

## ORIGINAL ARTICLE, MEDICINE

# Tranexamic Acid in Pertrochanteric Femoral Fracture: Is it a Safe Drug or Not?

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**Background:** There is a high incidence of blood transfusion following hip fractures in elderly patients.

**Aim:** The aim of this study is to evaluate the effectiveness and complications of use of tranexamic acid in proximal femur nailing surgery.

**Materials and methods:** Our sample group consisted of 90 patients suffering from pertrochanteric fractures surgically treated with osteosynthesis with SupernailGT(LimaCorporate). The classification system AO/OTA was used to divide the fractures into 31A1 (n=45) and 31A2 (n=45). The patients were divided into two groups: 47 patients were administered 15 mg of tranexamic acid per kg (group A) and 43 patients were administered placebo (group B). Blood counts were monitored daily to evaluate the rate of anemia. As a safety criterion, we monitored the possible occurrence of vascular events, symptomatic or not, over the 8 weeks post-surgery. Markers predicting mortality and deep venous thrombosis (DVE) were also monitored (fibrinogen D-dimer).

**Results:** Blood loss occurring post-surgery can be influenced by numerous factors that are not linked to the use or non-use of tranexamic acid. While closely monitoring hemoglobin levels daily, we observed that 42% of the patients in group A required blood transfusion as opposed to 60% in group B. The results of the markers predicting mortality (alpha1-acid glycoprotein; albumin LDL) and those of DVE were not statistically significant between the two groups in this study (p>0.05).

**Conclusion:** Based on this study, the use of tranexamic acid was statistically significant in reducing post-surgery blood loss.

**BACKGROUND**

The incidence of proximal femur fractures in the elderly is rising steadily, positioning them together with the wrist fractures at the top in order of frequency.<sup>1</sup> It is estimated that every year in Italy alone, more than 95,000 fractures occur - of these, about 40% are trochanteric fractures.<sup>2</sup> This type of fracture is associated with considerable post-operative blood loss.<sup>3</sup> The post-operative mortality rate decreases significantly by reducing blood loss.<sup>4</sup> The outcome of this population is extremely unfavorable.<sup>5,6</sup> Furthermore, one should consider the associated spending required of the Italian health system which amounts to 568 million Euro annually,

which should be added to all of the work relatives and health professionals do to manage a pathology this frequent in a country whose elderly population is steadily increasing.<sup>7,8</sup>

Surgical intervention with osteosynthesis allows for a premature recovery permitting mobilization and immediate loading, but at the expense of worsening the already present clinical conditions of the elderly patients, who are already jeopardized in most cases. One of the main problems is post-operative blood loss which is either due to the fracture itself or to the surgery. The use of allogeneic transfusions has high costs for the National Health System<sup>7,8</sup>, especially compared to

the expenditure for tranexamic acid, which is very cheap in comparison.<sup>9</sup> Additionally, one should not underestimate the need for a constant supply of blood donors to compensate the blood loss. Tranexamic acid is an antifibrinolytic drug whose administration during the perioperative period either by intravenous route or topically applied to the surgical field has been shown to reliably reduce blood loss and need for transfusion.<sup>10</sup>

The ability of this drug to effectively reduce post-operative blood loss has already been demonstrated in several surgical operations, including knee and hip arthroplasty which can result in major blood loss.<sup>14</sup> The surgeon and/or the anesthesiologist should consider the use of antifibrinolytic agents for patients undergoing major orthopaedic surgical procedures in which a large amount of blood loss can be expected.<sup>11</sup>

Studies on the use of tranexamic acid have shown interesting results, but its benefits have not yet been resolved.<sup>12-13</sup>

It is important to remember the adverse effects of the drug that are linked to a state of hypercoagulable blood.<sup>9</sup>

## MATERIALS AND METHODS

From March 2015 to September 2015, at Hospital Santa Maria della Misericordia of Perugia, from 216 patients suffering by proximal femoral fractures, we recruited 90 patients suffering from pertrochanteric fractures surgically treated with osteosynthesis with Supernail GT®(Lima™). The classification system AO/OTA was used to divide the fractures into 31A1 (n=45) and 31A2 (n=45). The Müller AO Classification of fractures is a system for classifying bone fractures. It is one of the few complete fracture classification systems to remain in use today after validation. The Orthopaedic Trauma Association in 2006 published a revision, unifying the Müller/AO and OTA systems into a single alphanumeric classification.

