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Comparison of the Effect of Dexamethasone and Tranexamic Acid, Separately or in Combination on Post-Rhinoplasty Edema and Ecchymosis

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Abstract

Background Dexamethasone and tranexamic acid are used to decrease post-rhinoplasty periorbital edema and ecchymosis. We compared the impact of each medication separately or in combination in this regard.

Methods A prospective, randomized triple-blinded study was undertaken on 60 patients who underwent primary open rhinoplasty. They were divided into four groups: Group D ($n = 15$) received 8 mg dexamethasone, group T ($n = 15$) received 10 mg/kg tranexamic acid, group DT ($n = 15$) received both 8 mg dexamethasone and 10 mg/kg tranexamic acid, and group P ($n = 15$) received neither medication and served as the placebo control group. The medications were given intravenously (IV) 1 h before and three doses every 8 h postoperatively. Digital photographs were taken on the first, third and seventh postoperative days. One expert examiner blinded to the study evaluated the periorbital edema and ecchymosis on a scale of 0–4. Periorbital edema and ecchymosis were examined in all groups.

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Results In group D, group T and group DT, periorbital edema and ecchymosis ratings were significantly lower compared with the control group ($p < 0.01$). No statistically significant difference was seen in preventing or decreasing both periorbital edema and ecchymosis among group D, group T and group DT.
Conclusion Tranexamic acid and dexamethasone, separately or in combination, had similar effects in reducing periorbital edema and ecchymosis in open rhinoplasty. Combined application did not show a significantly higher beneficial effect in this regard.
Level of Evidence III This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Rhinoplasty · Edema · Ecchymosis · Dexamethasone · Tranexamic acid · Periorbital

Introduction

Rhinoplasty is one of the most common and complex operations in esthetic plastic surgery [1]. Bruising and swelling are two commonly expected complications immediately after rhinoplasty [2]. They limit the exact postoperative evaluation of the result and can be cumbersome for both the patient and the surgeon. These sequelae may even cause potential candidates to dismiss rhinoplasty [3, 4]. Edema can delay the healing process of the involved tissues, and ecchymosis may lead to permanent pigmentation of the skin [4]. Different kinds of osteotomies are needed in most cases of rhinoplasty and can cause edema and ecchymosis [5]. Lateral osteotomy is the main cause of periorbital and paranasal swelling and ecchymosis [6].

Various methods and concepts have been proposed to decrease edema and ecchymosis with variable success. Suggested medical therapies include intraoperative hypotension, postoperative head elevation, ice packs, nasal packing, drainage tubes and medications such as corticosteroids, decongestants, tranexamic acid, fibrin sealants and lidocaine with epinephrine, herbal agents such as arnica montana, papain, melilotus, bromelain and α-chymotrypsin. Suggested surgical modifications include changing the sequence of osteotomy, external or internal, perforated or continuous lateral osteotomy, subperiosteal tunneling, preservation of periosteal attachment, using a sharp guarded micro-osteotome, piezosurgery or a diamond burr [6–10]. Traditionally, corticosteroids have been widely used in rhinoplasty to reduce the swelling and bruising [2]. Glucocorticoids diminish vascular permeability, leading to less exudation and decreased edema [5]. With a short course and low dose use of steroids, adverse events are minimal because most of the unwanted effects are related to their mineralocorticoid activity [5, 6]. Tranexamic acid is an antifibrinolytic agent and is presumed to prevent dissolution of the fibrin clot and reduce the intensity of bleeding [12]. It is used in certain surgical procedures to limit bleeding, and no adverse effect has been reported in the literature [13].

We present here a prospective triple-blinded study to compare the effect of tranexamic acid and dexamethasone, separately or in combination, on periorbital edema and ecchymosis in primary open rhinoplasty.

Patients and methods

We performed a prospective randomized triple-blinded (patient, surgeon and examiner) clinical trial from May 2015 to June 2017. We performed primary open rhinoplasty in 60 patients after informed consents were obtained. Considering the previous similar studies, the present study assumed an alpha error of 0.05 and 80% statistical power. Fifteen patients were needed in each group. Patients were randomly allocated to four groups via computer-generated random numbers table as follows:

- Group D ($n = 15$) received 8 mg intravenous (IV) dexamethasone.
- Group T ($n = 15$) received 10 mg/kg IV tranexamic acid.
- Group DT ($n = 15$) received 8 mg IV dexamethasone in addition to 10 mg/kg IV tranexamic acid.
- Group P ($n = 15$) received placebo as control group.

