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Prophylactic Effect of a Low Dose of Tranexamic Acid on Reducing Bleeding in Septorhinoplasty

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Abstract

Background: Intraoperative bleeding and postoperative periorbital edema and ecchymosis are the main concerns in septorhinoplasty surgery. Tranexamic acid, an antifibrinolytic agent, is used to reduce bleeding in nasal surgeries. The aim of this prospective double blind, randomized, controlled study was to assess the efficacy of a prophylactic low dose of tranexamic acid on bleeding and periorbital edema and ecchymosis in open septorhinoplasty.

Methods: 52 American Society of Anesthesiologists class I adult patients scheduled for open septorhinoplasty under total intravenous anesthesia were randomized into 3 groups to receive either a bolus dose of 500 mg oral or intravenous tranexamic acid or placebo prior to the surgery.

Results: There were no significant differences in the intraoperative bleeding between the groups. The grade of periorbital edema and ecchymosis on the first, third, and seventh days after surgery were similar in the three groups.

Conclusions: The efficacy of a prophylactic single dose of 500 mg tranexamic acid on the intraoperative bleeding and postoperative edema and ecchymosis was similar to that of placebo in open septorhinoplasty.

Keywords: Ecchymosis; Hemorrhage; Edema; Rhinoplasty; Tranexamic acid

Introduction

Bleeding during rhinoplasty is a major concern because bleeding in this limited surgical space restricts the surgeon's view and may result in prolonged operation and undesirable outcome. Moreover, intraoperative hemorrhage can aggravate postoperative eyelid edema and ecchymosis, which may cause stress and anxiety in the patients and delay their return to social activities [1,2]. To reduce these complications, several methods such as head elevation, vasoconstriction of the nasal mucosa, hypotensive anesthesia, modified surgical techniques, cold pack, and steroids are used [3,4]. Some have also used the antifibrinolytic agent tranexamic acid (TA) for this purpose [5]. TA is a synthetic plasminogen inhibitor, which reversibly blocks the lysine binding sites on plasminogen molecule, thus prevents fibrinolysis and stabilizes the blood clot [6]. TA has been given intravenously, orally, or topically to control bleeding in a number of facial, nasal and otorhinolaryngology surgical procedures without any major adverse effects [7-9]. In general, the recommended dosages for local fibrinolysis are 500mg to 1g intravenously 3 times daily or 1 to 1.5g orally 2 to 3 times daily. For general fibrinolysis, an intravenous single dose of 1g or 10 mg/kg is recommended [6]. However, numbers of studies that have evaluated TA on rhinoplasty bleeding are still limited and as far as we know, there is still no agreement on dosage, timing and administration route of TA in this type of surgery. However, in clinical practice, many rhinoplasty surgeons still prefer only one bolus dose of 500 mg of TA before surgery due to concerns about its thromboembolic complications. This prospective, controlled, randomized, double blind trial was conducted to determine whether this low single dose of TA is effective in reducing intraoperative bleeding and postoperative periorbital edema and ecchymosis in patients undergoing primary cosmetic open septorhinoplasty.The primary outcome measure was the amount of intraoperative blood loss and the secondary outcomes were the degree of postoperative periorbital edema and ecchymosis.

Materials and Methods

The Research Ethics Committee of Shahid Beheshti University of Medical Sciences in Tehran, Iran approved the study protocol on May 4, 2013 with protocol number 2013.464. Fifty-four American Society of Anaesthesiologists physical status class I adult patients, scheduled for primary cosmetic open septorhinoplasty under total intravenous anesthesia were included in the study. All patients gave their written informed consent for participation in the study prior to the surgery.

Patients

Exclusion criteria were pregnancy, known allergies to TA, coagulation disorders, history of thromboembolic disease, renal disease, oral contraceptive usage and anticoagulants or anti-platelets usage. Patients were randomized into one of three groups of 18 each by using a computer-generated random table. Then random allocations were covered in an envelope. Before surgery, a blind person drew the sealed envelope by chance and eligible patient was assigned to one of the 3 groups: Patients in oral TA group received 500 mg TA capsule (Caspian–Tamin Pharmaceutical Co. Rasht, Iran) 60 minutes before admission to operating room. Those in IV TA and placebo groups received identical looking placebo capsules. The nurses blinded to the study protocol administered the drugs. In the operating room, patients in IV TA group received 500 mg bolus dose of intravenous TA diluted

in normal saline, immediately after anesthesia induction. In the oral TA and placebo groups, the same volumes of normal saline administered intravenously. The IV study drugs were prepared and administered by anesthesia technicians not involved in the study. Patients were monitored with electrocardiogram, pulse oximetry (Spo2), noninvasive blood pressure and end-tidal carbon dioxide. General anesthesia was induced with sodium thiopental, fentanyl, midazolam, and atracurium and maintained with 100% oxygen, and continuous infusions of propofol and remifentanil.

