International Journal of Research in Orthopaedics
Pande A et al. Int J Res Orthop. 2019 Jul;5(4):639-644
http://www.ijoro.org

DOI: http://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20192676

Original Research Article

Assessing the effect of per operative intravenous injection of tranexamic acid in patients undergoing arthroscopic anterior cruciate ligament reconstruction

Ashish Pande[1], Ajit P. Bhaskarwar[2]*

Department of Orthopaedics, [1]Military Hospital, Kirkee, Pune, Maharashtra, [2]92 Base Hospital, Srinagar, Jammu and Kashmir, India

Received: 10 March 2019
Revised: 30 May 2019
Accepted: 01 June 2019

***Correspondence:**
Dr. Ajit P. Bhaskarwar,
E-mail: ajitbhaskarwar909@yahoo.com

ABSTRACT

Background: Anterior cruciate ligament (ACL) tear is a common injury sustained during contact games hampering performance of the sportsmen and thus requires promt management. Arthroscopic ACL reconstruction is commonly associated with postoperative knee effusion which affects the functional recovery. Various treatment modalities are available for managing effusion after ACL reconstruction, which are associated with various grades of success and side effects.
Methods: This prospective interventional study was carried out at tertiary care Orthopaedic centre. It involved 48 Young male athletes with ACL tear managed subsequently by arthroscopic ACL reconstruction. Subjects were divided into Injection group and non injection group by randomization and blinding was ensured. Postoperative rehabilitation, prophylactic antibiotic and chemoprophylaxis for DVT was kept standardised for all patients. Patients were assessed for pain at operative site by visual analogue scale, effusion of knee by classification of Coupens and Yates and Lysholm knee scoring at 2nd, 6th and 12th week postoperatively.
Results: During follow ups it was found that Injection group was having significant less incidence of effusion as compared with Non injection group; which also has reflected in functional recovery.
Conclusions: It can be concluded that use of inj tranexamic acid preoperative dose in case of patients undergoing ACL reconstruction is efficient to reduce the knee effusion.

Keywords: Knee effusion, Arthroscopic ACL reconstruction, Tranexamic acid

INTRODUCTION

The ACL injuries in contact games are one of common occurrences.[1] Anterior cruciate ligament (ACL) injuries are commonly seen injuries occurring in various contact sports i.e, kabaddi, football, basketball, handball, wrestling.[2,3] It leads an impact on the physical capabilities of the sportsman. And hence it is of great importance to have a cruciate ligament stabilized knee to continue or resume the sports activities.

Nowadays arthroscopic procedures are the preferred mode of management of surgeries of the intraarticular knee ligaments over open surgical procedures. However the postoperative knee range of motion, laxity shows no difference in either of them but immediate postoperative pain appears to be decreased in patients undergoing arthroscopic ACL reconstruction.[4]

Drains have been used in orthopaedic surgery with varying degrees of success for many years, specially in

intraarticular procedures to avoid post operative effusion. It is found that the effusion has toxic effect on chondrocytes and matrix and thus leads to postoperative fibrosis which results in difficulty in achieving the range of motion and also increases the risk of postoperative infections in the involved joint.[5,6]

Usually bleeding in case of ACL reconstruction occurs at intraarticular site as well as the graft donor site (hamstring or Bone patellar bone tendon graft) which adds to the formation of the knee effusion post operatively.[7]

Various ways of reducing the bleeding and formation of effusion involves use of tourniquet, drains, or antifibrinolytic chemotherapeutic agents like Inj Tranexamic acid (TXA).

TXA is an synthetic analogue of amino acid lycine and it acts by blocking competitively the plasminogen lycine binding site.[8] TXA is being used in general surgical procedures with considerable successful outcome in controlling the bleeding. And also the effectiveness of TXA in case of replacement surgeries around hip and knee has been proven with positive post operative rehabilitation and less need of blood transfusions posteoperative.[9,10]

The purpose of this study is to evaluate the efficacy of TXA to control bleeding and thus the effusion after ACL reconstruction, to minimize the associated pain, and to improve functional results.

METHODS

This is a prospective interventional study with the subjects evaluated at multiple points of time, carried out at a tertiary care Orthopaedic centre.

***Study design**:* Randomised control trial.

***Study place**:* Military Hospital Kirkee.

***Study duration**:* July 2017 to December 2018.

An approval from the institutional ethical committee was obtained prior to the study.