The patients were divided into two groups (**Table 1**): 47 patients who were administered tranexamic acid (group A) and 43 patients who received saline solution-placebo (group B). We used tranexamic acid, after authorization, in periods of non-availability of blood in the hospital, to decrease the demand for postoperative blood.

The exclusion criteria were (**Table 3**): polytrauma;

**Table 1.** Characteristics of the study sample divided into two groups: group A patients treated with tranexamic acid; group B patients treated with placebo (saline solution)

Characteristics	Tranexamic acid Group A (n= 47)	Tranexamic acid not used Group B (n=43)
Females [(n) (%)]	35 (16.45)	28 (12.04)
Males [(n) (%)]	12 (5.64)	15 (6.45)
Mean age (years)	84.3±8.3	84.3±8.3
Patients treated for osteoporosis	(90%)	(93%)
ASA physical status classification system	ASA I: 2 ASA II:21 ASA III:23 ASA IV:1	ASA I:2 ASA II:18 ASA III:20 ASA IV:3
BMI average (kg/m <sup>2</sup> )	28±8	28±8
Classification AO/OTA		
31-A1 [(n) (%)]	33 (15.51)	12 (5.16)
31-A2 [(n) (%)]	14 (6.58)	31 (13.33)
Pre-operative antibiotic prophylaxis	Cefazolin 2g I.V.	Cefazolin 2g I.V.
Tranexamic acid dose administered	15 mg/kg	Saline solution (same dose)
Average week of follow-up post surgery	8	8

patients operated more than 48 hours after the traumatic event; refusal of consent to participate in the study; dementia; patients whose relatives have not given their consent to participate; oral anticoagulant therapy; contraindications to treatment with tranexamic acid (a history of prior venous or arterial thrombosis, brain stroke, patients with creatinine clearance below 30 ml/min); patients who were administered tranexamic acid during or at the end of surgery; patients who require one or more transfusions before surgery; patients with INR > 1.2; patients with hematological diseases; patients who had the intra-operative complication of the migration of the intra-pelvic wire guide.<sup>15</sup>

All patients were treated with osteosynthesis technique with intra-medullary Gamma nail "Lima Sm Supernail Gt", head screws, anti-rotational

screws and dynamic distal locking screws.<sup>16</sup>

All patients received 2 g of intravenous cefazolin as preoperative antibiotic prophylaxis.

The sample consisted of 63 female patients (70%) and 27 male patients (30%). The mean age was 84.3±8.3 years, with a minimum of 61 and a maximum of 99 years. The mean BMI was 28 kg/m<sup>2</sup> (±8.0). The patients were monitored for 8 weeks.

The injection of tranexamic acid was carried out at the time of surgical incision. The dose used was 15 mg per kg. The other group of patients (group B) received the same dose of saline solution at the same time.

Regarding the type of anesthesia used, 76.88% of the patients were subjected to loco-regional anesthesia (LRA), while the remaining 12.23% were given general anesthesia (GA). Of these, 39.70%

**Table 2.** Comorbidity between the two study groups

Comorbidity	PS Group A (%)	PS Group B (%)
Cardiovascular diseases	15 (31.9%)	12 (27.9%)
Stroke	0 (0%)	0 (0%)
Respiratory diseases	4 (8.5%)	9 (20.9%)
Nephro-Urologic diseases	11 (23.4%)	17 (39.5%)
Diabetes mellitus	11 (23.4%)	7 (16.31%)
Rheumatic diseases	0 (0%)	0 (0%)
Parkinson's disease	0 (0%)	0 (0%)
Smokers	9 (19.1%)	12 (28.0%)
Use of steroids	2 (4.3%)	2 (4.7%)
Number of comorbidity for patient		
1	21 (44.7%)	18 (41.8%)
2	23 (48.9%)	20 (46.5%)
≥3	1 (2.1%)	3 (7.0%)

**Table 3.** Criteria for exclusion from the study

Exclusion criteria
Multi-trauma
Patients operated on > 48 hours after the event
Refusal to consent
Patients with dementia whose relatives refused consent
Oral anti-coagulant therapy
Contraindications for using tranexamic acid
Administered tranexamic acid before or after surgery
Transfusions before surgery
INR >1.2
Hematological disorders
Migration of the intra-pelvic guide wire as an intraoperative complication

in the group treated with tranexamic acid, and 37.19% in group B were subjected to the LRA.

