Does Tranexamic Acid Reduce Knee Swelling and Improve Early Function Following Arthroscopic Meniscectomy?

A Double-Blind Randomized Controlled Trial

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Background: Arthroscopic meniscectomy often results in rapid recovery and return to preinjury activities; however, postoperative hemarthrosis and swelling can lead to pain, decreased range of motion, and delayed return to work and leisure activities. Tranexamic acid (TXA) is a lysine-based inhibitor of plasminogen to plasmin that has gained popularity in arthroplasty surgery for reducing blood loss and, more recently, in anterior cruciate ligament reconstruction by reducing postoperative hemarthrosis, swelling, and pain while increasing function in the short term.

Purpose: To determine whether there is a role for TXA in improving the short-term results of swelling, pain, and function following arthroscopic meniscectomy.

Study Design: Randomized controlled trial; Level of evidence, 2.

Methods: We performed a prospective double-blinded randomized controlled trial in 41 patients undergoing arthroscopic meniscectomy by comparing patients treated with intravenous TXA with those treated with a placebo (normal saline). A single surgeon treated all patients. Following randomization, a dose of 1 g of TXA in 100 mL of normal saline (treatment group) or 100 mL of normal saline (placebo group) was given intravenously at induction prior to tourniquet inflation by the anesthetist. The anesthetist administering the TXA or placebo was not blinded, but all other clinicians involved were. Patients were evaluated by a blinded observer at postoperative days 3, 14, and 30, with the range of motion, swelling, pain levels (visual analog scale), and Lysholm and Tegner knee scores recorded.

Results: Patient demographics were similar in both groups. In the treatment group, there was a nonsignificant improvement in range of motion (P = .056) and swelling (P = .384) at 14 days; however, there was a significant improvement in the Tegner score at 3 days (P = .0064). The complication profile was similar between the groups.

Conclusion: The administration of 1 g of intravenous TXA in routine arthroscopic meniscectomy may improve early functional recovery without increased risk. A larger study is required to confirm these results and further evaluate any potential benefit.

Registration: ACTRN12618001600235 (Australian New Zealand Clinical Trials Registry).

Keywords: tranexamic acid; arthroscopy; meniscectomy; swelling; function

Arthroscopic meniscectomy is an established procedure with known long-term benefits in the correct patient population. This procedure has a low complication rate, with hemarthrosis recognized as one of the most common complications. In a study by Small, 23-25 21 experienced surgeons participated in a prospective study to analyze complications in arthroscopic surgery of the knee and other joints. Of 8741 procedures on the knee, hemarthrosis was reported in 101 cases (1.15%), and this accounted for 60.1% of all complications. Subsequently, a National Health Service–based cohort study prospectively collected admissions data on 301,701 operations performed between 2005 and 2010 and found a 0.27% rate of wound complications (which included wound infections and hematomas) within 30 days...
of knee arthroscopy, not including ligament reconstruction. In addition, this study found that the orthopaedic readmission rate within 30 days was 0.55%. Although the reason for readmission was not stated in this study, the associated literature would suggest that hemarthrosis would have had a large contribution to these readmissions.

Even without readmission, hemarthrosis may lead to increased postoperative pain and swelling, decreased range of motion (ROM), and reduced patient satisfaction. In the setting of anterior cruciate ligament (ACL) reconstruction, hemarthrosis has been shown to increase postoperative pain and delay rehabilitation and return to sport.\(^1\)

To reduce the effect of this complication, clinicians have utilized various methods. Initially, surgical drains were used after open meniscectomy, but a 1978 prospective quasi-randomized study of open meniscectomies showed no difference in postoperative pain or hemarthrosis rate at 3 weeks as well as no difference in the time to return to activities.\(^4\) In 2005, Tatari and colleagues\(^26\) assessed the effect of drain usage in arthroscopic knee procedures. They were unable to show any difference in postoperative pain or hemarthrosis risk between those who had a drain and those who did not, with a 15-day follow-up. More recently, several randomized controlled trials (RCTs) on arthroscopic ACL reconstructions have shown no difference in outcomes with the use of a surgical drain.\(^6,8,20\) Furthermore, the current use of drains in arthroscopic meniscectomy is very uncommon and impractical, as patients cannot be discharged while the drain is in situ.\(^4\)

