip stitched by No. 2 and No. 5 Ethibond sutures. The diameters of the folded tendons were determined by using sizing cylinders with incremental size changes of 0.5 mm. The femoral tunnel was created at the lateral femoral condyle through the anteromedial portal. The tibial tunnel was created with an ACL guide. The tunnel diameters were created

in the same manner as the diameter of the folded graft. At the femoral site, grafts were fixed with bioscrews. At the tibial site, grafts were fixed with bioscrews at 30○ of knee flexion. The screw and tunnel sizes were the same. After completion of the procedure, a suction drain (14 F–sized) was placed at the anterolateral aspect of the joint. At the end of the operation, 10 mL of TXA (100 mg/mL) was injected into the joint in the TXA group, and all drains were clamped for 2 hours.

Postoperative Regimen:

All of the patients received postoperative analgesia and prophylactic antibiotic. A compression bandage and ACL brace were routinely used postoperatively. The suction drain at the surgical site was removed 24 hours postoperatively, and the volume of drained blood was measured. The early reductions in Hb level were defined as the difference between the preoperative value and the postoperative sample taken 48 hours after surgery. Patients were discharged from the hospital when postoperative pain was manageable with oral analgesics. Discharge usually occurred between hospital days 2 and 3.

Approval Code: MS 4-2-2021

Results:

A total of 50 patients were available for follow-up (TXA group, n = 25; control group, n = 25) between February 2021 and April 2022.

Drain:

Postoperatively, patients receiving intra-articular injections of TXA showed a significant decrease in drainage within the first 24 hours (TXA group, 182±84.01 mL, and control group, 392±144.83 mL. and that was a statistically significant difference with P. value (<0.001) showing that the decrease in drainage volume was less in the TXA group than in the Control group table (1). Also, the amount of drainage was significantly reduced in TXA patients who underwent different meniscal procedures.

Hemoglobin level: The Mean difference in hemoglobin level was 2.3±0.74 (15.35 %) in the control group while it was 1.41±0.67 (9.76 %) in TXA group and that was a statistically significant difference with P. value (<0.001) showing that the decrease in HB level was less in TXA group than in the Control group (Table 2&3).

Hemarthrosis grade:

Postoperatively, patients receiving intra-articular injections of TXA showed a significant decrease in mean hemarthrosis grade within the first 2 weeks (TXA group, 0.24±0.47, and control group, 1.52±0.49 (Table 4). and that was a statistically significant difference with P. value (<0.001), The between-group difference in hemarthrosis grade after removing the drain was significant between the two groups until the end of week four.

Table 1: Comparison between control and TXA groups as regards drain volume.

Drain volume	WITH TRANEXAMIC ACID (n=25)	WITHOUT TRANEXAMIC ACID (n=25)	P. value
Range	50 – 350	200 – 700	<0.001**
Mean± SD	182±84.01	392±144.83	<0.001**
Median (IQ)	200(100-250)	350(300-500)	<0.001**

Table 2: Comparison between control and TXA groups as regards the decrease in Hb level.

	WITH TRANEXAMIC ACID (n=25)	WITHOUT TRANEXAMIC ACID (n=25)	P. value
Hb level pre-op.	14.44±1.21	14.98±1.1	0.105
Hb level 24hrs post-op.	13.03±0.97	12.69±1.26	0.285
Mean difference	1.41±0.67	2.3±0.74	<0.001**
% Of difference	9.76	15.35	0.865

Table 3: Comparison between control and TXA groups as regards the decrease in HB level preoperative and post-operative.

