ORIGINAL ARTICLE

https://doi.org/10.5125/jkaoms.2024.50.2.86
pISSN 2234-7550 · eISSN 2234-5930

Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study

Keisuke Harada[1], Noritaka Imamachi[2], Yuhei Matsuda[1], Masato Hirabayashi[3], Yoji Saito[3,4], Takahiro Kanno[1]

[1]*Department of Oral and Maxillofacial Surgery, Shimane University Faculty of Medicine, Izumo,* [2]*Department of Anesthesiology, Saitama Medical University, Saitama,* [3]*Department of Anesthesiology, Shimane University Faculty of Medicine, Izumo,* [4]*Department of Palliative Care, Shimane University Faculty of Medicine, Izumo, Japan*

Abstract (J Korean Assoc Oral Maxillofac Surg 2024;50:86-93)

Objectives: Orthognathic surgery is a surgical procedure performed by intraoral approach with established and safe techniques; however, excessive blood loss has been reported in rare cases. In response, investigative efforts to identify methods to reduce the amount of blood loss have been made. Among such methods, the administration of tranexamic acid was reported to reduce the amount of intraoperative blood loss. However, few studies to date have reported the effect of tranexamic acid in orthognathic surgery under hypotensive anesthesia. The present study aimed to investigate the effect of the administration of tranexamic acid on intraoperative blood loss in patients undergoing bimaxillary (maxillary and mandibular) orthognathic surgery under hypotensive anesthesia.

Patients and Methods: A total of 156 patients (mean age, 27.0±10.8 years) who underwent bimaxillary orthognathic surgery under hypotensive anesthesia performed by the same surgeon between June 2013 and February 2022 were included in this study. The following data were collected from the medical records of each patient: background factors (age, sex, and body mass index), use of tranexamic acid, surgical procedures, previous medical history, duration of surgery, American Society of Anesthesiology physical status findings before surgery, intraoperative blood loss as a primary outcome, in–out balance, and blood test results. Descriptive statistics were calculated for statistical analysis, and a *t*-test and the chi-squared test were used for between-group comparisons. Group comparisons were performed after 1:1 propensity score matching to adjust for confounding factors. Statistical significance was set at $P<0.05$.

Results: Comparison between the groups based on the use of tranexamic acid revealed a significant difference in operation time. Propensity score matching analysis revealed that intraoperative blood loss was significantly lower in the tranexamic acid group.

Conclusion: The administration of tranexamic acid was effective in reducing intraoperative blood loss in patients undergoing bimaxillary orthognathic surgery under hypotensive anesthesia.

Key words: Orthognathic surgery, Tranexamic acid, Anesthesia, Blood loss, Propensity score

[paper submitted 2024. 1. 19 / revised 2024. 4. 22 / accepted 2024. 4. 24]

I. Introduction

Dentofacial deformities are diagnosed based on the patient's chief complaint, findings of cephalometric analysis, masticatory function, mandibular movement, dental model analysis, computed tomography and magnetic resonance imaging, and the results of psychological assessment[1]. Long-term follow-up is important, as the treatment strategy for dentofacial deformity surgery includes both preoperative and postoperative orthodontic treatment in addition to surgery[1]. Orthognathic surgery is a surgical procedure performed by intraoral approach increasingly to correct dentofacial deformities in recent years. The most commonly used surgical techniques for orthognathic surgery include Le Fort I osteotomy (LF-I) for the maxilla and sagittal split ramus osteotomy (SSRO) and intraoral vertical ramus osteotomy (IVRO) for the mandible[2]. Although these techniques are well-established, complications may occur during the surger-

Takahiro Kanno
Department of Oral and Maxillofacial Surgery, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo 693-8501, Japan
TEL: +81-853-20-2301
E-mail: tkanno@med.shimane-u.ac.jp
ORCID: https://orcid.org/0000-0003-0635-9084

ies. Major complications include trigeminal sensory nerve damage, such as damage to the infraorbital, lingual, and inferior alveolar nerve bundles; postoperative infection; massive bleeding owing to damage to the descending palatine artery, sphenopalatine artery, or inferior alveolar artery; abnormal fractures; sleep apnea; dental root damage; and temporomandibular joint dysfunction[3-6]. Among those major complications, a large amount of intraoperative blood loss and associated blood transfusions are the complications that should be avoided perioperatively. In a previous study by Ulker et al.[7], intraoperative vascular complications were observed in 10 patients (5%) among 200 patients undergoing LF-I osteotomy. The most common source of bleeding was the descending palatine artery and pterygomaxillary plexus in eight patients (4%) and two patients (1%), respectively, and the causes of bleeding were maxillary down-fracture and separation of the pterygomaxillary junction in eight and two patients[7]. Separately, the mean intraoperative blood loss amounts during maxillary and mandibular osteotomy are approximately 345 mL and 436 mL as reported in previous studies[8,9].

