

Original Article

Comparison of two methods of bolus and infusion of Tranexamic acid to reduce blood loss in Total Knee Arthroplasty

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Abstract

Background: Until today, many studies conduct to determine the optimal dose and regimen of tranexamic acid to reduce the preoperative and postoperative blood loss in primary total knee arthroplasty. In this study, we were compared two different methods of administration (bolus and infusion).

Materials and Methods: Forty patients were randomized in two groups; all the patients received 500 mg tranexamic acid before tourniquet was turned on. Group (A) consisted of 20 patients (mean age: 64 ± 6.1 years) received 500 mg tranexamic acid ten minutes before tourniquet was loosened and group (B) (63.5 ± 7.7 years) received 500 mg tranexamic acid IV infusion during 6 hours from the time of tourniquet loosening (total dose of TA 1 g in both groups). Intraoperative blood loss, postoperative drainage (in 6 and 12 hours), blood transfusion (in 48 hours), hematocrit and hemoglobin decrease (6 and 12 hours later) were compared between two groups.

Results: The patients in group (B) had less blood loss intra- and postoperative in 6 and 12 hours, and also had less hemoglobin decrease and packed cell transfusion rate was significantly lower in these patients; compared to group (A).

Conclusion: Our study demonstrated that infusion administration of tranexamic acid in primary total knee arthroplasty was more effective to reduce perioperative blood loss and the demand for blood transfusion in 48 hours.

Keywords: tranexamic acid, total knee arthroplasty, blood transfusion

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Introduction

Total knee arthroplasty (TKA) is one of the most common procedures, for treating knee diseases such as end-staged knee osteoarthritis and rheumatoid arthritis (1). The prevalence is increasing greatly in aging societies, and it may cause large amounts of blood loss, ranging from 500 to 2000 ml after a single TKA procedure therefore need for blood transfusion

(2-5). As most patients were elderly, blood transfusion may cause more subsequent complications, such as transfusion reactions and even death. So an effective and safe method to decrease intra- and postoperative blood loss would be helpful (6, 7).

There are several suggestions for suppressing perioperative blood loss, including antifibrinolytic agents, intraoperative blood salvage and application

of tourniquet (6, 7). One of the pharmacological choices to prevent surgical bleeding is Tranexamic acid (TA), a widely used synthetic antifibrinolytic agent which prevents the activation of plasminogen to plasmin thus blocks the fibrinolytic action of plasmin on fibrin (8, 9). Many old and recent studies showed that TA can significantly reduce perioperative blood loss and thus need for blood transfusion (6-10), but there is limited information of its effectiveness, safety and method of administration in Iranian patients, so this study is aimed to compare two methods of administration (bolus and IV infusion) of TA in TKA patients.

Methods

The inclusion criteria were: 1) primary knee osteoarthritis, 2) unilateral TKA, 3) ASA I and II. The criteria for exclusion were: 1) ASA III and IV, 2) Pregnancy, 3) Addiction, 4) Autoimmune or inflammatory diseases, 5) Age < 50 years, 6) Severe anemia, 7) Malignant tumors, 8) History of pulmonary thromboemboli, 9) uncontrolled diseases, 10) primary neuropathy, 11) patients who did not cooperate.

The participants of our study were recruited from January 2016 to January 2017, who were randomly classified into two groups. All the patients received 500 mg TA before tourniquet turned on. First group (A) received 500 mg TA 10 minutes before tourniquet was loosened and second group (B) received 500 mg TA IV infusion during 6 hours from the time of tourniquet loosening (total dose of TA 1 g in both groups). Intraoperative blood loss, postoperative drainage (in 6 and 12 hours), blood transfusion (in 48 hours), hematocrit and hemoglobin decrease (6 and 12 hours later) were compared between two groups.

Surgical Procedure

TKA was performed under spinal anesthesia, surgical method was the same in all as a standard midline skin incision, and a medial arthrotomy were obtained. TKA was done same in all cases in both groups. Before the performing the procedure, a

tourniquet was used. Each group received TA the way which was mentioned before and then the drainage was placed, incision was sutured and bandaged the tourniquet was loosened.

Post-operative Follow Up

After the operation, the drainage was clamped for 4 hours. Blood transfusion was based on clinical symptoms and laboratory test results. If the Hb was less than 8 g/dl, blood transfusion was concerned. Hb level and the amount of blood drainage were recorded 6 and 12 hours after the procedure. Transfused packed cell was documented in 48 hours after the TKA operation.

Clinical Data Collection

The following data were recorded: 1) Age, 2) Sex, 3) Comorbidity diseases, 4) Intraoperative blood loss (measured by a same anesthesiologist by the net increase in gauze and the liquid of the drainage bottle minus the intraoperative flushing fluid.), 5) Hb, Hct, and Platelets before the surgery, followed by 6 and 12 hours after the surgery, 6) As mentioned previously, the amount of drainage blood 6 and 12 hours after the surgery, 7) Blood transfusion in 48 hours after the surgery. All the data and clinical evaluation were conducted by blinded independent clinicians.

