

ORIGINAL RESEARCH ARTICLE

Use of tranexamic acid as a blood-saving method in patients of liposuction and other aesthetic surgeries: a retrospective study

Octavio de Jesus Carrascal-Navarro*, Hernando Carrascal-Carrasquilla, Hernan Amaris-Jimenez, Giovanni Mera-Cruz, Javier Augusto Soto Ortega, Octavio Carrascal-Carrasquilla and Enrique Carlos Ramos Clason

Plastic and Aesthetic Surgery, Clínica Dhara, Bogotá, Colombia

Abstract

Introduction: Liposuction is among the most grueling procedures in esthetic plastic surgery. Despite the existing evidence of tranexamic acid (ATX) as a blood-saving method in surgeries of different surgical specialties, its use in plastic-esthetic surgery is scarce, especially in liposuction.

Goal: To determine the impact of ATX on blood loss in patients who have undergone liposuction surgical procedures.

Methods: A total of 102 patients met the inclusion requirement criteria. All of them received balanced general anesthesia. 10–15 mg/kg IV of ATX (1 g on average) was administered 20 min before surgery, and so it continued for the first 24 h of postoperative with 500 mg/IV every 8 h. Blood count samples were taken 12–20 h postoperative.

Results: The hematocrit showed a median of 42.6% presurgical and 33.5% postsurgical. On the other hand, the presurgical hemoglobin median was 14.2 g/Dl (Interquartile ranges [RIC]) 13.4–15) and postsurgical of 11.4 (RIC: 10.6–12.1); giving a median difference of presurgical and postsurgical hemoglobin of –2.8 (RIC: –3.6 to –2.1), the difference percentage of hemoglobin concerning the base was –19.5% (RIC: –25.0 to –14.9).

Conclusion: The use of ATX in liposuction seems to grant the same benefits in terms of bleeding reduction, hemoglobin stabilization, hematocrit, and necessity of transfusions compared with operations of other surgical specialties. The dose used in this study is adequate and safe in order to achieve these goals and is consistent with the literature. More analytic studies in the field are necessary to reinforce these hypotheses.

Keywords: *tranexamic acid; antifibrinolytics; aesthetic surgeries; liposuction; blood-saving methods; transfusions*

Received: 26 January 2022; Revised: 22 February 2022; Accepted: 11 March 2022; Published: 28 June 2022

Esthetic procedures have increased exponentially in the last years (1). According to global statistics from the International Society of Aesthetic Plastic Surgery (ISAPS) published in 2017, all over the world were performed 23,390,517 surgical procedures during that year. United States, Brazil, and Japan are the countries that are in the top three places where the most esthetic plastic surgeries are carried out, respectively. Colombia took seventh place with a total of 516,930 surgical procedures. Despite augmentation mammoplasty and liposuction represent the first and second place of the most commonly esthetic procedures carried out worldwide, liposuction took the first place in our country with a total of 65,700 procedures (2).

The procedure of liposuction consists on remodeling the body contour by aspiration of adipose subcutaneous tissue in different parts of the body using cannulae

connected to vacuum pumps, which are inserted through incisions adjacent to the area to be suctioned (3). Throughout years, the technique for this procedure has been modified, from the first dry to the wet, superwet, and tumescent techniques; these latter ones facilitated suction, reducing the trauma caused by the cannulae (4). Bleeding is still one of the most common complications, which increases when liposuction is performed in combination with other procedures or when it is a large-volume surgery, defined as a suction of over 5 L (2, 5, 6). This complication is inevitable because of the swinging movement of cannulae that vacuums fat and blood concomitantly, which causes microvascular trauma (7).

Blood loss and transfusions increase morbidity and mortality in patients scheduled for surgical procedures (8, 9), which makes it necessary to implement strategies during the perioperative period in order to reduce

bleeding. Among these, we have the preanesthetic assessment that provides information on the hemostatic condition of the patient in order to detect any alteration, optimize hemoglobin levels, indications for the moment of discharge and leave of the hospital, and start adding antiplatelet agents and anticoagulants, performing less invasive surgical procedures and the use of antifibrinolytic drugs, from which ϵ -aminocaproic acid and tranexamic acid (ATX) stand out, both are analog lisinic acids that compete for joint places of lysine on the plasminogen, inhibiting its activation to plasmin and therefore to fibrin hydrolysis (10).

