



## Original article

# Use of tranexamic acid for controlling bleeding in thoracolumbar scoliosis surgery with posterior instrumentation<sup>☆</sup>



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## ABSTRACT

**Objective:** Scoliosis surgery involves major blood loss and frequently requires blood transfusion. The cost and risks involved in using allogeneic blood have motivated investigation of methods capable of reducing patients' bleeding during operations. One of these methods is to use antifibrinolytic drugs, and tranexamic acid is among these. The aim of this study was to assess the use of this drug for controlling bleeding in surgery to treat idiopathic scoliosis.

**Methods:** This was a retrospective study in which the medical files of 40 patients who underwent thoracolumbar arthrodesis by means of a posterior route were analyzed. Of these cases, 21 used tranexamic acid and were placed in the test group. The others were placed in the control group. The mean volumes of bleeding during and after the operation and the need for blood transfusion were compared between the two groups.

**Results:** The group that used tranexamic acid had significantly less bleeding during the operation than the control group. There was no significant difference between the groups regarding postoperative bleeding and the need for blood transfusion.

**Conclusions:** Tranexamic acid was effective in reducing bleeding during the operation, as demonstrated in other studies. The correlation between its use and the reduction in the need for blood transfusion is multifactorial and could not be established in this study. We believe that tranexamic acid may be a useful resource and that it deserves greater attention in randomized double-blind prospective series, with proper control over variables that directly influence blood loss.

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## Uso do ácido tranexâmico no controle do sangramento em cirurgias de escoliose toracolombar com instrumentação posterior

### R E S U M O

#### Palavras-chave:

Ácido tranexâmico  
Escoliose/cirurgia  
Tempo de sangramento  
Transfusão de sangue

**Objetivo:** A cirurgia de escoliose envolve elevada perda sanguínea e necessita frequentemente de hemotransfusão. O custo e os riscos envolvidos no uso do sangue alogênico têm motivado pesquisas de métodos capazes de reduzir o sangramento operatório nos pacientes. Um desses métodos é o uso de drogas antifibrinolíticas, entre as quais está o ácido tranexâmico (ATX). O objetivo deste estudo foi verificar o uso dessa droga no controle do sangramento em cirurgias de escoliose idiopática.

**Métodos:** Estudo retrospectivo no qual foram analisados os prontuários de 40 pacientes submetidos à artrodese toracolombar por via posterior. Desses, apenas 21 usaram o ATX e foram relacionados no grupo teste. Os demais foram relacionados no grupo controle. Foram comparadas as médias de sangramento per e pós-operatório e a necessidade de hemotransfusão entre os dois grupos.

**Resultados:** O grupo que usou o ATX teve sangramento peroperatório significativamente menor do que o grupo controle. Não houve diferença significativa entre os grupos para o sangramento pós-operatório e a necessidade de hemotransfusão.

**Conclusões:** O ATX foi eficaz na redução do sangramento peroperatório, conforme demonstrado em outros estudos. A correlação entre o seu uso e a redução da necessidade de hemotransfusão é multifatorial e não pôde ser estabelecida neste trabalho. Acreditamos que o ácido tranexâmico possa ser um recurso útil e merece maior atenção em séries prospectivas, duplo-cegas, randomizadas, com o devido controle das variáveis que interferem diretamente na perda sanguínea.

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## Introduction

Surgical correction of scoliosis involves significant blood loss of multifactorial origin. The duration of the surgical procedure, the severity and type of the deformity, the technique used, the mean perioperative arterial pressure and the hemostasis strategies are among the variables that directly influence the amount of bleeding.<sup>1-6</sup>

Within this scenario, the need for blood transfusions is a reality that is of concern for surgeons and attracts the attention of researchers. Use of allogeneic blood with the aim of maintaining tissue perfusion and preventing injuries to target organs in patients with large-volume blood losses is not risk-free. Transmission of viral diseases, immunological reactions and reductions in coagulation factors are known to be complications of blood transfusion.<sup>1,2,4</sup>

Given this situation, a variety of strategies have already been proposed in attempts to diminish the dependence on allogeneic blood in major surgery. These include storage of autologous blood before the operation, normovolemic hemodilution, hypotensive anesthesia, use of a cell recovery machine and use of drugs with antifibrinolytic properties, such as aprotinin, epsilon-aminocaproic acid and tranexamic acid.<sup>6-10</sup>

Tranexamic acid is a synthetic antifibrinolytic drug that has the resultant effect of forming a reversible complex with plasminogen and plasmin. It inhibits fibrinolysis, prevents lysis of fibrin coagulum and acts toward partial blocking of the platelet aggregation induced by plasmin.<sup>11,12</sup> Because of its

low cost and because its side effects are small, studies have been conducted in different parts of the world in attempts to evaluate its efficacy for controlling perioperative bleeding in major surgery.<sup>2,7-12</sup>

In our institution, tranexamic acid has recently been used in operations to treat idiopathic scoliosis. The surgeons counted on its efficacy for reducing the bleeding consequent to the surgical procedure, thus hoping to reduce the risk for patients and to lead to lower need for blood transfusions.

