ASSESSMENT OF PRE- AND POST-OPERATIVE VALUES OF ERYTHROCYTES, HEMOGLOBIN, HEMATOCRIT AND DRAINAGE VOLUME AFTER ADMINISTRATION OF TRANEXAMIC ACID IN TOTAL HIP ARTHROPLASTY

Damjanovikj Dejan^{1,2}, Georgieva Daniela^{1,2}, Dzoleva Tolevska Roza^{1,2}, Atanasov Nenad^{1,2}, Majstorov Venjamin^{2,3}, Saveski Aleksandar^{1,2}, Atanasovski Igor^{1,2}, Komnenovikj Marina⁴, Zlateska Gjurikj Sofija^{2,5}, Zlateska Damjanovikj Aleksandra⁶

¹University Clinic for Orthopedic Surgery, Skopje, Republic of North Macedonia ²Faculty of Medicine, Ss. Cyril and Methodius Skopje, Republic of North Macedonia ³Institute of Pathophysiology and Nuclear Medicine, Skopje, Republic of North Macedonia ⁴Health Center, Skopje, Republic of North Macedonia ⁵University Clinic for Gynecology and Obstetrics, Skopje, Republic of North Macedonia ⁶PHI Fertty Clinic, Skopje, Republic of North Macedonia *e-mail:* damjanovicmkd@hotmail.com

Abstract

Total hip arthroplasty is a well-established and effective treatment for hip osteoarthritis. However, it is commonly associated with significant blood loss and an increased need for blood transfusions. Tranexamic acid, an antifibrinolytic agent, prevents the degradation of fibrin and preserves the integrity of the fibrin matrix. This study aimed to assess the pre- and postoperative levels of erythrocytes, hemoglobin, hematocrit, and drainage volume following intravenous administration of tranexamic acid during total hip arthroplasty.

A total of 40 patients participated in the study, divided into two groups: an experimental group receiving intravenous tranexamic acid and a control group not receiving the drug.

On the second postoperative day, the experimental group showed a smaller decrease in erythrocytes (0.2935 x 10^{12} /L), hemoglobin (11.093 g/L), and hematocrit (0.032) compared to the control group. Furthermore, the total drainage volume from the day of surgery and the first postoperative day was reduced by 137.65 ml in the experimental group.

Overall, the use of tranexamic acid proved to be a safe and effective strategy for minimizing postoperative declines in erythrocyte, hemoglobin, and hematocrit levels, while also reducing postoperative drainage volume. This ultimately leads to decreased blood loss and a lower requirement for blood transfusions.

Keywords: total hip arthroplasty, tranexamic acid, osteoarthritis, blood loss, blood transfusion

Introduction

Hip osteoarthritis is one of the most prevalent diseases in orthopedics, and total hip arthroplasty is among the most commonly performed procedures in orthopedic surgery, offering a proven and effective treatment that significantly enhances patients' quality of life^[1]. In the

1960s, total hip arthroplasty revolutionized the approach to treating osteoarthritis. Advances in bioengineering technology, prosthetic design, material development, and fixation durability for both cemented and uncemented prostheses, along with minimally invasive surgical techniques, have led to excellent long-term outcomes. Consequently, total hip arthroplasty is often regarded as the surgery of the century^[2].

However, one of the most significant challenges associated with total hip arthroplasty is excessive bleeding and a high demand for blood transfusions [3]. Reported blood loss can range from 1188 ml to 1651 ml, making it difficult to compare these values due to the various formulas used to calculate blood loss^[4-7]. The prevalence of allogeneic erythrocyte transfusions has been reported by several authors to be between 21% and 70% [8,9,10]. While blood transfusion can be lifesaving, it carries various risks, including transfusion-related lung injury, immunomodulation, pathogen transmission, and wound infections^[11-13].

To address blood loss and reduce the need for transfusions, several methods are employed, such as blood salvage, enhanced surgical hemostasis techniques, minimally invasive surgery, and stimulation of erythropoiesis with erythropoietin alpha. Although these methods have proven effective, they each involve additional costs^[14].

Recently, pharmacological agents known as antifibrinolytics have been studied for their potential to minimize blood loss during total arthroplasty. Among these, tranexamic acid has been found to be 7 to 10 times more effective in inhibiting fibrinolysis compared to epsilon aminocaproic acid^[15]. Tranexamic acid is a synthetic analog of the amino acid lysine, recognized for its ability to inhibit fibrinolysis by reversibly binding to 4 to 5 lysine receptor sites on plasminogen. This action reduces the conversion of plasminogen to plasmin, thereby preventing fibrin degradation and preserving the structure of the fibrin matrix^[16]. Tranexamic acid can be administered intravenously, orally, or locally. Despite the growing interest in its use to minimize blood loss, a universally accepted protocol for tranexamic acid administration in total hip arthroplasty has yet to be established.

