https://doi.org/10.31925/farmacia.2022.5.7 **ORIGINAL ARTICLE**

TRANEXAMIC ACID - MAKING MASSIVE BODY WEIGHT LOSS SKIN REDUCING SURGERY EASIER AND SAFER

CARMEN GIUGLEA [1,2#], ELENA-CRISTINA BURLACU [1]*, LAVINIA ALICE BĂLĂCEANU [1,2#], GEORGE TRAIAN ALEXANDRU BURCEA-DRAGOMIROIU [2#], IULIA MIHAELA GAVRILĂ [1,2], ANDREI MARIN [1,2], SILVIU-ADRIAN MARINESCU [2,3]

[1] *"Sf. Ioan" Clinical Emergency Hospital, Bucharest, Romania*
[2] *"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*
[3] *"Bagdasar-Arseni" Clinical Emergency Hospital, Bucharest, Romania*

**corresponding author: elena.burlacu89@gmail.com*
[#]*Authors with equal contribution.*

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Abstract

Plastic and aesthetic procedures in patients with massive body weight loss require a careful management regarding the correct strategy implemented prior, during and following surgery. Post-operative haemorrhage and haematoma formation are some of the most undesirable complications that often need reinterventions. Tranexamic acid (TXA) is a synthetic antifibrinolytic pharmaceutic drug that suppress of the lysine binding sites of plasminogen to plasmin by precluding plasminogen from fastening to the fibrin molecule. Its role is to decrease perioperative blood loss. The authors assessed their experience with 70 consecutive patients that underwent lower body lift surgery from July 2018 to July 2021. They were divided into 2 groups, 35 of them received perioperative TXA and another 35 served as control (no TXA). We assessed the complication rates, blood loss and transfusion risk in the 2 groups to demonstrate the efficiency of TXA as a support in the surgical protocol. This study shows that the use of TXA in patients with massive body weight loss skin reducing surgery has a significant role in perioperative blood loss and its complications.

Rezumat

Procedurile plastice și estetice la pacienții cu pierderi masive de greutate corporală necesită un management atent în ceea ce privește strategia corectă implementată înainte, în timpul și după operație. Hemoragia postoperatorie și formarea de hematoame sunt unele dintre cele mai nedorite complicații care necesită adesea reintervenții. Acidul tranexamic (TXA) este un medicament antifibrinolitic de sinteză care blochează situsurile de legare pentru lizină din plasminogen, împiedicând astfel transformarea plasminogenului în plasmină. Este folosit pentru a diminua pierderile de sânge perioperatorii. În cadrul studiului au fost evaluați 70 de pacienți care au suferit o intervenție chirurgicală de ridicare a părții inferioare a corpului în perioada iulie 2018 - iulie 2021. Aceștia au fost împărțiți în 2 grupuri, astfel: 35 dintre ei au primit TXA perioperator, iar ceilalți 35 au fost lot control (fără TXA). Au fost evaluate ratele complicațiilor, pierderile de sânge și riscul de transfuzie în cele 2 grupuri pentru a demonstra eficiența TXA ca suport în protocolul chirurgical. Acest studiu arată că utilizarea TXA la pacienții cu pierdere masivă de greutate corporală în urma unei intervenții chirurgicale de reducere a pielii are un rol semnificativ în ceea ce privește pierderea perioperatorie de sânge și complicațiile acesteia.

Keywords: TXA, massive body weight loss, postbariatric surgery

Introduction

The antifibrinolytic drug tranexamic acid (TXA) is currently used to preserve blood in surgeries where there is a high risk of significant bleeding [1]. It prevents clot disassembly by inhibiting the activation of plasminogen into plasmin, and intravenous administration reduces bleeding and transfusion requirements by approximately one-third [2]. Fear of undetected adverse effects has so far bounded routine use of intravenous tranexamic acid to high-risk surgeries. TXA is a synthetic lysine analogue with a molecular weight of 157.2 Daltons that inhibits the conversion of plasminogen into plasmin by preventing plasminogen from binding to fibrin molecules [3]. Furthermore, TXA inhibits plasmin activity directly, although only at higher doses [4]. Metabolism of TXA in the liver is inferior; however it achieves a renal clearance of 95% [5]. The half-life in adults is approximately 2.3 h, after the intravenous dose of 1 g [6, 7]. Routinely, TXA is used in doses that varies from 10 to 135 mg/kg bw, and the duration differs from a single bolus to multiple infusions lasting up to three days [5]. In the medical literature, up to now, there are no reports underlying the availability of severe side effects, even if it was used in high dosages and long-term administration [8, 9]. By passing the blood-brain barrier, tranexamic acid leads to cerebro-spinal fluid concentrations of approximately 10% of

