

The Influence of Tranexamic Acid for Controlling Blood Loss in Orthognathic Surgery

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Abstract

The purpose of this study was to evaluate the tranexamic acid influenced in the reduction of blood loss in patients underwent bilateral sagittal split ramus osteotomies. This randomized controlled trial was conducted in patients underwent bilateral sagittal split ramus osteotomies to correct the dentofacial deformities at the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University from February 2006 to October 2006. A total of 19 patients in this study were divided into 2 groups, 10 patients were treated with 10 mg/kg TXA and the others were assigned as a control group. Standard bilateral sagittal split ramus osteotomies procedures were performed in all patients. Independent sample t-test was used at a significant level of $p < .05$. The study demonstrated that the intraoperative blood loss reduced by 36.92% in the experimental group, but the change was not statistically significant. The postoperative blood loss, total blood loss, hemoglobin level at the 1st and 3rd postoperative day, the difference of hemoglobin level at the preoperative and the 1st postoperative day and the difference of hemoglobin level at the preoperative and the 3rd postoperative day in the experimental group were similar to that in the control group. No patients in both groups received blood transfusion. There were no reports of thromboembolic events, post operative infection and other complications of all cases. In conclusion, tranexamic acid showed some influences in reducing intraoperative blood loss but there was no statistically significant difference.

Key words: antifibrinolytic agent; orthognathic surgery; total blood loss; Tranexamic acid

Introduction

Although orthognathic surgery has been recognized as a safe operation with minimal morbidities, a major complication in orthognathic surgery is the potential to have excessive blood loss with several reports of life-threatening hemorrhage following the surgery.¹⁻⁵ The standard treatment for massive hemorrhage during operations by electrocautery, local ligation, use of hemostatic agents, packing the area or ligation of major vessels leading to the bleeding area. Hypotensive anesthesia was reported

as a well-established and effective method to reduce blood loss.⁶⁻¹⁰ Its disadvantages are brain anoxia and postoperative bleeding after the end of anesthesia due to ineffective intraoperative hemostasis. The use of antifibrinolytic drugs such as tranexamic acid (TXA) in the reduction of bleeding has also emerged as an additional approach. Previous reports on TXA in cardiac and joint replacement surgery demonstrated that TXA significantly reduced intraoperative and postoperative blood loss¹¹⁻¹⁴ and there were few reports of thrombotic events. However, very few studies assessed the use of TXA in orthognathic surgery. The objective of this study, thus, was to evaluate the effects of tranexamic acid in the reduction of blood loss in patients underwent bilateral sagittal split ramus osteotomies.

Material and method

Nineteen patients, ages ranged between 18 to 40 years, planned for bilateral sagittal split ramus osteotomies (BSSRO) at the Department of Oral & Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University from February 2006 to October 2006 participated in this study. The patients were fit and healthy and had no medical history of hematopoietic disorders, deep vein thrombosis, previous exposure to TXA, currently taking oral contraceptive pills or anticoagulants, ischemic heart disease, renal disease, liver cirrhosis, acquired defective color vision and allergy to TXA. Patients who had injury of major blood vessels during operation and bad splits were excluded from this study. The patients were randomly divided into two groups; a study group and a control group. This study was approved by the medical ethics committee for human research of the faculty. The patients were informed and consents were obtained from all patients participated in this study.

Samples of blood from each patient were collected for evaluation of hematological parameters (CBC; Hb, Hct, platelet count, BUN, Creatinine) before and after operation. All surgical procedures were performed under general anesthesia administered by only one anesthesiologist using the standard general anesthetic technique. Patients and drugs were randomized. Tranexamic acid (Transamin[®], Daiichi Pharmaceutical Co. Ltd., Thailand) 250 mg/5ml 2 ampoules or saline 20 ml 2 ampoules were prepared in a syringe labeled by a person who did not involve with the surgical procedure and administered by the anesthesiologist. In the TXA group, 10 mg/kg of TXA was administered intravenously five minutes before the incision. In the control group, 10 ml/kg of NSS was administered intravenously five minutes before the incision. Each surgical site was infiltrated with 3.6 ml of 2% lidocaine HCl with epinephrine 1:100,000 solution 5 minutes

