DOES INTRAVENOUS TRANEXAMIC ACID REDUCE BLOOD LOSS DURING SURGICALLY ASSISTED RAPID PALATAL EXPANSION?

Cerrahi Destekli Hızlı Üst Çene Genişletmesi Sırasında Damar İçi Traneksamik Asit Kullanımı Kan Kaybını Azaltır mı?

Emine AKBAŞ, Zerrin ÇEBİ, Erol CANSIZ, Sabri Cemil İŞLER, Sırmahan ÇAKARER

Received: 18/01/2017
Accepted:21/02/2017

ABSTRACT

Purpose: The purpose of this study was to evaluate the efficacy of tranexamic acid (TXA) in reducing blood loss during surgically assisted rapid palatal expansion (SARPE) procedure.

Subjects and Methods: A total of 34 patients (12 male, 22 female) who had been treated surgically under general anesthesia with SARPE including pterygoid disjunction for transverse maxillary deficiency (TMD) were included in this study. The study group (n=17) received intravenous (IV) TXA 10 mg/kg as a preoperative bolus; the control group (n=17) received normal saline solution. Preoperative and postoperative hemoglobin and hematocrit values, intraoperative blood loss, and any blood product transfusion were recorded.

Results: Blood loss during SARPE was statistically significantly less in the study group than the control group (p=0.0001).

Conclusion: Preoperative IV administration of TXA can effectively control blood loss during when SARPE with pterygoid disjunction is performed.

Keywords: Hemorrhage; maxillary expansion; SARPE; tranexamic acid; blood loss

How to cite: Akbas E, Cebi Z, Cansiz E, Isler SC, Cakarer S. Does intravenous tranexamic acid reduce blood loss during surgically assisted rapid palatal expansion?. J Istanb Univ Fac Dent 2017;51(3):32-37.
Introduction

Transverse maxillary deficiency (TMD) is one of the most common skeletal dysplasias observed in clinical practice (1). It can be treated with several techniques such as slow orthodontic expansion, rapid palatal expansion, and SARPE (2). The recommended technique for adult patients with TMD is SARPE because of the limited osteogenic activity of the palatal suture (3). SARPE is a well-established procedure to treat TMD with low morbidity, but some complications have also been described in the literature. Although this technique is considered to be relatively safe when compared to other orthognathic surgical methods, blood loss can occur and transfusion may be required (4-10). In particular, disjunction of the pterygomaxillary process combined with conventional SARPE osteotomy may increase the haemorrhagic complication rate depending on the damage to the pterygoid venous plexus (11). Tranexamic acid (TXA) is a reversible antifibrinolytic agent that completely blocks the conversion of plasminogen to plasmin. TXA inhibits the proteolytic action of plasmin on the fibrin clot and prevents thrombolysis, rather than the formation of a new clot. TXA has been reported to reduce bleeding in total knee arthroplasty, spinal surgery, and cardiac surgery (11). However, studies regarding the use of intravenous (IV) TXA during orthognathic surgery procedures performed on the well-vascularized head and face region are limited. Therefore, the aim of this study is to evaluate the efficacy of IV TXA in reducing blood loss during SARPE in combination with pterygomaxillary disjunction. The null hypothesis tested in this research is that the IV TXA does not have any effect on the examined variables related to blood loss during SARPE with pterygomaxillary disjunction procedure.

Subjects and Methods

Study Design

The study protocol was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Istanbul University, Faculty of Medicine (Ref. No: 27415); written informed consent was obtained from all patients. This study involved 34 patients who had undergone SARPE at Istanbul University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery from January 2014 through September 2015. The study criterion was the presence of TMD and use of SARPE with pterygomaxillary disjunction. The inclusion criteria were: skeletally mature patients diagnosed with TMD of >5 mm, good oral hygiene, and healthy periodontal structures. The exclusion criterion were previous surgery at donor and/or recipient sites, maxillary sinus disease, systemic disease that would contraindicate oral surgery, chronic periodontitis, use of anticoagulant drugs and smoking.

Study variables

The primary outcome variable was the amount of intraoperative bleeding. All patients were admitted to the hospital for preoperative assessment and anesthetic consultation 1 or 2 days before surgery. The medical history of each patient was recorded, and a blood sample was taken to evaluate complete blood count, international normalised ratio (INR), prothrombin time (PT), activated partial thromboplastin time (aPTT), and cross-matching. Body weight, age, gender, allergy, previous surgery, alcohol use, smoking, systemic disease, hospitalization period, duration of surgery, intraoperative blood loss, haemoglobin concentration, haematocrit, INR, PT, aPTT, and any complications were recorded. Postoperative haemoglobin concentration, haematocrit, aPTT, INR, and PT were measured on the day of surgery.