the plasma concentrations. That is why tranexamic acid is able to induce central nervous system hyper-excitability by obstructing the inhibitory neuro-transmitters gamma-aminobutyric acid and glycine from their action, and a 15 µg/mL cerebrospinal fluid concentration has been acknowledged as a threshold value for a possible excitatory effect. Administration of antifibrinolytics in major plastic and aesthetic surgery hasn't been settled as in others surgical fields such as orthopaedics, gynaecology, abdominal or cardiac surgery [10-12].

The interest in massive body weight loss surgery has been in a constant extension in the last decade due to the advancement of bariatric surgery [13, 14]. The patients that need to undergo body contouring surgery are often in a fragile equilibrium concerning their biological status and this is associated with a higher risk for surgical complications. Their level of haemoglobin and albumin are often in the lower edge of the normal parameters. By trying to minimise the blood loss we start to use the intravenous treatment with tranexamic acid during and immediately after surgery, on the basis that abdominoplasties are surgeries with large wound surfaces, which would allow for maximum absorption and retrieves a good model for a pharmacokinetic study. Regarding the blood conservation strategies, there are several inputs like costs and risks connected with blood transfusion, along with the struggling in getting blood products [1]. TXA has been proven his effectiveness in reducing blood loss during major orthopaedic surgeries [5]. Well-known anti-fibrinolytic agents, from which aprotinin is largely employed, have been linked with an increased occurrence of thrombotic complications like cerebral thrombosis, myocardial infarction, and renal dysfunction.

Materials and Methods

We perform a retrospective cohort study on benefits given by TXA regarding blood loss. All patients included in the study were admitted for surgery in the clinic after massive body weight loss. The inclusion criteria were: massive body weight loss (more than 30 kg), patients who needed one large or many surgical procedures for body contouring after massive body weight loss, BMI less than 25.15, no hypersensitivity to TXA, non-smokers, normal creatinine and glomerular filtration rate. The exclusion criteria were: less than 30 kg body weight loss, minor body contouring surgery, BMI greater than 25.15, hypersensitivity to TXA, renal insufficiency, smokers. The procedures were performed by a team of plastic surgeons in an interval of 3 years (July 2018 - July 2021). Body contouring procedures in our hospital could be referred as: circumferential abdominoplasty (lower body lifting) or classical abdominoplasty, simple or combined with brachioplasty, mastopexy, thigh lift or lipoaspiration. During all procedures the surgeon routinely placed 2 abdominal drains. The standard amount of 2 doses of tranexamic acid (vials of 500 mg/ 5 mL) was administrated intraoperative and immediately postoperative, *per* patient. All patients received low molecular weight heparin postoperatively 7 days as a preventive dose for thromboembolic events. We divided the patients into two groups: group A – patients who receive TXA perioperatively and group B – the patients who did not received TXA (the control group). Each group was formed by 35 patients. We analysed the quantity of blood loss by measuring the haemoglobin and haematocrit level, the need for blood transfusion, the drains aspect and quantity and the development of postoperative complications. The cohorts of patients were categorized by age, sex, BMI, body weight, creatinine level, glomerular filtration rate (Cockcroft-Gault), level of Hb and Ht preoperative and one day postoperative, postoperative blood transfusion and hematoma, aspect of the drains (Table I). The drains were maintained between 7 and 14 days and the aspect shift from sanguinolent to sero-sanguinolent to clear happen progressively. Each patient from group A received 0.5 g TXA (1 vial of 5 mL) slowly administered intravenously intraoperative and another 5ml vial immediately postoperative. Taking into consideration that the average body weight from the TXA group is 67 kg (minimum 55 kg – maximum 88 kg, an average dose of 14.9 mg/ kg was used (maximum 18.18, minimum 11.36 mg *per* kg). No side effects were noticed after administration. Statistical analyses were achieved using SPSS (IBM SPSS statistic 21.0.0, IBM Corp. Armonk, N.Y.). Independent-Samples t test was used for parametric variables. Pearson's chi-square test was used for analysing normal variables. Preoperative variable and postoperative outcome were compared using the Descriptive Statistics, Bivariate Correlations, Crosstabulations, One-Way ANOVA, Mann-Whitney U test, and chi-square as appropriate. P-value < 0.05 was considered statistically significant.

