The Effect of Tranexamic Acid on Blood Loss During Orthognathic Surgery: A Randomized Controlled Trial

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Purpose: Tranexamic acid has been used to reduce blood loss and the subsequent need for transfusion in orthopedic, spinal, and cardiac surgery. Orthognathic surgery can be associated with significant bleeding yet its efficacy in this setting is not clear. The purpose of this study was to investigate the effect of tranexamic acid on blood loss during bimaxillary osteotomy.

Patients and Methods: Seventy-three consecutive patients, scheduled for elective bimaxillary osteotomy, were included in this double blind, randomized, controlled trial. They received either a bolus of tranexamic acid (20 mg/kg) or placebo (normal saline) intravenously just before surgery. All patients received induced mild hypotension and had surgery according to a standard protocol. Intraoperative blood loss, operation time, transfusion of blood products, perioperative hemoglobin, and hematocrit were recorded.

Results: The total blood loss and blood loss during maxillary surgery was reduced significantly in the tranexamic acid group compared with the control group (878.6 ± 577.7 mL vs 1,257.2 ± 817.8 mL and 428.0 ± 233.3 mL vs 643.8 ± 430.0 mL, respectively; P < .05). Considering the duration of operation and the treatment groups only, the mean total blood loss in the control group was 422 mL more than that in the tranexamic acid group (P < .001). There was no significant difference in blood transfusion or the length of hospital stay between the 2 groups.

Conclusion: Preoperative intravenous bolus administration of tranexamic acid at 20 mg/kg reduces blood loss compared with placebo during bimaxillary osteotomy.

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Orthognathic surgery is a well-established method to correct various forms of dentofacial deformity. With the current standards of surgery and anesthesia, this elective procedure is considered relatively safe with good results. However, as the orofacial region is very vascular, significant blood loss can occur and a subsequent need for blood transfusion is often encountered.1 Adverse effects of blood transfusion include transmission of infectious disease, immunosuppression, and incompatibility reactions.2 Hypotension can be induced deliberately to minimize blood loss3 and has been reported to reduce total blood loss by as much as 40% and improve the surgical field by 27% in orthognathic surgery.4 However, there is a risk of ischemic complications5 with prolonged moderate hypotension especially in patients with altered baseline autoregulatory mechanisms (hypertension) or those likely to be particularly vulnerable (eg, diabetes, coronary artery disease, stroke, chronic renal failure). The Medical Protection Society has recently urged caution in this regard and it would seem prudent to investigate other methods to reduce bleeding. Tranexamic acid, a synthetic amino acid that inhibits fibrinolysis, has been shown to reduce blood loss and the need for blood transfusion in total knee arthroplasty,6,7 spine surgery,8 and cardiac surgery.9 Topical tranexamic acid has been used for treatment of postoperative bleeding in anticoagulated patients after oral surgery.10-16 Senghore and Harris17 showed that a single intravenous preoperative dose of tranexamic acid was effective in preventing excessive postoperative bleeding in healthy adult patients undergoing third molar extraction. The use of tranexamic acid in orthognathic surgery was evaluated by Zellin et al18 in...
a retrospective study. They reported that blood loss during orthognathic surgery under hypotensive anesthesia could be reduced significantly when a combination of tranexamic acid and desmopressin was added.\textsuperscript{18} Adverse events with tranexamic acid therapy including nausea or diarrhea, and occasionally orthostatic reaction, are uncommon.\textsuperscript{19} Isolated cases of thromboembolism after the use of tranexamic acid have been reported\textsuperscript{20}; however, these observations have not been confirmed by results of controlled clinical studies.\textsuperscript{7} Insufficient evidence is available regarding the use of tranexamic acid as the only pharmacologic means to reduce blood loss during orthognathic surgery.

The aim of this study was to assess the effect of a single intravenous preoperative dose of tranexamic acid on blood loss during bimaxillary osteotomy under mild controlled hypotension.