The objective of this study was to document the influence of tranexamic acid on the bleeding inherent to procedures for treating idiopathic scoliosis with posterior instrumentation, and to ascertain whether the expected reduction in bleeding was capable of reducing the need for blood transfusion.

## Methods

### Profile of the sample

This was a retrospective cohort study on 40 patients who underwent operations to correct idiopathic scoliosis between December 2012 and March 2013. The study was approved by the research ethics committee of the center where it was conducted (CAAE-15734413.6.0000.5273).

The medical files of patients who underwent arthrodesis via a posterior route with six or more levels of arthrodesis, whose bleeding consequent to the procedure was adequately

**Table 1 – Sample selection criteria.**

Inclusion criteria	
Age between 10 and 30 years	
Body mass index between the 5th and 95th percentiles for the age	
Idiopathic scoliosis	
Posterior arthrodesis with fusion of six or more levels	
Exclusion criteria	
Mean perioperative arterial pressure exceeding 85 mmHg	
Congenital or syndromic scoliosis	
Previous spinal surgery	
Use of the drug not in accordance with the standardized protocol	

documented, were analyzed. We used the selection criteria listed in [Table 1](#).

### Data analyzed

Data that were considered relevant for the statistical analyses were gathered from the medical files. These included: (1) patient's age; (2) patient's weight at the time of the operation; (3) duration of the procedure from the time of the skin incision until its closure; (4) severity of the deformity; (5) bleeding documented in the medical file; and (6) use of blood transfusions.

The number of levels subjected to arthrodesis was used as a variable for estimating the severity of the deformities.

The perioperative bleeding estimated in this study was measured as the blood collected through the suction drains of the surgical site during the operation plus the blood absorbed in the surgical compressive dressings. For the calculations, the density of human blood was taken to be 1.053 g/mL and the quantity of saline solution used for irrigation of the surgical site was discounted.

The postoperative bleeding was also taken into consideration and was estimated from the output of the vacuum drains that were installed subcutaneously over the first 24 h after the operation.

### Surgical technique

Three teams participated in the operations on the patients selected. Basically, the surgical technique involved a skin incision on the midline above the spinal processes, followed by dissection of the soft tissues until achieving exposure of the vertebrae. Careful hemostasis was undertaken. The ligaments and facets were released in order to gain spinal mobility, and pedicle screws and pins were used to enable correction and stabilization of the deformity. Autologous grafts coming from the spinal processes and iliac crest were used to enable vertebral fusion. Vacuum suction drains were positioned in the subcutaneous layer in order to allow adequate drainage of the surgical wound during the postoperative period.

### Use of the drug

In our institution, we follow a protocol in which tranexamic acid is used at an attack dose of 100 mg/kg of body weight, administered over the 30-minute period prior to making the skin incision. A maximum dose of 2 g of the drug is observed. After the incision has been made, continual infusion is maintained at the rate of 30 mg/kg/h until the end of the procedure,

**Table 2 – Profiles of the groups studied.**

	Control	Tranexamic acid	p-Value
Number of patients	19	21	
Age (years)	21.6 ± 8.0	18.0 ± 4.4	0.1463
Weight (kg)	51.8 ± 5.9	55.5 ± 6.1	0.0628
Number of levels fused	9.2 ± 2.3	9.4 ± 2.2	0.7624
Duration of operation (h)	4.3 ± 1.4	4.0 ± 1.2	0.5291

i.e. when the skin has been closed. This protocol has already been used safely in other centers.<sup>2,13</sup>

### Division of the groups

Among the 40 patients selected, 21 received tranexamic acid in accordance with the administration protocol (test group), while the other 19 were operated without receiving the drug (control group).

### Evaluation of complications

The patients involved in the study remained in hospital for an average of five days after the operation. After this period, they started to undergo periodic outpatient follow-ups. A search was made in the medical files of the patients who received tranexamic acid with the aim of identifying any possible complications relating to use of the drug, especially those resulting from thromboembolic events, including venous thrombosis, pulmonary embolism, arterial occlusion, kidney failure, etc.

