A Comparison Study between 1 gram and 2 grams of Tranexamic Acid for Reducing Blood Loss and Transfusion Requirements in Total Knee Arthroplasty

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Objective: *To compare the effectiveness between 1 g and 2 g of tranexamic acid on blood loss and packed red cell transfusion requirements in total knee arthroplasty (TKA) in Thai patients.*
Methods: *This study evaluates the use of TXA in 50 TKA performed in a single surgeon at Priest Hospital between 2014 and 2020. The initial 25 patients underwent surgery with TXA 1 g (TXA1 group) while the subsequent 25 patients all received 2 g TXA (TXA2 group). Perioperative blood loss, postoperative blood loss, total blood loss, postoperative 24hr Hct, total PRC transfusion, and deep vein thrombosis (DVT) were examined.*
Results: *Total blood loss and postoperative blood loss were significantly higher in the TXA1 group than the TXA2 group (473.2 cc vs 290.6 cc; p-value < 0.001 and 399.6 cc vs 228.2 cc ; p-value < 0.001 respectively). Postoperative 24hr Hct were lower in the TXA1 group than the TXA2 group significantly (33.6±3.0 vs 37.0±4.4; p-value 0.002). However, the transfusion requirements were the same. None of the patients developed DVT.*
Conclusion: *TXA 2 g can reduce total blood loss more than TXA 1 g significantly without increasing the risk of postoperative DVT.*

Keywords: *Tranexamic acid, Total Knee Arthroplasty*

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Introduction

Total Knee Arthroplasty (TKA) is a major operation that can cause a lot of hemorrhages both during and after the operation. Post-operative anemia results in a prolonged hospital stay and delayed rehabilitation[1]. Moreover, some patients need an allogenic blood transfusion, which may increase not only the risk of transfusion-transmitted diseases but also the risk of postoperative infections[2]. The mortality rate for mismatched transfusion is about 10% due to shock, renal failure, and bleeding[3].

Currently, there are many methods for reducing allogeneic blood transfusions, such as preoperative autologous blood transfusions, red blood cell salvages, and hypotensive anesthesia[4]. The use of antifibrinolytic drugs, such as tranexamic acid (TXA), are the other options for decreasing blood loss and blood transfusion in orthopedic surgery[5, 6] without increasing the risk of deep vein thrombosis (DVT), pulmonary embolism, and infection[7].

A previous study found that 1 g TXA, by comparison with no TXA, can reduce postoperative blood loss, total blood loss, and total PRC transfusion significantly[8]. This study aimed to evaluate the effect on a treatment of a higher dose of TXA (2 g) compared with the previously used lower dose (1 g).

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Material and Methods

This retrospective cohort study was approved by the research ethics committee. From 2014 – 2020, patients who underwent primary TKA for osteoarthritis by a single surgeon at Priest Hospital were included. Exclusion criteria were allergy to TXA, history of severe ischemic heart disease, pulmonary embolism, deep vein thrombosis, coagulopathy, hepatic or renal failure.

Fifty patients were divided into two groups: the TXA1 group, which represented 25 patients who received 1 g of TXA, and the TXA2 group, which represented 25 patients who received 2 g of TXA. Both groups were received TXA 15 minutes before incision and LMWH (Enoxaparin) for the prevention of DVT after removing the radivac drain postoperatively. The data to be collected are as follows:

1. Perioperative blood loss was estimated and recorded by the anesthesiologist.
2. Postoperative blood loss was recorded from blood in the radivac drain.
3. Total blood loss was the total amount of perioperative and postoperative blood loss.
4. Postoperative 24hr Hct was the least Hct within 24 hours after surgery.
5. Total PRC transfusion was the unit of PRC that was transfused after surgery.

6. Venous thromboembolic complications, such as deep vein thrombosis and pulmonary embolism, were assessed clinically after surgery.

The sample size was determined using the same data as the previous study[8], a minimum of 19 patients in each group were needed. Differences between groups were compared using the Chi-squared test and independent t-test. A STATA version 22.0 was used for all statistical analyses. A *p*-value less than 0.05 was considered significant.

