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Original Research Article

Effect of tranexamic acid and total knee arthroplasty on perioperative coagulation indices and blood loss in patients with knee osteoarthritis

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Abstract

Purpose: *To study the effect of the combination of tranexamic acid and total knee arthroplasty (TKA) on perioperative coagulation indices and blood loss in patients with knee osteoarthritis (KOA).*
Methods: *A total of 78 KOA patients who received TKA in Second Affiliated Hospital of Qiqihar Medical College from July 2020 to July 2022 were recruited and randomized to study and control groups in a ratio of 1:1 (n = 39). Patients in control group received 0.9 % sodium chloride, while those in study group were treated with 0.9 % sodium chloride plus tranexamic acid after TKA. Parameters evaluated include intraoperative bleeding, drainage volume, occult blood loss, and total blood loss.*
Results: *The two groups of patients had similar intraoperative blood loss ($p > 0.05$). Tranexamic acid significantly reduced postoperative drainage volume, occult blood loss, and total blood loss in TKA patients ($p < 0.05$). Before and after treatment, no intergroup differences were seen in prothrombin time, activated partial thromboplastin time, fibrinogen, and D-dimer (D-D) levels ($p > 0.05$). The D-D levels of all patients showed a significant increase after TKA ($p < 0.05$). Patients with tranexamic acid exhibited significantly higher serum hemoglobin (Hb) concentrations and lower serum white blood cell count (WBC) than those without tranexamic acid during TKA ($p < 0.05$).*
Conclusion: *Tranexamic acid plus TKA effectively reduces the intraoperative blood loss of KOA patients, restores knee function, improves serological condition, and lowers the incidence of postoperative complications and transfusion risk. Multicenter large-scale trials are, however, required prior to application in clinical practice.*

Keywords: *Tranexamic acid, Total knee arthroplasty, Knee osteoarthritis, Perioperative period, Coagulation index, Blood loss*

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INTRODUCTION

Knee osteoarthritis (KOA) is a progressive and degenerative knee disease caused by joint trauma or excessive strain [1], and elderly people are more susceptible to KOA. Common clinical manifestations of KOA are swelling and deformed joints with significant pain, which

severely compromise the daily quality of life of patients [2].

Total knee arthroplasty (TKA) is the ultimate clinical treatment option for KOA and is performed by replacing the diseased joint so as to relieve knee pain and improve the function of the patient's limbs [3]. The effectiveness of TKA in the treatment of KOA patients has been substantiated in other clinical studies [3-5]. However, research has indicated that TKA may cause severe trauma and heavy bleeding, which is difficult to manage in the elderly population due to their weak physique [5].

It has been shown that KOA patients treated with TKA had a postoperative bleeding volume of about 1.5 L and a transfusion rate of about 57 % [6]. Moreover, most patients required postoperative allogeneic or autologous blood transfusion, which may significantly increase the risk of infectious diseases and hemolytic reactions. Intraoperative bleeding can be managed by tourniquets, but their release is associated with abnormal fibrinolytic-coagulation mechanisms and increased postoperative bleeding [7]. Previously, drugs and controlled hypotension were frequently employed clinically to reduce postoperative bleeding and transfusion rates in patients with TKA [8]. Tranexamic acid inhibits fibrinolysis and achieve hemostasis by blocking the lysine-binding site of fibrinogen [9] and can also block urokinase-type plasminogen activators. Therefore, it may affect several processes associated with surgery and wound healing other than fibrinolysis. However, topical tranexamic acid may also have positive effects other than reduce bleeding. Documented beneficial effects include a reduction in inflammatory reactions during surgery and a reduction in melasma and erythema in dermatology. To date, no study has demonstrated the association between tranexamic acid use and increased risk of complications in joint replacement surgery [10]. The current research was performed to study the effect of tranexamic acid plus TKA on perioperative coagulation and blood loss in patients with KOA.

METHODS

Patients and ethical approval

A total of 78 KOA patients who received TKA in the Second Affiliated Hospital of Qiqihar Medical College from July 2020 to July 2022 were recruited and randomized to study and control groups in a ratio of 1:1, with 39 patients in each group. The patients in the control group received 0.9 % sodium chloride, while those in the study group were treated with 0.9 % sodium chloride plus tranexamic acid. The study complied with the requirements of the guidelines of Declaration of Helsinki [11] and was approved by the ethics committee of the Second Affiliated Hospital of Qiqihar Medical College (approval no. Q0220301). All patients were well informed and duly signed the relevant consent forms for this study.

