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Tranexamic Acid in Rhytidectomy: A Split-Face Multi-Institutional Study

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Abstract

Background: Tranexamic acid (TXA) has the ability to reduce intraoperative bleeding and facilitate hemostasis in addition to its anti-inflammatory properties that can potentially aid in recovery among patients who underwent rhytidectomy.

Objective: To compare postoperative ecchymosis in patients who underwent rhytidectomy with TXA added to the tumescent anesthetic.

Methods: A multi-institutional, single-blind study was performed on patients who underwent rhytidectomy. The sidedness of the face was randomized to receive either local anesthetic with TXA or without, prior to incision for rhytidectomy. The primary outcome was postoperative ecchymosis that was graded by the surgeons at the 1 week postoperative time frame in standard photograph review.

Results: A total of 70 patients, mean age 62.1, were enrolled in the study. The surface area of postoperative ecchymosis at 1 week was shown to be significantly less on the side of the face that received local anesthetic infiltration prior to incision with TXA than the side that had local anesthetic without TXA ($p < 0.001$). These results were consistent with subjective measurements of postoperative ecchymosis graded at 1 week with two blinded investigators to the sidedness of the face that received TXA ($p < 0.001$).

Conclusions: TXA may potentially facilitate a reduction in postoperative ecchymosis in patients undergoing rhytidectomy.

Introduction

Tranexamic acid (TXA) has grown in popularity in facial plastic surgery procedures to aid in hemostasis. TXA works as an antifibrinolytic agent preventing the activation of plasminogen to plasmin and the enzymatic degradation of fibrin clot. This cascade reduces plasmin-induced platelet activation leading to a higher circulating platelet count to aid clotting as the surgical procedure progresses.[1] TXA became popular after its discovery in 1957 and since has become a household name among cardiac and orthopedic surgeons to reduce blood loss, improve operative visibility, and reduce the need for transfusion while proving to be a safe addition to their surgical procedures.[2–4] In recent years, its benefits have been recognized in facial plastic surgery and thus incorporated into many of our procedures.[5–17]

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KEY POINTS

Question: Does the addition of tranexamic acid to local anesthetic prior to incision for facelift surgery facilitate postoperative reduction of bruising?

Findings: In our multi-institutional, prospective, split-face study of 70 patients, we found that the addition of tranexamic acid to local anesthetic significantly decreased postoperative bruising compared with the side of the face that was not treated with tranexamic acid.

Meaning: The use of tranexamic acid in local anesthetic prior to facelift surgery can potentially decrease postoperative bruising.

Minimizing blood loss and achieving hemostasis are critical in surgeries such as rhytidectomy to prevent complications such as hematoma and wound healing compromise. However, as plastic surgery continues to improve operative procedures, our attention has focused on creating experiences for patients that lead to improved postoperative recovery. As its off-label use in facial plastic surgery has evolved, many studies focus on its hemostatic properties in bleeding, preventing hematoma, limiting drain use, and shortening operative times. Because of TXA's different mechanisms of action and prolonged hemostatic effect lasting up to 24 h, it is thought to prevent rebound bleeding seen with epinephrine and its complications, which plagues 1–15% of all cases.[18]

Multiple prior studies using TXA in facelift surgeries have focused on bleeding and prevention, but little have objectively looked at its effects on postoperative healing or ecchymosis reduction.[11,12,15–17] Some other surgeries such as blepharoplasty and rhinoplasty have incorporated the use of TXA with promising results in respect to decreased bleeding and bruising.[13,14]

TXA has been known for its ability to reduce intraoperative blood loss, with theories suggesting it may also have properties that enhance recovery through reduction of postoperative ecchymosis. Plasminogen not only undergoes fibrinolysis but also binds with receptors on some inflammatory cells and also blocks the plasminogen inflammatory cascade.[19,20] Numerous methods have been studied to decrease postoperative ecchymosis and are regularly employed such as postoperative head elevation and cool compress application in conjunction with medications and supplements such as corticosteroids, *Arnica montana*, and bromelain. While all facilitate the recovery process, TXA may also be a useful addition to reduce postoperative ecchymosis.

