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Original Article

Reducing Blood Loss by Intravenous Tranexamic Acid in Minimally Invasive Total Knee Arthroplasty for Geriatric Patients

Chun-Liang Liu [a], Man-Kuan Au [b], Che-Sheng Wen [b *]

[a] *Department of Orthopaedic Surgery, China Medical University Hsinchu Hospital, Hsinchu, Taiwan,* [b] *Department of Orthopaedic Surgery, Cheng Hsin General Hospital, Taipei, Taiwan*

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SUMMARY

Background: Reducing blood loss is an important issue in total knee arthroplasty (TKA), especially for geriatric patients, who are often less tolerable to anemia. Tranexamic acid (TXA) is a widely studied agent to reduce blood loss in TKA. The safety and efficacy has been proved. Minimally invasive total knee arthroplasty (MIS-TKA), as a subgroup of the TKA, was believed to have the same benefit from the TXA, although direct investigation was not much. In this study, we aimed to confirm the efficacy and safety of TXA in the MIS-TKA.
Methods: We reviewed a series of 64 primary MIS-TKA procedures performed by a single surgeon from March 2013 to June 2013. The patients was divided into two groups according to the usage of TXA during operation or not. The hemoglobin, blood loss amount from drainage, amount of blood transfusion needed, hospital stay and complications were recorded and compared.
Results: The total blood loss amount from drains in postoperative two days was significantly lower in TXA group then control group ($p < 0.001$). The postoperative decrease in hemoglobin and transfusion rates were also significantly less in TXA group then control group ($p = 0.001$, 0.03 respectively). There was no symptomatic venous thromboembolism event or other major adverse event in either group.
Conclusion: Intravenous TXA significantly reduced blood loss and transfusion rate without increasing the risk of complications in MIS-TKA. The efficacy and safety of TXA in MIS-TKA appears to be as good as in conventional TKA and make it safer for geriatric patients undergoing MIS-TKA.

1. Introduction

Blood loss is a major concern in total knee arthroplasty (TKA), and it is associated with a higher rate of complications. Most patients requiring TKA aregeriatric patients and anemia was a common diagnosis in this group. The prevalence of anemia depends on age and associated co-morbidities or chronic inflammatory conditions.[1,2] Besides, postoperative anemia is less tolerable in elderly. Thus, appropriate management of blood loss is even more important in TKA for geriatric patients. Various methods have been proposed to reduce blood loss in the perioperative period.[3,4] Tranexamic acid (TXA) is an antifibrinolytic agent commonly used to reduce blood loss after TKA. The effectiveness and safety of TXA have been studied.[5–19] Since most patients who need knee arthroplasty are elderly with osteoarthritis, most patients involved in the study are geriatric patients and the safety was confirmed by the previous studies. However, few studies have investigated the application of TXA in minimally invasive total knee arthroplasty (MIS-TKA),[18,19] Since some studies have reported that MIS-TKA itself can also reduce blood loss,[20–24] we are not sure if TXA still works significantly in MIS-TKA. We used TXA in MIS-TKA procedures as empiric usage since middle of April 2013, though we were not sure about the significance at that time. The aim of this study was to confirm that TXA in MIS-TKA still significantly reduces blood loss and is as safe as it is in conventional TKA.

2. Methods

We reviewed a series of 64 primary MIS-TKA procedures performed by a single surgeon from March 2013 to June 2013 because we began to use TXA in all MIS-TKA as empiric routine since middle of April 2013. Patients who have history of thromboembolism did not received TXA during surgery, since it was considered as contraindication of tranexamic acid. Two patients with atrial fibrillation who needed anticoagulants and one patient who had a history of deep vein thrombosis did not received TXA during the MIS-TKA for safety concern and were excluded from the study. In addition, four patients with a pre-operative hemoglobin level of less than 10 g/dL, and one patient with severe varus deformity and bone loss in both knees who needed bone grafting during surgery were also excluded due to prolonged operation time and more blood loss. Five patients with coronary artery disease who were receiving antiplatelet therapy were included, however the antiplatelet medications were stopped seven days before surgery and resumed two days after surgery.

The remaining 55 knees were then divided into two groups

* Corresponding author. Department of Orthopaedic Surgery, Cheng Hsin General Hospital, No.45, Zhenxing St., Beitou Dist., Taipei City, Taiwan (R.O.C.)
E-mail addresses: a102090@cmu.edu.tw (C.-S. Wen)

(Fig. 1). The patients in the control group (29 knees) did not receive any pharmacological agents except for routine hemostasis with electrocoagulation during surgery, and those in the TXA group (26 knees) received one gram of intravenous TXA (Transamin 1 g/10 mL; Daiichi-Sankyo Propharma Co., LTD., Osaka, Japan) 15 minutes before incision and another one gram when the tourniquet was deflated.

