

Use of tranexamic acid in users served in federal district public air pre-hospital service

RESUMO | Objetivo: analisar o uso do ácido tranexâmico (TXA) no serviço pré-hospitalar aéreo público do Distrito Federal. Método: estudo descritivo com delineamento transversal e abordagem. O estudo engloba a análise documental de dados secundários provenientes dos prontuários eletrônicos e fichas de atendimento do Serviço Aeromédico (SA) do Distrito Federal (DF). Resultados: O correu redução no grau de choque e melhora dos parâmetros hemodinâmicos do momento Pré-Hospitalar (APH) para o intra-hospitalar após uso do TXA. Conclusão: observou-se no presente estudo que o uso do TXA associado a outras medidas de controle de hemorragia mostrou-se eficaz para melhora da condição hemodinâmica dos pacientes. A reposição volêmica dos pacientes ainda no período pré-hospitalar e demais medidas para contenção de hemorragia mostraram-se efetiva para reanimação em graus severos de choque. A administração do TXA no APH ocorreu na 1ª hora do atendimento com dosagem de 1g com melhora nos dos parâmetros clínicos.

Descritores: Choque hemorrágico; Ácido tranexâmico; Atendimento pré-hospitalar.

ABSTRACT | Objective: to analyze the use of tranexamic acid (TXA) in the pre-hospital public air service in the Federal District. Method: descriptive study with cross-sectional design and quantitative approach. The study encompasses the documentary analysis of secondary data from the electronic medical records and attendance sheets of the Aeromedical Service (SA) of the Federal District (DF). Results: There was a reduction in the degree of shock and improvement in hemodynamic parameters from the Pre-Hospital (APH) to the in-hospital moment after using TXA. Conclusion: it was observed in the present study that the use of TXA associated with other hemorrhage control measures proved to be effective in improving the hemodynamic condition of patients. Volemic resuscitation of patients in the pre-hospital period and other measures to contain bleeding proved to be effective for resuscitation in severe degrees of shock. The administration of TXA in the APH occurred in the 1st hour of care with a dosage of 1g, with improvement in the clinical parameters.

Keywords: Hemorrhagic shock; Tranexamic acid; Pre-hospital care.

RESUMEN | Objetivo: analizar el uso del ácido tranexâmico (TXA) en el servicio público aéreo prehospitalario en el Distrito Federal. Método: estudio descriptivo con diseño transversal y enfoque cuantitativo. El estudio abarca el análisis documental de datos secundarios de las historias clínicas electrónicas y planillas de asistencia del Servicio Aeromédico (SA) del Distrito Federal (DF). Resultados: Hubo una reducción en el grado de shock y mejoría en los parámetros hemodinámicos desde el momento Pre-Hospitalario (HAP) hasta el intrahospitalario después de utilizar ATX. Conclusión: se observó en el presente estudio que el uso de ATX asociado a otras medidas de control de la hemorragia demostró ser eficaz en la mejoría del estado hemodinámico de los pacientes. La reanimación volémica de pacientes en el período prehospitalario y otras medidas para contener el sangrado demostraron ser efectivas para la reanimación en grados severos de shock. La administración de TXA en el HAP se produjo en la 1ª hora de atención con dosis de 1g, con mejoría de los parámetros clínicos

Palabras claves: Choque hemorrágico; Ácido tranexâmico; Atención prehospitalaria.

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INTRODUÇÃO

In Brazil each year approximately 40,000 people die as a result of trauma caused by traffic accidents. Brazil ranks fourth among record-breaking countries for road deaths, behind China, India and Nigeria.¹ According to the Department of Informatics of the Unified Health System (DATASUS), traffic accidents in Brazil caused 91,000 deaths in 2019, generating one of the greatest significant impacts on the economy for Brazilian society.²

Trauma represents a serious public health problem, due to its high mortality and disability rates. Patients affected by trauma have large blood losses which lead to hemorrhage and hypovolemic shock.^{2,3,4}

In this context, the Advanced Trauma Life Support (ATLS) highlights important recommendations regarding volume replacement according to the hemorrhage classification, since the evolution of hypovolemic shock of the hemorrhagic type can lead to permanent complications for the patient. Thus, identification of the clinical class of severity of hemorrhagic shock is crucial during trauma patient care.³

