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ORIGINAL ARTICLE

A comparative analysis of the role of Tranexamic acid as an independent variable in reducing intraoperative blood loss in patients undergoing conventional total knee arthroplasty versus computer-assisted total knee arthroplasty

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Abstract
Background Blood loss in total knee arthroplasty (TKA) is an area of significant concern as it has an effect on patient morbidity and hospital stay. Among many different modalities to reduce blood loss, the use of Tranexamic acid has become a standard procedure nowadays. The aim of our study was to determine if Tranexamic acid alone decreases blood loss as an independent variable irrespective of other blood loss preserving measures.
Method This prospective non-randomized study included patients undergoing unilateral TKA by conventional method (Group 1) and computer-assisted TKA (Group 2). All the patients in both groups received Tranexamic acid in a dose of 10 mg/kg body weight prior to inflation of tourniquet. Blood loss in both the groups was calculated using Nadler's formula, and haemoglobin (Hb) level was calculated on day one and day three after surgery.
Results The mean drop of Hb in Group 1 was 1.608 and 1.56 g/dl in Group 2 which was statistically significant ($p < 0.001$); however, none of the patients in either of the groups actually required any blood transfusion postoperatively. Although there was a significant drop in haemoglobin and haematocrit in both the groups, on comparison, there was no significant difference in blood loss and fall in Hb levels between the groups ($p > 0.001$).
Conclusion Tranexamic acid decreases blood loss in patients undergoing TKA independent of all the other blood conserving procedures.

Keywords Tranexamic acid · CAS · Sub-vastus approach · Para-patellar approach · Blood loss

Introduction

Total knee arthroplasty (TKA) is a major surgical intervention which at times can lead to significant drop in haemoglobin, requiring postsurgery blood transfusion [1]. The various measures which have been described to reduce the intraoperative blood loss include the use of tourniquet [2], minimally invasive muscle sparing approach [3], use of antifibrinolytics [4] and diathermy coagulation. A meta-analysis of various randomized control trials (RCT) has shown that early tourniquet release before wound closure for haemostasis may increase blood loss after total knee arthroplasty [5]. One of the other postulated mechanisms to reduce intraoperative blood loss is to avoid opening the intramedullary canal by use of computer-assisted surgery (CAS) which uses a tracker to mark the points for component position instead of an intramedullary jig [6].

The predominant antifibrinolytic that has shown to have effect on reducing blood loss following surgery is Tranexamic acid (TXA) which is the most studied method. The administration of intravenous TXA has shown to reduce blood loss [7] and amount of blood required for transfusions [8] and therefore decreasing the fall in haemoglobin (Hb) [9] following total knee arthroplasty. Various studies comparing patients who received TXA compared to those who did not receive TXA showed significantly reduced hidden blood loss as well [10, 11].

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Even though all the above factors have individually proven to affect the drop in haemoglobin level postoperatively, no study has analysed their cumulative effect on blood loss and drop in haemoglobin. We postulated that antifibrinolytic use is an independent variable which reduces the blood loss significantly without any significant contribution of other variables. The aim of our study is to do a comparative analysis of drop in haemoglobin levels in patients undergoing TKA by conventional intramedullary femoral jig, using a medial para-patellar approach and wound closure after deflating tourniquet with patients undergoing TKA by CAS, using subvastus approach and wound closure under tourniquet control.

Materials and methods

The study protocol was approved by the Institute Ethics Committee and was conducted according to the principles established in the Declaration of Helsinki. Consent for the publication of clinical details, radiographs and photographs was obtained from the patients. This prospective non-randomized multicentre trial was performed between January 2015 and October 2015, wherein 200 consecutive patients with primary osteoarthritis of knee joint were included in the study. Group A consisted of 100 consecutive patients (64 females and 36 males) who underwent conventional TKA with intramedullary femoral alignment guide using medial para-patellar approach and in whom wound closure was done after deflating tourniquet. Group B consisted of 100 patients (74 females and 26 males) who underwent CAS knee arthroplasty using sub-vastus approach and in whom wound closure was done under tourniquet control. All the patients in both groups received Tranexamic acid in a dose of 10 mg/kg body weight prior to inflation of tourniquet.

Patients with morbid obesity (BMI > 40), those undergoing bilateral knee arthroplasty, revision surgery or complex primary TKR requiring augments or femoral/tibial stem, having bleeding diathesis, on oral anticoagulant treatment and those suffering from renal disease precluding the use of Enoxaparin were excluded from study.