All of the procedures were performed by the same surgeon with the mini-midvastus approach and the minimally invasive techniques modified from Haas et al.[22] The skin incision was around 9 cm in length. The arthrotomy was made by splitting the vastus medialis obliquus muscle 2 cm in line with its fibers from the superomedial pole of the patella and extended down medially by the patella to 2 cm below the tibial joint line. We made patella cut first to make more operating space. Then, the patella was subluxed, but not everted throughout the procedure. We also made distal femur and proximal tibia cuts with knee in semi-extended position to decrease soft tissue tension during cutting, while more attention should be paid to avoid posterior neurovascular bundle injury. The whole procedure was done with the principle of minimizing soft tissue trauma and tension (Fig. 2). All of the operations were for unilateral knee replacement under spinal anesthesia. A tourniquet with the pressure of 280 mmHg was applied throughout the procedures (before the skin incision to completion of skin closure). The prostheses were the same (NexGen LPS Flex Mobile, Zimmer, USA) and were cemented at all components. A intraarticular drain (Hemovac, Zimmer, USA) was used in every patient, and the evacuator was fully compressed to maintain negative pressure. The drain was not clamped until it was removed. The drain was left in place until the daily drainage amount was less than 100 mL, and every patient had the drain for a least 48 hours.

All of the patients underwent a rehabilitation program from postoperative day 1, and tried standing and then walking with the support of a walker from postoperative day 2. An intermittent pneumatic compression device (IPCD) was used in all of the patients immediately after the operation to prevent thromboembolism, however no anticoagulants were used. Blood transfusions of packed red blood cells were given to the patients if their hemoglobin level fell to less than 9 g/dL, and to those with symptoms of anemia. The patients were discharged when the range of motion of the operated knee was more than 90° and the wound was clear without discharge.

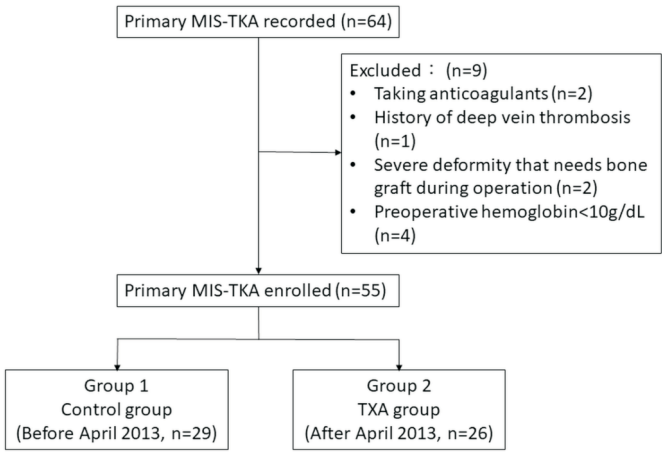

Fig. 1. Patient selection flow diagram. The patients of both groups are mainly divided by time, because we began to use TXA in all MIS-TKA as empiric routine since April 2013. MIS-TKA: minimally invasive total knee arthroplasty, TXA: tranexamic acid.

We recorded the age, gender, body mass index (BMI), preoperative hemoglobin and coagulating function of all patients. The wound length, surgical time, blood loss amount from drainage, hemoglobin level on postoperative day one, rate and amount of blood transfusion, hospital stay, and complications were also recorded and analyzed. Continuous variables were compared using the Student's t test, and categorical variables were compared using the chi-squared test. All the materials and methods of this study had received approval from ethical committee of Cheng-Hsin General Hospital.

3. Results

The demographics of the patients in both groups showed no significant differences in age, gender or body mass index. The preoperative hemoglobin level and coagulation function were also similar (Table 1).

The blood loss collected from the drains on the first postoperative day was 434.3 ± 232.9 mL in the control group and 219.2 ± 149.1 mL in the TXA group. The drainage amount on the second day was 135.3 ± 65.9 mL in the control group and 152.0 ± 88.9 mL in the TXA group. The total amount of drainage (postoperative day 1 + postoperative day 2) was 569.7 ± 266.7 mL in the control group and 371.2 ± 203.1 mL in the TXA group. Blood loss on postoperative day 1 and the sum of postoperative day 1 and 2 was significantly lower in the TXA group (both $p < 0.001$), however there was no significant difference in blood loss on postoperative day 2 between the two