Hb	WITH TRANEXAMIC ACID (n=25)	WITHOUT TRANEXAMIC ACID (n=25)	P. value
Preoperative			
Range	12 - 16.6	12 – 17	
Mean±SD	14.44±1.21	14.98±1.1	0.150ns
Postoperative			
Range	10.8 - 14.9	10.2 - 14.8	
Mean±SD	13.03±0.97	12.69±1.26	0.285ns
P. value	<0.001**	<0.001**	

Table 4: Comparison between control and TXA groups as regards a decrease in hemarthrosis grade

Hemarthrosis grade	WITH TRANEXAMIC ACID (n=25)		WITHOUTTRANEXAMIC ACID (n=25)		P. value
	No.	%	No.	%	
Follow up after 2 days					
1	12	60.0	0	0.0	
2	8	40.0	8	40.0	<0.001**
3	0	0	12	60.0	
Follow up after 2 weeks					
0	14	70	0	0	
1	6	30	11	55	<0.001**
2	0	0	9	45	
Mean±SD	0.24±0.47		1.52±0.49		
Follow up after 4 weeks					
0	20	100	15	75	
1	0	0	5	25	0.009**

Discussion

A total of 50 patients (from Benha University Hospital, ElHelmia Military Hospital and Maadi Military Hospital) were available for follow-up (TXA group, n = 25; control group, n = 25) between February 2021 and April 2022. The patients were injected intraarticularly and their postoperative drain were evaluated.

According to the demographic data, the age ranged from 18 to 41 years, the average age 24.36±6.96 as regard Control group, and ranged from 20 to 50 years, the average age 28.68±6.81 as regard Tranexamic Acid (TXA) group.

In this study assessed the hemostatic effect of intra-articular injection of TXA after ACLR on various parameters related to drain output, hemoglobin level, and hemarthrosis grade. We found that all parameters are lower with the use of the tranexamic acid group as opposed to the control group as decrease postoperative drain output on the first day. The hemarthrosis grade and drop in hemoglobin levels were also significantly reduced in the early postoperative period. This difference was statistically significant.

When comparing between control and TXA groups as regards drain volume, it was concluded that postoperatively, patients receiving intra-articular injections of TXA showed a significant decrease in drainage within the first 24 hours (TXA group, 182±84.01 mL, and control group, 392±144.83 mL. That was a statistically significant difference with P. value (<0.001) showing that the decrease in drainage volume was less in the TXA group than in the Control group

Drains have been commonly used in ACL surgery to evacuate intraarticular spaces or harvest-site hematoma to accelerate rehabilitation and postoperative outcomes. [6] Felli et al. reported a drainage amount of 59.3 ± 29.5 mL in their IV TXA group and 133.3 ± 56.1 mL in their control group (P < .001). [7]

Chiang et al. have shown that IV or intraarticular (IA) TXA administration may reduce postoperative hemarthrosis, thereby decreasing pain, promoting better rehabilitation, and improving functional outcomes in the short-term period after ACL reconstruction. [2] Sarzaeem et al. reported that IA injection of TXA was more effective at decreasing postoperative drainage after TKA. [8]

Chiang et al. administered 10 mL (100 mg/mL) of intraarticular TXA into the joint at the end of the operation, instead of IV TXA, which showed a significant improvement in hemarthrosis grade and drainage output (mean 6 SD, 56.1 6 34.1 vs 80.1 6 48 mL) within the first 24 hours. [2]

Many strategies have been proposed to reduce the incidence rate of postoperative complications in ACL reconstruction.[9]

The therapeutic effect of tranexamic acid is apparent when the fibrin clot gets prematurely dissolved by proteolysis of plasmin. The tranexamic acid molecule works at an active bleeding site of the wound and not within the blood vessels. Thus, its presence within the clot may be considered effective irrespective of the route of administration. While at therapeutic concentration, the antifibrinolytic action of tranexamic acid involves competitive inhibition of fibrinolysis, at a higher concentration it also acts as a weak non-competitive inhibitor of fibrinolysis .[10]

In this small study, it is that the use of TXA might further decrease intra-

articular bleeding compared with the joints with only closed suction drains in the early postoperative period.

It implied that the beneficial effect of drains in the early postoperative period could be enhanced by the use of TXA in ACLR patients. However, its clinical significance still needs to be clarified.