Procedure

The present study includes 48 consecutive patients who underwent arthroscopic ACL reconstruction with autologus ipsilateral hamstring tendon graft.

Inclusion criteria

Inclusion criteria were young athlete of age group (20 to 45 yrs of age), with less than 01 year time since injury; willing to be the part of surgery and follow the explained post operative rehabilitation protocol.

Exclusion criteria

Exclusion criteria were bleeding / clotting disorders, preoperative anticoagulation therapy, renal disorder or insufficiency, allergic to TXA, significant large preoperative swelling (grade 3 or 4 effusion), or a revision case.

Total of 48 persons were evaluated clinically with or without radiological (MRI) evaluation and were enrolled prospectively to be the part of study.

Mode of injury was twisting injury of the knee during 09 feet ditch jump (48%), twisting injury knee during organized games i.e, basketball, volleyball, hockey, handball (32%) and Road traffic accidents (20%).

Categorization into the injection and control group was done with computer generated randomization.

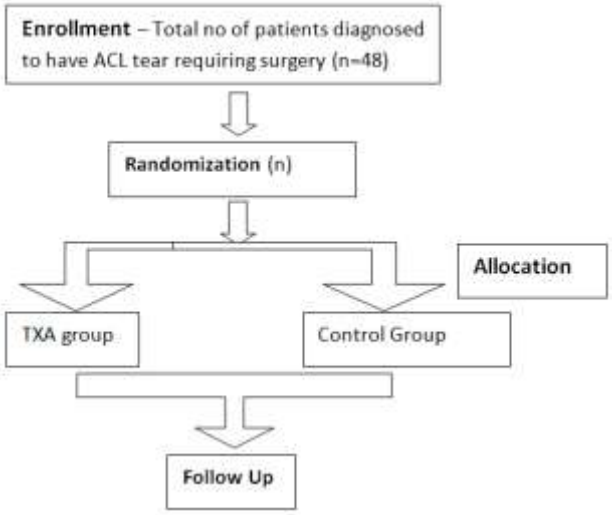

Figure 1: Study design.

Patients randomized to injection group who received the Inj Tranexamic Acid 1 gram IV (Pause, 500 mg /5 ml, Emcure) and control group who received saline solution. The surgeon, observer, and patients were blinded to the study.

Single dose of Inj Tranexamic acid 10 ml was injected before inflating the tourniquet and same volume of placebo was injected in the control drug group. Regional anesthesia in the form of spinal anesthesia was used in all the patients. Pneumatic tourniquet (Zimmer) was used in every case. Surgical procedure was standardized i.e., standard two portal technique with anterolateral and anteromedial portal. Ipsilateral Hamstring (semitendinosus) tendon graft was quadrupled and ends were stitched (with Ultrabraid, white suture and needle assembly) and femoral cortical fixating suspensor device (Retro button, closed loop, Titanium + UHMWPE, Arthrex) was used. Graft fixation in tibial tunnel was done with bio-interferance screw (Full thread, Poly L

Lactic Acid, Arthrex) with augmentation done by suture disc (suturefix, Biotek) in 07 cases. Meniscus balancing procedures were performed before the fixation of graft. The stability and placement of graft (to rule out impingement) were rechecked after the fixation of graft. In none of the cases the drain was inserted. Post operatively all of the patients have been given with prophylactic antibiotic (Inj Cefotaxim 1 gm 8 hrly for 36 hrs), oral analgesics (Tab tramadol / Paracetamol) on requirement basis. Pneumatic cryotherapy (Cool wrap) was given to all of the patients. For DVT prophylaxis early post operative mobilization, early rehabilitation exercises and chemoprophylaxis with Tab Aspirin 350 mg per day was ensured. Assessment of the operative wound was done on 4th post operative day (in 100% of patients). First assessment of effusion was done at the time of wound inspection and the grading was done according to the classification of Coupens and Yates (graded subjectively from 0-4).[11]

Table 1: Clinical grading of hemarthrosis.

Grade	Description
0	No detectable fluid
1	Fluid present with fluid wave
2	Palpable fluid in suprapatellar space
3	Ballotable patella
4	Tense hemarthrosis

Subsequently patient was reassessed on of 14th post operative date and on 6th week post surgery.

