

Protocol

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Implementation of prophylactic and systematic tranexamic acid administration in the surgical safety checklist for adult patients: a protocol proposal

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ABSTRACT

Background: The administration of tranexamic acid (TXA) in the surgical context has proven to be effective in reducing perioperative bleeding, both in cardiac and noncardiac surgery. Its low price and ease of use make it particularly advantageous. Despite existing evidence and international recommendations supporting its use in surgery, TXA remains underutilized and inconsistently used in surgery.

Methods: Furthermore, integrating this recommendation into the 'safe surgery' approach by establishing a consistent process may enhance its beneficial effect on patient clinical outcomes. Therefore, to increase and standardize the use of tranexamic acid in surgery, we considered including prophylactic administration of TXA in the 'surgical safety checklist' (SSC) at our hospital and implemented a protocol for its systematic prophylactic administration in adult surgical patients at risk of moderate to high blood loss.

Conclusions: A protocol based on current evidence, an innovative initiative implemented in a pioneering manner was presented at Unidade Local de Saúde São João.

Keywords: Tranexamic acid, Blood loss, Surgical, Surgical procedures, Operative, Perioperative care, Clinical protocols

INTRODUCTION

Tranexamic acid (TXA) is a synthetic antifibrinolytic, a lysine analogue that binds to the plasminogen lysine receptor, thereby preventing its activation into plasmin and inhibiting fibrinolysis.^{1,2}

TXA has demonstrated potential to reduce intra- and postoperative bleeding in cardiac, orthopedic, hepatic, abdominal, pelvic, gynecological, and urological surgeries, decreasing the need for blood transfusions without increasing the incidence of thrombotic events or other significant adverse effects.¹⁻¹³ This safety is underscored by several studies that demonstrated TXA's efficacy and safety in the surgical setting, both in cardiac and noncardiac surgery, making it an efficient, safe, easy, and low-cost measure.^{10,14-17}

Since the systematic and prophylactic administration of TXA can minimize blood loss and exposure to allogeneic blood transfusion, it constitutes an important measure of the patient blood management (PBM) strategy.

PBM is a multidisciplinary and patient-centered approach to improve patient outcomes by managing and conserving the patient's blood, reducing blood loss, and increasing tolerance to anemia. This strategy is applicable across various contexts where hemorrhage may occur; however, evidence indicates it exerts a more significant influence in perioperative patients.¹⁸ Within surgical settings, PBM encompasses optimizing preoperative hemoglobin levels, enhancing the patient's tolerance to anemia, and minimizing intraoperative bleeding through the use of antifibrinolytic agents such as TXA.¹⁹⁻²¹

Thus, given the strong evidence that TXA administration reduces peri- and postoperative bleeding as well as the need for transfusion, without significantly increasing thrombotic risk, its use offers a clear benefit to patients undergoing surgeries with moderate or high hemorrhagic risk. Accordingly, prophylactic administration of TXA is recommended with a "level of evidence A" for orthopedic and cardiac surgeries, and with a "level of evidence B" for other surgeries with moderate to high hemorrhagic risk, defined by the World Health Organization (WHO) as those with an expected blood loss greater than 500 milliliters (ml) in adults.^{6,8}

In this context, Unidade Local de Saúde São João, a university hospital with approximately 1,100 beds and all surgical specialties, where over sixty-four thousand surgeries are performed annually, developed a protocol based on an extensive review of the latest recommendations regarding this subject.

The intention was to establish a standardized, evidence-based protocol for the systematic use of TXA in adult surgical patients. To guarantee that this protocol respects the state-of-the-art and prioritizes patient safety, as well as to ensure that our recommendations are consistent with

international guidelines and with the best scientific evidence, we obtained review and approval from the Quality and Patient Safety Unit, the Pharmacy and Therapeutics Committee, and the Clinical Direction of our hospital.

Under this protocol, since February 2025, prophylactic TXA has been routinely administered to all adult patients undergoing procedures in Unidade Local de Saúde São João with expected moderate to high blood loss.