The rate of anemia was calculated by daily monitoring of patients' blood count. Transfusion of packed red blood cells was used if the hemoglobin levels were less than 8.5 g/dl. The parameters for transfusion for high-risk patients (cardiac patients with the New York Heart Association index greater than 3 and patients with respiratory failure) was 9 g/dl.<sup>17</sup>

All patients received Ringer's lactate during surgery and fluid therapy for 12 hours postoperatively.

The concentration of hemoglobin was measured with HemoCueHb 201+ everyday postoperatively.<sup>18</sup> Death predictors were measured at patients' arrival, in the early postoperative phase, and at discharge using three related values: alpha 1-acid glycoprotein ( $\alpha$ 1ag); albumin (Alb); the low density lipoprotein (LDL) cholesterol.<sup>19</sup> The risk thrombo-embolic markers (D-dimer and fibrinogen) were also evaluated at patients' arrival, after surgery, at discharge, after the first and third months.<sup>20-21</sup>

Patients were discharged with instructions to perform a CBC-electrolyte control within 4 days and to show them to their GP or doctor of the host health facility for rehabilitation. All patients were instructed to: use partial load of up to 50% of body weight for the operated limb, do isometric exercises, venous pump exercises, and breathing exercises for 40 days. The next clinical and radiographic check-up was after 40 days for subsequent provisions and analysis of the effected blood tests.

The patients were also contacted by telephone both after four days and at 4 and 8 weeks to assess the normal traumatologic follow-up of these fractures. The safety of the drug was evaluated by monitoring both arterial and venous vascular post-operative complications, both symptomatic and asymptomatic, diagnosed by ultrasonography, complicated by a possible pulmonary thrombo-embolism, or stroke (the latter two confirmed by computed tomography), or cutaneous ischemia and acute coronary syndromes.<sup>22</sup>

#### STATISTICAL ANALYSIS

Whether or not a transfusion was required was taken into consideration as a primary effect. This was evaluated statistically using the two-sided Fisher's exact test. The effect of risk factors for RBC transfusion on the primary study outcome was evaluated by multi-variable logistic regression analysis. Covariates for logistic regression analysis were selected on

the basis of their clinical and biological plausibility. They were first analysed for univariate influence on RBC transfusion. Only variables with a P-value less than 0.25 were included in the multivariable analysis. Treatment effect of tranexamic acid was adjusted for those risk factors that were identified at multivariate analysis.

Survival rates were evaluated using the Kaplan-Meier indicator with the log-rank-test. Odds ratio (OR), hazard-ratio (HR), or number needed to treat (NNT) are presented with 95% confidence intervals. Data were analysed using  $\chi^2$  test or Fisher's exact test and Student's t-test or Mann-Whitney U-test when appropriate. A two-tailed P-value of less than 0.05 was considered to indicate statistical significance.

The efficacy endpoint was the proportion of patients receiving at least 1 U of allogenic RBC transfusion according to transfusion protocol. For statistical analysis of the parameters of death predictors [ $\alpha$ 1-acid glycoprotein ( $\alpha$ 1ag)], albumin (Alb), low-density lipoprotein (LDL)] and markers of DVT risk (D-dimer and fibrinogen), the Student t-test with  $p < 0.05$  was used.