ATX is one of the most studied and used antifibrinolytics in several countries; at high concentrations, it blocks plasmin in a noncompetitive fashion. The union of ATX to plasminogen is 6 to 10 times stronger than the one with aminocaproic acid (11); this has been proven in different studies to reduce blood losses and transfusion requirements in a significant number of situations. The evidence of its use in esthetic plastic surgery and especially liposuction is limited. Therefore, our goal is to determine the impact on blood loss in patients who undergo this surgical procedure.

Methods

We made an observational, descriptive retrospective study of adult patients who underwent liposuction and/or other esthetic procedure at Clínica Dhara in Bogotá—Colombia, which has a team of 20 plastic surgeons who work in the institution, from which two random surgeons were selected, and the liposuctions carried out by them during September 2016 and 2018 were collected.

As inclusion criteria were selected patients of both genders, with ages ranging between 18 and 60 years old, with body mass index (BMI) > 18 and < 32 kg/m², classification American Society of Anesthesiology (ASA) I and II, who had presurgical hemoglobin ≥ 12 g/dL. Patients who were taking anticoagulants were allergic to ATX or had any coagulation disorder were excluded. By applying the treatments described, we obtained a total of 102 patients.

All patients received balanced general anesthesia, which during the induction was used with lidocaine 1 mg/kg, fentanyl 2 mcg/kg, propofol 1.5 mg/kg, and rocuronium 0.3 mg/kg; the maintenance concurred with sevoflurane 2%, Remifentanyl 0.15–0.4 mcg/kg/min (adjusted according to intraoperative analgesia requirements) and dexmedetomidine 0.1 mcg/kg/min. Analgesia was carried out with ketorolac 30 mg/IV and dipyrone 40 mg/kg IV. For postoperative, profilaxis of vomit and nausea was administered dexamethasone 8 mg/IV and ondansetron 4 mg/IV. In patients allergic to AINES, acetaminophen 1 g/IV was used. All patients were administered a dose of 10–15 mg/kg/IV of ATX (1 g on average) 20 min before the procedure and continued for 24 h postoperative with a dose of 500 mg/IV every 8 h. Liposuctions were carried out under

the superwet technique (lipoinjection-suction relation 2:1), the blends were prepared with Ringer lactate 1000 cc + 3cc of lidocaine 2% + 1 mg of epinefrin + baking soda 1 mEq (maximum dose allowed of epinefrin 5 mg and lidocaine 7 mg/kg), the places selected by the surgeon were lipoinjected and between 10 and 30 min were awaited for liposuction.

A blood sample was taken to control the blood count between 12 and 20 h of postoperative. The transfusion criteria of this institution include hemoglobin levels lower than 8 g/dL postoperative or between 8 and 9 in symptomatic patients. Two units of red blood cells packed were reserved for patients with negative Rhesus Factor (RH) factor.

Results

A total of 102 patients who underwent liposuction plus other esthetic surgeries between September 2016 and September 2018 were obtained. Among the results, we found that the average age of patients was 39 years old with a standard deviation of (DE) 9 years, 90% of them were female and the rest were male. BMI average was 21.21 (DE 2.8); being the normal weight the most frequent nutritional status with 52%, followed by overweight with 43.1%; 87.3% of patients were ASA-1 and the rest ASA-2 (Table 1).

Among the most performed surgical procedures associated to liposuction, we find gluteal lipoinjection with 58.8%, mammoplasty 28.4%, abdominoplasty 20.6%, and mastopexy 19.6% (Fig. 1). Concerning the intraoperative findings, it can be observed that the average duration of average of the infiltrated tumescent solution was in 5.185 cc and the liposucted 3269 cc. As for the composition of the liposucted, a total fat average of 1980 cc was obtained, representing a total of 60% and thus was also estimated an approximate bleeding average of 640 cc from the tests that evaluated the behavior of bleeding. The hematocrit had a median of 42.6% presurgical and 33.5% postsurgical; the presurgical hemoglobin median was 14.2 g/dL (RIC: 13.4–15). On the other hand, the postsurgical hemoglobin was 11.4 (RIC: 10.6–12.1), giving an average difference between preoperative and postoperative hemoglobin of -2.8 (RIC: -3.6 to -2.1), which represented -19.5% (RIC: -25.0 a -14.9) of hemoglobin difference concerning the base (Table 2).