Patients with effusion were observed for development of fever and progression of effusion over a period of 2 wks. Un-resolving effusion of grade 3+ and inadequate flexion (less than 90 degree at 2 wks) were subjected to aspiration. And the samples were assessed for detection of growth of infective organisms. None of the samples collected (case group -3 and control group – 07) showed growth on standard culture for 48 hrs.

Evaluation of clinical out come

Patient were assessed post operatively for pain with visual analogue scale (VAS), assessment of effusion was done with classification of Coupens and Yates, the scoring was done with Lysholm knee score as well as development complications were documented.[11,12]

Statistical analysis

The data was analysed using SPSS software.

Comparison was made between two groups with clinical assessment of effusion with grade III on 4th post operative day and grade II on 14th post operative day was considered significant. The statistical calculations were made according to recommendations of Kelsey et al.[13]

Table 2: Statistical calculations.

Two-sided confidence level (1-alpha)	**95**
Power(% chance of detecting)	80
Ratio of controls to cases	1
Hypothetical proportion of controls with exposure	40
Hypothetical proportion of cases with exposure:	80
Least extreme odds ratio to be detected:	6.00

Table 3: Sample size.

	Kelsey[13]
Sample size – drug group	24
Sample size – non drug group	24
Total sample size:	48

Categorical variables were described by Frequency tables. Descriptive statistics (n, mean, median, SD, and range) were tabulated for continuous variables. None of the variables, except age and ROM were normally distributed based on the Shapiro-Wilk test. Therefore, the Student t test was used to analyze the statistical significance of age & ROM values between the groups. Analyses for non-normally distributed data were conducted using the nonparametric Mann-Whitney U test. A power analysis was conducted, and P value of 0.05 was considered statistically significant.

RESULTS

A total of 48 patients were enrolled after an informed consent (24 in the TXA group, and 24 in the Non drug group) and completed the study. The hospitalization period and the mode of regional anesthesia (spinal) was kept similar between the groups.

The mean knee effusion (graded as per classification of Coupens and Yates) at the end of weeks 2 and 6 wks were significantly lower in the TXA group than the control group (p=0.001) (Table 3). The VAS score in the TXA group decreased from a median of 3 on day 1 to 2.5 on day 3, whereas it dropped from 6 to5 in the control group. The VAS scores of the TXA group at the end of weeks 2 and 6 were lower than those of the control group significantly (p=0.001). The other major outcome was the Lysholm score after weeks 2, 6 and 12 wks. The mean Lysholm score at the end of week 2 was 41.58 (SD- 5.05) in the control group and 53.83 (SD 10.63) in the TXA group; at the end of 6weeks, it was 58.54 (SD- 7.13) in the control group and 70.70(SD- 6.07) in the TXA group. The Lysholm score at the review after 12 weeks was 71.83(SD-4.25) in control group and 83.70(SD- 5.32) in TXA group. A significant difference in Lysholm scores was observed between the two groups (p=0.001) at all the reviews (2nd 6th and 12th post operative week) (Table 5).

Table 4: Patient characteristics.

Sr no	Characteristic	Control group (n=24)	TXA group (n=24)
1	Age (Average, year)	29.33	29.75
2	Operative time (min)	45±10	43±8
3	Hospitalization period (days)	13±5	13±4
4	Associated meniscal injury	14	13
5	Hospitalization period, (days)	14±2	14±2
6	Spinal/epidural block	24	24

The rehabilitation protocol (close chain exercises, active knee range of motion, quadriceps strengthening and hamstring stretching exercises) for both of the groups was kept same throughout.

The ROM achieved was similar between the groups at the end of week 6, the mean was 120.26±7.8 degree in the TXA group and 116.45±7.8 degree in the control group. However the range of motion at the end of 2nd week was significantly more in TXA group (95.25±5.5 degree) as compared with the control group (84.21±2.5 degree).

Table 5: Clinical assessment at followup.