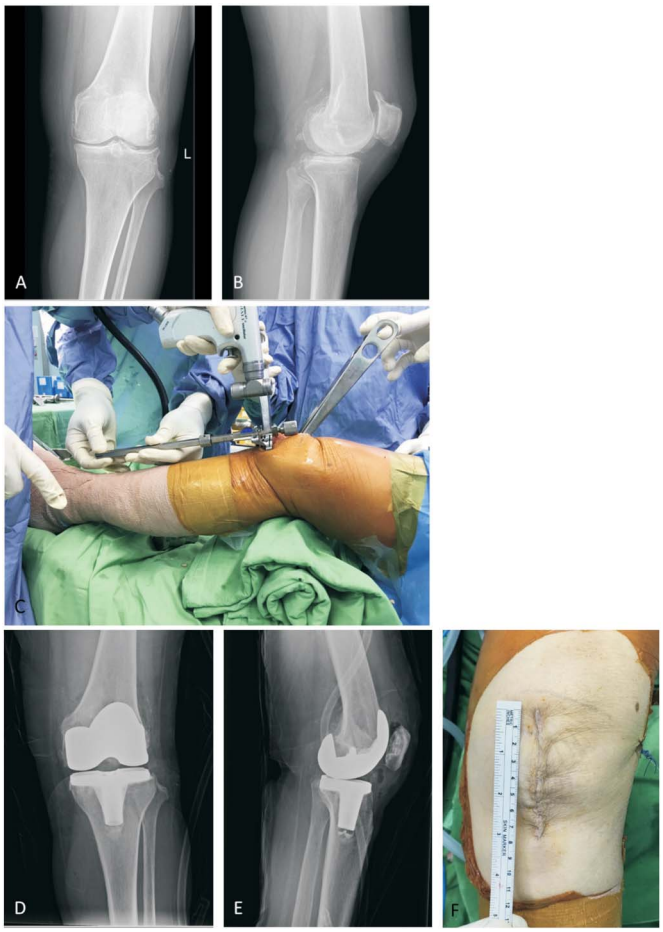

Fig. 2. Case demonstration. A and B, pre-operative AP and lateral knee radiographs. C, cutting tibia with knee in semi-extended position. D and E, post-operative radiographs. F, wound size was 8 cm (3.1 inches) in this case.

Table 1
Patient demographics.

	Control group (n = 29)	TXA group (n = 26)	p value
Age (years)[a]	73.2 ± 8.5 (53–91)	74.3 ± 7.9 (60–87)	0.622
Sex (female n. and %)	25, 86.2%	19, 73.1%	0.224
BMI (kg/m²)[a]	26.8 ± 3.6 (21.6–32.9)	28.5 ± 6.0 (22.7–47.3)	0.203
PT (s)[a]	10.1 ± 0.5 (9.3–11.4)	10.3 ± 0.6(9.2–11.7)	0.175
aPTT (s)[a]	27.1 ± 1.3 (23.6–29.8)	27.9 ± 2.2 (24.0–32.4)	0.124
Hemoglobin (g/dL)[a]	12.3 ± 1.4 (10.1–14.8)	12.9 ± 1.6 (10.0–15.7)	0.149
Platelet ($10^3/\mu L$)[a]	215.9 ± 76.1 (111–435)	209.6 ± 44.7 (101–274)	0.715

a: Values are presented as mean ± standard deviation (range).
BMI: body mass index; TXA: tranexamic acid; PT: prothrombin time; aPTT: activated partial thromboplastin time.

groups (p = 0.430). The postoperative decrease in hemoglobin was 2.3 ± 0.9 g/dL in the control group and 1.5 ± 0.8 g/dL in the TXA group. The decrease in hemoglobin was also significantly lower in the TXA group (p = 0.001).

The transfusion rate was 31.0% in the control group and 7.7% in the TXA group, with 0.8 ± 1.0 units of transfusion in the control group and 0.2 ± 0.7 in the TXA group. Both the rate and units needed for transfusion were significantly lower in the TXA group (p = 0.030 and 0.025, respectively).

There were no significant differences in the surgical time, blood loss during surgery, wound length and hospital stay between the two groups (Table 2). In addition, no symptomatic venous thromboembolism events, poor wound healing, deep infection or other major adverse events were noted in either group.

The reduction in blood loss with TXA therapy was most effective at postoperative day 1 and less significant at postoperative day 2, however the total amount of drainage (postoperative day 1 plus day 2) was still significantly lower when using TXA. In addition, TXA significantly reduced blood loss and transfusion rate without increasing the risk of complications in MIS-TKA. The effectiveness and safety of TXA in MIS-TKA appears to be as good as in conventional TKA.