**Patients and Methods**

**PATIENT SELECTION**

This study was approved by the ethics committee of the Faculty of Dentistry, University of Hong Kong. All American Society of Anesthesiologists (ASA) Class I patients between 16 and 40 years of age scheduled for bimaxillary osteotomy at Queen Mary Hospital between November 2005 to January 2008 were consecutively recruited to the study after written informed consent. Patients who had bone disease (eg, fibrous dysplasia), cleft lip and palate, craniofacial syndromes (eg, hemifacial microsomia, Treacher Collins Syndrome), or scheduled to receive simultaneous rhinoplasty, temporomandibular joint surgery, or bone graft harvest were excluded from consideration.

**PREOPERATIVE PREPARATION**

All patients were admitted to the hospital for preoperative assessment and anesthetic consultation 1 to 3 days before operation. After routine history taking and clinical examination, a blood sample was taken for complete blood picture (CBP), prothrombin time (PT), activated partial thromboplastin time (APTT), liver function tests (LFT), renal function tests (RFT), random glucose (RG), and cross matching. Three measurements of blood pressure were taken at 1 hour, 5 hours, and 9 hours after admission.

**RANDOMIZATION**

Patients were randomized by computer generated numbers to receive 20 mL study drug (20 mg/kg tranexamic acid or 0.9% normal saline) immediately before surgery. Sealed envelopes containing the information of the randomization allocation were prepared and kept by clerical staff not involved in the study. The specific envelope was transferred to a specific member of the surgical team not involved in the surgery just before the induction of anesthesia. The study drug was prepared by this surgeon accordingly and was transferred to the anesthetist for administration over 15 minutes after induction of anesthesia. The envelope was sealed again and kept in the patient’s folder until the end of the study period. All members of the surgical team, nursing staff, and the anesthetist were unaware of the allocation. Subject enrollment and allocation is summarized in a CONSORT flow diagram (Fig 1).

**ANESTHETIC PROTOCOL**

Patients did not receive premedication. Anesthesia was induced with propofol (2-3 mg/kg), remifentanil (0.5 \(\mu\)g/kg/min) infusion with rocuronium (0.5 mg/kg) for muscle relaxation. After nasoendotracheal intubation, a urinary catheter was inserted. Anesthesia was maintained with isoflurane in an air/oxygen mix delivered by intermittent positive pressure ventilation to normocapnia, and a remifentanil infusion (0.15-0.5 \(\mu\)g/kg/min). No positive end-expiratory pressure was applied. Blood pressure was monitored continuously by radial artery catheter or blood pressure cuff at 5-minute intervals and maintained at 25% to 30% below the mean preoperative level by incremental doses of labetrol and/or metoprolol. A temperature probe, continuous oxygen saturation, and electrocardiogram were used. The patient was positioned supine with a 15° head up tilt, and care was taken to avoid obstruction of venous return from the head.

**INTRAOPERATIVE PROCEDURE**

Penicillin G, dexamethasone, and the study drug were given intravenously just before commencement of the surgery. If the patient was allergic to penicillin, clindamycin was used instead. The operation was carried out by qualified surgical staff with the assistance of surgical trainees, or by senior surgical trainees under supervision at this training centre. The surgical procedures comprised of a combination of maxillary and mandibular osteotomies, including:

1. Maxillary surgery:
   - Le Fort I with or without segmentalization;
   - Anterior maxillary (Wunderer) osteotomy;
   - Posterior maxillary (Schuchardt) osteotomy; or
   - Le Fort I maxillary distraction.
2. Mandibular surgery:
   - Anterior subapical (Hofer) osteotomy;
   - Body (Step) osteotomy;
   - Sagittal split ramus osteotomy;
   - Vertical subsigmoid osteotomy;
   - Genioplasty; or
   - Mandibular body osteotomy and distraction.
The estimated blood loss (EBL) was measured hourly and after completion of each surgical procedure (such as the subapical or Wunderer part of the operation) by calculating the difference in weight between the fluid in suction bottles, blood-soaked gauze, and the irrigation fluid used. Perioperatively, all patients received standard fluid replacement therapy with crystalloids (0.9% saline or lactated Ringer’s solution) at 4 mL/kg/hour or 3 times the EBL to maintain urine output greater than 0.5 mL/kg/hour. When 15% of the estimated blood volume (EBV) was lost, hydroxyethyl starch (Voluven; Fresenius Kabi Pharmaceutical, Bad Homburg, Germany) was given on a matching basis (mL for mL) or according to the vital signs (pulse and blood pressure) and urine output (L/mg/kg/hour). Packed red cells were transfused when the EBL was greater than 25% of the EBV (70 mL/kg for males, 65 mL/kg for females), and the hemoglobin level was less than 8 g/dL as measured by the HemoCue B-hemoglobin photometer (HemoCue AB, Angelholm, Sweden).

Blood samples were taken at 4, 24, and 48 hours postoperatively for CBP, PT, and APTT.

Blood loss was estimated by calculating the difference in pre- and postoperative hemoglobin and hematocrit values according to the following formulae (assuming the blood volume was normalized at 48 hours postoperatively and the hemoglobin level could be raised by 1 g/dL for every pack of red blood cells transfused):

1. \[ \text{Hb}_{\text{loss}} = \text{Hb}_{\text{pre}} \times \frac{\text{Hb}_{\text{post}}}{\text{Hb}_{\text{pre}}} + t \]
2. \[ \text{RBCL} = \left( \frac{\text{Hct}_{\text{pre}} \times \text{Hct}_{\text{post}}}{2} \right) \] (adapted from Hurle et al.

Abbreviations: BV, blood volume (mL) [70 mL/kg for males, 65 mL/kg for females]; CBL, calculated blood loss (mL); Hb post, hemoglobin level at postoperative 48 hours (g/dL); Hb pre, preoperative hemoglobin level (g/dL); Hct pre, preoperative hematocrit level (%); RBCL, red blood cell loss (mL); t, unit of packed red cells transfused.

POWER ESTIMATION AND STATISTICAL ANALYSIS

According to an internal clinical audit of this training center in 2005 to 2006, the blood loss of bimax-
illary osteotomy was within a range of 600 mL to 2,000 mL, with a mean of 1,000 mL and standard deviation (SD) of 350 mL (unpublished data). Previous studies showed the use of tranexamic acid to be associated with a reduction of intraoperative blood loss by 30% to 50%. A power analysis using these assumptions showed that 22 patients per group offered a 80% chance to detect a 30% difference between the 2 groups at the 0.05 level of significance using a two-sample \( t \) test.

Statistical analysis was carried out using SPSS for Windows (version 13.0; SPSS, Chicago, IL) to compare the study and control groups in terms of baseline information, intraoperative, and postoperative findings. When comparing the 2 groups, continuous data were summarized by means and SD and analyzed using the 2-sample \( t \) test and confidence intervals. Tables were used to summarize and compare categorical variables between treatment groups, and the data were analyzed using \( \chi^2 \) tests. Logistic regression was used when analyzing binary outcome and ANCOVA was applied to identify which variables were independently predictive for total blood loss. Results of the statistical tests were considered to be significant if the \( P \) value was less than .05.

### Results

Seventy-three consecutive patients were included in the study initially. However, 12 patients had to be excluded due primarily to incomplete data collection (9 patients), or postoperative re-intubation/re-operation (3 patients). Therefore, only 61 sets of data could be analyzed.