The primary objective of this study was to evaluate the pre- and postoperative values of erythrocytes, hemoglobin, hematocrit, and drainage volume after administration of tranexamic acid in patients undergoing total hip arthroplasty.

Materials and methods

This study was designed as a prospective, single-center clinical trial. Informed consent for voluntary participation in the study and for the procedure itself was obtained from patients undergoing total uncemented hip arthroplasty. The study was conducted at the University Clinic for Orthopedic Diseases in a duration of 12 months, involving 40 patients over the age of 18, in whom the diagnosis of hip osteoarthritis was clinically and radiographically confirmed with an indication for surgical treatment. Only patients with normal hematological status and hemostasis were included. Patients were excluded if they had: coagulopathy, rheumatoid arthritis, chronic anticoagulant or corticosteroid therapy, infectious diseases, malignancies, the need for revision surgery, hypersensitivity to tranexamic acid, a coronary or vascular stent placed within the last 6 months, deep vein thrombosis, fixation of the prosthetic components with bone cement, or intravenous or oral therapy with tranexamic acid during the treatment.

Before surgery, all patients had their height and weight measured, a complete blood count, hemostasis assessment, and evaluation by an anesthesiologist. All patients received antibiotic and antithrombotic prophylaxis with low molecular weight heparin according to protocol. An anterolateral approach to the proximal femur was used following the Watson-Jones technique.

Patients were randomly divided into two groups. The first group served as the control one, while the second was the experimental group, consisting of 20 patients each. The control group followed the established surgical protocol for total hip arthroplasty at the University Clinic for Orthopedic Diseases in Skopje. In the experimental group, tranexamic acid was administered before the skin incision according to the recommended dosage of 1 gram via slow intravenous infusion (1 ml/minute). The indication for intraoperative erythrocyte transfusion was determined by the anesthesiologist. The indication for postoperative erythrocyte transfusion was established when hemoglobin levels fell below 9 g/dL or when the patient exhibited clinical signs of anemia, such as fatigue, palpitations, pallor, tachycardia, tachypnea, and hypotension.

Throughout the study, preoperative values of erythrocytes, hemoglobin, and hematocrit were recorded. Postoperative values included the volume of drainage on the day of surgery and the first postoperative day, measured with a digital scale, as well as the values of erythrocytes, hemoglobin, and hematocrit on the second postoperative day, and the number of transfusions.

Results

This study included 40 patients, of whom 20 (50%) were men and 20 (50%) were women. Patients involved in the study were aged between 41 and 81 years, with an average age of 59.65 years. Patients' demographic data are presented in Table 1.

Table 1. Demographic data of patients in the experimental and control groups \overline{x} +SD (Values are statistically significant at p<0.05)

Group	Experimental	Control	Significance
Age (years)	58.25±9.689	61.2±5.578	NO
Body Mass Index	28.669±4.103	31.25 ± 4.569	NO
Gender (male/female)	10/10	10/10	NO

t-test; no - no statistically significant difference; yes - statistically significant at p < 0.05

Patients in the control group were insignificantly older and heavier, but without a statistical significance. Both groups had equal representation of men and women.

As part of the preoperative preparation, all patients underwent a complete blood count. The average values of erythrocytes, hemoglobin, and hematocrit in both groups were within the reference ranges. The preoperative values of erythrocytes, hemoglobin, and hematocrit in the groups are presented in Table 2.

Table 2. Preoperative values of erythrocytes, hemoglobin, and hematocrit $\bar{x}\pm SD$ (Values are statistically significant at p<0.05)

Group	Experimental	Control	Significance
Erythrocytes 10 ¹² /L	4.7445±0.449	4.64±0.392	NO
Hemoglobin/L	142±15.53	139.2±13.801	NO
Hematocrit	0.423 ± 0.041	0.4115 ± 0.041	NO

t-test; no - no statistically significant difference; yes - statistically significant at p<0.05

The average values of erythrocytes, hemoglobin, and hematocrit were higher in the experimental group, but without a significant statistical difference. The values of erythrocytes,

hemoglobin, and hematocrit from the second postoperative day of both groups were recorded and are presented in Table 3.

