

# Topical Tranexamic Acid to Reduce Postoperative Blood Loss in Total Knee Arthroplasty

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## Introduction

Total knee arthroplasty alleviates pain and restores function in patients with osteoarthritis of the knee, but it is associated with postoperative blood loss resulting in anemia and allogeneic blood transfusion in 10% to 38% of patients<sup>1,2</sup>. Currently available blood conservation modalities to reduce the need for allogeneic blood transfusion do not reduce the amount of intraoperative blood loss or prevent the postoperative reduction in hemoglobin level. Preoperative autologous blood donation is costly; does not eliminate the risks of clerical errors or bacterial contamination; and may be unused, leaving patients anemic<sup>3</sup>. Intravenous administration of the antifibrinolytic agent tranexamic acid has been shown to reduce postoperative bleeding and the need for transfusion<sup>4,5</sup>. Tranexamic acid is a synthetic antifibrinolytic drug that prevents the breakdown of fibrin (the primary component of blood clots), thereby stabilizing blood hemostasis and reducing blood loss under conditions that promote fibrinolysis<sup>6</sup>. Increased fibrinolysis can result in excessive or recurrent bleeding. However, systemic inhibition of fibrinolysis carries the risk of thromboembolic events such as deep-vein thrombosis or pulmonary embolism<sup>7,8</sup>.

The advantages of topical application of tranexamic acid over intravenous administration are that this method of delivery is both “target-directed” and “safe” to use to reduce postoperative bleeding. Direct application at the site of bleeding attenuates the marked increase in local fibrinolysis associated with surgical trauma and release of the tourniquet<sup>9</sup>.

The safety of intravenous/systemic use of tranexamic acid to reduce surgical blood loss has been questioned recently<sup>10</sup>. Minimal systemic absorption of tranexamic acid has occurred when the medication has been applied directly into the surgical wound in total knee arthroplasty<sup>11</sup> and when it has been applied locally in other types of surgery<sup>12</sup>. Topical fibrin sealants reduce blood loss but are costly;

also, they are derived from human plasma, so the risk of transmission of infective agents is not completely eliminated<sup>13,14</sup>. Tranexamic acid is completely synthetic, has no human blood products, and can be used in patients who refuse blood products. Tranexamic acid is a generic and inexpensive medication that is available as a preservative-free liquid, does not need to be reconstituted, and is easy to apply.

The preparation and topical application of tranexamic acid proceeds in three stages:

1. Prepare tranexamic acid solution.
2. Apply tranexamic acid.
3. Remove tranexamic acid.

## Step 1: Prepare Solution

Prepare tranexamic acid solution using aseptic technique.

Prepare the 3-g solution by combining three vials of sterile (preservative-free) tranexamic acid with 70 mL of sterile normal saline solution for a total volume of 100 mL. Each 10-mL vial contains 1 g of tranexamic acid (Cyklokapron, 100 mg/mL; Sandoz, Boucherville, Quebec, Canada). If you are using the 1.5-g solution, prepare it by combining 1.5 g of tranexamic acid (15 mL) and 85 mL of sterile normal saline solution for a total volume of 100 mL.

## Step 2: Apply Solution

Apply tranexamic acid solution to the open joint and soft-tissue surfaces.

After all components are cemented into place, with the pneumatic tourniquet inflated and the knee in extension, apply the tranexamic acid

solution to the open joint and soft-tissue surfaces using a bulb syringe (Fig. 1).

Leave the solution in contact with the tissues for five minutes.

### Step 3: Remove Solution and Close

Remove tranexamic acid, keeping the tourniquet inflated until the wound is closed and the dressing is applied.

After five minutes, remove the remaining tranexamic acid solution by placing the suction tip on the cemented component without suctioning other parts of the joint and surrounding soft tissues. Some solution may be absorbed into the tissue.

Do not irrigate the wound again.

Keep the tourniquet inflated until the wound is closed and the dressing is applied (Fig. 2).

### Results & Preop./Postop. Images

We showed, in a prospective, double-blinded, placebo-controlled randomized trial, that topical application of tranexamic acid directly into the surgical wound prior to closure at the end of a total knee arthroplasty reduces postoperative bleeding by 20% to 25%, or 300 to 400 mL<sup>11</sup>. This resulted in 16% to 17% higher postoperative hemoglobin levels compared with those in the placebo group. There was minimal systemic absorption, and no difference in the rates of deep-vein thrombosis or pulmonary embolism between patients who received tranexamic acid and those who received the placebo.

### What to Watch For

#### Indications

Primary or revision total knee arthroplasty performed with a pneumatic tourniquet.

#### Contraindications

Allergy to tranexamic acid.

History of thromboembolic disease (for example, deep-vein thrombosis, pulmonary embolus, or cerebral vascular accident).

Pregnancy and breast-feeding. Tranexamic acid crosses the placenta and is passed into breast milk during lactation.

Disturbance of color vision is a contraindication to use of tranexamic acid, and retinal

changes can be caused by long-term use and large doses<sup>15</sup>.

