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Randomised Controlled Trial
Orthognathic Surgery

The effect of different dosage regimens of tranexamic acid on blood loss in bimaxillary osteotomy: a randomized, double-blind, placebo-controlled study

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Abstract. The purpose of this study was to compare the effects of three dosage regimens of intravenous tranexamic acid and normal saline placebo on blood loss and the requirement for transfusion during bimaxillary osteotomy. A prospective, randomized, double-blind, placebo-controlled study was performed. Eighty patients scheduled for elective bimaxillary osteotomy were divided into four groups: a placebo group and three groups receiving a single dose of tranexamic acid 10, 15, or 20 mg/kg body weight after the induction of anaesthesia. Demographic data, the anaesthetic time, the operative time, and the experience of the surgical team were similar in the four groups. Patients receiving placebo had increased blood loss compared to those receiving tranexamic acid. No significant difference in blood loss was found among those who received 10, 15, or 20 mg/kg body weight of tranexamic acid. There was no significant difference in transfusion requirement, amount of 24-h postoperative vacuum drainage, length of hospital stay, or complications among the four groups. Prophylactic tranexamic acid decreased bleeding during bimaxillary osteotomy. Of the three dosages of tranexamic acid studied, the most efficacious and cost-effective dose to reduce bleeding was 10 mg/kg body weight.

Key words: tranexamic acid; orthognathic surgery; blood loss in bimaxillary surgery.

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Blood loss and the need for transfusion during bimaxillary osteotomy are the major concerns of oral and maxillofacial surgeons. Bleeding is generally less than the limits set for blood transfusion; however it may occasionally be heavier, and preparations for reserving blood should be considered[1]. The blood loss during bimaxillary osteotomy at the Faculty of Dentistry, Mahidol University is reported to vary from 200 ml to 3400 ml[2]. Several measures have been used to reduce operative bleeding, including the use of controlled hypotensive anaesthesia[3–5], tranexamic acid[6–10], aprotinin[11], and desmopressin[12].

Tranexamic acid is a synthetic lysine analogue and antifibrinolytic agent that has been shown to decrease blood loss in many types of surgery, such as total hip and knee arthroplasty[13–15], spinal surgery[16], cardiac surgery[17], and even third molar extraction[18]. It has also been used in dentistry and oral surgery as a mouthwash for patients with anticoagulation or haemorrhagic problems[19,20]. Several authors have found that tranexamic acid can reduce blood loss during bimaxillary osteotomy[6–9]. However the most appropriate dose of tranexamic acid remains an issue.

This study compared the effects of three different dosage regimens of a single preoperative intravenous dose of tranexamic acid and saline placebo on blood loss during bimaxillary osteotomy.

Patients and methods

This randomized, double-blind clinical trial was performed in the Faculty of Dentistry, Mahidol University from June 2012 to March 2014. The study protocol followed the Declaration of Helsinki on medical protocol and was approved by the Institutional Review Board of the Faculty of Dentistry and Pharmacy, Mahidol University.

The sample size was calculated based on previous data on average blood loss during bimaxillary osteotomy reported at the study institution (854.8 ± 442.8 ml). It was estimated that 20 patients would be needed in each group to have 80% power to detect a 500-ml blood loss difference at a significance level of 0.05. Thus the study population was composed of 80 patients who were scheduled for bimaxillary orthognathic surgery.

Written informed consent was obtained from the patients during the preoperative period. All patients were 18–35 years of age, healthy, and physical status 1 according to the American Society of Anesthesiologists (ASA) classification. Patients with a known allergy to the study drug, a history or a risk of thromboembolism (including taking oral contraceptive pills), or a body mass index (BMI) more than 30 kg/m^2 were excluded. Patients undergoing a segmental Le Fort I osteotomy or additional procedures such as genioplasty or angle reduction were also excluded.

