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# The Effect of Intravenous Tranexamic Acid on Postoperative Ecchymoses after Upper Blepharoplasty

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**Background:** Tranexamic acid has been increasingly used in facial plastic surgery to improve perioperative hemostasis. While subcutaneous tranexamic acid has been found to not significantly decrease postoperative ecchymoses following upper blepharoplasty, systemic administration has not previously been studied.
**Methods:** A total of 325 patients undergoing upper blepharoplasty were randomly assigned to either receive intravenous tranexamic acid or serve as a control. Patients in the experimental group were administered 1 g of tranexamic acid intravenously 10 minutes before surgical incision. A similar upper blepharoplasty technique was performed by two American Society of Ophthalmic Plastic and Reconstructive Surgery-trained surgeons. Follow-up was conducted at a median of 8 days post-surgery. Patient photographs were evaluated by two independent graders to rate ecchymoses on a scale of 0 (least) to 10 (most).
**Results:** Of the 325 included patients, 138 patients received intravenous tranexamic acid and 187 patients did not. The average ecchymosis rating for the control group at day 8 was 5.8 ± 1.7, while the average rating for the tranexamic acid group at the same time point was 4.1 ± 1.6 ($P < 0.0001$). There was a trend toward decreased ecchymoses in the tranexamic acid group at earlier and later postoperative time-points that did not reach statistical significance. No hemorrhagic or systemic embolic complications occurred.
**Conclusions:** Systemic tranexamic acid may reduce postoperative ecchymoses after upper blepharoplasty surgery, reaching significance at the eighth post-operative day, which may lead to improved patient satisfaction and decreased occupational downtime. *(Plast Reconstr Surg Glob Open 2024; 12:e6089; doi: 10.1097/GOX.0000000000006089; Published online 26 August 2024.)*

## INTRODUCTION

Upper blepharoplasty is among the top five most common procedures performed in the United States.[1–3] Although surgical satisfaction rates are generally high, postoperative periorbital ecchymoses may limit patient contentment and prolong occupational downtime. Thus, numerous investigations of methods to optimize perioperative hemostasis have been performed.[1] A randomized-controlled-trial comparing scalpel and electrocautery skin incision techniques did not find differences in postoperative hemostasis.[4] Although routine application of cold compresses following surgery may alleviate pain, the efficacy in ecchymosis and edema reduction has not been proven.[5] Evaluation of Arnica and Bromelain supplementation have not demonstrated a statistically significant difference in ecchymoses compared with placebo.[1,6,7] Fibrin glue application was demonstrated to decrease postoperative ecchymoses only in patients on antithrombotic agents.[8] Recent studies investigating the effects of magnesium sulfate wet dressing on ecchymosis following blepharoplasty demonstrated

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promising hemostatic results, though the application is limited due to concerns of skin irritation.[9]

Tranexamic acid (TXA) has been recently adopted in various surgical specialties to reduce blood loss and speed postoperative recovery.[10] TXA was first patented in 1957 and is a synthetic lysine analog that promotes coagulation through multiple pathways.[10] TXA inhibits the conversion of plasminogen to plasmin, thereby preventing fibrin clot breakdown.[11] The medication also blocks plasmin-induced platelet activation, promoting coagulation.[11,12] Additionally, TXA may play an antiinflammatory role in the healing process.[13] TXA may be administered intravenously or subcutaneously at the time of surgery. Many surgeons have favored the use of locally administered TXA to limit systemic absorption and decrease the need for epinephrine, which can induce vasospasm, increased blood pressure, and tachycardia.[10] Although prior studies investigating subcutaneous TXA for blepharoplasty suggested a slightly decreased ecchymosis formation, the difference was not statistically significant.[14] However, studies investigating TXA in patients undergoing rhinoplasty and rhytidectomy have found a statistically significant decrease in ecchymoses compared with placebo when used in both intravenous and topical forms, without a compromise in safety.[15–18] In this study, we evaluated the use of systemic intravenous TXA in patients undergoing upper blepharoplasty to determine safety and its effect on postoperative ecchymosis.

## Takeaways

**Question:** Does intravenous tranexamic acid (TXA) reduce ecchymoses after upper blepharoplasty?

**Findings:** Patients who were randomly assigned to receive intravenous TXA had fewer apparent ecchymoses 1 week after upper blepharoplasty compared with controls.

