Research Article

Pharmaceutical BIOPROCESSING

Comparison of the effect of intravenous and intra-articular injection of tranexamic acid on blood loss in total knee arthroplasty

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Objective: To compare the effect of intravenous and intra-articular injection of tranexamic acid on blood loss in total knee arthroplasty (TKA).

Methods: A total of 90 patients treated with total knee arthroplasty in our hospital from August 2015 to August 2016 were selected as the objects and divided into observation group and control group according to different treatment methods with 45 cases in each group. The control group were given intravenous drip of 10 mg/kg tranexamic acid during anesthetic induction with the maximum dose of 1 g while the observation group were treated by intra-articular injection of 1 g tranexamic acid after finishing suture but before loosening tourniquet. After that, the blood loss, blood coagulation and the incidence of deep venous thrombosis were observed in the two groups.

Results: In the observation group, the postoperative drainage volume was (252.21 ± 63.98) mL, the occult blood loss was (603.21 ± 59.96) mL and the total blood loss was (923.12 ± 286.21) mL, significantly less than those in the control group, they were respectively (545.21 ± 61.98) mL, (882.21 ± 113.96) mL and (1223.13 ± 386.25) mL and the difference in between was of statistical significance ($P<0.05$); there were no significant differences in blood coagulation (PT, APTT, INR) and the incidence of deep vein thrombosis (DVT) between the two groups of no statistical value ($P>0.05$).

Conclusion: Intraarticular injection of tranexamic acid can effectively control blood loss after TKA treatment and avoid the occurrence of deep vein thrombosis, thus worth popularizing.

Keywords: tranexamic acid ▪ total knee arthroplasty ▪ intraarticular ▪ intravenous drip

Introduction

TKA is a new technique for treating knee joint disease and has gradually developed when artificial hip replacement manages to be successfully applied in the modern time. Despite its good effects in eradicating advanced knee pain, it also has such defects as the large volume of bleeding, serious surgical trauma and high difficulty of stemming bleeding [1]. Massive bleeding during total knee arthroplasty is mainly based on two factors: (a) fibrinolytic reaction activated by surgical trauma (b) during operation, tourniquet is used to cause ischemia and anoxia, resulting in microcirculation disturbance and accumulation of various harmful metabolites. In addition, after the release of the tourniquet in the distal limb prone to ischemia reperfusion injury, activated neutrophils aggregation and a series of inflammatory mediators, leading to tissue plasminogen activator protein release of vascular endothelial cells after injury, further increase the fibrinolytic reaction [2]. It is confirmed by the study that tranexamic acid can play the effect of hemostasis by inhibiting fibrinolysis [3,4]. The tranexamic acid can be used for stopping bleeding through intravenous drip or intra articular injection and there remains no systematic report about the hemostatic effect of different administration methods. In this study, we aimed to explore the effect of intra-articular injection and intravenous infusion of tranexamic acid on blood loss in total knee arthroplasty with the details reported as follows:

Data and methods

General information

A total of 90 patients treated with total knee arthroplasty in our hospital from August 2015 to August 2016 were selected as the objects and divided into observation group and control group according to different treatment methods with 45 cases in each group. In the observation group there were 24 males and 21 females, aged 47-82 with an average age of (63.12 ±.82) years, 1-2 years in duration with an average duration of (1.23 ± 0.24) years; In the control group, there were 26 males and 19 females, aged 46-81 with an average age of (62.23 ± 7.14) years, 2-3 years in duration with an average duration of (1.53 ± 0.64) years; There was no statistically significant difference in general information and condition between the two groups of comparability (P>0.05).

Methods

Two groups of patients were treated with total knee arthroplasty and operated by the same surgeon with following surgical procedure: pueumatic tourniquet was applied in the operation and the pressure in patients was adjusted to 35-40kPa according to their actual conditions and under general or epidural anesthesia the median incision was conducted in front of knee joint. Patella medial joint capsules were opened to expose the knee joint, the anterior cruciate ligament was cut off, the osteophyte formation on the edge of joint was snapped off, residual meniscus were removed and the internal or lateral collateral ligament was properly relaxed with the knees flexed over 90°. The angle between femoral anatomic axis and lower mechanical axis was measured according to preoperative X-ray of lower extremity to determine hallux valgus angle. With the external rotation angle under control, bone cut was implemented respectively in the distal femur, ankles and angular surface with stabilized prosthesis after total knee arthroplasty followed by implement of intercondylar prosthesis and intramedullary or extramedullary localization. Osteotomy was conducted 1-2 cm away from the lowest point of distal tibial plateau. Suitable type was chosen for test mode and the installation was completed followed by test of lower extremity, joint activity and varus or valgus balance. Articular cavities were flushed and arranged in turn with the fixation of tibia of corresponding type and the cement solidification from femur to bone; the observation group, besides the above treatment, were additionally given intra-articular injection of tranexamic acid as follow: after the suture of joint capsules, 100 mL tranexamic acid (Fuzhou Haiwang Fu Pharmaceutical Co. Ltd., H20059504,5 mL:0.5 g * 5/box) was injected to the articular cavities in patients, Then drainage tube was closed followed by closure of incision one by one and the tourniquet was released followed by bandaging with appropriate compression; the control group were given intravenous drip of tranexamic acid 10 mg/kg which was diluted by 5%-10% glucose during anesthesia induction with its maximum dose of dripping less than 1.0 g.

