Invited lecture/Review

The Use of Tranexamic Acid in Orthopaedic Surgery

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Abstract:
New surgical techniques (minimally invasive surgery – (MIS), laparoscopic surgery), meticulous consideration of haemostasis, use of robots, Cell Saver and tranexamic acid, new transfusion criteria and single red blood cell (RBC) unit ordering have greatly changed clinical practices. Implementation of these therapeutic options along with other practices has significantly contributed to the effectiveness of the patient blood management approach to surgical patients. In recent years use of anti-fibrinolytic agent tranexamic acid (TXA) has been introduced at our department and intravenous administration as well as topical TXA administration were successfully implemented. Use of topical TXA was effective at reducing both post-operative red blood cell loss and transfusion rates with good tolerance and no clinically relevant adverse events. Within 6 years of Patient Blood Management (PBM) protocol implementation in our institution, the total number of transfusions was reduced by 76 % and the percentage of patients requiring transfusion fell from 38 % to 9 %.

Keywords: Tranexamic acid; Blood loss; Orthopaedic surgery; Endoprosthesis; Joint arthroplasty

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1. Tranexamic acid

Tranexamic acid (also referred to as TXA) is a drug commonly prescribed in order to control bleeding in patients. As it helps blood to clot it is most commonly used for nosebleeds and heavy periods. Tranexamic acid has also proven to be beneficial for patients who suffer from excessive bleeding and are about to undergo surgical or dental procedures (NHS, 2020).

Tranexamic acid is a synthetic derivative of the amino acid lysine with a chemical formula $C_8H_{15}NO_2$, as shown in **Figure 1** (DrugBank, 2023).

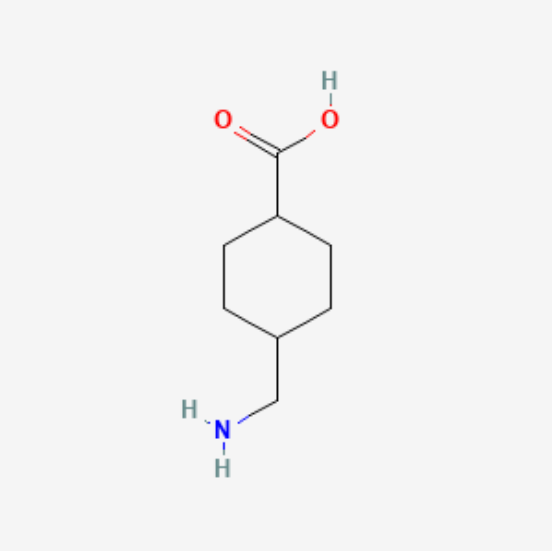

Figure 1: Chemical structure of tranexamic acid (National Center for Biotechnology Information, 2023).

Tranexamic acid is an antifibrinolytic which competitively and reversibly inhibits the activation of plasminogen to plasmin. It does so by binding to several sites of plasminogen, one of which is a high-affinity site which is involved in binding fibrin. The binding of fibrin and plasminogen induces fibrinolysis, that is, the breakdown of fibrin in the blood. Bound tranexamic acid occupies the necessary sites on plasminogen, thus preventing fibrinolysis and stabilising the blood clot (Drugbank, 2023).

Tranexamic acid may be administered to patients either orally in the form of tablets, or intravenously via injection. It is only available with a doctor's prescription and is only available for patients over 12 years of age (Mayo Clinic, 2023). Tranexamic acid is provided as 500mg tablets. The normal dose prescribed for adult patients is 2-3 tablets, taken 3 times per day. The time intervals should be spaced out as evenly as possible. For patients with kidney problems, prescribed doses are normally lower (NHS, 2020).

2. Clinical use of tranexamic acid

A beneficial finding regarding tranexamic acid has been that there are little to no common side effects with tranexamic acid tablets, however, with tranexamic acid injections, patients might experience nausea, diarrhoea and itchy skin.

Additionally, tranexamic acid can be taken with most other medicines (NHS, 2020). All this makes for a useful medication used in surgical procedures, such as orthopaedic ones.

Orthopaedic surgery, especially total joint arthroplasty (**Figure 2**), is commonly associated with major blood loss, and patients require blood transfusion to avoid postoperative anaemia. It has been reported that up to almost 40% of patients undergoing primary total hip

arthroplasty and almost 25% of patients undergoing total knee arthroplasty require such transfusion, as the average blood loss during said surgeries ranges between 1000 and 2000 ml of blood (Kim et al., 2015).