One of the measures to prevent intraoperative bleeding includes the use of hypotensive anesthesia and the administration of tranexamic acid. Hypotensive anesthesia is an anesthesia technique where blood pressure is intentionally lowered so as to reduce intraoperative blood loss and improve the quality of surgery[10]. This approach has also been reported to improve the visibility of the surgical field and shorten the operative time[11,12]. Hypotensive anesthesia is mainly used in the fields of orthopedic spine surgery and total hip replacement; however, it is also known to reduce intraoperative blood loss in patients undergoing orthognathic surgery and was also adopted for this study[13-15].

Tranexamic acid, a synthetic amino acid with antiplasminic properties widely recognized to be a hemostatic agent, is used to control bleeding owing to increased fibrinolysis[16]. A multicenter, randomized controlled trial conducted in 2010 at 284 centers across 44 countries revealed that the administration of tranexamic acid to trauma patients was effective in reducing all-cause mortality and deaths by bleeding. Moreover, it was found to improve the prognosis for patient survival. Based on these findings, tranexamic acid has been used in the management of intraoperative hemorrhage[17]. Although tranexamic acid has been used in orthopedic joint-replacement surgery and open heart surgery[18,19], it may induce complications like hypotension, nausea and vomiting, diarrhea, allergic dermatitis, visual disturbances, and color blindness. Notably, the risk of thromboembolism is high when its intravenous administration is completed rapidly[20-22].

Although hypotensive anesthesia and tranexamic acid can both be used for controlling intraoperative bleeding, it is unclear whether these measures must be implemented simultaneously in orthognathic surgery. Therefore, the present study aimed to investigate the effect of the administration of tranexamic acid on reducing blood loss in patients undergoing bimaxillary orthognathic surgery under hypotensive anesthesia.

II. Patients and Methods

1. Data collection

Data were collected from the medical records of eligible patients according to the inclusion criteria in a single-center, retrospective, observational study. Patients with non-craniomaxillofacial syndromic dentofacial deformity who visited the Department of Oral and Maxillofacial Surgery of Shimane University Hospital between June 2013 and February 2022 and underwent bimaxillary orthognathic surgery, including maxillary and mandibular osteotomies, under hypotensive anesthesia performed by the same experienced oral-maxillofacial surgeon on a single surgical team were included in this study. We excluded patients (1) with hemorrhagic diathesis, (2) who were receiving anticoagulants or antiplatelet drugs, or (3) who were receiving maxillary or mandibular orthognathic surgery only. This study was approved by the Medical Research Ethics Committee, Shimane University Faculty of Medicine (No. 20220120-1) and the written informed consent was obtained from all patients.

2. Background data

Data for the following variables were collected: age (years), sex (male/female), body mass index (kg/m^2), surgical technique (LF-I for the maxilla and bilateral sagittal split ramus osteotomy [BSSRO] alone or in combination with IVRO for the mandible; additional simultaneous surgeries included genioplasty, multiple-segment osteotomy, mandibular midline osteotomy, and tooth extraction), existence of systemic disease (hypertension, liver disease, diabetes mellitus, and abnormal blood clotting), duration of surgery, American Society of Anesthesiology physical status (ASA-PS), in–out balance (mL), and results of blood tests (hemoglobin change [g/dL], hematocrit change [%], preoperative platelet count [10^4/μL], and preoperative international normalized ratio of prothrom-

