Transfusion and Apheresis Science 49 (2013) 574–577

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Effectiveness of oral Tranexamic acid administration on blood loss after knee artroplasty: A randomized clinical trial

Mohammad Alipour [a], Masoomeh Tabari [a,*], Mohammadreza Keramati [b], Azam Moradi Zarmehri [c], Hadi Makhmalbaf [d]

[a] Department of Anesthesiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[b] Department of Hematopathology and Blood Banking, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[c] Department of Anesthesiology, Mashhad University of Medical Sciences, Mashhad, Iran
[d] Department of Orthopedic Surgery, Mashhad University of Medical Sciences, Mashhad, Iran

ARTICLE INFO

Article history:
Received 6 November 2012
Received in revised form 28 April 2013
Accepted 18 September 2013

Keywords:
Oral Tranexamic acid
Bleeding
Knee arthroplasty

ABSTRACT

Introduction: Some studies have proved that Tranexamic acid infusion is associated with a decrease in blood loss during and after surgery. Due to the availability of an oral form of the drug, the rapid and complete absorption of it and ease of administration without need for specific instruments, we evaluated the effectiveness of the oral form in decreasing blood loss after total knee arthroplasty.

Materials and methods: In this double-blind, randomized, parallel clinical trial study, we evaluated 53 patients undergoing knee arthroplasty admitted to Ghaem hospital, Mashhad in 2012. Patients with any history of severe ischemic heart diseases, renal failure, cirrhosis, history of bleeding disorders or thromboembolic events, were excluded from the study.

Materials and methods: The patients were randomly allocated into 27 patients with and 26 patients without Tranexamic acid. Blood loss (mL) at 12 and at 24 h and hematocrit at 24 h were measured postoperatively. The results were analyzed with SPSS software (11.5 version) using independent and paired sample *t*-tests. A *p*-value $\leqslant 0.05$ was considered to be significant.

Results: The average blood loss after 12 h of surgery in the control and Tranexamic acid groups were 462.9 (±147.4) and 274.6 (±139) mL, respectively ($p < 0.001$) and after 24 h of surgery they were 588.8 (±193) and 364 (±165.1) mL, respectively ($p < 0.001$).

Results: The mean decrease in the hematocrit after surgery was 4.7% in the Tranexamic acid group and 6.8% in the control group ($p = 0.016$).

Conclusion: Prescription of oral Tranexamic acid before knee arthroplasty can cause remarkable decrease in blood loss after surgery and also less decrease in hematocrit. The advantages of the oral route of the drug versus the intravenous form is that it can be used routinely as a safe and effective way to decrease bleeding after surgery.

1. Introduction

Nowadays, total knee arthroplasty (TKA) is done for many diseases including rheumatoid arthritis and osteoarthritis. Using a tourniquet during TKA has resulted in minimum bleeding during the surgery; however, it can cause severe bleeding can occur after. Surgery and the use of a tourniquet during TKA both activate the fibrinolytic system in the regional blood causing remarkable bleeding postoperatively [1–3]. Because of extensive blood loss especially after surgery, many patients require blood transfusion [4,5] and this, in turn, increases the risk of hemolytic and

* Corresponding author. Tel./fax: +98 5118417402.
E-mail address: Tabarim@mums.ac.ir (M. Tabari).

1473-0502/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.transci.2013.09.005

non-hemolytic transfusion reactions and transmission of infectious diseases [4,6].

Many studies have shown that routine prescription of Tranexamic acid during TKA for patients without a history of thromboembolic events reduces postoperative bleeding and the need for transfusion and, even in the patients who receive a transfusion, it decreases the number of transfused units [5,7–10]. The reason for this is that Tranexamic acid forms a reversible complex with plasminogen (with the amino acid lysine) and prevents its activation. Furthermore, Tranexamic acid interferes with the function and activation of plasmin and acts as an antifibrinolytic agent [1]. Even though Tranexamic acid through inhibition of the fibrinolytic system, can in theory, increase the rate of thromboembolic events, in many studies these complications have not been seen although blood transfusion has been clearly reduced [4,7,8]. Tranexamic acid can be administered orally or as an intravenous infusion. Since the oral form is available and its absorption is quick and complete, it is speculated that it has the same effect in bleeding prevention compared with the IV form. In one study, postoperative bleeding in the second 12 h after surgery, in patients with TKA who had reviewed the oral form had no notable difference from the patients administered the IV form; However, bleeding in both groups was significantly less than in the control group [3].