Surgery

At the beginning of the operation, topical phenylephrine 0.25% was applied for nasal mucosal decongestion and 10 ml solution of 1% lidocaine +1:100.000 epinephrine was injected into the transcolumellar and marginal incision sites and osteotomy lines. Steroid was not given throughout the perioperative period. Arterial blood pressure and heart rate were recorded every 15 minutes during the operation and systolic blood pressure was kept around 80-90 mmHg. During the surgery, patients were placed in a 30 degrees head elevation. The same senior otolaryngology resident using the same surgical technique with skin flap elevation, septoplasty, hump resection, bilateral external osteotomies without periosteal elevation, and tip plasty, performed all operations.

The total volume of intraoperative hemorrhage was assessed at the end of surgery by measuring the amount of absorbed blood to the surgical gauzes (measured as the weight difference between gauzes before and after surgery) and blood volume in the suction bottle. Surgical nurses not involved in the study calculated the amount of bleeding. After completion of the surgery, intranasal packing and an external nasal splint were used in all patients. The patients, surgeon, anesthesiologists and caregivers were blinded to the group allocation.

The same-blinded otolaryngology resident using a scale of 0-4 [10] evaluated periorbital edema and ecchymosis on first, third, and seventh postoperative days. The scale for eyelid edema was: 0= none; 1+= minimal; 2+= covering to the iris; 3+= extending to the pupil; 4+= massive edema with the eyelid close. Ecchymosis scale consisted of 0= none, +1= in the medial canthus, +2= extending to the pupil, +3= past the pupil, +4= extending to the lateral canthus. Patients were discharged from hospital on the first day after surgery. The nasal packs removed on the third and the nasal splint on the seventh days after surgery. Any postoperative complications were recorded.

Statistical analysis

Data were analyzed using SPSS software version 22.0; IBM. The normal distribution of the variables was evaluated with the Kolmogorov-Smirnov analysis. Kruskal wallis one-way analysis of variance test was used for the comparison of the age, weight, height, operation time, and the amount of intraoperative bleeding between three groups. Scores of periorbital edema and ecchymosis in each postoperative day were compared between the groups using the Fisher's exact test and repeated measures ANOVA. The changes in the edema and ecchymosis scores in each group were analyzed using Friedman test. All variables are expressed as mean ± standard deviation and numbers or percentages. A P-value less than 0.05 was considered statistically significant.

Results

Two patients (1 in the IV TA group and 1 in the oral TA group) were excluded from the study, because they lost follow-up visit. 52 patients (22 women and 30 men between the ages of 18-51 years) were analyzed (17 in IV TA, 18 in placebo and 17 in oral TA group). Figure 1 shows the CONSORT participant flow diagram. There was no significant differences between the 3 groups in age, sex, weight, height, surgery length, the amount of intraoperative bleeding (Table 1) and periorbital edema and ecchymosis scores on postoperative days 1,3 and 7 (Table 2). None of the patients had severe edema and ecchymosis (grade 3 or 4) in all assessment days after surgery. However, a statistically significant decrease in edema and ecchymosis scores over time was observed in each group between 1,3 and 7 postoperative days (P=0.0001) (Table 3). No complication related to the TA usage was detected.

Discussion

In the present study, we compared the prophylactic effect of one dose of 500 mg IV or oral TA with the placebo on the amount of intraoperative bleeding and the grade of postoperative periorbital edema and ecchymosis in primary open septorhinoplasty. Considering the mean age of patients in this study, the prescribed dose of TA was less than 10 mg/Kg. We found that 500mg systemic TA did not have a clinical benefit in reduction of the studied variables versus placebo. In most patients, the edema and ecchymosis scores reduced after the first postoperative day and reached grade 1 or less on the third day after surgery. On the seventh postoperative day, the eyelid edema was resolved in majority of the patients and none of them had ecchymosis. No side effects related to the TA were detected. The limitation of this study was that the surgeon's satisfaction with the surgical field and patient satisfaction after surgery were not assessed. Some may also point out the non-equivalence of IV and oral TA doses as the weakness of the study. However, the purpose of this study was not to compare intravenous and oral methods.

Contrary to the results of our study, in previous studies, the use of TA causes a significant reduction in intraoperative bleeding and postoperative edema and ecchymosis compared with placebo in rhinoplastic surgeries. Eftekharian and Rajabzadeh showed that preoperative use of a single dose of 1g oral TA compared to placebo significantly decreases blood loss and improves surgeons' satisfaction with the surgical site in rhinoplasty patients [11]. Beikaei, et al. evaluated the efficacy of a single bolus dose of 10mg/kg IV TA on hemostasis during open rhinoplasty. They observed that patients given TA significantly have fewer intraoperative bleeding than placebo [12]. However, none of these two studies provides information on postoperative edema and ecchymosis. In the study of Sakallioglu et al, 1g TA was given orally before open septorhinoplasty with additional 3 g daily doses for 5 days. The authors found that oral TA is significantly more effective than IV methylprednisolone or placebo for reduction of bleeding during surgery. They also showed that TA significantly reduces postoperative periorbital edema and ecchymosis compared with placebo group [13]. Ghavimi et al showed that administration of 10mg/Kg IV TA before rhinoplasty significantly reduces intraoperative bleeding, eyelid edema and periorbital ecchymosis and increases surgeon satisfaction compared to the control group [14]. However, there was no significant TA related side effect in our experience and the earlier studies. The difference between our findings with previous studies may be due to their higher TA doses and differences in drug administration time. Another potential reason could be a relatively