In another prospective randomized study, it evaluated 80 patients (40 in the TXA group and 40 in the control group), the main finding of this randomized trial is that a single IV administration of TXA 20 to 30 minutes before tourniquet release in patients who underwent ACL reconstruction surgery reduced the blood volume in suction drainage, amount of hemarthrosis, and postoperative pain during the first 2 weeks. TXA use improved early phase outcomes in the postoperative period after ACL reconstruction. .[7]

In another prospective randomized study, a total of 300 patients were enrolled (151 in TXA group and 149 control group,) the results of this prospective, randomized study show that intraarticular injection of TXA could significantly reduce postoperative intra-articular bleeding in the first 24 hours after ACL reconstruction. TXA injection also decreases pain and the grade of hemarthrosis in the early postoperative period. .[2]

In the study of Karaaslan et al. the intravenous administration of TXA could reduce postoperative drainage volume and hemarthrosis following ACLR and alleviate pain and knee swelling, similar to the results of the previous study. .[11]

In the study of Johns et al., tranexamic acid use in ACL reconstruction cases resulted in a mean reduction of 61.5 mL in postoperative drain output at 24 hours (95% CI, –95.51 to 227.46; P = .0004), lower hemarthrosis grade (P < 00001).

Some studies reported that IV administration of TXA could reduce the amount of drainage blood and postoperative hemarthrosis without side effects after ACL reconstruction. [3]

The topical use of TXA could significantly decrease intra-articular bleeding during the first postoperative day. Also, a significant decrease in the grading of hemarthrosis was noted, and none of our patients required aspiration during the follow-up period. Previous studies have concluded that, although TXA may penetrate large joints efficiently after IV administration, it has a relatively short half-life (2 hours) and might remain just above the effective plasma concentration for only 4 to 6 hours. [12]

Postoperatively, patients receiving intra-articular injections of TXA showed a significant decrease in mean hemarthrosis grade within the first 2 weeks (TXA group, 0.24±0.47, and control group, 1.52±0.49. and that was a statistically significant difference with P. value (<0.001), The between-group difference in hemarthrosis grade after removing the drain was significant between the two groups until the end of week four

Hemarthrosis accounts for 60% of all ACL reconstruction complications. Hemarthrosis creates many adverse effects, including increased susceptibility to infection, potential toxic effects to the cartilage, possible subsequent synovitis and arthrofibrosis, the onset of fever episodes, delayed rehabilitation, and prolonged hospital stay. These aspects negatively affect the outcomes of patients and result in increased costs. Minimizing postoperative intra-articular hemarthrosis may be potentially advantageous for recovery in ACLR patients. Our study reported the positive

effects of TXA in reducing hemarthrosis after ACL reconstruction. [4]

Some researchers concluded that there was no statistically significant difference in blood loss and transfusion rates between IA and IV use in TKA. [13]

TXA has anti-inflammatory effects as a plasmin inhibitor and minimizes hemarthrosis formation, which causes inflammation, painful swelling and tension on the joint capsule and soft tissues,5 and possibly a toxic effect on articular cartilage.[14]

According to Johns et al. the use of intravenous tranexamic acid in ACL reconstruction surgery results in reduced joint drain output and hemarthrosis. [3]

Conclusion

The results of this prospective, randomized study show that Intraarticular injection of TXA could significantly reduce the amount of suction drainage in the first 24 hours postoperative and reduced the need for aspiration of the knee in patients who underwent arthroscopic ACL reconstruction.

TXA injection may also decrease pain and the grade of hemarthrosis in the early postoperative period Consequently, TXA reduced pain and improved knee ROM in the early postoperative period. No systemic side effects or need for aspiration was noted during the follow-up period. Therefore, intra-articular injection of TXA could be considered an effective, efficient, and reproducible method for reducing blood loss and hemarthrosis, with the potential to reduce patient discomfort after arthroscopic ACL reconstruction (ACLR).

