Study of the Tranexamic Acid Influence on Blood Loss in Arthroplasty

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Within the period 2010-2012, a prospective study has been conducted in order to examine the blood-saving effect of the tranexamic acid (TXA) in total knee (TKA) and hip arthroplasty. There were 100 TKA, 50 total hip replacements. A total of 3.000 mg/30 mL TXA + 60 ml saline solution has been injected intra-articular at closure into the knee joint through a closed suction drain and then the tourniquet was released. In hip joint, the injection was performed at the end of the skin closure. Then the drain was closed for 6 hours and then activated. Total blood loss was calculated from the maximum loss of hemoglobin (Hb). The hemoglobin levels, the volumes from drainage and pre- and post-operatively leg diameters (thigh, suprapatellar portion and calf girth) have been analyzed post-operatively. All patients were followed clinically to detect presence of venous thromboembolism (VTE). The results revealed that post-operative decrease in Hb level was significantly reduced after tranexamic injection (1.7 units), whereas the need for postoperative blood transfusion decreased by 90%. The mean postoperatively blood loss in drainage was 150 mL (50-325 mL). Furthermore, knee joint swelling after operation was significantly reduced. There wasn’t any systemic reaction or clinical symptoms of deep venous thrombosis (DVT).

Keywords: tranexamic acid, total knee replacement, total hip replacement, blood loss

Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine with antifibrinolytic activity. Its chemical name is Trans-4-(Aminomethyl) cyclohexanecarboxylic acid or Cyklokapron. With strong affinity for the five lysine-binding sites of plasminogen, tranexamic acid competitively inhibits the activation of plasminogen to plasmin, resulting in inhibition of fibrinolysis; at higher concentrations, this agent noncompetitively inhibits plasmin. This agent has a longer half-life, is approximately ten times more potent, and is less toxic than aminocaproic acid, which possesses similar mechanisms of action. Therefore, by competitively inhibiting the conversion of plasminogen to plasmin, tranexamic acid allows mature fibrin clots to be maintained and coagulation to continue uninhibited.

After intravenous administration it has been proven to reduce blood loss after routine total knee replacement (TKR), primary and revision hip arthroplasty [1-3], decreasing by at least 50% the transfusion rate [4, 5]. However, there are a lot of controversies regarding the dosage and timing of administration of this drug during surgery, the studies and meta-studies thereof failing to reach a stable consensus. There is also a concern regarding the side effects of this drug when systemically administered, the patient being at high risk to develop thrombosis [5-7]. Some of the contraindications of intravenous administration are: DVT history, visual problems with color disturbances, renal function disorders. The following side effects have been signaled: nausea, vomiting and diarrhea, dizziness, hypotension, rash (allergic reaction), over dosage (rare), even convulsions by the direct SNC impairing, inhibiting the GABA-receptor [7-10].

In order to avoid such risks and especially the potential risk of thrombosis, another way of drug administration is contemplated. Therefore intra-articular administration becomes very attractive for all the patients [8].

Total hip and knee arthroplasties are excellent procedures for patients with arthritic joints, representing widely used treatment methods, considering the current demographical conditions. This surgery is, however, associated with important blood losses both during and after the intervention and with significant transfusion rates [4, 5, 11, 12]. According to the medical reports, blood losses ranged between (1450-1790) mL which led to anemia for most patients. The post-operative anemia in elderly patients is of utmost importance due to the low hematopoietic reserve. Adverse effects of anemia include need for transfusion, longer hospital stay and increased associated costs. Specialized studies indicate that 11-21% of TKA patents and 16-37% of THA patients receive transfusions [4]. Although, the incidence is low, such transfusions can generate serious complications, such as viral infections and graft-versus-host disease etc. For a long period of time, only two methods have been used to avoid allogenic blood transfusions. One is by transfusing autologous blood, including the autologous pre-op blood donation and blood saving during and after surgery. The other is by reducing blood loss by means of techniques such as controlled hypotension, clamping of the drain tube, application of fibrin sponges, compressive bandages and cryotherapy. Subsequently, intravenously administered antifibrinolytic substances have been used, the most useful proving to be the tranexamic acid [2, 3, 13] due to its antifibrinolytic power ten times higher than the Epsilon-aminocaproic acid [5].

Experimental part

Within the period 2010-2012, a prospective study has been concluded in order to examine the blood-saving effect of TEA in total knee and hip arthroplasty. It included 100 knees undergoing unilateral primary cemented TKA and 50 cemented and cementless THA. They were divided into...
two groups. The study group underwent retrograde intra-articular injection of TXA via the drain at the end of the operation. A total of 3,000mg/30mL TXA + 60mL saline solution containing has been injected intra-articular at closure into the knee joint through a closed suction drain and then the tourniquet was released. In hip joint, the injection was performed at the end of the skin closure. Then the drain was closed for 6 h and then activated. For the control group the aspirating drain has been used from the very beginning. Informed consent was obtained from each patient. The single exclusion criteria have been the contraindications of tranexamic acid and the revision arthroplasties.