Surgical procedure

All the surgeries were performed by two senior authors (AVGR, KKE) who were well versed with both the surgical techniques. Spinal anaesthesia and tourniquet were used in all the cases. Intravenous Tranexamic acid was given in all cases prior to inflation of tourniquet. In patients undergoing conventional TKA (Group A), medial para-patellar arthrotomy was used with a femur first technique in whom medullary canal of femur was opened and an intramedullary guide was used to make the coronal cut of femur and the entry hole closed by bone plug before implantation. All the patients had tourniquet deflated before wound closure. In patients undergoing navigated TKA (Group B), sub-vastus approach was used for arthrotomy and Ortho Pilot (B Braun, Aesculap, Tutlingen) 5.1 femur first computer-aided, imageless navigation system was used which avoids opening the femoral medullary canal. In these patients, tourniquet was deflated after the completion of wound closure. In both the groups, no postoperative intraarticular wound drain was placed. Periarticular infiltration of a mixture of local anaesthetic diluted in normal saline was performed after bone cuts in both groups, and a postoperative single shot adductor canal block was given. All patients received three doses of cefazolin 1 g as antibiotic prophylaxis and had similar postoperative analgesic protocol including 100 mg celecoxib twice daily, 75 mg pregabalin twice daily and paracetamol 1 g three times daily. All the patients received 150 mg oral aspirin for 6 weeks after surgery along with calf pumps for deep vein thrombo-prophylaxis during their hospital stay.

Both the groups followed a standard postoperative rehabilitation programme which involved early mobilization. The haemoglobin (Hb) level was recorded on the day preceding the surgery and on the third postoperative day. Intraoperative blood loss was assessed by weighing sponges and measuring suction volume, and the patient's blood volume (PBV) was calculated using the formula described by Nadler et al. [12], i.e., patient blood volume $= \text{kl} \times \text{height}\ (\text{m})3 + \text{k2} \times \text{weight}\ (\text{kg}) + \text{k3}$, where k is constant, whose values are, $\text{kl} = 0.3669$, $\text{k2} = 0.03219$, $\text{k3} = 0.6041$ for men; $\text{kl} = 0.3561$, $\text{k2} = 0.03308$, $\text{k3} = 0.1833$ for women. The total red cell volume was calculated by multiplying the haematocrit with PBV, and total haemoglobin loss was calculated by subtracting the postoperative haemoglobin level and units of blood transfused from preoperative haemoglobin loss.

Statistical analysis

Data were analysed using SPSS version 20 (IBM Co., Armonk, NY, USA) software. Data were represented in mean ± SD/median (range), and Wilcoxon rank-sum test was used for comparing two groups for blood transfusion, total RBC volume loss, total blood volume loss, hidden blood loss and total haemoglobin loss. Student t test was used to compare two continuous variables, and correlation was done using Karl Pearson/Spearman correlation coefficient. Categorical variables were compared using χ^2/Fisher exact test. A p value < 0.05 was taken as statistically significant.

Results

The two groups were similar with respect to age, gender, weight, height, BMI, comorbidities, preoperative haemoglobin and haematocrit (Table 1). Right knee was replaced in 108 (52 in conventional and 56 in navigated) patients, and left knee was replaced in 92 (48 in conventional and 44 in navigated) patients. The mean tourniquet time in conventional TKA was 57.53 min (range, 40–83 min), while in navigated TKA was 66.73 min (range, 48–92 min) which was not clinically significant ($p = 0.832$). The mean preoperative Hb was 12.44 g/dl (range 9–16 g/dl and SD: 1.528) in the conventional group and 12.064 g/dl (range 8.6–17.7 g/dl and SD: 1.73) in the navigated group ($p = 0.832$). The mean postoperative Hb was 10.82 g/dl (range 8–14 g/dl and SD: 1.334) in the conventional group and 10.504 g/dl (6.7–15.2 g/dl and SD: 1.66) in the navigated group ($p = 0.832$) which again was not statistically significant. The mean drop of Hb in conventional group was 1.608 and 1.56 g/dl in navigated TKA, and the mean drop of haematocrit in conventional group was 4.59 and 4.21 in navigated group. The loss of haemoglobin and haematocrit in both the groups was statistically significant ($p < 0.001$); however, none of the patients in either of the groups actually required any blood transfusion post operatively. The threshold for blood transfusion was set as a Hb value <9 g/dl. Although there was a significant drop in haemoglobin and haematocrit in both the groups, on comparison, there was no significant difference in blood loss and fall in Hb levels between the groups ($p > 0.001$) (Table 2).