Thus, many surgeons prefer to reduce the risk of hemarthrosis after arthroscopic meniscectomy with the application of a compressive bandage. Despite the widespread use of compressive bandages however, there remains a lack of evidence that compressive bandages decrease postoperative pain, swelling, or hemarthrosis.\(^7\)

Tranexamic acid (TXA) is a lysine-based inhibitor of plasminogen, which has gained popularity in orthopaedic practice over the past decade after being shown to decrease blood loss in hip and knee arthroplasty. TXA in the setting of total knee arthroplasty has been shown to reduce postoperative swelling and drain output. In an RCT, Ishida et al\(^14\) injected 2000 mg of TXA into the joint at closure and showed that this produced decreased knee swelling at 1 week. In 2015, a prospective double-blinded RCT in 105 patients undergoing arthroscopic ACL reconstruction showed that the use of intravenous TXA before tourniquet inflation and for 3 hours postoperatively led to decreased pain, reduced rates of hemarthrosis, and improved knee function in the early postoperative period, without an increased risk in infection or deep vein thrombosis.\(^17\)

The safety of intravenous TXA has been well documented. In 2011, a Cochrane review that included 65 trials (4842 patients) undergoing cardiac, orthopaedic, gynecological, and vascular procedures found no association with the use of TXA and risk of myocardial infarction, stroke, thromboembolic events, or renal failure.\(^12\) Kagoma and colleagues\(^16\) performed a meta-analysis that compared the outcomes between controls and patients who received intravenous antifibrinolytics in hip and knee arthroplasty. They evaluated 27 studies that included 1637 patients. For all antifibrinolytics, they found that the relative risk for venous thromboembolism was 0.95 (95% CI, 0.80-1.10; \(P = .531\)). The risk difference specifically for TXA was 0.01 (95% CI, –0.04 to 0.02). A further meta-analysis was performed by Yang and colleagues,\(^28\) who specifically looked at the use of TXA in the setting of total knee arthroplasty. This included 15 studies and 837 patients. Neither deep venous thrombosis (from 13 studies) nor pulmonary embolism (6 studies) was found to be associated with the use of TXA. In addition, 2 large retrospective cohort studies found no association with the use of TXA and risk of venous thromboembolism.\(^10,21\)

In the setting of knee arthroscopy, the rates of venous thromboembolism have ranged from 0.11% to 0.34%, which is lower than the reported rate in the arthroplasty studies previously mentioned.\(^18,25,25\) Hence, it is likely that administering TXA in the lower-risk setting of arthroscopic meniscectomy would not cause a significant increase in risk. Thus, the aim of this study was to serve as a pilot study to determine if the administration of TXA results in an improvement in pain, swelling, and function during the early postoperative period following arthroscopic meniscectomy.

**METHODS**

This was a double-blind RCT to investigate the analgesic benefit, functional outcomes, and complication risk of intravenous TXA in early postoperative recovery from arthroscopic meniscectomy. Ethical approval was obtained from the Southern Health Ethics Committee, New Zealand. The trial was registered at the Australian New Zealand Clinical Trials Registry.

**Enrollment**

Patients scheduled for arthroscopic meniscectomy from April to October 2018 were screened for enrollment with a screening and enrollment form (see Appendix). Indications

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Ethical approval for this study was obtained from the Southern Health and Disability Ethics Committee, New Zealand (18/STH/10).
for meniscectomy included a painful knee with locking, clicking, or instability with (1) positive examination findings using the McMurray test or (2) joint line tenderness and the presence of an isolated meniscal tear on magnetic resonance imaging. Exclusion criteria were as follows: age younger than 18 years, a history of bleeding or clotting disorder, pregnancy, current oral contraceptive pill use, preoperative anticoagulation therapy other than aspirin, known renal disorder, allergy to local anesthetics or TXA, large preoperative swelling (grade 3 or 4 effusion), concurrent ligament injury, prior ACL reconstruction, microfracture, and revision surgery. Patients were given a copy of a patient information sheet and the informed consent form.

