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**OCENA BEZPIECZEŃSTWA I EFEKTYWNOŚCI
STOSOWANIA KWASU TRANEKSAMOWEGO
PODCZAS WYBRANYCH ORTOPEDYCZNYCH ZABIEGÓW
CHIRURGICZNYCH**

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

STRESZCZENIE W JEZYKU ANGIELSKIM

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EVALUATION OF THE SAFETY AND EFFICACY OF TRANEXAMIC ACID DURING SELECTED ORTHOPAEDIC SURGICAL PROCEDURES

Introduction

Orthopaedic surgery, which includes procedures such as total shoulder arthroplasty (TSA), total hip arthroplasty (THA), and total knee arthroplasty (TKA), is one of the most commonly performed types of surgery worldwide. As the population ages and the prevalence of osteoarthritis rises, we anticipate a further surge in these procedures in the upcoming years. According to epidemiological data, in developed countries alone, the number of knee and hip arthroplasty surgeries is increasing by several percent each year, placing a significant burden on health systems. The increased number of surgeries also presents challenges in optimizing postoperative care, including minimizing complications that can affect the length of hospitalization and patients' quality of life. Significant blood loss is one of the main issues orthopaedic surgeons face when performing TSA, THA, and TKA, which can lead to complications associated with the need for transfusion. Blood loss during and after surgery not only poses a health risk to patients, but also increases the risk of infection, delays the healing process, and prolongs recovery time. Consequently, the need to develop strategies that effectively reduce bleeding is one of the priorities of modern orthopaedic surgery. The use of modern pharmacological approaches, such as tranexamic acid (TXA), are effective tools to reduce blood loss. Tranexamic acid, a synthetic antifibrinolytic agent, has gained significant interest in recent years, particularly in the context of orthopaedic surgery. Its mechanism of action is based on blocking the binding of plasminogen to fibrin, resulting in inhibition of blood clot dissolution. This action makes TXA particularly useful in procedures where blood loss is a significant clinical problem. In orthopaedic surgery, especially in joint replacement surgeries such as hip, knee, and shoulder arthroplasty, blood loss is one of the most serious challenges, often leading to the need for blood transfusions and prolonged hospitalization of patients. Consequently, the search for effective methods to reduce bleeding is crucial to improving patient outcomes and safety.

Aim of study

The main objective of this study is to evaluate the efficacy and safety of tranexamic acid (TXA) in limiting blood loss and reducing the need for blood transfusions in patients undergoing

selected orthopaedic surgical procedures, such as total shoulder arthroplasty (TSA), hip arthroplasty (THA), and knee arthroplasty (TKA). This study aims to evaluate the effect of TXA on improving clinical outcomes, reducing complications, and decreasing patient hospitalization time.

Material and methods

The dissertation's monothematic series of publications consisted of five studies.

We designed and conducted the first paper as a systematic literature review and meta-analysis to evaluate the efficacy and safety of tranexamic acid in shoulder arthroplasty. We conducted the study and the other three meta-analyses in accordance with PRISMA international standards. Four databases were searched to identify studies meeting the inclusion criteria: PubMed, Scopus, Web of Science, and Cochrane, using predefined keywords. On 1 December 2021, we conducted the final search and included 10 studies that met the required criteria in the final analysis.

The second study was a single-center, retrospective observational study to evaluate the efficacy of tranexamic acid in hip and knee arthroplasty surgery. The study included 77 patients operated on between January and December 2023 in the Department of Trauma and Orthopaedic Surgery at the Ruda Śląska City Hospital. Of the participants, 33 patients underwent hip arthroplasty, and the rest underwent knee arthroplasty.

The third study, which also involved a systematic review and meta-analysis, examined the effectiveness and safety of tranexamic acid in total knee arthroplasty. For this purpose, databases such as PubMed, Central, Web of Science, and Scopus were searched, and the last search was performed on 23 March 2022. The analysis ultimately included 52 studies.

The aim of the fourth study was to evaluate the efficacy and safety of tranexamic acid administered by two methods, intravenously and topically, in knee arthroplasty procedures. A search of Medline, Embase, Scopus, and Cochrane databases using defined keywords ended on 20 December 2021, and 23 studies were included in the meta-analysis.

The fifth study aimed to assess the effectiveness and safety of administering tranexamic acid through delivery and intravenous routes during hip arthroplasty. The study searched BioMed Central, PubMed, EMBASE, Scopus, and Cochrane databases. The final database search took place on 12 January 2024, and 18 studies were included in the analysis.