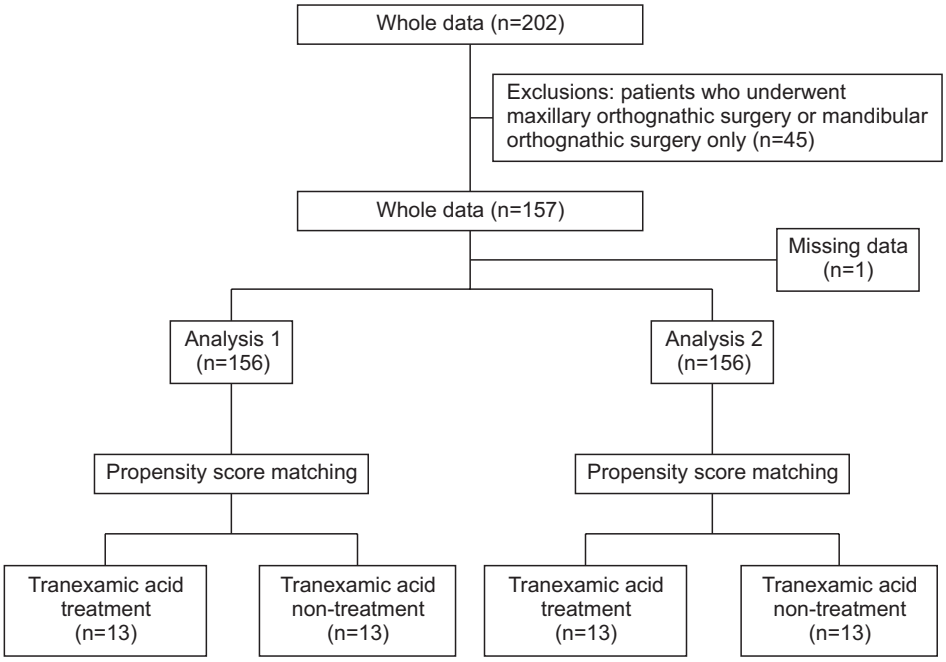

Fig. 1. Flowchart from patient enrollment to analysis.
Keisuke Harada et al: Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study. J Korean Assoc Oral Maxillofac Surg 2024

bin time [PT-INR]). The requirement for blood transfusions and the incidence rates of postoperative pulmonary emboli and seizures were also investigated.

3. Usage protocol of tranexamic acid

The patients were divided into two groups; among them, the treatment group received continuous intravenous administration of 1 g of tranexamic acid intraoperatively, while the non-treatment group did not receive tranexamic acid during the surgery. However, both groups received continuous intravenous administration of 1 g of tranexamic acid postoperatively over a 12-hour period.

4. Hypotensive anesthesia

Hypotensive anesthesia was based on the definition provided by the Japanese National Health Insurance and usually involved systemic management of patients with a target of 40% reduction in systolic blood pressure or 60 to 70 mmHg reduction in mean arterial pressure.

5. Outcome measures

The primary outcome was the amount of intraoperative blood loss. Secondary outcomes included changes in hemoglobin and hematocrit levels, the duration of surgery, postoperative blood loss, and the incidence of postoperative pulmonary emboli. Data regarding intraoperative and postoperative blood loss (mL) were gathered from the medical records.

6. Statistical analysis

Descriptive data (as percentage or mean±standard deviation values) were selected for the statistical analyses, and their normality was confirmed using the Shapiro–Wilk test. The chi-squared test and *t*-tests were used to perform between-group comparisons. Propensity scores were calculated via logistic regression analysis, and 1:1 propensity score matching was performed to adjust for confounding factors (sex, age, body mass index, operative time, and ASA-PS). Analysis 1 focused on intraoperative blood loss, while Analysis 2 focused on postoperative bleeding.(Fig. 1) Group comparisons were performed using IBM SPSS Statistics software (ver. 26; IBM Corp.). Two-tailed *P*-values were calculated for all analyses, and the alpha level of significance was set at $P<0.05$.

III. Results

1. Patient characteristics

Table 1 summarizes the patient characteristics. A total of 156 patients with a mean age of 27.0±10.8 years were enrolled in this study. Among these 156 patients, 47 (30.1%) were males. Tranexamic acid was administered to 139 patients (89.1%). The mean duration of surgery was 197.6±38.3

minutes, and the mean volume of intraoperative blood loss was 124.0±38.3 mL. Blood transfusions were not required in any of the included cases, and no instance of postoperative pulmonary embolism or seizure occurred.

Table 1. Descriptive statistics of included patients who underwent bimaxillary orthognathic surgery for dentofacial deformity (n=156)

Variable	Category	Value
Sex	Male	47 (30.1)
	Female	109 (69.9)
Age (yr)		27.0±10.8
Body mass index (kg/m^2)		21.3±3.1
Tranexamic acid	No use	17 (10.9)
	Use	139 (89.1)
Type of surgery	LF1+BSSRO (yes)	156±100
Multiple answers allowed	IVRO (yes)	6 (3.8)
	Genioplasty (yes)	5 (3.2)
	Multi-segment osteotomy (yes)	2 (1.3)
	Mandibular midline osteotomy (yes)	1 (0.6)
	Tooth extraction (yes)	2 (1.3)
Systemic disease	Hypertension	4±0
	Liver disease	14±0
	Diabetes mellitus	1±0
	Abnormal blood clotting	3±0
Operation time (min)		197.6±38.3
ASA-PS	Class 1	70 (44.9)
	Class 2	86 (55.1)
Intraoperative blood loss (mL)		124.0±38.3
In–out balance (mL)		876.8±506.6
Blood test	Hemoglobin change (g/dL)	−1.9±1.0
	Hematocrit change (%)	−5.8±4.2
	Preoperative platelet in count (10^4/μL)	253.6±50.3
	Preoperative PT-INR in preoperation	0.984±0.07

(LF-1: Le Fort I osteotomy, BSSRO: bilateral sagittal split ramus osteotomy, IVRO: intraoral vertical ramus osteotomy, ASA-PS: American Society of Anesthesiology physical status, PT-INR: international normalized ratio of prothrombin time)

Values are presented as number (%) or mean±standard deviation.