References

1. NBLyman S, Koulouvaris P, Sherman S, Do H, Mandl LA, Marx RG. Epidemiology of anterior cruciate ligament reconstruction: trends, readmissions, and subsequent knee surgery. JBJS. 2009;91(10):2321-8

2. Chiang E-R, Chen K-H, Wang S-T, Ma H-L, Chang M-C, Liu CL, et al. Intra-articular injection of tranexamic acid reduced postoperative hemarthrosis in arthroscopic anterior cruciate ligament reconstruction: A prospective randomized study. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2019;35(7):2127-32.

3. Johns WL, Walley KC, Hammoud S, Gonzalez TA, Ciccotti MG, Patel NK. Tranexamic Acid in Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. Am J Sports Med. 2021 Dec;49(14):4030-4041..

4. Bahl V, Goyal A, Jain V, Joshi D, Chaudhary D. Effect of haemarthrosis on the rehabilitation of anterior cruciate ligament reconstruction-single bundle versus double bundle. Journal of orthopaedic surgery and research. 2013;8(1):5.

5. Liu X, Liu J, Sun GJIJoS. A comparison of combined intravenous and topical administration of tranexamic acid with intravenous tranexamic acid alone for blood loss reduction after total hip arthroplasty: a meta-analysis. Int J Surg. 2017;41:34-43.

6. Karahan M, Erol B, Bekiroglu N, Uyan DJTAJoSM. Effect of drain placed in the donor site in the early postoperative period after arthroscopically assisted anterior cruciate ligament reconstruction with quadrupled hamstring tendons. Am J Sports Med. 2005 Jun;33(6):900-6.

7. Felli L, Revello S, Burastero G, Gatto P, Carletti A, Formica M, Alessio-Mazzola M. Single Intravenous Administration of Tranexamic Acid in Anterior Cruciate Ligament Reconstruction to Reduce Postoperative Hemarthrosis and Increase Functional Outcomes in the Early Phase of Postoperative Rehabilitation: A Randomized Controlled Trial. Arthroscopy. 2019 Jan;35(1):149-157.

8. Sarzaeem MM, Razi M, Kazemian G, Moghaddam ME, Rasi AM, Karimi M. Comparing efficacy of three methods of tranexamic acid administration in reducing hemoglobin drop following total knee arthroplasty. J Arthroplasty. 2014 Aug;29(8):1521-4.

9. Jameson S, Dowen D, James P, Serrano-Pedraza I, Reed M, Deehan DJTJoB, et al. The burden of arthroscopy of the knee: a contemporary analysis of data from the English NHS. 2011;93(10):1327-33.

10. Verstraete MJD. Clinical application of inhibitors of fibrinolysis. 1985;29(3):236-61.

11. Karaaslan F, Karaoğlu S, Yurdakul EJTAjosm. Reducing intraarticular hemarthrosis after arthroscopic anterior cruciate ligament reconstruction by the administration of intravenous tranexamic acid: a prospective, randomized controlled trial. Am J Sports Med. 2015 Nov;43(11):2720-6.

12. Ahlberg A, Eriksson O, Kjellman H. Diffusion of tranexamic acid to the joint. Acta Orthop Scand. 1976 Oct;47(5):486-8.

13. Wang H, Shen B, Zeng Y. Comparison of topical versus intravenous tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled and prospective cohort trials. Knee. 2014 Dec;21(6):987-93.

14. Yue C, Kang P, Yang P, Xie J, Pei F. Topical application of tranexamic acid in primary total hip arthroplasty: a randomized double-blind controlled trial. J Arthroplasty. 2014 Dec;29(12):2452-6.

To cite this article: Mohamed S. Shawky, Ali M. Elmasry, Abdelsamie M. Halawa. Effect of Tranexamic Acid Local Injection in Anterior Cruciate Ligament Reconstruction on Blood Loss. BMFJ XXX, DOI: 10.21608/bmfj.2024.318393.2194