Blinding

Following consent, patients were randomized to receive either intravenous TXA (1 g in 100 mL of normal saline) or a placebo (100 mL of normal saline). A randomization schedule was created at the initiation of the study based on an atmospheric noise randomization generator found at www.random.org. Patients were given a study number and a study category of A or B to ensure blinding of the clinical investigators. Patients were also blind to which group they were in during the course of the trial but could elicit this information by enquiry when the trial was complete. The TXA or placebo was administered by the anesthetist (R.P.; who was not blinded to the patient group) at induction and prior to inflation of the tourniquet.

Operative Intervention

All arthroscopies were performed under general anesthesia by 1 surgeon (G.J.H.). A tourniquet was applied at 300 mm Hg prior to the incision. Standard arthroscopic instruments were used. The amount of meniscal debridement was at the discretion of the primary surgeon. Local anesthetic (20 mL of 0.25% levobupivacaine) was injected into the knee joint at the conclusion of the case. Port sites were not closed and were dressed with absorbable dressings. Patients were discharged on the day of surgery when pain was manageable and they were safe mobilizing with crutches. They were given a prescription for nonopioid oral analgesia per their preferences and medical conditions and instruction for active and passive ROM exercises of the knee. No postoperative chemoprophyaxis for venous thromboembolism was prescribed, and there were no formal physical therapy referrals.

Clinical Evaluation

Patient information, including age, sex, comorbidities, height, weight, duration of surgery, and tourniquet application as well as all complications, was recorded on the day of surgery. The following outcome measures were assessed at baseline (preoperatively) and postoperative days 3, 14, and 30 (in an outpatient setting): pain (assessed with a visual analog scale [VAS] from 0-5), swelling (measured as the circumference at the superior patellar border [suprapatellar girth] and the maximum circumference of the calf [calf girth]), ROM (measured with a goniometer), and there were no formal physical therapy referrals.

Lysholm knee score,19 and the Tegner activity scale.27 Clinical evaluations were performed by 1 examiner at each time point (J.H.M., M.N., or G.J.H.).

Statistical Analysis

A VAS score difference of 2 points at postoperative day 14 was deemed clinically significant (based on work by Karaaslan et al17). For the superiority comparison between the study arms, the independent-samples t test was used with inferences made at the .05 level of significance.

RESULTS

Figure 1 shows the CONSORT (Consolidated Standards of Reporting Trials) flow diagram for the study. A total of 45 patients were randomized to the treatment (intervention) and placebo groups. Patient baseline demographics are shown in Table 1. The VAS scores, clinical measurements, and functional scores are summarized in Table 2. The only statistically significant difference between the groups was in the 3-day postoperative Tegner activity scale, in which the TXA group had a mean score of 2.7 (95% CI, 2.2-3.1), while the control group had a score of 1.7 (95% CI, 1.2-2.3; P = .0064). There was a nonsignificant trend toward improved ROM (P = .056) and reduced suprapatellar circumference (P = .384) at 14 days in the TXA group versus control. There were no adverse events or complications in any patient.

DISCUSSION

This pilot study is the first to investigate the short-term benefits of TXA in patients undergoing arthroscopic meniscectomy. While TXA is frequently used in many other surgical procedures and is known to reduce blood loss and transfusion requirement in larger orthopaedic procedures such as hip and knee replacement, its benefit in arthroscopic knee meniscectomy remains unknown.5,22

The paucity of data on the use of TXA in arthroscopic meniscectomy is likely driven by the minimal blood loss usually expected in these procedures. However, postoperative hemarthrosis has been implicated as the most common complication of arthroscopic knee procedures.25 This complication is known to cause temporary changes to cartilage and synovium histology, but it can also reduce ROM and increase postoperative pain, which may negatively affect the patient’s early postoperative recovery and return to normal function.1,13,23

