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**Ocena efektywności i bezpieczeństwa stosowania kwasu
traneksamowego w warunkach medycyny ratunkowej**

**Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki medyczne**

STRESZCZENIE W JĘZYKU ANGIELSKIM

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Obrona rozprawy doktorskiej przed Radą Dyscypliny Nauk Medycznych
Warszawskiego Uniwersytetu Medycznego

Warszawa 2022

ASSESSMENT OF THE EFFECTIVENESS AND SAFETY OF TRANEXAMIC ACID USE IN EMERGENCY MEDICINE

Introduction

According to data from the World Health Organization, injuries account for 8% of global mortality and are considered a serious threat to public health worldwide. According to scientific studies, heavy bleeding is the most common cause of premature death of injured people. About 25% of trauma patients experienced acute coagulopathy as a side effect, and up to 40% of them died as a result of hemorrhagic shock. Tranexamic acid is an antifibrinolytic drug that has been associated with increased survival in patients with bleeding injuries. In addition to transfusing blood products, tranexamic acid is considered a key hemostatic strategy in the treatment of pre-hospital bleeding worldwide. Scientific evidence has clearly shown that early treatment of acute coagulopathies and haemorrhagic shock significantly minimizes traumatic deaths. Bleeding leading to haemodynamic instability should be treated with fluid resuscitation, permissive hypotension, and administration of tranexamic acid, which allows for initial protection of the casualty and allows time for rapid transport to the nearest appropriate center. Tranexamic acid is a cost-effective antifibrinolytic drug and its early administration after injury within 3 hours of injury in both in-hospital and pre-hospital care shows a significant reduction in the mortality rate among patients with trauma-induced haemorrhagic shock.

Aim of the study

The common goal of the series of works included in the monothematic series of publications constituting the basis of this doctoral dissertation is to assess the effectiveness and safety of the use of tranexamic acid in patients with traumatic hemorrhage in the setting of emergency medicine.

Material and methods

The series of publications constituting the doctoral thesis includes four publications.

The first work is a review of the various uses of tranexamic acid in emergency medicine. The work is a specific introduction to the considerations on the use of TXA in patients with traumatic hemorrhage. Apart from introducing the reader to the possibilities of using tranexamic acid, he also describes the mechanism of action of TXA.

The second work on the efficacy and safety of tranexamic acid use in adult trauma hemorrhage patients was designed as a systematic review and meta-analysis. For this purpose, the use of predefined keywords was used to search electronic writing databases, including: PubMed, EMBASE, Scopus, Web of Science, and Cochrane Central. The last database search took place on January 10, 2021. 17 articles were eventually included in the meta-analysis.

The third paper was designed in a similar way to the second paper, but related to the use of TXA in pediatric patients with traumatic hemorrhage. The study was published as a research letter to the editor. The work was carried out on the basis of searching databases using predefined keyword layouts. Among the databases that were searched were, among others PubMed, EMBASE, Scopus, and the Cochrane Central database. After verification of the articles obtained in the course of the search, four studies were finally included in the meta-analysis.

The aim of the fourth study was to evaluate the use of tranexamic acid in patients with traumatic injuries of the central nervous system. The study was also designed and conducted as a systematic review and meta-analysis. To this end, electronic literature databases (PubMed, EMBASE, Scopus, Web of Science, Cochrane Central) were searched from their creation to April 10, 2021. After thorough verification of the original searched references, nine studies were included for the final meta-analysis.

Results

In a study evaluating the effectiveness and safety of TXA in adult patients with traumatic haemorrhage, the use of tranexamic acid reduced in-hospital mortality in adult patients with traumatic haemorrhage. However, as shown by the sub-analysis, this dependence concerned only the use of TXA in the civil emergency medicine environment (OR = 0.69; 95% CI: 0.51 to 0.93; $p = 0.02$), in the case of applications in the battlefield of such no relationship was noted (OR = 1.44; 95% CI: 0.85 - 2.45; $p = 0.18$). The use of tranexamic acid compared to the group treated without TXA was also associated with a lower volume of blood transfused (MD = -1.27; 95% CI: -3.64 to -1.09; $p = 0.29$), as well as lower risk of complications in the form of myocardial infarction (26.9% and 38.7%, respectively).

In the meta-analysis that assessed the use of tranexamic acid in pediatric patients with traumatic haemorrhage, the use of TXA resulted in a reduction in in-hospital mortality compared to the group of patients who did not use TXA (1.8% and 3.6%, respectively), however, these differences were not statistically significant (OR = 1.77;

95% CI: 0.32 to 9.73; $p = 0.51$). The use of TXA compared to the non-TXA group was associated with a higher frequency of seizures (0.4% and 0%, respectively; OR = 15.06; 95% CI: 0.86 to 263.78; $p = 0, 06$) and a comparable risk of thromboembolic disorders (0.3% and 0.2%; OR = 0.72; 95% CI: 0.19 - 2.70; $p = 0.62$).

In a third study designed to assess the efficacy and safety of tranexamic acid in adult traumatic brain injury patients, the 28-day / in-hospital mortality rate in patients treated with TXA was 17.8%, compared to 19 in patients treated without TXA. 3% (OR = 0.92; 95% CI: 0.83 - 1.01; $p = 0.08$). The neurological status of patients defined in the Glasgow Coma Scale below 4 points (in the 28-day observation period) was observed in 29.8% of patients treated with TXA and 34.8% of patients treated without TXA (OR = 0.91; 95% CI: 0, 45 to 1.82; $p = 0.78$).

Conclusions

The conducted research allows for the following conclusions:

- Tranexamic acid is a safe antifibrinolytic drug that should be introduced into the Polish procedures for the treatment of outgoing medical emergency teams in adult patients with traumatic haemorrhages.
- It is necessary to conduct a standardized multicentre study to assess the effectiveness of the use and safety of tranexamic acid in pediatric trauma patients.
- The use of tranexamic acid in patients with traumatic brain injury does not have a statistically significant effect on the reduction of in-hospital mortality among patients.