4. Discussion

TKA in a common operation in geriatric patients. Due to age or other co-morbidities, geriatric patients has more frequent diagnosis of preoperative anemia and less tolerance of postoperative anemia. Thus, appropriate blood conservation during this operation is an important issue in this group. TXA can decrease postoperative bleeding by acting on the fibrinolytic system. However, there are concerns about the safety of the systemic administration of TXA and the risk of thromboembolic events. Many studies have investigated the use of TXA in conventional total knee arthroplasty and total hip arthroplasty, and it has been shown to be effective in reducing blood loss without increasing adverse events such as thromboembolic complications.[9,13] However, most studies excluded the high risk groups. The common contraindication of TXA includes known allergy to TXA, severe cardiopulmonary disease, and hematological or thromboembolism disease.[25] No study has investigated its use in TKA for patients who are at high risk of thromboembolism. In addition, only two reports have discussed the blood conservation effect in MIS-TKA.[18,19] Both of these studies reported a good blood saving effect with the use of TXA in MIS-TKA, and both used low-molecular-weight heparin (LMWH) to prevent thromboembolism after surgery. To exclude the LMWH effect on blood loss after surgery, we use IPCD but no LMWH for the prevention of thromboembolism in this study.

Many different protocols have been proposed for the use of TXA, however there is currently no consensus as to the most appropriate and safest dose or route of TXA administration.[10,13,25] We used one gram (within the general dose of 10–20 mg/kg) of intravenous TXA preoperatively and one gram when the tourniquet was released, and this appeared to be safe and practical. The results showed a significant decrease in blood loss on the first day, total blood loss, and the rate and amount of transfusion, and there was no increase in the rate of complications including thromboembolism. Thus, it seemed to be as safe and effective as in conventional TKA.

Since most patients undergoing TKA are geriatric patients and are less able to tolerate inadequate oxygen supply, well blood management is crucial. Historical averages for the decrease in hemoglobin after conventional unilateral TKA are approximately 3 to 4 g/dL,[26] because of a combined effect of blood loss and hemodilution. Mainstay treatment of postoperative anemia is blood transfusion. However, allogeneic transfusions carry certain risks, such as disease transmission and reactions, clerical error and infection.[27,28] To decrease the risk of blood transfusion, tools and techniques to limit blood loss during operation are important. In our study, the mean decrease of hemoglobin in MIS-TKA was minimized

Table 2
Postoperative data.

	Control group (n = 29)	TXA group (n = 26)	p value
Wound length (cm)[a]	9.2 ± 1.3 (6–11)	9.5 ± 1.5 (6–12)	0.561
Operative times (minutes)[a]	99.1 ± 15.5 (70–140)	100.6 ± 11.3 (80–120)	0.699
Hospital stay (days)[a]	8.0 ± 1.3 (6–11)	7.6 ± 2.0 (5–12)	0.443
Drainage from H/V (mL)[a]			
Day 1	434.3 ± 232.9 (65–840)	219.2 ± 149.1 (25–540)	< 0.001*
Day 2	135.3 ± 65.9 (10–280)	152.0 ± 88.9 (10–380)	0.430
Day 1 + Day 2	569.7 ± 266.7 (170–1000)	371.2 ± 203.1 (95–740)	< 0.001*
Hemoglobin on post-OP day 1 (g/dL)[a]	10.1 ± 1.3 (8.1–12.8)	11.5 ± 1.6 (9.0–14.6)	0.001*
Decreased hemoglobin on day 1 (g/dL)[a]	2.3 ± 0.9 (0.9–4.7)	1.5 ± 0.8 (0.4–3.6)	0.001*
Blood transfusion (n, %)	9, 31%	2, 7.7%	0.030*
Mean transfusion units[a]	0.8 ± 1.0 (0–2)	0.2 ± 0.7 (0–2)	0.025*

a: Values are presented as mean ± standard deviation (range), *: p < 0.05.
TXA: tranexamic acid, H/V: Hemovac, post-OP: postoperative.

to 2.3 g/dL without TXA and even lower to 1.5 g/dL when TXA was used.

Though there are some concerns about the thromboembolic complications caused by TXA, several studies and meta-analysis have shown its safety when certain high risk patients – such as those with recent stents or history of thromboembolism disease – were avoided.[9,13] TXA is an efficacious, cost-effective and safe for most geriatric patients undergoing MIS-TKA if there is no contra-indication.

The limitations of this study include the retrospective study design and small sample size. However, all patients in this study underwent the MIS-TKA procedure by the same surgeon, which decreased the variation of surgical techniques by different surgeons. Besides, the results of the analysis showed significant differences with an alpha value set at 0.05. The sample size may be too small to show all possible complications in both groups. In addition, we excluded patients at high risk of thromboembolism and those taking anticoagulants. Furthermore, we only checked the hemoglobin level on the first postoperative day, which may not show the trend and difference in hemoglobin in both groups, and it may have decreased even more on the following days. However, we still found a significant difference in the hemoglobin level on postoperative day 1.

Since only few studies have investigated the application of TXA in MIS-TKA, and as the optimal dose and route are still unclear, further prospective, randomized, double-blinded studies with a larger sample size are needed to confirm our findings.

Conflict of interest

There is no potential financial or non-financial conflict of interest to all authors of this article.

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