COSMETIC

Serum Concentrations and Pharmacokinetics of Tranexamic Acid after Two Means of Topical Administration in Massive Weight Loss Skin-Reducing Surgery

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Background: Topical administration of tranexamic acid to reduce bleeding is receiving increasing attention, as it is inexpensive, simple, and possibly beneficial in most surgery. Concerns regarding potential systemic adverse effects such as thromboembolic events and seizures may prevent general use of tranexamic acid. Although serum concentrations after topical application are assumed to be low, proper pharmacokinetic studies of tranexamic acid after topical application are lacking.

Methods: The authors have investigated systemic absorption of tranexamic acid after two means of topical administration in patients undergoing abdominoplasty after massive weight loss: a bolus of 200 ml of 5 mg/ml into the wound cavity versus moistening the wound surface with 20 ml of 25 mg/ml. Twelve patients were recruited in each group. Serum concentrations achieved were compared with those after administration of 1 g as an intravenous bolus to arthroplasty patients. Serial blood samples for tranexamic acid analysis were obtained for up to 24 hours.

Results: After intravenous administration, the peak serum concentration was 66.1 ± 13.0 μg/ml after 6 ± 2 minutes. Peak serum concentration after topical moistening was 5.2 ± 2.6 μg/ml after 80 ± 33 minutes, and in the topical bolus group, it was 4.9 ± 1.8 μg/ml after 359 ± 70 minutes. Topical moistening resulted in homogenous and predictable absorption across the individuals included, whereas topical bolus administration caused variable and unpredictable serum concentrations.

Conclusion: Topical administration of tranexamic acid in patients undergoing abdominoplasty results in low serum concentrations, which are highly unlikely to cause systemic effects. (*Plast. Reconstr. Surg.* 143: 1169e, 2019.)

The antifibrinolytic drug tranexamic acid is routinely used for blood conservation in surgery with high risk of significant bleeding.[1] Tranexamic acid prevents clot breakdown by inhibiting the activation of plasminogen to plasmin, and intravenous use reduces bleeding and

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transfusion needs by approximately one-third.[2] Fear of unrecognized adverse effects has so far limited routine use of intravenous tranexamic acid to high-risk surgery.

A drug that prevents bleeding may also promote thrombosis.[3] However, no increased risk of vascular occlusive events has been shown after intravenous use[4–8] and this worry may be unwarranted. In contrast, increasing attention is given to reports of a tranexamic acid–associated dose-dependent increased risk of nonischemic convulsive seizures, particularly in cardiac surgery.[9–13]

In vitro studies suggest that the minimum plasma concentration that significantly inhibits fibrinolysis is approximately 5 μg/ml in children and 10 μg/ml in adults.[14–16] In clinical practice, doses vary greatly, and some regimens advocate doses causing plasma levels above 150 μg/ml.[17–20] Tranexamic acid passes the blood-brain barrier and results in cerebrospinal fluid concentrations of approximately 10% of the plasma concentrations. Tranexamic acid may cause central nervous system hyperexcitability by blocking the action of the inhibitory neurotransmitters gamma-aminobutyric acid and glycine,[21–23] and a cerebrospinal fluid concentration of 15 μg/ml has been postulated as a threshold value for a potentially excitatory effect.[22–24]

Topical application of tranexamic acid can provide adequate concentrations in the wound with a low systemic concentration and thus lessen the risk of systemic adverse events. Topical application is receiving increasing attention, as it is inexpensive and simple, and may reduce bleeding from all surgical surfaces.[25] Large studies from joint replacement surgery have confirmed that topical use of tranexamic acid reduces blood loss at least as well as intravenous administration.[26–30] Studies from cardiac and thoracic surgery are fewer, smaller, and not unambiguous.[31–38] Studies on topical use of tranexamic acid from other surgical areas have so far been scarce.[39–46]

Topical use of tranexamic acid in surgery consists mostly of administration as a bolus into a confined space or by adding it to the irrigation fluid.[26] Moistening a wound surface can be performed with a small volume with a high drug concentration,[46] whereas irrigation or local bolus administration needs larger volumes with lower drug concentrations.[26] The lowest tranexamic acid concentration that can be administered in a solution and still have a topical hemostatic effect is unknown, but concentrations below 5 mg/ml have been shown to be effective.[37,38,47] In oral and dental surgery, a high-concentration mouthwash (48 mg/ml) has been reported but is not commercially available.[43,48,49] Only a few studies have measured systemic tranexamic acid concentrations after topical use in surgery, and then mostly at a single time point, rendering peak levels uncertain and precluding a complete pharmacokinetic analysis.[33,41,50,51]