Keisuke Harada et al: Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study. J Korean Assoc Oral Maxillofac Surg 2024

2. Group comparison

Table 2 presents the results of the comparisons between the treatment and the non-treatment groups. The operation time was significantly increased in the non-treatment group (248.2±37.4 minutes) compared to the treatment group (191.4±33.7 minutes; P<0.05).

3. Group comparison using propensity score matching

Tables 3 and 4 present the results of between-group comparisons performed following propensity score matching. Twenty-six patients were matched after adjusting for sex, age, body mass index, duration of surgery, and ASA-PS. Notably, the amount of intraoperative bleeding was significantly reduced in the treatment group (53.1±52.5 mL) compared to the non-treatment group (145.8±79.4 mL; P<0.05).

IV. Discussion

The major findings of this study were that tranexamic acid reduced both the amount of intraoperative blood loss and the operation time in patients undergoing bimaxillary orthognathic surgery under hypotensive anesthesia. Additionally, no pulmonary embolisms or other complications attributable to transamine usage occurred, confirming that transamine can be used safely in patients undergoing bimaxillary orthognathic surgery.

Surgical stress or surgical trauma activates the fibrinolytic system by stimulating the release of tissue plasminogen activator, the primary enzyme responsible for the conversion of plasminogen to plasmin[23,24]. Tranexamic acid is a synthetic fibrinolysis inhibitor that blocks the lysine-binding sites on

Table 2. Comparison of clinical data between the tranexamic acid treatment group and the non-treatment group (n=156)

Variable	Category	Tranexamic acid treatment (n=139)	Tranexamic acid non-treatment (n=17)	P-value
Sex	Male	40 (28.8)	7 (41.2)	0.40
	Female	99 (71.2)	10 (58.8)	
Age (yr)		27.3±11.1	24.8±8.1	0.38
Body mass index (kg/m^2)		21.3±3.2	21.9±2.2	0.45
Operation time (min)		191.4±33.7	248.2±37.4	<0.001*
ASA-PS		1.58±0.5	1.4±0.5	0.08
Intraoperative blood loss (mL)		120.0±152.4	156.8±100.9	0.33
In–out balance (mL)		902.6±504.8	665.6±485.6	0.07
Blood test	Hemoglobin change (g/dL)	−1.9±1.1	−1.7±0.8	0.40
	Hematocrit change (%)	−5.9±4.4	−5.1±2.0	0.45

(ASA-PS: American Society of Anesthesiology physical status)

*P<0.05.

Values are presented as number (%) or mean±standard deviation.

Keisuke Harada et al: Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study. J Korean Assoc Oral Maxillofac Surg 2024

Table 3. Comparison of the propensity matched data between the tranexamic acid treatment group and the non-treatment group (n=26)

Variable	Category	Tranexamic acid treatment (n=13)	Tranexamic acid non-treatment (n=13)	*P*-value
Sex	Male	3 (23.1)	5 (38.5)	0.67
	Female	10 (76.9)	8 (61.5)	
Age (yr)		21.9±5.9	24.2±7.6	0.38
Body mass index (kg/m^2)		22.6±4.1	21.9±1.8	0.57
Operation time (min)		233.9±34.1	238.5±34.0	0.74
ASA-PS		1.5±0.5	1.4±0.5	0.71
Intraoperative blood loss (mL)		53.1±52.5	145.8±79.4	0.002*
In–out balance (mL)		983.1±419.4	665.0±533.1	0.10
Blood test	Hemoglobin change (g/dL)	−1.9±0.7	−1.7±0.9	0.58
	Hematocrit change (%)	−6.0±0.7	−5.2±2.1	0.42

(ASA-PS: American Society of Anesthesiology physical status)
*P<0.05.
Values are presented as number (%) or mean±standard deviation.
The propensity score method was used to adjust for sex, age, body mass index, operative time, and ASA-PS.
Keisuke Harada et al: Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study. J Korean Assoc Oral Maxillofac Surg 2024

Table 4. Comparison of propensity matched data between the tranexamic acid treatment group and the non-treatment group (n=26)