	Tranexamic acid group	Control group	P value
Lysholm score, mean value			
Postoperative week 02	53.83 (SD 10.63)	41.58 (SD- 5.05)	<0.001
Postoperative week 06	70.70 (SD- 6.07)	58.54 (SD- 7.13)	<0.001
Postoperative week 12	83.70 (SD- 5.32)	71.83 (SD-4.25)	<0.001
VAS (median range)			
Postoperative week 02	2 (1-4)	4 (2-5)	<0.001
Postoperative week 06	1 (0-2)	2 (1-3)	<0.001
Postoperative week 12	0-1	0-1	
Effusion (mean value)			
Postoperative week 02	1.6 (SD- 0.7)	2.1 (SD-1.01)	<0.001
Postoperative week 06	0.37 (SD- 0.49)	0.75 (SD-0.060)	<0.001
Postoperative week 12	0.00	0.16 (SD-0.38)	<0.001

The need for aspiration at the end of 2 wks was significantly less in TXA group as compared to control group (3 patients in case group whereas 7 in control group). However the aspiration sample sent for evaluation did not show any growth. Post operatively all of the patients were screened for the development of DVT by clinical suspicion, Moses and Homan sign and Color Doppler study in case of high suspicion; none of the patients developed DVT.

DISCUSSION

Arthroscopic ACL reconstruction is the common and reproducible procedure and has become the treatment of choice for the anterior knee instability due to ACL insufficiency. It requires a high degree of technical efficiency and infrastructure. Despite of being a less invasive surgery; it is associated with various postoperative complications. Out of it effusion is the commonest.[14] Effusion imparts a negative effect in achieving range of motion post operatively and thus reduces the level of strength of muscle. Thus the efforts directed towards reducing the postoperative knee effusion in turn improves the ROM of the knee and functional outcome. Amongst the various modalities to reduce the postoperative effusion of knee Inj tranexamic acid administration is one of the choice. Administration of Inj.Tranexamic acid single dose has less contraindications and little systemic complications. However it significantly reduces the postoperative effusion in knee. Inj Tranexamic acid has been used in various major surgeries to reduce the blood loss and thus reduces the requirement of blood transfusions. We have performed this study to evaluate the effect of tranexamic acid in reducing the effusion in knee and its effect on postoperative rehabilitation in attaining knee function. Hemearthrosis occurred during postoperative period has a toxic effect of articular cartilage and also increases susceptibility to infections leading to increased immediate morbidity and ultimately the poor results.[15] Inserting a drain in knee during surgery or aspiration postoperatively in order to manage the hemearthrosis is distressing and also increases the chances of infection.[16] In this study it was found that occurrence of postoperative hemearthrosis, postoperative pain, requirement of aspiration of knee were significantly higher in control group not receiving the TXA injection. Lysholm score calculated at all the follow-ups (2nd, 6th and 12 th week postoperatively) were significantly higher in TXA group than control group.

TXA has been used in major orthopaedic surgeries and is found to be effective in reducing the bleeding.[17] It was found to be effective and safe. In our study also all of the patients have tolerated the single dose of TXA without any adverse reaction. However in some large scale studies where TXA was used some patients were found to develop side effects.[18] The quantity of bleeding occurring in an ACL surgeries depends on the reconstruction procedure and type of graft harvested.[19] It is also found

that type of anesthesia to some extent makes a difference in the amount of bleeding, however in our study the type of anesthesia was kept same for all of the patients in both groups (spinal anesthesia).

In order to monitor the occurrence of hemarthrosis and facilitate its drainage the intraarticular blood drains can also be used.But the chances of its blockage due to the clots and probability of transmission of infection has reduced the use of drain. Thus avoiding hemearthrosis becomes a more practical and logical solution for the postoperative effusion. Hemarthrosis found to be associated with the pain in early postoperative period and thus affects the attainment of range of motion. In our study the functional scoring done postoperatively has clearly brought out the difference between the case and control group on subsequent follow ups. A weakness of our study was that we have not measured the amount of blood collected in the joint postoperatively which could have been done with the use of drain to quantitatively compare the physiological effectiveness of drug in controlling the postoperative bleeding. But by avoiding the use of drain and comparing the outcome of the supervised physiotherapy and not the amount of bleed, we have compared the practical and ergonomical effectiveness of TXA for reducing the complication of hemarthrosis after ACL surgery.