The aim of this study was to investigate the degree of systemic absorption after two means of topical routine prophylactic application in patients having large wound surface areas: (1) moistening the wound surface before closure with 20 ml of tranexamic acid 25 mg/ml[46,52] or (2) instilling a bolus of 200 ml tranexamic acid 5 mg/ml into the wound cavity retrogradely by means of drains after closure. We also compared the systemic tranexamic acid concentrations achieved by these two methods with standard intravenous prophylactic administration of 1 g of tranexamic acid in hip replacement surgery.

PATIENTS AND METHODS

Patients older than 18 years undergoing skin-reducing abdominoplasty after massive weight loss were consecutively recruited from two plastic surgical clinics in Trondheim, Norway. St. Olav's University Hospital routinely moistens the wound surfaces with 20 ml of 25 mg/ml tranexamic acid (the topical moistening group), based on a previous study from our group showing the efficacy of this method.[46] The application is demonstrated in a video.[52] Twenty milliliters is a sufficient volume to moisten even large wounds, and 25 mg/ml is unlikely to be toxic.[53,54] Aleris Medical Center instills a bolus of 200 ml of 5 mg/ml tranexamic acid mixed with local anesthesia into the wound cavity retrogradely by means of the drains after wound closure (the topical bolus group). This concentration is lower than in the topical moistening group, but 5 mg/ml has had effect in published studies.[37,47] Both clinics practice prophylactic topical tranexamic acid in all surgery, but abdominoplasties have the largest wound surfaces, which would allow for maximum absorption and thus constitute a good model for a pharmacokinetic study. Patients undergoing hip replacement surgery and routinely receiving 1 g tranexamic acid intravenously constituted the reference group (the intravenous bolus group) and were consecutively recruited from the Department of Orthopedics at St. Olav's University Hospital.

Patients were not eligible for inclusion if they (1) were pregnant or nursing, (2) had a known allergy to tranexamic acid, (3) had a known history of a thromboembolic event, or (4) had an

estimated glomerular filtration rate less than 60 ml/minute. Twelve patients were recruited in each of the three groups. The Regional Committee for Medical and Health Research Ethics in Mid Norway and the Norwegian Medicines Agency approved the study. Written informed consent was obtained from all participants.

Interventions

Age, sex, height, body weight, body mass index, serum creatinine concentration, and estimated glomerular filtration rate were registered for all participants. The weight of the resected tissue was registered for the abdominoplasty groups and the maximum width and length of the wound were measured to allow calculation of an elliptical wound surface area (in square centimeters) as $\pi \times$ (length/2) × (width/2).

In the topical moistening group, the wound surface was moistened with 20 ml of tranexamic acid 25 mg/ml (total dose, 500 mg) after completion of hemostasis and directly before wound closure, with no further swabbing of the wound. Drains were activated after completion of the wound closure, which was at least 45 minutes after tranexamic acid application. The dose of 500 mg is half of that given in the other two groups. However, 20 ml is enough to moisten even larger surfaces,[52] and doubling the volume would only cause more spill without increasing the absorbed dose. Doubling the concentration was not done, as potential local toxic effects of 50 mg/ml are not yet clarified, and 25 mg/ml has proven efficient.[46] In the topical bolus group, 200 ml of tranexamic acid 5 mg/ml (total dose, 1 g) was instilled into the wound cavity by means of the drains after wound closure. Drains were clamped for 1 hour thereafter. In the intravenous bolus group, 1 g tranexamic acid diluted in 100 mg 0.9% sodium chloride was administered intravenous immediately before surgery.

Blood samples for the analysis of tranexamic acid were obtained before drug administration, and after 10 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours. The intravenous bolus group also had a sample taken at 5 minutes, whereas the two topical groups had an additional sample taken the next morning. In the topical bolus group, the last eight patients had an additional sample obtained after 8 hours, as early analyses suggested that the peak serum concentration of tranexamic acid in this group could take place later than 6 hours. All blood samples were centrifuged at 2000 relative centrifugal force for 10 minutes within 15 to 30 minutes after sampling. Thereafter, serum was pipetted off, transferred to polypropylene tubes, and stored at −80°C until analysis.