When comparing general intraoperative findings and the presurgical and postsurgical tests among the four main esthetic procedures carried out, there were no differences except for the one among the mammoplasty and abdominoplasty groups, where it was observed that in some mammoplasty groups there was a higher average of lipoinfiltrated liquids in relation to the one of abdominoplasty and a median of hematocrit statistically lower than in abdominoplasty (Table 3).

Discussion

ATX was discovered early in the decade of 1960 by the couple of spouses Shosuke and Utako Okamoto, encouraged by the search of a new antifibrinolytic more powerful than the aminocaproic acid of clinical use in postchildbirth hemorrhage (12). In 2009, the World Health Organization

(WHO) included it in the list of essential medical drugs to be used in heart surgery procedures that require cardiopulmonary derivation to reduce perioperative blood losses (13). However, with the publication of important studies such as Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage (CRASH)-2 (14) and the WOMAN (15), in which ATX reduced mortality in polytraumatized patients except for patients with head trauma (16) and in postchildbirth hemorrhage, respectively; its use in other scenarios has increased.

In recent years, the use of ATX has been implemented in surgeries in which it is anticipated to have significant

Table 1. General characteristics of the study sample

Variables	N	%
Age $\bar{X} \pm DE$	39.5 \pm 9.5	
Sex		
F	92	90.2
M	10	9.8
BMI $\bar{X} \pm DE$	21.21 \pm 2.8	
Normal weight	53	52.0
Overweight	44	43.1
Obesity	5	4.90
ASA		
1	89	87.3
2	13	12.7
Procedure		
Glute lipoinjection	60	58.8
Mammoplasty	29	28.4
Abdominoplasty	21	20.6
Mastopexy	20	19.6
Rhinoplasty	4	3.9
Implant retirement	3	2.9
Blepharoplasty	2	2.0
Dewlap liposuction	2	2.0
Vaginoplasty	2	2.0
Others	4	3.9

Table 2. General and paraclinical intraoperative, presurgical, and postsurgical findings

Variables	$\bar{X} \pm DE$ Me (RIC)
Surgical time $\bar{X} \pm DE$	234 \pm 85
Estimation of fat suction and bleeding $\bar{X} \pm DE$	
Lipoinfiltration	5,185 \pm 1,803
Liposuctioned	3,269 \pm 1,170
Total fat cc	1,980 \pm 843
Suctioned fat percentage	60.0 \pm 15%
Approximate bleeding cc	644 \pm 302
Paraclinic Me (RIC)	
Presurgical hematocrit	42.6 (40.1 – 45.0)
Postsurgical hematocrit	33.5 (31.5 – 35.7)
Presurgical Hb	14.2 (13.4 – 15.0)
Postsurgical Hb	11.4 (10.6 – 12.1)
Hemoglobin difference	-2.8 (-3.6 to -2.1)
Hb difference percentage	-19.5 (-25.0 to -14.9)

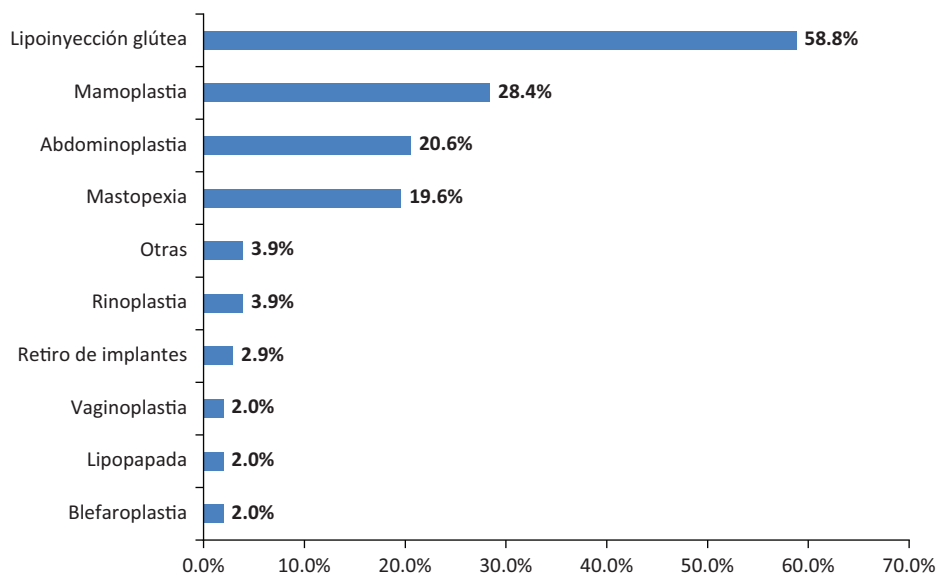


Fig. 1. Frequency of esthetic procedures in the sample studied.