Statistical analysis

SPSS version 21 software was used in order to analyze the data. Patients group were compared using student's T-test but in cases when data was not distributed normally Mann-Whitney U-test was used. When differences were statistically significant, Chi-square test or Fischer's exact test were used in order to compare findings. $P < 0.05$ was considered significant.

Results

There were 40 patients with mean age of 63.55 ± 6.9 years (50% males and 50% females) and each group consists of 20 individuals. There were no significant differences between two groups considering age, gender, body mass index, operation time, Hb and Hct values and comorbidities before surgery.

Table 1: Preoperative basic clinical data of patients in the two groups ($x \pm s$).

Basic Data	Infusion Group	Bolus Group	T value	P value
Age	63.5 \pm 7.7	64 \pm 6.1	0.3442	>0.05
Body mass index (BMI)	27.3 \pm 1.9	26.9 \pm 2.5	0.2653	>0.05
Gender (male/female)	11/9	9/11	0.3622	>0.05
Preoperative hemoglobin (g/dl)	15.25 \pm 1.35	14.31 \pm 1.61	1.9821	>0.05

Table 2: Comparison of observed postoperative indices between two groups.

Observed indices	Infusion Group	Bolus Group	T value	P value
Intraoperative blood loss (cc)	245 \pm 87	322 \pm 81	2.897	0.006
Hb decrease in 6 hrs (g/dl)	0.81 \pm 0.35	1.35 \pm 0.77	2.932	0.007
Hb decrease in 12 hrs (g/dl)	1.031 \pm 0.326	1.81 \pm 0.87	3.734	0.001
Blood drainage in 6 hrs (cc)	157 \pm 46	400 \pm 70	9.828	0.000
Blood drainage in 12 hrs (cc)	132.5 \pm 37	290 \pm 86	6.791	0.000
Blood transfusion rate (cc)	0%	25 % (5/20)	5.714	0.017

The total bleeding (intraoperative blood loss plus the amount of blood drainage in 6 and 12 hours after surgery) ($P=0.000$), the total postoperative drainage ($P=0.000$), and drainage in 6 and 12 hours after surgery ($P=0.000$ for both), intraoperative blood loss ($P=0.008$) and Hb decrease in 6 and 12 hours ($P=0.007$ and $P=0.001$ respectively) significantly differed between the two groups. Blood transfusion (12.5%) was only needed in 5 cases which were in TA bolus group ($P=0.047$). No deaths or allergic reaction were reported in both groups.

Discussion

TKA causes major perioperative blood loss due to enhanced fibrinolytic activity (2). TA can be used intravenous, intramuscular, local joint cavity injection

and as oral route. The results of our study indicated that antifibrinolytic therapy with TA infusion significantly reduced total blood loss compared to bolus administration of TA, which in turn reduced the amount of blood transfusion required.

There were several systemic reviews and meta-analysis that evaluated the role of TA in total hemorrhage following TKA. All of these studies showed that it was significant decrease in the amount of total blood loss in different routes of administering TA. Peng et al. showed that single intravenous dose of TA before tourniquet loosening can significantly reduce post-operative hemorrhage and blood transfusion (11). Lee et al. reported similar results in which TA causes significant decrease in perioperative blood loss without exacerbating complications (5).

Other similar studies also demonstrated that blood loss can be reduced by 20-31%, administering TA in TKA (12).

Maniar et al compared the effect of pre-, intra- and postoperative administration of TA on blood loss which showed that preoperative use of TA is superior to others (13). In another study MacGilirray et al. compared the efficacy of different doses of TA on blood loss in TKA procedures, which showed significant difference between placebo group and TA group (14). Some studies have reported shorter time to peak value in intravenous rather than intramuscular injection or oral route administration. In another study Mutsuzaki et al (15) showed that TA injection via the drainage duct after TKA and also keeping the drainage closed for one hour can reduce 643 ml of blood loss so decreases 21% of allogenic blood transfusion rate.

TA caused no complication in our study; its administration did not increase the risk of thrombosis and reduced local skin ecchymosis after TKA. A meta-analysis by Alshryda et al. reported topical TA is an effective and safe way in order to reduce the need for blood transfusion. There was no higher rate of thromboembolic events in TA group compared to control group (16). In another similar study there were no more risks of complications in patients received TA after TKA (12). Xiao et al. mentioned that as high doses of TA may increase the risk of thrombosis, it is not recommended in patients with a history of PE (17).

Conclusion

Our study demonstrated that infusion administration of tranexamic acid in primary total knee arthroplasty was more effective to reduce perioperative blood loss and the demand for blood transfusion in 48 hours.

Acknowledgment

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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