Bone Bleeding During Total Hip Arthroplasty After Administration of Tranexamic Acid

Narendra Garneti, MSc, MRCS, and Jeremy Field, BSc, ChM, FRCS, FRCS(Orth)

Abstract: Numerous methods of controlling bleeding during total hip arthroplasty have been used. Thromboplastic agents have been used with some success, but the resultant fibrin layer interposed between the bone and cement weakens the interface. Topical freezing saline and hypotensive anesthesia have proved to be the most effective to date. The goal of this randomized, double blind, controlled study is to determine the effect of a single bolus dose of tranexamic acid, administered at the time of anesthesia, on bleeding during primary total hip arthroplasty. Fifty patients were randomized to receive either 10 mg/kg of tranexamic acid or a similar volume of normal saline as a preoperative bolus. Patients were not given pharmacologic thrombotic prophylaxis until 48 hours after surgery. The goal was to measure blood loss from the femoral canal at the time of surgery. An estimate of the internal and external blood loss during and after surgery was performed, and the transfusion requirement was recorded. No significant difference was found between the groups in terms of blood loss from the femoral canal, the perioperative bleeding, and postoperative hemoglobin. In the group that received tranexamic acid, a greater number of patients required transfusion than in the placebo group. The results of this study do not support the routine use of tranexamic acid in primary total hip arthroplasty. Key words: total hip arthroplasty, tranexamic acid, blood loss, femoral canal, transfusion.

Bleeding during total hip arthroplasty (THA) is a problem for 2 major reasons. The requirement for blood transfusion carries with it the risk of well-recognized complications, including transfusion reactions (ABO incompatibility) and transmission of infectious agents (human immunodeficiency virus and hepatitis viruses). Bleeding from the exposed bone surfaces (femoral canal and acetabulum) during cementation has been shown to reduce the strength of the bone-cement interface [1] and, by blood lamination, the strength of the cement itself [2–4]. These conditions may lead to aseptic loosening and premature implant failure.

Numerous methods of controlling bleeding from the femoral canal have been used. Thromboplastic agents have been used with some success [5], but the resultant fibrin layer interposed between the bone and cement weakens the interface [6]. Topical freezing saline and hypotensive anesthesia have proved to be the most effective to date [7]. Tranexamic acid (Cyklokapron, Pharmacia, Bucks, UK) is a synthetic antifibrinolytic drug used to prevent bleeding. It is a trans-stereo isomer of a synthetic amino acid. It is a white odorless powder that forms white crystals, which are soluble in water, acids, and alkalis, and slightly soluble in alcohol, but remain insoluble in organic solvents. Tran-
examic acid produces antifibrinolytic effects by competitively inhibiting the activation of plasminogen to plasmin [8,9]. It saturates the lysine binding sites of human plasminogen, displacing plasminogen from the fibrin surface, which results in inhibition of fibrinolysis [10,11]. The apparent elimination half-life of tranexamic acid is 80 to 120 minutes [12]. Tranexamic acid effectively suppresses fibrinolysis by inhibiting tissue plasminogen activator and plasmin activity, with a clear reduction of perioperative blood loss in patients undergoing cardiopulmonary bypass surgery [13].

Its effectiveness has been tested in orthopaedic surgery, but most studies have concentrated on its ability to reduce postoperative bleeding and the need for blood transfusion after knee arthroplasty [14]. It is effective in inhibiting plasmin activity, shortening the bleeding time, and improving the platelet function in patients with severe disease [15].

Tranexamic acid is not routinely used in primary THA. The goal of the current study was to determine the effect of a single bolus dose of tranexamic acid, administered at anesthesia, on bleeding from the femoral canal at the time of cementation of the femoral component of a primary THA. In addition, an estimate of the intraoperative and postoperative blood loss was performed in an attempt to clarify further the role of tranexamic acid in controlling bleeding during primary THA.

**Methods**

**Patients**

This was a double blind, randomized trial approved by the local ethics committee. Fifty patients with a diagnosis of primary osteoarthritis of the hip necessitating THA were recruited. Patients were treated by surgeons of different grades (consultants, registrars, staff grades, senior house officers). The junior staff were appropriately supervised. Signed consent to participate in the study was obtained from each patient. Preoperative and postoperative (48 hours) measures of hemoglobin concentrations were obtained. Patients were randomized using a random number technique to receive either 10 mg/kg of intravenous tranexamic acid or a similar volume of normal saline (placebo) as a bolus at anesthesia. A dose of 10 mg/kg was suggested by the Drug Information Department at Cheltenham General Hospital, after contacting Pharmacia. The patient, anesthetist, and surgeon were all unaware of which solution was given. Each patient received spinal anesthesia.