Table I

Patients' data and variables

	TXA Group	**Non-TXA Group**
Age	36.51 years old (min. 21 – max. 60)	39.85 years old (min. 21 – max. 61)
Sex	4 M; 31 F	4 M; 31 F
BMI	23.88 (min. 20.96 – max. 25.15)	23.19 (min 19.33 – max 25.15)
Weight	67.14 kg (min. 55 kg – max. 88 kg)	62,34 (min 52 kg – max 79 kg)
Hb level preoperatory	12.72 g/dl (min. 10.1 – max. 14.4)	13.51 g/dl (min 9.8 – max 17.1)

	TXA Group	Non-TXA Group
Ht level preoperatory	37,92 % (min. 30.7 – max. 42.7)	40.38 % (min 31.2 – max 48)
Hb level postoperatory	11.03 g/dl (min 8.6 – max 13.9)	10.05 g/dl (min 6.7 – max 12.1)
Ht level postoperatory	30.16 % (min 24.2 – max 36.2)	28.05 % (min 21.6 – max 33.8)
Blood transfusion	0 patients	2 patients
Postoperative hematoma	1 patient	5 patients
Drain aspect shift	< 36 hours	> 36 hours
Creatinine level	0.84 mg/dl (min 0.7 – max 0.99)	0.82 mg/dl (min. 0.68 – max. 0.94)
RFG	99.85 (min. 67 – max. 153)	94.85 (min. 68 – max. 139)

Results and Discussion

The sample size estimation was set considering the study performed by Maniar *et al*. In this regard, for the mean difference of 250 mL of intraoperative blood loss between the groups, in order to be detected with a standard deviation of 50 mL, a power of 80%, and alpha error at 0.05%, a minimum of 35 patients in each group were required.

The preoperative levels of haemoglobin and haematocrit had an average of 12.72 mg/dL and 37.92% in the TXA group and 13.51mg/dL and 40.38 in the non-TXA group. The postoperative Hb level and blood loss were significantly lower and higher in the control group, respectively – with an average of Hb level of 10.5 mg/dL in the non-TXA group as compared with 11.3 in the TXA group. We found a difference of Hb level of 1.42 mg/dL in the TXA group *versus* 3.01 mg/dL in the non-TXA group, having a strong statistical correlation with a p = 0.002 (Figure 1).

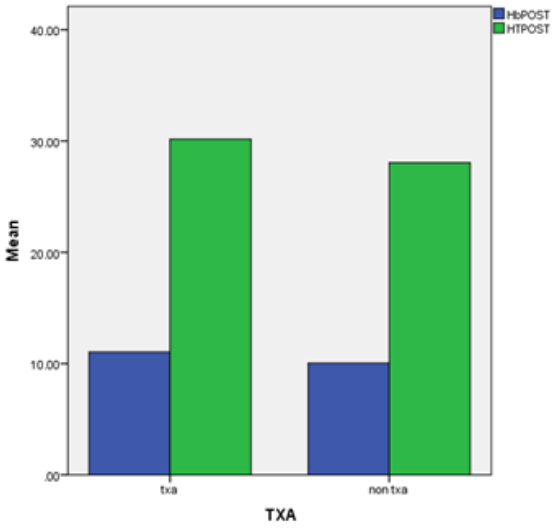

Figure 1.
Postoperative haemoglobin and haematocrit levels

The haematocrit level dropped from 37.92% in the TXA group to 30.16% in the first day postoperative, and from 40.38% to 27.96% in the non-TXA group. Likewise, there was found a strong statistical correlation between the two groups, with a result of 7.76% loss of Ht level in the first group *versus* 12.42% loss in the second group (Figures 2, 3, 4 and 5).

In addition, the rate of blood transfusion was significantly greater in the control group – 2 patients needed 2 units of blood transfusion, on the grounds that their Hb levels reached 6.9 and 6.7 mg/dL, and the heamatrocrit reached 24%, respectively 23.6%. No patient from the TXA group needed blood transfusion (P = 0.01) (Figure 5).