Analysis of Tranexamic Acid in Serum

Tranexamic acid concentrations in serum were determined by an ultra-high performance liquid chromatography tandem mass spectrometry method specifically developed for sensitive and precise analysis of low tranexamic acid concentrations. (**See Appendix, Supplemental Digital Content 1**, for details of the analysis of tranexamic acid in serum, *http://links.lww.com/PRS/D466*.)

Pharmacokinetic Analysis

Maximum measured peak serum concentration and the times to achieve these concentrations were obtained directly from the measured values. Other pharmacokinetic variables were calculated using the pharmacokinetic program package Kinetica, version 5.0 (ThermoFisher Scientific, Waltham, Mass.).

Area under the time–serum concentration curve was calculated using a mixed log-linear model with extrapolation to infinity. Clearance (Cl) was calculated as dose per area under the time–serum concentration curve. By applying a noncompartment model, the parameter estimate describing the decrease of the log-concentration (λ_z) was calculated using the best-fit log-linear regression line of the samples representing the elimination phase. The elimination half-life was calculated as $\ln2/\lambda_z$. Volume of distribution was calculated as Cl/λ_z. Mean residence time was calculated as area under the serum concentration-time product versus time curve from zero to infinity/area under the time–serum concentration curve.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Version 25 (IBM Corp., Armonk, N.Y.). Descriptive data are presented as mean ± 1 SD or median (interquartile range) as appropriate. Categorical variables were compared using Fisher's exact test, and continuous variables were compared using an independent samples *t* test. Associations between continuous variables were analyzed using the Pearson correlation coefficient. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Patient characteristics are summarized in Table 1. There were no significant differences between the two topical groups with regard to age,

Table 1. Demographic Characteristics and Pharmacokinetic Data for 36 Patients Receiving Routine Prophylactic Tranexamic Acid When Undergoing Hip Arthroplasty (Intravenous Bolus Group) and Abdominoplasty (Topical Bolus Group and Topical Moistening Group)

	Intravenous Bolus Group (1 g TXA)	Topical Bolus Group (1 g TXA)	Topical Moistening Group (500 mg TXA)
Patients			
No.	12	12	12
Male-to-female ratio	6:6	1:11	2:10
Age, yr			
Mean ± SD	62 ± 11	41 ± 11	43 ± 13
Range	45–81	25–63	22–68
Body weight, kg			
Mean ± SD	82.3 ± 17.4	74.9 ± 10.3	73.8 ± 7.3
Range	54–107	59–95	60–83
BMI, kg/m^2			
Mean ± SD	27.2 ± 5.4	25.7 ± 2.4	25.9 ± 2.7
Range	16.9–34.9	20.7–31.0	22.0–30.5
eGFR, ml/min			
Mean ± SD	98.1 ± 16.9	122.4 ± 14.7	113.1 ± 16.3
Range	74–120	103–153	85–136
Wound area, cm^2			
Mean ± SD	—	1091 ± 388	879 ± 383
Range	—	491–1802	346–1571
Pannus weight, g			
Mean ± SD	—	1420 ± 623	1630 ± 756
Range	—	635–2495	581–3065
Mean C_{max} ± SD, µg/ml	66.1 ± 13.0	4.9 ± 1.8	5.2 ± 2.6
Mean t_{max} ± SD, min	6.2 ± 2.2	359 ± 70	80 ± 33
$t_{1/2}$, min			
Mean ± SD	114 ± 12		253 ± 32
Median (IQR)		500 (415–823)*	
AUC, (µg/ml) × hr			
Mean ± SD	99.1 ± 20.0		31.3 ± 9.7
Median (IQR)		92.6 (63.7–130.8)*	
Clearance, ml/min			
Mean ± SD	174 ± 33		292 ± 96†
Median (IQR)		181 (129–263)*†	
MRT, min			
Mean ± SD	151 ± 19		377 ± 57
Median (IQR)		902 (768–1312)*	
Volume of distribution, liters			
Mean ± SD	28.5 ± 5.0		107.6 ± 38.5
Median (IQR)		186.6 (131.4–206.9)*	

TXA, tranexamic acid; BMI, body mass index; eGFR, estimated glomerular filtration rate; C_{max}, maximum (peak) serum concentration; t_{max}, time to maximum concentration; $t_{1/2}$, elimination half-life; IQR, interquartile range; AUC, area under the concentration-time curve; MRT, mean residence time.