There was no significant difference in demographic data and baseline hemodynamic data between the treatment groups (Table 1). The blood loss during anterior mandibular surgery, maxillary surgery, ramus surgery, and the total blood loss was reduced in the tranexamic acid group. A statistical difference was observed during maxillary surgery (428.0 vs 643.8 mL; \( P < .05 \)) and total blood loss (878.6 vs 1,257.2 mL; \( P < .05 \)) (Table 2). Further statistical analysis using ANCOVA showed that both the operation time and treatment group (\( P < .001 \)) affected the total blood loss. Considering both variables in the analysis, the total blood loss in the control group was 422 mL greater than that in the tranexamic acid group. The total blood loss increased as the operation time increased (Fig 2). However, there was no significant difference in total operation, percentage of transfusion, and length of hospital stay between treatment groups. Logistic regression showed that total blood loss was the only factor that affected the chance of transfusion (\( P < .05 \)). The length of hospital stay was associated with perioperative transfusion and duration of surgery (\( P < .05 \)). For both groups, significant reduction in hemoglobin (Hb) and hematocrit (Hct) levels was observed at 4, 24, and 48 hours postoperatively.

### Table 1. DEMOGRAPHIC CHARACTERISTICS AND PREOPERATIVE COMPARISON OF THE TREATMENT GROUPS

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Tranexamic Acid Group (n = 32)</th>
<th>Control Group (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>22/10</td>
<td>18/11</td>
</tr>
<tr>
<td>Age (y)</td>
<td>23.9 ± 6.1</td>
<td>22.8 ± 4.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>56.3 ± 9.3</td>
<td>57.7 ± 11.7</td>
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<tr>
<td>Smoking habit</td>
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<td>4</td>
</tr>
<tr>
<td>Drinking habit</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blood volume (mL)</td>
<td>3,761.3 ± 731.4</td>
<td>3,866.5 ± 877.8</td>
</tr>
<tr>
<td>Diagnosis of maxilla</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillary hypoplasia in AP</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Maxillary hypoplasia in transverse</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Maxillary dentoalveolar hyperplasia in AP</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Vertical maxillary excess</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Maxillary hypoplasia in vertical</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Diagnosis of mandible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandibular hypoplasia in AP</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Mandibular hyperplasia in AP</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Mandibular dentoalveolar hyperplasia</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Asymmetric mandibular hyperplasia</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Hemimandibular hyperplasia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Unilateral condylar hyperplasia</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Geniohipoplasia</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Geniohyperplasia</td>
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<td>0</td>
</tr>
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</table>

Abbreviation: AP, anteroposterior.

Continuous data are expressed in mean ± SD. Study groups were compared by 2-sample \( t \) test or \( \chi^2 \) test, as appropriate.
platelet count also was decreased significantly and the PT was prolonged until 24 hours postoperatively. The APTT was reduced significantly during 4 to 48 hours postoperatively. No significant difference in the postoperative hematologic results between 2 groups was observed (Table 3).

There were 3 incidences of perioperative hemorrhage during maxillary osteotomy. One was due to laceration of the descending palatine artery that was cauterized. Oozing from the pterygoid plexus was encountered in the other 2 cases. All 3 were controlled by packing absorbable hemostat (Surgicel; Johnson & Johnson, Ethicon Inc, Somerville, MA) and gauze in the wound. No blood transfusion was required in these cases. No adverse reactions or thromboembolic events were observed. There were no transfusion reactions in any patient receiving blood in this study.

**Discussion**

Randomized controlled trials (RCT) are considered the best method to investigate the value of an intervention because they are designed to minimize possible bias and maximize attribution. Although RCT is
difficult to use in surgical care,27 we tried to reduce the possible effects of confounding factors in this study by randomization and strict anesthetic and surgical protocols in an attempt to generate the strongest evidence for the effect of tranexamic acid in orthognathic surgery.

The biologic half life was reported to be 1.9 hours28 and according to Pilbrant et al,29 after intravenous administration of 1 gram tranexamic acid, the drug is eliminated in 3 exponential phases with over 95% excretion in urine. As cited by Dunn and Goa,30 other studies showed that around 30% of the intravenous dose of 10 mg/kg of tranexamic acid was detected in the urine during the first hour after administration. The total excretion rose to 45% after 3 hours and approximately 90% after 24 hours. There is no consensus on the best time for administration of this drug. Most studies advocate the use of tranexamic acid administered just before the surgical incision and continued until the patients becomes hemodynamically stable and at least 1 hour after the surgical incision. The drug was not discontinued until the patients become free of any signs of hemorrhage.

