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Tranexamic Acid Treatment Reduces Blood Loss After Elective and Semi-Urgent Reverse Total Shoulder Arthroplasty

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Abstract

Introduction: Post operative blood loss after reverse shoulder arthroplasty (RSA) is associated with the need for blood transfusion and prolonged hospital stay, among other complications. Tranexamic acid (TXA) reduces perioperative blood loss and is effective when delivered systemically or locally. We compared the effects of TXA on perioperative blood loss between elective and semi-urgent RSA. **Methods:** We retrospectively reviewed patients who underwent either elective or semi-urgent RSA for fracture repair, with and without TXA treatment. Demographics, clinical records, and laboratory results were collected and analyzed to compare peripheral blood hemoglobin concentrations before and after surgery, the need for blood transfusion, and length of hospital stay between the 2 groups. **Results:** In a cohort of 158 patients, 91 (58%) underwent elective RSA. TXA was administered in 91 (58%) patients from the entire group. TXA administration was associated with a significant decrease in post operative hemoglobin concentration reduction in both the elective and fracture groups (P = .026 and P = .018, respectively), a significant decrease in post operative blood transfusion rates (P = .004 and P = .003, respectively), and a decrease in the need for prolonged hospitalization (P = .038 and P = .009, respectively). **Discussion:** The local application of TXA during RSA yielded a significant reduction in perioperative blood loss. We showed a significant positive effect of local TXA administration during RSA that is comparable for both elective and semi-urgent patients. Due to the baseline characteristics of fracture patients, their clinical benefits may be more notable. **Conclusions:** The positive outcomes for surgical patients with the use of TXA during RSA can possibly cause future consideration in clinical practice.

Keywords

reverse shoulder arthroplasty, tranexamic acid, postoperative blood loss

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Introduction

Reverse shoulder arthroplasty (RSA) has been gaining popularity in the last 2 decades, making it the most commonly performed shoulder arthroplasty globally.[1] Stability between the articular components of this semi-constrained prosthetic joint is achieved by distal traction of the arm, thereby creating a dead space. The increased dead space created by the change in anatomy in RSA may explain the excess blood loss. Together with other causes for blood loss such as the indication for surgery, patient characteristics and surgical technique, this dead space may potentially be filled with blood after surgery. Hence, both estimated blood loss and blood transfusion rates are

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significantly higher in patients who underwent RSA than in those who underwent anatomic shoulder arthroplasty.[2-5] Decreasing post operative bleeding after RSA may help reduce the incidence of these complications and facilitate the current trend of same-day surgery.

RSA is primarily designed to treat cuff tear arthropathy. The indications for RSA have expanded over time and it is currently widely used to treat comminuted fractures of the proximal humerus in older adults. In cases like these, surgery is performed shortly after trauma, and patients often presents with decreased baseline hemoglobin concentrations.[6]

Tranexamic acid (TXA) is an inexpensive and effective drug for reducing perioperative blood loss in joint arthroplasty surgery.[4,5,7-11] TXA inhibits plasminogen activation by binding plasmin to fibrin, leading to clot stabilization and reduced bleeding. TXA treatment has been used for more than 2 decades in hip and knee joint replacements and has been shown to be safely and effectively associated with decreased transfusion rates and shorter lengths of hospital stay.[7] Intravenous, oral, and topical administrations are similarly effective in primary and revision surgeries.[4] Despite early concerns, no increase in thrombotic and thromboembolic events have been linked to TXA administration, even in patients with a history of thrombotic events and other risk factors.[12] In recent years, TXA administration was shown effective in shoulder surgery, and specifically shoulder arthroplasty.[3,13,14]

Since lower preoperative hemoglobin, higher perioperative blood loss, and higher blood transfusion rates are associated with RSA in treatment of fractures, we hypothesized that perioperative TXA application may have critical clinical value for this subgroup of patients.