*Median value (interquartile range) given instead of mean ± SD because the distribution was extremely skewed, with four subjects having improbably high values (improbably low values for clearance).

†Apparent clearance (i.e., Cl/F, where F is the fraction absorbed).

sex, body mass index, estimated glomerular filtration rate, weight of resected tissue, and wound surface area. Patients in the intravenous group were significantly older ($p < 0.001$), had significantly lower estimated glomerular filtration rate ($p = 0.002$), and had a more homogenous male-to-female ratio than the two topical groups combined ($p = 0.036$).

Pharmacokinetic data in the three groups are summarized in Table 1. Average serum concentrations over time are presented in Figure 1, with exact concentrations at identical time points shown in Supplemental Digital Content 2. (**See Table, Supplemental Digital Content 2**, which shows serum concentrations of tranexamic acid at comparable selected sampling times in the intravenous bolus group, the topical bolus group, and the topical moistening group. Data are presented as means ± SD. All concentrations are in micrograms per milliliter, *http://links.lww.com/PRS/D467*.) Peak serum concentration was considerably lower and occurred later in the two topical groups than in the intravenous bolus group (Table 1). Elimination half-life and mean residence time were also longer in the two topical groups than in the intravenous bolus group (Table 1).

Serum concentration over time data for each patient are presented. [**See Figure, Supplemental Digital Content 3**, which shows individual values for serum concentration (in micrograms per
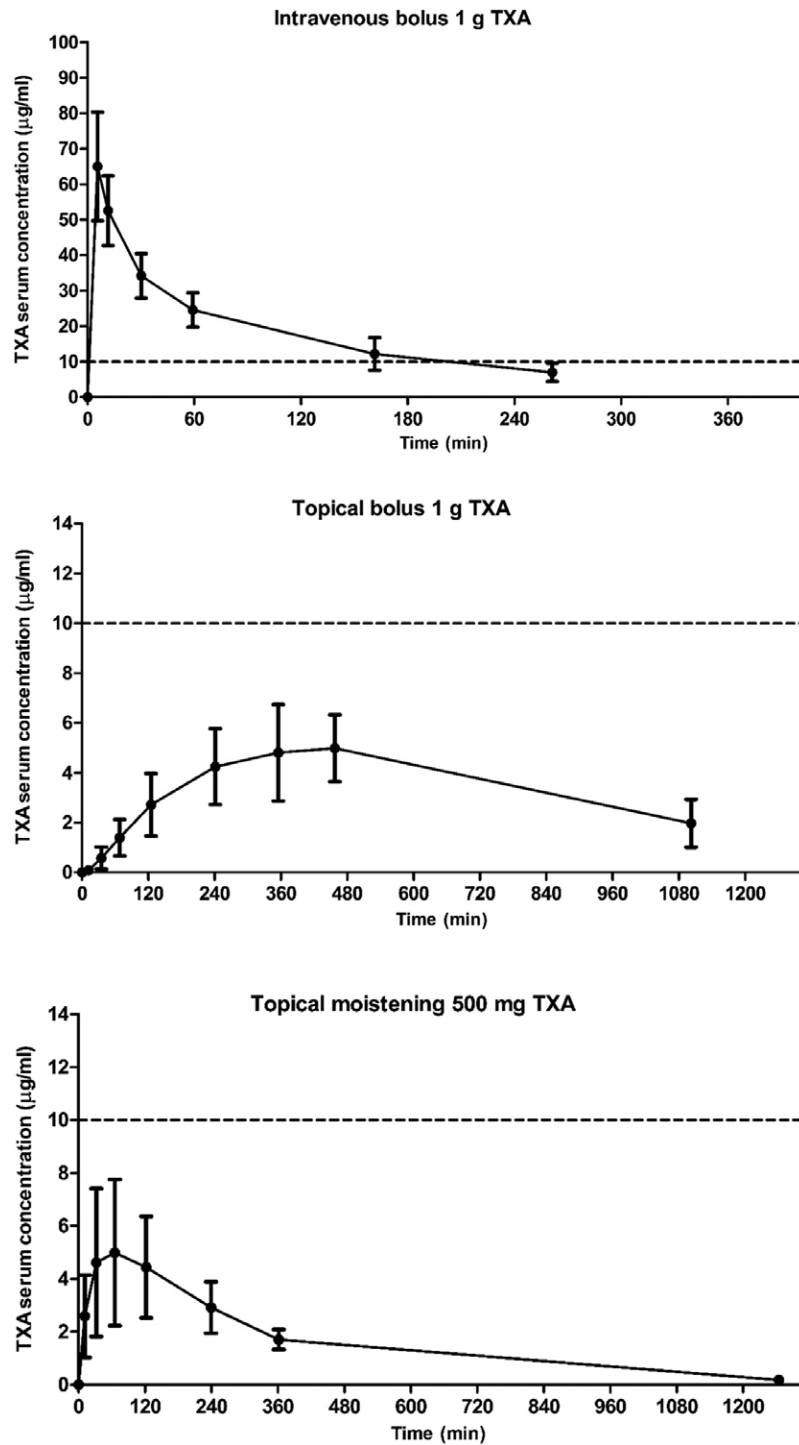
Fig. 1. Mean serum concentration versus time (minutes) after (*above*) intravenous bolus administration of 1 g of tranexamic acid (*TXA*); (*center*) topical bolus administration of 1 g of tranexamic acid; or (*below*) topical moistening with 500 mg of tranexamic acid. *Error bars* = 1 SD. The *dotted line* represents a concentration of 10 μg/ml, which is considered a threshold value for inhibition of fibrinolysis in adults. Individual patient curves are presented in Supplemental Digital Content 3 through 5.