**Intraoperative and Postoperative Protocol**

Blood loss during surgery was measured by weighing swabs and recording the amount returned through the suction apparatus, less lavage solution. After the femoral canal was prepared and a cement restrictor inserted, an estimate of blood loss from the femoral canal was made using the technique described by Bannister et al. [7]. A small surgical swab was inserted fully into the femoral canal and left for 2 minutes. This swab was used to stabilize bleeding from the femur. Four swabs were subsequently inserted in a similar fashion, each for one minute. These swabs were then weighed, and the difference between the wet weight and the dry weight gave a representation of the blood loss from the femoral canal during the procedure. A recording of the blood pressure was obtained at estimating femoral canal blood loss. At the end of surgery, 2 vacuum drains were inserted into the patient, one deep and one superficial. These were used to record postoperative blood loss by measuring the total drainage at 48 hours. A sample of blood was taken 48 hours postoperatively to give a recording of the hemoglobin and platelet count.

All patients were given regular medication perioperatively. None of them received medication that will influence surgical blood loss. Thrombo-embolic deterrent stockings and foot pumps were used postoperatively, but no patient received pharmacologic thrombotic prophylaxis for 48 hours after surgery. All patients underwent Belfast scan or a duplex scan or venogram on the fifth postoperative day to detect the presence or absence of deep vein thrombosis.

**Analysis**

Results from the 2 groups were analyzed using the Mann Whitney U test. A P value of <.05 was regarded as statistically significant. All results are expressed as mean ± standard deviation.

**Results**

All patients underwent cemented primary THA. The mean arterial blood pressure at the time of measurement of blood loss from the femoral canal was similar in both groups.

The 2 groups were similar in terms of age (69.6 ± 11.99 years for the tranexamic acid vs 67.6 ± 11.4 years for the placebo group) and, preoperative and postoperative hemoglobin concentrations. No statistically significant difference was found in preoperative and postoperative hemoglobin in the 2 groups (preoperative hemoglobin, $P = .644$; postoperative hemoglobin, $P = .564$).
The amount of cumulative blood lost in the swabs from the femoral canal was not statistically significant ($P = .799$). We found a mean loss of 32 ± 18 mL for the tranexamic acid group and 33 ± 15 mL in the placebo group. Also, no statistically significant difference was found in any of the individual swabs (Table 1, Fig. 1).

No significant statistical difference was found in the amount of blood loss retrieved by the suction apparatus between the 2 groups ($P = .906$; mean loss of 638 ± 545 mL for the tranexamic acid group and 552 ± 357 mL for the placebo group).

The amount of blood lost in the drains at 48 hours after surgery was not statistically significant between the 2 groups. A mean drainage of 411 ± 220 mL for the tranexamic acid group and 353 ± 311 mL for the placebo group ($P = .246$).

Internal and external blood loss measures were obtained by adding blood loss through the swabs, suction, and drains. The size of the femoral implant and the degree of surgical aggression may have influenced the overall surgical blood loss. No statistically significant difference was found in the amount of internal and external blood loss in the 2 groups. A mean loss of 1443 ± 809 mL in the tranexamic acid group and 1340 ± 665 mL in the placebo group was found ($P = .822$; Fig. 2).

A greater number of patients in the tranexamic acid group required a transfusion than in the placebo group; 64% (16 of 25) of patients in the tranexamic acid group required transfusion compared with 56% (14 of 25) in the placebo group. Perhaps this was because of the different transfusion strategies of the anesthetists, one of whom transfused most patients unless they were young and healthy. We established no defined criteria for administering blood transfusion in this trial, and this could be a source of bias. For patients who required transfusion, the median units of blood transfused were the same in the 2 groups. In the tranexamic acid group, 14 patients received 2 units, one patient received 4 units, and one patient received 5 units. In the placebo group, 12 patients received 1 unit and 2 patients received 3 units.

No patient had a clinically proven deep vein thrombosis after surgery, but 53% of the patients who received tranexamic acid had a positive Belfast scan performed on the fifth postoperative day. These patients subsequently underwent duplex scanning or venogram. All results were negative. In the placebo group, 39% of the patients had a positive Belfast scan result, but none had a positive duplex scan or venogram result. One patient in the tranexamic acid group was readmitted to the hospital after discharge with chest pain. He had a pulmonary embolism, confirmed on ventilation-perfusion scan, and underwent appropriate treatment. We are not certain if these results were in any way influenced by tranexamic acid.

