The Routine Use of Tranexamic Acid in Hip and Knee Replacements


Abstract

Purpose: Our aim was to determine whether the administration of intravenous tranexamic acid is a safe and effective means of reducing blood loss associated with hip and knee replacement surgery.

Method: Sequential cohort study analysing hemoglobin titers, transfusion rates, and the occurrence of venous thromboembolism in patients undergoing hip and knee replacements with and without the administration of tranexamic acid at the time of induction. Finally, a cost benefit analysis was performed.

Results: Two hundred and seventy-three patients were included in our study. We demonstrated that 1 gram of tranexamic acid administered intravenously at the time of induction significantly reduces operative blood loss and transfusion rates (p < 0.05). Moreover, the use of tranexamic acid reduces the costs associated with surgery.

Conclusions: The administration of 1 gram of intravenous tranexamic acid is a safe and effective means of reducing operative blood loss and blood transfusion rates in patients undergoing hip and knee replacements.

There can be no doubting the transforming role of joint replacements in patients afflicted with disabling and debilitating conditions of the hip and knee. Indeed, the Lancet went as far as to describe total hip replacements to be the operation of the century. The success of joint replacements is reflected by the fact that, in 2009, 79,413 total hip replacements and 84,527 total knee replacements were performed in England and Wales. Nonetheless postoperative complications do occur and include venous thromboembolism, deep infection, and in the case of hip replacements, dislocation. A further complication is intraoperative blood loss culminating in anemia. In the case of total hip and total knee replacements, hemoglobin on average falls by 3 g/dL perioperatively. The consequences of such blood loss impact both the individual patient and the healthcare system in general. The individual can expect an increased risk of infection, a delayed postoperative recovery, and poorer physical functioning. The healthcare system in general, on the other hand, can expect a high demand for allogenic blood and an increased financial burden. As such, the prevention and early treatment of postoperative anemia is a concern for orthopaedic surgeons, anesthetists, and public health physicians.

Preoperative measures aimed at preventing postoperative anemia include the use of iron supplementation and recombinant human erythropoietin in patients with pre-existing anemia. Intraoperative measures include the use of a tourniquet and the use of tranexamic acid. Postoperative measures include closely monitoring the use of anticoagulation and allogenic blood transfusion.

Tranexamic acid is an antifibrinolytic that inhibits the conversion of plasminogen to plasmin. The role of tranexamic acid in reducing blood loss has been long recognized in specialties such as cardiac and dental surgery. There is now a growing corpus of evidence supporting the use of tranexamic acid in patients undergoing a total knee or total hip replacement.
The purpose of this study is to determine the efficacy of tranexamic acid in reducing operative blood loss and the role of tranexamic acid in decreasing the need for allogenic blood transfusions in patients undergoing primary total knee and total hip replacements. A further aim is to determine the cost benefit of routinely administering tranexamic acid to all patients undergoing total hip and total knee replacements.

Materials and Methods

The study period of 24 months included 12 months prior to and 12 months following the introduction of tranexamic acid as a blood conserving technique in patients undergoing either a primary total knee or a primary total hip replacement. Our study consisted of four groups.

Group 1, the total hip replacement intervention group, comprised all patients who had their total hip replacement performed between January 1, 2010, and December 31, 2010. All received the intervention being considered, 1 gram of intravenous tranexamic acid administered at the time of induction.

Group 2, the total hip replacement control group, comprised all patients who had their operation performed between January 1, 2009, and December 31, 2009. None of the patients in this group received the intervention being considered.

Group 3, the total knee replacement intervention group, comprised all patients who had their total knee replacement performed between January 1, 2010, and December 31, 2010. All received the intervention being considered, 1 gram of intravenous tranexamic acid administered prior to tourniquet inflation at the time of induction.

Group 4, the total knee replacement control group, comprised all patients who had their operation performed between January 1, 2009, and December 31, 2009. None of the patients in this group received the intervention being considered.

The primary outcome measures were perioperative change in hemoglobin and the proportion of patients requiring an allogenic blood transfusion. The secondary outcome measures were the frequency of clinical postoperative venous thromboembolism and the cost effectiveness of our intervention. With regards to venous thromboembolism, only those patients with clinical manifestations suggestive of a deep venous thrombosis or pulmonary embolus were investigated further by performing a venous duplex scan or a computerized tomography pulmonary angiogram.

The primary surgeon remained unchanged in all four groups, and all procedures were performed within a single National Health Service trust. Surgical technique and implant used remained consistent. Drains were not routinely inserted, and hemoglobin measurements were typically obtained within 2 days of surgery in all four groups. In the case of total hip replacements, an anterolateral approach was utilized. Uncemented femoral and acetabular components were implanted on every occasion (the Corail Total Hip System manufactured by DePuy Orthopaedics, Inc.). In the case of total knee replacements, an anterolateral approach was utilized. A Press Fit Condylar Sigma Knee manufactured by DePuy Orthopaedics, Inc., was inserted on every occasion. On the first postoperative day, all patients were commenced on a daily dose of 5,000 units of subcutaneous dalteparin sodium. Our policy regarding anesthesia remained unchanged throughout the study; all patients received a spinal anesthetic with the exception of those that declined a spinal anesthetic and those in which one was clinically contraindicated. Patients were routinely followed up for a year following their operation.

Demographic data including age, gender, and preoperative American Society of Anesthesiologists (ASA) Score were recorded. Pre- and postoperative blood results were analyzed and details of all allogenic blood transfusions documented.