CONCLUSION

The results of this prospective, randomized study shows that TXA reduces the amount of postoperative hemarthrosis and the need for aspiration of the knee in patients who underwent arthroscopic ACL reconstruction. Consequently, TXA reduces the post-operative pain and improved knee ROM in the early postoperative period without side effects. This administration route of TXA (single Intravenous dose, preoperatively) significantly reduced blood loss and the need for aspiration of the knee associated with ACL reconstruction. We consider the methods employed in this study to be effective, efficient, and reproducible for reducing the postoperative hemarthrosis, with the potential to reduce patient discomfort and helps in rehabilitation after arthroscopic ACL reconstruction.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Dragoo JL, Braun HJ, Durham JL, Chen MR, Harris AH. Incidence and risk factors for injuries to the anterior cruciate ligament in National Collegiate Athletic Association football: data from the 2004-2005 through 2008-2009. National Collegiate Athletic Association Injury Surveillance System. Am J Sports Med. 2012;40(5):990-5.
2. Singh G, Garg S, Damle S.G, Dhindsa A, Kaur A, Singla S. A study of sports related occurrence of traumatic orodental injuries and associated risk factors in high school students in north India. Asian J Sports Med. 2014;5(3):e22766.
3. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. J Athl Train. 2007;42(2):311–9.
4. Levy, David M, Erickson, Brandon J. Bach, Bernard R. Jr. Open versus arthroscopic anterior cruciate ligament reconstruction: a systematic review of randomized controlled trials. Current Orthop Pract. 2017;28(5):449–52.
5. Salzler MJ, Lin A, Miller CD, Herold S, Irrgang JJ, Harner CD. Complications after arthroscopic Knee surgery . Am J Sports Med. 2014;42(2):292-6.
6. Simpson LA, Barrett JP Jr: Factors associated with poor results following arthroscopic subcutaneous lateral retinacular release. Clin Orthop. 1984;186:165–171.
7. Karahan M, Erol B, Bekiroglu N, Uyan D. 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;33(6):900-6.
8. Camarasa MA, Olle G, Serra-Prat M, et al. Efficacy of aminocaproic, tranexamic acids in the control of bleeding during total knee replacement: a randomized clinical trial. Br J Anaesth. 2006;96(5):576-82.
9. Cid J, Lozano M. Tranexamic acid reduces allogeneic red cell transfusions in patients undergoing total knee arthroplasty: results of a meta-analysis of randomized controlled trials. Transfusion. 2005;45(8):1302-7.
10. Zohar E, Ellis M, Ifrach N, Stern A, Sapir O, Fredman B. The postoperative blood-sparing efficacy of oral versus intravenous tranexamic acid after total knee replacement. Anesth Analg. 2004;99(6):1679-83.
11. Coupens SD, Yates CK. The effect of tourniquet use and hemovac drainage on postoperative hemarthrosis. Arthroscopy. 1991;7(3):278-82.
12. Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. Res Nurs Health. 1990;13(4):227-36.
13. Kelsey JL, Whittemore AS, Evans AS, Thompson WD. Methods in Observational Epidemiology 2nd Edition, Oxford University Press; 1996.
14. Small NC. Complications in arthroscopic surgery performed by experienced arthroscopists. Arthroscopy. 1988;4(3):215-21.
15. Simpson LA, Barrett JP Jr. Factors associated with poor results following arthroscopic subcutaneous lateral retinacular release. Clin Orthop Relat Res. 1984;186:165-71.
16. Khalifa TE, Al Mahozi A, Dhaif B. Intra-articular drain versus no drain after arthroscopic anterior

cruciate ligament reconstruction: a randomized prospective clinical trial. Bahrain Med Bull. 2008;30(1):9-11.
17. Zufferey P, Merquiol F, Laporte S, Decousus H, Mismetti P, Auboyer C, et al. Do antifibrinolytics reduce allogeneic blood transfusion in orthopedic surgery? Anesthesiology. 2006;105(5):1034-46.
18. Swendsen H, Galante JM, Bateni GHS, Scherer LA, Schermer CR. Tranexamic Acid use in Trauma: Effective but not with Consequences. J Trauma Treat. 2013;2:179.
19. Pape D, Seil R, Adam F. Blood loss in anterior cruciate ligament (ACL) reconstruction with and without intercondylar notchplasty: does it affect the clinical outcome. Arch Orthop Trauma Surg. 2001;121(10):574-7.

Cite this article as: Pande A, Bhaskarwar AP. Assessing the effect of per operative intravenous injection of tranexamic acid in patients undergoing arthroscopic anterior cruciate ligament reconstruction. Int J Res Orthop 2019;5:639-44.