**Meaning:** The use of intraoperative intravenous TXA significantly reduces ecchymoses 1-week after upper blepharoplasty.

## METHODS

Patients presenting for an isolated upper blepharoplasty procedure at one of the two surgery centers from February 2019 through May 2021 were included. The patients who met inclusion criteria were randomized to either the intravenous TXA group or control groups by an automated random group assignment. Exclusion criteria included patients with underlying hypercoagulabile medical disorders, history of blood clots, and use of medications known to prolong ecchymosis. Patients in the experimental group were administered 1 g of TXA intravenously 10 minutes before surgical incision. All patients received the same 3 mL of local anesthetic mixture consisting of a 1:1 mixture of lidocaine with 1:100,000 epinephrine and 0.5% bupivacaine in each upper lid. A similar upper blepharoplasty technique was performed by two American Society of Ophthalmic Plastic and Reconstructive Surgery–trained oculoplastic surgeons, which included a skin-only resection flap with scalpel and medial fat pad debulking (Fig. 1). Immediately postoperatively, ice packs were applied to the bilateral surgical sites for 15–20 minutes. Standard postoperative instructions were given for home care to include a regular icing protocol and activity restrictions for the first postoperative week. Patients were instructed to avoid over-the-counter medications and supplements that may increase ecchymosis. Postoperative follow-up was conducted at a median of 8 days (range 1–27 days), and patient photographs were taken during the visit. Photographs were independently evaluated by two American Society of Ophthalmic Plastic and Reconstructive Surgery–trained oculoplastic surgeons blinded to the treatment group to quantitively rate ecchymoses on a scale of 0 (least) to 10 (most) (Fig. 2). A standardized ecchymosis scale with example patient photographs was provided to the graders for their reference during the grading process. Data were grouped according to postoperative day to assess differences in postoperative ecchymosis longitudinally. Statistical analyses were performed via two-tailed $t$ test, with a $P$ value of less than 0.05 considered significant. The patients and the independent graders of the postoperative photographs were blinded to treatment group. The study was performed with HIPAA-compliance and institutional review board approval, in accordance to the Declaration of Helsinki.

## RESULTS

A total of 325 patients were included. Of these, 138 patients received intravenous TXA and 187 patients did not receive TXA. Such discrepancy exists because each patient was truly randomized to the treatment or control