All hip arthroplasties have been carried out by modified Hardinge approach. Great part of the bleeding sources have been identified and cauterized. Stryker Omnifit and Zimmer (Trilogy acetabular system and VerSys or Metablocstem) implants have been used.

All knee arthroplasties have been performed by standard medial parapatellar approach under tourniquet control. The cemented, posterior stabilized prostheses have been exclusively used, the kneecap prosthesis being used in approx. 30% of the cases.

The used implants were either Stryker Scorpio or Zimmer NexGen. Intraoperative blood loss was negligible in all patients because the tourniquet was not deflated until wound closure. The average duration of the surgical interventions was of 1 h and 20 min. All surgeries have been performed under spinal anesthesia. No autologous blood has been collected for any patient and no cell saver machines have been used during surgery. After surgery, all patients received a prophylactic antibiotic treatment with Cefazolin 1g/12h for 3 days and they all benefited from thromboprophylaxis with Fraxiparine 0.4mL, 1 per day for 3 weeks. Passive mobilization began in the first day after surgery. The suture threads have been extracted after 21 days.

The transfusion criteria of the patients were substantiated on the postoperative Hb measurement, the trigger value being 8g/dL or values ranging between 8-9g/dL if acute anemia clinical signs were present. The blood loss-related measurements included: loss through the drain tube, preoperative Hb and Hb in 1st and 7th day after surgery, total postoperative blood loss, need for autogenic or allogenic blood transfusions, and the transfusion rate. The level of Hb was determined by Automated Hematology System Sysmex XT-4000 using the power of fluorescent flow cytometry and hydrodynamic focusing technologies. Total blood loss was calculated from the maximum loss of hemoglobin, as per the specific formulas adjusted according to the bodyweight and height of the patients.

The operating time has been recorded and the D-dimer levels were assessed 7 days after the surgery. The wound condition (skin necrosis, hematoma, infection) and the possibility of deep venous thrombosis (DVT) and/or pulmonary embolism (PE) have been monitored for 4 weeks after the operation. The leg diameters (thigh, suprapatellar portion and calf girth) have been measured pre- and post-operatively (day 1 and 7). The suprapatellar girth was used as index of intra-articular swelling.

All data were reported using summary statistics including means and standard deviations for quantitative data, frequencies and percentages for qualitative data.

**Results and discussions**

The need for post-operative blood transfusion decreased by 90%. The average postoperative blood loss in drainage was 150 mL (50-325 mL). Furthermore, knee joint swelling after operation was significantly reduced (approx. 30%) after TXA administration (fig. 1), the other mean girth of the limb (thigh and calf girth) being also smaller than the control group (fig. 2 and fig. 3). All other girths begin to reduce from day 14, when the differences become equal in average for the study group (0.8 cm).
The results revealed that post-operative decrease in Hb level was significantly reduced after tranexamic injection, the apparent and total blood losses in the group receiving TXA were significantly lower than those in the control group (fig. 4).

Due to the antifibrinolytic effect there is at least a theoretical risk of thromboembolism if TXA is used even when intra-articularly administered [14, 15]. TXA does not impact on the fibrinolysis in the venous walls [15] and for this reason our study did not point out any increase of thromboembolic complications. Furthermore, the D-dimers level has been quite similar in the two groups, smaller in the study group as compared to the controlled group. The incidence of subcutaneous and intraarticular hematomas has been low in patients who received TXA because of the small amount of bleeding after prosthetic surgery.

Conclusions
Three aspects were clarified in the present study
Firstly, the most important finding of the present study was that intra-articular retrograde injection of TXA via the drain at the end of the operation and then clamping the drain for 6 h effectively reduced postoperative blood loss and thus the need for blood transfusion decreasing the blood loss in hip and knee arthroplasty by more than 50% and decreasing the need for transfusion by over 90%.

Secondly, TXA also reduced knee joint swelling; however, this second conclusion is dependent upon other factors that might modify the girths of the lower limb (inflammation of soft tissues, renal dysfunctions, etc.). Thirdly, the method proves that the thromboembolic complications of any kind, possibly related to a different administration of the drug, are avoided. The method is simple, easy to perform, suitable for all patients and understandable for clinicians. From the four administration alternatives of TXA (oral, intravenous, intramuscular and intraarticular), the intraarticular administration represents the safest and most comfortable method, the procedure being safe without any systemic reaction or septic complications. An economical approach allows us to conclude that the use of tranexamic acid decreases the hospital stay of prosthetic patients, decreases the complications related to bleeding and the possible side effects as well as the afferent costs.

Last but not least, it allows the patient’s reintegration in society and the resumption of the independent activity in the briefest delay possible.

References

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