Results

A meta-analysis evaluating the efficacy and safety of tranexamic acid (TXA) in shoulder arthroplasty showed that the mean blood loss in the TXA-treated group was 0.66 ± 0.52 liters, compared with 0.834 ± 0.592 liters in the control group (MD = -0.15; 95% CI: -0.23 to -0.07; $p < 0.001$). Furthermore, the use of TXA contributed to a significant reduction in hemoglobin fall, which was 2.2 ± 1.0 g/dl in the TXA group, compared with 2.7 ± 1.1 g/dl in the control group (MD = -0.51; 95% CI: -0.57 to -0.44; $p < 0.001$). The reduction in hemocrit values was also more pronounced in the control group ($7.9 \pm 3.1\%$) than in the TXA group ($6.1 \pm 2.7\%$) (MD = -1.43; 95% CI: -2.27 to -0.59; $p < 0.001$). The value of drainage discharge was also lower in the TXA treatment group (110.5 ± 100.4 ml) compared to the control group (222.9 ± 187.2 ml) (MD = -92.51; 95% CI: -141.09 to -43.93; $p < 0.001$).

The use of TXA reduced the need for blood transfusion (12.5% in the TXA group vs. 32.0% in the group without TXA) in a retrospective study of patients undergoing hip arthroplasty (THA). In contrast, for knee arthroplasty (TKA), the difference was more pronounced, with 20% of patients in the TXA group requiring transfusion, compared to 83.3% of patients in the control group. The decrease in hemoglobin on the first day after surgery was less in the TXA group (mean change: 1.48 g/dl in THA and 1.05 g/dl in TKA) than in the group without TXA (2.4 g/dl and 2.31 g/dl for THA and TKA, respectively).

Another meta-analysis examining the efficacy and safety of TXA in total knee arthroplasty showed that the mean change in hemoglobin level in the TXA group was 3.4 ± 3.1 , compared with 4.03 ± 2.62 in the control group (MD = -1.30; 95% CI: -1.57 to -1.03; $I^2 = 99\%$; $p < 0.001$). Total blood loss was significantly lower in the TXA group (MD = -391.51; 95% CI: -454.29 to -328.73; $p < 0.001$). There was also less blood loss during surgery (MD = -32.10; 95% CI: -50.63 to -13.58; $p < 0.001$) and within 24 hours after surgery, as measured by drainage (MD = -228.68; 95% CI: -293.31 to -164.05; $p < 0.001$). These findings pertain to both intravenous and topical TXA administration. Blood transfusions were needed in 11.2% of patients in the TXA group, compared with 34.3% in the control group (OR = 0.16; 95% CI: 0.11 to 0.22; $p < 0.001$). Deep vein thrombosis (DVT) occurred in 4.6% of patients in the TXA group and 5.8% in the control group (OR = 0.81; 95% CI: 0.49 to 1.35; $p = 0.42$), and pulmonary embolism affected 0.5% and 1.4% of patients, respectively (OR = 0.44; 95% CI: 0.15 to 1.36; $p = 0.15$).

The results of a systematic review and meta-analysis on the use of tranexamic acid (TXA) in knee arthroplasty showed that both intravenous (IV-TXA) and topical (T-TXA) administration were effective in reducing blood loss. In an analysis involving 23 studies with 3,363 patients, there were no statistically significant differences in total blood loss between the two administration methods (IV-TXA: 874.8 ± 349.7 ml vs. T-TXA: 844.9 ± 366.6 ml). However, differences in the volume of blood removed by drainage were significant, with T-TXA (302.9 ± 182.6 ml) superior to IV-TXA (377.9 ± 191.9 ml). Analysis of the change in hemoglobin levels showed no significant differences between the two groups, where the decrease in hemoglobin was 2.4 ± 1.1 g/dl in both groups. In terms of the need for blood transfusion, slightly fewer patients in the IV-TXA group required transfusion (10.9%) compared to the T-TXA group (15.4%), although this difference did not reach statistical significance.

A meta-analysis comparing intrathecal and intravenous administration of TXA in hip arthroplasty showed that the decrease in hemoglobin levels after intravenous administration of TXA compared with intrathecal administration was not statistically significantly different (SMD = -0.08; 95% CI: -0.41 to 0.24; $p=0.61$). Total blood loss averaged 935 ± 527 ml in the intravenous group and 962 ± 519 ml in the delivery group (SMD = -0.07; 95% CI: -0.19 to 0.05; $p=0.23$). Blood transfusions were needed in 8.1% of patients treated intravenously and in 8.3% of patients treated with delivery (OR = 0.95; 95% CI: 0.66 to 1.38; $p=0.79$).

Conclusions

Studies show that the use of tranexamic acid (TXA) in orthopedic surgery, such as shoulder, hip, and knee arthroplasty, significantly reduces blood loss and the need for transfusions. The results of numerous systematic analyses and meta-analyses confirm both the efficacy and safety of TXA, regardless of the method of administration - intravenous or topical. Additionally, TXA does not increase the risk of thromboembolic complications, making it a valuable agent in optimizing surgical outcomes. By reducing bleeding and improving surgical rates, TXA has the potential for further use in standard orthopaedic protocols, with the potential to improve the quality of life for patients undergoing these complex procedures.