before making incisions. Then, standard BSSRO procedures were performed. The mandibles were set back or advanced as presurgical planned. Each osteotomy site was fixed with a four hole titanium miniplate and four 2.0 mm titanium screws 7 or 5.5 mm in length. A vacuum drain was applied at each osteotomy site before wound closing. The surgical wound was sutured with resorbable sutures and maxillo-mandibular fixation was applied for one week. Patients were given 1.2 g amoxicillin-clavulanate intravenously before surgery and a single dose 8 hour postoperatively and then continued with 625 mg oral regimen every 8 hours for five days. Patients who were allergic to penicillin were given 600 mg clindamycin and 300 mg oral regimen using the same period as amoxicillin-clavulanate. Intravenous dexamethasone 8 mg was given preoperatively and then every 12 hours for 3 days. Postoperative nausea and vomiting were controlled by 10 mg metoclopramide given intramuscularly as required. Early post operative pain was control with 40 mg parecoxib and once the patients were able to take oral fluid, they were given 200 mg ibuprofen syrup. Patients were fed with liquid diet until the maxillo-mandibular fixation removed. Any postoperative complications detected were recorded and treated. Patients were kept in the hospital for 3 days then discharged once the condition was good for discharge.

The intraoperative blood loss was assessed from the blood in the suction container and the blood soaked surgical sponges, gauzes and swabs. Postoperative blood loss was measured from vacuum drains which were retained until the 2nd postoperative days or until postoperative blood loss was less than 20 ml/day for each side. The total blood loss was the combination of the intraoperative blood loss and the postoperative blood loss. Postoperative Hb level was measured at the first and third postoperative days. Any patients whose Hct reduced more than 25%¹⁵ of the baseline or Hb was below 7 g/dl⁷ on the second postoperative day and developed clinical symptoms of anemia, a blood transfusion would be considered.¹⁵ The amount of blood transfused would be recorded if there was any blood transfusion. The patients were evaluated for postoperative thrombosis with the Homan's sign (calf pain with forcible dorsiflexion of the feet), edema, pain, tenderness, increased warmth and changes in skin color (redness) in legs during hospitalization and at the out patient clinic on the 1st, 2nd and 4th weeks postoperatively. Signs of prolonged drainage or infection and abnormal findings would be noted and treated.

Total blood loss was measured from all blood in the suction container in the theatre, the blood in the suction drains from the wound sites and all the blood soaked swabs and gauzes used during

the operation. Hemoglobin level was recorded at preoperative, the first and the third postoperative days. All data collected from 19 patients were analyzed with SPSS for Windows version 11.5. *P*-values lesser than .05 were considered statistically significant.

Results

The demographic data was shown in Table 1. All patients were in ASA I category and no contraindication for TXA. There were no differences in mean ages, body weight, preoperative Hb and

gender between both groups in the demographic data. As shown in Table 2, the mean intraoperative blood loss of the experimental group was 198.96 ± 227.07 ml and the control group was 315.43 ± 294.99 ml. As shown in Table 1, the mean intraoperative blood loss per minute of the experimental group was 1.55 ml / minute and the control group was 1.93 ml/minute. The difference of blood loss from both groups was 0.38 ml/minute (19.96%). The mean postoperative blood loss of the experimental group was 115.35 ± 43.54 ml and the control group was 117.33 ± 32.89 ml. The mean total blood loss in the experimental group was 314.31 ± 233.49 ml and the control

Table 1 Summary of the patients' demographic data

	Tranexamic acid (n =10)	Control group (n = 9)
Age (year)	25.4 ± 5.15	25.22 ± 4.09
Body weight (Kg.)	58.86 ± 11.31	57.5 ± 15.58
Preoperative Hb (g/dl)	12.53 ± 1.12	12.92 ± 1.74
Surgery time (minutes)	128.1 ± 47.34	163.22 ± 31.02
Gender (male/female)	4/6	3/6
Intraoperative blood loss per minute (ml/minute)	1.55	1.93

Table 2 Summary of the patients' intraoperative blood loss, postoperative blood loss, total blood loss