In this study, we aimed to compare the effects of TXA treatment on perioperative blood loss and transfusion rates between elective primary RSA and RSA in the treatment of acute fractures.

Methods

This retrospective cohort study was approved by the Institutional Review Board of our institution (IRB number: HMO-0514-19). The need for informed consent was waived due to the retrospective nature of the study.

Study Design

In September 2016, we incorporated the routine use of local TXA in shoulder arthroplasty, which is applied to the shoulder at the end of surgery. We reviewed the hospital records of the patients who underwent RSA between January 2014 and December 2019. Patients who underwent elective and semi-urgent primary RSA were included in the study. Patients who had undergone revision surgery were excluded. From this cohort, we excluded patients who underwent surgery for proximal humeral malunion following conservative or surgical treatment of fractures and those who underwent RSA following tumor resection. The reason for their exclusion was the variable nature of these procedures and excess soft tissue dissection compared with the standard surgical course of primary RSA.

Group Allocation

We divided the patients into 2 groups. The first group included patients who underwent RSA until August 2016, who did not receive TXA (non-TXA group), and the second included those who underwent RSA from September 2016 onwards with TXA treatment (TXA group). We further divided these groups according to the indication for surgery. Patients who underwent elective surgery for rotator cuff tear arthropathy, irreparable rotator cuff tear, osteoarthritis, or inflammatory arthritis comprised the first subgroup (elective group) and those who underwent semi-urgent surgery for acute proximal humeral fractures comprised the second subgroup (fracture group).

Surgical Technique

All surgical procedures were performed by 1 of 2 fellowship-trained orthopedic surgeons (O.S. and S.B.) in a beach chair position using a deltopectoral approach with a mechanical arm holder. The Delta Xtend (DePuy Synthes, Warsaw, IN, USA) and Aequalis (Wright, Memphis, TN, USA) RSA systems were used. The long head of the biceps tendon was tenotomized or tenodesed. In elective cases, the subscapularis was peeled off the lesser tuberosity to allow access to the joint, whereas in acute fractures, the tuberosities were separated and held by sutures through the corresponding rotator cuff tendons. The humeral head was then removed or cut at a 20° retroverted angle using an intramedullary guide. Glenoid exposure and capsular release were performed and a glenoid baseplate with a glenosphere was implanted. Next, the humerus was prepared and the humeral component inserted. When stable fixation could not be established using the press fit technique or the bone quality seemed compromised, cementation of the humeral component was performed. In elective cases, the subscapularis tendon was reattached to the lesser tuberosity. In acute fracture cases, the tuberosities were reattached to the proximal humerus using several no. 5 non-absorbable Ethibond sutures (Ethicon, Bridgewater, NJ, USA) through the proximal humerus bone, humeral implant, and rotator cuff.

Table 1. Patient Demographics.

	Elective (n = 91)	Fracture (n = 67)	*P*-Value
Sex female/male (%)	72/19 (79%/21%)	57/10 (85%/15%)	>.05
Age at time of surgery mean [standard deviation]	72.73 [8.53]	74.74 [6.93]	>.05
Antiplatelet or anticoagulation therapy yes/no (%)	42/49 (46.2%/53.8%)	26/41 (38.8%/61/2%)	>.05

Stability and range of motion were examined. A Hemovac drain (Zimmer Biomet, Warsaw, IN, USA) was placed in the shoulder joint, and the incision was closed in layers. The operated shoulder was immobilized using a brace for two–six weeks. Post operative blood transfusion in these elderly patients was indicated by a combination of clinically significant anemia as expressed by tachycardia, hypotension, reported dizziness and/or weakness associated with significant decrease from baseline hemoglobin or peripheral blood hemoglobin under 10 mg%.

TXA Administration

In the TXA group, 10 mL of 1000 mg TXA (Tel Aviv, Teva, Israel) was administered to the shoulder joint through the drain after wound closure. The drain was then sealed for 2 hours.