milliliter) over time (in minutes) in 12 patients receiving intravenous bolus administration of 1 g of tranexamic acid (*TXA*), *http://links.lww.com/PRS/D468*. **See Figure, Supplemental Digital Content 4**, which shows individual values for serum concentration (in micrograms per milliliter) over time (in minutes) in 12 patients receiving topical bolus administration of 1 g of tranexamic acid (*TXA*), *http://links.lww.com/PRS/D469*. **See Figure, Supplemental Digital Content 5**, which shows individual values for serum concentration (in micrograms per milliliter) over time (in minutes) in 12 patients receiving topical moistening with 500 mg of tranexamic acid (*TXA*), *http://links.lww.com/PRS/D470*.] When using a serum concentration of 10 μg/ml as a threshold for clinical antifibrinolytic effect in adults, intravenous bolus administration maintained above-threshold values for at least 150 minutes in all patients. In contrast, serum levels above 10 μg/ml were not seen in any patients in the topical bolus group and in only one patient in the topical moistening group.

Peak serum concentration was inversely correlated to body weight in the intravenous bolus group ($r = -0.695$; $p = 0.012$). In the topical moistening group, a similar albeit nonsignificant inverse correlation was seen ($r = -0.454$; $p = 0.138$), whereas no correlation was seen in the topical bolus group ($r = 0.130$; $p = 0.688$). Peak serum concentration was not correlated to wound surface area in either the topical bolus group ($r = -0.278$; $p = 0.382$) or the moistening group ($r = -0.219$; $p = 0.494$).

Adverse events were registered for the topical groups, as topical administration is still off-label. There was one postoperative hematoma in the topical moistening group that was managed conservatively, and one postoperative wound infection requiring antibiotics in the topical bolus group. There were no cases of thromboembolic events in either group.

DISCUSSION

This study demonstrates that moistening a large wound surface with a 25-mg/ml tranexamic acid solution, or instilling a bolus of 200 ml tranexamic acid 5 mg/ml into a large wound cavity, results in very low serum tranexamic acid levels compared to an intravenous bolus of 1 g of tranexamic acid. The mode of administration clearly accounts for the differences between the intravenous bolus group and the two topical groups. Although patients in the intravenous bolus group were on average 20 years older than those in the topical groups and had significantly lower estimated glomerular filtration rate, group interdiversity should not influence the general descriptive observations of this study.