According to the classification of hemorrhages, replacement of up to 2000 liters of crystalloids (ringer lactate or 0.9% saline solution) is recommended for class I and II. In class III and VI fluid infusion and blood transfusion.³ In addition to the aforementioned replacements, the ATLS recommends the administration of tranexamic acid (TXA) in patients with severe bleeding within 3 hours after the trauma.^{3,4}

Patients who are victims of hemorrhagic shock may develop trauma-induced coag-

ulopathy. Traumatic coagulopathy is characterized by vascular damage with failure to produce hemostasis due to tissue damage. It occurs after traumatic injury accompanied by inflammatory processes and dysfunction in the coagulation process, anticoagulation and fibrinolysis.^{5,6}

The coagulopathy generated by the traumatized patient, once not reversed, increases the number of deaths, and the administration of TXA is a possibility of controlling the hemorrhage by providing the inhibition of the competitiveness of fibrinolysis.⁷

TXA is derived from the synthetic amino acid lysine discovered in 1962 by Shosuke and Okamoto. Its use inhibits fibrinolysis, increases clot stability and blocks the interaction of plasminogen and plasmin with fibrin. After the interruption of this interaction, the formation of plasmin is prevented. This mechanism is the main factor responsible for fibrinolysis.⁸

By reducing blood loss, its clinical administration for trauma patients is being studied, but there are reports of benefits, with increased survival in patients with trauma and significant bleeding.⁴

A study carried out in 2010 with 20,211 participants provides evidence of the benefit of using TXA in trauma patients with successful administration at a loading dose of 1 g of TXA infused over 10 minutes, followed by an intravenous infusion of 1 g within 8 hours. Decreases hemorrhage mortality without increasing fatal and non-fatal vascular occlusive events.^{5,8}

It is suggested by the CRASH-3 study to administer TXA to trauma victims during care, intravenously, at the site of the incident as soon as possible⁶ and includes the pre-hospital care (PHC), since patients with hemorrhagic trauma tend to worsen and progress to death.⁵ According to European guidelines for the control of severe bleeding and coagulopathies resulting from trauma, the early use of TXA is indicated as a preventive measure for bleeding complications.^{7,9}

However, the use of TXA for traumatized patients facilitates in-hospital use.⁶ According to European guidelines for the control of severe bleeding and coagulopathies resulting

from trauma, the early use of TXA is indicated as a preventive measure for bleeding complications. Its use in PHC is under discussion, although its effectiveness when administered early has already been demonstrated.^{7,9}

There is safety in the use of TXA in PHC, however some authors believe that more studies are needed comparing the effectiveness of the drug administered in PHC with its use in a hospital environment. In the PHC, it was effective with a reduction in mortality when applied within 3 hours after the occurrence of the trauma.^{8,9}

The use of TXA in the aeromedical service (AS) is described in a study carried out in 2013 with the administration of TXA in patients with severe hemorrhage and describes that TXA is an important out-of-hospital adjunct in the treatment of severe hemorrhage in trauma, where it increases the chance of life in the final outcome of the patient.¹⁰

The current study is justified by analyzing the use of TXA in the pre-hospital service. The results may trigger a discussion for the adoption of strategies and protocols to optimize their use in PHC and contribute to an increase in the chance of survival of patients with hemorrhagic trauma, as well as in the evolution of the final outcome until the in-hospital service.

It aims to analyze the use of TXA in patients suffering from severe hemorrhagic shock treated by a public pre-hospital air service in the Federal District.

METHOD

This is a descriptive cross-sectional study with a quantitative approach. The study encompasses the documentary analysis of secondary data from the electronic medical records and service records of the Aeromedical Service (AS) of the Federal District (DF).

Held at the Operational Aviation Group (GAVOP - Grupo de Aviação Operacional) of the Federal District Military Fire Brigade (CBMDF - Corpo de Bombeiros Militar do Distrito Federal), in partnership with the Mobile Emergency Care Service of the Federal District (SAMU DF) and the Trauma Center of the Instituto Hospital de Base do Distrito

Federal (IHBDF - Instituto Hospital de Base do Distrito Federal).

The analysis of the electronic medical records was carried out in the MV system of the IHBDF, the unit where the patients were referred, in addition to the SA care sheets and records books of the pre- and intra-hospital care sectors of patients seen from May 2021 to June 2022.

The study included patients whose electronic medical records and SA care records mentioned the administration of tranexamic acid during care in the condition of severe hemorrhagic shock. Excluded from the study were patients whose electronic medical record or registration form was not located or had incomplete or ineligible information and children up to 12 years old.