![Graph](image)

**FIGURE 2.** Relationship between total blood loss and operation time.

Table 3. **POSTOPERATIVE HEMATOLOGIC COMPARISON BETWEEN TREATMENT GROUPS**

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative (4 h)</th>
<th>Postoperative (24 h)</th>
<th>Postoperative (48 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hb level (g/dL)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>13.5 ± 1.8</td>
<td>11.0 ± 1.9*</td>
<td>11.1 ± 2.1*</td>
<td>11.0 ± 2.1*</td>
</tr>
<tr>
<td>C</td>
<td>13.8 ± 1.2</td>
<td>10.4 ± 1.6*</td>
<td>10.6 ± 1.6*</td>
<td>10.2 ± 1.6*</td>
</tr>
<tr>
<td><strong>Hct level (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>39.6 ± 4.8</td>
<td>33.4 ± 8.0*</td>
<td>32.5 ± 6.1*</td>
<td>32.2 ± 6.0*</td>
</tr>
<tr>
<td>C</td>
<td>40.3 ± 5.1</td>
<td>30.4 ± 4.9*</td>
<td>30.8 ± 4.7*</td>
<td>29.7 ± 4.8*</td>
</tr>
<tr>
<td><strong>Platelet level (×10^9/L)</strong></td>
<td>246.0 ± 54.5</td>
<td>217.8 ± 43.3*</td>
<td>232.8 ± 53.5*</td>
<td>246.2 ± 55.3</td>
</tr>
<tr>
<td>T</td>
<td>260.9 ± 50.7</td>
<td>226.0 ± 55.6*</td>
<td>234.5 ± 64.0*</td>
<td>245.7 ± 56.3</td>
</tr>
<tr>
<td>C</td>
<td>260.9 ± 50.7</td>
<td>226.0 ± 55.6*</td>
<td>234.5 ± 64.0*</td>
<td>245.7 ± 56.3</td>
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<tr>
<td><strong>PT (s)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>11.7 ± 1.0</td>
<td>12.8 ± 1.1*</td>
<td>12.7 ± 1.1*</td>
<td>11.7 ± 0.7</td>
</tr>
<tr>
<td>C</td>
<td>11.5 ± 0.8</td>
<td>13.4 ± 1.3*</td>
<td>12.8 ± 0.9*</td>
<td>12.0 ± 1.1</td>
</tr>
<tr>
<td><strong>APTT (s)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>30.0 ± 2.8</td>
<td>26.6 ± 3.7*</td>
<td>28.2 ± 3.1*</td>
<td>27.3 ± 1.9*</td>
</tr>
<tr>
<td>C</td>
<td>29.9 ± 2.0</td>
<td>26.5 ± 2.2*</td>
<td>28.4 ± 1.9*</td>
<td>27.6 ± 2.3*</td>
</tr>
</tbody>
</table>

*Abbreviations: APTT, activated partial thromboplastin time; C, control group; Hb, hemoglobin; Hct, hematocrit; PT, prothrombin time; T, tranexamic acid group.
Continuous data expressed in mean ± SD.

*Statistically significant difference compared to preoperative value (P < .05).
acid preoperatively with or without continuous infusion intraoperatively. Different dosages have been reported in the literature, ranging from a bolus administration of 1 gram regardless of body weight\textsuperscript{18} to 100 mg/kg over 15 minutes, continued with an infusion of 10 mg/kg/hour until wound closure.\textsuperscript{31} Horrow et al\textsuperscript{32} showed that prophylactic tranexamic acid at 10 mg/kg followed by 1 mg/kg/hour for 12 hours decreases bleeding after extracorporeal circulation. Larger doses do not provide additional hemostatic benefit. In view of the duration of surgery and the pharmacodynamics of tranexamic acid, we chose to give a bolus injection of 20 mg/kg on induction of anesthesia. This should provide therapeutic plasma concentrations (5 to 10 mg/L)\textsuperscript{30} for 10 hours after administration, which should cover the longest possible duration of orthognathic cases in the study.