#### RESULTS

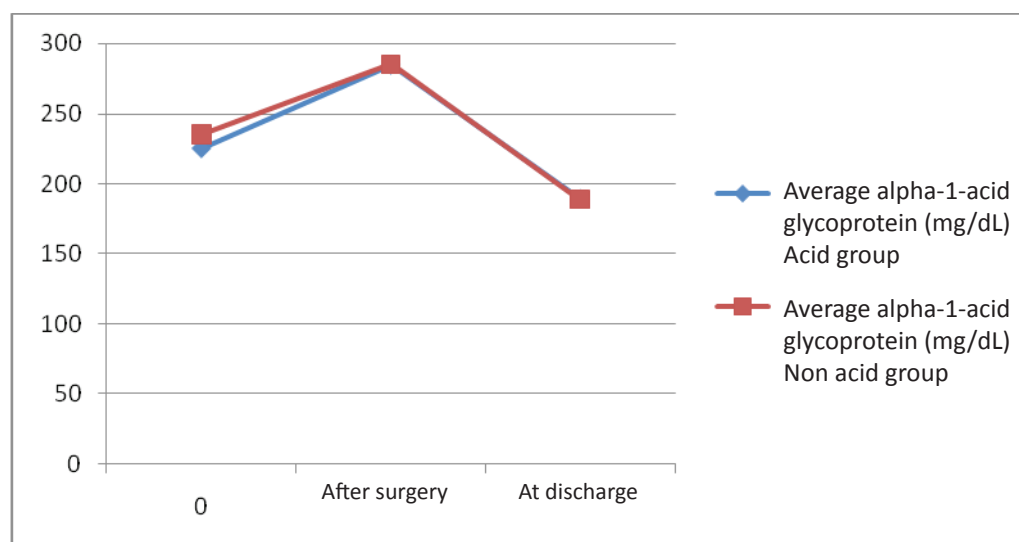
The average length of hospital stay was 6 days post-operatively with a minimum of 4 to a maximum of 8 days without any statistically significant difference between the two groups in the average duration of hospital stay.

Considering the group of patients treated with tranexamic acid, it was observed that 42.55% (n=20) needed 1 bag of red blood cells since they all had hemoglobin values less than 8.5 g/dl. The percentage of patients in the group B needing a bag of packed red blood cells was 60.46% (n=26). It should also be noted that in group A only 3 patients had to be given additional bags; while in group B, 5 patients needed more bags. Based on the P value, there was no statistically difference between the two groups with  $p = 0.06$ . No patients received transfusions in the period between the moment of trauma to the moment of surgery. No patient underwent postoperative transfusion of blood derivatives of any kind (**Table 9**).

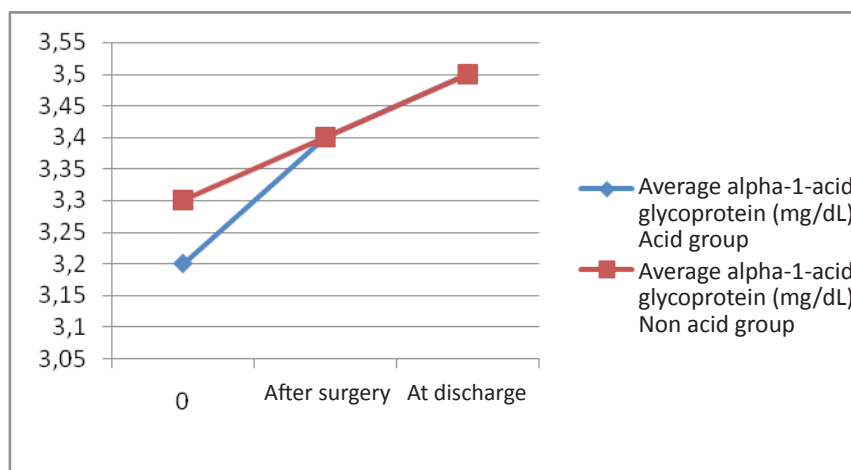
The Odds Ratio for the percentage of hemoglobin loss was statistically significant considering that the risk of hemoglobin loss was 99% of group A patients versus 97% of patients in group B. The resulting P-value is 0.03%. This indicates that there is a difference in the hemoglobin levels between

**Table 4.** Trend of alpha-1-acid glycoprotein (n.v. 55-120 mg/dL) during hospitalization of follow up in the two groups

Time	Average alpha-1-acid glycoprotein (Mg/Dl) acid group	Average alpha-1-acid glycoprotein (Mg/Dl) Non acid group
0	225.3 (range 160-380)	235.2 (range 65-390)
After surgery	284.6 (range 178-424)	285.1 (range 180-420)
At discharge	189.3 (range 154-228)	188.9 (range 146-234)

