Blood Control in Total Knee Arthroplasty

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The total knee arthroplasty (TKA), as any surgical procedure, is liable to a series of post-operative complications, such as, particularly in this procedure, excessive blood loss associated, prolonged hospitalization, with an increase in hospital expenses and a decrease in patient satisfaction.

Aiming to minimize intra- and postoperative bleeding as well as their complications, some alternatives are constantly studied. Among them, we find in the literature the use of hypotensive anesthesia, tourniquet use, intraopera- tive blood salvage, re-infusion drains, radiofrequency bipolar, or manipulation of the coagulation cascade, adrenaline, fibrin glue sprays, FloSeal®, auto-transfusion, as the most common procedures. The use of the plasminogen-activator inhibitor tranexamic acid (TA) has arisen interest as an inexpensive agent to be held in surgical procedures worldwide. Thus, the analysis of the clinical efficacy of the use of TA in reducing blood loss in TKA is of paramount importance as the current literature lacks clarity regarding the best dosage and the most effective timing of administration.

Different dosages and method of TA application can be found in the literature and can be shown in Table 1, according to the RCTs analysed.

Author and publishing year	Type of Intervention
Aguilera X et al., 2013	Use of fibrin glue, fibrinogen and troponin, and intravenous tranexamic acid
Pachauri et al., 2013	02 doses of tranexamic acid, injection, first dose one hour preoperatively and six hours postoperatively
Kim TK et al., 2013	01 dose before incision and a dose (10mg.kg-1) of tranexamic acid before tourniquet deflation
Roy SP et al., 2012	Use of tranexamic acid, 5ml, administered intra-articularly after the procedure
Wong J et al., 2010	Use of tranexamic acid 1.5 to 3.0 g applied for five minutes in the joint at the end of surgery
Kankar PN et al., 2009	Use of tranexamic acid 10mg.kg-1 just before inflation of the tourniquet followed by 1mg.kg-1 until the end of the procedure
Camaras et al., 2006	Use of tranexamic acid 10mg.kg-1 just before inflation of the tourniquet followed by 1mg.kg-1 until the end of the procedure

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At our institution, we performed a systematic review selecting papers analysing the effectiveness of TA in TKA over the last 10 years. In the first search, 59 articles were found of which seven randomized control trials (RCT) met the inclusion criteria and were selected with a total sample of 948 patients. After the analysis of and the comparison between the studies included in this work we can conclude that the use of TA in TKA, whether unilateral or bilateral, reduces blood loss in peri- and postoperative procedures significantly when compared to other antifibrinolytic agent. With the reduction of total blood loss, decrease in hemoglobin and haematocrit rate, and the reduction in the need for blood transfusions, the use of tranexamic acid has being demonstrated to be safe with no increase in side effects, such as venous thromboembolism. The use of TA as a hemostasis mechanism can reduce costs and shorten hospital stays, also avoiding the use of autologous blood transfusion.

The TA, synthetic antifibrinolytic agent, presents in its formula the trans isomer of the 4-amino-methyl-cyclohexane carboxylic acid (Transamin®), a synthetic derivative of the lysine amino acid, which acts through competition inhibiting the activation of both the plasminogen and the plasmin. This formula is strongly attracted to the lysine binding both in the plasminogen and the plasmin, thus competitively inhibiting plasmin activation and activity. Its action is fundamentally based on the slowing of the process of fibrinolysis (potent inhibitor of plasmin fibrinolytic action), a later stage to clot formation, causing the time of fibrin network dissolution to extend (Dunn & Goa, 1999).

This way, clotting is preserved, despite not resulting in activation of the coagulation cascade. These properties increase the haemostatic efficiency of the substance, reducing the intensity and the risk of bleeding in surgical procedures, as well as traumatisms and diseases with bleeding tendencies. The acid in question has rapid absorption; about 90% of an intravenous dose is excreted through urine in 24 hours, with a plasma half-life of approximately 2 hours, while maintaining therapeutic levels for 6–8 hours. (Kim, 2014)

Based on the meta-analysis by Tan et al., in 2013, in our institution, the TA is administered at a dose of 10mg/kg before inflating the tourniquet, repeating the dose right before its released. A new dose may be applied six hours after the end of surgery, which has been demonstrated as effective when it comes to after surgery hemostasis improvement. (Maniar et al., 2012)

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When comparing the use of intravenous tranexamic acid with fibrin glue and hemostasis using Tissucol (fibrinogen and thrombin). The results of this study revealed less blood loss in the group, which used tranexamic acid as hemostasis when compared with the use of Tissucol.

Nonetheless, in this study, the use of TA added to the topical application of fibrin glue around osseous tissues presented no benefits on this combined procedure. No complications were reported in any group. In this study we observed a small number of patients in each group, which may have influenced the results collected. (Aguilera et al., 2013) The TA has also the advantage of being significantly less expensive than fibrin spray. (Molloy et al., 2007)

The topical application of TA, which is also used in different methods of application, is gaining popularity due to existing concerns about the safety of intravenously applied TA. As long as the topical application works directly on the source of bleeding, it may be considered a safe and effective method, which reduces the systemic effects. In a meta-analysis, Panteli et al. (2013) confirmed the efficacy and safety of topical TA, using a dosage of 50mg to 3g of TA associated with saline solution from 5ml to 100ml. Topical application methods vary among authors, the most common ones being the application for 5 min before removing the tourniquet and 3–5 min after the operation. The dosage above 2g of topic TA has proven more effective in reducing blood transfusion after TKA. (Dang and Schwarzkopf, 2013)

Despite the use of TA, both intravenously and topically, TKA postoperative bleeding remains an issued to be solved. New agents must be produced with greater effectiveness in transfusion rate reduction.

To date the amount of published studies, with a large number of RCTs and systematic reviews, give us the necessary support for their use, which should be used more widely. More studies should be carried out in order to standardize the optimal method of application, in regards to the the frequency, time of administration and dosage. A cost–benefit analysis should be undertaken to quantify its salutary effects in decreasing perioperative blood transfusions, minimizing transfusion related complications, and reducing overall health care costs. (Georgiadis et al., 2013)

01 Table 1 Methods of application cited in articles.
02 Fig 1 Chemical structure of tranexamic acid. (Dang and Schwarzkopf, 2013)