The mean total blood loss in the tranexamic acid group and the control group was 878.6 mL and 1,257.2 mL, respectively, which was higher in comparison to previous studies.\textsuperscript{1,33} This may be due to several reasons. First, many of our cases involved segmental osteotomies in both the maxilla and mandible leading to multiple bone cuts and additional cancellous bone and intrabony capillaries exposure. The increased complexity of the surgical procedures in the context of a training center often resulted in prolonged operation time and increased blood loss. Furthermore, the level of controlled hypotension was variable in this study. For safety reasons, we intended to lower the mean blood pressure by no more than 25% to 30% compared with the preoperative level and consequently we did not feel it was ethical to pursue this aggressively. The lower limit of the target mean blood pressure for all patients was above 50 mm Hg. Although a standard anesthetic protocol was implemented, less than 50% of cases had a mean blood pressure reduction within the range of 25% to 30% of preoperative values (Table 2). Often, the mean blood pressure was only slightly reduced.

Blood loss was estimated intraoperatively as described in Patients and Methods. Blood on surgical drapes, gowns, and instruments was difficult to quantify accurately. Although a throat pack was placed in every case, a small amount of blood might still have been swallowed. The suction bottle contained not only irrigation fluid and blood, but also saliva and bone powder produced during the osteotomy. All these uncertainties contributed to the inaccuracy of blood loss estimation although these would apply to all cases. There was a discrepancy between estimated blood loss measured intraoperatively and calculated blood loss by comparison of pre- and postoperative hemoglobin and hematocrit levels. The calculation was done based on 2 assumptions: the blood volume would have normalized by 48 hours postoperatively and 1 pack (320 mL) of red blood cells transfused could raise the hemoglobin by approximately 1 g/dL. There might still be hemodilution due to postoperative intravenous fluid administration and the rise in Hb level varied in different individuals depending on the body size. Furthermore, postoperative bleeding was not measured. No suction drains were used in intraoral wounds and a significant amount of blood could have been swallowed during the early postoperative period (concealed blood loss). Therefore, the post-operative Hb and Hct values only supplement the estimation of blood loss, and may not represent the true blood loss.

In this study, we were only able to show a significant decrease in blood loss in the tranexamic acid group during maxillary surgery and the whole operation, but not for the mandibular surgery. The maxilla is more vascular than the mandible. Blood loss during maxillary surgery, therefore, accounts for a large percentage of the total blood loss. The extent of reduction of blood loss during the mandibular surgery did not reach statistical significance probably because of the small sample size. The data was affected by many variables, including the complexity and combination of different surgical procedures, different surgeons, and different levels of blood pressure. The total blood loss in the treatment group was 422 mL less than the control group, which was not only significant statistically, but is also a clinically significant amount. The total operation time was not significantly different but the mean surgical time for ramus surgery was 31 minutes longer in the treatment group than in the control group. This might be due to increased surgical time for adaptation and placement of distractors during mandibular body distraction (range = 1 hour to 3 hours 20 minutes). Three cases of mandibular body distraction were randomized to receive tranexamic acid whereas only 1 case was in the control group. Although the operation time for ramus surgery was increased significantly in the treatment group, the blood loss during this procedure was less than that in the control group (287.0 ± 216.3 mL vs 329.3 ± 233.4 mL, respectively). We were not able to show a statistically significant reduction of transfusion in the treatment group, nevertheless, the percentage of patients requiring transfusion in the control group was larger than the treatment group (24.1% vs 12.5%). The high transfusion rate may be related to the increased blood loss that was mentioned above. A total of 11 patients received transfusion (4 in the treatment group, 7 in the control group). Both the mean blood loss and the operation time for these patients were higher in the control group than the treatment group (2,291 ± 831.7 mL, 505 minutes ± 94 minutes vs 1,732 ± 856.8 mL, 469 minutes ± 118 minutes). Twenty-eight patients had long operations (>6 hours). Nine of them received blood transfusion (6 in
TRANEXAMIC ACID EFFECTS ON BLOOD LOSS

the control group, 3 in the treatment group). These findings suggest that tranexamic acid may be useful in reducing blood loss, especially when the total operation time is long (Fig 2). There was no clinical or statistical difference in the length of hospital stay between the 2 groups of patients.