Data Collection

We reviewed all patients' data in the hospital registry, including demographics, medical illnesses, indications for surgery, preoperative and postoperative day 1 (POD 1) hemoglobin levels, and the number of blood units transfused. Post operative blood transfusion was indicated when peripheral blood hemoglobin <10 g% was associated with clinical signs and symptoms of tachycardia, hypotension, palpitations, and dizziness, among other relevant symptoms.

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corp, Armonk, NY, USA). The two-sample *t*-test was used to compare quantitative variables between the 2 groups. The Chi-square and Fisher's exact tests were applied to assess the association between categorical variables. A multivariate logistic regression model was used to simultaneously assess the effect of several variables on a dependent, dichotomous variable. Two-sided *P* values ≤.05 or less were considered statistically significant.

Results

We identified 182 patients who underwent RSA between January 2014 and December 2019 at our hospital. We excluded 24 patients who underwent surgery for fracture malunion or revision surgery. Therefore, our cohort comprised 158 patients. Sex, age at the time of surgery, and antiplatelet or anticoagulant use were not significantly different between patients in the elective and fracture groups (Table 1).

Study Group Characteristics

Elective RSA was performed on 91 patients (58%). Of those, 50 (32%) had irreparable massive rotator cuff tears or cuff tear arthropathy, and 41 (26%) had osteoarthritis of the glenohumeral joint. The remaining 67 patients (42%) underwent acute comminuted proximal humeral fracture repair. TXA was used in 59 patients (65%) in the elective group and 32 patients (48%) in the fracture group.

Hemoglobin Concentrations

In the elective group, the mean hemoglobin level decreased from 12.9 g% preoperatively to 10.781 g% on POD 1 in the non-TXA group and from 13.312 g% preoperatively to 11.626 g% on POD 1 in the TXA group. In the fracture group, the mean hemoglobin level decreased from 11.924 g% preoperatively to 9.818 g% on POD 1 in the non-TXA group and from 11.747 g% preoperatively to 10.222 g% on POD 1 in the TXA group. The decrease in hemoglobin concentrations was significantly smaller in the TXA group in both the elective and fracture groups (P = .026 and P = .018, respectively) (Table 2).

Blood Transfusions

In the elective group, blood transfusions were performed in 15.6% of the patients in the non-TXA, and no patients in the TXA group needed blood transfusion. In the fracture group, blood transfusions were performed in 47.1% of the patients in the non-TXA group and in 12.1% of the TXA group. This reduction in blood transfusion rates was significant in both the elective and fracture groups (P = .004 and P = .003, respectively; Table 3). We conducted multivariate analysis to identify the independent factors associated with the

Table 2. Perioperative Hemodynamics.

	Non-TXA (n = 67)	TXA (n = 91)	*P*-Value
Elective			
Mean pre-op Hgb (median) [SD]	12.919 (12.800) [1.149]	13.312 (13.300) [1.302]	**.026**
Mean POD 1 Hgb (median) [SD]	10.781 (11.050) [1.296]	11.626 (11.600) [1.182]	
Mean pre-op to POD 1 Hgb difference (median) [SD]	−2.137 (−2.050) [1.036]	−1.736 (−1.500) [1.017]	
Fracture			
Mean pre-op Hgb (median) [SD]	11.924 (12.050) [1.341]	11.747 (11.600) [1.670]	**.018**
Mean POD 1 Hgb (median) [SD]	9.818 (9.900) [1.084]	10.222 (10.500) [1.282]	
Mean pre-op to POD 1 Hgb difference mean (median) [SD]	−2.105 (−2.100) [1.543]	−1.525 (−1.350) [1.056]	
Total			
Mean pre-op Hgb (median) [SD]	12.406 (12.550) [1.339]	12.762 (12.900) [1.618]	**.016**
Mean POD 1 Hgb (median) [SD]	10.285 (10.400) [1.278]	11.121 (11.100) [1.388]	
Mean pre-op to POD 1 Hgb difference (median) [SD]	−2.121 (−2.100) [1.312]	−1.660 (−1.500) [1.030]	

[a]Peripheral blood hemoglobin (mean, median, and SD) before (preoperative) and 1 day after surgery (P-value using Mann-Whitney test).
SD, standard deviation; Hgb, hemoglobin; Pre-op, preoperative; POD 1, post operative day 1; TXA, tranexamic acid.