Variable	Category	Tranexamic acid treatment (n=13)	Tranexamic acid non-treatment (n=13)	*P*-value
Sex	Male	4 (30.8)	5 (38.5)	>0.99
	Female	9 (69.2)	8 (61.5)	
Age (yr)		24.9±13.7	24.2±7.6	0.88
Body mass index (kg/m^2)		23.2±4.3	21.9±1.8	0.33
Operation time (min)		237.2±27.8	238.5±34.0	0.92
ASA-PS		1.5±0.5	1.4±0.5	0.45
Post-bleeding (mL)		87.2±30.5	86.5±26.6	0.95
In–out balance (mL)		933.8±439.9	665.0±533.1	0.17
Blood test	Hemoglobin change (g/dL)	−1.8±0.8	−1.7±0.9	0.71
	Hematocrit change (%)	−3.5±8.5	−5.2±2.1	0.53

(ASA-PS: American Society of Anesthesiology physical status)
Values are presented as number (%) or mean±standard deviation.
The propensity score method was used to adjust for sex, age, body mass index, operative time, and ASA-PS.
Keisuke Harada et al: Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study. J Korean Assoc Oral Maxillofac Surg 2024

plasminogen[25]. The plasminogen–tranexamic acid complex then detaches from the fibrin surface and inhibits plasmin from binding with fibrinogen and fibrin monomers, delaying fibrinolysis[25].

Compression hemostasis is especially difficult to perform in patients undergoing maxillary osteotomies, as the wound is open. The primary source of bleeding may be vessels located in the soft tissue, such as the gingiva and nasal mucosa, or the bone marrow. Tranexamic acid is also used as a hemostatic agent in nasal surgery, and it has been shown to improve the visibility of the surgical field in nasal surgery[26]. The antifibrinolytic properties of tranexamic acid act on the bone marrow to reduce bleeding[27]. The results of this study also suggest that the administration of tranexamic acid during a state of increased fibrinolysis may reduce bleeding by delaying fibrinolysis.

No optimal dosage nor duration of tranexamic acid administration to achieve hemostatic effects during surgery has been established; however, the therapeutic plasma concentration of tranexamic acid is 10 ng/mL, and an 80% reduction in plasmin activity is considered necessary[28,29]. The same mechanism of action may have been effective in suppressing plasmin activity by >80% during the anesthetic management of patients undergoing bimaxillary orthognathic surgery in the present study. The observed reduction in the duration of surgery may be attributed to an improvement in the visibility of the surgical field owing to the reduction of intraoperative blood loss via the mechanism of action described above[11].

The administration of tranexamic acid before surgery had no effect on the amount of postoperative blood loss or the blood test results. The minimum concentration of tranexamic acid required to inhibit fibrinolysis is 5 to 10 mg/L for significant inhibition, with concentrations of 10 to 15 mg/L ensuring maximum inhibition of fibrinolysis[30]. Benoni et al.[31] reported that postoperative plasminogen levels were significantly lower in their study's tranexamic acid group

compared to those in the placebo group. Tranexamic acid interferes with the measurement of plasminogen and has been reported to reduce measured plasminogen levels by 16%[31]. Thus, a total dose of 1 g of tranexamic acid is considered sufficient for patients undergoing bimaxillary orthognathic surgery under hypotensive anesthesia, as there is no evidence supporting the administration of higher doses[32]. However, an intravenous administration of 10 mg/kg of tranexamic acid maintains the plasma concentration for only 3 hours[20]. Therefore, the continuous administration of 1 g of tranexamic acid postoperatively is considered necessary to suppress postoperative bleeding, as the preoperative administration of 1 g of tranexamic acid alone cannot be expected to suppress postoperative bleeding.

Activation of fibrinolysis is a cascade process and most likely to be inhibited in its early stages[33]. In other words, it may be sufficient to administer tranexamic acid preoperatively, as the findings are consistent with reports that tranexamic acid has little effect when administered after massive bleeding[33]. Therefore, an effect of preoperative administration of a 1-g dose of tranexamic acid on postoperative bleeding in long orthognathic surgery was not expected.

A randomized controlled trial conducted by Jozefowicz et al.[16] reported a mean reduction in blood loss of approximately 193 mL with the administration of tranexamic acid. A meta-analysis by Siotou et al.[34] reported that the use of tranexamic acid reduces intraoperative blood loss by approximately 217.18 mL. However, few studies to date have examined the effects of both hypotensive anesthesia and tranexamic acid, as hypotensive anesthesia was not used in such a combination in the abovementioned studies. Salma et al.[8], who conducted their study using both hypotensive anesthesia and tranexamic acid, concluded that a 10% reduction in intraoperative blood loss can be expected with the use of tranexamic acid under hypotensive anesthesia. It is worth noting here that these studies reported bleeding volumes ranging from 391 to 875 mL. Systematic reviews have also reported that 300 to 400 mL of blood loss is common[16]. A difference that should be noted here is that the average intraoperative blood loss in the present study was only 124 mL, which is far less than the range of 391 to 875 mL reported in the previous study[16]. Thus, the use of hypotensive anesthesia and tranexamic acid may be effective regardless of the skill of the surgeon, suggesting that tranexamic acid may be used even in bimaxillary orthognathic operations that may be completed in a short time with limited blood loss.