Results

Comparison of demographic data between both groups were no statistically significant differences, except preoperative Hct. TXA2 has a significantly preoperative HCT higher than TXA1 (41.3 ± 3.9 vs 39.2 ± 2.6 ; $p = 0.028$). Perioperative blood loss of the TXA1 group was more than the TXA2 group (73.6 cc vs 61.2 cc), but the difference was not statistically significant ($p = 0.422$). Postoperative and total blood loss in the TXA2 group compare with the TXA1 group (399.6 cc vs 228.2 cc and 473.2 cc vs 290.6 cc respectively) was reduced significantly ($p < 0.001$). Postoperative 24hr Hct of the TXA1 group was significantly lower than the TXA2 group (33.6 ± 3.0 vs 37.0 ± 4.4 ; $p = 0.002$). Two units of PRC transfusion were needed in both groups, so the difference was not significant. The demographic data and pre-and post-operative parameters of both groups were shown in table 1 and table 2 respectively.

Table 1 Demographic data.

TKA	TXA1 (n=25)	TXA2 (n=25)	*P*-value
Age (years)	68.5±7.2	67.6±6.1	0.614
Gender (M:F)	25:0	25:0	1.000
Preoperative Hct (%)	39.2±2.6	41.3±3.9	0.028
BMI (kg/m²)	24.5±3.1	26.1±2.8	0.064

Table 2 Pre-and post-operative parameters of both groups.

TKA	TXA1 (n=25)	TXA2 (n=25)	*P*-value
Tourniquet Time (min)	110.5±21.2	112.2±18.5	0.767
Perioperative blood loss (cc)	73.6 (0-200)	61.2 (10-200)	0.422
Postoperative blood loss (cc)	399.6 (150-850)	228.2 (20-400)	< 0.001
Total blood loss (cc)	473.2 (200-950)	290.6 (30-500)	< 0.001
Postoperative 24hr Hct (%)	33.6±3.0	37.0±4.4	0.002
Total PRC transfused (units)	2	2	1.000
No. of patients with DVT	0	0	-

Discussion

The risk factors of blood loss in TKA are gender and tourniquet time[9]. The male gender tends to lose more blood than the female, especially in postoperative blood loss. And the more tourniquet time, the greater total blood loss. Massive blood loss from total knee arthroplasty can relate to other complications, especially cardiovascular complications. The treatment with allogeneic blood transfusions are high cost[10] and may result in complications, such as HIV or hepatitis viral infection[2]. Moreover, the risk of postoperative infection, such as urinary tract infection, in patients treated with blood transfusion is higher than the patients without blood transfusion[11]. Some methods substitute the use of allogeneic blood transfusions, but with some disadvantages. For example, an autologous blood transfusion may be safe, but it can cause wasting of blood and unnecessary expenses[12]. Red blood cell salvage can cause clotting problems due to dilutional coagulopathy because only normal saline is mixed with RBCs[13]. And hypotensive anesthesia is potentially unsafe in some patients, because of the risk of reduced perfusion to important organs and tissues, especially in the brain, heart, and kidneys[14].

Tranexamic acid (TXA) is an antifibrinolytic agent that inhibits fibrinolysis by blocking the lysine-binding sites of plasminogen[15]. Binding of TXA to plasminogen inhibits the conversion of plasminogen into active plasmin, which prevents the lysis of blood clots. TXA had little effect when administered at the end of surgery and 3 hours later[16] because once plasminogen is bound to the fibrin surface, TXA is no longer effective[17]. TXA is widely and safely used medication in massive blood loss conditions, such as acute upper gastrointestinal bleeding, or due to surgery, such as cardiothoracic surgery, gynecological surgery, etc[18, 19]. The CRASH-2 trial found that the uses of TXA in traumatic patients are safe and decreasing mortality rates[20]. TXA can be

administered locally or intravenously with the same good effectiveness[21-24]. In total knee and total hip arthroplasty, there are many study[2,4,7,25-29], including my previous study[8], report that the TXA can reduce blood loss from surgery and decrease the volume of blood transfusions significantly.