Table 3. Post Operative Blood Transfusion.

	Non-TXA (n = 67)	TXA (n = 91)	*P*-Value
Elective			
Patients requiring blood transfusion N (%)	5 (15.6)	0 (0)	**.004**
Fracture			
Patients requiring blood transfusion N (%)	16 (47.1)	4 (12.1)	**.003**
Total			
Patients requiring blood transfusion N (%)	21 (31.8)	4 (4.3)	**<.001**

[a]Blood transfusion following surgery in each subgroup-number and percentage of transfused patients-before [non-TXA] or after [TXA] incorporation of TXA into the standard treatment protocol (*P*-value according to Fisher's exact test).
TXA, tranexamic acid.

need for post operative blood transfusion. In this analysis, indication for surgery (elective vs fracture) and TXA administration were found to be significant independent factors ($P = .001$ and $P < .001$, respectively).

Perioperative Hospitalization

For the elective group, prolonged hospital stay (defined as hospitalization > 2 days, as per our surgical protocol) occurred in 46.9% of the patients in the non-TXA and 25.4% in the TXA group. In the fracture group, hospitalization > 2 days occurred in 76.5% of the patients in the non-TXA and in 45.5% of the TXA group. This reduction in hospitalization duration was significant in both the elective and fracture groups ($P = .038$ and $P = .009$, respectively; Table 4). We conducted a multivariate analysis to identify independent factors associated with the duration of hospitalization. Age, indication for surgery (elective vs fracture), and TXA administration were significant independent factors (P = .037, $P = .004$, and $P = .002$, respectively).

Discussion

In this retrospective cohort study, we found that the local administration of TXA during RSA was associated with a statistically significant reduction in perioperative blood loss. This was indicated by a significantly smaller decrease in hemoglobin concentrations and lower blood transfusion rates following surgery. We also found that the effect of TXA treatment was significant in both elective primary RSA and RSA performed for comminuted fractures of the proximal humerus in older adults. This supports a previously published study demonstrating the effectiveness of topical application of TXA in reducing blood loss, which was comparable to systemic administration.[13]

Since TXA is considered an effective treatment for reducing perioperative blood loss, it is commonly utilized in various arthroplasties of the knee, hip, and shoulder joints.[3,4,15] Carbone et al (2020) noted that the use of perioperative TXA administration in shoulder arthroplasty increased dramatically from nearly no use in 2010 to approximately 30% in 2016.[12] TXA administration has been shown to be safe with no associated increase in

Table 4. Hospitalization Days and Patients Requiring Prolonged Stay.

	Non-TXA (n = 67)	TXA (n = 91)	*P*-Value
Elective			
Days of post operative hospitalization			
Mean (median) [SD]	2.94 (2.00) [1.318]	2.27 (2.00) [.611]	**.038**
Patients requiring prolonged hospitalization N (%)	15 (46.9)	15 (25.4)	
Fracture			
Days of hospitalization			
Mean (median) [SD]	3.35 (3.00) [1.203]	3.09 (2.00) [1.809]	**.009**
Patients requiring prolonged hospitalization N (%)	26 (76.5)	15 (45.5)	
Total			
Days of hospitalization			
Mean (median)	3.15 (3.00) [1.268]	2.57 (2.00) [1.243]	**<.001**
Patients requiring prolonged hospitalization N (%)	42 (62.1)	30 (32.6)	