Table 3. Comparison of general and paraclinical intraoperative, presurgical, and postsurgical findings among the main surgical procedures

Variables	Glute lipoinjection N = 60	Mammoplasty N = 29	Abdominoplasty N = 21	Mastopexy N = 20	Value P*	Value P†	Value P‡	Value P§	Value P	Value P¶
Estimation of fat and bleeding suction $\bar{X} \pm DE$										
Lipofiltration	5,453 ± 1,609	5,927 ± 1,659	4,828 ± 1,685	5,310 ± 1,789	0.2004	0.1343	0.7381	0.0260	0.2210	0.3804
Liposuction	3,426 ± 1,070	3,533 ± 983	2,980 ± 1,092	3,185 ± 1,437	0.6531	0.1064	0.4264	0.0676	0.3185	0.6106
Total fat cc	2,049 ± 770	2,224 ± 659	1,824 ± 744	1,838 ± 964	0.2962	0.2481	0.3230	0.0504	0.1025	0.9580
Suctioned fat Percentage	59.1 ± 11.8	63.7 ± 15.9	61.0 ± 17.5	56.3 ± 16.0	0.1270	0.5774	0.4128	0.5702	0.1175	0.3782
Approximate bleeding cc	688 ± 261	654 ± 309	578 ± 300	673 ± 339	0.5868	0.1140	0.8340	0.3899	0.8704	0.3483
Paraclinic Me (RIC)										
Presurgical hematocrit	42.2 (39.8 – 44.9)	41.0 (39.1 – 42.6)	42.5 (41.0 – 44.0)	42.4 (39.4 – 44.1)	0.1719	0.5389	0.9998	0.0459	0.2338	0.6292
Postsurgical hematocrit	33.1 (31.4 – 35.4)	32.5 (31.1 – 34.0)	32.8 (31.1 – 34.5)	32.2 (31.5 – 34.6)	0.2495	0.9871	0.3280	0.3762	0.9432	0.4974
Presurgical Hb	14.0 (13.1 – 14.9)	13.6 (13.1 – 14.5)	14.5 (13.5 – 15.0)	13.9 (13.1 – 14.7)	0.4252	0.3882	0.8067	0.1453	0.6762	0.3818
Post-surgical Hb	11.3 (10.5 – 12.1)	11.4 (10.5 – 11.6)	11.0 (10.7 – 11.7)	10.9 (11.6 – 11.4)	0.6677	0.8715	0.3306	0.8981	0.4823	0.4485
Hemoglobin difference	-2.6 (-3.6 a -2.1)	-3.1 (-3.5 a -2.0)	-2.8 (-3.9 a -2.3)	-2.9 (-3.7 a -2.1)	0.8678	0.4341	0.5556	0.4425	0.6688	0.8858
Hb difference percentage	-18.8 (-25.3 a -14.9)	-21.4 (-24.8 a -14.9)	-21.5 (-26.5 a -16.7)	-21.4 (-24.6 a -16.1)	0.9198	0.4441	0.6054	0.5686	0.8787	0.8449

*Value P comparing the glute lipoinjection group versus mammoplasty.

†Value P comparing the glute lipoinjection group versus abdominoplasty.

‡Value P comparing the glute lipoinjection group versus mastopexy.

§Value P comparing the mammoplasty group versus abdominoplasty.

||Value P comparing the mammoplasty group versus mastopexy.

¶Value P comparing the abdominoplasty group versus mastopexy.

blood losses, in different surgical specialties (17–22). In tibial osteotomy, Kim K-I et al. in South Korea found that bleeding in drains on the first postoperative day, as well as total bleeding accumulated, was less in the group of ATX compared with the control group (502.4 ± 294.9 mL) versus (882.7 ± 482.0 mL) (23). Even though losses were fewer in this study compared to this currently described in this paper, that may be caused due to the subjective quantification carried out intraoperatively. While in theirs, quantification was objective by the drains in hemovac during the first two postsurgery days taking into account that in the intraoperative stage; bleeding was null because of the use of a tourniquet. The South Korean study also reported hemoglobin levels on the first post-surgery of 11.8 g/dL, which are similar to the results obtained in this current study. The previous findings are also consistent with the ones described by Palanisamy JV et al. in Korea in patients who underwent tibial osteotomy (24).