The tranexamic acid concentration needed to inhibit fibrinolysis in vitro starts at approximately 10 μg/ml in adults and approximately 5 μg/ml in children.[15,16] Fibrinolysis is inhibited by more than 90 percent at tranexamic acid concentrations of approximately 20 μg/ml, and a concentration of 100 μg/ml provides a 98 percent inhibition.[14] In our study, topical application gave a mean peak serum concentration of 4.9 μg/ml in the bolus group and 5.2 μg/ml in the moistening group. The systemic antifibrinolytic effect should therefore be negligible. It would therefore appear safe to use these topical methods also in patients with increased risk of thromboembolic events[55] or at the donor sites for free flaps. However, we have not found any published studies on the effect of topical application directly onto microvascular anastomoses, and we have personally not used topical tranexamic acid at recipient sites.

Tranexamic acid passes the blood-brain barrier, reaching a concentration in cerebrospinal fluid of approximately 10% of that in plasma, although the degree of passage may vary considerably.[22,24] A plasma level of 5 μg/ml after topical application may thus cause a concentration of approximately 0.5 to 1 μg/ml in the brain.[24] As a cerebrospinal fluid concentration of at least 15 μg/ml has been necessary in experimental settings to increase the excitatory potential of tranexamic acid,[22] it is highly unlikely that a concentration of approximately 0.5 to 1 μg/ml may precipitate seizures. However, caution may be warranted should topical solutions come in direct contact with the central nervous system. Studies from topical use in spine surgery have not addressed this issue,[56] and the possibility of seizures is not common knowledge outside of the cardiac surgery community.[8] Any topical use in neurosurgery should be discouraged, as accidental intrathecal administration in humans[57–60] and direct topical application to the central nervous system in animal studies[61–63] have caused seizures.

Our findings after intravenous administration of 1 g of tranexamic acid are in accordance with earlier pharmacokinetic data.[64–67] Concentrations remained above 10 μg/ml for approximately 2.5 hours, which was well beyond the end of surgery in all patients.

The topical bolus group presented heterogeneous results both for the total amount of

absorbed drug and for its elimination (Fig. 1, *center*) (**see Figure, Supplemental Digital Content 4**, *http://links.lww.com/PRS/D469*). Interindividual differences regarding the extent to which the drains actually eliminated the instilled fluids, patient mobility to stir up and distribute fluids, and wound cavity topography with nooks and crevices where fluid deposits reside are all factors that may add to the heterogeneity of this group. In four subjects in this group, the absorption was particularly low and irregular during the approximately 20 hours we followed them with serum concentrations measurements. Consequently, the area under the time–serum concentration curve calculations were uncertain because of a considerable degree of extrapolation; also, the elimination half-life, clearance, mean residence time, and volume of distribution values were correspondingly affected. We therefore present median values for these variables in this group in Table 1.

In the topical moistening group, tranexamic acid was smeared manually onto the wound surface. Moistening the entire wound surface was thus ensured under visual supervision, which may be beneficial for large wounds. A film is left on the wound surface and surplus volume is left to spill. We used a volume of 20 ml tranexamic acid 25 mg/ml (i.e., the total administered dose was 500 mg, which is half of the dose given to the other two groups). Abdominoplasties create large wounds, but 20 ml is still enough to moisten even larger surfaces.[52] Doubling the volume would only cause more spill without increasing the absorbed dose. We chose not to double the drug concentration for this pharmacokinetic study, as our published routine method has shown that a concentration of 25 mg/ml[46] is sufficient for an adequate clinical effect and because potential local toxic effects of higher concentrations are not yet clarified. We assume that a doubling of the drug concentration would have caused a doubling of the serum concentration, as demonstrated by Wong et al.,[51] who reported that an equal volume (100-ml) bolus of either 15 or 30 mg/ml tranexamic acid intraarticularly after knee arthroplasty resulted in serum concentrations of 4.5 μg/ml versus 8.5 μg/ml.