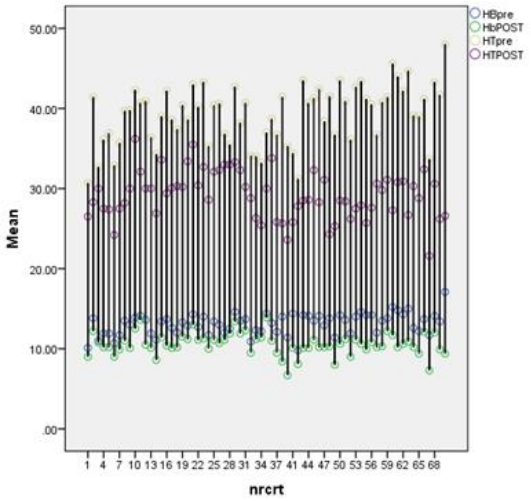

Figure 2.
Haemoglobin and haematocrit drop line

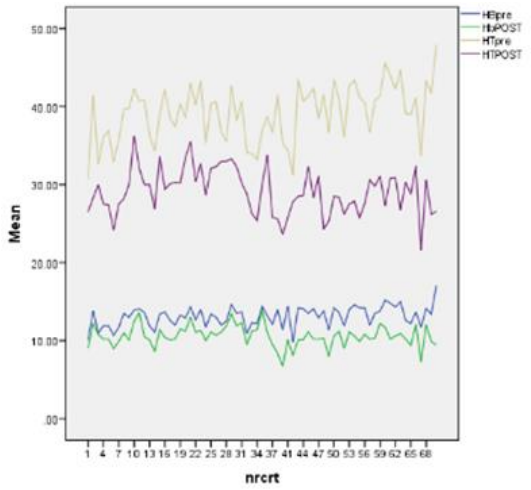

Figure 3.
Preoperative and postoperative haemoglobin and haematocrit level

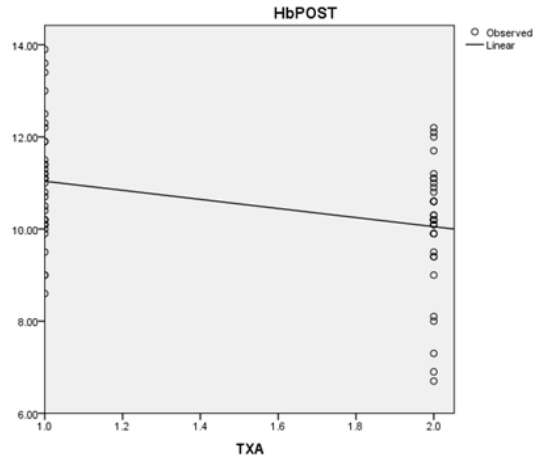

Figure 4.
Haemoglobin drop curve

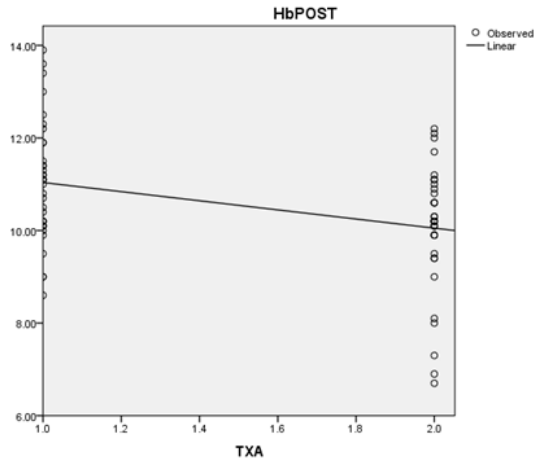

Figure 5.
Haematocrit drop curve

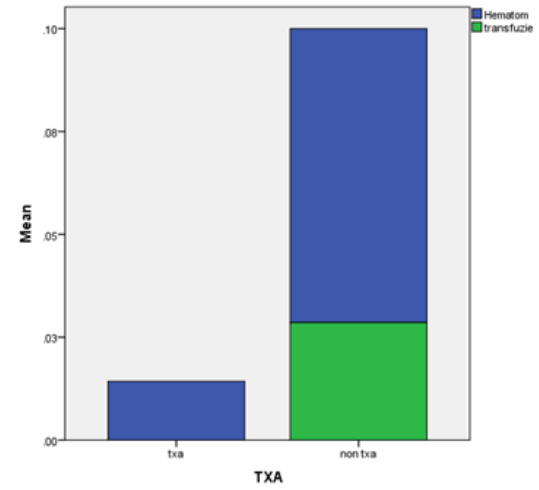

Figure 5.
Postoperative complications

The aspect of the drainage changed faster from sero-sanguinolent to serous, in less than 36 hours compared with the other group, more than 36 hours. (P = 0.11) (Figure 7). However, the duration of maintaining the drainage tubes did not differ significantly in terms of measured variables (p = 0.73). No patient experienced a thromboembolic accident in our study. The most often local complications following intervention were haematomas, seromas and wound dehiscences. We analysed the presence of hematomas in both groups and noticed a lower risk of hematoma formation in the TXA group. In the TXA group we found one patient that developed a postoperative haematoma as compared with 5 patients in the non-TXA group (p = 0.09) (Figure 6).