On the other hand, a meta-analysis of 2,720 cases of hip and knee arthroplasty showed a decrease in blood loss in patients who were given ATX in comparison with the control group in hip arthroplasty (Mean differences [MDs]: -318.49; 95% confidence intervals [CIs]:

-398.04 to 238.94; $P < 0.00001$) as well as knee arthroplasty (MDs: -321.78; 95% CIs: -413.25 to -213.08; $P < 0.00001$) (25). Blood losses were higher than the ones of this current study, which could be caused to the more gruesome character of these surgeries and quantification as much as in the intraoperative stage as in the postsurgical.

Farrow et al., in a systematic revision on hip surgery, analyzed six studies concerning the postsurgical level of hemoglobin that reported higher levels of it in postsurgical than in those that received intravenous ATX compared with a placebo group, with hemoglobin averages ranging between 10.1 and 10.5 g/dL. It also showed that there was 46% less risk of blood transfusion in patients who received intravenous ATX compared with a placebo group (RR: 0.54; 95% CI: 0.35 to 0.85; I²: 78%; inconsistency (χ^2) $P \leq 0.0001$; $n = 750$) (26). In this current study, no transfusion was required.

The use of antifibrinolytic agents (ATX, ϵ -aminocaproic acid and aprotinine) in spine surgery was studied by Guang Li et al. in a meta-analysis where it was observed that the use of these agents reduces perioperative blood losses and transfusion requirements. Moreover, another relevant result showed ATX as more effective compared

to other antifibrinolytic agents to reduce intraoperative bleeding, total blood loss, and transfusions (27).

In the specialty of plastic-esthetic surgery, despite different procedures such as breast surgeries, abdominoplasty, and liposuction producing important blood losses and may require transfusion in some cases, the use of ATX has been studied very little in spite of its well-known benefits (28). In craniofacial surgeries, ATX produced a reduction in the average of blood losses of 18.2 mL/kg ($P = 0.00001$) and a reduction in blood transfusion of 8.7 mL/kg ($P = 0.00001$) (29).

Although it is a gruesome procedure secondary to the use of suction cannulae, there is little evidence about ATX in liposuction. In Brazil, in a nonrandomized double-blind clinical trial of 20 patients who underwent liposuction, blood loss volume per lipoaspired liter was a 56.2% lower in the tranexamic group in comparison with the control group ($P < 0.001$). The hematocrit levels on day 7 after surgery were 48% lower in ATX in contrast with the control ($P = 0.001$). Additionally, a drop of 1% was found in the level of hematocrit after liposuction of 812 ± 432 mL in the group of ATX and of 379 ± 204 mL in the control group (30). Despite the study on this paper was not experimental, the results related to the bleeding magnitude and blood count parameters were similar, highlighting the fact that postsurgical levels of hemoglobin did not get close to the transfusion criteria so it was not necessary for any of our patients. The average duration of a surgery in this current study was 3.9 h because in all patients another esthetic procedure apart from the liposuction was practiced, which can be inferred as factors (duration and another procedure) that can increase blood losses.

For what concerns, the ATX dose in *in vitro* and *in vivo* tests, it has been found that its effective plasmatic concentration is 10 µg/mL or 10–15 mg/L (31, 32), which is achieved with doses of 10 mg/kg or 1 g, reaching its maximum plasmatic concentration 3 h later, keeping a therapeutic effect up to 17 h in tissues (33), this dose of 1 g could be enough in most adults, which would not justify using higher dosages (34). After giving the dose of 10 mg/kg of ATX, its average cycle is approximately 80 min, with renal elimination of 30% in the first hour, 55% in the third, and 90% 24 h later (35). Some cases of seizures associated with ATX have been reported (mostly in heart surgery), associated with high doses. The evidence suggests as antagonistic mechanism competitive γ -aminobutyric acid GABA receptors type A and glycine, reducing inhibitory neurotransmission. Thus, the simplest strategy to reduce this adverse effect is the use of recommended doses and their adjustment in patients with kidney failures, because the elimination of ATX is carried out through them (36, 37); hypersensitivity to the drug is contraindicated, surgeries in which there is continuous vascular occlusion, traces of thrombosis, and in patients with macroscopic hematuria,

given that it represents a risk for the development of obstructions of ureters by clots (38).