Medications were prepared by nurses unaware of the study nature and were applied 1 h before and three doses every 8 h after surgery. Patients with a history of peptic ulcers, diabetes mellitus, body dysmorphic disorder, tuberculosis, herpes simplex, hypertension, known allergy to dexamethasone and tranexamic acid, preoperative use of anticoagulant therapy 5 days before operation, hematologic and fibrinolytic disorders were excluded from the study.

All operations were performed by the last author using the same technique and instruments under general anesthesia. All rhinoplasties during the study period included dorsal hump removal as well as lateral and medial osteotomies in similar fashion. We kept the mean arterial blood pressure between 90 and 100 mmHg during the operation and documented the time of operation and any complications that occurred. All patients were discharged on the first postoperative day although rhinoplasty is routinely performed in an outpatient setting. Head elevation and ice packs were ordered for 48 h postoperatively. Acetaminophen (325 mg, four times a day) and cephalexin

(500 mg, four times a day) were administered for 7 days. Intranasal antibiotic-soaked non-absorbable packs were placed for all patients, which were removed on the third postoperative day. Digital photographs were obtained on the first, third and seventh postoperative days. An expert examiner at our institution, who was blinded to the study, evaluated patient photographs and scored the eyelid edema and ecchymosis based on the scale described by Gurlek et al. (2006) (Table 1) [14].

The average extent of ecchymosis and severity of edema were compared among the groups using a Kruskal–Wallis test and within the groups using a Friedman test. All p values <0.05 were considered to be statistically significant. Pairwise comparisons within and between groups were performed using Wilcoxon and Mann–Whitney tests based on Bonferroni correction (statistical significance at $p < 0.01$). Kruskal–Wallis, Chi square and analysis of variance (ANOVA) tests were used to compare demographic data and operation time between groups. SPSS 16.0 was used for all statistical analysis.

Results

We enrolled 60 patients [27 men and 33 women; age range, 18–39 years; mean age (SD), 27.35 (6.0) years]. The demographic data of patients (age, weight, gender) and operation times are presented in Table 2. We observed no statistically significant difference among the four groups for any of the variables considered (all $p > 0.05$).

Periorbital edema and ecchymosis on postoperative days 1, 3 and 7 are shown in Figs. 1, 2, 3, 4. No complications were observed during the study period for any patient. Figures 5, 6, 7, 8 show periorbital edema and ecchymosis on the seventh postoperative day in four patients of different groups.

Results regarding postoperative edema and ecchymosis on postoperative days 1, 3 and 7 are presented in Table 3. In group D, group T and group DT, periorbital edema and ecchymosis scores were significantly lower compared with the control group ($p < 0.01$). However, there was no statistically significant difference when comparing the periorbital edema or ecchymosis among groups D, T and DT on postoperative days 1, 3 and 7.

Table 1 Scoring system for edema and ecchymosis

Rating	Edema	Ecchymosis
0	None	None
+ 1	Minimal	In the medial canthus
+ 2	Covering to the iris	Extending to the pupil
+ 3	Extending to the pupil	Past the pupil
+ 4	Massive edema	Extending to the lateral canthus

Discussion

In a cosmetic surgery like rhinoplasty, periorbital edema and ecchymosis can fade the cosmetic results and can lead to dissatisfaction for both the surgeon and the patient. Many attempts have been undertaken to minimize these morbidities [3, 5, 6, 11].

