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COMPARATIVE STUDY OF TOURNIQUET V/S TRANEXAMIC ACID USE ON BLOOD LOSS IN TOTAL KNEE ARTHROPLASTY

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ABSTRACT: CONTEXT: Total knee replacement (TKR) is often carried out using a tourniquet to minimize intraoperative blood loss. However, its application enhances local fibrinolysis, resulting in excessive blood loss during the post-operative period. Fibrinolytic profile varies in different regions and races. Tranexamic acid has been shown to reduce post-operative blood loss and the need for transfusion in TKR. However, there is paucity of literature from the Indian population and the efficacy of the agent has not been tested in Indian patients undergoing TKR. **AIMS:** Effect of tranexamic acid without use of tourniquet V/S tourniquet use on blood loss in TKR surgery in the Indian population. **SETTING AND DESIGN:** In this study, 40 patients undergoing unilateral TKR were randomly divided into two groups. **METHODS:** All patients were conducted under spinal anaesthesia using injection bupivacaine 0.5% heavy 12-15 mg. One group received 10 mg/kg tranexamic acid, intravenous (IV), half an hour before deflation of the tourniquet without use of tourniquet, with a second dose of 2 mg/kg administered 3 hours after the first dose. Other group underwent TKR under tourniquet which was inflated before surgery and deflated after compression.

KEYWORDS: Antifibrinolytics, blood loss, Fibrinolytic, Knee replacement, Tourniquet, Tranexamic acid, Transfusion.

INTRODUCTION: In recent years there has been an increasing awareness of the potential risks in allogenic blood transfusion, such as viral transmission, organic lesion and ABO incompatibility.^{1,2} Total knee arthroplasty (TKA) is associated with marked blood loss, so how to avoid blood transfusion has long been a concern among clinicians.^{3,4} Apparently, minimizing peri- and postoperative blood loss is the most direct way to avoid allogenic blood transfusion. Several techniques, such as autologous blood transfusion, intraoperative blood saving etc, have been adopted to reduce the need for allogenic blood transfusion. Nowadays, tourniquet is routinely used in TKA. It not only reduces blood loss during operation but also makes a operation field clear. However, it should be emphasized that the use of tourniquet activates the local fibrinolytic system and greatly increases blood loss after operation.⁵ Tranexamic acid (TA) is an analogue of lysine,⁶ which has powerful antifibrinolytic potency through blocking the lysine-binding sites of plasminogen molecule and is mainly used in bleeding caused by acute or chronic, localized or systemic accentuation of fibrinolysis. To minimise blood loss, orthopaedic surgeons are accustomed to using a tourniquet in TKA, which could certainly reduce the intraoperative blood loss.

Multiple previous studies have shown a reduction in blood loss and postoperative transfusion requirements with the use of TEA in patients undergoing unilateral total knee arthroplasty.⁷⁻¹⁴ However, there is limited literature¹⁵ regarding the use of TEA in patients undergoing concurrent bilateral TKA. These are the patients expected to be associated with higher transfusion requirement and thus more likely to benefit from such antifibrinolytic therapy.

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Patients and Methods: Forty patients were randomised into two groups: one group underwent operation with a tourniquet and one with intravenous Tranexamic acid but without tourniquet period starting in 2008 involving all patients who underwent primary TKA performed in our institution. The approval of the Institutional Review Board and informed consent from all participants were obtained. Forty consecutive patients suffering from primary osteoarthritis (OA) and rheumatoid arthritis (RA) were recruited into the study. Exclusion criteria were specified as follows: bilateral TKA either simultaneously or staged at less than three-month intervals, diabetes, haemostatic defect, a history of peripheral vascular disease, presence of malignant tumour, preoperative level of Hb less than 10g/l and previous thromboembolism.

Twenty primary knee replacement patients were randomly allocated to group A, with tourniquet in TKA. There are three main strategies for the use of a tourniquet in TKR:

1. The tourniquet may be inflated before the incision and deflated following confirmed hardening of the cement.
2. It can be inflated prior to cement application and deflated following hardening.
3. It can be inflated before the initial incision and deflated following completion of skin closure.

Twenty patients were allocated to group B, which receive an intraoperative intravenous (IV) dose of 1 g of TXA 15 minutes before skin incision for total knee replacement. After 3 hours, a second dose of 1 g of TXA or an equivalent volume of placebo (saline) was administered IV. TXA was given to the patient on the next day at the dose of 10mg/ml BD.

The final result of this randomisation was to have 20 patients in each of the groups. Neither patients nor nurses were informed as to whether or not a tourniquet was used. The patients in the two groups were well matched for age, gender, preoperative Hb, Intraoperative blood loss, Post-operative blood loss, Total Blood loss, Post op Hb on day 1 and Post op Hb on day 3.