### Statistical analysis

The results were expressed as means ± SD (standard deviation). For comparisons, Student's *t* test or the Mann-Whitney test was used, when appropriate. Correlations between the study variables were determined using the Spearman or Pearson correlation coefficient. The nominal variables were evaluated using the Chi-square test. Results were accepted as statistically significant with  $p < 0.05$ . The statistical analyses were performed using the Stata 11.2 software (StataCorp, Texas, USA).

## Results

### Comparison between the test group (tranexamic acid) and the control group

Overall, the groups studied were comparable and there was no significant difference between them regarding age, body weight, number of levels subjected to arthrodesis and duration of the operation ([Table 2](#)).

### Mean blood loss

The mean perioperative blood loss among the patients who received tranexamic acid was 747.6 ± 265.9 mL. In the control group, it was 996 ± 342.0 mL, with a statistically significant difference ( $p = 0.01$ ) ([Table 3](#)).

**Table 3 – Mean amount of bleeding in the groups studied.**

	Control	Tranexamic acid
Perioperative loss (mL)	996.0 ± 342.0	747.6 ± 265.9
Postoperative loss (mL)	410.5 ± 215.2	349.8 ± 268.4
Total loss (mL)	1406.5 ± 372.1	1097.3 ± 323.9

In relation to postoperative bleeding, we observed that the control group presented a mean bleeding level that was 60.7 mL greater than that of the patients who received tranexamic acid. This difference was not statistically significant.

#### Percentage perioperative blood volume loss

Since the blood volume of each individual is a variable link directly to body weight, the percentage perioperative blood volume loss of each patient was estimated by taking the mean volume of 70 mL per kg of body weight. In this manner, an index capable of correlating the volume of blood lost during the operation with the estimated total blood volume could be created.

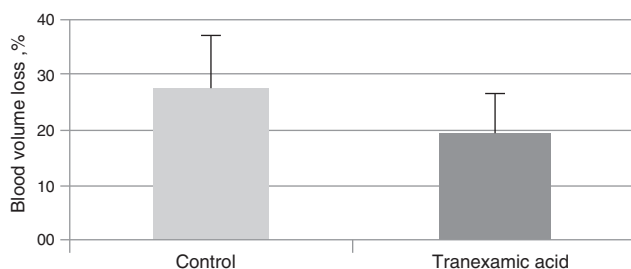
It was observed that the percentage perioperative blood volume loss in the tranexamic acid group (mean of 19.4 ± 7%) was significantly lower than that of the control group (mean of 27.6 ± 9.4%) ( $p=0.008$ ) (Fig. 1).

We also observed that there was a positive linear correlation between the percentage perioperative blood volume loss and the duration of the operation, for both groups ( $r=0.369$ ;  $p=0.0191$ ).

#### Relationship between the percentage perioperative blood volume loss and the number of levels subjected to arthrodesis (loss/level)

Another important variable considered in analyzing the results was the number of levels subjected to arthrodesis. Patients with curves that are more severe generally require procedures that encompass larger numbers of vertebrae. This is directly reflected in the duration of the surgical procedure and the amount of perioperative bleeding. In view of this reality, we created an index correlating the percentage perioperative blood volume loss and the number of levels subjected to arthrodesis (loss/level).

We observed that the tranexamic acid group had a significantly lower loss/level ratio than that of the control group ( $p=0.01$ ) (Table 4).



**Fig. 1 – Comparison between percentage blood volume losses in the control and test groups.**

**Table 4 – Percentage perioperative blood volume loss.**

	Control	Tranexamic acid	p-Value
Blood volume loss (%)	27.6 ± 9.4	19.4 ± 7.0	0.0083
Number of levels subjected to arthrodesis	9.2 ± 2.3	9.4 ± 2.2	0.7624
Loss/level	3.2 ± 1.3	2.1 ± 0.6	0.0101

#### Relationship between the percentage perioperative blood volume loss, the number of levels subjected to arthrodesis and the duration of the operation

Considering that the percentage perioperative blood volume loss has direct relationships with the number of levels subjected to arthrodesis and the duration of the operation, we applied linear regression in order to analyze the relationship between the use of tranexamic acid and the percentage perioperative blood volume loss, controlled for the number levels subjected to arthrodesis and the duration of the operation. We found that use of this drug reduced the percentage blood volume loss by 7.1% ( $p=0.001$ ).