The patients were assigned randomly to one of four groups by a computer-generated random number: a placebo group (group 0) and three groups receiving a single dose of tranexamic acid of 10 mg/kg (group 10), 15 mg/kg (group 15), or 20 mg/kg (group 20) body weight after the induction of anaesthesia.

Preoperative investigations included a complete blood cell count, chest radiography, and test for hepatitis B surface antigen and human immunodeficiency virus antibodies. A unit of typed and screened blood was prepared. Patients were instructed not to eat for 8 h before surgery. Baseline arterial blood pressure, pulse rate, and oxygen saturation were measured before the induction of anaesthesia.

All patients underwent a standardized anaesthetic technique consisting of intravenous induction with midazolam 0.05 mg/kg, fentanyl 1 μg/kg, and propofol 2 mg/kg. Nasotracheal intubation was performed 5 min after cisatracurium administration. Anaesthesia was maintained with 50% nitrous oxide in oxygen, cisatracurium, fentanyl, and 1–2% sevoflurane as required. Patients were placed in a 15° head-up position. Intraoperative monitoring consisted of non-invasive blood pressure monitoring, electrocardiography, pulse oximetry, capnometry, and urine output. Ventilation was controlled to maintain end-tidal carbon dioxide tension at 30–35 mmHg. Controlled hypotension was started at the incision by titrating intravenous nitroglycerin to obtain a mean arterial pressure within the target range of 65–75 mmHg. Nitroglycerin was tapered off after the last screw was fixed. After the induction of anaesthesia, the patients were given 100 ml of normal saline solution or 100 ml of tranexamic acid by intravenous drip over the course of 30 min, according to the study group assigned; identical 100-ml bags were used, identified only by a random number. The study drugs were prepared and coded by an anaesthesia nurse who was not involved in clinical treatment, and were given by another independent anaesthesia nurse. The surgeon and anaesthesiologist were blinded to the study drug.

All patients received standard fluid replacement therapy with crystalloids (acetated Ringer's solution) to maintain urine output greater than 0.5 ml/kg/h. Hydroxyethyl starch (Voluven; Fresenius Kabi Pharmaceutical, Bad Homburg, Germany) was given when 15% of the estimated blood volume (EBV) was lost. Allogeneic packed red blood cells were transfused if the haematocrit fell to less than 21%; all such transfusions were recorded.

The primary outcome was the intraoperative blood loss and the number of patients receiving a transfusion of allogeneic blood products. The blood loss was calculated from the difference between the fluid in the suction canisters and the irrigation fluid used plus the amount of blood in the surgical gauze estimated by weight. The secondary outcomes included the difference between preoperative and 24-h postoperative haematocrit, the volume of 24-h postoperative vacuum drainage, and the length of hospital stay. Any thromboembolic or other complications occurring during the hospital stay were recorded.

Age, sex, BMI, baseline haemodynamic values, baseline haematocrit, anaesthetic time (time from induction to extubation), duration of hypotensive anaesthesia, operative time (time from incision to the last suture), and experience of the surgical team were compared between the four groups. The study institute is a training centre for oral and maxillofacial surgery where several surgeons at various stages of expertise and training perform orthognathic surgery. The different levels of expertise can be one of the reasons for high intraoperative blood loss and transfusion requirements. An experienced surgeon was defined as one who had performed at least 200 cases of any type of orthognathic surgery and had more than 5 years of experience.

The statistical analysis was conducted using SPSS for Windows version 13.0 software (SPSS Inc., Chicago, IL, USA). Parametric data were reported as the mean and standard deviation and non-parametric data were reported as counts. Changes in parametric variables were analyzed using one-way analysis of variance (ANOVA) and post-hoc comparisons using the Tukey honestly significant difference (HSD) test. Non-parametric variables were compared using the χ^2 test. A P-value of <0.05 was considered significant.

Results

All 80 patients completed the study. No significant differences were found between the four patient groups in demographic characteristics, baseline haemody-

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