The Effect of Tranexamic Acid Administration on Perioperative Bleeding in Patients Undergoing Knee or Hip Arthroplasty: A Single-Centre Retrospective Study

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Abstract

Objective: Tranexamic acid (TXA) has been used to reduce perioperative bleeding in various surgeries because of its antifibrinolytic effect. Recently, patients undergoing orthopaedic surgery in our institution received a loading dose of TXA (1000 mg) before surgery, followed by 100 mg h\(^{-1}\) until the end of surgery. The purpose of the present study was to evaluate the efficacy of TXA administration on the perioperative blood loss in patients undergoing knee arthroplasty or hip arthroplasty.

Methods: A retrospective cross-sectional study was conducted for the records in patients who underwent surgery without TXA administration (control group) and patients who underwent surgery with TXA administration (TXA group). Amount of intraoperative blood loss, intraoperative transfusion volume, intraoperative blood transfusion volume, postoperative blood transfusion volume, changes in haemoglobin concentrations (ΔHb) and estimated blood loss were collected. Data were adjusted by propensity score method.

Results: A total of 126 (63 in the control group and 63 in the TXA group) patients were included during the study period. Intraoperative infusion, postoperative transfusion, ΔHb and estimated blood loss were significantly reduced in the TXA group, although there were no significant differences in the volumes of intraoperative transfusion and blood loss.

Conclusion: The administration of TXA (loading dose of 1000 mg and continuous infusion of 100 mg h\(^{-1}\)) reduced postoperative transfusion and perioperative blood loss. These results indicated that TXA administration is useful for reducing perioperative blood loss in patients undergoing knee or hip arthroplasty.

Keywords: Arthroplasty, tranexamic acid, transfusion

Introduction

It is known that perioperative anaemia affects morbidity and mortality and increases the risk of surgical site infection (1, 2). Tranexamic acid (TXA) has been used to reduce perioperative bleeding and transfusion in various surgeries because of its antifibrinolytic effect (3-6). The number of total knee arthroplasty (TKA) and total hip arthroplasty (THA) procedures has been increasing worldwide (7). However, previous reports have shown that TKA and THA surgeries are associated with considerable blood loss, thereby necessitating perioperative blood transfusion in approximately 30% of the patients (8, 9). Allogeneic blood transfusion is expensive and accompanied with the risk of infection, transfusion-related acute lung injury and transfusion-associated circulatory overload. To reduce the need for allogeneic transfusion, some studies have reported the effect of TXA on perioperative bleeding; however, there is insufficient information about the ideal dosage, timing and continuous infusion (7). Patients who were scheduled to undergo orthopaedic surgery at our institution between July 2016 and June 2017 received a loading dose of TXA (1000 mg) before surgery, followed by 100 mg h\(^{-1}\) until the end of surgery.
Therefore, the aim of the present study was to retrospectively investigate perioperative blood loss in patients who underwent knee arthroplasty or hip arthroplasty 1 year before and after the administration of TXA.

**Methods**

**Study design and data source**
A retrospective single-centre, cross-sectional study between January 2015 and June 2017 at our institution was conducted. The study was approved by the Akita University Ethics Committee of our institution on 18 October 2017 (approval no. 1862). All data were extracted from the clinical database in our institution.

**Patients**
Patients who underwent unilateral primary THA, TKA or unicompartmental knee arthroplasty (UKA) at our institution were selected. One hundred thirty-five patients were enrolled in this study. Demographic data on sex, age, height, weight, American Society of Anaesthesiologists Physical Status, duration of surgery, type of surgery (THA, TKA or UKA) and type of anaesthesia were collected. Patients who did not receive TXA (control group) were those who underwent surgery between January 2015 and December 2015, whereas those who received TXA (TXA group) underwent surgery between July 2016 and June 2017. TKA and UKA surgeries were performed using a tourniquet.

**Study intervention and outcomes**
TXA was infused (1000 mg) before surgery as a loading dose and 100 mg h$^{-1}$ continuously until the end of surgery in the TXA group. The total doses of TXA were confirmed from the anaesthesia records. The control group did not receive any placebo drug. Induction and maintenance of anaesthesia was entrusted to the discretion of the anaesthesiologist in charge. From the anaesthesia records, the choice of epidural or femoral perineural anaesthesia was at the discretion of the anaesthesiologist. Primary outcome was perioperative estimated blood loss, which was calculated using the modified Zufferey’s method (10). In brief, the value was expressed as $1000 \times (\Delta Hb \times \text{blood volume} + \text{the total amount of transfused Hb}/\text{preoperative Hb})$. $\Delta Hb$ was obtained by the subtraction of the Hb value on the preoperative day and postoperative day 4. Secondary outcomes included intraoperative blood loss, $\Delta Hb$, intraoperative infusion (amount of crystalloid and colloid infusion), intraoperative transfusion and postoperative transfusion. The criteria for transfusion depended on the discretion of the anaesthesiologist in charge. From postoperative day 1, all patients received 3000 IU (30 mg) of enoxaparin daily for 2 weeks as prevention against venous thromboembolism.

