Original Article *นิพนธ์ต้นฉบับ*

Effect of Tranexamic acid (TEA) on Blood Loss in Total Knee Arthroplasty (TKA)

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Abstract Surgical trauma and pneumatic tourniquet in orthopedic procedures are reported to enhance local fibrinolysis. However, the use of short-term antifibrinolytic therapy may reduce post-operative blood loss. The purpose of this control study was to investigate the effect of tranexamic acid (TEA) on blood loss in total knee arthroplasty (TKA). This prospective control study included, patients with primary osteoarthritis that had cemented total knee arthroplasty performed between February 1, 2009 and February 28, 2010. They received either tranexamic acid 10 mg/kg (n=21) intravenous injection just before deflation of the tourniquet (single low dose) or did not receive tranexamic acid (n=33). Postoperative drainage system was measured. Both groups had similar characteristics. Mean total blood loss was 482 ml in the tranexamic acid group and 745 ml in the control group ($p > 0.1$). In conclusion, short-term tranexamic acid therapy (single low dose) was not significantly reducing total blood loss in total knee arthroplasty.

Key words: **tranexamic acid, post operative blood loss, total knee arthroplasty**

Introduction

Nowadays, orthopedic practices to treat degenerative diseases increased due to human longevity. In generally, most of degenerative diseases can affect quality of life and osteoarthritis of the knee (OA knee) is one of them. Total knee arthroplasty (TKA) is a good choice for the treatment of advance osteoarthritis of the knee. However, blood loss and blood transfusion after TKA are one of the most common post-operative complications and can result in increasing incident of postoperative hypotension, immunological reaction and transmission of disease[1,2].

There are many factors influencing post-operative blood loss. The major cause was fibrinolysis which can be attributed to surgical trauma[3,4] and the pneumatic tourniquet[5-8]. Some studies have reported that 65 percent of drainage volume occurs in the first 8 hours post-operatively[9,10]. Recently, several studies have shown that intravenous administration of the antifibrinolytic agent, tranexamic acid (TEA) reduced

postoperative bleeding and the need for a blood transfusion[11-13,25]. Tranexamic acid (TEA) is a competitive inhibitor of plasminogen and at much higher concentrations, a noncompetitive inhibitor of plasmin[14-16]. However, the dosage and the route of administration are not standardized. From the previous literature, the dosage used might range from 10 to 20 mg/kg and many different routes of administration included high dose before operation (single high dose)[17], high dose after release tourniquet (single high dose)[17], pre-operative low dose and before deflated tourniquet (double low dose)[17], low dose before deflated tourniquet and repeated at 3 hours later (double low dose)[18] and temporary clamping of drain combined with tranexamic acid[25]. Most of the studies presented the appropriate dose of tranexmic acid (TEA) to reduce post-operative blood loss in TKA patients was 20 mg/kg. however, one study found tranexamic acid (TEA) did not moderate fibrinolytic effect and reduced post-operative blood loos or transfusion[19]. If lower dosage of tranexamic acid (TEA) (10 mg/kg) can be used effectively, the cost of TKA becomes lower. Therefore, the purpose of this study was to explain efficacy of low dose intravenous tranexamic acid (TEA) on reducing post-operative bleeding in TKA by comparing the volume of post-operative blood in TKA patient who had received intravenous injection tranexamic acid (TEA) 10 mg/kg before deflated tourniquet (single low dose) and TKA patient who had not received tranexamic acid (TEA).

Methods

Study design

Prospective control study

Materials and methods

The protocol of this research was reviewed and approved by ethics committee of Rajavithi Hospital. The inclusion criteria were the patient with primary osteoarthritis of the knee, stopped non-steroidal anti-inflammatory drugs (NSAIDs) one week before surgery, classified with American Society of Anesthesiologists (ASA) Physical Status between class I and III and underwent primary total knee arthroplasty during the period between 1st February 2009 and 28th February 2010. The secondary osteoarthritis of the knee including rheumatoid arthritis (RA) or tuberculosis (TB), the revision total knee arthroplasty, congenital or acquired coagulopathy and history of thromboembolism disease were excluded.