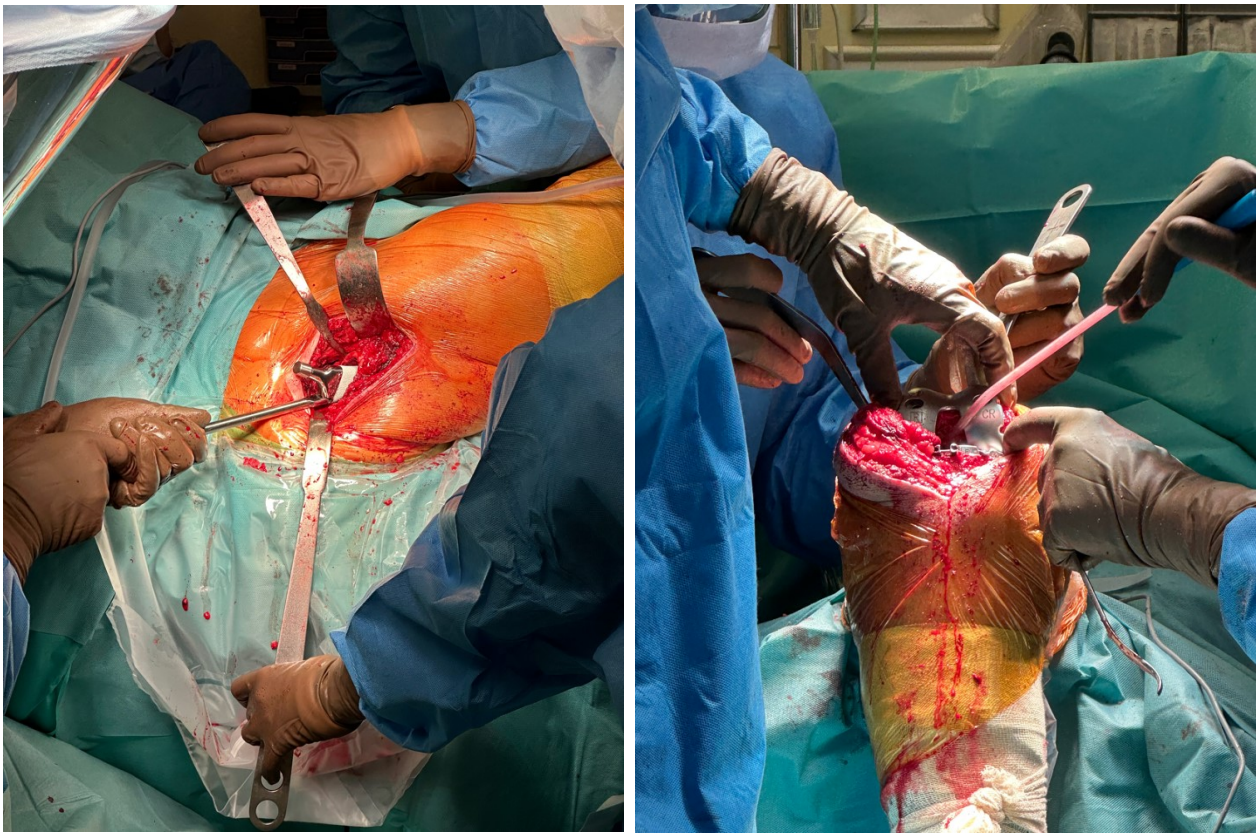

Figure 2: Left: Primary total hip arthroplasty surgery. Right: Primary total knee arthroplasty surgery (Author's own photographs).

Attempts to minimize blood loss during surgery, as well as the need for patient blood transfusions, have been made. The use of haemostatic agents, such as tranexamic acid and the use of Cell Saver, have considerably increased in orthopaedic lower limb surgery (Reale et al., 2021).

Clinical studies show that multiple administrations of tranexamic acid have proven to be useful in reducing patient blood loss, postoperative pain, and markers of inflammation, all without a significant increase in the incidence of thromboembolic events compared to placebo and single-dose tranexamic acid groups. Findings also show a more favourable hospital stay length and a lesser need for expensive blood transfusions which might, in rare cases, lead to unnecessary secondary patient infections (Haratian et al., 2021).

3. Conclusion and the use of tranexamic acid at the Department for Orthopaedic Surgery, University Medical Centre Ljubljana

With the help of minimally invasive surgical methods, updated transfusion threshold guidelines, and recently rising tranexamic acid usage, transfusion rates at the Department for Orthopaedic surgery of Ljubljana have been dropped by over 80% during the past ten years. The overall number of transfusions was decreased by 76% within 6 years of the Patient Blood Management protocol's implementation, and the proportion of patients needing transfusions decreased from 38% to 9%. Use of topical TXA was effective at reducing both post-operative red blood cell loss and transfusion rates with good tolerance and no clinically relevant adverse events.

It is certain that a multidisciplinary approach is required for the implementation of Patient Blood Management program and reduction of blood loss in surgery. Surgeons, general practitioners, as well as anaesthesiologists, play a pivotal role.

Clinical practices for red blood cell transfusion have significantly changed as a result of new surgical techniques (including MIS, laparoscopic surgery, robots), rigorous consideration of haemostasis, use of Cell-Saver, and most recently, use of tranexamic acid, new transfusion criteria, and single red blood cell unit ordering. The effectiveness of the patient blood management approach to surgical patients will be greatly enhanced by the implementation of this therapeutic option along with other procedures (early detection and treatment of pre-operative and post-operative anaemia, a restrictive transfusion strategy, policy of transfusing single units of red blood cells, etc.).

Our experience and statistical data demonstrate a significant decline in the number of transfusions and the proportion of patients who required transfusions in recent years. The causes for this include new surgical procedures, increased public awareness of the drawbacks of blood transfusions, and the introduction of innovative techniques and agents, such as tranexamic acid.

Conflicts of Interest: The authors declare no conflict of interest.

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