Surgical Technique

The same surgical team treated all of the patients, and surgery was performed under general anesthesia by the same surgeon. The same type of fixed hyrax palatal expansion device was used for all of the patients, and the devices were applied 1 or 2 days before SARPE. All patients underwent general anesthesia with nasotracheal intubation. After the induction of general anesthesia, infiltration of local anesthetic (articaine-HCl, Ultracaine, Sanofi, Istanbul, Turkey) was performed to provide haemostasis around the operative site. Before osteotomy and separation of the palatal suture, the expansion device was activated by preloading to facilitate separation (Figure 1). A full-thickness incision at the deepest site of the maxillary buccal vestibular sulcus, extending from the first molar to the contralateral first molar, was performed. A mucoperiosteal flap was elevated, exposing the maxilla from the anterior maxillary process to the zygomatic buttresses. The anterior attachment of medial nasal cartilage and anterior...
Blood loss during SARPE

nasal spine was separated, and the nasal mucosa lining the inferomedial site of the nasal airway was elevated. After elevation of the flaps, a Le Fort I osteotomy and maxillary anterior vertical osteotomy were performed by using a Lindemann bur (2 mm in diameter, 23 mm in length) (Figure 2). Bilateral pterygomaxillary separation was performed by using a curved chisel osteotome, and lateral nasal osteotomies were performed by using guided chisel osteotomes. Finally, transpalatal osteotomy was performed by using a straight chisel osteotome and the preloaded palatal suture was separated (Figure 3). After the separation process, the expansion device was deactivated and the flap was closed.

![Figure 1. Preloading of the expansion device to facilitate palatal separation](image1)

![Figure 2. Vertical and horizontal osteotomies.](image2)

Statistical analysis

Statistical analysis was performed using NCSS (Number Cruncher Statistical System) 2007 Statistical Software (NCSS, LLC, Kaysville, UT, USA) for the comparison of intraoperative blood loss in study and control groups. An independent t-test was used for the evaluation of descriptive statistical methods (mean, standard deviation) in addition to paired comparisons. Qualitative data were evaluated by using the chi-square test. p-values less than 0.05 were considered as statistically significant (p<0.05).

Results

No significant difference was observed among control and study groups for the age and gender variables. Differences in average weights between control and study groups were not significant either. On the other hand, the mean amount of intraoperative blood loss in the group which had received IV TXA was found to be significantly less than that of the controls (p=0.0001) (Table 1).

| Table 1. Statistical differences between control and study group (TXA: Tranexamic acid, SD: standard deviation). |
|----------------------------------------------------|----------------------------------------------------|--------------|
| Control Group | TXA Group | p |
| Age (mean±SD) | 22.18±5.66 | 22±4.54 | 0.921 |
| Gender | Male | 6 | 9 | 0.301 |
| | (35.29%) | (52.94%) |
| Female | 14 | 8 | (64.71%) | (47.06%) |
| Weight (mean±SD kg) | 62.76±13.45 | 67.06±14.54 | 0.378 |
| Blood Loss (mean±SD cc) | 219.71±72.96 | 52.65±17.51 | 0.0001 |
Discussion

TXA is a synthetic analogue of the amino acid lysine that inhibits fibrinolysis by blocking the conversion of plasminogen to plasmin (11). TXA has been shown to reduce blood loss and the need for blood transfusion in a variety of operations such as total knee arthroplasty (12, 13), spine surgery (14), cardiac surgery (15), caesarean section, and tonsillectomy (16). Although the effectiveness of TXA for the reduction of blood loss during operations has been well-documented, there is a ongoing debate about the timing, dosage, and method of use. The terminal half-life of TXA is 1.9 hours and it is mostly eliminated in the urine (17). The duration of the operation may be the most important factor in determining the timing of TXA administration. Although a single preoperative dose of TXA for operations shorter than 1.9 hours can be adequate, continuous infusions may be required for longer operations (18). Senghore et al. (19) reported that a single IV preoperative dose of TXA was effective in preventing postoperative bleeding in healthy patients undergoing third molar surgery. SARPE is a relatively short procedure when compared to other orthognathic surgery interventions. In this research, only a single preoperative dose of TXA was used in the study group. Additional doses may be required if the operation is longer than 1.9 hours.