Confirmation of the effectiveness of the drug in reducing postoperative bleeding in these patients can lead to a decrease in blood transfusion and thus reduce transfusion complications. Indeed, the oral form is easy to use and cheap and does not require specific equipment for administration. Therefore, we evaluated the effectiveness of the oral form of Tranexamic acid on postoperative bleeding in patients undergoing TKA.

2. Materials and methods

In this double-blind, randomized, parallel clinical trial, 65 adult patients, candidates for TKA, were studied in the Ghaem teaching hospital, Mashhad, Iran in 2012. After approval of the study by the local ethical committee, written informed consents were obtained from all patients. Before Surgery, PT, INR, aPTT and CBC tests were requested for all patients. Patients with any history of ischemic heart disease, renal insufficiency, Cirrhosis, bleeding disorders, thromboembolic events and those with a recent intake of anticoagulant or non-steroid anti-inflammatory drugs were excluded from the study. Finally, 53 patients were included in the study. According to the results of a previous study [3] with a power of 80% and an α of 5%, a sample size of 26 partipiciants was calculated for each group. According to computer generated random numbers, patients were assigned to two groups including a Tranexamic acid group, ($n = 26$) and a control group ($n = 27$). Outcome assessors were kept blinded to the allocation. For the case group, initially, 1 g of oral Tranexamic acid was prescribed 2 h before the surgery and it was continued every 6 h for 18 h after surgery. The control group did not receive the drug. To prevent deep vein thrombosis, one day before the surgery Enoxaparin with a dose of 40 mg daily was started and maintained for 2 weeks.

2.1. Anesthetic and surgical measures

After arrival in the operating room, all patients received usual care including monitoring of blood pressure, capnography, electrocardiogram, heart rate and arterial pulse oximetry. Subsequently, standard general anesthesia was done for all patients. For this, the patients were premedicated with Midazolam and Sufentanyl and then induction was done with Thiopental and Atracorium and finally, for maintenance of anesthesia, Propofol, 50% nitrous oxide, 50% oxygen, atracorium and Sufentanyl were administered. Before the incision a pneumatic tourniquet was used around the thigh and removed after the knee prosthesis was fixed in place and homeostasis was established. During surgery, Ringer's and/or normal saline was infused to maintain the heart rate and blood pressure at about 20% of base level and the urinary output at about 100 cc/h. The bleeding rate in surgery drains was measured 12 and 24 h after surgery. We also measured the patients' hematocrit before and 24 h after surgery. All surgeries were carried out by the same surgeon. We also clinically examined the patients 6 weeks after the surgery for evaluation of thrombotic complications.

2.2. Statistical analysis

Data were analyzed using statistical software, SPSS (version 11.5). Initially descriptive analysis of demographic data was performed. Noting the normal distribution of variables, the means of continuous variables were compared with an independent sample *t*-test and paired *t*-test. A *p*-value of $\leqslant 0.05$ was considered to be significant.

3. Results

Out of 53 patients, 22 (41.5%) cases were male and 31 (58.5%) cases female. The average (±SD) age and age range of the patients were 65.8 (±11.5) and 34–88 years, respectively. Average age, height, weight and body mass index (BMI) in the two groups had no significant differences

Table 1
Mean age, weight, height and BMI in the both treatment and control groups (with and without use of Tranexamic acid) in patients undergoing TKA.

General characteristic	Mean	±SD	*p*-Value
Age			
Control	63.11	12.4	0.83
Case	68.6	10	
Weight			
Control	75.9	11.4	0.334
Case	72.6	12.9	
Height			
Control	161.2	12	0.298
Case	157.9	9.5	
BMI			
Control	29.3	3.7	0.741
Case	28.9	3.9	