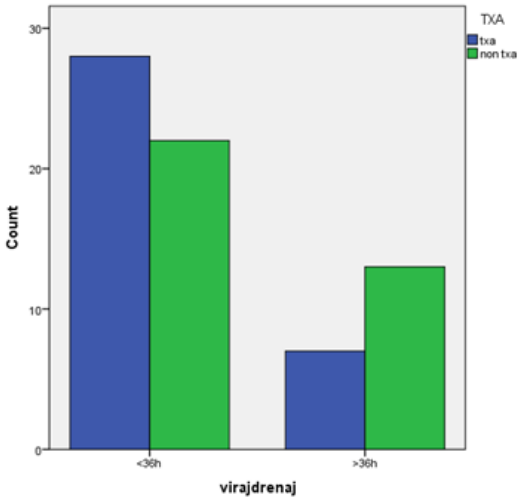

Figure 6.
Drainage colour changing

No thromboembolic complications such as deep venous thrombosis or lung embolism were found in these patients at 12 months follow-up. No cases of acute kidney injury were found in the patients receiving TXA.

There is an extensive research available on the effects and benefits of tranexamic acid in various areas of surgery, however, few information are known about the effect of tranexamic acid in massive body weight loss skin reducing surgery. TXA was primarily discovered in 1962 by to independent research groups [15, 16]. The studies had found that the trans form of 4-(aminometil)- cyclohexane-carbonic acid had antifibrinolytic properties [16]. Some of the initial randomized studies examining the efficacity of TA in lessening blood loss in orthopaedic surgery were published in 1997 by Hiippala *et al.* [17]. Increased fibrinolytic activity has been argued to be a substantial factor for increased blood loss during massive surgery. TXA counteracts the fibrinolytic process by indirectly blocking the lysine-binding sites on plasminogen, in a reversible manner. This consequently prevents the connection of fibrin in the plasminogen plasmin tissue activator complex, and as follows the degradation of fibrin is secluded [18, 19]. The most common administration course for

TXA in the studies that were published along the 60 years period is the intravenous route [20]. TXA is contraindicated in patients with hyper sensibility or allergy to this substance, venous or arterial thrombosis history, intrinsic risk for thrombosis or thrombo-embolism, renal failure, subarachnoid haemorrhage and epileptic seizures [21]. In the latest years TXA has begun to revive and its use has been included in the plastic surgery domain in both divisions – reconstructive and aesthetic field [22, 23].

Aytuluk *et al*. considered the advantages of TXA lower doses with a mixture in TKA (Total Knee Arthroplasty). They determined that a total dose of 10 mg *per* kg of TXA intravenous infusion initiated 15 minutes prior to surgery until wound closure can substantially decrease blood loss and the intraoperative infusion treatment is beneficial than the divided dose administration [5]. Maniar *et al*. investigated different quantities, timings, and modules of administration to calculate the most effective system of TXA in achieving a maximum reduction of blood loss in total knee arthroplasty. The conclusion was that TXA administered perioperatively, in an attrition of drain loss as well as total blood loss, was most effective [24]. Thipparampall *et al*. gathered that a bolus of TXA (10 mg *per* kg bw and 1 mg *per* kg bw *per* hour for a 4-hour period) is more convenient than a single dose in in order to decrease perioperative blood loss in patients undergoing hip surgeries. That can be translated in reducing the transfusion of blood products without expanding the appearance risk of thromboembolic events [25]. Zufferey *et al*. studied if the supplementation of the iv infusion to bolus dose had better results in decreasing blood loss in primary hip arthroplasty and deduced that additional perioperative administration of TXA did not acquire any further reduction in blood loss [26].

Conclusions

Haemorrhage and transfusion impact the wider health service by increasing postoperative hospitalisation, also with a blood donor supply under substantial pressure to continue to recruit plenty donors, the benefits of reducing transfusion rates are clear. TXA is a useful antifibrinolytic drug to reduce postoperative blood loss, Hb drop rate, the need of blood transfusion and drainage quantity in patients undergoing skin reducing surgery procedure following massive body weight loss. TXA should be considered for routine administration in postbariatric surgery and approving and extending the indications for its use would be an advantageous part to decrease haemorrhage complications.

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Conflict of interest

The authors declare no conflict of interest.

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