Evidence is not enough yet to prove that ATX increases the risk of thrombus stroke events in comparison to control groups, in orthopedic, major heart, and trauma surgery, which are scenarios where this drug has been used the most (39, 40). ATX seems to have an anti-inflammatory effect by inhibiting plasmin formation, which participates in the inflammatory response (41, 42), which makes it a very attractive molecule to reduce edema, ecchymosis, and postsurgery bruises, improving patients' recovery. In this study, there were no episodes defined as adverse to the use of ATX. However, it is necessary to make a use of the drug in all cases.

Conclusion

ATX use in liposuction seems to bring the same benefits in terms of bleeding reduction, hemoglobin and hematocrit stabilization and necessity of transfusions compared with surgeries of other surgical specialties. The doses used in this study are adequate and safe to accomplish these goals and are consistent with the literature. More analytic studies in the field are necessary to strengthen this hypothesis.

Ethical responsibilities

Protection of people and animals: The authors state that they did not perform any experiments on humans or animals for this research.

Data confidentiality: The authors declare that they have followed their work protocols in the publication of patient data.

Right to privacy and informed consent: The authors attest that there is no patient data in this article.

Acknowledgements

The authors express their gratitude to Dr. Enrique Carlos Ramos, methodological consultant who oriented us in the design and process of making this study.

Conflict of interest and funding

The authors declare that there is no conflict of interest for them with this study. The authors state that the execution of this study was carried out with their own funds.

References

1. Kaoutzanis C, Gupta V, Winocour J, Layliev J, Ramirez R, Grotting JC, et al. Cosmetic liposuction: preoperative risk factors, major complication rates, and safety of combined procedures. *Aesthet Surg J* 2017; 37(6): 680–94. doi: 10.1093/asj/sjw243
2. Plastic Surgery Statistics | Global Plastic Surgery Statistics [Internet]. ISAPS. Available from: <https://www.isaps.org/medical-professionals/isaps-global-statistics/> [cited 28 November 2018].
3. Iverson RE, Lynch DJ, American society of plastic surgeons committee on patient safety. Practice advisory on liposuction.