We crudely estimated the true net dose administered (i.e., the absorbed dose) in the topical moistening group by comparing the area under the time–serum concentration curve values in this group with the area under the time–serum concentration curve values in the intravenous bolus group, assuming that the true clearance in the

two groups was the same. Mean net administered dose in the moistening group could then be estimated to be 316 ± 98 mg. Drains were not activated until at least 45 minutes after application, as closing of abdominoplasties takes time. Much of the absorption had presumably occurred at drain activation, and as the drug is applied as an evenly distributed film, little can be expected to have escaped through the drains, as time to maximum concentration had taken place already at 80 ± 33 minutes. Elimination half-life was 253 ± 32 minutes and mean residence time was 377 ± 57 minutes, with a small interindividual variability. Elimination is thus slower than after intravenous bolus administration, and also somewhat slower but comparable to the elimination reported after intramuscular injection.[68] Drug applied as a film would be expected to be quickly absorbed because of its short diffusion distance, with correspondingly little drug acting as a depot within the wound cavity. In contrast, the prolonged elimination is probably attributable to a certain extent of tissue drug deposition (e.g., subcutaneously). Unabsorbed film will be diluted by wound effusions, and whether concentrations lower than 25 mg/ml may be effective in a moistening technique is not known.

Systemic absorption of topically applied drugs is a product of concentration, contact surface area, volume, and time.[69] In our topical moistening group, neither the absorbed dose (as measured by the area under the time–serum concentration curve) nor the peak serum concentration was related to the wound surface area. One may speculate whether microstructural topographic differences or tissue vascularization may affect absorption and contact area to a larger extent than the surface area.

This study has some limitations, but also some strengths, that should be acknowledged. As intravenous tranexamic acid is not used routinely for bleeding prophylaxis in abdominoplasties and this was a descriptive study of methods already used for routine prophylaxis, we had to choose a completely different patient group (hip arthroplasties) to describe pharmacokinetics after intravenous use, with resulting differences in age, estimated glomerular filtration rate, and sex distribution.[70,71] Group interdiversity would, however, not be expected to significantly influence the general descriptive observations of this study. According to standard methodology, we have derived pharmacokinetic data from serum concentrations, but topical administration also allows for various nonbiological routes

of elimination (e.g., through the drains and into absorbent materials). We did not collect fluids from these alternative external pathways, and thus the true amount of absorbed drug is uncertain. In the topical moistening group, a collection and analysis of all absorbing material in the operating field could have been of value, whereas in the bolus group, both drain fluid analysis and not least prolonged blood sampling would have given more accurate results. Blood sampling beyond 24 hours was, however, not practically feasible in our routine surgery setting. It could also be considered a weakness that we have included only 12 patients in each group; however, such a number is generally regarded sufficient to provide a representative pharmacokinetic picture. Nevertheless, the topical bolus group could have benefited from a larger population because of the heterogeneity of the data in this group.

Strengths of the study include the frequent and timely blood sampling from the subjects (with the possible exception of the topical bolus group), allowing us to estimate reliable pharmacokinetic data. The sensitive and precise analytical method developed to accurately describe the low serum tranexamic acid levels expected from topical administration is also a significant strength. Finally, we consider it being a strength that we have studied patients with very large surgical wounds; thus, our study most likely represents a "worst case" scenario regarding drug absorption after topical administration.

Topical use of tranexamic acid is becoming widespread but is still off-label. The optimum dose and mode of administration for topical use of tranexamic acid are uncertain, and more efficacy studies are needed. Moistening of the wound surface before closure under visual and manual control ensures that a homogenous film of drug is applied to the entire wound surface. Pharmacokinetics in the topical moistening group was homogenous and predictable, and thus this mode of drug administration can be considered standardized and reproducible. When instilling a topical bolus into a closed wound cavity, the volume of the bolus must be adjusted to the size of the cavity. In large wound cavities, the bolus may reside in various locations, and contact with the entire wound surface is not ensured. This is reflected by the unpredictable and highly variable pharmacokinetics we observed in the topical bolus group. In patients with large wound cavities, we would thus advocate the use of topical moistening of the wound surface rather than topical bolus instillation.

CONCLUSIONS

In patients undergoing abdominoplasty, topical application of tranexamic acid—either with moistening with 20 ml of 25 mg/ml solution or by administration of a bolus of 200 ml of 5 mg/ml into the wound cavity—resulted in mean maximum (peak) serum concentration values of approximately 5 µg/ml, which is below the 10-µg/ml limit considered to cause any systemic antifibrinolytic effect in adults. Moreover, these concentrations are much lower than those being associated with a possible risk of seizures.

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