Some clinical trials of IV and topical administration of TXA in maxillofacial surgery have been reported. Karimi et al. (20) showed that the preoperative IV administration of TXA significantly reduced intraoperative bleeding in bimaxillary surgery. In addition, Sankar et al. (21) observed that IV administration of TXA was effective in controlling blood loss and in improving the visibility of the surgical area, but had no significant effect on the incidence of blood transfusion or duration of surgery in orthognathic operations. In addition to IV administration of TXA, its topical use as an irrigation fluid or mouthwash has been suggested as a useful method for the management of postoperative bleeding after oral surgery in patients who are receiving anticoagulant therapy (22-27). Carter et al. (24) showed that the effectiveness of 4.8% TXA mouthwash was the same as autologous fibrin glue in warfarin-treated patients undergoing dental extraction. In addition, Sindet-Pedersen et al. (26) found that 4.8% TXA mouthwash was effective in bleeding prevention after oral surgery in anticoagulant-treated patients.

Hypotensive anesthesia is a basic technique for intraoperative bleeding management, and some studies used TXA in combination with hypotensive anesthesia during orthognathic operations (28). Although hypotensive anesthesia alone is a useful method for reducing intraoperative bleeding, it is very difficult to distinguish the effectiveness of TXA when used in combination with hypotensive anesthesia. Therefore, TXA administration was used without hypotensive anesthesia in this study. Authors used IV TXA (10 mg/kg) in the study group, based on a report about therapeutic plasma concentrations (29). Some studies reported the use of different dosages of TXA ranging from 10 to 100 mg/kg (18). However, it is also known that larger doses of TXA have no additional effect on haemostasis.

The maxillofacial region is a vulnerable area for haemorrhagic complications due to its well-vascularized anatomic structures, and these complications may occur during orthognathic procedures (30). Although SARPE is considered to be a relatively safe procedure, it may cause haemorrhagic complications which are usually related to the pterygomaxillary disjunction process (31). No consensus has been reached regarding the requirement for pterygomaxillary disjunction during SARPE (31). Although some researchers suggest that pterygoid disjunction is not required, authors believe that it is essential for the long-term stability of maxillary expansion, as separating the palatal suture without pterygoid disjunction can be difficult in some cases. During SARPE with pterygomaxillary disjunction, damages to the venous plexus may lead to haemorrhagic complications due to short distance between the plexus and the osteotomy lines. Therefore, authors routinely use TXA for the management of intraoperative bleeding during SARPE with pterygomaxillary disjunction. Findings of the present study regarding the effects of TXA on blood loss during SARPE procedures are consistent with those of the previous studies (20, 32, 33). In addition, no adverse reactions or complications were observed.

Conclusion

The present study demonstrated that preoperative IV administration of TXA significantly reduced intraoperative bleeding in SARPE with pterygomaxillary disjunction.
Blood loss during SARPE

Source of funding
None declared.

Conflict of interest
None declared.