Observation index and evaluation standard

The occult blood loss, drainage volume 24 h after operation, the total blood loss, rate of blood transfusion and blood coagulation function were observed between the two groups in which the function of blood coagulation included prothrombin time (PT), activated partial thromboplastin time (APTT) and international normalized ratio (INR); the incidence of deep vein thrombosis was assessed as follow: color doppler ultrasound was given to both lower extremities in patients 7 days after operation (DVT) followed by the observation of the occurrence of DVT.

Statistical processing

All the data were processed by SPSS 21 statistical software in which the measurement data were expressed by "mean ± standard deviation" ($\bar{x}$ ±s) and the count data "n (%)". The comparison between groups was expressed by χ2, and P<0.05 suggested there was statistically significant difference between the two groups.

Results

Comparison of blood loss between the two groups

After treatment, the total blood loss in the observation group was significantly lower than that in the control group (P<0.05), as shown in **TABLE 1**.

Comparison of coagulation function between the two groups

After treatment, there was no significant difference in coagulation function between the two groups (P>0.05), as shown in **TABLE 2**.

Comparison of deep venous thrombosis rates between the two groups

After treatment, there was no difference in the incidence of venous thrombosis between the two groups (P>0.05), as shown in **TABLE 3**.

Discussion

TKA was accompanied by the operation of synovectomy, osteotomy and femoral reaming, which will give rise to postoperative complications like large blood loss and wide as well as constant bleeding. The use of tourniquet will cause the ischemia and reperfusion injury in lower extremity, thereby leading to release of tissue plasminogen activator (TPA) in blood endothelium, facilitating fiber solution reaction and finally increasing the amount of bleeding. All these adverse reactions should be taken seriously and active measures are required to be taken according to the cause of bleeding in clinical treatment [5-8].

In this study, we compared the effect of intravenous and intra-articular injection of tranexamic acid on blood loss in total knee arthroplasty and found that compared with the control group, the postoperative drainage volume, occult blood loss and total blood loss in the observation group were significantly lower with statistically significant difference in between and no significant difference was found in the incidence rate of deep vein thrombosis (DVT) as well as blood coagulation function (PT, APTT, INR), suggesting that in knee arthroplasty the intra-articular injection of tranexamic acid can effectively reduce the amount of bleeding perhaps because 6 h after the intravenous drip of tranexamic acid, the drug concentration will be reduced to be less than the minimum value which can maintain the balance of fibrinolytic system, which will hinder the degradation of fiber protein in the other parts and thus greatly reduce the hemostatic function. The intra-articular injection enables the tranexamic acid to strongly adsorb for a long time on plasmin and lysine binding site (LBS) in fibrin affinity of plasminogen, which inhibits the combination of plasmin and plasminogen with fiber protein and thus strongly hinders the fibrin decomposition induced by plasmin [9-13]; With the presence of anti-plasmin like serum alpha 2 macroglobulin, the tranexamic acid has more obvious anti fibrinolytic function with more significant effect of hemostasis and also plays a role in preventing enhancement of vascular permeability, allergic reaction and inflammatory lesions [14,15]. Due to the limitations like objective conditions and actual research level, the long-term effect in the two groups needs further verification in clinical practices.

In summary, the intra-articular injection of tranexamic acid has significant hemostatic effect for TKA surgery and it can effectively reduce the occult blood loss, postoperative drainage volume as well as total blood loss and prevent the incidence of deep venous

Table 1. Comparison of blood loss between the two groups ($\bar{x}$ ± s, mL)

Groups	Postoperative drainage	Occult blood loss	Total blood loss
Observation group (n=45)	252.21 ± 63.98	603.21 ± 59.96	923.12 ± 286.21
Control group (n=45)	545.21 ± 61.98	882.21 ± 113.96	1223.13 ± 386.25
t	7.027	8.036	9.145
p	< 0.05	< 0.05	< 0.05

Table 2. Comparison of coagulation function between the two groups ($\bar{x}$ ±s)

Groups	PT (s)	APPT (s)	INR
Observation group (n=45)	13.21 ± 1.21	32.01 ± 1.96	1.12 ± 0.21
Control group (n=45)	12.82 ± 0.98	33.21 ± 1.72	1.13 ± 0.25
t	6.005	8.128	8.803
p	< 0.05	< 0.05	< 0.05
Note: compared with the control group, P>0.05.			

Table 3. Comparison of deep venous thrombosis between the two groups [n (%)]

Groups	DTV (+)	DTV (-)
Observation group (n=45)	1 (2.22)	44 (97.78)
Control group (n=45)	1 (2.22)	43 (95.56)
$\chi 2$	0.361	0.449
p	> 0.05	> 0.05

thrombosis and improve the prognosis in patients of practical application value.

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