Jalali et al. [15] and Sakallioglu et al. [3] compared the effect of tranexamic acid and a steroid on post-rhinoplasty periorbital edema and ecchymosis before. However, there is no study reporting the effect of the combined use of them to date. Also, no study in the English literature compared the efficacy of tranexamic acid and dexamethasone on periorbital edema and ecchymosis in open rhinoplasty. Goldman et al. were the first to present an article supporting the use of steroids to control the unpleasant side effects of rhinoplasty [4]. The use of steroids to reduce postoperative edema is broadly practiced in facial surgery [5]. Most studies have found steroids useful although some studies reported that steroids are of no benefit [11, 16, 17]. Although the literature supports the use of steroids to reduce post-rhinoplasty swelling and bruising, only a minority of surgeons in the UK regularly use them in their practice [6, 11]. At present, there is still no consensus on the use of steroids and it is not the standard of care for all facial plastic surgeons [4]. Steroids are gene-active hormones, and their beneficial or toxic effects may last from a few hours to several days and do not correlate directly with serum concentrations [11]. Among the many different steroids, dexamethasone appears to be the most appropriate due to its highest anti-inflammatory effect with relatively early onset of action in addition to a prolonged biological half-life of more than 36 h [5]. Gurlek et al. [14] observed no significant differences among the various kinds of steroids administered in equivalent doses. Totonchi and Guyuron [2] found that both arnica and corticosteroids might be effective in decreasing edema during the early post-rhinoplasty period. Arnica does not seem to diminish ecchymosis. Besides, the delay in resolution of ecchymosis for patients receiving corticosteroids may outweigh the benefit of reducing edema during the early postoperative period [2]. The only objectively measured report by Berinstein et al. showed a single preoperative dose of dexamethasone increases post-rhinoplasty edema [4, 18]. Gutierrez et al. [4] observed no statistically significant difference in the decrease of both ecchymosis and edema between placebo and high-dose long-acting dexamethasone. Additionally, it was reported that steroids can cause various complications and should not be used in aesthetic

Table 2 Demographic data and operation time

Variable	Group D	Group T	Group DT	Group P	*P* value
Age (year)	27.40 ± 6.71	26.20 ± 5.0	28.52 ± 6.14	27.27 ± 6.48	[1]0.72
Weight (kg)	71.87 ± 8.10	70.27 ± 5.72	73.07 ± 9.17	69.60 ± 5.80	[1]0.77
Operation time (min)	177.33 ± 17.71	183.67 ± 16.95	186.33 ± 15.29	178.33 ± 14.47	[2]0.37
Gender (%)					
M	5 (33.3)	8 (53.3)	7 (46.7)	7(46.7)	[3]0.73
F	10 (66.7)	7 (46.7)	8 (53.3)	8 (53.3)	