References

1. Handelman CS. Nonsurgical rapid maxillary alveolar expansion in adults: A clinical evaluation. Angle Orthod 1997;67(4):291-305; discussion 306-298.
2. Verlinden CR, Gooris PG, Becking AG. Complications in transpalatal distraction osteogenesis: A retrospective clinical study. J Oral Maxillofac Surg 2011;69(3):899-905.
3. Babacan H, Sokucu O, Doruk C, Ay S. Rapid maxillary expansion and surgically assisted rapid maxillary expansion effects on nasal volume. Angle Ortho 2006;76(1):66-71.
4. Greenbaum KR, Zachrisson BU. The effect of palatal expansion therapy on the periodontal supporting tissues. Am J Orthod 1982;81(1):12-21.
5. Haas AJ. Long-term posttreatment evaluation of rapid palatal expansion. Angle Orthod 1980;50(3):189-217.
6. Langford SR, Sims MR. Root surface resorption, repair, and periodontal attachment following rapid maxillary expansion in man. Am J Orthod 1982;81(2):108-115.
7. Lamigan DT, Mintz SM. Complications of surgically assisted rapid palatal expansion: Review of the literature and report of a case. J Oral Maxillofac Surg 2002;60(1):104-110.
8. Mommertaes MY. Transpalatal distraction as a method of maxillary expansion. Br J Oral Maxillofac Surg 1999;37(4):268-272.
9. Song G, Yang P, Hu J, Zhu S, Li Y, Wang Q. The effect of tranexamic acid on blood loss in orthognathic surgery: A meta-analysis of randomized controlled trials. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115(5):595-600.
10. Timms DJ. A study of basal movement with rapid maxillary expansion. Am J Orthod 1980;77(5):500-507.
11. Hynes M, Calder P, Scott G. The use of tranexamic acid to reduce blood loss during total knee arthroplasty. Knee 2003;10(4):375-377.
12. Ho KM, Ismail H. Use of intravenous tranexamic acid to reduce allogeneic blood transfusion in total hip and knee arthroplasty: A meta-analysis. Anaesth Intensive Care 2003;31(5):529-537.
13. Neilipovitz DT. Tranexamic acid for major spinal surgery. Eur Spine J 2004;13 Suppl 1:S62-65.
14. Laupacis A, Ferguson D. Drugs to minimize perioperative blood loss in cardiac surgery: Meta-analyses using perioperative blood transfusion as the outcome. The international study of perioperative transfusion (ISPOT) investigators. Anesth Analg 1997;85(6):1258-1267.
15. Dunn CJ, Goa KL. Tranexamic acid: A review of its use in surgery and other indications. Drugs 1999;57(6):1005-1032.
16. Patatanian E, Fugate SE. Hemostatic mouthwashes in anticoagulated patients undergoing dental extraction. Ann Pharmacother 2006;40(12):2205-2210.
17. Sethna NF, Zurakowski D, Brustowitz RM, Bacsik J, Sullivan LJ, Shapiro F. Tranexamic acid reduces intraoperative blood loss in pediatric patients undergoing scoliosis surgery. Anesthesiology 2005;102(4):727-732.
18. Andersson L, Nilsson IM, Colleen S, Granstrand B, Melander B. Role of urokinase and tissue activator in sustaining bleeding and the management thereof with eca and amca. Ann NY Acad Sci 1968;146(2):642-658.
19. 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 1999;186(2):642-658.
20. Karimi A, Mohammadi SS, Hasheminasab M. Efficacy of tranexamic acid on blood loss during bimaxillary osteotomy: A randomized double blind clinical trial. Saudi J Anaesth 2012;6(1):41-45.
21. Sankar D, Krishnan R, Veerabahu M, Vikraman B. Evaluation of the efficacy of tranexamic acid on blood loss in orthognathic surgery. A prospective, randomized clinical study. Int J Oral Maxillofac Surg 2012;41(6):713-717.
22. Borea G, Montebugnoli L, Capuzzi P, Magelli C. Tranexamic acid as a mouthwash in anticoagulant-treated patients undergoing oral surgery. An alternative method to discontinuing anticoagulant therapy. Oral Surg Oral Med Oral Pathol Oral Radiol 1993;75(1):29-31.
23. Carter G, Goss A. Tranexamic acid mouthwash--a prospective randomized study of a 2-day regimen vs 5-day regimen to prevent postoperative bleeding in anticoagulated patients requiring dental extractions. Int J Oral Maxillofac Surg 2003;32(5):504-507.
24. Carter G, Goss A, Lloyd J, Tocchetti R. Tranexamic acid mouthwash versus autologous fibrin glue in patients taking warfarin undergoing dental extractions: A randomized prospective clinical study. J Oral Maxillofac Surg 2003;61(12):1432-1435.

25. Ramstrom G, Sindet-Pedersen S, Hall G, Blomback M, Alander U. Prevention of postsurgical bleeding in oral surgery using tranexamic acid without dose modification of oral anticoagulants. J Oral Maxillofac Surg 1993;51(11):1211-1216.

26. Sindet-Pedersen S, Ramstrom G, Bernvil S, Blomback M. Hemostatic effect of tranexamic acid mouthwash in anticoagulant-treated patients undergoing oral surgery. N Engl J Med 1989;320(13):840-843.

27. Souto JC, Oliver A, Zuazu-Jausoro I, Vives A, Fontcuberta J. Oral surgery in anticoagulated patients without reducing the dose of oral anticoagulant: A prospective randomized study. J Oral Maxillofac Surg 1996;54(1):27-32; discussion 323.

28. Zellin G, Rasmussen L, Palsson J, Kahnberg KE. Evaluation of hemorrhage depressors on blood loss during orthognathic surgery: A retrospective study. J Oral Maxillofac Surg 2004;62(6):662-666.

29. Robl MT, Farrell BB, Tucker MR. Complications in orthognathic surgery: A report of 1,000 cases. Oral Maxillofac Surg Clin North Am 2014;26(4):599-609.

30. Hamedi Sangsari A, Sadri-Eshkevari P, Al-Dam A, Friedrich RE, Freymiller E, Rashad A. Surgically assisted rapid palatomaxillary expansion with or without pterygomaxillary disjunction: A systematic review and meta-analysis. J Oral Maxillofac Surg 2016;74(2):338-348.

31. Kilic E, Kilic B, Kurt G, Sakin C, Alkan A. Effects of surgically assisted rapid palatal expansion with and without pterygomaxillary disjunction on dental and skeletal structures: A retrospective review. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115(2):167-174.

32. Choi WS, Irwin MG, Samman N. The effect of tranexamic acid on blood loss during orthognathic surgery: A randomized controlled trial. J Oral Maxillofac Surg 2009;67(1):125-133.

33. Eriksson O, Kjellman H, Pilbrant A, Schaﬄong M. Pharmacokinetics of tranexamic acid after intravenous administration to normal volunteers. Eur J Clin Pharmacol 1974;7(5):375-380.