In this single-blinded, split-face, randomized, multi-institutional study, we compare the association of including TXA in the local anesthetic injection during rhytidectomy, with a control side of the anesthetic only, and measuring the bruising at 5–9 days postoperatively using standardized photographs and a blinded surgeon survey.

Methods

This prospective, multi-institutional, randomized investigation was performed by three board-certified facial plastic surgeons from October 2020 to May 2022 in New York, Alabama, and Indiana. Institutional review board (IRB) approval was granted at each of the three surgical offices prior to the initiation of the study: Pearl IRB #34127, NYMC IRB #14065, and WCG Clinic #20220402. Patients over the age of 18 were stratified into one of two groups that met the inclusion criteria for the study: any English-speaking male or female patients over the age of 18 undergoing traditional rhytidectomy for signs and symptoms of aging predetermined by the facial plastic surgeon can be candidates for rhytidectomy; this includes those with rhytids, loss of fat (volume), jowling, loose or excess skin, laxity of skin, and loss of youthful contours of the face. Exclusion criteria included those unable to understand the research protocol, those with incomplete medical records, those lost to follow up, who are current smokers or who could not be off blood-thinning agents, and those with allergies or contraindications to anesthetic agents and vulnerable populations (adults unable to consent, individuals who are not yet adults, wards of the state/prisoners). Each patient served as her/his own control, randomized to receive local anesthetic with TXA to their right or the left side. All identifying patient health information was removed prior to randomization.

All patients underwent either a deep plane or a biplanar superficial musculoaponeurotic system (SMAS) imbrication cervicofacial rhytidectomy. Local anesthetic solution was infiltrated along all the areas to be undermined during the rhytidectomy after anesthesia induction. The control and study side each received equal parts of the local anesthetic, with the only difference being the addition of TXA. All patients had a concentration of 1 mg/mL of TXA added to their tumescent solution and infiltrated in a subcutaneous plane for the randomized side of their face. The nature of the infiltration solution at each site was unknown to the surgeon and blinded assessors. The primary outcome was percentage of ecchymoses on the left and right sides. Photo documentation was taken in the standard 5-view Frankfort plane series preoperatively and postoperatively on day 7. An objective analysis of ecchymosis was calculated using ImageJ software. In the lateral Frankfort horizontal position, a tracing tool was used to calculate the surface area of the entire patient's face and neck that was infiltrated with local anesthetic prior to rhytidectomy. We employed a similar grading system used by Fayman et al. who employed a similar split-sided study using TXA in tumescent solution infiltrated to one flank in

patients undergoing liposuction and compared with ImageJ software to the other flank that did not receive TXA. They found that TXA consistently resulted in a smaller area of ecchymosis similar to our study.[21] This measurement remained constant for every individual patient in each postoperative standardized photograph. Again, using the tracing tool, the surface area of ecchymosis was outlined and calculated on postoperative day 7 (average 7.2 ± 2.6). The surface area of ecchymosis was expressed as percentages.

Secondary outcomes included a subjective questionnaire that required grading of the postoperative ecchymosis by two blinded investigators to delineate between the sides of the face that received TXA. Patient eyes were concealed, and identity was removed before pictures in both the lateral and oblique views were analyzed independently. Ecchymosis was graded on a Likert scale that ranged bruising from 0% to 100%. Ecchymosis scores ranged from 0 to 4 and converted into percentages. The scale is recorded as follows for ecchymosis:

0–1, mild to moderate: (0–24% of the face)
0–2, 1–2 moderate: (25–49% of the face)
0–3, 2–3 moderate-severe: (50–74% of the face)
3–4 severe: (75–100% of the face).

Complications such as postoperative hematoma, seroma, flap necrosis, infection, and delayed wound healing in the immediate postoperative period were recorded.