	Tranexamic acid (n =10)	Control group (n = 9)	<i>p</i> -value*
Intraoperative blood loss (ml)	98.96 ± 227.07	315.43 ± 294.99	.346
Postoperative blood loss (ml)	115.35 ± 43.54	117.33 ± 32.89	.913
Total blood loss (ml)	314.31 ± 233.49	432.76 ± 318.31	.364

* t-test with level of significance .05

group was 432.76 ± 318.31 ml. The intraoperative, postoperative and total blood loss in the experimental group was not significantly different from the control group ($p > .05$). As shown in Table 1, the operation time in the experimental group was not significantly different from the control group ($p = .076$) and the operation time was not correlated to the intraoperative blood loss.

The comparisons of preoperative Hb, the Hb on the 1st and 3rd postoperative days are share in Tables, the difference between the preoperative Hb and the Hb on the 1st postoperative day and the difference between the preoperative Hb and the Hb on the 3rd postoperative day in the TXA group were not significantly different from those in the control group. No patients in both groups required blood transfusion. There were no problems from thromboembolic events and other complications in all patients during 4 weeks postoperative review.

Discussion

Tranexamic acid (TXA) is a synthetic antifibrinolytic drug released in 1970s.²² It may be useful when hemorrhage cannot be staunched e.g. in prostatectomy, dental extraction in hemophiliacs, menorrhagia, cardiopulmonary bypass and orthopedic surgery. It is a trans-stereo isomer of a synthetic amino acid, introduced to competitively inhibit the activation of plasminogen to plasmin. It saturates the lysine binding sites of human plasminogen, displacing plasminogen from the fibrin surface which results in inhibition of fibrinolysis, preserves platelet function and reduces intraoperative blood loss and thus reduces the need for blood transfusions.²³ The results in this study, the intraoperative blood loss in the TXA group was lower than the patients in the control group, but this was

not statistically significant ($p > .05$). However, the data analyzed to reduce blood loss per minute was 19.69%. Similar to several previous studies, the surgeons were familiar with the procedure and operation time was short. There was only a small amount of blood loss in the BSSRO procedure, so it was difficult to demonstrate the significant hemostatic effect of TXA of patients in the study group while there were statistically significant in the cardiac¹⁶ and orthopedic surgery.¹¹⁻¹⁴ Estimations of operative blood loss used in most operating rooms are not exactly accurate. The measurement of weight of the sponges and gauzes used, the volume of fluid used for irrigation and the blood that was collected in the tissue space and the blood on the surgical drapes and surgeon gowns and gloves were factors that made the measurement of actual blood loss far from accuracy. However, the study was designed to avoid these factors and made the measurement as accurate as possible. In this study, the operating time was not correlated with the intraoperative blood loss. It would be dependent on individual patient's anatomy and each surgery condition.

There was no significant reduction of Hb on the 1st and 3rd postoperative days and no signs of anemia, so there were no patients in both groups required blood transfusion. The Hb level on the 1st and 3rd postoperative days, the difference between the preoperative Hb and the Hb on the 1st postoperative day and the difference between the preoperative Hb and the Hb on the 3rd postoperative day in the experiment group were not significantly different compared to the control group. There were very few changes in Hb in the experiment group which corresponded to the changes in blood loss.

The period of this study was short and the sample size was small. However the data demonstrated normal distributed statistic. There was no massive bleeding during operation in any cases

Table 3 Summary of the patients' preoperative hemoglobin, the hemoglobin of 1st postoperative day, the hemoglobin of 3rd postoperative day

	Tranexamic acid (n =10)	Control group (n = 9)	p-value*
Preoperative Hb (g/dl)	12.53 ± 1.12	12.92 ± 1.74	.563
1st postoperative Hb (g/dl)	11.57 ± 1.22	11.15 ± 1.0	.432
3rd postoperative Hb (g/dl)	10.68 ± 1.88	11.22 ± 1.16	.471

* t-test with level of significance .05

because it was operated by experienced surgeons. Luz et al reported that no patients in the single-jaw surgery required blood transfusion during operation or postoperatively.¹⁹ Samman et al also found that blood transfusion was not necessary for a single-jaw surgery, although 27% of their bimaxillary osteotomy patients required blood transfusion.²⁰ Gong et al found that the amount of blood loss in bimaxillary osteotomy procedures was 899 ml (range 200 to 1,800 ml).²¹ There are more blood loss in other procedures in orthognathic surgery. It would have been better if the same experiment were conducted on bimaxillary surgery or other more extensive orthognathic surgeries than the BSSRO could be done which may show the different outcome and the hemostatic efficacy of TXA in surgery. The study in a larger sample size is preferred for a more predictable result.