**Statistical analyses**
According to our previous records of anaesthesia and other similar studies, we assumed that the difference between perioperative blood loss was 400 mL and standard deviation was 750 mL. Based on the above, we calculated that a sample size of 57 patients per group would be required to achieve a power of 80% with a two-sided α risk of 0.05. The propensity score matched pair analysis was applied to reduce the effect of confounding factors. Student’s t-test, Mann-Whitney U test and McNemar test were employed for the analysis of results. Propensity score matched pair analysis for demographic data was done using EZR version 1.36 (The R Foundation for Statistical Computing, Vienna, Austria) (11). Comparison between the two groups was performed using StatView version 5.0 (SAS Institute, Cary, NC, USA) and JMP version 14.1 (SAS Institute). Normally distributed values were expressed as mean±SD, and non-normally distributed data were expressed as median (25$^{th}$-75$^{th}$ percentile). A p value <0.05 was considered statistically significant.

**Results**
This retrospective cross-sectional study consisted of 135 (98 THA, 29 TKA and 8 UKA) patients between January 2015 and June 2017, of whom 63 were in the control group and 72 were in the TXA group (Figure 1). Demographic data are summarised in Table 1. All data except for the duration of surgery and activated partial thromboplastin time (aPTT) were similar between the two groups. To adjust this confounding factor, 87.5% (n=63) of patients in the TXA group were matched with similar patients in the control group through propensity score matching. Both matched and unmatched data are described in Table 1.

Within the matched data, perioperative estimated blood loss and $\Delta Hb$ in the TXA group were significantly less than those in the control group (p=0.01) (Figure 2a and b). However, the mean intraoperative blood loss did not differ between the two groups (Figure 2c).

**Main Points:**
- Tranexamic acid has been used to reduce perioperative bleeding and transfusion in various surgeries.
- The ideal dosage, timing and continuous infusion of tranexamic acid has not been fully elucidated.
- Loading dose and intraoperative continuous infusion of tranexamic acid were used in patients with orthopaedic surgery.
- Tranexamic acid reduced postoperative transfusion and perioperative blood loss.
- No patient developed adverse effects.
Although the volumes of intraoperative red blood cell transfusion were similar between the two groups, the volume of postoperative transfusion was significantly less in patients given TXA (Table 2). There was no significant difference in the number of patients who required at least 1 U of allogeneic red blood cells in the perioperative period (21 patients in the TXA group and 22 patients in the control group). No patient received other blood products, such as fresh frozen plasma and platelet concentrate.

The intraoperative infusion in the TXA group (1489±808 mL) was significantly less than that in the control group (1880±851 mL, p<0.01). No patient was diagnosed with pulmonary embolism (PE), deep vein thrombosis (DVT) or myocardial infarction using spiral computed tomography or electrocardiogram.
In the present study, we found that perioperative blood loss (estimated blood loss and ΔHb) and volume of postoperative transfusion were less in patients who were given TXA, whereas the volumes of intraoperative blood loss and transfusion were similar between patients with and without TXA. These results were consistent with previous similar studies showing that TXA decreased not only blood loss but also need for perioperative infusion (12). In addition, our results showed significant reduction in need for intraoperative infusion in the TXA group due to decrease in intraoperative blood loss.

Many studies have reported the effect of TXA on perioperative blood loss and transfusion. However, the doses of TXA evaluated were different among the studies that included patients undergoing THA or TKA. We used 1000 mg TXA before surgery as loading dose and 100 mg h⁻¹ continuous infusion until the end of surgery. Oremus et al. (13) showed that TXA reduces perioperative blood loss but not intraoperative blood loss in patients who underwent THA and TKA. Clave et al. (14) also indicated the same effect of TXA in patients who underwent THA. Although our results also indicated reduction in perioperative blood loss, the dose of TXA in their literature was greater than that of our study. Oremus et al.
The authors declared that this study has some limitations. First, we could not completely adjust the duration of surgery and the aPTT between the two groups, although we used the propensity score analysis. The main reason is that the surgical time acts as an intermediate rather than a confounding variable. Although the aPTT in the TXA group was statistically less significant than that in the control group, both values were within the normal range. Thus, this difference may be ignored clinically. Second, the surgical position for THA was different in the two groups. It was the transition period of the surgical position from the end of 2015 to 2016. Almost all patients in the control group underwent surgery in the lateral decubitus position, whereas patients in the TXA group were in the jack knife position. Third, there were no exact criteria for blood transfusion in our retrospective study. Most of us considered red blood cell transfusion in cases with Hb <8 g dL\(^{-1}\) though it depended on the decision of the anaesthesiologist. Additional prospective or systematic large study should be conducted to reduce these confounding factors.

**Conclusion**

We observed that infusion of TXA decreased perioperative blood loss and the need for transfusion without any adverse events in patients undergoing TKA and THA. These results indicated that TXA administration is useful for reducing perioperative blood loss.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Akita University (Approval no. 1862).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - T.G.; Design - A.N., T.G.; Supervision - T.G.; Resources - T.G.; Materials - T.G.; Data Collection and/or Processing - A.N., K.M.; Analysis and/or Interpretation - A.N., T.G.; Literature Search - A.N.; Writing Manuscript - A.N., T.G.; Critical Review - T.G., K.M.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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