smaller number of patients in our study. Indeed, larger clinical trials are recommended to investigate the effect of lower doses of TA on rhinoplasty bleeding [11,12]. Furthermore, some evidence suggests that external osteotomy technique decreases bony and soft tissue trauma during rhinoplasty [3]. In the current study, the use of this surgical approach along with local vasoconstriction of nasal mucosa, preserving mild hypotension, and head elevation during surgery may be the possible causes for the similarity of the results among the TA and placebo usage. Based on this study, the efficacy of a 500 mg dosage of TA was not superior to the above-mentioned factors. We concluded that the efficacy of a prophylactic single dose of 500 mg intravenous or oral TA on the amount of bleeding during open septorhinoplasty and postoperative degree of periorbital edema and ecchymosis was similar to that of placebo.

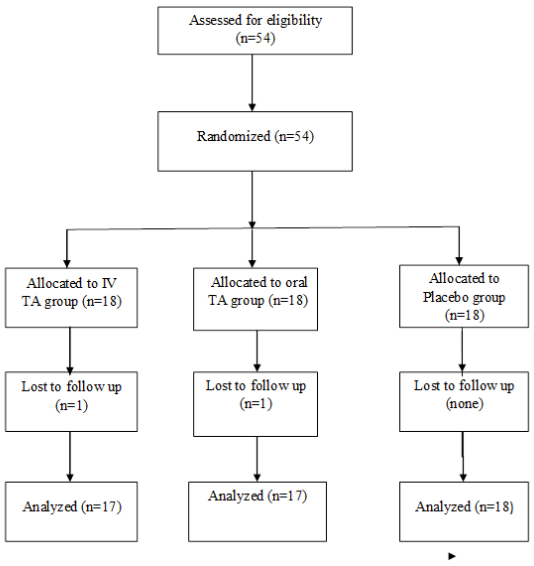

Figure 1: CONSORT Flow diagram of study patients. TA: tranexamic acid.

	IV TA(n=17)	Oral TA(n=17)	Placebo(n=18)	P Value
Age (year)	26.88 ± 5.73	25.76 ± 4.61	28.55 ± 9.50	0.842
Sex (F/m)	8/9	4/13	10/8	0.158
Weight (Kg)	70.82 ± 9.76	74.58 ± 7.07	69.77 ± 8.61	0.333
Height (cm)	174.05 ± 7.13	177.47 ± 6.13	172.72 ± 7.38	0.148
Surgery length (min)	205.88 ± 24.38	199.11 ± 19.14	221.11 ± 36.40	0.213
Intraoperative bleeding(ml)	120.58 ± 32.15	120.88 ± 46.17	130.55 ± 43.34	0.876

Table 1: Characteristics of the patients in tranexamic acid (TA) and placebo groups.

There were no significant differences between the three groups (P>0.05). Data are expressed as mean ± SD and number.

	IV TA (n=17)	Oral TA (n=17)	Placebo (n=18)	P Value
First POD Scores				
Ecchymosis (o/+1)	6/11	5/12	7/11	0.933
Edema (o/+1/+2)	1/11/5	2/12/3	1/14/3	0.834
Third POD Scores				
Ecchymosis (o/+1)	14/3	12/5	16/2	0.377
Edema (o/+1/+2)	9/8/0	4/12/1	7/8/3	0.177
Seventh POD Scores				
Ecchymosis (o/+1)	17/0	17/0	18/0	-
Edema (o/+1/+2)	15/2/0	15/2/0	13/5/0	0.465

Table 2: Distribution of postoperative periorbital edema and ecchymosis scores of study patients in tranexamic acid (TA) and placebo groups on postoperative days 1,3,7.

There were no significant differences between the 3 groups (P>0.05). Data are expressed as the number of patients. POD: postoperative day.

	First POD	Third POD	Seventh POD	P Value
IV TA group (n=17)				
Ecchymosis score	0.64 ± 0.49	0.17 ± 0.39	0.00 ± 0.00	0.000
Edema score	1.23 ± 0.56	0.47 ± 0.51	0.11 ± 0.33	0.000
Oral TA group (n=17)				
Ecchymosis score	0.70 ± 0.46	0.29 ± 0.46	0.00 ± 0.00	0.000
Edema score	1.05 ± 0.55	0.82 ± 0.52	0.11 ± 0.33	0.000
Placebo group (n=18)				
Ecchymosis score	0.61 ± 0.50	0.11 ± 0.32	0.00 ± 0.00	0.000
Edema score	1.11 ± 0.47	0.77 ± 0.73	0.27 ± 0.46	0.000

Table 3: Scores of postoperative periorbital ecchymosis and edema in tranexamic acid (TA) and placebo groups.

The changes in ecchymosis and edema scores between 1,3 and 7 days after surgery were statistically significant in each group (P<0.05). Data are expressed as mean ± SD. POD: postoperative day.

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