To register the research data, a data collection instrument was adopted, whose elaboration followed the recognition of indicators related to pre- and intra-hospital care. This instrument underwent a validation process by five judges with expertise in trauma patient care and pre-hospital care. Such judges were selected by Lattes curriculum by the platform of the National Council for Scientific and Technological Development (CNPQ).

The instrument was developed following two stages: axis I and axis II. Axis I is related to PHC data and axis II to in-hospital data. In both stages of the instrument, there are indicators to be filled in regarding the epidemiological and clinical profile of the patient.

Data analysis was performed in SPSS and distributions were made in absolute and relative frequency of qualitative variables and measures of central tendency and dispersion of quantitative variables. For analysis of variance and association between dependent and independent variables, the Kruskal-Wallis and Chi-square tests were applied. For all tests, a significance level of 5% was adopted (p -value ≤ 0.05).

The clinical and sociodemographic aspects of the patients assisted were studied, in addition to aspects related to the consultations. The dependent variable considered was care provided to victims of severe hemorrhagic shock who used TXA in the first 3 hours in a pre-hospital air service. The variables

sex, age, condition, clinical condition, shock management and outcome were analyzed as independent variables in this study.

This study is part of a thematic project: clinical and epidemiological profile and outcome of users treated at a public air pre-hospital service in the Federal District in the management of tranexamic acid. It was submitted to the Research Ethics Committee of the Health Sciences Teaching and Research Foundation (FEPECS) with CAAE: 43498921.6.0000.5553 and the IHBDF Ethics Committee with CAAE: 4349892.6.3001.8153.

RESULTS

A total of 51 consultations performed by the Aeromedical Service (AS) from May 2021 to June 2022 were analyzed. There was a higher prevalence of male patients, with a mean age of 38.74 years. Among the nature of the injuries, there was a prevalence of traumatic brain injury - TBI (24.35%), limbs (21.78%), abdomen (17.94%), chest (12.08%), face (5.13%), crushing (3.84%), amputation, cervical and urogenital injuries (1.28%) (Table 1).

The use of TXA and other hemorrhage containment measures did not show statistical significance for the primary outcome of reduction in mortality within 30 days after the use of TXA ($p=0.333$).

There was also no statistical significance

for the use of TXA that favors early patient discharge ($p = 0.503$), as well as for hemorrhage control in the pre-hospital setting ($p = 0.451$) (Table 2).

However, a reduction in the degree of shock and improvement in hemodynamic parameters from the pre-hospital to the in-hospital moment after the use of TXA and other measures for hemorrhage control were observed.

The techniques applied for hemorrhage control in this investigation did not show statistical significance on the outcome of the patients treated (Table 2).

The administration of TXA can be performed in the first hour in the pre-hospital context, having occurred in an average of 34.16 min. after the trauma (median of 30 min and SD of 28.33). Likewise, volume replacement using blood products also occurred predominantly in the first hour after arrival at the hospital, with 74.51% of patients and 3.92% after 24 hours of care (Table 3).

The present study identified a significant improvement in hemodynamic parameters, in heart rate (HR) ($p = 0.046$), respiratory rate (RR) ($p = 0.035$) and blood pressure (BP) ($p = 0.000$) when related to the first consultation, at 1 hour and 24 hours after trauma with administration of TXA (Table 4).

When comparing the patient's HR at the time of initial care and at 24 hours, it was observed that there was a sig-

Table 1. Main injuries affected in trauma victims, 2022.

Injury/Aggravation	Freq	%
TBI	19	24,35
Abdominal trauma	14	17,94
Pelvic trauma	8	10,25
Facial trauma	4	5,13
Chest trauma	10	12,08
Limb fracture	17	21,78
Crushing	3	3,84
Amputation	1	1,28
Cervical trauma	1	1,28
Urogenital trauma	1	1,28

Kruskal-Wallis test.
Source: Authors, 2022.



nificant reduction in the parameters ($p = 0.01$), as well as, a significant reduction in respiratory rate was also identified in the same period ($p = 0.01$). BP reduction, unlike respiratory rate and heart rate, showed a significant reduction in the first hour interval ($p = 0.01$) (Table 5).