**Table 5.** Trend of Alb (n.v. 3-5 g/dL) during hospitalization of follow up in the two groups

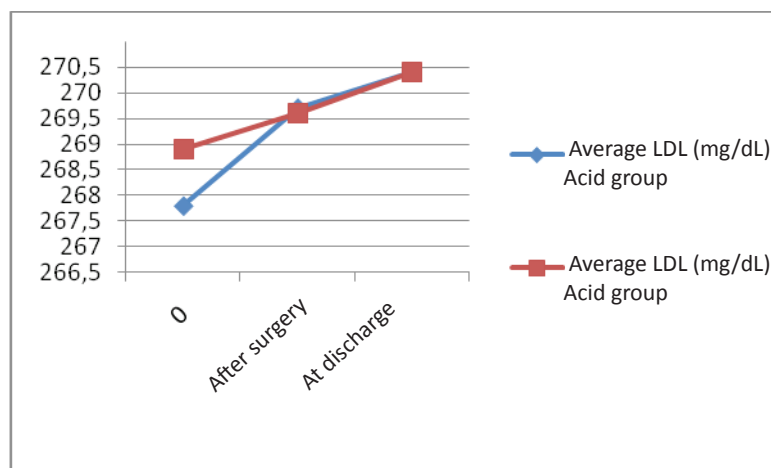
Time	Average Alb (g/dL) acid group	Average Alb (g/dL) non acid group
0	3.2 (range 2.4-5.6)	3.3 (range 2.4-5.6)
After surgery	3.4 (range 2.6-6)	3.4 (range 2.4-5.6)
At discharge	3.5 (range 2.4-5.6)	3.5 (range 2.4-5.6)





**Table 6.** Trend of LDL (n.v. < 200 mg/dL) during hospitalization of follow-up in the two groups

Time	Average LDL (mg/dL) acid Group	Average LDL (mg/dL) non acid group
0	267.8 (range 168-340)	268.9 (range 156-356 )
After surgery	269.7 (range 172-338)	269.6 (range 159-351)
At discharge	270.4 (range 163-348 )	270.4 (range 161-354 )

**Table 7.** Trend of fibrinogen (n.v. 200-400 mg/dL) during three months of follow up in the two groups

Time	Average fibrinogen (mg/dL) Acid	Average fibrinogen (mg/dL) Non Acid
0	643 range 543.2–742.8	641 range 541.2–740.8
After surgery	626.6 range 527.7–724.4	624 range 525.9–730.4
At discharge	683 range 604.2–761.8	684 range 602.4–759.9
1 <sup>st</sup> month	431 range 362.1–499.9	432.1 range 363–501.1
3 <sup>rd</sup> month	206.9 range 158.1–265.7	206.1 range 160.2–164.7

**Table 8.** Trend of D-dimer changes (n.v. 50-500 ng/mL) during three months of follow up in the two groups

Time	Average D-dimer (ng/mL) acid	Average D-dimer (ng/mL) non acid
0	697 range 594.8–799.2	699.6 range 596.2–800.2
After surgery	771 range 658.8–883.2	768.1 range 655.9–880.9
At discharge	776.2 range 662.9–889.5	777.4 range 663.4–890.5
1 <sup>st</sup> month	499 range 414.6–583.4	501.1 range 418.2–580.9
3 <sup>rd</sup> month	155.1 range 119.1–187.1	153 range 121.8–189.8

**Table 9.** HB before surgery and after surgery in groups A and B

	Tranexamic acid Group A (n= 47)	Tranexamic acid not used Group B (n=43)
Hb average before surgery [(g/dl) (min-max)]	11.2 [10-13]	11.3 [10-13]
Hb average after surgery [(g/dl) (min-max)]	9.8 [9.5-10.4]	9.5 [9.1-10.1]
Hb average before discharge [(g/dl) (min-max)]	10.2 [10-10.8]	10.0 [9.6-10.2]
Hb average 4 days post-discharge [(g/dl) (min-max)]	10.3 [9.9-10.7]	10.1 [9.5-10.3]
Hb average at 8 weeks [(g/dl) (min-max)]	11.2 [10.8-11.5]	11.0 [10.8-11.2]
Transfusions		
1 U.I. [(n) (%)]	20 [42.55%]	26 [60.46%]
>1 U.I. [(n) (%)]	3 [1.41%]	5 [2.15%]
Transfusions before surgery (n)	0	0