Table 3. Values of erythrocytes, hemoglobin, and hematocrit from the second postoperative day $\bar{x}\pm SD$ (Values are statistically significant at p<0.05)

Group	Experimental	Control	Significance
Erythrocytes 10 ¹² /L	3.85±0.375	3.5565±0.461	YES
Hemoglobin/L	117.473±10.591	106.1±13.380	YES
Hematocrit	0.345 ± 0.041	0.313±0.045	YES

t-test; no - no statistically significant difference; yes - statistically significant at p<0.05

The values of erythrocytes, hemoglobin, and hematocrit recorded on the second postoperative day were statistically significantly higher in the experimental group. The difference in the level of erythrocytes was 0.2935 x 10^{12} /L, in hemoglobin 11.093 g/L, and in hematocrit 0.032. Considering the number and distribution of erythrocyte transfusions across both groups, the actual difference between the control and experimental groups was even greater.

The volume of the drainage pump was measured during the day of surgery (day zero) and the first postoperative day. The measured values are presented in Table 4.

Table 4. Volume of postoperative drainage measured on the day of surgery and the first postoperative day. $\bar{x}\pm$ SD (Values are statistically significant at p<0.05)

Group	Experimental	Control	Significance
Day of surgery	301.1±93.59	428.57±228.150	YES
First postoperative day	179.4 ± 83.505	89.4±107.607	NO
Total	480.5±163.898	618.15±196.323	YES
t-test: no - no statistically significant difference; yes - statistically significant at $n<0.05$			

t-test; no - no statistically significant difference; yes - statistically significant at p<0.05 $\,$

The volume of postoperative drainage in both groups differed significantly. In patients from the experimental group, the average measured volume on the day of surgery was 301.1 ± 93.5 ml, which was 127.47 ml less than in the control group, where it was 428.57 ± 228.150 ml. On the first postoperative day, the measured volume in the experimental group averaged 179.4 ± 83.505 ml, which was 10 ml less than in the control group, where it was 189.4 ± 107.607 ml. The total measured volume in the experimental group was 137.65 ml less than the measured volume in the control group.

Table 5shows the distribution of transfusions made in relation to the intraoperative and postoperative periods.

	• •	
Group	Experimental	Control
Intraoperative transfusion	0	5
Postoperative transfusion	3	15
Total	3	20

Table 5. Distribution of intraoperative and postoperative erythrocytetransfusions (bag with decanted erythrocytes of 350 ml)

In the control group, five units of erythrocytes of 350 ml were given during the intraoperative period, and 15 units were given in the postoperative period. This was significantly more than in the experimental group, where three units were given in the postoperative period.

Discussion

Tranexamic acid is a synthetic amino acid that serves as a competitive inhibitor of plasminogen, effectively reducing fibrinolysis. Surgical trauma triggers the release of tPa (tissue plasminogen activator), which activates fibrinolysis. Typically, fibrinolysis is inhibited 24 hours post-surgery. However, antifibrinolytics like tranexamic acid can obstruct the conversion of plasminogen to plasmin in the early stages, thereby minimizing postoperative blood loss. Since its introduction in total hip arthroplasty in 2000, tranexamic acid has shown potential to significantly alter blood loss management during the procedure. Despite this, a standardized protocol has yet to be established due to considerable variability in administration methodologies, dosing, duration, and timing^[17,18].

The results of this study revealed significant differences between the two groups. The experimental group experienced a lesser decrease in erythrocytes, averaging 0.2935 x 10^{12} /L, a smaller reduction in hemoglobin, averaging 11.093 g/L, and a reduced drop in hematocrit, averaging 0.032. On the day of surgery, the volume of postoperative drainage in the experimental group was 127.47 ml lower than that of the control group, and it was 10 ml less than in the control group on the first postoperative day. Overall, the total drainage volume was 137.65 ml less in the experimental group. Furthermore, the number of transfusions was significantly lower in the experimental group, with 20 transfusions compared to only 3 in the control group.

The findings indicate that the application of tranexamic acid during total hip arthroplasty results in decreased blood loss and reduced transfusion requirements. This reduction leads to fewer associated adverse effects and risks, providing a pharmacoeconomic benefit. Additionally, a decrease in postoperative drainage volume will likely shorten the duration of necessary postoperative drainage.

Conclusion

The use of tranexamic acid as a standard protocol in total hip arthroplasty is a safe and effective method to reduce the decrease in postoperative values of erythrocytes, hemoglobin, and hematocrit, as well as to decrease the volume of postoperative drainage, ultimately resulting in less blood loss and a lower need for blood transfusion.