#### Need for blood transfusion

In the control group, the mean blood volume transfused was 176.3 ± 252.6 mL per patient. In the test group, it was 111.1 ± 216.5 mL. Blood transfusion was required for 47.4% of the control group and 28.6% of the group that received the drug, i.e. the drug reduced the need for transfusion by 18.8%. The Chi-square test did not show any evidence capable of correlating the use of the drug with this reduction, for a 95% confidence level ( $p=0.220$ ).

#### Complications resulting from use of tranexamic acid

During the postoperative follow-up period, there were no clinical or surgical complications attributable to use of tranexamic acid.

#### Discussion

Our results showed that the group that used tranexamic acid had a lower mean level of perioperative bleeding. Other studies that have analyzed this relationship have obtained similar results.<sup>2,8-14</sup>

The percentage perioperative blood volume loss provides a closer representation of the systemic consequences resulting from blood loss than does direct analysis of the bleeding in absolute values. This is because by correlating bleeding, blood volume and body weight, data of greater reliability regarding the impact of blood loss on patients' homeostasis are furnished. Our results showed that the group that used tranexamic acid had lower percentage perioperative blood volume loss and reproduced the findings of another retrospective cohort study that used the same index.<sup>13</sup>

The postoperative loss was also lower in the group that used tranexamic acid, but this difference was non-significant.

In our study, certain factors may explain these results. The plasma half-life of this drug is relatively short (3.1 h) and its effect cannot be guaranteed throughout the 24-h period subsequent to the surgical procedure. Moreover, the chances that the material discharged through the drain might have also included seroma and other tissue degradation products was not taken into consideration by the professionals who measured the contents of the collection flasks and, thus, measurement bias may have occurred. Only one study has demonstrated a significant difference in postoperative bleeding between groups that used this drug and groups that used placebo.<sup>10</sup>

The reduction in the need for transfusion observed in the group that used tranexamic acid was not significant for the number of patients involved. Although studies with different designs have obtained similar results,<sup>2,8-11,13-23</sup> we take the view that the model of our study was not the most appropriate one for analyzing this outcome. Furthermore, we noted that there was no standardization of the parameters used by surgical and anesthesia teams with regard to using homologous or autologous blood. Use of mean arterial pressure greater than 85 mmHg as an exclusion criterion may not have been sufficient to neutralize the influence of higher blood pressure levels on perioperative bleeding. We believe that keeping mean arterial pressure within a band would be more appropriate for controlling the impact of this variable on blood loss, as has been shown in some published series.<sup>3-5,24-26</sup> The technical skill of each surgeon with regard to controlling hemostasis and the pedicular instrumentation is another important variable that should be taken into consideration. This may have interfered with the results between the groups, given that three different teams operated on the patients studied.<sup>3,26</sup>

Since the risk of complications inherent to using homologous blood is directly proportional to the quantity of blood used,<sup>27,28</sup> the decrease in blood loss in the group that used tranexamic acid should be valued. Moreover, the reduction in perioperative blood loss may also diminish the risk of death, but this is a theoretical proposition that has not been assessed in any study.

The groups studied were statistically similar regarding age group, body weight, during of the operation and severity of the deformity, which diminished the interference of these variables in the study.<sup>3-5</sup>

The meta-analyses available still do not bring together numbers capable of guaranteeing the safety of tranexamic acid, for use in accordance with the protocol presented.<sup>25,27</sup> In the present study, no complications were attributed to use of tranexamic acid. The number of complications reported in the literature so far has been very small and comparable with those seen in using placebo,<sup>26-29</sup> but the seriousness of the possible thromboembolic events makes it essential to implement regular follow-up for these patients.

The protocol for using tranexamic acid that was analyzed in the present study has already been applied by other authors. Its efficacy has been compared with placebo and with other antifibrinolytic drugs, and the results relating to its efficacy and safety have been promising.<sup>2,8,14,25,27</sup> Studies using tranexamic acid at lower doses have not achieved the same proportional reduction in perioperative bleeding.<sup>20,23</sup>

## Conclusion

Use of tranexamic acid is a low-cost, effective and safe option for reducing perioperative bleeding during operations to treat scoliosis with posterior instrumentation. Its efficacy in reducing the need for blood transfusion is a multifactorial phenomenon that could not be demonstrated in the present study.

Randomized prospective clinical studies with proper blinding of the surgical and anesthesia teams thus become necessary in order to evaluate the impact of tranexamic acid on the need for blood transfusion and contribute toward rationalizing protocols so as to make them more effective and safer in using this drug.

## Conflicts of interest

The authors declare no conflicts of interest.

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