METHODS

Indications and contraindications

Indications

Systematic prophylactic administration of tranexamic acid (TXA) is recommended for adult patients undergoing selected surgical procedures. These include cardiac surgery, otorhinolaryngological procedures such as adenoidectomy and tonsillectomy, and plastic or reconstructive surgeries, such as abdominoplasty. TXA prophylaxis is also recommended for orthopedic procedures with moderate to high bleeding risk, such as revision or total arthroplasty of the hip, knee, or shoulder, arthroplasty for femoral neck fracture, elective spinal surgery, and for elective intracranial or spinal neurosurgical procedures with moderate to high hemorrhagic risk and expected blood loss over 500 ml. In addition, TXA is indicated for urological surgeries of the lower genitourinary tract (prostate and bladder procedures), major gynecological surgeries (myomectomy and hysterectomy performed for fibroids, endometriosis, or malignancy), and obstetric surgeries with postpartum hemorrhage when predicted blood loss exceeds 500 ml. Prophylactic TXA may also be considered for other surgeries associated with moderate to high bleeding risk and expected blood loss greater than 500 ml.^{1-9,11-13,17,22-25}

The protocol does not apply to children or adolescents (under 18 years of age). TXA administration for pediatric patients may continue according to clinical indications, as this statement does not include pediatric patients.

Contraindications

The systematic prophylactic administration of TXA should not be performed in the following situations: hypersensitivity to the active substance or any of the excipients; severe renal impairment (GFR<30 ml/min/1.73 m²); disseminated intravascular coagulation (DIC); recent venous or arterial thrombosis (within the last 3 months); recent acute myocardial infarction (AMI) or stroke (within the last 3 months); severe thrombophilia or other very relevant hypercoagulable conditions, previously diagnosed, to be evaluated by immunohemotherapy; previous history of epilepsy, only in situations where it is desired to administer more than 4 g of tranexamic acid in 24 hours (h); upper urinary tract hematuria; patients with

severe and complex polytrauma, tranexamic use beyond 3 hours post-injury should be considered on a case-by-case basis by the surgical team, depending on the patient's clinical situation.^{20,24,26-28}