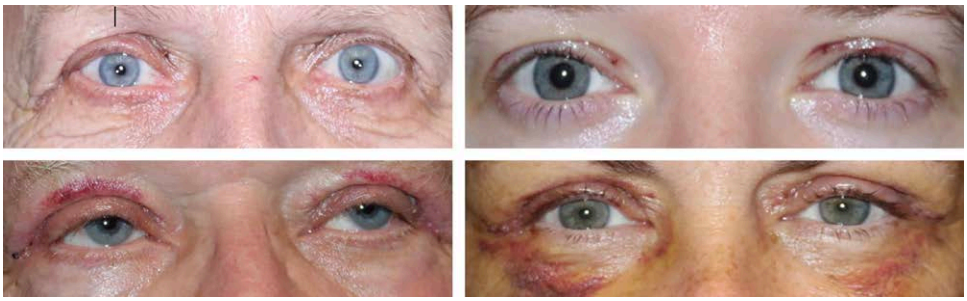

**Fig. 1.** Example patient photographs taken at the postoperative visit day 8 for ecchymosis grading.

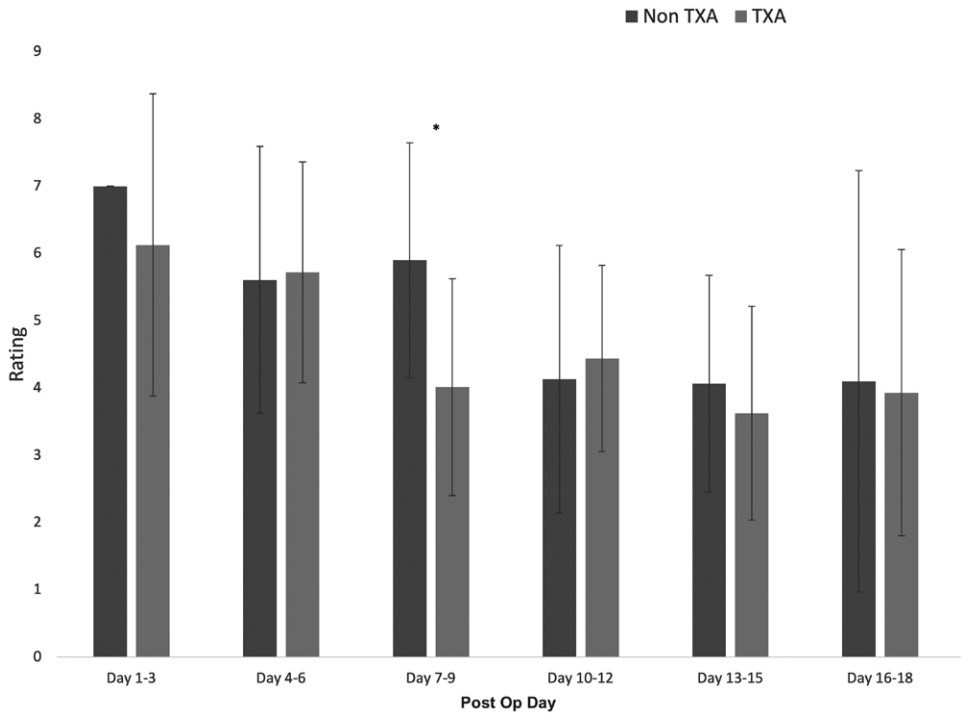


**Fig. 2.** Graphical representation of average ecchymosis grading for 3-day postoperative time intervals comparing the TXA cohort (light gray) with the non-TXA cohort (dark gray). SD is depicted by the black error bars. The asterisk depicts statistically significant difference in ecchymosis grading between the TXA and non-TXA cohorts at days 7–9.

group via an automated random group assignment, rather than a preset requirement for a certain number of patients in each group. The average age of patients was 62 years in the TXA group and 64 years in the non-TXA group. There was no statistically significant difference in age or gender between the TXA group and the non-TXA group (Table 1).

Patients were evaluated at a median 8 days after surgery (range 1–18 days). The average ecchymosis rating for the non-TXA group at day 8 was $5.8 \pm 1.7$, whereas the average rating for the TXA group at the same time point was $4.1 \pm 1.6$ ($P < 0.0001$). (**See figure, Supplemental Digital Content 1,** which displays the representative intraoperative photograph demonstrating a skin-only upper eyelid blepharoplasty resection flap with medial fat pad excision. **http://links.lww.com/PRSGO/D445**.) Although there was no statistical difference at earlier or later timepoints following surgery, there was a trend toward decreased ecchymoses in the TXA group for all but the postoperative days 4–6 and 10–12 time points (Table 2). There were no TXA-related adverse reactions; hematologic complications, including retrobulbar hematoma; or systemic thrombic complications in either group.

## DISCUSSION

Although ecchymoses are inevitable and typically minor following upper blepharoplasty, reducing postoperative bruising is a goal of surgeons and patients alike to increase patient satisfaction and decrease postsurgical downtime.[19] Significant and slowly resolving ecchymoses may also lead to prolonged hyperpigmentation through cutaneous staining from red blood cell product degradation.[20] TXA, as an antifibrinolytic drug, has been found to significantly decrease bleeding after some surgery types.[15] The randomized controlled study presented herein found a statistically significant reduction in postoperative ecchymosis in patients undergoing blepharoplasty at the 1-week postoperative time period, specifically at postoperative day 8, with a trend toward fewer ecchymoses at earlier and later time points. These data suggest that systemic TXA may have a beneficial role in decreasing ecchymoses postblepharoplasty.