The PT was prolonged postoperatively, presumably due to hemodilution, but this phenomenon was not observed in other studies.32,34 Deep vein thrombosis (DVT) and pulmonary embolism (PE) are considered to be rare in Asia. Cheuk et al35 reported that the overall annual incidences of DVT and PE in Hong Kong were 17.1 and 3.9 per 100,000 population, respectively, representing significantly lower figures than those reported in Western countries. The majority of DVTs and PEs were not associated with surgery, with an overall incidence of postoperative DVT and PE of only 0.13% and 0.04%, respectively. Therefore, routine thromboprophylaxis was not given in this study in keeping with the accepted standard of care in this population. No adverse reactions or complications associated with the use of tranexamic acid was observed in this study; however, no special investigations were carried out as a routine to look for silent thromboembolism. The potential for this antifibrinolytic agent to be associated with an increased risk of thromboembolic events has been a concern, especially after major surgery. There was no evidence of an increased incidence in thromboembolism in patients using tranexamic acid during total knee arthroplasty7,20,36 or liver transplantation.37 A retrospective case-controlled study also showed no increased risk of venous thrombosis in women taking tranexamic acid for menorrhagia.30 Theoretically, tranexamic acid does not alter blood clotting. It is a clot stabilizer that slows the dissolution of the blood clot and does not initiate blood clot formation spontaneously. Benoni et al23 suggested the reason tranexamic acid was not associated with thromboembolic events is that its effects are more pronounced in operative wounds than in peripheral venous vessels. Nevertheless, vascular thrombosis has been reported, although at a low incidence rate, in prospective controlled studies.30,40 Casati41 raised a concern that the use of high doses of tranexamic acid in patients with preexisting vascular disease might facilitate the formation of thrombus and result in stroke. Thiagarajamny et al42 reviewed 12 articles and found that 5 prospective randomized trials reported myocardial ischemia, pulmonary embolism, and neurologic dysfunction. To date, there is no strong evidence available showing a definite risk of thromboembolism associated with the use of tranexamic acid. However, it should be used with caution and should be avoided in patients with a high risk for thrombosis (eg, history of a thromboembolic event or a family history of thromboembolic disease). Because tranexamic acid is excreted in the urine, dose reduction may also be required in patients with renal insufficiency.

Other drugs have been shown to be effective in reducing blood loss during surgery. These include aprotinin,43,44 epsilon-aminocaproic acid,45 desmopressin,46 and recombinant factor VII.47 However, tranexamic acid was considered to be more cost effective and easiest to handle compared with other drugs.48,49 Besides pharmacologic methods, other blood-saving strategies are also available. Mild hypotension50,52 normovolemic hemodilution,53,56 preoperative autologous blood donation,33 cell salvage techniques,57,58 positioning the operating table 20° head-up, avoiding venous obstruction, and maintaining hypocapnia have been used individually or in combination to minimize blood loss and transfusion. This involves special knowledge and skill as well as intensive monitoring. Moreover, the cost of autologous blood donation and cell salvage is much higher than the use of tranexamic acid while achieving a similar clinical outcome in conjunction with the above techniques.

A single preoperative dose (20 mg/kg) of tranexamic acid given intravenously immediately before surgery reduced blood loss during maxillary osteotomy and bimaxillary osteotomy but had no significant effect on the incidence of blood transfusion or length of hospital stay. No adverse reaction or complication associated with the use of tranexamic acid was noted in this study.

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17. Senghore N, Harris M: The effect of tranexamic acid (Cyclokapron) on blood loss after third molar extraction under a day case general anaesthetic. Br Dent J 186:634, 1999