Intra-articular administration of tranexamic acid in total hip arthroplasty

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ABSTRACT

Purpose. To evaluate the effectiveness of intra-articular tranexamic acid (TXA) in reducing blood loss and the need for blood transfusion during total hip arthroplasty (THA).

Methods. Records of 19 men and 31 women aged 46 to 83 (mean, 62) years who underwent primary THA with intra-articular administration of TXA were reviewed. They were compared with a matched cohort of 17 men and 33 women aged 40 to 87 (mean, 62) years who underwent the same procedure by the same surgeon without use of TXA. Postoperatively, a standard thromboembolic prophylaxis protocol was followed. A serum haemoglobin level of <80 g/l was the trigger for blood transfusion.

Results. The 2 groups were comparable in terms of age, gender, body mass index, side involved, and anaesthesia method. No patient developed infection, wound haematoma, symptomatic deep vein thrombosis, or pulmonary embolism within 30 days. Compared with controls, patients in the TXA group had a higher median postoperative serum haemoglobin level (103 vs. 112 g/l, p=0.013), lower median drop in serum haemoglobin level (31 vs. 20 g/l, p<0.001), lower median total blood loss (900 vs. 575 ml, p<0.001), and lower transfusion rate (32% vs. 10%, p=0.007). The TXA treatment cost S$19.50 per patient, whereas one unit of allogenic blood cost S$123 per patient. Respectively in the control and TXA groups, the mean cost per patient was S$39.36 and S$31.80, indicating a 19% difference.

Conclusion. Intra-articular administration of TXA is a cost-effective and safe means to reduce blood loss and the need for blood transfusion during THA, without increasing the risk of thromboembolic events.

Key words: arthroplasty, replacement, hip; blood loss, surgical; blood transfusion; tranexamic acid

INTRODUCTION

Total hip arthroplasty (THA) is associated with considerable blood loss, with 16% to 37% of patients requiring allogenic blood transfusion.1 Blood
transfusion is associated with risks of viral infections, transfusion-related reactions, and fluid overload, as well as increased length of hospital stay and costs. Blood-conserving strategies including hypotensive anaesthesia, intra-operative blood salvage, and erythropoietin and anti-fibrinolytic agents are thus suggested.

Tranexamic acid (TXA) is a synthetic anti-fibrinolytic agent that inhibits the activation of plasminogen to plasmin, which is an enzyme that degrades fibrin clots, fibrinogen, and procoagulant factors V and VIII. At a higher concentration, TXA acts directly to inhibit plasmin activation and binding of plasmin to fibrin, thereby inhibiting fibrin degradation. It reduces the breakdown of fibrin clots that are already formed; it is not a procoagulant per se but rather it supports the coagulation process already in progress. Thus, TXA is well suited to reduce postoperative bleeding, where surgical haemostasis is achieved and fibrinolytic activity needs to be suppressed to maintain haemostasis, without promoting venous thrombus formation. The use of TXA does not increase the thromboembolic risk. It has been used to reduce blood loss in cardiac surgery, liver transplantation, and gynaecology. The trauma of surgery activates fibrinolysis by promoting the release of tissue plasminogen activator. Although the body naturally inhibits fibrinolysis within 24 hours of surgery, anti-fibrinolytic agents such as TXA may block the activation of plasminogen to plasmin earlier and thereby decrease peri-operative blood loss.

Intravenous TXA is commonly used. Intra-articular administration of TXA is effective in reducing blood loss during total knee arthroplasty (TKA), but in THA, its effect remains controversial. This study evaluated the effectiveness of intra-articular TXA in reducing blood loss and the need for blood transfusion during THA.

**MATERIALS AND METHODS**

This study was approved by the Centralised Institutional Review Board of SingHealth (CIRB: 2013/871/D) and carried out in accordance with the Declaration of Helsinki. Based on the difference in postoperative blood transfusion incidence with or without TXA, to detect a significant difference between 2.3% and 19.3% at a power of 0.80, a sample size of at least 48 patients in each group was required (one-sided test, with a type-I error of 0.05).

Records of 19 men and 31 women aged 46 to 83 (mean, 62) years who underwent primary THA were compared with a matched cohort of 17 men and 33 women aged 40 to 87 (mean, 62) years who underwent the same procedure by the same surgeon without use of TXA between May 2009 and April 2011. The patients were matched for preoperative serum haemoglobin level and body mass index (BMI); both were predictors for the need for blood transfusion after THA. Patients with a history of thromboembolic disease or bleeding disorder, or in use of anticoagulant drugs were excluded.

THA was performed through the posterior approach, and major bleeders were cauterised in a standard fashion. Patients in the TXA group received 1500 mg of TXA (Cyklokapron, Pfizer, New York, USA) diluted in 100 ml of 0.9% sodium chloride as a wash poured into the wound after implantation of the uncemented acetabular and femoral components (DePuy Synthes Total Hip System, Warsaw [IN], USA). After at least 5 minutes of contact time, the TXA fluid was then suctioned out sufficiently to allow repair of the external rotators and capsule. Deep fascia, subcutaneous and skin were closed in a standard fashion. No drain was used. Intravenous fluid substitution (1 litre) in the form of 0.9% sodium chloride was given.

Postoperatively, a standard thromboembolic prophylaxis protocol was followed. Pneumatic calf pumps were given until ambulation. Subcutaneous Clexane (Sanofi, Paris, France) 40 mg once daily was given on day 1 and continued until discharge. Physiotherapy was started with the aim of early mobilisation. Patients with deep vein thrombosis symptoms were evaluated using ultrasonography (for the lower limb) and computed tomography (for the chest). Patients were discharged once they could walk independently with or without a walking aid.