Although no prior studies have assessed the use of TXA in knee arthroscopic meniscectomy, 2 previous prospective RCTs assessed its benefits in ACL reconstruction.9,17 Both studies showed a reduced volume of drainage and less hemarthrosis in the early postoperative period. The more recent RCT by Felli and colleagues9 also demonstrated improvements in pain, ROM, and quadriceps strength during the first 2 weeks. In the current study, we found better Tegner activity scores at 3 days postoperatively with the
use of TXA, although this difference was no longer significant at 14 and 30 days postoperatively, suggesting that any benefit of TXA in this setting is during the early postoperative period. This is consistent with any likely benefit relating to lower levels of hemarthrosis, which is supported by our findings of lower suprapatella circumferences postoperatively in the TXA group, although this failed to reach statistical significance. Despite reaching statistical significance, the difference in Tegner scores between the groups at 3 days postoperatively was small and therefore may not be clinically meaningful, especially when there was no significant change from baseline and it was not sustained at the later time points. It is worth noting that there were no significant differences in pain scores, swelling, and ROM between the treatment and control groups at any of the time points assessed.

Despite the potential benefits of TXA identified in this study, there are a number of study limitations that should be recognized. First, the number of patients enrolled was small, as it was intended as a pilot study for a larger RCT. It is therefore possible that increased numbers may yield different results. This is particularly relevant to potential complications, as none of the participants in this pilot study experienced any adverse events. Known potential side effects of TXA include thromboembolic events, visual disturbances, and hypersensitivity reactions, including anaphylaxis. Patients with a history of any thromboembolic event or known hypersensitivity to TXA were excluded from this study. However, as detailed in the introduction,
a number of studies have shown no significant increase in thromboembolic events when TXA was used perioperatively.\textsuperscript{10,12,21,28} Given that the clinical difference between groups in this study was small, further investigation with a larger cohort is necessary before adopting TXA administration as a part of routine practice in arthroscopic meniscectomies, as it is possible that any potential benefits would not be of sufficient magnitude to justify even a low risk of adverse events.

A second limitation is the precision of the measurements chosen—long-arm goniometers were used in this trial for the measurement of ROM for practical reasons and easy accessibility, but these have been shown to have variance in measurements up to 10\textsuperscript{\%}.\textsuperscript{11} We did not exclude silent venous thromboembolism via Doppler venograms or other means, in view of the relatively low expected risk as detailed earlier. Last, we administered either 1 g of TXA or a placebo and therefore did not investigate different doses of TXA, which may be required in future studies.

\textbf{CONCLUSION}

This study showed that the administration of 1 g of intravenous TXA in routine arthroscopic meniscectomy was associated with better mean Tegner scores at postoperative day 3 without any identified increased risk. No sustained benefit at 2 weeks or 1 month postoperatively was seen, nor were there any significant differences in other measures. A larger study is required to confirm these results and establish if there is sufficient early benefit of TXA to justify its use in arthroscopic meniscectomy.
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A Comparative Outcome Study Using Tranexamic Acid in Arthroscopic Meniscectomy

| Patient Study ID Number | Patient Initials | Date | DD | MM | YYYY |
|-------------------------|-----------------|------|----|----|------|

**Inclusion Criteria:** you must be able to answer **yes** to the following questions to include this patient in this study.

1. Is the patient 18 years or older? **YES**
2. Is the patient undergoing an arthroscopic meniscectomy? **YES**

**Exclusion Criteria:** You must answer **no** to the following questions to include the patient in this study.

1. Has the patient had previous surgery on the same knee without any type of reconstruction, such as ACL, PCL, LCL, or MCL reconstruction? **NO**
2. Does the patient have a history of kidney disease or dysfunction? **NO**
3. Does the patient have a history of clotting disorders including a history of thromboembolism or thrombosis (such as deep venous thrombosis, pulmonary thromboembolism)? **NO**
4. Does the patient have a history of bleeding disorder? **NO**
5. Is the patient pregnant? **NO**
6. Is the patient breastfeeding? **NO**
7. Does the patient have a known hypersensitivity to tranexamic acid? **NO**
8. Will the patient **not** be able to follow cessation of anticoagulants as usual? **NO**
9. Is there another reason to exclude this patient from this study? If yes, specify: 

**Patient Status:**
- **INCLUDED** (Proceed to Consent, Contact Information, and Patient Questionnaire forms)
- **EXCLUDED**
- **MISSED** (Was eligible, but missed due to error)