Age, weight and operation time were presented as mean ± SD

[1] Kruskal–Wallis test

[2] Analysis of variance (ANOVA) test

[3] Chi-square test

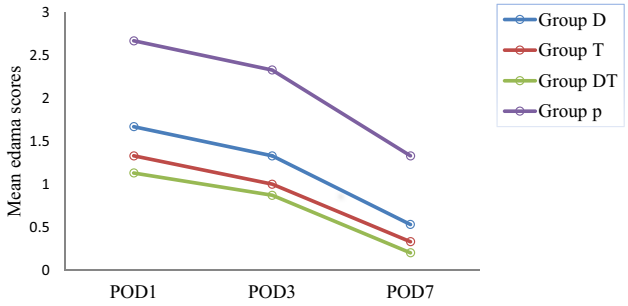

Fig. 1 Mean edema ratings of upper eyelids. POD indicates postoperative day

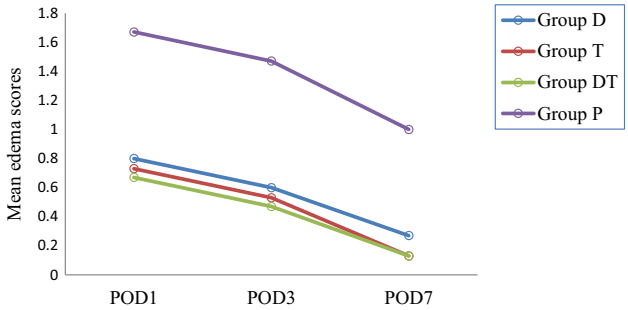

Fig. 2 Mean edema ratings of lower eyelids

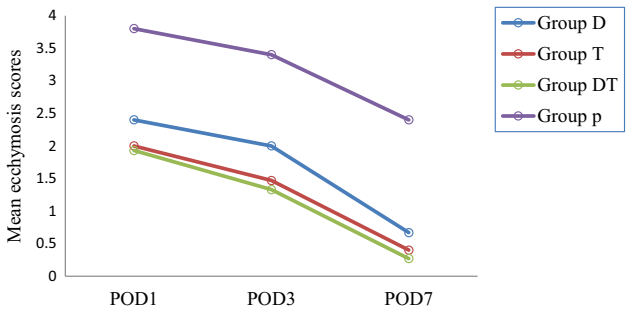

Fig. 3 Mean ecchymosis ratings of upper eyelids

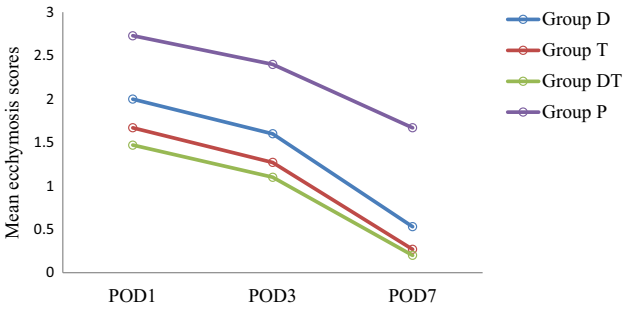

Fig. 4 Mean ecchymosis ratings of lower eyelids

Fig. 5 View of a patient from group D presented on the seventh postoperative day. Upper and lower eyelid edema and ecchymosis scores are, respectively, + 2, + 1, + 4, + 4

surgery [14]. Kara and Gokalan [19] showed that use of a single dose of dexamethasone (either preoperatively or postoperatively) had a significant effect in reducing upper and lower eyelid edema and upper eyelid ecchymosis for the first 2 days in rhinoplasty. Considering the time of

Fig. 6 View of a patient from group T presented on the seventh postoperative day. Upper and lower eyelid edema and ecchymosis scores are, respectively, 0, 0, + 2, + 2

Fig. 7 View of a patient from group DT presented on the seventh postoperative day. Upper and lower eyelid edema and ecchymosis scores are, respectively, + 1, 0, + 1, + 1

application, Hatef et al. [20] concluded that preoperative administration was superior to postoperative and extended application was superior to single. Hwang et al. [21] showed that multiple dose administration of steroids had more benefits in reducing post-rhinoplasty edema and ecchymosis compared to a single dose regimen. Kargi et al. [22] stated that if the first dose was given before osteotomy, triple-dose steroid application was the best to reduce post-rhinoplasty edema and ecchymosis. A recent meta-analysis failed to show steroid advantages after postoperative day 3 [4].

Tranexamic acid is a very valuable drug to reduce almost any kind of bleeding [23]. Experience with tranexamic acid started as soon as it was released from

Fig. 8 View of a patient from group P presented on the seventh postoperative day. Upper and lower eyelid edema and ecchymosis scores are, respectively, + 2, + 1, + 4, + 4

Shosuke Okamoto's lab in the early 1960s. In the clotting cascade, it stabilizes the fibrin clot and reduces total bleeding [13]. It is cheap and has principally few contraindications and is included in the WHO's list of essential medicines [23]. Tranexamic acid is well tolerated, but nausea and diarrhea are the most common adverse events. Increased risk of thrombosis with the drug has not been demonstrated in clinical trials [24]. It is safe and effective and can be recommended for routine uses including epistaxis, menorrhagia and gastrointestinal hemorrhage. Its antifibrinolytic effect is about ten times more than that of aminocaproic acid [25, 26]. Our findings are consistent with the study of Jalali et al. [15]. They observed no significant difference in edema and ecchymosis between the dexamethasone group and the tranexamic acid group on the third day after closed rhinoplasty. Our study confirms the findings of Ghavimi et al. [27]. They demonstrated the effectiveness of tranexamic acid usage on the periorbital edema and ecchymosis on first day after closed rhinoplasty. Our findings are also comparable with the study of Sakallioglu et al. [3]. They found no significant difference, clinically or statistically, in decreasing post-rhinoplasty edema and ecchymosis between application of methylprednisolone intravenously and oral tranexamic acid on the postoperative first, third and seventh days. In the current study, dexamethasone and tranexamic acid, separately or in combination, showed no statistically significant difference in decreasing periorbital edema or ecchymosis, although one may expect that combined application would lead to a significantly higher effect. However, larger clinical trials could bring more light on this issue specially looking at the figures it appears that there is a trend toward combination therapy providing the least edema and ecchymosis.