Inclusion and exclusion criteria

Inclusion criteria

Patients who were diagnosed with KOA by clinically relevant tests, treated with TKA, diagnosed with unilateral lesions, and aged between 55 and 75 years old were included.

Exclusion criteria

Patients with allergies or related contraindications to drugs and surgical procedures in this study, coagulation disorders, serious organ diseases, serious infectious diseases, immune diseases, recent use of anticoagulants, deep vein thrombosis, severe deformity or internal or external fracture of the knee joint, mental disorders or cognitive disorders, or inability to cooperate completely with this study were excluded.

Treatments

In both groups, the patients were treated with TKA, and the surgery was performed by the same group of surgeons. The medial parapatellar approach was adopted as the surgical approach and combined lumbar and rigid anesthesia were administered. A tourniquet was applied to the affected thigh, and an incision was made in the anterior median of the knee joint. The joint cavity was accessed medially from the parapatellar area, the patella was turned laterally, and the femur and tibia were cut posteriorly to release the soft tissue. The femoral and tibial prostheses were secured with bone cement, polyethylene spacers were installed, and the patellar surface was trimmed, followed by the placement of drainage tubes in the posterior joint cavity. The tourniquet was released, and the surgery was concluded by using an elastic bandage cotton pad for pressure bandaging.

In the study group, when the tourniquet was released, 1 g of tranexamic acid (Shanghai Xinyi Jinzhu Pharmaceutical Co. Ltd., State Drug Administration H31021856) dissolved in 100 mL 0.9 % sodium chloride injection was administered

intravenously, at an infusion rate at 50 drops/minute and an interval of 3 h between doses. The control group was administered an equal amount of 0.9 % sodium chloride injection. Patients in both groups were given nursing care such as anti-infection and rehabilitation training after surgery. A 60-day follow-up was carried out after discharge.

Parameters evaluated

Blood loss

The relevant blood loss parameters of the patients including intraoperative bleeding, 1d drainage volume, occult blood loss, and total blood loss were recorded.

Coagulation

Before and after surgery, 5 mL of morning fasting elbow venous blood was collected and centrifuged to obtain serum. The prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (Fg), and D-dimer (D-D) levels were measured using a fully automated biochemical analyzer.

Hospital for Special Surgery Knee-Rating Scale (HSS) scores

Before surgery and after follow-up, patients' knee function was evaluated using the HSS, which was scored from 0 to 100, with higher scores indicating better recovery of knee function.

Serological parameters

Before and after surgery, 5 mL of fasting elbow venous blood was collected and centrifuged to obtain serum. The serum white blood cell count (WBC) and hemoglobin (Hb) levels of patients were determined using an enzyme-linked immunosorbent assay (ELISA).

Complications

Complications including subcutaneous petechiae, deep vein thrombosis, swelling of the lower extremities, pulmonary embolism, and the percentage of patients requiring blood transfusion were recorded.

Statistical analysis

GraphPad Prism 8 was used to plot graphics, while SPSS 26.0 was employed for data analyses. Count data are expressed as (n (%)) and tested using chi-square test. Measurement data are expressed as mean ± standard deviation (SD) and tested using a *t*-test. $P < 0.05$ indicates that the difference was statistically significant.

RESULTS

Baseline profiles of patients

The two arms were well-balanced in terms of baseline profiles of the patients ($p > 0.05$; Table 1)

Blood loss indices

The two groups of patients had similar intraoperative blood loss ($p > 0.05$). Tranexamic acid significantly reduced the postoperative 1-day drainage volume, occult blood loss, and total blood loss in TKA ($p < 0.05$; Table 2).

Table 1: Baseline profiles of patient (n = 39)

Parameter	Study group	Control group	t/x²	*P*-value
Sex			0.206	0.65
Male	17	19		
Female	22	20		
Age (years)	64.06±4.32	64.17±4.39	-0.112	0.911
BMI (kg/m²)	23.08±1.74	23.15±1.84	-0.173	0.863
Disease duration (years)	8.72±2.93	8.83±2.95	-0.165	0.869
Affected sides			0.054	0.817
Left	15	16		
Right	24	23		
Underlying disease				
Hypertension	21	24	0.473	0.492
Diabetes mellitus	10	11	0.065	0.799
History of heart disease	5	4	0.126	0.723
History of cerebrovascular disease	7	5	0.394	0.53

Table 2: Blood loss indices (mean ± SD, n = 39)

