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Original Research Article

Impact of age, gender and body mass index on the efficacy of tranexamic acid in total knee arthroplasty

Rui Viegas[1]*, Abhishek Kumar[2], Maria M. Carvalho[3], João Vide[1], Ana P. Fontes[3], João P. Sousa[3]

[1]Department of Orthopaedics, Hospital Beatriz Ângelo, Loures, Portugal
[2]Department of Orthopaedics, Fortis Hospital, Kangra, Himachal Pradesh, India
[3]Department of Orthopaedics, Hospital Particular do Algarve, Gambelas, Portugal

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***Correspondence:**
Dr. Rui Viegas,
E-mail: rui.viegas@hotmail.com

ABSTRACT

Background: Tranexamic acid (TXA) is effective and safe in decreasing blood loss and transfusion rate in total knee arthroplasty (TKA). Few studies focused on the role of patients' characteristics on the efficacy of TXA in TKA. The purpose of this study was to conduct a retrospective analysis to investigate if age, gender and BMI influence the efficacy of TXA in reducing perioperative blood loss in TKA.
Methods: We did an observational study including 366 consecutive patients undergoing TKA in Hospital Particular do Algarve between January 2011 and April 2019 which were divided in two groups: intraoperative administration of intravenous TXA (TXA Group) and no administration of TXA (Control Group). The perioperative blood loss between groups and their relation with age, gender and BMI was compared.
Results: Of the 366 patients, 225 (61%) received TXA. In both groups, age did not correlate to the blood loss. Women in the TXA group had less perioperative blood loss than in the control group. No such difference was found for men. The normal weight group showed no difference in perioperative blood loss with or without TXA administration. However, there was a statistically significant difference in the overweight and obese groups. The mean perioperative blood loss was higher in the control group (854±342 ml) than in the TXA group (720±335 ml).
Conclusions: TXA administration is efficient in controlling TKA associated hemorrhage in overweight and obese individuals and in women but it doesn't have that effect in normal weight patients or in men.

Keywords: Age, Body mass index, Blood loss, Gender, Tranexamic acid, Total knee arthroplasty

INTRODUCTION

Total knee arthroplasty (TKA) is a widely used procedure in the treatment of osteoarthritis, providing pain relief and good functional outcomes. Due to population ageing and increasing levels of obesity, the number of TKAs is expected to increase in the next decades.[1,2] TKA represents major surgery and is associated with substantial bleeding – over 85% of patients undergoing TKA are anemic after surgery.[3,4] Perioperative blood management strategies assume a central role in minimizing blood loss and the need for allogenic blood transfusions.[5]

Tranexamic acid (TXA) is an intraoperative blood management strategy. This antifibrinolytic agent inhibits the activation of plasminogen to plasmin, preventing fibrin degradation and promoting clot stabilization.[6] In TKA, the use of TXA is effective and safe in decreasing blood loss and transfusion rate.[7] The perioperative blood

loss and consequent need of transfusion increases the risk of surgical site infection, providing poorer outcomes.[8,9] This strengthens blood conservation as a very important aspect in TKA.

Patients characteristics like age, gender and body mass index (BMI) may influence perioperative blood loss.[9,10] However, few studies focused on the role of these characteristics on the efficacy of TXA in TKA.

The purpose of this study was to conduct a retrospective analysis to investigate if age, gender and BMI influence the efficacy of TXA in reducing perioperative blood loss in TKA.

METHODS

We did an observational, correlational, retrospective study including 366 consecutive patients undergoing TKA in Hospital Particular do Algarve between January 2011 and April 2019 which were divided in two groups: intraoperative administration of intravenous TXA (TXA Group) and no administration of TXA (Control Group).

The perioperative blood loss between the groups and their relation with age, gender and BMI was compared. The BMI was stratified into three categories: normal weight (<25), overweight (25-29.9) and obesity (≥30). The use of TXA refers to the administration of a bolus of 1g intravenously 15 minutes before opening the tourniquet.

Age, sex, height and weight were collected. Hemoglobin (Hb) and hematocrit (Hct) were measured a week before surgery and 24 hours after surgery. The necessity of allogenic blood transfusion and the number of units administrated were also recorded.

The perioperative blood loss was estimated using the Gross equation:[11]

$$Blood\ loss\ (ml) = \text{Blood volume} \times \frac{\text{Preoperative Hct} - \text{Postoperative Hct}}{\text{Average between Preoperative and Postoperative HCT}}$$

In which blood volume = k1 × [height (m)]3 + k2 × body weight (kg) + k3. For males, k1 = 0.3669, k2 = 0.03219, and k3 = 0.6041; for females, k1 = 0.3561, k2 = 0.03308, and k3 = 0.1833.