**Table 10.** Vascular and death events

	Tranexamic acid Group A (n= 47)	Not Used Tranexamic Acid Group B (n=43)
Vascular and death event [(no.) (%)]	9 (19.15)	3(6.98)
Asymptomatic distal DVT [(no.) (%)]	1(2.13)	0 (0)
Asymptomatic proximal DVT [(no.) (%)]	1(2.13)	0 (0)
Acute coronary syndrome [(no.) (%)]	3 (6.38)	0 (0)
Stroke [(no.) (%)]	1(2.13)	0 (0)
Death [(no.) (%)]	4 (8.51)	3 (6.98)

the two groups, regardless of transfusions, which is higher in group B with respect to the group treated with tranexamic acid.

Regarding the safety of tranexamic acid, at 8 week follow-up, cardiovascular complications were detected (some resulting in death) in 9 patients in group A and in 3 in group B (HR 2.7 with  $p=0.1$ ). It was reported that four patients in group A and 3 patients in group B died. The increased risk of using this drug, therefore, was not statistically significant (**Table 10**).

Upon admission to the emergency room, the average value of  $\alpha$ 1ag was 225.3 mg/dl (range 160-380) in the tranexamic acid group while the average was 235.2 mg/dl (range of 165-390) in the group B (**Table 4**). There was no statistical

difference between the two groups ( $p > 0.05$ ). At blood sampling after surgery, the average value of  $\alpha$ 1ag was 284.6 mg/dl (range 178-424) in the group treated with tranexamic acid, while the average was 285.1 mg/dl (180-420) in group B ( $p>0.05$ ) (**Table 4**).

At discharge, the average value of  $\alpha$ 1ag was 189.3 mg/dl (range 154-228) in the group treated with tranexamic acid, while the average was 188.9 mg/dl (146-234) for the patients in group B (**Table 4**). There were no statistical differences between the two groups ( $p>0.05$ ). There was no statistical difference ( $p> 0.05$ ) between the input and output values between the various groups.

The same situation was discovered at emergency room admission for the average value of Alb, which

was 3.2 g/dl (range 2.4-5.6) in the tranexamic acid group while the average was 3.3 g/dl (2.4-5.6 range) in group B (**Table 5**). There was no statistical difference between the two groups ( $p>0.05$ ). At blood sampling after surgery, the average value of Alb was 3.4 g/dl (range 2.8-6) in the group with tranexamic acid, while in group B, the average was 3.4 g/dl (range 2.8-6) ( $p>0.05$ ) (**Table 5**).

At discharge, the average value of Alb was 3.5 g/dl (2.4-5.6 range) in the tranexamic acid group, while the average was 3.5 g/dl (range 2.4-5.6) in group B (**Table 5**). There was no statistical difference between the two groups ( $p>0.05$ ). There was no statistical difference ( $p>0.05$ ) between the input and output values between the various groups (**Table 5**).

The same situation was discovered at the emergency room admission for the average value of LDL was 267.8 mg/dl (range 168-340) in the tranexamic acid group while the average was 268.9 mg/dl (range 156-356) for group B patients (**Table 6**). There was no statistical difference between the two groups ( $p>0.05$ ). At blood sampling after surgery, the average value of LDL was 269.7 mg/dl (range 172-338) in the group with tranexamic acid, the same parameter being 269.6 mg/dl (range 159-351) in group B ( $p>0.05$ ) (**Table 6**).

At discharge, the average value of LDL was 270.4 mg/dl (range 163-348) in the tranexamic acid group, while the average was 270.4 mg/dl (range 161-354) in group B (**Table 6**). There was no statistical difference between the two groups ( $p>0.05$ ). There was no statistical difference ( $p>0.05$ ) between the input and output values between the various groups (**Table 6**).

Regarding the fibrinogen values, the average value after the intervention was 626.6 mg/dl for group A and 624 mg/dl for group B, with no statistical difference between the two groups ( $p>0.05$ ). The same was true for the values at discharge (683 mg/dL for group A and 684 mg/dL for group B); the first month (group A - 431 mg/dl and group B - 432.1 mg/dl); the third month (206.9 mg/dl for group A and 206.1 mg/dl for Group B patients) (**Table 7**).