The effectiveness of tranexamic acid observed in the present study may be attributed in part to the operative time at our department being 197.6±38.3 minutes, which is faster than that of other centers, and the use of a single dose of 1 g to sufficiently control intraoperative hemorrhage.

The results of this study are also consistent with reports that the administration of tranexamic acid does not directly correlate with fibrinolytic variables (D-dimer and fibrinogen-/fibrin-degradation products)[35]. Therefore, the administration of tranexamic acid for bimaxillary orthognathic surgery under hypotensive anesthesia should be initiated preoperatively to achieve a limited hemostatic effect intraoperatively.

One of the disadvantages of the administration of tranexamic acid is the risk of venous thromboembolism. Thus, the dosage for patients with a history of myocardial infarction or cerebral thrombosis should be considered carefully. However, previous clinical studies have reported low incidence rates of venous thrombosis in both the placebo and tranexamic acid groups and also that the incidence of venous thromboembolic events did not differ between tranexamic acid and control groups[36,37]. As a highly safe drug, tranexamic acid could be considered as one of the methods to effectively control bleeding in orthognathic surgery.

This study has three main limitations due to the following reasons. First, the duration of hypotensive anesthesia intraoperatively was not standardized. Second, the optimal plasma concentration of tranexamic acid and activation of the fibrinolytic system were not assessed. Third, the detailed surgical techniques for the directions of placement of the osteotomy segments with or without additional surgical involvement and the device used for osteosynthesis were not standardized, which may have affected the results. However, the study data were obtained for analysis from those patients who underwent surgeries performed by the same experienced oral and maxillofacial surgeon on a single surgical team over the study period. Future research should include a randomized controlled trial with a constant dose of tranexamic acid and standardized duration of hypotensive anesthesia.

V. Conclusion

A reduction in intraoperative blood loss was observed following the administration of tranexamic acid in patients undergoing orthognathic surgery under hypotensive anesthesia. In addition, it was suggested that a decrease in intraoperative blood loss may be associated with a reduction in operative time.

ORCID

Keisuke Harada, *https://orcid.org/0000-0002-7497-6191*
Noritaka Imamachi, *https://orcid.org/0000-0002-8972-7665*
Yuhei Matsuda, *https://orcid.org/0000-0001-8922-3582*
Masato Hirabayashi, *https://orcid.org/0000-0003-1866-1862*
Yoji Saito, *https://orcid.org/0000-0002-4497-1381*
Takahiro Kanno, *https://orcid.org/0000-0003-0635-9084*

Authors' Contributions

K.H., N.I., and M.H. participated in data collection and writing the manuscript. N.I., Y.M., Y.S., and T.K. participated in the study design and performed the statistical analysis. N.I., Y.S., and T.K. participated in the study design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Funding

No funding to declare.

Acknowledgments

We would like to express our appreciation to the staff members of the Department of Oral and Maxillofacial Surgery and the Department of Anesthesiology of the Shimane University Faculty of Medicine.