Group	Intraoperative blood loss	Postoperative 1-day drainage volume	Occult blood loss	Total blood loss
Control (mL)	113.41±27.42	488.54±68.72	635.73±184.76	1237.68±280.90
Study (mL)	114.29±27.26	193.62±38.28	324.69±102.37	632.60±167.91
T	-0.142	23.414	9.196	11.547
P-value	0.887	<0.001	<0.001	<0.001

Coagulation parameters

In the study group, the preoperative and postoperative prothrombin time (PT) was 12.84 ± 1.86 s, 13.08 ± 2.11 s, APTT was 32.64 ± 4.79 s, 33.02 ± 5.19 s, Fg was 3.85 ± 0.47 g/L, 3.82 ± 0.48 g/L, and D-D level was 0.24 ± 0.12 mg/L, 0.93 ± 0.42 mg/L. In the control group, the preoperative and postoperative PT was 12.79 ± 1.93 s, 13.06 ± 2.13 s, APTT was 32.87 ± 4.82 s, 33.07 ± 5.24 s, Fg was 3.87 ± 0.52 g/L, 3.83 ± 0.51 g/L, and D-D level was 0.26 ± 0.11 mg/L, 0.95 ± 0.39 mg/L. Before and after the treatment, no intergroup differences were seen in PT, activated APTT, Fg, and D-D levels ($P > 0.05$). The D-D levels of all patients showed a significant increase after TKA ($P < 0.05$) (Figure 1).

HSS scores

The HSS in the control group before surgery and after follow-up was 52.47 ± 5.38 and 73.69 ± 8.24. The HSS in the study group before surgery and after follow-up was 52.76 ± 5.41 and 89.87 ± 10.68. Total knee arthroplasty with tranexamic acid provided more improvement in knee function of the patients versus without tranexamic aid, evinced by the markedly elevated HSS scores of patients in the experimental group ($p < 0.05$) (Figure 2).

Serological indices

Patients with tranexamic acid exhibited significantly higher serum Hb concentrations and lower serum WBC than those without tranexamic acid during TKA ($p < 0.05$) (Table 3).

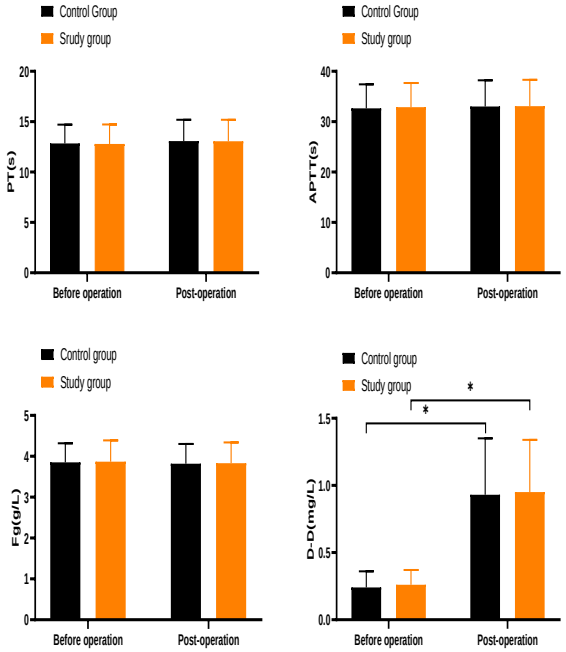

Figure 1: Comparison of PT, APTT, Fg, and D-D levels between the two groups. *$P < 0.05$

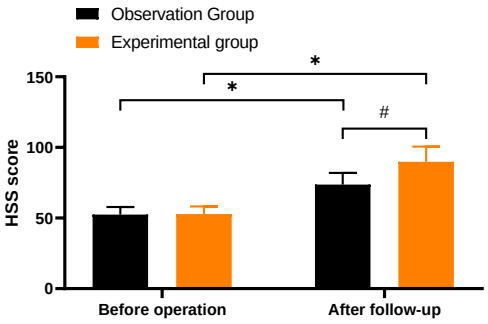

Figure 2: HSS scores of the two groups of patients (n = 39). *$P < 0.05$ versus control

Table 3: Serological indices ((mean ± SD, n = 39)

Group	Hb (g/L)		WBC (×10^9/L)	
	Preoperative	Postoperative	Preoperative	Postoperative
Control	120.49±7.32	81.58±10.36	16.43±4.84	11.23±2.59
Study	120.27±7.43	87.62±9.74	15.97±5.16	7.62±1.84
t	0.132	-2.653	0.406	7.096
P-value	0.895	0.01	0.686	<0.001