Regarding the D-dimer values, the average value after the intervention was 771 ng/mL for group A and 768.1 ng/dl for group B, with no statistical difference between the two groups ( $p>0.05$ ). The same was true for the values at discharge (776.2 ng/mL for group A and 777.4 ng/mL for group B patients); the first month: 499 ng/mL in group

A and 501.1 ng/mL in group B; the third month: 155.1 ng/mL in group A and 153 ng/mL in group B (**Table 8**).

## DISCUSSION

Tranexamic acid (TXA), a synthetic derivative of the amino-acid lysine, has been used to reduce blood loss and transfusion requirements in patients undergoing orthopedic surgeries based on its antifibrinolytic properties. By competitively blocking the lysine-binding sites on plasminogen, TXA is able to reduce the local degradation of fibrin by plasmin.<sup>23</sup>

The efficacy of the use of TXA in orthopedic surgery has been proven but its proper use is still unclear.<sup>24</sup> Also, we don't know the real consequences using TXA in fractures. Furthermore, the optimal dosing and time of TXA administration is still debated.<sup>25</sup>

Petrochanteric fractures and their surgical treatment leads to a blood loss so significant that it requires the need for concentrated red blood cell transfusions in the pre-operative stages differing from intracapsular femoral fractures. In 2014, Barbour et al. reported that the highest inflammatory marker levels were correlated with an increased risk of fracture in elderly people.<sup>26</sup> The mortality in our study population of patients over 75 is linked more to the chronic inflammatory state and comorbidities rather than whether tranexamic acid is used or not. In our study, about 1 of 2 patients underwent a transfusion; which are satisfactory results in comparison with those reported by Hou et al.<sup>27</sup> in which the need for transfusions in patients treated for this type of fracture was  $3.1\pm 1.47$  IU.<sup>27</sup>

It is an interesting value that could be reduced by administering TXA to the patient. Our study also highlights the increased risk of symptomatic and asymptomatic DVT, pulmonary thromboembolism, stroke, brain stroke and acute coronary syndrome in group A as opposed to group B. These events are not statistically significant. Our results agree with those of the literature as shown by the systematic review by Farrow et al.<sup>28</sup> and Mayeux et al.<sup>29</sup> Tranexamic acid was administered before incision and not during or at the end of surgery so as not to greatly affect the blood loss, as proposed by Gaused et al.<sup>30</sup> The dose used was 15 mg/kg, which differed from that used by Gaused (1g in 100 cc of saline solution).<sup>30</sup> The reduction in haemoglobin levels of the sample examined turned out to be statistically significant, and the data are in line with the international literature.<sup>30,31</sup> By reducing



blood loss, the use of TXA reduces hospital costs by reducing the need of transfusions, reducing laboratory costs and hospital days.<sup>32</sup>

The values obtained in this study regarding mortality predictor markers and possible DVT are in line with recent literature, as demonstrated by the values of Fischer et al.<sup>20</sup> and Wiseman et al.<sup>21</sup> In the first case, the three biomarkers taken into consideration are associated with all of the causes of mortality, and are involved in various pathophysiological mechanisms, including inflammation and in maintaining the homeostasis. The alfa-1 acid glycoprotein is an acute phase protein that increases in response to infections and inflammation.<sup>33</sup> Its levels are associated with all causes of mortality in elderly people with cardiovascular as well as tumor genesis. It must, however, be associated with other predictor markers to have a higher sensitivity.<sup>34</sup>

The plasma albumin is a marker of liver and kidney function, nutritional status and inflammation.<sup>35</sup> Low circulating levels of this protein result in an increase in vascular and non-vascular mortality. It is correlated with an increased susceptibility to various diseases and fragility in elderly people.<sup>36</sup>

Even LDL levels correlate with increased risk of mortality, especially if associated with alpha 1-acid glycoprotein, which determines a level of low-grade chronic inflammation in the individual.<sup>37</sup>