All the patients included had symptomatic arthrosis resistant to conservative treatment and were operated by the same team with constant presence of the senior surgeon. Surgeries were performed with a tourniquet inflated at the beginning of the surgery and released after dressing the sutured wound. All operations were done by conventional medial parapatellar approach. Patients received a cemented implant without replacement of patella and with preservation of the posterior cruciate ligament. If preservation of the posterior cruciate ligament was not possible, an ultra-congruent implant was used. The capsule was closed with continuous suture without use of an intra-articular drain. We performed peri and intra-articular instillation of ropivacaine and the knee was in flexion for 15 minutes after tourniquet release. Chemical thromboprophylaxis with enoxaparin 40 mg once daily for the first 30 postoperative days was used for each patient. Transfusion triggers were Hb<7 g/dl and Hb<8 g/dl in patients with symptomatic anemia or cardiovascular disease.[12]

The comparative analysis between the two subsamples were performed using the Mann-Whitney test for the categorical variables and the Student t-test for independent samples for numeric variables. The comparative analysis between BMI classes involved the Kruskall-Wallis test. The correlation between dependent and independent variables was performed using the Spearman or Pearson tests, according to the type of variables involved. We considered a 5% significance level for all inferential analysis. We performed all statistical analysis with SPSS version 26.0 (SPSS, Chicago, IL, USA).

RESULTS

Of the 366 patients, 225 (61%) received TXA. The preoperative characteristics of the patients are presented in Table 1. Both groups had similar characteristics concerning to age, gender, BMI, basal Hb and basal Hct (p>0.05).

Table 1: Patients characteristics.

Parameters	Control (n=141)	TXA (n=225)
Age (years)	69.24±7.93	71.04±7.81
Female (%)	68.80	66.70
BMI (kg/m^2)	29.44±4.80	29.40±4.74
Basal Hg (g/dl)	13.90±1.40	13.63±1.53
Basal HCT (%)	41.57±3.68	40.54±4.32

Age

In both groups, age did not correlate to the blood loss (p=0.991 in control group and p=0.812 in the TXA Group).

Gender

A significant difference was found in perioperative blood loss in women, with a mean blood loss of 637±0307 ml in the TXA group and 816±23 ml in the control group (p<0.001). No significant difference was found in perioperative blood loss for men: 885±330 ml in the TXA group and 939±368 ml in the control group (p=0.607).

BMI

The normal weight group showed no difference in perioperative blood loss with or without TXA

administration (p=0.806). However, there was a statistically significant difference in the overweight (p=0.035) and obese groups (p=0.009) as presented in Table 2.

Table 2: Differences in blood loss in control group and TXA group by BMI.

		N	Blood loss mean (ml)	SD	P value
Obesity	Control	59	899	321	0.009
	TXA	94	732	345	
Overweight	Control	60	850	365	0.035
	TXA	93	707	341	
Normal weight	Control	22	746	321	0.806
	TXA	38	717	299	

Blood loss

The mean perioperative blood loss was higher in the control group (854±342 ml) than in the TXA group (720±335 ml) (p<0.001). Four patients needed allogenic blood transfusion, all of them belonging to the control group. Three of those patients received 1 unit of red blood cells and one patient received 2 units.

DISCUSSION

The results of this study showed globally that the administration of TXA decreases perioperative blood loss after TKA. However, the benefit of TXA was not equal in the whole population. We found that gender and BMI influence the effect of this drug and that age doesn't have that capacity. In a specific manner, TXA administration is more protective in women, overweight and obese individuals.

Most of the previous studies over TXA have shown its blood sparing action in TKA and there's various meta-analysis pointing in this direction.[7,13,14] However, few of those studies investigated this action in relation with gender, age and BMI.

Regarding perioperative blood loss in TKA with intravenous TXA administration, literature reports range from 600 ml to 1600 ml.[15,16] In our series we report a mean perioperative blood loss of 720 mL, which is within the expected values.

Concerning age, El Beheiry et al concluded that TXA had a similar hemoglobin-sparing effect in patients over 65 years old undergoing primary total hip arthroplasty compared with younger patients.[21] We also reported that age didn't influence perioperative bleeding because no correlation was found between blood loss and age in both control and TXA Groups.

Secher et al found a hemostatic effect of TXA in women and none in men who underwent bimaxillary orthognathic surgery.[17] Rajesparan et al found that in total hip replacement, the reduction in blood loss after a single dose of 1g of intravenous TXA was more pronounced in women than in men.[18] Our results are consistent with these findings: the administration of TXA reduced the perioperative blood loss in women and had no such effect in men. We thought that the gender differences could be related to the fact that we didn't adapt the dose of TXA to the body weight. However, there was no weight difference between males and females in our study. Furthermore, there's evidence supporting that a 1g dose should be sufficient to decrease surgical blood loss.[19,20]

It is known that obesity carries a higher risk of developing complications following TKA.[22,23] In these patients, it is particularly important to prevent and minimize blood loss to obtain good postoperative results. Meng et al and Tuttle et al found that obese patients can benefit to a greater extent of TXA than patients with normal weight.[24,25] Our results are coherent with the previously cited. We demonstrated that the benefit of TXA in diminishing blood loss was only present in overweight and obese patients and was not present in normal weight patients. One possible explanation for this effect is that obese patients have increased levels of plasminogen activator inhibitor-1, which is an inhibitor of fibrinolysis. TXA is also an inhibitor of fibrinolysis and there could be a synergistic effect between them.[24]

This study has several strengths, such as, a large population and a single surgical and perioperative protocol. However, some limitations are present: the retrospective nature of the study and taking place in a single center. Further multi-center randomized controlled trials in larger populations are required to clarify the population's characteristics which influence the efficacy of TXA.

CONCLUSION

TXA administration is efficient in controlling TKA associated hemorrhage in overweight and obese individuals and in women but it doesn't have that effect in normal weight patients or in men.

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