SURGICAL TECHNIQUE: Standard techniques were used in all of the cases. Spinal type of anaesthesia was chosen. All procedures were performed by four similar staff surgeons. The implant used was the type of posterior cruciate ligament-substituting total knee prosthetic components (STRYKER). A midvastus approach was used through an anterior midline skin incision. Bone cuts and soft tissue balancing were done in the same sequence. The patella was not replaced in either group. The patella was reshaped to match the shape of the femoral component trochlea better and the soft tissue around the patella was cauterised with an electric scalpel to partly destroy the innervation of the patellar. To reduce the blood loss from the femoral canal an intramedullary plug with bone grafts was used before closure of the wound. In group A tourniquet was used. The tourniquet was inflated to 100mmHg above the systolic blood pressure after the leg was elevated and exsanguinated, and deflation was performed after the wound was closed and the compressive dressing applied.

In group B I/V Tranexamic acid was used and the active bleeding points were promptly sealed with electric coagulation.

Intraoperative and postoperative blood loss was estimated by two different methods. The first was a standard clinical method where approximate blood loss was taken as volume of blood recovered in the suction apparatus, drains and calculation of blood loss from sponges used during surgery. Each half soaked sponge was calculated as 25 ml of blood, and a fully soaked one as 50 ml. This estimation was done by senior resident or consultant.

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The second method was based on changes in Hb level. Assuming that blood volume (BV) on the third day after surgery was the same as that before surgery, we calculated the loss of Hb using the formula.

$$\text{Hb loss} = \text{BV} \times (\text{Hb}_i - \text{Hb}_e) \times 0.001 + \text{Hb}_t$$

Note: Hb_i - Hb concentration before surgery; Hb_e - Hb concentration on the third day after surgery; Hb_t - total amount of allogenic Hb transfused; BV - blood volume taken as 7% of total body weight of the patient and is calculated by Nadler's formula.

A unit of banked blood was considered to contain 52g Hb. The blood loss (ml) was related to the patients' preoperative Hb value (g/l) (blood loss=1000×Hb loss/Hbi). Results were analysed using Student's paired test. None of the patients were transfused during the operation. The transfusion trigger was a haemoglobin level less than 9g/dl measured at the 24th postoperative hour. Drains were used in the wounds.

Post-operative Management: A uniform perioperative regimen was used in all of the cases. Antibiotic treatment with second-generation cephalosporin was infused intravenously (One dose preoperatively and for the next 2 days). The quantity of saline transfused intravenously within 24 h postoperatively was 2, 500~3, 000 ml. Every patient was evaluated to decide whether blood transfusion was needed according to the result of the haemoglobin level measured at the 24th postoperative hour. Thus, the patients' haematocrit levels were well matched, not being lowered due to saline infusion or increased because of blood transfusion. All patients received standard thromboprophylaxis in the form of administration of low molecular weight heparin, pneumatic venous compression pumps and early mobilisation. The wound dressing was changed when soaked or bandaged so tightly as to hinder the blood circulation of the extremity. The affected limb was elevated to exceed the heart level. Ice bags were placed around the affected knees. Continuous passive movement was not used. Active isometric quadriceps, initiative straight leg raising and extending-flexing motion was encouraged just after operation, and walking with part weight-bearing was permitted 24 hours postoperatively under the supervision of a physiotherapist. The study data were documented by a surgeon who did not attend the operation.

Outcome Assessment: Research indexes included patient age and sex, preoperative hb, intraoperative blood loss (IBL), postoperative wound blood loss (PWBL), calculated total blood loss (CBL), free haemoglobin level measured at the 1st and 3rd post op day:

- **IBL:** Assessed by adding the amount of the volume in suction bottles after reduction of wound irrigation fluid and the net blood weight of the sponges used during the procedure.
- **PWBL:** Soaked dressings were weighed and converted to volume. Due to evaporation from the soaked dressings before changing, there was an error between calculated volume and actual volume. So we increased the thickness of the dressings and the frequency of changing.
- **CBL:** Calculated using the formula reported by Nadler et al and Gross. The Hct value used in the formula was measured at the 3rd post op day.

RESULTS: Sixteen females and twenty four males were included in the study which suffered from osteoarthritis and rheumatoid arthritis. Mean age of the patients in both the groups was comparable ranging from 55 years to 80. The average duration of the symptoms before consultation was 14

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months (Range 8 months-24 months). Mean pre-op hb of both the groups was 12.765gm% (range 11-14.5gm%). The mean intraoperative blood loss in the tourniquet group shown in Table 2 is 1160ml as compared to tranexamic acid shown in Table 1 in which the mean intra operative blood loss is 1370 ml. The mean postoperative blood loss in tourniquet group is 640 ml as compared to the tranexamic acid in which the postop blood loss is 350ml. Mean total blood loss in tourniquet group is 1795ml compared to tranexamic acid groups in which 1720 ml was mean total blood loss. Post op hb on day 1 in tourniquet group was 10.24gm% and 11.2gm% on post op day 3 compared to 10.7gm% on post op day 1 and 11.6gm% on post op day 3 in tranexamic acid group. The results are shown in Table 1 of tranexamic acid.