Table 3 Ratings of edema and ecchymosis in the groups on different days

Variable	Group D	Group T	Group DT	Group P	*P* value[1]
Upper eyelid edema					
POD1	1.67 ± 0.90[a]	1.33 ± 0.48[a]	1.13 ± 0.74[a]	2.67 ± 0.61[a]*	<0.001
POD3	1.33 ± 0.72[a]	1.00 ± 0.65[a]	0.87 ± 0.51[a]	2.33 ± 0.61[a]*	<0.001
POD7	0.53 ± 0.51[b]	0.33 ± 0.61[b]	0.20 ± 0.41[b]	1.33 ± 0.61[b]*	<0.001
P value[2]	<0.0001	<0.0001	<0.0001	<0.0001	
Lower eyelid edema					
POD1	0.80 ± 0.86[a]	0.73 ± 0.79[a]	0.67 ± 0.81[a]	1.67 ± 0.97[a]*	0.01
POD3	0.60 ± 0.73[a]	0.53 ± 0.91[ab]	0.47 ± 1.06[a]	1.47 ± 0.99[a]*	0.004
POD7	0.27 ± 0.45[a]	0.13 ± 0.35[b]	0.13 ± 0.51[a]	1 ± 0.75[b]*	<0.001
P value[2]	0.072	0.044	0.08	0.001	
Upper eyelid ecchymosis					
POD1	2.40 ± 1.12[a]	2.00 ± 0.84[a]	1.93 ± 0.96[a]	3.8 ± 0.41[a]*	<0.001
POD3	2.00 ± 1.41[a]	1.47 ± 0.74[a]	1.33 ± 1.11[a]	3.4 ± 0.5[a]*	<0.001
POD7	0.67 ± 0.97[b]	0.40 ± 0.63[c]	0.27 ± 0.59[b]	2.4 ± 0.75[b]*	<0.001
P value[2]	<0.0001	<0.0001	<0.0001	<0.0001	
Lower eyelid ecchymosis					
POD1	2.00 ± 0.84[a]	1.67 ± 1.04[a]	1.47 ± 1.06[a]	2.73 ± 0.45[a]*	0.001
POD3	1.60 ± 1.05[a]	1.27 ± 0.88[ab]	1.1 ± 0.74[a]	2.4 ± 0.5[a]*	<0.001
POD7	0.53 ± 0.74[b]	0.27 ± 0.79[b]	0.20 ± 0.41[b]	1.67 ± 0.61[b]*	<0.001
P value[2]	0.001	0.001	0.002	<0.0001	

Identical letters mean no statistically significant within each group

Ratings were presented as mean ± SD

POD postoperative day

* Means statistically, it is significantly different among the groups

[1] Kruskal–Wallis test

[2] Friedman test

The limitations of the present study were the small sample size and inclusion of only one examiner. Using objective techniques, for example, MRI, volumetric three-dimensional stereophotogrammetry, stereolithography and ultrasonography, for measuring edema and Photoshop for determining the intensity and extent of ecchymosis would add to the strength of the study. Nevertheless, comparing the efficacy of tranexamic acid and dexamethasone on postoperative complications, patient and surgeon satisfaction, intraoperative bleeding and operative field visibility in rhinoplasty would be a worthwhile point to investigate by further studies. Additionally, different types of steroids, dosages, routes of administration and dosing schedules of tranexamic acid and dexamethasone should be considered in future studies.

Conclusion

Tranexamic acid and dexamethasone are each helpful in reducing periorbital edema and ecchymosis in open rhinoplasty patients and should be used thoughtfully based on patient allergies and potential side effects. Combination therapy, however, does not appear to provide significant added benefit.

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Compliance with ethical standards

Conflicts of interest We have no conflict of interest to declare.

Ethics statement/confirmation of patients' permission We have no financial interest and we did not have any financial or material support concerning this study. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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