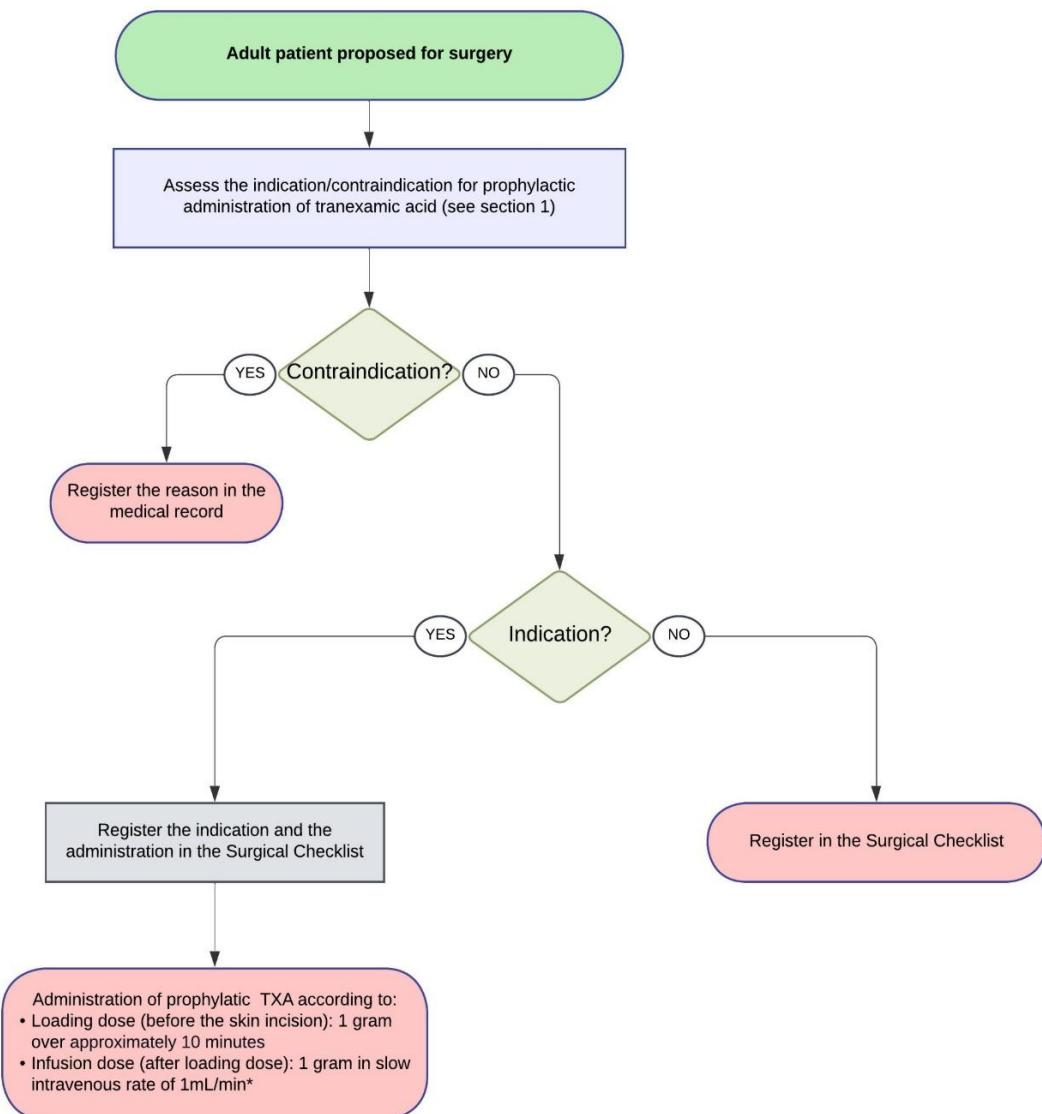
Dosing and administration

As part of an integrated effort by the surgical team, the surgeon is responsible for prescribing prophylactic TXA, and the anesthesiologist is responsible for ensuring its timely administration and proper documentation in the patient's medical record if there is a contraindication to TXA use. Administration should occur in the operating

room before the skin incision to ensure adequate tissue levels during the incision.²⁹

Systematic prophylactic administration of TXA should be performed in patients older than 17 years and 364 days in the surgeries stated in this document, as shown in Figure 1.

The initial dose is 1g of TXA, diluted in 10 ml of normal saline, administered intravenously before the skin incision. During surgery, give a continuous intravenous infusion of 1 g of TXA diluted in 250 ml of normal saline at a slow rate of 1 ml/min. This infusion must begin after the initial dose mentioned above.^{1,9,12,27}



* The infusion should not be interrupted, maintaining it even after the end of the surgery.

Figure 1: Protocol flowchart for the systematic prophylactic administration of tranexamic acid.

In patients with mild to moderate renal disease, administration of TXA is not contraindicated; however,

TXA dosage should be reduced according to the serum creatinine level (Table 1).²⁴

Adverse events

Some of the adverse events that may occur with the administration of this drug, as listed in the TXA summary of product characteristics, are: allergic dermatitis; diarrhea, nausea or vomiting; visual disturbances (including changes in color perception); general malaise with hypotension, with or without loss of consciousness (usually after a very rapid intravenous injection); arterial or venous thrombosis in any location; seizures; hypersensitivity reactions, including anaphylaxis.²⁴

Table 1: Tranexamic acid dose adjustment based on serum creatinine levels in patients with renal impairment.

Serum creatinine level (mg/dl)	IV dosage
1.35 to 2.82	10 mg/kg every 12 hours
2.82 to 5.65	10 mg/kg every 24 hours
>5.65	5 mg/kg every 24 hours

Levels of responsibility

The surgeon is responsible for assessing the indication or contraindication for the prophylactic TXA use. If indicated, the surgeon must prescribe TXA. If the administration is contraindicated, the surgeon must document the reason for the absence of a prescription in the patient's medical record.

The anesthesiologist must confirm that there is no contraindication to the administration of TXA, ensure the administration before surgical incision, and verify the correct recording of this procedure.

The nurse anesthetist should administer TXA prophylaxis immediately before the skin incision.

The circulation nurse, responsible for completing the surgical safety checklist (SSC), must record the indication for TXA prophylaxis, its administration, and the exact administration time. This information should be filed in the SSC.

In situations not mentioned in this protocol, the hematology service should be contacted.