DISCUSSION

When assessing mortality, it was observed that 6.38% of the cases that evolved to death were related to the surgery in the first hours of hospital admission and related to more severe degrees of shock and injuries. Similar results could be observed in a randomized, double-blind study where the administration of TXA in patients with greater clinical viability may be associated with a benefit in survival.¹⁰

In this investigation, it was shown that TBI had a high incidence (24.35%) revealing a prevalence that can also be recognized worldwide.^{4,12} It was also noticed in this investigation that the use of TXA and other hemorrhage control measures in TBI victims was not associated with death and occlusive vascular events in the first 24 hours after the trauma.¹²

Such findings could be noticed in a recent study with 12,639 patients who suffered TBI with the use of TXA in the first 3 hours, with a reduction in mortality in the first 24 hours of 20% and vascular occlusive events occurred in only 1.6%.¹²

Patients who used TXA also adopted volume resuscitation as a concomitant measure, with volume replacement occurring in 97.87% of cases with a mean infusion of 640 ml of ringer lactate, 0.9% saline solution or both in the first 20 to 40 minutes of care in the pre-hospital setting of victims who presented with severe hemorrhagic shock. Volume resuscitation associated with the use of TXA has already been proven to be effective, respecting the recommen-

Table 2. Control and outcome of patients using TXA, 2022.

Outcome/Control	KW	Pvalor
Hemorrhagic control x Initial TXA time	10,91	0,451
Desfecho inicial x Tempo inicial	39,27	0,503

Kruskal-Wallis test.
Source: Authors, 2022.

Table 3. Patients who received blood transfusion, 2022.

Red blood cell concentrate (admission 1st hour)	Freq (%)	Red blood cell concentrate (24 hours later)	Freq (%)
Yes	38 (74,51)	Yes	2 (3,92)
No	13 (25,49)	No	49 (96,08)

Kruskal-Wallis test.
Source: Authors, 2022.

Table 4. Analysis of blood pressure, heart rate and respiratory rate in the first consultation, 1 hour and 24 hours after the trauma with the use of TXA, 2022.

Variable	KW	Pvalue
FC	6,16	0,046
FR	6,71	0,035
PA	26,56	0,00

Kruskal-Wallis test.
Source: Authors, 2022.

Table 5. Blood pressure, respiratory rate and heart rate crosses: first visit, 1h and 24h later, 2022.

Crossings	Pvalor
Heart Rate	
1 service - 1 hour	0,07
1 service - 24 hours	0,01
1 hour - 24 hours	0,15
Respiratory rate	
1 service - 1 hour	0,21
1 service - 24 hours	0,01
1 h - 24 h	0,04
Blood Pressure	
1 service - 1 hour	0,00
1 service - 24h	0,00
1 hour - 24h	0,01

Kruskal-Wallis test.
Source: Authors, 2022.

dation of up to 2000 ml of crystalloid infusion.¹³

Volemic replacement using blood

products in patients with hemorrhagic shock in the present study was performed in the first hour of care in most

patients (74.51%). The administration of volume and blood products help to correct deficiencies in oxygen transport, replenish the losses of elements in the coagulation cascade, restoring tissue perfusion.^{13,14}

It was possible to identify a reduction in hemodynamic signs (heart rate $p = 0.01$, respiratory rate $p = 0.01$ and blood pressure $p = 0.00$) during the first visit and 24 hours after the trauma. The reduction of instability in these patients increased survival by 93.62%. It is known that the reduction of the signs of hemorrhagic shock when identified and treated in the first 24 hours after the incident brings the patient a lower risk of mortality and leads to a better

prognosis.^{15,16,17}

As for the administration of TXA in the present study, it occurred in the first hour of care (mean: 34.52, SD: 29.11) with a loading dose of 1 g in 100 ml of saline solution, which could contribute to the clinical improvement between the first hour and 24 hours after the treatment. The use of TXA in PHC proved to be effective when administered in the first 3 hours of care.¹⁸ In another study, the administration of TXA in the PHC was reported, the patients.¹⁰

CONCLUSION

The current study identified that the use of TXA associated with other

hemorrhage control measures became effective. The injury that most affected the patients is related to traumatic brain injury. The degree of shock showed a reduction when compared to its classification in the initial care, increasing the survival of patients. Volemic replacement was initially performed with Ringer's lactate followed by 0.9% saline solution. Patients who died were related to surgical procedures. The administration of TXA in the PHC occurred in the 1st hour of care with a dosage of 1g. Patients who received TXA administration and volume replacement achieved improvements in clinical parameters between 1h and 24h after the trauma.

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