In this study, we compare the effect of TXA, a higher dose (TXA2) with a lower dose (TXA1). The gender and tourniquet time that affecting blood loss of both groups are not significantly different. Even though preoperative Hct of TXA2 group is higher than TXA1 group statistically significant, it is not clinically significant (41.3% VS 39.2%). Perioperative blood loss was not differenced significantly, but the postoperative and total blood loss was reduced significantly in the group of a higher dose (TXA2). These results are similar to the previous study that the TXA effect only after surgery not during surgery. Although postoperative 24hr Hct is better significantly in the higher dose group (TXA2), the need for blood transfusion in both groups is not different. There are no thromboembolic complications in both groups.

The limitations of the study are selection bias from a retrospective cohort study design and small sample size. Furthermore, the results of postoperative 24hr Hct may be biased by the significant difference of Hct in both groups preoperatively.

Conclusion

TXA 2 g can reduce total blood loss more than TXA 1 g significantly without increasing the risk of postoperative DVT. Therefore, for more effectiveness, we can use TXA 2 g in TKA operation safely.

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เปรียบเทียบการใช้ยา Tranexamic Acid ขนาด 1 กรัม และ 2 กรัม ในการลดการสูญเสียโลหิตจากการผ่าตัดเปลี่ยนข้อเข่าเทียม

ประมุข วนัสบดีกุล, พบ

วัตถุประสงค์: *เพื่อเปรียบเทียบผลของยา Tranexamic acid (TXA) ขนาด 1 กรัม กับ 2 กรัม ในการลดการสูญเสียโลหิตและลดการเปลี่ยนถ่ายโลหิต ทั้งระหว่างและภายหลังการผ่าตัดเปลี่ยนข้อเข่าเทียม (TKA)*

วิธีการศึกษา: *ศึกษาพระภิกษุไทยที่เข้ารับการผ่าตัด TKA ที่โรงพยาบาลสงฆ์ ตั้งแต่ปี พ.ศ.2557 - 2563 จำนวน 50 ราย แบ่งเป็น TXA 1 กรัม (TXA1) 25 ราย และ 2 กรัม (TXA2) 25 ราย เปรียบเทียบปริมาณโลหิตที่สูญเสียจากการผ่าตัด, ปริมาณความเข้มข้นเลือดที่น้อยที่สุดภายใน 24 ชั่วโมงหลังผ่าตัด, ปริมาณโลหิตที่ใช้ในการเปลี่ยนถ่ายโลหิต, และการเกิดลิ่มเลือดอุดตันในหลอดเลือดดำ (DVT)*

ผลการศึกษา: *ปริมาณการสูญเสียโลหิตโดยรวมในกลุ่ม TXA1 สูงกว่ากลุ่ม TXA2 อย่างมีนัยสำคัญ (p-value < 0.001) โดยเฉพาะการสูญเสียโลหิตภายหลังการผ่าตัด (p-value < 0.001) ปริมาณความเข้มข้นเลือดหลังผ่าตัดในกลุ่ม TXA1 น้อยกว่ากลุ่ม TXA2 อย่างมีนัยสำคัญ (p-value 0.002), อย่างไรก็ตามปริมาณโลหิตที่ใช้ในการเปลี่ยนถ่ายโลหิตกลุ่ม TXA1 ไม่แตกต่างจากกลุ่ม TXA2 และทั้งสองกลุ่มไม่พบการเกิด DVT*

สรุป: *TXA ขนาด 2 กรัม สามารถลดปริมาณโลหิตที่สูญเสียจากการผ่าตัดเปลี่ยนข้อเข่าได้อย่างมีนัยสำคัญเมื่อเทียบกับขนาด 1 กรัม โดยไม่เพิ่มความเสี่ยงในการเกิด DVT*