Outcome measures included duration of surgery, wound complications and thromboembolic events within 30 days of surgery, postoperative drop in serum haemoglobin level, total blood loss, transfusion rate, and length of hospital stay. A serum haemoglobin level of <80 g/l was the trigger for blood transfusion. Total blood loss was calculated by the haemoglobin balance method. Patient’s blood volume was equal to (k1×height2 in m) + (k2×weight in kg) + k3, where k1=0.3669, k2=0.03219, and k3=0.6041 for men, and k1=0.3561, k2=0.03308, and k3=0.1833 for women. The loss of haemoglobin (in g) was equal to the patient’s blood volume×(preoperative minus postoperative serum haemoglobin level [g/l])×0.001 + the amount of haemoglobin transfused (in g). Total blood loss (in ml) was equal to 1000×loss of haemoglobin (in g) /
Normality was tested using the Shapiro-Wilk test. Continuous variables with non-normal distribution (pre- and post-operative serum haemoglobin level, postoperative drop in serum haemoglobin level, total blood loss, length of hospital stay, and duration of surgery) were compared using the Mann-Whitney U test. Continuous variables with normal distribution (age and BMI) were compared using the Student’s unpaired t-test. Categorical variables (gender, side involved, anaesthesia method, transfusion rate, and postoperative complications) were compared using the Pearson Chi-Square test. A p value of <0.05 was considered statistically significant.

RESULTS

The 2 groups were comparable in terms of age, gender, BMI, side involved, and anaesthesia method (Table). No patient developed infection, wound haematoma, symptomatic deep vein thrombosis, or pulmonary embolism within 30 days. Compared with controls, patients in the TXA group had a higher median postoperative serum haemoglobin level (103 vs. 112 g/l, p=0.013), lower median drop in serum haemoglobin level (31 vs. 20 g/l, p<0.001), lower median total blood loss (900 vs. 575 ml, p<0.001), and lower transfusion rate (32% vs. 10%, p=0.007) [Table].

TXA treatment cost S$19.50 per patient, whereas one unit of allogenic blood cost S$123 per patient. Respectively in the control and TXA groups, the total cost for TXA treatment and blood transfusion was S$1968 and S$1590, and the mean cost per patient was S$39.36 and S$31.80, indicating a 19% difference.

DISCUSSION

A meta-analysis has shown that TXA reduces the blood transfusion rate by a third. Compared with intravenous TXA, intra-articular TXA provides a maximum concentration at the bleeding site, with minimal systemic absorption. The use of intra-articular TXA in THA may not be as effective as in TKA, because the use of a tourniquet in TKA results in negligible intra-operative blood loss (but notable postoperative blood loss), whereas in THA a greater proportion of blood is lost intra-operatively.

Intra-articular administration of TXA significantly reduces haemoglobin drop and total blood loss during THA, but is less effective in reducing the need for blood transfusion: some studies report a 14% to 20% reduction, but others report no difference. It also reduces the length of hospital stay by 0.6 to 1 day, with minimal or no increase in infection or venous thromboembolic events.

In our study, total blood loss was calculated by the haemoglobin balance method. It can also be estimated by: (1) subtracting the total amount of wash given from the total suction volume intra-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Tranexamic acid group</th>
<th>Matched controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (range): age (years)</td>
<td>62 (46–83)</td>
<td>62 (40–87)</td>
<td>0.741</td>
</tr>
<tr>
<td>No. of male:female</td>
<td>19:31</td>
<td>17:33</td>
<td>0.677</td>
</tr>
<tr>
<td>Mean (range): body mass index (kg/m²)</td>
<td>27.0 (20.8–35.0)</td>
<td>27.0 (20.0–35.8)</td>
<td>0.947</td>
</tr>
<tr>
<td>Side involved (no. of patients)</td>
<td></td>
<td></td>
<td>0.841</td>
</tr>
<tr>
<td>Left</td>
<td>27</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>23</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Anaesthesia method (no. of patients)</td>
<td></td>
<td></td>
<td>0.110</td>
</tr>
<tr>
<td>General</td>
<td>21</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Neuraxial</td>
<td>29</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Diagnosis (no. of patients)</td>
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</tr>
<tr>
<td>Osteoarthritis</td>
<td>38</td>
<td>38</td>
<td></td>
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<tr>
<td>Avascular necrosis</td>
<td>12</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range): serum haemoglobin level (g/l)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preop</td>
<td>134 (17)</td>
<td>133 (23)</td>
<td>0.697</td>
</tr>
<tr>
<td>Postop</td>
<td>112 (23)</td>
<td>103 (22)</td>
<td>0.013</td>
</tr>
<tr>
<td>Drop</td>
<td>20 (11)</td>
<td>31 (16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median (interquartile range): total blood loss (ml)</td>
<td>575 (414)</td>
<td>900 (508)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. (%) of patients receiving blood transfusion</td>
<td>5 (10)</td>
<td>16 (32)</td>
<td>0.007</td>
</tr>
<tr>
<td>Median (interquartile range): length of hospital stay (days)</td>
<td>3 (2)</td>
<td>4 (2)</td>
<td>0.226</td>
</tr>
</tbody>
</table>
operatively, or (2) weighing the swabs after use and calculating the increase from original dry weight (1 g difference = 1 ml). Nonetheless, blood loss was underestimated by 64% when clinical methods of measuring suction bottles and blood-soaked swabs were used. The haemoglobin balance method is less likely to underestimate the total blood loss.

One limitation of this study was its retrospective nature. In addition, pain score, range of movement, Oxford Hip Score, and Short Form-36 score were not reported.

CONCLUSION

Intra-articular administration of TXA is a cost-effective and safe means to reduce blood loss and the need for blood transfusion during THA, without increasing the risk of thromboembolic events.

DISCLOSURE

No conflicts of interest were declared by the authors.

REFERENCES