Monitoring and evaluation

The assessment of the implementation of this protocol must be carried out periodically. The implementation of this protocol is monitored and evaluated through the following indicators:

Process indicators

The process indicators comprise the absolute number of surgeries with prophylactic TXA administration, the

proportion of surgeries with prophylactic TXA administration, and the absolute number and proportion of surgeries with a documented contraindication to TXA use. All results were stratified by surgery type.

Results for outcome

Outcome indicators include having another surgery within 24 hours, dying on the day of surgery (which includes during or up to 24 hours after surgery), dying in the hospital after surgery, the typical number of red blood cell packs given during and after surgery, and the average days spent in the hospital. All results were grouped by surgery type.

DISCUSSION

TXA use in the surgical setting is a strategy that has proven to be effective in reducing perioperative bleeding and, thus, reducing postoperative anemia which is associated with an increased risk of infection, longer hospital stays, heart failure, and death.^{19,30} Therefore, the application of this protocol intends to be an essential tool integrated into the PBM program.

Furthermore, TXA is an affordable, widely accessible pharmacologic agent with no special storage requirements. So, the implementation of systematic prophylactic administration of TXA in surgery would safely improve patient outcomes at low cost, as evidence demonstrates.^{19,31}

Following several societies' recommendations, TXA was already used in surgery at Unidade Local de Saúde São João, as evidence supports that it safely reduces surgical bleeding. However, its use has been inconsistent and insufficiently standardized, varying by department and professional. Data from the UK, Australia, and New Zealand reveal high rates of non-use of TXA even in eligible surgical patients and high variability across surgical specialties.^{32,33}

Thus, implementing standardized, evidence-based protocols is crucial to establishing consistent and systematic use of TXA in adult surgical patients. To promote the utilization of TXA in surgery, we considered including it in the SSC. The SSC was created by the WHO to reduce mortality and complications related to surgical interventions by focusing on a sequence of routine activities that help mitigate specific risks. SSC was developed by the WHO to reduce mortality and complications associated with surgical interventions by emphasizing a sequence of routine activities designed to mitigate specific risks. The objective is clear: to delineate a set of procedures to be performed before, during, and after surgery that are well-defined and have a robust scientific basis, which, when correctly executed, can save lives.^{17,34} Currently, our hospital has a digital version of the SSC, integrated into the information system,

highlighting the essential nature of its use in all surgical procedures performed.

As there is evidence that TXA administration is both beneficial and safe in reducing bleeding during surgery, including this recommendation in the SSC can enhance the impact of this measure and its outcomes. Some literature states that the evidence supports the inclusion of TXA on the WHO "surgical safety checklist", and The Joint Royal Colleges TXA in Surgery Implementation Group has made a proposal for the WHO to consider its inclusion.^{19,30,35,36} So, we have implemented this protocol at Unidade Local de Saúde São João, which ensures that prophylactic TXA is routinely administered to all adult patients undergoing procedures with an expected moderate to high blood loss. So, situations in which its use is not indicated or is contraindicated will be exceptions and must be justified.

To ensure compliance with the protocol, the clinical information system was modified to integrate this protocol within the hospital's electronic medical record system. In order to optimize protocol application, we included the item "TXA was administered" in the SSC section corresponding to the period before skin incision. The possible answers are "yes", "no" (demanding the reason) or "not applicable" if the prophylactic administration of TXA is not considered appropriate (for example, in surgeries expected to have mild blood loss of less than 500 ml).

At this stage, this document focuses exclusively on outlining the protocol. However, preliminary data indicate a 50% increase in the use of intravenous TXA in surgical settings since the protocol's introduction, suggesting that it is being effectively implemented and adopted in clinical practice. A subsequent analysis will be conducted to evaluate the proper implementation of the protocol and its effects on TXA use, red blood cell concentrates (RBC) consumption, case fatality rates, and length of hospital stay.

CONCLUSION

In conclusion, with this protocol, we intend to promote routine and systematic prophylactic administration of TXA in adult surgical patients, ensuring that its benefits are maximized. We believe that the wider use of TXA will enhance surgical outcomes and safety, while preventing unnecessary blood transfusions, thereby allowing for better blood stock management and availability of healthcare resources for other critical areas. Therefore, we consider it of utmost importance to include the prophylactic and systematic administration of TXA as an integral part of the 'safe surgery' program for adult patients.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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