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The Efficacy of Amicar Versus Tranexamic Acid in Pediatric Spinal Deformity Surgery: A Prospective, Randomized, Double-Blinded Pilot Study

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Abstract

Study Design: Single-center, prospective, randomized, double-blinded trial.
Objectives: To compare blood loss, allogenic transfusion requirements, and coagulation parameters between pediatric spinal deformity patients receiving aminocaproic acid (Amicar) or tranexamic acid (TXA) during posterior spinal fusion.
Summary of Background Data: Amicar and TXA have been shown to decrease blood loss in pediatric spinal deformity cases compared with controls. The difference in efficacy between these medications in this population has not been reported.
Methods: Enrolled patients were randomized to receive either Amicar or TXA during scoliosis surgery. Baseline demographic and deformity comparisons were collected. Intraoperative comparisons included estimated and calculated blood loss, number of levels instrumented, number of osteotomies, operative time, and allogenic transfusion requirements. Preoperative and postoperative hemoglobin, platelets, prothrombin time, partial prothrombin time (PTT), international normalized ratio (INR), and fibrinogen were recorded.
Results: A total of 47 patients were enrolled with data available for review (N = 25, Amicar; N = 22, TXA). No difference in cohorts was found in demographics, preoperative hemoglobin, platelets, prothrombin time, PTT, INR, initial Cobb angle, average number of: levels fused, patients with osteotomies and osteotomies, operative time, and final Cobb angles. Estimated blood loss was significantly less (about 221 mL) than the calculated blood loss in both groups (p = .003). Estimated blood loss (1,088 vs. 726 mL; p = .055) and calculated blood loss (1,366 vs. 903 mL; p = .13) trended higher in the Amicar group. Although no difference in allogenic transfusion rates (20% vs. 14%) was observed, average volumes transfused were significantly higher in the Amicar cohort (1,014 vs. 461 mL; p = .03). The TXA cohort demonstrated a statistically significant smaller change in INR, a lower PTT, and greater fibrinogen levels postoperatively.
Conclusions: Compared with Amicar, TXA use was associated with a lower allogenic transfusion requirement, less alteration in postoperative clotting studies, and a trend toward lower blood loss in pediatric posterior spinal fusion patients.

Keywords: Scoliosis; Blood loss; Antifibrinolytics; Amicar; Tranexamic acid

Introduction

Previous reports have shown the efficacy of using aprotinin [1], aminocaproic acid (Amicar (Xanodyne Pharmaceuticals, Inc, Newport, KY)) [2-4], and tranexamic acid TXA [5-8] in decreasing blood loss in scoliosis surgery. These agents are thought to decrease blood loss by their

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antifibrinolytic properties. These products have been effective in cardiac surgery [9,10], arthroplasty [11-13], and scoliosis surgery [1,3,4,6-8]. Previous studies demonstrated decreased blood loss when comparing the use of the antifibrinolytic agents with a control [2,4,6-8] in the spinal deformity population. Amicar decreased blood loss at an average of 400–600 mL/patient [4], and TXA by 40% [7], compared with controls.

The purpose of this study was to determine which antifibrinolytic agent used during posterior spinal fusion for scoliosis was more effective at minimizing perioperative blood loss and need for transfusion, using a prospective, randomized, double-blinded trial. Because previous studies have demonstrated the primary effect of Amicar to be in decreasing postoperative drainage [2], and because the researchers do not routinely use postoperative wound drains, the hypothesis was that TXA would be more effective at controlling blood loss in patients undergoing posterior spinal instrumentation and fusion than would Amicar.

Materials and Methods

The authors performed a single-center, prospective, randomized, double-blinded comparison between TXA and Amicar. After they obtained institutional review board approval, they offered enrollment int the study to all patients scheduled to undergo posterior spinal fusion by the pediatric spinal deformity service, from January 2009 to December 2010. Each patient was preoperatively evaluated by the pediatric blood avoidance service. This service consisted of pediatric intensivists and nurses with interest in minimizing pediatric patient exposure to allogenic blood products during high-risk procedures. During this evaluation, the study was explained and interested patients provided consent. Those refusing randomization were given the agent of choice of the anesthetist at the time of surgery, as was current practice; thus, all patients received Amicar or TXA, unless a contraindication for antifibrinolytic treatment was found. Preoperative laboratory values obtained included hemoglobin, platelets, prothrombin time (PT), partial prothrombin time (PTT), international normalized ratio (INR), and fibrinogen. The basic inclusion criterion for recruitment was a patient with idiopathic or neuromuscular scoliosis younger than 18 years of age, undergoing posterior spinal fusion. Medical exclusion criteria were inability to obtain a full consent, patient or parent refusal to participate, personal or family history of bleeding or clotting disorders, abnormal preoperative clotting studies or von Willebrand screen, patients at risk for clotting as a result of long-term oral contraceptive use, and severe immobility. Patients were routinely given back any salvage blood from the Cell Saver unit (Haemonetics, Braintree, MA). A standard transfusion trigger of hemoglobin less than 7 or patient symptomology was used throughout the study period. A study process flowchart (Appendix 1, Supplemental Digital Content 1) and our blood avoidance protocol (Appendix 2, Supplemental Digital Content 2) are available for review.

Method for assigning subjects to treatment groups

Upon consent to the study, randomization was performed by a member of the blood avoidance team using a block, blinded method. At least 24 hours in advance of surgery, the blood avoidance service (BAS) staff member drew an envelope and provided the pediatric staff pharmacist with a sealed envelope containing a drug-specific order set. The pharmacist prepared the study medication, labeled it as either study medication A or study medication B, and delivered it to the anesthesiologist in a fashion that was indistinguishable in terms of which drug was going to be used. The drug used in the study was blinded to all care providers (blood avoidance team, surgeon, anesthesiologist, and surgical and postoperative nursing staff) throughout the study period. Only the pharmacist knew what drug had been used. If the anesthesiologist or surgeon suspected drug-related side effects, the nature of the infusion was revealed.

Treatment regimen

A core group of pediatric staff pharmacists prepared medications for both treatment arms. All medications were prepared and secured in the pediatric satellite pharmacy. Medications were delivered by the pharmacy to the pediatric anesthesiologist before surgery. Amicar and TXA were diluted to a final concentration of 10 mg/mL. Whether using Amicar or TXA, the first syringe contained an initial bolus dose of 100 mg/kg, which was to be given once over 30 minutes at the beginning of the operative procedure. A second syringe was prepared for study medications A and B with the same final concentration of 10 mg/mL, and a continuous infusion was initiated to run at 10 mg/kg/hour for the duration of the surgical procedure. At the completion of the surgery, a third prepared syringe was started. The Amicar syringe contained the same contents as the second syringe, 10 mg/mL, and was run at the same rate of 10 mg/kg once over the next 24 hours postoperatively. (This is the routine method for Amicar administration postoperatively.) For the TXA group, the third syringe contained normal saline, which was infused at the same weight-based rate as calculated for Amicar over the next 24 hours postoperatively. The TXA was discontinued after the procedure because 90% of it is eliminated at 24 hours; however Amicar infusion must be continued postoperatively because it is excreted much faster, at 4 to 6 hours. The pediatric staff pharmacist notified nursing staff of the time the postoperative infusion was to be complete. Medications were recorded in the medication administration record as medication A or B.

All procedures were performed by the same 2 fellowship-trained orthopedic surgeons working simultaneous as a team. Typically, these procedures used electrocautery, subperiosteal dissection, topical hemostatic agents, and the Cell Saver blood salvage system. For the first patient, the