Conflict of interest statement. None declared

References

- 1. Räsänen P, Paavolainen P, Sintonen H, Koivisto AM, Blom M, Ryynänen OP, *et al.* Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. *ActaOrthop* 2007; 78(1): 108-115. doi: 10.1080/17453670610013501.
- 2. Learmonth ID, Young C, Rorabeck C. The operation of the century: total hip replacement. *Lancet* 2007; 370(9597): 1508-1519. doi: 10.1016/S0140-6736(07)60457-7.
- 3. Vuille-Lessard E, Boudreault D, Girard F, Ruel M, Chagnon M, Hardy JF. Red blood cell transfusion practice in elective orthopedic surgery: a multicenter cohort study. *Transfusion* 2010; 50(10): 2117-2124. doi: 10.1111/j.1537-2995.2010.02697.x.
- Hays MB, Mayfield JF. Total blood loss in major joint arthroplasty. A comparison of cemented and noncemented hip and knee operations. *J Arthroplasty* 1988; 3 Suppl: S47-9. doi: 10.1016/s0883-5403(88)80008-1.

- 5. Sehat KR, Evans RL, Newman JH. Hidden blood loss following hip and knee arthroplasty. Correct management of blood loss should take hidden loss into account. *J Bone Joint Surg Br* 2004; 86(4): 561-565. PMID: 15174554.
- 6. Billote DB, Glisson SN, Green D, Wixson RL. A prospective, randomized study of preoperative autologous donation for hip replacement surgery. *J Bone Joint Surg Am* 2002; 84(8): 1299-1304. doi: 10.2106/00004623-200208000-00002.
- 7. Charrois O, Kahwaji A, Vastel L, Rosencher N, Courpied JP. Blood loss in total hip arthroplasty for rapidly destructive coxarthrosis. *IntOrthop* 2001; 25(1): 22-24. doi: 10.1007/s002640000210.
- Stanworth SJ, Cockburn HA, Boralessa H, Contreras M. Which groups of patients are transfused? A study of red cell usage in London and southeast England. *Vox Sang* 2002; 83(4): 352-357. doi: 10.1046/j.1423-0410.2002.00237.x.
- 9. Jans Ø, Kehlet H, Hussain Z, Johansson PI. Transfusion practice in hip arthroplasty-a nationwide study. *Vox Sang* 2011; 100(4): 374-380. doi: 10.1111/j.1423-0410.2010.01428.x.
- Browne JA, Adib F, Brown TE, Novicoff WM. Transfusion rates are increasing following total hip arthroplasty: risk factors and outcomes. *J Arthroplasty* 2013; 28(8 Suppl): 34-37. doi: 10.1016/j.arth.2013.03.035.
- 11. Spiess BD. Transfusion of blood products affects outcome in cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2004; 8(4): 267-281. doi: 10.1177/108925320400800402.
- 12. Rawn J. The silent risks of blood transfusion. *CurrOpinAnaesthesiol* 2008; 21(5): 664-668. doi: 10.1097/ACO.0b013e32830f1fd1.
- Taneja A, El-Bakoury A, Khong H, Railton P, Sharma R, Johnston KD, *et al.* Association between Allogeneic Blood Transfusion and Wound Infection after Total Hip or Knee Arthroplasty: A Retrospective Case-Control Study. *J Bone Jt Infect* 2019; 4(2): 99-105. doi: 10.7150/jbji.30636.
- 14. Juraj M, Jaroslav V, Gažová A, Žufková V, Kyselovič J, Šteňo B. Evaluation of efficacy and safety of systemic and topical intra-articular administration of tranexamic acid in primary unilateral total hip arthroplasty. *Medicine (Baltimore)* 2021; 100(26): e26565. doi: 10.1097/MD.00000000026565.
- 15. Nilsson IM. Clinical pharmacology of aminocaproic and tranexamic acids. J ClinPatholSuppl (R CollPathol). 1980; 14: 41-47. PMID: 7000846.
- 16. Cai J, Ribkoff J, Olson S, Raghunathan V, Al-Samkari H, DeLoughery TG, *et al.* The many roles of tranexamic acid: An overview of the clinical indications for TXA in medical and surgical patients. *Eur J Haematol* 2020; 104(2): 79-87. doi: 10.1111/ejh.13348.
- 17. Wei W, Wei B. Comparison of topical and intravenous tranexamic acid on blood loss and transfusion rates in total hip arthroplasty. *J Arthroplasty* 2014; 29(11): 2113-2116. doi: 10.1016/j.arth.2014.07.019.
- Ekbäck, Gustav MD*; Axelsson, Kjell MD, PhD*; Ryttberg, Lars MD†; Edlund, Bror MD, PhD‡; Kjellberg, Jill Chief CRNA*; Weckström, Johan MD†; Carlsson, Olle PhD§; Schött, Ulf MD, PhD*. Tranexamic Acid Reduces Blood Loss in Total Hip Replacement Surgery. *Anesthesia & Analgesia* 2000; 91(5): 1124-1130. doi: 10.1213/00000539-200011000-00014.