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The Spine Journal 15 (2015) 752–761

THE SPINE JOURNAL

Review Article

Efficacy of tranexamic acid on surgical bleeding in spine surgery: a meta-analysis

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Received 4 April 2014; revised 17 November 2014; accepted 8 January 2015

Abstract

BACKGROUND CONTEXT: Spine surgery is usually associated with large amount of blood loss, necessitating blood transfusions. Blood loss-associated morbidity can be because of direct risks, such as hypotension and organ damage, or as a result of blood transfusions. The antifibrinolytic, tranexamic acid (TXA), is a lysine analog that inhibits activation of plasminogen and has shown to be beneficial in reducing surgical blood loss.

PURPOSE: To consolidate the findings of randomized controlled trials (RCTs) investigating the use of TXA on surgical bleeding in spine surgery.

STUDY DESIGN: A metaanalysis.

STUDY SAMPLE: Randomized controlled trials investigating the effectiveness of intravenous TXA in reducing blood loss in spine surgery, compared with a placebo/no treatment group.

METHODS: MEDLINE, Embase, Cochrane controlled trials register, and Google Scholar were used to identify RCTs published before January 2014 that examined the effectiveness of intravenous TXA on reduction of blood loss and blood transfusions, compared with a placebo/no treatment group in spine surgery. Metaanalysis was performed using RevMan 5. Weighted mean difference with 95% confidence intervals was used to summarize the findings across the trials for continuous outcomes. Dichotomous data were expressed as risk ratios with 95% confidence intervals. A $p<.05$ was considered statistically significant.

RESULTS: Eleven RCTs were included for TXA (644 total patients). Tranexamic acid reduced intraoperative, postoperative, and total blood loss by an average of 219 mL ([−322, −116], $p<.05$), 119 mL ([−141, −98], $p<.05$), and 202 mL ([−299, −105], $p<.05$), respectively. Tranexamic acid led to a reduction in proportion of patients who received a blood transfusion (risk ratio

FDA device/drug status: Not approved for this indication (Tranexamic acid).

Author disclosures: ***TC:*** Nothing to disclose. ***SPM:*** Nothing to disclose. ***KB:*** Nothing to disclose. ***KS:*** Nothing to disclose. ***RNR:*** Nothing to disclose. ***VL:*** Stock Ownership: Nemaris, Inc.; Consulting: MSD (D); Speaking and/or Teaching Arrangements: MSD (D), DePuy (D), K2M (D); Board of Directors: Nemaris, Inc.; Research support (Investigator Salary, Staff/Materials): DePuy (D), ISSG (D), SRS (D), NIH (D, Paid directly to institution); Grants: DePuy (D), ISSG (D), SRS (D), NIH (No. 5R01AR0551764, D, Paid directly to institution). ***FJS:*** Royalties: MSD (D), K2M (D); Stock Ownership: Nemaris, Inc.; Consulting: MSD (D), Depuy (D), K2M (D); Speaking and/or Teaching Arrangements: MSD (D), Nemaris, Inc., K2M (D); Board of Directors: Nemaris, Inc.; Research support (Investigator Salary, Staff/Materials): DePuy (D), MSD (D), AO (B, Paid directly to institution); Grants: DePuy (D), MSD (D), AO (B, Paid directly to institution). ***BSL:*** Royalties: DePuy Spine; Stock Ownership: Paradigm Spine (9272 Units), Spine Search (5 Units); Private Investments: Paradigm Spine (E); Consulting: DePuy Spine (D); Speaking and/or Teaching Arrangements: DePuy Spine, K2M (C); Trips/Travel: K2M; Board of Directors: Spine Search (no value); Scientific Advisory Board/Other Office: DePuy Spine (no value); Grants: Setting Scoliosis Straight Foundation (D per year, Paid directly to institution), AOSpine (D, Paid directly to institution), John and Marcella Fox Fund (B, Paid directly to institution), OREF (C, Paid directly to institution). ***TJE:*** Royalties: K2M (F/year); Stock Ownership: Fastenetix (F/year); Speaking and/or Teaching Arrangements: K2M, DePuy (B); Trips/Travel: K2M (B); Research support (Investigator Salary, Staff/Materials): Paradigm Spine (F/year, Paid directly to institution), Fridolin (E/year, Paid directly to institution); Fellowship Support: OREF: Orthopaedic Research & Education Foundation (E/year, Paid directly to institution), OMEGA: Orthopedic Medical Education Grants Association (E/year, Paid directly to institution), AOSpine (E/year, Paid directly to institution).