[a]Duration (mean, median, and SD) and need for prolonged hospitalization (number and percentage) in each subgroup before [non-TXA] or after [TXA] incorporation of TXA into the standard treatment protocol (*P*-value according to Pearson's chi-square test).
TXA, tranexamic acid.

thromboembolic events, even in patients with a documented history of either deep vein thrombosis, pulmonary emboli, myocardial infarction, renal disease, or ischemic stroke/transient ischemic attack.[12]

In a recent meta-analysis, Ye et al (2020) found that oral and intravenous administration of TXA had similar hemodynamic effects on primary hip and knee replacement patients with a significantly lower cost of the oral approach.[4] Zhang et al (2019) prospectively investigated the safety and efficacy of periarticular TXA injection following primary knee arthroplasty and compared it with intravenous administration. They showed that periarticular TXA injection and systemic administration had similar effects in lowering perioperative total blood loss. No delayed wound healing or increase in the risk of deep vein thrombosis and pulmonary emboli were found.[16] Yoon et al (2020) showed similar results in lowering blood loss when periarticular injection of TXA was used in RSA.[13] Our results are consistent with the current literature, which suggest a possible beneficial effect of periarticular TXA injection on blood loss following RSA.

Even though the effect of TXA on reducing blood loss following RSA was significant in both the elective and fracture groups TXA administration in RSA seems to be clinically more significant in acute fracture cases. This may be due to soft tissue injury in patients with fractures. In addition, patients who underwent acute surgery for fracture had significantly lower baseline preoperative hemoglobin levels (11.9 g% vs 12.9 g% respectively). Therefore, a higher number of patients in the fracture group, who were not treated with TXA, had clinically significant post operative anemia compared with non-TXA elective patients. While we are not aware of any relation between the utilization of drain and blood loss, we did use drains for the first 24 hours aiming to minimize hematoma and thereby reduce the risk of infection.

In a retrospective analysis of 265 shoulder arthroplasties, Burns et al (2019) reported that patients with a history of anemia, a preoperative hemoglobin concentration <10.9 g%, and an intraoperative estimated blood loss of 300 mL are at higher risk for transfusion after TSA.[17] In their study, these 3 factors were highly associated with blood transfusions, with a sensitivity of 80.0% and a specificity of 99.6%. Moreover, these 3 factors often characterize patients who undergo RSA,[18] and preoperative anemia and post operative blood loss are common in patients with fractures. Transfusion rate in our study is somewhat higher than reported in some (but not all) studies. Yet, transfusion policy did not change in our service during the study period. Same is true for the surgical skills of the 2 well experienced fellowship trained surgeons who performed all surgeries. It is therefore suggested that under similar conditions local application of TXA carries significant potential benefit for RSA patients and specifically when performed to treat complex fractures.

Prolonged hospitalization is a known indicator of a less favorable clinical course. In addition, it is associated with increased costs and burdens on the healthcare system. Assimilation of TXA treatment into our RSA protocol resulted in a 50% reduction in the number of patients requiring longer-than-routine hospitalization. The effect exerted by TXA was statistically significant for both elective and fracture patients, yet it was more prominent in fracture RSA cases.

Although the evidence does not support increased risk-associated systemic TXA administration,[13] some authors

suggest using topical or local TXA. In our study, TXA administration was associated with significantly lower post operative blood loss, which was more significant in the fracture group. Hence, topical use of TXA may obviate concerns that may still be associated with systemic administration of TXA in these patients.

The limitations of our study include the retrospective design and a medium-sized patient cohort. Despite these limitations, our results indicate a statistically significant positive effect related to local TXA use in RSA surgeries for both elective and fracture patients.

Conclusion

TXA reduces blood loss after RSA in both elective and fracture surgeries. Local TXA application in RSA for fracture repair seems to yield a significant clinical benefit due to the patients' baseline characteristics. Surgeons can safely consider incorporating TXA as part of their RSA protocol with the aim to improve patient outcomes.

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