Surgical techniques: All surgery procedure were performed by the same surgeon, using the midvastus approach[20]. All patients had spinal anesthesia; a dose of 2gm cefazolin was given intravenously 1 hour before operation. A tourniquet was applied over the thigh after squeezed and inflated to 350mm Hg before skin incision, the tourniquet was not released before skin closure. All patients received a posterior stabilized cemented prosthesis without patellar resurfacing. The femoral canal for intramedullary guiding was routinely plugged with bone. The author used one intraarticular drain (10-gouge) connecting to vacuum bottle. All knees were placed in compressive bandages and splint without clamped drainage.

In both groups, a standard post-operative rehabilitation protocol, including continuous passive motion of the knee and muscle strengthening exercise at one day postoperatively were followed. All drains were removed within 48 hours and the total volumes in the bottle were measured.

Data collection: The author collected volume of blood loss in the control group (patients who did not receive tranexamic acid), which were performed TKA between 1st February 2009 and 30th September 2009. For the tranexamic acid (TEA) group, the volume of blood loss in patients who underwent TKA

between 1st September 2009 and 28st February 2010 and received intravenous tranexamic acid 10mg/kg between skin closures and before deflated tourniquet by anesthetist, were collected.

The sample sizes were calculated from the pilot study, the mean of blood loss in TEA group and control group were 558 ml. and 745 ml. respectively, and the standard deviation was 287. To obtain a statistical power of 0.8 and alpha error of 0.05, 29 patients were required in each group. Within the time limitation of this study, a total of 58 patients were enrolled, 33 were patients in control group and 25 were patients in TEA group. Four patients were excluded from this group, one RA, one TB, one revision TKA and one patient who had history of thromboembolic disease.

Statistical analysis: the analysis was carried out using Statistical Package for Social Science. Descriptive analysis was used for the age, sex, weight, height, and duration of the tourniquet time. Using unpaired t-test to compare the mean blood loss between TEA group and control group, p-value of less than 0.05 was taken as significant.

Results

Fifty-two patients who underwent unilateral cemented TKA at Rajavithi Hospital were identified. The demographics data (age, gender, weight, height, and tourniquet time) were similar in both groups. Besides, osteoarthritis was more common in females than males (Table 1).

For the post-operative blood loss, the mean blood loss in the TEA group was 482 ml. (range 200-860 ml.) and the mean blood loss in the control group was 745 ml. (range 340-1560 ml.), respectively. Although the mean blood loss was found to be lower for the TEA group, no statistically significant difference in blood loss between these two groups could be reported ($p > 0.1$).

No patients in either group suffered any clinically significant thromboembolic event during post-operative course.

Discussion

Tranexamic acid (4-(aminomethyl) cyclohexanecarboxylic acid) - TEA) is one of antifibrinolyic amino acids that as competitive inhibitor of plasminogen and play as weak noncompetitive inhibitor of plasmin[14-16]. After TEA diffuse into the blood circulation, it cannot bind with serum albumin, consequently, increased binding to plasminogen[21]. Moreover, the TEA can rapidly diffuse into the synovial membrane and collected in joint fluid[22]. However, the TEA has a biological half-life of 3 hours within joint fluid; thus, intravenous TEA is the most rapid route of administration and can reduce post-operative

Table 1 The demographics data and total blood loss of both groups.

	Control	TEA*	p - value
Number of patients	33	21	
Mean age (yrs)(range)	66 (58-75)	67 (59-74)	
Female : male	32 : 1	20 : 1	
Mean weight (kg)	65	67	
Mean height (cm)	156	158	
Mean tourniquet time (minutes)	112	117	
Blood loss (ml)	745 (340-1,560)	482(200-860)	p> 0.1

**TEA =Tranexamic Acid*

Table 2 The dosage of tranexamic acid (TEA) in difference weight

Body weight (kg.)	Dosage of tranexamic acid (TEA)
40-50	2 Vial (500 mg.)
51-60	21/2 Vial (625 mg.)
61-70	3 Vial (750 mg.)
>75	4 Vial (1000 mg.)

blood loss in TKA patients.

Several studies reported that the TEA was efficient in reducing blood loss in patients who had been performed total knee arthroplasty (TKA) in difference route and time of administration included high dose before operation (single high dose)[17], high dose after deflated tourniquet (single high dose)[17], pre-operative low dose and before deflated tourniquet (double low dose)[17], low dose before deflated tourniquet and repeated at 3 hours later (double low dose)[18].

