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Safety of a High-Dose Tranexamic Acid Protocol in Complex Adult Spinal Deformity: Analysis of 100 Consecutive Cases

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Abstract

Study Design: Retrospective review of high-dose tranexamic acid (TXA) use in consecutive patients.
Objective: To determine the safety profile of a high-dose TXA protocol in complex adult spinal deformity patients.
Summary of Background Data: Adult spinal deformity (ASD) surgery may involve significant amounts of blood loss, especially when various osteotomy techniques are used. Antifibrinolytic agents such as TXA have been used to reduce intraoperative blood loss. However, there is no universally accepted dosing protocol for its use during complex ASD surgery.
Methods: Consecutive patients undergoing spinal deformity correction over a 14-month period at a single institution were identified. Inclusion criteria were adults (age ⩾18 years) who underwent posterior spinal fusion of at least 5 levels and use of our standard TXA protocol of 50 mg/kg intravenous loading dose followed by a 5-mg/kg/h infusion until skin closure. Patient demographics, estimated blood loss (EBL), operative time, transfusion rates, complications, and other procedure-specific information were recorded.
Results: A total of 100 adult patients were included. All operative procedures were performed by the senior surgeon. The mean age was 47.3 years, and 71% of patients were female. Average body mass index was 24.9. The average fusion length was 14 levels; 33/100 patients had fusion constructs of 17 levels or more. Pedicle subtraction osteotomy was performed in 9 patients and vertebral column resections were performed in 14 patients. There were 45/100 patients who had a primary procedure, whereas the rest were revisions. Mean EBL was 1,336 mL (98 mL/level, 31% estimated blood volume). There were three thromboembolic complications, including one pulmonary embolism and two deep vein thromboses (DVTs), which were all treated successfully with anticoagulation. There were no cases of myocardial infarction, seizure, stroke, or acute renal failure.
Conclusions: This is the first study to demonstrate the use of high-dose TXA in a complex ASD population. Larger prospective studies are needed to assess the efficacy and safety of high-dose TXA in ASD.
Level of Evidence: Level IV, therapeutic.

Keywords: Tranexamic acid; Adult spine deformity; Vertebral column resection; Pedicle subtraction osteotomy; antifibrinolytic

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Introduction

Adult spinal deformity (ASD) surgery can be associated with significant blood loss because of various factors such as extensive soft tissue dissection, long segment instrumentation, epidural bleeding from multilevel neural element decompression, as well significant blood loss that can occur during osteotomies [1-3]. Increased blood loss has both direct and indirect effects on the clinical outcome. The direct effects of significant blood loss include hemodynamic instability, end organ dysfunction from hypoperfusion, and coagulopathy from loss of clotting factors and platelets, as well as activation of fibrinolysis pathway. Indirect effects of blood loss include complications inherent to blood transition such as transfusion reaction, hypersensitivity, acute lung injury, and increased risk for infection [1,4].

Various strategies have been utilized by spine surgeons to reduce blood loss in an effort to minimize the complications associated with blood loss. These strategies include hypotensive anesthesia during exposure, hemodilution, intraoperative cell salvage system, and pharmacologic agents. Tranexamic acid (TXA) is a synthetic antifibrinolytic amino acid used in various surgical fields, including cardiac, transplant, gynecologic, orthopedic, and spinal surgery [2,5]. It is a lysine analog that reversibly binds receptor sites on plasma and plasminogen to inhibit plasminogen activation [5,6]. Multiple studies have documented TXA usage, resulting in significant decrease in intraoperative blood loss during spinal surgery [2,7-12].

Various TXA dosing regimens have been reported in the spine surgery literature with no established guidelines. Dosing ranges from a single dose of 15 mg/kg to a very high-dose regimen of 100-mg/kg loading dose followed by 10 mg/kg/h infusion during surgery until skin closure [2,8,13]. There have been very few reports of high-dose ($>$50 mg/kg) TXA usage in ASD [2,12].

The potential adverse effects of using TXA have been a major concern for clinicians, especially when high doses of TXA are used in elderly patients. TXA has been shown to decrease seizure threshold in patients undergoing cardiac surgery [14]. It also has the theoretical risk of thromboembolic disease, although a recent systematic review of randomized trials showed thromboembolic complications to be very rare [12]. Case reports exist for cerebral thrombosis, arterial thrombosis, and acute renal failure, but these events are rare as well [6].

The high-dose TXA dosing protocol at our institution was jointly determined by the spine and anesthesia departments to be a 50-mg/kg loading dose followed by a 5-mg/kg/h infusion. This dosing was felt to be a compromise between the efficacy of the 100-mg/kg dosing reported in pediatric spinal deformity, while being below the high dosages associated with seizures in the cardiac literature. It has been demonstrated in the cardiac literature that high-dose TXA ($\geqslant$100 mg/kg) use is associated with postoperative seizures [15]. This dosage has also been previously studied and reported on in the cardiac and obstetrical literature [16,17].

We aim to investigate the efficacy and safety profile of a high-dose TXA protocol (loading dose of 50 mg/kg followed by 5 mg/kg/h infusion until skin closure) in ASD patients at our institution over a 14-month period with a review of the pertinent literature.

Material and Methods

Study design

Patients who underwent ASD surgery at a single institution between September 2015 and November 2016 were identified. Inclusion criteria were adults (age $\geqslant$18 years) with spinal deformities such as scoliosis, kyphosis, and flatback syndrome who had underwent posterior spinal fusion surgery of at least 5 levels and use of our standard TXA protocol of 50-mg/kg intravenous loading dose followed by a 5-mg/kg/h infusion until skin closure. Patient demographics, medical comorbidity, procedure type, fusion levels, osteotomy type and levels, estimated blood loss, cellsaver collection, intraoperative and postoperative blood transfusion requirement, as well as complications such as myocardial infarction (MI), acute renal failure, stroke, seizure, deep vein thrombosis (DVT) and pulmonary embolism (PE) in the perioperative period were recorded. Estimated blood volume was calculated as the patient's weight (in kilograms) $\times$ 70 mL/kg. Patients who had staged three-column osteotomies (3COs) were counted as two separate procedures with the osteotomies attributed accordingly.

Anesthetic technique

A similar anesthetic technique was used in all patients. Patients were premedicated with midazolam (1−4 mg) and fentanyl (50−150 μg). General anesthesia was induced with propofol (1.5−2.5 mg/kg), lidocaine (50−100 mg), and rocuronium (30−40 mg) or succinylcholine (120−200 mg) to facilitate intubation. Anesthesia was maintained with propofol (60−200 μg/kg/min) and remifentanil (0.1−0.8 μg/kg/min). Depth of anesthesia was monitored by vital signs and bispectral index monitoring.

TXA was given as a bolus of 50 mg/kg after induction and before incision, followed by a continuous infusion of 5 mg/kg/h during the whole procedure until the wound was closed. Mean arterial pressure (MAP) was maintained at 70 mmHg during the dissection phase until spine was exposed, and MAP was raised to 90 mmHg during the correction phase of surgery. MAP was raised to higher mean pressures if there were any changes in SSEP or MEP. Transfusion threshold was not rigidly defined. Usually blood was transfused or cellsaver given once hematocrit was below 25. Transfusion threshold depended on the