Conclusion

Tranexamic acid has some influences in reducing intraoperative blood loss but there was no statistically significant difference.

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บทความวิชาการ

การศึกษาแนวโน้มของยาทรานเอ็กซามิกแอซิดต่อการลดปริมาณเลือดที่ออกในการผ่าตัดขากรรไกรร่วมกับการจัดฟัน

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บทคัดย่อ

วัตถุประสงค์ของการศึกษานี้เพื่อศึกษาแนวโน้มของยาทรานเอ็กซามิกแอซิดต่อการลดปริมาณเลือดที่ออกในการผ่าตัดขากรรไกรร่วมกับการจัดฟัน การศึกษานี้เป็นงานวิจัยแบบสุ่มเชิงทดลอง โดยกลุ่มตัวอย่างได้จากผู้ป่วยที่ได้รับการผ่าตัดขากรรไกรร่วมกับการจัดฟันแบบไบแล็ทเทอเรียลแซจิทอลสปริทเรมส์ฮอสติโอโตมี ที่คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ในช่วงเดือนกุมภาพันธ์ พ.ศ. 2549 จนถึงเดือนตุลาคม พ.ศ. 2549 ได้จำนวนกลุ่มตัวอย่างทั้งหมดจำนวน 19 คน โดยแบ่งเป็นกลุ่มที่ได้รับยาทรานเอ็กซามิกแอซิด (10 มิลลิกรัมต่อน้ำหนักตัว 1 กิโลกรัม) จำนวน 10 คน และกลุ่มควบคุมที่ไม่ได้รับยาจำนวน 9 คน ผู้ป่วยทั้ง 2 กลุ่มได้รับการผ่าตัดโดยวิธีการมาตรฐาน ผลการศึกษาพบว่าปริมาณการสูญเสียเลือดเฉลี่ยที่ออกระหว่างการผ่าตัดในกลุ่มที่ได้รับยามีค่าน้อยกว่าในกลุ่มที่ไม่ได้รับยาร้อยละ 36.92 แต่เมื่อทำการทดสอบสมมติฐานเพื่อเปรียบเทียบในทั้ง 2 กลุ่ม ด้วยแบบทดสอบที่ระดับนัยสำคัญ .05 พบว่าปริมาณการสูญเสียเลือดที่ออกเฉลี่ยของกลุ่มที่ได้รับยาไม่มีความแตกต่างกันทางสถิติที่ระดับนัยสำคัญ .05 สำหรับปริมาณเลือดเฉลี่ยที่ออกหลังและทั้งหมดของการผ่าตัดระดับฮีมโกลบินหลังการผ่าตัดวันที่ 1 และวันที่ 3 และค่าการเปลี่ยนแปลงระดับฮีมโกลบินก่อนและหลังผ่าตัดวันที่ 1 และก่อนและหลังผ่าตัดวันที่ 3 ในกลุ่มที่ได้รับยามีความแตกต่างกับกลุ่มที่ไม่ได้รับยาอย่างไม่มีนัยสำคัญทางสถิติที่ระดับนัยสำคัญ .05 ไม่มีผู้ป่วยในทั้งสองกลุ่มที่ได้รับเลือดภายหลังการผ่าตัด ไม่พบภาวะแทรกซ้อนและภาวะการฉีกขาดเนื้อเยื่อใด ๆ ในผู้ป่วยทั้ง 2 กลุ่ม โดยสรุปยาทรานเอ็กซามิกแอซิดมีอิทธิพลในการช่วยลดปริมาณเลือดที่ออกในระหว่างการผ่าตัดแต่มีความแตกต่างอย่างไม่มีนัยสำคัญทางสถิติ