Sl. No.	Age/Sex	Preop Hb	Intra op blood loss	Post op blood loss	Total Blood Loss	Post op Hb on day 1	Post op Hb on day 3
1	63/m	12.5	1250 ml	350 ml	1600 ml	10.2	11
2	67/m	11.2	1300 ml	400 ml	1700 ml	9.8	10.8
3	65/m	13	1200 ml	450 ml	1650 ml	11.8	12.3
4	75/m	12.6	1300 ml	500 ml	1800 ml	11	11.6
5	87/f	11	1200 ml	300 ml	1500 ml	9.2	10.2
6	75/f	12.3	1400 ml	500 ml	1900 ml	10.2	10.6
7	67/m	13.2	1250 ml	450 ml	1700 ml	12	12.7
8	68/f	14	1300 ml	250 ml	1550 ml	12.8	13.1
9	69/f	13.8	1400 ml	300 ml	1700 ml	11	12.3
10	71/m	14	1450 ml	300 ml	1750 ml	12	12.9
11	72/m	12.3	1500 ml	300 ml	1800 ml	10.7	11.3
12	73/f	11.2	1450 ml	250 ml	1700 ml	9.8	10.2
13	80/m	12.8	1350 ml	400 ml	1750 ml	10	10.9
14	73/f	11.9	1450 ml	250 ml	1700 ml	9.3	10.5
15	55/m	14	1500 ml	300 ml	1800 ml	12.4	13
16	65/m	13.4	1450 ml	350 ml	1800 ml	11.8	12
17	68/f	14.5	1500 ml	400 ml	1900 ml	12	12.3
18	69/m	12	1450 ml	500 ml	1950 ml	9	11.1
19	70/f	13	1300 ml	250 ml	1550 ml	10.6	11.6
20	72/m	12.6	1400 ml	200 ml	1600ml	10.1	11.7
MEAN		12.765 gm%	1370 ml	350 ml	1720 ml	10.7 gm%	11.6 gm%

Table 1

The result is shown in Table 2 are of tourniquet group.

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Sl. No.	Age/Sex	Pre-op Hb	Intra op blood loss	Post-op blood loss	Total Blood Loss	Post-op Hb on day 1	Post-op Hb on day 3
1	63/m	12.5	1050 ml	650 ml	1650 ml	9.5	10.7
2	67/m	11.2	1300 ml	700 ml	2000 ml	9	11.4
3	65/m	13	1000 ml	650 ml	1650 ml	10.8	11.8
4	75/m	12.6	1200 ml	700 ml	1900 ml	10.6	11.2
5	87/f	11	1100 ml	500 ml	1600 ml	9	10.4
6	75/f	12.3	1100 ml	800 ml	1900 ml	10.2	11
7	67/m	13.2	1150 ml	650 ml	1800 ml	11.2	12.3
8	68/f	14	1250 ml	450 ml	1700 ml	11.6	12
9	69/f	13.8	1250 ml	550 ml	1800 ml	10.4	10.8
10	71/m	14	1250 ml	600 ml	1850 ml	11.6	11.9
11	72/m	12.3	1200 ml	600 ml	1800 ml	10.3	10.8
12	73/f	11.2	1150 ml	650 ml	1800 ml	9.2	10
13	80/m	12.8	1150 ml	700 ml	1850 ml	9.5	10.1
14	73/f	11.9	1050 ml	550 ml	1550 ml	9.4	10
15	55/m	14	1000 ml	700 ml	1700 ml	11.3	12.1
16	65/m	13.4	1450 ml	650 ml	2100 ml	10.1	11.8
17	68/f	14.5	1200 ml	800 ml	2000 ml	11.2	11.9
18	69/m	12	1150 ml	700 ml	1850 ml	9	11.3
19	70/f	13	1100 ml	550 ml	1650 ml	10.8	11.4
20	72/m	12.6	1100 ml	650 ml	1750 ml	10.2	11
MEAN		12.765 gm%	1160 ml	640 ml	1795 ml	10.245 gm%	11.2 gm%

Table 2

DISCUSSION: TKA can be associated with a significant blood loss. In order to reduce the intraoperative blood loss, a tourniquet was regularly used in TKA. However, orthopaedic implant procedures differ from more general procedures and bleeding may continue for many hours after completion of the operation and much of this may be occult. The mechanism of the hidden blood loss is generally accepted as the residual blood into the joint, extravasation into the tissues,^{16,17} and loss due to haemolysis.¹⁸ Extravasation into the tissues can induce limb swelling and subcutaneous ecchymosis. The extent of haemolysis can be evaluated through free haemoglobin concentration.