Statistical analysis was performed using SPSS (version 24), IBM SPSS Statistics. A 20% decrease in ecchymosis between sides was considered by the investigators to be potentially clinically relevant, given the majority of studies that look at postoperative reduction in bruising find clinical relevance between 15% and 30%.[22–26] Using a power of 0.90, and a two-tailed alpha of 0.05, we estimated 45 patients to be clinically relevant and aimed to enroll at least 60 to account for any dropouts. Based on these calculations, if the expected effect size is medium (0.5) or larger, the sample size of 45 (with a target enrollment of 60 to account for dropouts) should be sufficient to achieve a power of 0.90 at a significance level of 0.05. The Mann–Whitney–Wilcoxon signed rank test was used to compare the percentage of ecchymosis on postoperative day 7 between the control and study sides. A 2-tailed paired samples *t*-test was used to compare results of subjective ecchymosis scores between the two sides on the blinded questionnaire. Categorical variables were evaluated via Pearson chi-square tests and assessed using frequencies and percentages. A p value of <0.05 was selected for statistical significance.

Results

A total of 70 patients from our surgeon practice sites (2 males, 68 females, mean age 62.1 ± 8.3) were enrolled in the study from October 2020 to May 2022 (Table 1). No significant difference was noted between the age and gender among patients when stratified by site. Patients were regularly seen multiple times between days 1 and 14 in their immediate postoperative period, and standardized photographs in the Frankfort horizontal plane were used on day 7 (average 7.2 ± 2.6) for image analysis with Image J. The volume of anesthetic injected was controlled to be equal among the left and right sides with the only difference being the addition of TXA. No patients in the study had a history of prior or current smoking or prior thromboembolic events.

A visual assessment of postoperative ecchymosis was analyzed from standardized photographs taken at their 1-week postoperative visit. Using ImageJ software, a blinded investigator compared and calculated the area of bruising on the left and right sides of the face of each patient. The control side was noted to have an average percent surface area of 28.5 ± 12.1 between the three surgical sites with noticeable ecchymosis at 1 week postoperative, compared with the TXA that had an average percent ecchymosis surface area of 20.8 ± 10.2. This was statistically significant ($p < 0.001$) (Fig. 1). Results were calculated before and after controlling for patients who experienced postoperative hematoma, which would lead to more ecchymosis, in order to isolate the impact of this variable on overall outcomes and ensure the accuracy and reliability of the findings. Similar results were noted on the side that received TXA where patients were

Table 1. Patient characteristics by surgeon practice site

Variable	*Surgeon practice site 1*	*Surgeon practice site 2*	*Surgeon practice site 3*	*Total average*	p-*Value*
Age (years) (mean, SD) Range	60.7 ± 7.1 (49–72)	63.7 ± 7.9 (43–79)	60.3 ± 8.7 (44–77)	62.1 ± 8.3 (43–79)	0.25*
Sex	0—M (0%) 10—F (100%)	1—M (3.1%) 30—F (96.9%)	1—M (3.3%) 29—F (96.7%)	2—M (2.9%) 68—F (97.1%)	0.82*
Mean Follow-up time ImageJ analysis of ecchymosis				7.2 ± 2.6	

p-Values were calculated using a chi-square test for discrete variables and a *t*-test for continuous variables.
*None of the *p* values reached statistical significance.
SD, standard deviation.