Ethics Approval and Consent to Participate

This study was approved by the Medical Research Ethics Committee, Shimane University Faculty of Medicine (No. 20220120-1), and the written informed consent was obtained from all patients.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Weiss RO 2nd, Ong AA, Reddy LV, Bahmanyar S, Vincent AG, Ducic Y. Orthognathic surgery-LeFort I osteotomy. Facial Plast Surg 2021;37:703-8. https://doi.org/10.1055/s-0041-1735308
2. Lee KT, Lin SS, Hsu KJ, Tsai CY, Lee YH, Chang YJ, et al. Intraoperative blood loss and postoperative pain in the sagittal split ramus osteotomy and intraoral vertical ramus osteotomy: a literature review. Biomed Res Int 2021;2021:4439867. https://doi.org/10.1155/2021/4439867
3. Alister Herdener JP, Uribe F, Barreda M, Olate S, Fariña R. Delayed bleeding of sphenopalatine artery as a complication in Le Fort I osteotomy. J Craniofac Surg 2021;32:e493-5. https://doi.org/10.1097/scs.0000000000007455
4. Yang HJ, Jung YE, Kwon IJ, Lee JY, Hwang SJ. Airway changes and prevalence of obstructive sleep apnoea after bimaxillary orthognathic surgery with large mandibular setback. Int J Oral Maxillofac Surg 2020;49:342-9. https://doi.org/10.1016/j.ijom.2019.07.012
5. Remschmidt B, Schwaiger M, Gaessler J, Wallner J, Zemann W, Schwaiger M. Surgical site infections in orthognathic surgery: prolonged versus single-dose antibiotic prophylaxis. Int J Oral Maxillofac Surg 2023;52:219-26. https://doi.org/10.1016/j.ijom.2022.06.002
6. Dujoncquoy JP, Ferri J, Raoul G, Kleinheinz J. Temporomandibular joint dysfunction and orthognathic surgery: a retrospective study. Head Face Med 2010;6:27. https://doi.org/10.1186/1746-160x-6-27
7. Ulker O, Demirbas AE, Kutuk N, Kilic E, Alkan A. Vascular complications in Le Fort I osteotomy: incidence, reasons, and management of the intraoperative hemorrhage. J Craniofac Surg 2021;32:325-8. https://doi.org/10.1097/scs.0000000000007152
8. Salma RG, Al-Shammari FM, Al-Garni BA, Al-Qarzaee MA. Operative time, blood loss, hemoglobin drop, blood transfusion, and hospital stay in orthognathic surgery. Oral Maxillofac Surg 2017;21:259-66. https://doi.org/10.1007/s10006-017-0626-1
9. Piñeiro-Aguilar A, Somoza-Martín M, Gandara-Rey JM, García-García A. Blood loss in orthognathic surgery: a systematic review. J Oral Maxillofac Surg 2011;69:885-92. https://doi.org/10.1016/j.joms.2010.07.019
10. Lin S, McKenna SJ, Yao CF, Chen YR, Chen C. Effects of hypotensive anesthesia on reducing intraoperative blood loss, duration of operation, and quality of surgical field during orthognathic surgery: a systematic review and meta-analysis of randomized controlled trials. J Oral Maxillofac Surg 2017;75:73-86. https://doi.org/10.1016/j.joms.2016.07.012
11. Gallagher DM, Milliken RA. Induced hypotension for orthognathic surgery. J Oral Surg 1979;37:47-51.
12. Elsharnouby NM, Elsharnouby MM. Magnesium sulphate as a technique of hypotensive anaesthesia. Br J Anaesth 2006;96:727-31. https://doi.org/10.1093/bja/ael085
13. Jiang J, Zhou R, Li B, Xue F. Is deliberate hypotension a safe technique for orthopedic surgery?: a systematic review and meta-analysis of parallel randomized controlled trials. J Orthop Surg Res 2019;14:409. https://doi.org/10.1186/s13018-019-1473-6
14. Dutton RP. Controlled hypotension for spinal surgery. Eur Spine J 2004;13(Suppl 1):S66-71. https://doi.org/10.1007/s00586-004-0756-7
15. Zhang Q, Yin S, Huang K, Wang M, Xie H, Liao R, et al. [Effectiveness and safety of tranexamic acid combined with intraoperative controlled hypotension on reducing perioperative blood loss in primary total hip arthroplasty]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi 2021;35:1133-40. Chinese. https://doi.org/10.7507/1002-1892.202103230
16. Jozefowicz E, Sabourdin N, Lambelin V, Lejeune V, Delassus R, Tavernier B. The effect of tranexamic acid on blood loss in orthognathic surgery: a randomized, placebo-controlled, equivalence study. Int J Oral Maxillofac Surg 2022;51:637-42. https://doi.org/10.1016/j.ijom.2021.08.018
17. Williams-Johnson JA, McDonald AH, Strachan GG, Williams EW. Effects of tranexamic acid on death, vascular occlusive events, and

blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. West Indian Med J 2010;59:612-24.
18. Berebichez-Fridman R, Castillo-Vázquez FG, Berebichez-Fastlicht E. [Applications of tranexamic acid in orthopaedics and traumatology]. Acta Ortop Mex 2021;35:539-46. Spanish.
19. Alaifan T, Alenazy A, Xiang Wang D, Fernando SM, Spence J, Belley-Cote E, et al. Tranexamic acid in cardiac surgery: a systematic review and meta-analysis (protocol). BMJ Open 2019;9:e028585. https://doi.org/10.1136/bmjopen-2018-028585
20. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. Drugs 1999;57:1005-32. https://doi.org/10.2165/00003495-199957060-00017
21. Sundström A, Seaman H, Kieler H, Alfredsson L. The risk of venous thromboembolism associated with the use of tranexamic acid and other drugs used to treat menorrhagia: a case-control study using the General Practice Research Database. BJOG 2009;116:91-7. https://doi.org/10.1111/j.1471-0528.2008.01926.x
22. Kim DH, Kim S, Kang H, Jin HJ, Hwang SH. Efficacy of tranexamic acid on operative bleeding in endoscopic sinus surgery: a meta-analysis and systematic review. Laryngoscope 2019;129:800-7. https://doi.org/10.1002/lary.27766
23. Murphy WG, Davies MJ, Eduardo A. The haemostatic response to surgery and trauma. Br J Anaesth 1993;70:205-13. https://doi.org/10.1093/bja/70.2.205
24. Levin EG, Marzec U, Anderson J, Harker LA. Thrombin stimulates tissue plasminogen activator release from cultured human endothelial cells. J Clin Invest 1984;74:1988-95. https://doi.org/10.1172/jci111620
25. Hoylaerts M, Lijnen HR, Collen D. Studies on the mechanism of the antifibrinolytic action of tranexamic acid. Biochim Biophys Acta 1981;673:75-85.
26. Ping WD, Zhao QM, Sun HF, Lu HS, Li F. Role of tranexamic acid in nasal surgery: a systemic review and meta-analysis of randomized control trial. Medicine (Baltimore) 2019;98:e15202. https://doi.org/10.1097/md.0000000000015202
27. Pereira EG, Carvalho MM, Oliveira T, Sacramento T, Cruz H, Viegas R, et al. Benefits of tranexamic acid in total knee arthroplasty: a classification and regression tree analysis in function of instrumentation, BMI, and gender. J Knee Surg 2023;36:173-80. https://doi.org/10.1055/s-0041-1731455
28. Andersson L, Nilsoon IM, Colleen S, Granstrand B, Melander B. Role of urokinase and tissue activator in sustaining bleeding and the management thereof with EACA and AMCA. Ann N Y Acad Sci 1968;146:642-58. https://doi.org/10.1111/j.1749-6632.1968.tb20322.x
29. Nilsson IM. Clinical pharmacology of aminocaproic and tranexamic acids. J Clin Pathol Suppl (R Coll Pathol) 1980;14:41-7.
30. Niego B, Horvath A, Coughlin PB, Pugsley MK, Medcalf RL. Desmoteplase-mediated plasminogen activation and clot lysis are inhibited by the lysine analogue tranexamic acid. Blood Coagul Fibrinolysis 2008;19:322-4. https://doi.org/10.1097/mbc.0b013e3282f54568
31. Benoni G, Lethagen S, Fredin H. The effect of tranexamic acid on local and plasma fibrinolysis during total knee arthroplasty. Thromb Res 1997;85:195-206. https://doi.org/10.1016/s0049-3848(97)00004-2
32. Ker K, Prieto-Merino D, Roberts I. Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss. Br J Surg 2013;100:1271-9. https://doi.org/10.1002/bjs.9193
33. Levi M, ten Cate JW. [Antifibrinolytic therapy]. Ned Tijdschr Geneeskd 1995;139:613-7. Dutch.
34. Siotou K, Siotos C, Azizi A, Cheah MA, Seal SM, Redett RJ, et al. The role of antifibrinolytics in reducing blood loss during craniofacial or orthognathic surgical procedures: a meta-analysis. J Oral Maxillofac Surg 2019;77:1245-60. https://doi.org/10.1016/j.joms.2019.01.032
35. Tarazi JM, Zois TP, Bohm A, Mont MA, Scuderi GR. Elevated preoperative D-dimer levels do not impact the effect of tranexamic acid on revision total knee arthroplasty. Orthop Clin North Am 2022;53:139-43. https://doi.org/10.1016/j.ocl.2021.12.001
36. Wright GP, Wolf AM, Waldherr TL, Ritz-Holland D, Laney ED, Chapman HA, et al. Preoperative tranexamic acid does not reduce transfusion rates in major oncologic surgery: results of a randomized, double-blind, and placebo-controlled trial. J Surg Oncol 2020;122:1037-42. https://doi.org/10.1002/jso.26142
37. Heyns M, Knight P, Steve AK, Yeung JK. A single preoperative dose of tranexamic acid reduces perioperative blood loss: a meta-analysis. Ann Surg 2021;273:75-81. https://doi.org/10.1097/sla.0000000000003793

How to cite this article: Harada K, Imamachi N, Matsuda Y, Hirabayashi M, Saito Y, Kanno T. Effect of tranexamic acid on blood loss reduction in patients undergoing orthognathic surgery under hypotensive anesthesia: a single-center, retrospective, observational study. J Korean Assoc Oral Maxillofac Surg 2024;50:86-93. https://doi.org/10.5125/jkaoms.2024.50.2.86