Table 4: Complications and number of patients requiring blood transfusion (mean ± SD, n = 39)

Complication	Control	Study	χ^2	*P*-value
Subcutaneous petechiae	3	1	-	-
Deep vein thrombosis	1	0	-	-
Swelling of lower extremities	3	0	-	-
Pulmonary embolism	1	0	-	-
Total incidence (%)	20.51% (8/39)	2.56% (1/39)	6.155	0.013
The percentage of people requiring blood transfusion (%)	23.08% (9/39)	5.13% (2/39)	5.186	0.023

Complications and number of patients requiring blood transfusion

The incidence of complications in the control group was 20.51 %, and the percentage of the number of people requiring blood transfusion was 23.08 %. The incidence of complications in the study group was 2.56 %, and the percentage of people requiring blood transfusion was 5.13 %. Total knee arthroplasty with tranexamic acid resulted in a lower incidence of complications and fewer cases requiring blood transfusion than TKA without tranexamic acid ($p < 0.05$; Table 4).

DISCUSSION

Knee osteoarthritis is a common chronic degenerative orthopedic disease. In recent years, with a continued increase in the aging of the population and the increasing number of obese people in China, the prevalence of KOA has shown a significant increase, thereby constituting the most common bone disease that endangers people's life and health safety [12]. Total knee arthroplasty effectively mitigates the clinical symptoms of KOA patients and restores the function and stability of the diseased knee joint [13].

However, research indicates that TKA requires osteotomy and resection of the tibia and femur, resulting in high surgical trauma [14}. Moreover, TKA often requires the use of a tourniquet to control intraoperative bleeding, but the rapid congestion of the lower extremity after release may lead to rupture and massive bleeding of local microvessels [15]. Ischemia-reperfusion injury may drive the activation of the fibrinolytic system, which further aggravates postoperative bleeding in patients [16]. In addition, a large local accumulation of blood may aggravate the pain in the affected limb, compromising the joint function recovery of patients [17]. Massive bleeding after TKA is frequently managed by hemostatic drugs, intraoperative autologous blood transfusion, and allogeneic transfusion, but the outcomes are mostly clinically unsatisfactory [18].

Previous research has reported a suboptimal clinical efficacy of hemostatic drugs such as enzyme-inhibiting peptides and aminoacetic acid as antifibrinolytic drugs [19]. Allogeneic blood transfusion is limited by its increased risk of hepatitis and AIDS [20], while intraoperative autologous blood transfusion requires a high turnover of hospital beds and related hardware and equipment, which similarly prevents its widespread use in clinical practice [21].

Tranexamic acid is a synthetic antifibrinolytic drug, and numerous studies [22] have demonstrated that tranexamic acid effectively reduces perioperative bleeding and the risk of postoperative transfusion. Tranexamic acid blocks the lysine binding site of the fibrinogen molecule, thereby preventing fibrinolysis and antifibrinolytic activation, resulting in effective hemostasis [23]. The results of the present study were consistent with previous results [24], suggesting that tranexamic acid is effective in reducing postoperative blood loss, improving serological conditions, and promoting functional recovery of the knee joint. Smith *et al* [25] found that tranexamic acid significantly reduces the risk of allogeneic transfusion and several complications, which was consistent with the results in the present study. Previous studies indicated that the use of tranexamic acid would affect the coagulation function of patients [26,27], while in the present study, no intergroup differences were observed in the PT, APTT, Fg, and D-D levels both preoperatively and postoperatively while the D-D levels of all patients showed a significant increase after TKA. The current results indicated no significant implications for the coagulation function of patients from tranexamic acid, which is at variance with the findings of previous related studies. The discrepancy may lie in the different sample sizes included and the different determination criteria. In the current study, postoperative D-D levels were significantly higher in both groups, which may be associated with surgical stimulation and reduced activity of the patients.

Limitations of this study

This study has the following shortcomings: The small sample size of this study may lead to

biased results. The effects of different dosing times and doses on treatment effects were not studied in depth, and the short follow-up of this study failed to assess the difference in long-term patient outcomes.

CONCLUSION

The use of the combination of TKA and tranexamic acid in the management of KOA effectively reduces intraoperative blood loss, restores knee function, improves serological conditions, and lowers the incidence of postoperative complications and transfusion risk. Large-scale multi-center trials using several dosing conditions are, however, required prior to the application of this findings in clinical practice.

DECLARATIONS

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Funding

None provided.

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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