Discussion

Our results in both the groups show that there is no significant difference in blood loss between them despite in one of the groups (Group B) using the various proven methods to minimize blood loss like muscle sparing approach, computer-assisted surgery and tourniquet deflation after closure. The only common denomination to minimize blood loss in both the groups was the use of Tranexamic acid, which led us to the conclusion that the use of Tranexamic acid alone would lead to a significant reduction in blood loss and therefore is a single most important independent variable that can be used in arthroplasty to reduce bleeding. Numerous studies have proven the efficacy of Tranexamic acid in blood conservation in arthroplasty, yet none of them have studied the role of Tranexamic acid as an isolated variable in preventing blood loss. Our study concludes that the use of Tranexamic acid alone can reduce blood loss significantly in total knee arthroplasty irrespective of the approach, technique of surgery and the timing of wound closure.

Blood loss after total knee arthroplasty is significant complication intraoperatively sometimes necessitating blood transfusion which can predispose to potential transfusion associated risks like immune sensitization, infections, transfusion-related acute lung injury, increased length of hospital stay and total cost of surgery [8]. There are several methods described to reduce the intraoperative bleeding such as minimally invasive surgery, the use of tourniquet, diathermy, sealing of the intramedullary femoral canal and use of antifibrinolytic agents.

Various studies have shown that the use of CAS total knee replacement results in reduced blood loss and thereby requirement for blood transfusion. Avoidance of opening of the medullary canal is postulated as the mechanism of decreasing blood loss in navigated knee replacement surgery [9]. However, the amount of surgical time in navigated knee replacement is more than a conventional knee replacement and therefore results in tissue anoxia and thereby activation of thrombolytic mechanisms leading to increased bleeding [10]. In our study, the tourniquet time in CAS total knee replacement group was more than conventional knee replacement; however, this difference was not statistically significant. The difference was because in CAS group; the tourniquet was deflated after wound closure. In the authors' experience, there was no significant difference in duration of surgery between the two groups as

Table 1 Baseline parameters

Factor	Conventional TKA	Navigated TKA	*p* value
Age	62.67 ± 8.238	62.89 ± 7.143	0.840
Height	115.92 ± 71.411	124.58 ± 66.928	0.126
Weight	71.32 ± 11.404	70.55 ± 11.107	0.629
Body mass index	27.57 ± 4.591	27.08 ± 3.620	0.403
Hypertension	56	53	
Diabetes mellitus	30	26	
Pre-op haemoglobin	12.47 ± 1.553	12.61 ± 1.235	0.832
Post-op haemoglobin	10.82 ± 1.373	10.62 ± 1.852	0.387
Tourniquet time	57.53 ± 10.380	66.73 ± 10.333	0.362

Table 2 Measurement of comprehensive blood loss in both the groups

Blood loss	Conventional TKA	Navigated TKA	*p* value
Total RBC volume loss (ml)	320 ± 89	280 ± 79	0.625
Measured RBC loss (ml)	130 ± 65	122 ± 39	0.0821
Hidden RBC loss (ml)	190 ± 66	161 ± 56	0.873
Intraoperative blood loss (ml)	172 ± 71	162 ± 50	0.298
Postoperative drain	0	0	–
Blood transfusion	0	0	–
Total blood loss (g/dl)	1.608 (0.45−3.3)	1.56 (0.6−4.3)	0.961
Total blood loss (ml)	812 ± 78	725 ± 63	0.711

Values are presented as mean ± standard deviation

each of them were very well experienced in their individual techniques and having had performed more than thousand knee arthroplasties each.

The use of a tourniquet during total knee arthroplasty aids in better visualization of structures, reduced intraoperative bleeding and better cementation [11]. The timing of tourniquet release has a bearing on the amount of blood loss, and early release for haemostasis is associated with increased blood loss during primary knee arthroplasty. However, tourniquet release after wound closure can increase the rate of reoperation [5]. In our study, there was no significant difference in the amount of blood loss between the two groups which employed different techniques of tourniquet release.

Total knee arthroplasty through the sub-vastus approach results in earlier unassisted straight-leg raise, less total blood loss, less opiate consumption, and better knee flexion at 1 week after surgery when compared with those undergoing through the para-patellar approach [12]. However, in our study, the approach as an independent variable did not show any statistically significant difference in the amount of blood loss.

Tranexamic acid, which can be administered either intravenously or by intraarticular route, has been proven to reduce intraoperative blood loss significantly in orthopaedic surgery, and this has been increasingly documented in a number of studies published over the last decade [13–15]. This drug has shown to reduce blood loss by stabilizing formed clots and prevent the degradation of fibrin by reversibly inhibiting the lysine binding site on plasminogen. This impairs plasminogen's linkage with fibrin to become plasmin, which normally creates a fibrinolytic effect and dissolves clots. We administered intravenous Tranexamic acid before inflation of the tourniquet in all our cases and this has been a well-described technique during orthopaedic surgery [16, 17].