The fibrinogen protein produced by the liver can increase not only in various inflammatory conditions. It can create a hypercoagulable state with a risk of DVT, especially in surgically treated patients.<sup>38</sup> An increase in D-dimer is also associated with the latter, which is produced from the degradation of fibrin and is an index of hypercoagulable.<sup>39</sup>

In the literature, there are many studies that are in favor of using tranexamic acid and recommend its use to help greatly to reduce bleeding with a statistically insignificant risk of related side effects.<sup>40-44</sup>

In relation to this, we have searched in the most authoritative scientific journals, studies related to our own, which would propose conflicting results with respect to ours. In particular, we searched for the safety levels of the drug in question and the risk-benefit value. We did not find any study that discourages the use of tranexamic acid; all studies show some episodes of adverse events, but not statistically significant in line with our results. Our adverse events are not statistically significant

because we are speaking about old patients in whom a few of this events are possible. For these reasons it is impossible to declare the correlation of these adverse events with administration of TXA. The use of this drug in traumatology is growing, but using and timing of administration are not still clear.

The limitation of our study was the small number of enrolled patients. The research is progressing and we are not excluding the possibility of utilizing tranexamic acid for other types of fractures. Reducing blood loss does not only mean a reduction of costs, above all it means reducing the risk of worsening the clinical condition of patients that in our case were mostly elderly.

## CONCLUSIONS

In conclusion, it is clear that if on one hand we have a decreased percentage in the loss of hemoglobin, we cannot guarantee, on the other hand, a reduction in the need for transfusions and therefore a reduction in government spending. With the increase in pro-thrombotic risk, even if it is not statistically significant, it does not appear that the statistical power of the sample analyzed is such to call for the creation of a unique protocol for the management of these types of patients with proximal femoral fractures. It is possible that this type of approach can be extended to other types of fractures and major orthopedic surgery. For this reason, further studies are needed to enhance its use. In our view, this study is just a beginning. Further insights, with greater case histories, will be needed to create guide lines for proximal femoral fractures

## ACKNOWLEDGMENTS

### CONFLICT OF INTEREST STATEMENT

All authors declare no financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

### HUMAN AND ANIMAL RIGHT

For this type of study any statement relating to studies on humans and animals is not required. Patients gave their informed consent prior to being included in the study. All procedures involving human participants were in accordance with the 1964

Helsinki declaration and its later amendments.

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## Транексамовая кислота при пертхроантерном переломе бедренной кости: безопасное лекарство или нет?

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**Введение:** Существует высокая частота необходимости переливания крови после переломов бедренной кости у пациентов пожилого возраста.

**Цель:** Целью данного исследования является оценка эффективности и вероятных осложнений при применении транексамовой кислоты при операции для введения проксимального бедренного стержня.

**Методы:** Наша группа состояла из 90 пациентов с пертхроантерным переломом, перенёвших хирургическое лечение с применением остеосинтеза SupernailGT(LimaCorporate). Была использована АО/ОТА (Ассоциация остеосинтеза/ Ассоциация ортопедических травм) классификационная система для распределения переломов в 31A1 (n=45) и 31A2 (n=45). Больные были распределены в группы. 47 больным был предписан приём 15мг /кг транексамовой кислоты (Группа А) и 43 больным был предписан приём плацебо (Группа Б). Проводился ежедневный мониторинг за показателями крови больных, с целью выявления частоты анемии. В качестве критерия безопасности мы наблюдали за вероятностью наступления сосудистых проявлений с наличием или без наличия симптомов в течение 8 недель после операции. Были прослежены и маркеры смертности и тромбоза глубоких вен (ТГВ) - (фибриноген D-димер).

**Результаты:** Послеоперационная кровопотеря может быть обусловлена целым рядом факторов, не связанных с приёмом или отсутствием приёма транексамовой кислоты. Во время пунктуального и ежедневного наблюдения за уровнями гемоглобина, нами было установлено, что 42% больных из группы А нуждались в переливании крови по сравнению с 62% из группы Б. Показатели маркеров смертности (альфа – 1 – кислый гликопротеин; альбумин LDL) и ТГВ не являлись статистически значимыми для сравнения двух групп настоящего исследования (p>0.05).

**Заключение:** На основе данного исследования было установлено, что приём транексамовой кислоты является статистически значимым при уменьшении послеоперационной кровопотери.