All statistical analyzes were performed using SPSS version 18.0 (SPSS Inc., Chicago, Illinois) or Microsoft Excel 2007 (Microsoft Corp., Redmond, Washington). Categorical data were analyzed using the chi-squared test. Continuous date were analyzed using either the Shapiro-Wilk test or Student’s t-test. Our null hypotheses were that there would be no difference in our primary or secondary outcome measures between groups 1 and 2 and groups 3 and 4.

Results

A total of 273 patients were included in our study. Patients in the intervention groups did not differ significantly from

<table>
<thead>
<tr>
<th>Table 1 Summary of the Study Group</th>
<th>Group 1: Tranexamic acid administered prior to THR</th>
<th>Group 2: Tranexamic acid not administered prior to THR</th>
<th>Group 3: Tranexamic acid administered prior to TKR</th>
<th>Group 4: Tranexamic acid not administered prior to TKR</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>57</td>
<td>74</td>
<td>76</td>
<td>66</td>
</tr>
<tr>
<td>Percentage male</td>
<td>31.6</td>
<td>37.8</td>
<td>31.6</td>
<td>42.4</td>
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<tr>
<td>Percentage female</td>
<td>68.4</td>
<td>62.2</td>
<td>68.4</td>
<td>57.7</td>
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<tr>
<td>Mean age</td>
<td>69.8</td>
<td>71.0</td>
<td>68.4</td>
<td>67.8</td>
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<td>Percentage ASA 1 &amp; 2</td>
<td>84.2</td>
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<tr>
<td>Percentage ASA 3 &amp; 4</td>
<td>15.8</td>
<td>14.9</td>
<td>10.5</td>
<td>12.1</td>
</tr>
<tr>
<td>Preoperative hemoglobin (g/dL)</td>
<td>13.1</td>
<td>13.3</td>
<td>13.5</td>
<td>13.4</td>
</tr>
</tbody>
</table>
patients in the control groups with regards to age, gender, preoperative hemoglobin, or ASA score ($p > 0.05$) (Table 1).

With the exception of 13 patients who presented with femoral neck fracture, all patients were pre-assessed 1 month prior to their operation. A preoperative hemoglobin was obtained at this stage. Postoperative blood tests were typically obtained within 2 days of surgery.

Our primary outcome indicator was the fall in hemoglobin postoperatively. This differed significantly between our intervention and control groups. Intravenously administering 1 gram of tranexamic acid preoperatively resulted in a smaller drop in hemoglobin in patients undergoing either a total knee replacement ($p < 0.05$) or a total hip replacement ($p < 0.05$) (Fig. 1).

A total of nine patients, three following a total hip replacement and six following a total knee replacement, required a postoperative allogenic blood transfusion. All patients were transfused 2 units of blood. None of these patients had received tranexamic acid preoperatively. Allogenic blood transfusions were not necessary in a single patient that had received tranexamic acid preoperatively. The indication for blood transfusion was a symptomatic hemoglobin level of less than or equal to 8.0 g/dL. Alternative interventions such as the administration of erythropoietin were not utilized in any of our four groups.

According to the NHS Blood and Transplant Department the cost of a unit of blood is £124.21 ($205). Consequently, £2235.78 ($3,690) was spent on allogenic blood transfusions in those patients not receiving tranexamic acid. This averages at £15.96 ($26) per patient. Conversely, the cost of administering 1 gram of tranexamic acid is £3.10 ($5.05) per patient according to the British National Formulary. As a result, the routine use of tranexamic acid results in a saving of £12.86 ($20.95) per patient.

None of the patients in our four groups had their recovery complicated by a venous thromboembolism.

**Discussion**

In the present study, we focus on the role of tranexamic acid in reducing operative blood loss. Operative blood loss is a complication that has significant repercussions for both the individual and health care in general. It is recognized that operative blood loss and subsequent anemia increases a patient’s risk of complications such as infection.$^6,14$ Smaller, earlier studies have demonstrated that tranexamic acid results in reduced operative blood loss reflected both by the volume of blood in the patient’s drain and a patient’s hemoglobin titer.$^{15-17}$ Our larger study mirrors these findings. In our study, every effort was made to ensure surgical technique, implant, and primary surgeon remained consistent throughout.

Postoperative allogenic blood transfusion is a treatment option for intraoperative blood loss, but it is by no means a panacea. Although uncommon, the risk of transfusion related complications is not negligible. Immunologic complications (such as acute hemolytic reactions), infective complications (such as hepatitis C transmission), and non-immunologic complications (such as transfusion associated lung injury) can have a deleterious effect on orthopaedic patients. Moreover, allogenic blood is a scarce resource with orthopaedic hip and knee surgery estimated to account for 8% of all usage.$^7$ Our study demonstrated that the use of tranexamic acid in patients undergoing hip and knee replacements can reduce the burden placed on blood transfusion services.

Increasingly physicians operating within nationalized, insurance, and consumer funded healthcare systems are faced with the dual challenge of achieving better results while simultaneously reducing costs. Our study demonstrates that these seemingly paradoxical goals are simultaneously achievable. The use of tranexamic acid in our unit reduced costs while concurrently improving outcomes. Consequently, we would suggest that professional and national bodies need to publish guidance on the routine use of tranexamic acid in patients undergoing hip and knee replacements.

Finally, one concern regarding tranexamic acid is that it may result in an increase in the risk of venous thromboembolism. Our study did not demonstrate an increased risk of venous thromboembolism in those receiving tranexamic acid. This is consistent with the findings of earlier studies and meta-analyses.$^{13}$

**Conclusions**

The administration of 1 gram of intravenous tranexamic acid is a safe and effective means of reducing operative blood loss and allogenic blood transfusion rates in patients undergoing hip and knee replacements.

**Disclosure Statement**

None of the authors have a financial or proprietary interest in the subject matter or materials discussed, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony.

**References**