Our study does have some limitations. Lack of randomization may account for some amount of bias in selection of patient even though there was no significant difference in the age, body mass index and comorbidities of the patients in both the groups. There are several studies to show that Tranexamic acid can significantly reduce the blood loss during TKR. Since the two groups employed completely different protocols and surgical technique with none of the uncommon factors between them shown to influence the amount of blood loss significantly and with Tranexamic acid administration as the only common factor, it shows that Tranexamic acid alone can independently reduce the blood loss irrespective of the technique. However, we do recognize that a study with a control group in each of the categories would be more powerful to show the influence of Tranexamic acid as an independent factor to reduce blood loss.

In conclusion, this study has shown that the use of Tranexamic acid decreases the loss of blood and requirement for blood transfusion in patients undergoing total knee arthroplasty independent of all the other blood conserving procedures and should be recommended for all patients undergoing arthroplasty as a standard of care practice.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest in publishing this research work.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Bierbaum BE, Callaghan JJ, Galante JO, Rubash HE, Tooms RE, Welch RB (1999) An analysis of blood management in patients having a total hip or knee arthroplasty. J Bone Joint Surg Am 81(1):2–10

2. Vandenbussche E, Duranthon LD, Couturier M, Pidhorz L, Augereau B (2002) The effect of tourniquet use in total knee arthroplasty. Int Orthop 26(5):306–309
3. Tria AJ Jr, Coon TM (2003) Minimal incision total knee arthroplasty: early experience. Clin Orthop Relat Res 416:185–190
4. Samama CM (2004) A direct antifibrinolytic agent in major orthopedic surgery. Orthopedics 27(6 Suppl):675–680
5. Rama KR, Apsingi S, Poovali S, Jetti A (2007) Timing of tourniquet release in knee arthroplasty. Meta-analysis of randomized, controlled trials. J Bone Joint Surg Am 89(4):699–705
6. Kalairajah Y, Simpson D, Cossey AJ, Verrall GM, Spriggins AJ (2005) Blood loss after total knee replacement: effects of computer-assisted surgery. J Bone Joint Surg Br 87-B(11):1480–1482
7. Benoni G, Fredin H (1996) Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: a prospective, randomised, double-blind study of 86 patients. J Bone Joint Surg Br 78:434–440
8. Seol YJ, Seon JK, Lee SH, Jin C, Prakash J, Park YJ, Song EK (2016) Effect of tranexamic acid on blood loss and blood transfusion reduction after total knee arthroplasty. Knee Surg Relat Res 28(3):188–193. doi:10.5792/ksrr.2016.28.3.188
9. Hynes M, Calder P, Scott G (2003) The use of tranexamic acid to reduce blood loss during total knee arthroplasty. Knee 10:375–377
10. Akgül T, Büget M, Salduz A, Edipoğlu İS, Ekinci M, Küçükay S, Şen C (2016) Efficacy of preoperative administration of single high dose intravenous tranexamic acid in reducing blood loss in total knee arthroplasty: a prospective clinical study. Acta Orthop Traumatol Turc 50(4):429–431. doi:10.1016/j.aott.2016.06.007
11. Huang GP, Jia XF, Xiang Z, Ji Y, Wu GY, Tang Y, Li J, Zhang J (2016) Tranexamic acid reduces hidden blood loss in patients undergoing total knee arthroplasty: a comparative study and meta-analysis. Med Sci Monit 10(22):797–802
12. Nadler SB, Hidalgo JH, Bloch T (1962) Prediction of blood volume in normal human adults. Surgery 51(2):224–232
13. Friedman R, Homering M, Holberg G, Berkowitz SD (2014) Allogeneic blood transfusions and postoperative infections after total hip or knee arthroplasty. J Bone Joint Surg Am 96:272e8
14. Chauhan SK, Scott RG, Breidahl W, Beaver RJ (2004) Computer assisted knee arthroplasty versus a conventional jig-based technique: a randomised, prospective trial. J Bone Joint Surg Br 86-B(3):372–377
15. Petäjä J, Myllynen P, Myllyla G, Vahtera E (1987) Fibrinolysis after application of a pneumatic tourniquet. Acta Chir Scand 153(11–12):647–651
16. Alcelik I, Pollock RD, Sukeik M, Bettany-Saltikov J, Armstrong PM, Fismer P (2012) A comparison of outcomes with and without a tourniquet in total knee arthroplasty: a systematic review and meta-analysis of randomized controlled trials. J Arthroplast 27(3):331–340
17. Roysam GS, Oakley MJ (2001) Subvastus approach for total knee arthroplasty: a prospective, randomized, and observer-blinded trial. J Arthroplast 16:454–457