The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

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http://dx.doi.org/10.1016/j.spinee.2015.01.013

0.67 [0.54, 0.83], p<.05) relative to placebo. There was one myocardial infarction (MI) in the TXA group and one deep vein thrombosis (DVT) in placebo.
CONCLUSIONS: Tranexamic acid reduces surgical bleeding and transfusion requirements in patients undergoing spine surgery. Tranexamic acid does not appear to be associated with an increased incidence of pulmonary embolism, DVT, or MI.

Keywords: Antifibrinolytics; Tranexamic acid; Epsilon-aminocaproic acid; Spine surgery; Blood loss; Transfusion rate; Adult spine deformity

Introduction

Spine surgery is usually associated with large amount of perioperative blood loss that may be attributed, at least in part, to the large wound surfaces, long operating times, and involvement of richly supplied cancellous bone. Although the amount of perioperative blood loss may vary widely across procedures, dependent on both surgical and nonsurgical factors, blood loss remains a major concern in the setting of spine surgery. Significant blood loss is associated with complications such as hypotension, end organ damage, or coagulopathy. Allogenic blood transfusions present additional risks, including hemolytic transfusion reactions, transfusion-related acute lung injuries, infection transmission, and immune modulation effects. Because of the significant risks and complications associated with blood loss and allogenic transfusions, efforts to identify safe and effective ways of minimizing blood loss during spine surgery are crucial.

Blood conservation strategies have been effectively used to reduce surgical bleeding and the need for allogenic transfusions in various surgical procedures. Such techniques include regional anesthesia, hypotensive anesthesia, intraoperative blood salvage, acute normovolemic hemodilution, and administration of intravenous, intramuscular, and oral medications [1,2]. Furthermore, the administration of antifibrinolytics, such as tranexamic acid (TXA) and epsilon-aminocaproic acid (EACA), has been shown to reduce bleeding in various surgeries including cardiac, trauma, hip, and knee arthroplasty, gynecological, and urologic procedures [3–11]. Tranexamic acid acts by competitively blocking the lysine-binding sites of plasminogen, thereby inhibiting fibrinolysis and blood clot degradation [8,10,12–16].

Recent research in spine surgery has demonstrated the efficacy of TXA to reduce perioperative blood loss and allogeneic blood transfusion in patients undergoing spine surgery, however, optimal dosing and duration is still unclear [2]. In spine surgery, the use of antifibrinolytics is not considered as routine. There are concerns regarding the safety profile of these drugs, including increased incidence of thromboembolic events, such as deep vein thromboses (DVTs), pulmonary embolisms (PEs), and myocardial infarctions (MIs), and increased incidence of seizures with moderate to high doses of TXA [17]. This metaanalysis investigated the efficacy of TXA on blood loss during spine surgery.

Methods

The metaanalysis was performed in accordance to published guidelines of the Cochrane Collaboration and Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) [18].

Literature search

Literature searches were conducted using MEDLINE, Cochrane central register of controlled trials, Embase, and Google Scholar by three independent reviewers. Medical Subject Heading terms included ‘‘tranexamic acid,’’ ‘‘epsilon-aminocaproic acid,’’ ‘‘amicar,’’ and ‘‘antifibrinolytics,’’ and the literature search was refined to randomized controlled trials (RCTs) in spine surgery. Reference lists of trials and reviews were also examined. No restrictions on language or publication year were applied. The last date of the search was December 31, 2013.

Study selection

A systematic review of medical literature was conducted for all RCTs that compared the efficacy of intravenous TXA with no or placebo treatment in spine surgery. All age groups were included. Studies were excluded if they were nonrandomized trials, retrospectively designed trials, or trials of low quality. Three reviewers independently selected eligible publications and any disagreement was settled by discussion with a fourth reviewer.

Validity assessment

Assessment of quality was done as outlined by Jadad et al. [19]. Assessments were conducted for each study by two independent reviewers and the criteria have been outlined in Table 1. Included studies were graded according to a three-category risk of bias scale. Studies that had a score of 0 to 1, 2 to 3, and 4 to 5 of a maximum score of 5 were classified to be of high, medium, and low bias, respectively. Studies graded as having a medium or high risk of bias were discussed among all reviewers to determine inclusion/exclusion.

Data collection and extraction

Each complete study report was thoroughly reviewed independently by two researchers to ensure that all data were collected entirely and accurately. The senior author made final decisions determining which studies would be