While TXA is classically known to enhance hemostasis via inhibition of plasminogen activation into plasmin, there are other antiinflammatory benefits to limiting plasmin formation.[13] Plasmin promotes production of cytokines and the inflammatory cascade, which results in poorer postoperative outcomes, including prolonged erythema, edema, and pain.[13] Prior studies have investigated oral TXA after open septorhinoplasty and have found an improved reduction of periorbital edema and ecchymosis after using a combination of TXA and intravenous methylprednisolone compared with TXA alone.[21] Future studies in oculofacial surgery that incorporate various additional antiinflammatory agents to synergistically enhance the therapeutic effects of TXA postoperatively may be informative. The hemostatic benefits of TXA may also lead to decreased cautery requirements and operative time.[22] Risks of TXA include thromboembolic complications and

**Table 1. Patient Demographics**

| | TXA (n = 138) | Non-TXA (n = 187) | *P* |
|---|---|---|---|
| Age (average, in years) | 62 | 64 | 0.28 |
| Female | 101 | 129 | 0.66 |
| Male | 37 | 58 | 0.49 |

**Table 2. Average Ecchymosis Grading for Postoperative Time Intervals Comparing Patients in the TXA and Non-TXA Groups**

| | Average Ecchymosis Grading (0–10 Scale) | | |
|---|---|---|---|
| | TXA | Non-TXA | *P* |
| Postoperative day 1–3 | 6.13 | 7.00 | 0.17 |
| Postoperative day 4–6 | 5.72 | 5.60 | 0.85 |
| Postoperative day 7–9 | 4.01 | 5.90 | <0.0001* |
| Postoperative day 10–12 | 4.44 | 4.13 | 0.51 |
| Postoperative day 13–15 | 3.63 | 4.06 | 0.29 |
| Postoperative day 16–18 | 3.93 | 4.10 | 0.91 |

*$P < 0.05$ considered statistically significant.

seizures, and it cannot be used in patients with associated predisposition.[23]

Sagiv et al demonstrated a trend toward reduced postoperative ecchymoses with subcutaneous injection of TXA in upper blepharoplasty compared with placebo that did not reach statistical significance in 34 treated patients.[14] The current study instead used intravenous TXA, as is more commonly used in the plastic surgery literature, and confirmed significantly reduced ecchymoses. The reason for this significance may be multifactorial. The current study had a markedly larger enrollment of 325 total patients. Furthermore, the route of TXA administration also likely plays a role in its efficacy. These authors propose that systemic TXA may work more effectively than subcutaneous forms via faster time to peak concentration, as highlighted in physiologic models.[24] Additionally, the incorporation of TXA to a local anesthesia mixture may dilute alternative hemostatic agents such as epinephrine, which may be additive in effect when combining with systemic TXA. These authors suggest future head-to-head comparison study of multiple routes of administration (subcutaneous versus oral versus intravenous) for further assessment of superiority.

One hypothesis for why statistically significant effects were not observed in the earlier postoperative period is due to the smaller number of patients presenting for a postoperative appointment earlier than 1 week. Additionally, postoperative swelling was likely more pronounced initially and potentially led to higher ecchymosis scores being given by graders. With a majority of patients being seen for follow-up on day 8, a smaller sample size in the later postoperative period could have also led to less significant results, as well as influences from inherent limitations.

This study has several limitations. Although there was an effort to ensure photography parity with equal lighting and angle, as well as distance from camera to patient, any slight variability present could alter ecchymosis ratings. Furthermore, patient adherence to recommended postoperative interventions that may influence ecchymoses, including application of cold compresses and activity limitation, may differ between the two patient groups. Variability in postoperative follow-up time was present but accounted for statistically by comparing only those patients who presented during the same postoperative 3-day interval. Surgical factors such as operative time, cautery time and other postoperative outcome measures, such as long-term healing, were not assessed between the two groups. Note must be made that, although trends toward decreased ecchymoses were seen in early and late postoperative periods, statistical significance was only reached on day 8, and therefore, a full risks and benefits discussion must still be completed between the patient and the surgeon, which is personalized and outside the scope of this article.

Systemic TXA reduces postoperative ecchymoses 1-week after upper blepharoplasty surgery, which may lead to increased patient satisfaction, decreased social and occupational downtime, and reduced risk for prolonged hyperpigmentation. Further studies comparing oral and systemic forms of TXA, to optimize both efficacy and safety, would be of benefit. Additionally, testing in other periorbital procedures, including lower blepharoplasty, could potentially be pursued.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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## DISCLOSURE

*The authors have no financial interest to declare in relation to the content of this article.*

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