### Table 1. Femoral Canal Blood Lost in the Swabs

<table>
<thead>
<tr>
<th></th>
<th>Mean Blood Loss in the TA Group</th>
<th>Mean Blood Loss in the Placebo Group</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swab 1</td>
<td>12 ± 7 mL</td>
<td>12 ± 6 mL</td>
<td>.822</td>
</tr>
<tr>
<td>Swab 2</td>
<td>7 ± 4 mL</td>
<td>8 ± 5 mL</td>
<td>.620</td>
</tr>
<tr>
<td>Swab 3</td>
<td>7 ± 4 mL</td>
<td>7 ± 3 mL</td>
<td>.499</td>
</tr>
<tr>
<td>Swab 4</td>
<td>7 ± 4 mL</td>
<td>6 ± 3 mL</td>
<td>.480</td>
</tr>
</tbody>
</table>

Abbreviation: TA, tranexamic acid.

**Fig. 1.** Mean blood loss from the femoral canal for tranexamic acid (Cyklokapron) and placebo groups.

**Fig. 2.** Mean and median total blood loss for tranexamic acid (Cyklokapron) and placebo groups.
Discussion

Bone bleeding from the femoral canal at THA was not affected by administration of a single bolus dose of tranexamic acid. However, neither was intraoperative blood loss or postoperative blood loss. We should stress that estimating blood loss during surgery by recording the amount returned by suction apparatus and that collected in vacuum drains is an inexact method, but it is currently the best available and has been used in numerous previous studies.

Our results are in contrast to those of other authors, who have shown reduced bleeding by 35% [16]. Ido et al. [17] reported a significant reduction in postoperative blood loss in patients undergoing THA who were given tranexamic acid, with no severe complications, such as venous or pulmonary thromboembolism. Benoni et al. [18] showed a blood loss of 0.76 L in the tranexamic acid group compared with 1 L in the placebo group in a randomized double-blind trial involving 40 patients. Tranexamic acid administered at the end of surgery does not reduce postoperative blood loss [19].

The reasons for these discrepancies are unclear. Patient numbers, surgical time, dose, duration, time of administration of the drug in relation to surgery, and number of times the drug is administered may be contributing factors. Benoni et al. [18] used a bolus dose of 10 mg/kg intravenously just before surgery. Ekbak et al. [16] used 2 bolus doses of 10 mg/kg of tranexamic acid, the first just before surgical incision and the second 3 hours later. In addition, a continuous infusion of tranexamic acid 1 mg/kg/h for 10 hours, was given after the first bolus dose. No increase in the frequency of peripheral venous thrombosis was seen between the tranexamic acid group and the control group. Neither reports discussed how the dosage of tranexamic acid used was determined.

We used a single bolus dose of 10 mg/kg given intravenously at induction of anesthesia. The half-life of tranexamic acid is approximately 2 hours, which would cover the duration of surgery. A longer duration of administration may be more appropriate for longer procedures.

In other orthopaedic procedures, authors have shown tranexamic acid to be of use in reducing blood loss and transfusion requirements in knee arthroplasty and scoliosis surgery [14,20–22]. The volume of blood lost in these procedures may be lesser or greater than during primary THA, and a direct comparison with the results of these studies is of limited value.

The amount of cumulative blood lost in the swabs and femoral canal blood lost in all 4 swabs in the group treated with tranexamic acid did not reach statistical significance. The surface area of the reamed femoral canal is large in comparison with the potential bleeding area from other surgical sites (eg, the venous graft used during coronary artery bypass graft surgery). The normal high pressure arterial flow from the nutrient artery toward the cortex is reversed when the femoral neck is fractured or osteotomized, as is the norm during THA [23]. This situation may explain, at least in part, why tranexamic acid appears not to have such a significant effect during THA, particularly when considering bleeding from exposed bone surfaces.

In this randomized, double-blind, controlled study, no significant difference was found in blood loss or transfusion requirement between the 2 groups treated with either tranexamic acid or placebo. The findings of this study do not support the use of tranexamic acid to replace or augment other, more acceptable methods of reducing femoral canal bleeding (eg, hypotensive and regional anaesthesia and saline lavage) or be used to reduce total blood loss.

Acknowledgment

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