Renal failure. Topical administration of tranexamic acid is associated with minimal systemic absorption; however, this medication is eliminated by glomerular filtration and can accumulate in patients with renal failure.

#### Pitfalls & Challenges

The solution should be used within twenty-four hours after preparation.

The volume of study medication used in our study (100 mL) can be too large for the joint space in some patients.

### Clinical Comments

In our study, we did not directly investigate the effect of tranexamic acid on the local tissue, prosthetic joint, or healing of the wound. We inferred that the topical application of tranexamic acid did not affect postoperative wound-healing or patient function on the basis of a lack of a significant difference between placebo and tranexamic acid groups with regard to postoperative knee flexion, visual analogue pain scores, length of hospital stay, time to the start of rehabilitation, and improvement in functional scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) six weeks after surgery. A group from the United Kingdom has recently investigated the effect of tranexamic acid on artificial joint materials. The results of their work will help to clarify the effect of tranexamic acid on joint prostheses (Dr. Sattar Alshryda, personal communication). Notably, topical application of tranexamic acid in other types of surgery has not been reported to be associated with adverse effects on wound-healing<sup>16-19</sup>.

In our study, we did not include patients who had undergone revision total knee arthroplasty as we had a limited number of such patients. However, we believe that patients undergoing revision surgery may receive an even greater benefit from the use of topical tranexamic acid, and we recommend and use the medication in this patient population.

We found that the total volume of medication used in our original study (100 mL) can be too large for the joint space in some patients, and since completing the study we have used a smaller total volume of tranexamic acid solution, usually 80 mL. This volume of tranexamic acid solution still ensures contact of the medication with the tissue surfaces of the knee. The volume of the tranexamic acid solution and the duration for which the medication was left in place in our study were based on studies of topical administration of tranexamic acid in cardiac surgery<sup>14</sup>. In those

randomized trials, the tranexamic acid was diluted with sterile normal saline solution to a volume of 100 mL. The medication or placebo (an equal amount of saline solution) was poured into the pericardial cavity and/or over the mediastinal tissues at the end of the surgery and before the closure of the median sternot-

omy and was left for two to five minutes. We did not compare different durations for which the medication was left in place. It is possible that a shorter duration of application is also effective for reducing postoperative blood loss.

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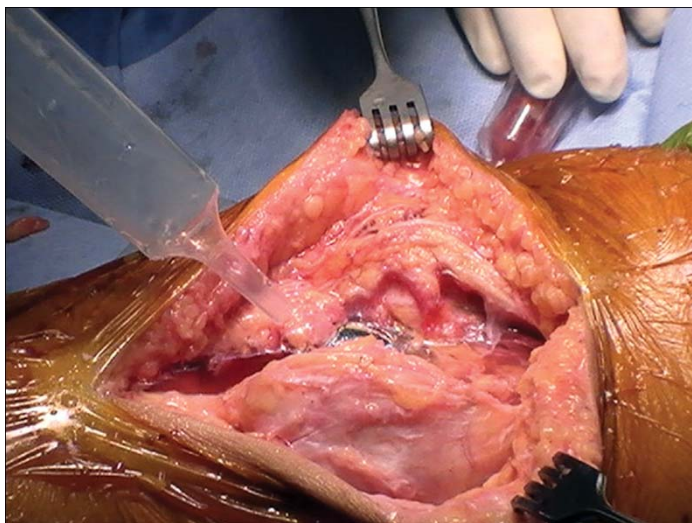
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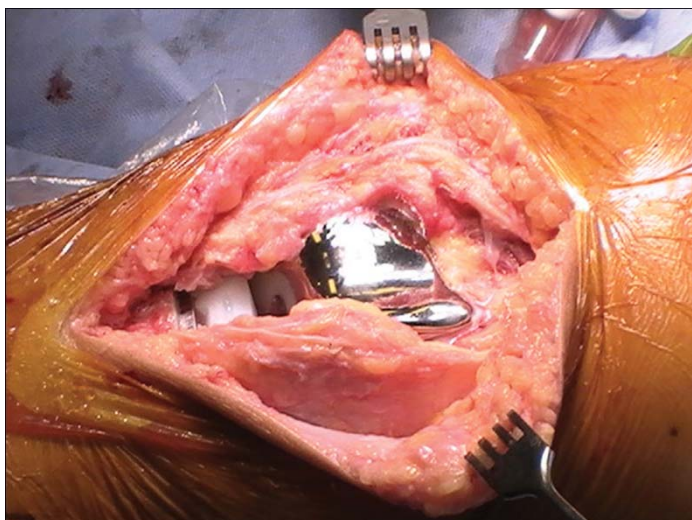
## Figures

**Fig. 1.** Application of tranexamic acid solution to open joint and soft-tissue surfaces with use of a bulb syringe.

**Fig. 2.** With the tourniquet still inflated, wait five minutes and then remove the remaining tranexamic acid solution. Then close the wound without further irrigation.



**Fig. 1**



**Fig. 2**