Blood loss and its replacement are a serious problem in elective knee replacement surgeries, and are attended to through numerous blood conservation strategies. The present study shows nearly 60% reduction in post-operative blood loss with prophylaxis, using tranexamic acid. The results of this study can be broadly comparable with other similar studies. Hippala and colleagues in two studies demonstrated 45% and 48% reduction in blood loss with the use of tranexamic acid in TKR.^{19,20} Another study showed that tranexamic acid in knee arthroplasty reduces blood loss by nearly 50% and the number of transfused blood units by one-third, with treatment.²¹

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There are many contradictory publications about the effect of a tourniquet on blood loss following TKA.²²⁻²⁶ We calculated the hidden blood loss from Tetro et al.'s²⁴ and Vandenbussche et al.'s²⁵ experiment results and reached different conclusions: using a tourniquet in TKA increased the hidden blood loss in Tetro et al.'s study and the contrary conclusion was reached in Vandenbussche et al.'s study. Our results are consistent with the study of Tetro and associates. The reason for this may be: Firstly, the ischaemic conditions caused by the use of a tourniquet could induce sustained local reactive hyperaemia, lasting several hours after tourniquet deflation. This would in turn promote more haemorrhage into the traumatised tissue and out of the incision within the postoperative period.²⁷⁻²⁹ Secondly, the increased fibrinolytic activity associated with tourniquet-induced ischaemia promotes bleeding into the local tissues following the procedure.^{30,31,28,32}

Thirdly, the superoxide substances generated in tourniquet-induced ischaemia-reperfusion conditions induces the increased permeability of small vessels, which promotes exosmosis of blood constituents. Fourthly, haemocytolysis could be induced by superoxide substances generated in ischaemia-reperfusion conditions and compression caused by an inflated tourniquet. Fifthly, in this study we deflated the tourniquet after the wound was closed and bandaged, in contrast to the method of releasing the tourniquet before wound closure, and allowing control of bleeding, much more blood flow to the affected limb and increase in the proportion of the hidden blood loss in the total blood loss. Our results contrasted with those of Vandenbussche et al.,²⁵ which might be attributed to the fact that the patients they selected were more difficult and their operating time was much longer than ours.

The present study demonstrated that twice the number of patients in the placebo group required blood transfusion when compared to the tranexamic acid group. A meta-analysis of nine randomized control studies demonstrated that the use of tranexamic acid for patients undergoing TKR significantly reduces the proportion of patients requiring blood transfusion.³³ Other clinical studies have demonstrated a decrease in the percentage of patients receiving transfusion with tranexamic acid therapy.³⁴ A study by Lozano and colleagues demonstrated that only 17.6% patients on tranexamic acid received red blood cells transfusion, while 54% of patients in the control group needed the same in TKR.³⁵ Alvarez and workers also reported similar findings. They used same bolus dose. Authors questioned the usefulness of the postoperative reinfusion drains and autologous transfusion in addition to reduction of blood loss and transfusion after administration of tranexamic acid.³⁶

Appel et al.³⁷ and Ömeroğlu et al.³⁸ reported that using a tourniquet could lead to ultrastructural damage of the skeletal muscle distal to the cuff, even rhabdomyolysis, which may be the first step towards muscular atrophy and muscle weakness. In this study, the active knee flexion and straight leg raising activities in the early postoperative period in group B were better than in group A, which might be explained by the foregoing. Furthermore, we consider that the swelling of the affected limb caused by the hidden blood loss can also interfere with rehabilitation. The swelling increases the tension of the soft tissue around the knee so as to hinder the knee flexion movement. Meanwhile, the weight of the affected limb also increased, which means that straight leg raising activities need more muscle force. Although the active knee flexion at the seventh postoperative day did not show a significant difference between the two groups, the more effective rehabilitation exercise in the relatively early period should improve the patients' recovery confidence, decrease the incidence of complications lying in bed and improve the patients' satisfaction.

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We conclude that compared with patients undergoing TKA using a tourniquet with those who used tranexamic acid resulted in reduction in blood loss and the amount of blood transfusion required in patients undergoing total knee replacement surgery. Routine administration of tranexamic acid benefits patients undergoing TKR. Though our study shows that using only TXA without tourniquet results in less overall blood loss than using tourniquet but further larger studies are required to make this as a routine practice.

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