Some studies showed that no significant difference in the risk of venous thromboembolism (DVT) and pulmonary embolism (PE)) in patients who underwent total knee arthroplasty (TKA), both with and without tranexamic acid (TEA) injection[17,18]. This is similar in this study, no thromboembolic events occurred.

In the present study, the use of intravenous tranexamic acid (TEA) 10 mg/kg (low dose) before deflating the tourniquet without clamped drainage could not reduce post-operative blood loss in patients who underwent total knee arthroplasty. According to previous report, the recommended dosage of tranexamic acid (TEA) to reduce post-operative blood loss should be 20 mg/kg[23,24].

There are many factors affecting to postoperative blood loss. Temporary clamping of drain combined with intravenous tranexamic acid 10 mg/kg perioperative and then 1,500 mg per day oral formed tranxamic acid was given 5 day after operation can reduce blood loss significantly[25]. Clamping drainage 4 hours after total knee arthroplasty significantly enhanced less postoperative blood loss and fewer blood transfusions[26]. Dosage and duration of admistration, long duration of operation may affect more bleeding in operative field and postoperative blood loss.

This study had some inherent limitation, including; first, the study population was small; second, the author observed only clinical thromboembolism complication without specific investigation. Third, There were no mechanical assist for bleeding control after operation (Clamping drainage). Forth, The dosage regimen in this study was just only single low dose of tranexamic acid because the author tried to control cost effectiveness and postoperative protocol of the study without drainage clamp that may not be enough for bleeding control after operation.

Conclusion

The short-term intravenous tranexamic acid therapy 10 mg/kg (single low dose) before deflated tourniquet did not significantly reduce total blood loss in total knee arthroplasty.

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บทคัดย่อ **ผลของยา Tranexamic Acid (TEA) ต่อภาวะการเสียเลือดหลังการผ่าตัดเปลี่ยนผิวข้อเข่าเทียม**

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วารสารวิชาการสาธารณสุข **2556; 22:383-388.**

ขบวนการเกิด fibrinolysis ในการทำหัตการทางออร์โธปิดิกส์นั้นสามารถเกิดขึ้นได้ทั้งจากในขั้นตอนของการผ่าตัดและจากการใช้ทูนิเกต์ อย่างไรก็ตามการใช้ยา antifibrinolytic ในระยะสั้น ๆ พบว่าสามารถช่วยลดการเสียเลือดภายหลังการผ่าตัดได้วัตถุประสงค์ของการศึกษา prospective control study ครั้งนี้เพื่อต้องการศึกษาผลของยาtranexamic acid (TEA) ต่อภาวะการเสียเลือดหลังการผ่าตัดเปลี่ยนผิวข้อเข่าเทียม ในผู้ป่วยข้อเข่าเสื่อมที่ได้รับการผ่าตัดเปลี่ยนผิวข้อเข่าเทียมชนิดมีสารยึด ตั้งแต่วันที่ 1 กุมภาพันธ์ 2552 ถึงวันที่ 28 กุมภาพันธ์ 2553 โดยการเปรียบเทียบปริมาณของเหลวและเลือดในท่อระบาย หลังการผ่าตัดในผู้ป่วยกลุ่มที่ได้รับการฉีดยา tranexamic acid ขนาด 10 mg/kg จำนวน 21 รายและกลุ่มที่ไม่ได้รับการฉีดยา tranexamic acid อีก 33 ราย ผลการศึกษาทั้งสองกลุ่มการศึกษามีข้อมูลพื้นฐานที่ไม่แตกต่างกันค่าเฉลี่ยของการเสียเลือดของกลุ่มที่ได้รับยาฉีดและไม่ได้รับยาฉีดคือ 482 มล. และ 745มล. ตามลำดับซึ่งพบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p > 0.1$)

สรุปผลการใช้ยาฉีด tranexamic acid ระยะสั้น (single low dose) ไม่สามารถลดการเสียเลือดหลังการผ่าตัดเปลี่ยนผิวข้อเข่าเทียมได้อย่างมีนัยสำคัญทางสถิติ

คำสำคัญ: **กรดทรานสมิก, การเสียเลือดหลังผ่าตัด, การผ่าตัดเปลี่ยนผิวข้อเข่าเทียม**