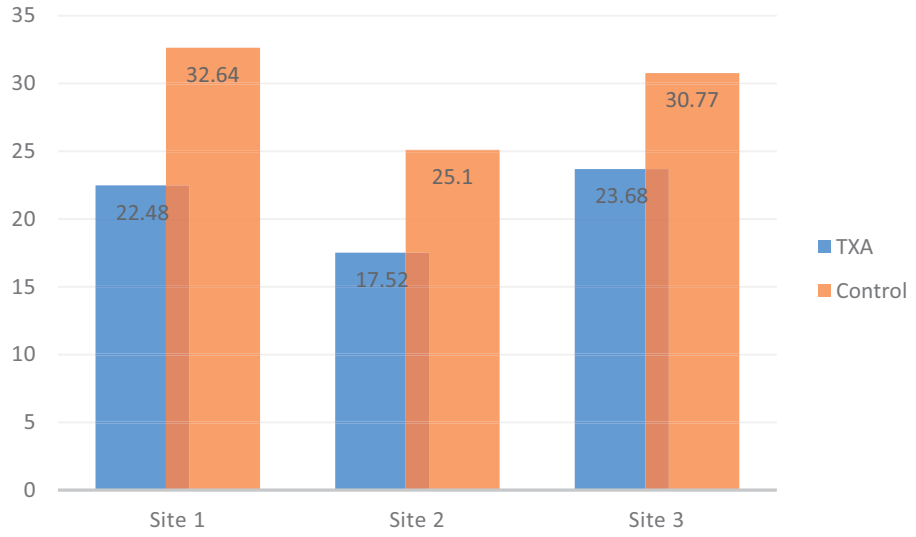

Fig. 1. Postoperative ecchymosis measured by blinded observer (%) stratified by the side of the face TXA (blue) and control (orange) at each surgeon practice site. TXA—side of the face that received tumescent anesthetic with TXA (blue). Control—tumescent anesthetic without TXA (orange). TXA, tranexamic acid.

significantly less bruised ($p < 0.001$). No differences were noted between the three surgeon practice sites when their control and study groups were compared. Results were similar notwithstanding different surgeons performing the procedures (Table 2).

Ecchymosis was subjectively scored by two blinded investigators to the sidedness and patient on a Likert scale with average scores compared between the study and the control groups. The TXA side had an average graded ecchymosis score of 0.9 ±0.5 (20.9% ± 11.4) compared with the side without TXA 1.2 ± 0.6 (29.5% ± 14.1) which reached statistical significance ($p < 0.001$) (Table 3). The first blinded investigator was able to correctly identify the TXA side of the face 84.3% of the time, while the second investigator was able to correctly identify the TXA side of the face 85.7% of the time. Between the two investigators, 14/70 patients (20%) were incorrectly assumed to have received TXA on the side of the face that did not receive TXA. In patients where the side of the face was incorrectly identified as having received TXA, the average percent difference in bruising between sides was less than 3.8% ± 3.7. Patients who showed a greater percentage of ecchymosis between their left and right sides of the face were more noticeable to blinded investigators. The objective measurements of ecchymosis were then compared with the subjective scorings completed. Consistent results were noted notwithstanding two different scoring systems.

Operative times were slightly higher on the control side with an average 50.3 ± 15.1 compared with the TXA side of 48.2 ± 13.7 min but did not reach statistical significance ($p = 0.22$). A single-sided hematoma occurred in two (2.8%) patients in the cohort, all occurring on the control side ($p = 0.77$). Among the control group, six

Table 2. Percentage of postoperative ecchymosis on the face between surgical practice sites, stratified by sidedness

	Study (tranexamic acid) side	*Control (tranexamic acid) side*	p-*Value*
Surgeon practice site 1	22.5 ± 8.4	32.6 ± 10.5	0.01*
Surgeon practice site 2	17.5 ± 10.1	25.1 ± 13.1	0.03*
Surgeon practice site 3	23.7 ± 10.2	30.8 ± 10.9	0.02*
Total (all cases)	20.8 ± 10.2	28.5 ± 12.1	<0.001*
Total (all cases) excluding hematoma	20.9 ± 10.3	28.2 ± 11.9	<0.001*

p-Values were calculated using the Mann–Whitney–Wilcoxon signed rank test.

*Statistical significance <0.05.