- Plast Reconstr Surg 2004; 113(5): 1478–90; discussion 1491–5. doi: 10.1097/01.PRS.0000111591.62685.F8
4. Abdelaal MM, Aboelatta YA. Comparison of blood loss in laser lipolysis vs traditional liposuction. *Aesthet Surg J* 2014; 34(6): 907–12. doi: 10.1177/1090820X14536904
 5. Kaoutzanis C, Winocour J, Gupta V, Ganesh Kumar N, Sarosiek K, Wormer B, et al. Incidence and risk factors for major hematomas in aesthetic surgery: analysis of 129,007 patients. *Aesthet Surg J* 2017; 37(10): 1175–85. doi: 10.1093/asj/sjx062
 6. Choudry UH, Hyza P, Lane J, Petty P. The importance of pre-operative hemoglobin evaluation in large volume liposuction: lessons learned from our 15-year experience. *Ann Plast Surg* 2008; 61(3): 230–4. doi: 10.1097/SAP.0b013e31815bf341
 7. Rosique RG, Rosique MJF, Rabelo MQ. Does Postoperative erythropoietin reduce transfusions and hemodynamic instability following liposuction, either alone or associated with abdominoplasty or mammoplasty? A comparative, prospective study of 50 consecutive patients. *Aesthetic Plast Surg* 2017; 41(1): 98–101. doi: 10.1007/s00266-016-0748-0
 8. Gilliss BM, Looney MR, Gropper MA. Reducing noninfectious risks of blood transfusion. *Anesthesiology* 2011; 115(3): 635–49. doi: 10.1097/ALN.0b013e31822a22d9
 9. Kordzadeh A, Askari A, Parsa AD, Browne T, Panayiotopoulos YP. The clinical implication of blood product transfusion on morbidity and mortality of ruptured abdominal aortic aneurysm. *Clin Appl Thromb Hemost* 2017; 23(6): 601–6. doi: 10.1177/1076029615624548
 10. Hogg K, Weitz JI. Blood coagulation and anticoagulant, fibrinolytic, and antiplatelet drugs. In: Brunton LL, Hilal-Dandan R, Knollmann BC, eds. *Goodman & Gilman's: the pharmacological basis of therapeutics* [Internet]. 13th ed. New York, NY: McGraw-Hill Education; 2017. Available from: accessmedicine.mhmedical.com/content.aspx?aid=1154981387 [cited 6 November 2018].
 11. Ng W, Jerath A, Wąsowicz M. Tranexamic acid: a clinical review. *Anaesthesiol Intensive Ther* 2015; 47(4): 339–50. doi: 10.5603/AIT.a2015.0011
 12. Watts G. Utako Okamoto. *Lancet* 2016; 387(10035): 2286. doi: 10.1016/S0140-6736(16)30697-3
 13. WHO | Tranexamic acid (Inclusion) [Internet]. WHO. Available from: http://www.who.int/selection_medicines/committees/expert/17/application/tranexamic/en/ [cited 8 November 2018].
 14. CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet* 2010; 376(9734): 23–32. doi: 10.1016/S0140-6736(10)60835-5
 15. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2017; 389(10084): 2105–16. doi: 10.1016/S0140-6736(17)30638-4
 16. Study) C-2 C (Intracranial B. Effect of tranexamic acid in traumatic brain injury: a nested randomised, placebo controlled trial (CRASH-2 Intracranial Bleeding Study). *BMJ* 2011; 343: d3795. doi: 10.1136/bmj.d3795
 17. Xiong H, Liu Y, Zeng Y, Wu Y, Shen B. The efficacy and safety of combined administration of intravenous and topical tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled trials. *BMC Musculoskelet Disord* 2018; 19(1): 321. doi: 10.1186/s12891-018-2181-9
 18. Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, Painter T, et al. Tranexamic acid in patients undergoing coronary-artery surgery. *N Engl J Med* 2017; 376(2): 136–48. doi: 10.1056/NEJMoal606424
 19. Wang G, Xie G, Jiang T, Wang Y, Wang W, Ji H, et al. Tranexamic acid reduces blood loss after off-pump coronary surgery: a prospective, randomized, double-blind, placebo-controlled study. *Anesth Analg* 2012; 115(2): 239–43. doi: 10.1213/ANE.0b013e3182264a11
 20. Wang D, Wang L, Wang Y, Lin X. The efficiency and safety of tranexamic acid for reducing blood loss in open myomectomy. *Medicine (Baltimore)* 2017; 96(23): e7072. doi: 10.1097/MD.0000000000007072
 21. Kurnik NM, Pflibsen LR, Bristol RE, Singh DJ. Tranexamic acid reduces blood loss in craniostomosis surgery. *J Craniofac Surg* 2017; 28(5): 1325–9. doi: 10.1097/SCS.0000000000003731
 22. Martin DT, Gries H, Esmonde N, Diggs B, Koh J, Selden NR, et al. Implementation of a tranexamic acid protocol to reduce blood loss during cranial vault remodeling for craniostomosis. *J Craniofac Surg* 2016; 27(6): 1527–31. doi: 10.1097/SCS.0000000000002835
 23. Kim K-I, Kim HJ, Kim GB, Bae SH. Tranexamic acid is effective for blood management in open-wedge high tibial osteotomy. *Orthop Traumatol Surg Res* 2018; 104(7): 1003–7. doi: 10.1016/j.otsr.2018.07.019
 24. Palanisamy JV, Das S, Moon KH, Kim DH, Kim TK. Intravenous tranexamic acid reduces postoperative blood loss after high tibial osteotomy. *Clin Orthop Relat Res* 2018; 476(11): 2148–54. doi: 10.1097/CORR.0000000000000378
 25. Wei Z, Liu M. The effectiveness and safety of tranexamic acid in total hip or knee arthroplasty: a meta-analysis of 2720 cases. *Transfus Med* 2015; 25(3): 151–62. doi: 10.1111/tme.12212
 26. Farrow LS, Smith TO, Ashcroft GP, Myint PK. A systematic review of tranexamic acid in hip fracture surgery. *Br J Clin Pharmacol* 2016; 82(6): 1458–70. doi: 10.1111/bcp.13079
 27. Li G, Sun T-W, Luo G, Zhang C. Efficacy of antifibrinolytic agents on surgical bleeding and transfusion requirements in spine surgery: a meta-analysis. *Eur Spine J* 2017; 26(1): 140–54. doi: 10.1007/s00586-016-4792-x
 28. Rohrich RJ, Cho M-J. The role of tranexamic acid in plastic surgery: review and technical considerations. *Plast Reconstr Surg* 2018; 141(2): 507–15. doi: 10.1097/PRS.00000000000003926
 29. Murphy GRF, Glass GE, Jain A. The efficacy and safety of tranexamic acid in cranio-maxillofacial and plastic surgery. *J Craniofac Surg* 2016; 27(2): 374–9. doi: 10.1097/SCS.0000000000002250
 30. Cansancao AL, Condé-Green A, David JA, Cansancao B, Vidigal RA. Use of tranexamic acid to reduce blood loss in liposuction. *Plast Reconstr Surg* 2018; 141(5): 1132–5. doi: 10.1097/PRS.0000000000004282
 31. Pilbrant A, Schannong M, Vessman J. Pharmacokinetics and bioavailability of tranexamic acid. *Eur J Clin Pharmacol* 1981; 20(1): 65–72. doi: 10.1007/BF00554669
 32. Benoni G, Björkman S, Fredin H. Application of pharmacokinetic data from healthy volunteers for the prediction of plasma concentrations of tranexamic acid in surgical patients. *Clin Drug Invest* 1995; 10(5): 280–7. doi: 10.2165/00044011-199510050-00005
 33. Lanoisélée J, Zufferey PJ, Ollier E, Hodin S, Delavenne X, PeriOperative Tranexamic acid in hip arthroplasty (PORTO) study investigators. Is tranexamic acid exposure related to blood loss in hip arthroplasty? A pharmacokinetic-pharmacodynamic study. *Br J Clin Pharmacol* 2018; 84(2): 310–9. doi: 10.1111/bcp.13460