Table 3. Percent of correctly identifying the study (TXA) and control (no TXA) side of the face by blinded investigators

	Study (TXA) side	*Control (no TXA) side*	p-*Value*
Ecchymosis percent scores (mean, SD) 1 week postoperative	20.9 ± 11.4	29. 5 ± 14.1	<0.001*
Ecchymosis graded scores (mean, SD) 1 week postoperative	0.9 ± 0.5	1.2 ± 0.6	<0.001*
Operative time (minutes, SD)	48.2 ± 13.7	50.3 ± 15.1	0.22
Hematoma (%)	0 (0)	2 (2.86%)	0.39
Seroma (%)	0 (0)	6 (8.57%)	0.38
Delayed healing	0 (0)	0 (0)	1

Postoperative complications compared between control and study group. *p*-Values were calculated using a *t*-test or for continuous variables and a *t*-test for discrete variables.

*Statistical significance <0.05.

TXA, tranexamic acid.

patients were found to have a single-sided seroma compared with zero patients in the TXA group (8.6%). One patient in the control group (1.4%) required prolonged placement of a seroma catheter. No patient displayed signs of delayed wound healing, necrosis, or infection in the study (Table 3) or had any systemic complications such as thromboembolic, major cardiac, or neurological events.

Discussion

As surgical techniques have evolved in the safety and efficacy of a rhytidectomy, there has been a shift toward speeding up recovery time, enhancing wound healing, and preventing complications. Commonly patients are motivated toward cosmetic surgery by significant life events, stressing the importance of returning to their daily routine as soon as possible. Significant ecchymosis after surgery can adversely impact a patient's experience, satisfaction, and perceived success of the operation.[21] TXA has been used widely for years by other surgical services for its well-known hemostatic ability[20,27–29] and now may be found to have secondary wound healing benefit because of the intimate relationship between the fibrinolytic and pro-inflammatory pathways that it inhibits.[1,21,30] Our study focused on postoperative ecchymosis reduction, and we found that in addition to its hemostatic abilities consistent with other literature, the addition of TXA in local anesthetic during rhytidectomy decreased ecchymosis through both subjective and objective results.

While standardized photography is consistently taken during the recovery period, we noted in our study that the seventh postoperative day was when the height of postoperative ecchymosis was observed and could be most consistently quantified between the left and right sides. Several studies utilizing TXA in rhinoplasty have been done in relation to postoperative periorbital edema and ecchymosis with noticeable subjective improvement among the TXA groups in all studies, whether or not it has reached significance.[7,10,14] While many studies using TXA in various forms in rhytidectomy have shown potential benefits to facilitate decreased bleeding, only another rhytidectomy study to date delved into an analysis of postoperative ecchymosis.[11,12,15–17] Fathimani et al. performed a retrospective cohort study of 70 patients who underwent cervicofacial rhytidectomy with tumescent solution with or without TXA. They looked at time till ecchymosis resolution and found that 60% of patients in the TXA group had bruising cleared within 7 days compared with 0% in the non-TXA group, and only 2.2% of the TXA group still had bruising by day 28 compared with 52% of the non-TXA group.[31]

Although ecchymosis is common after surgical procedures, no validated standardized grading scales exist for the face. Many studies are small and rely on simplistic measurements, which require a well-powered study to reach statistical significance. The Surgeon Periorbital Rating of Edema and Ecchymosis questionnaire is one of the first grading scales to quantify and reliably rate periorbital edema and ecchymosis that can be used after some facial surgery such as blepharoplasty and rhinoplasty but fails to address the larger areas of the face affected in rhytidectomy.[32] Creating a streamlined questionnaire and grading system as we sought to accomplish in our study gives investigators performing the grading a more objective approach to measuring postoperative ecchymosis. Blinded investigators consistently ranked the side that received TXA to have less ecchymosis than the control that showed statistical significance. When asked to stratify the patients between the side they believed to have received TXA, blinded investigators were able to correctly assign the study (TXA) side over 84% of the time. In patients where the sidedness to TXA was incorrectly chosen, we saw a narrow difference in their objective ecchymosis scores between the control and study sides with a percent difference of 3.8%.