34. Hunt BJ. The current place of tranexamic acid in the management of bleeding. *Anaesthesia* 2015; 70 Suppl 1: 50–3, e18. doi: 10.1111/anae.12910
35. Levy JH, Koster A, Quinones QJ, Milling TJ, Key NS. Antifibrinolytic therapy and perioperative considerations. *Anesthesiology* 2018; 128(3): 657–70. doi: 10.1097/ALN.0000000000001997
36. Lecker I, Wang D-S, Whissell PD, Avramescu S, Mazer CD, Orser BA. Tranexamic acid-associated seizures: causes and treatment. *Ann Neurol* 2016; 79(1): 18–26. doi: 10.1002/ana.24558
37. Lin Z, Xiaoyi Z. Tranexamic acid-associated seizures: a meta-analysis. *Seizure* 2016; 36: 70–3. doi: 10.1016/j.seizure.2016.02.011
38. Ramirez RJ, Spinella PC, Bochicchio GV. Tranexamic acid update in trauma. *Crit Care Clin* 2017; 33(1): 85–99. doi: 10.1016/j.ccc.2016.08.004
39. Tengborn L, Blombäck M, Berntorp E. Tranexamic acid – an old drug still going strong and making a revival. *Thromb Res* 2015; 135(2): 231–42. doi: 10.1016/j.thromres.2014.11.012
40. Ross J, Al-Shahi Salman R. The frequency of thrombotic events among adults given antifibrinolytic drugs for spontaneous bleeding: systematic review and meta-analysis of observational studies and randomized trials. *Curr Drug Saf* 2012; 7(1): 44–54. doi: 10.2174/157488612800492744
41. Teng Y, Feng C, Liu Y, Jin H, Gao Y, Li T. Anti-inflammatory effect of tranexamic acid against trauma-hemorrhagic shock-induced acute lung injury in rats. *Exp Anim* 2018; 67(3): 313–20. doi: 10.1538/expanim.17-0143
42. Jimenez JJ, Iribarren JL, Lorente L, Rodriguez JM, Hernandez D, Nassar I, et al. Tranexamic acid attenuates inflammatory response in cardiopulmonary bypass surgery through blockade of fibrinolysis: a case control study followed by a randomized double-blind controlled trial. *Crit Care* 2007; 11(6): R117. doi: 10.1186/cc6173

***Octavio de Jesus Carrascal-Navarro**

Email: octaviocarrascal@gmail.com