Using the ImageJ software to quantify and give an objective measurement for ecchymosis, we could correlate our perceived benefit and results from the questionnaire with actual objective results. The results are consistent in showing a significant difference in objective measurements for ecchymosis between the control and study sides of the patient's face that received TXA (Fig. 2). Many surgeons employ postoperative regimens that also try to reduce postoperative inflammation with promising results that work systemically to aid the patient in recovery. Bruising is generally less extensive with a deep plane facelift compared with a SMAS facelift given the dissection occurs beneath the SMAS layer, with minimal trauma to blood vessels and less disruption of the skin's blood supply, resulting in reduced bruising. Conversely, the SMAS facelift involves more superficial tissue manipulation, which can cause more vascular disruption.[33] The advantage of a split-face study even among three different surgical sites where techniques and potential postoperative regimens differ is that using patients as their own control allowed us to determine solely the effect of TXA on the patient's recovery and eliminate inter-patient variability, which is common for differences in postoperative ecchymosis and recovery.

Local complications were recorded for each patient, and sidedness remained blinded until the conclusion of the study. All postoperative hematomas (2/70) and seromas (6/70) were noted to be on the side that did not receive TXA. While the incidence of postoperative seromas and hematomas remains low in rhytidectomy, they can cause prolonged recovery and wound healing compromise. Although our results did not reach statistical significance because of the small population size, they are worth mentioning as a potential benefit in reducing these frustrating complications. No infections or delayed wound healing was noted in any patient in our study. No

Fig. 2. Patients demonstrating the difference between the side of their face that received tranexamic acid (TXA) compared with the side that did not at 1 week postop. All were correctly guessed by blinded investigators. Example of a patient whose sidedness was incorrectly chosen by blinded investigators.

thrombotic or systemic events occurred in patients receiving TXA, which is consistent with the literature noting its low systemic risk profile.[7,11,20,27,34] Operative times were also noted to be shorter on the TXA side of the face (48.1 min) compared with the control side (50.3 min). While this did not reach statistical significance, there could be a slight advantage of using TXA as an aid in hemostasis throughout the operation. Epinephrine is commonly used in local anesthetic during rhytidectomy and was used as part of the mixture in our study, so maintaining a bloodless field is a common practice even prior to the advent of TXA's introduction. However, rebound bleeding is a concern once the epinephrine's vasoconstrictive properties wear off, begging the question of whether TXA could be a safer alternative eliminating the risk of rebound bleeding and postoperative complications such as hematoma. More studies are warranted to further pursue this possibility.

Most recently, a survey study among facial plastic surgeons sought to investigate the incidence and nature of TXA-related complications with cutaneous flap surgery. Among the respondents, 121 complications were reported with flap necrosis in an unusual pattern being the most common. In addition to recall bias being a limited of survey studies, various concentrations and routes of administration for TXA were used, which begs more research to be conducted in its use during facial plastic procedures.[35]

Limitations include a small population size and potential variability among rhytidectomy techniques. While patients remained their own control, we believe that this limitation is negligible given our strong results.

Conclusions

In conclusion, our split-face study demonstrated a trend toward potentially reducing postoperative ecchymosis. It is our hope that these preliminary results from our split-face study will encourage more research in the use of TXA for many of our facial plastic surgery procedures and further explore its effects on postoperative recovery and healing.

Authors' Contributions

J.A.K.: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, validation, visualization, and writing—original draft as well as reviewing and editing. Article approved prior to submission. M.A.: Conceptualization, formal analysis, investigation, methodology, project administration, resources, supervision, validation, visualization, and reviewing and editing of the publication. Article approved prior to submission. S.H.: Conceptualization, data curation, resources, visualization, and reviewing and editing of the publication. Article approved prior to submission. D.E.R.: Conceptualization, data curation, formal analysis, funding acquisition, project administration, resources, supervision, visualization, and reviewing and editing of the publication. Article approved prior to submission. S.P.: Project administration, funding acquisition, project administration, resources, supervision, and reviewing and editing of the publication. Article approved prior to submission. M.H.: Project administration, funding acquisition,

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Supplementary Material

Supplementary Figure S1

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