formation or analgesic requirements when comparing patients with and without drain use [1].

In 2007, a Cochrane Database Systematic Review evaluated 36 studies regarding the use of closed suction surgical wound drainage after orthopaedic surgery and reported only one study specific to shoulder surgeries by Gartsman et al. [2]. This level II, randomized trial evaluated length of hospital stay, wound dehiscence, infection, reoperation rates and hematomas in patients undergoing TSA, hemiarthroplasty, rotator cuff repair and anterior shoulder instability surgery and found no differences between patients who did or did not receive a drain [3].

Overall, there are few available studies, and these are not sufficiently powered to detect a difference in infection rates after shoulder arthroplasty.

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QUESTION 4: What is the role of tranexamic acid (TXA) during primary or revision shoulder arthroplasty (SA) in decreasing the risk of periprosthetic joint infection (PJI)?

RECOMMENDATION: There is no evidence to support routine use of TXA in patients undergoing shoulder arthroplasty for the prophylaxis of PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Patients undergoing SA may experience variable degrees of perioperative bleeding and blood loss, which in the most severe cases, may result in complications including hematoma formation [1], acute symptomatic anemia and the need for blood transfusions [2–4]. It has been suggested that there is an association between blood transfusion and wound hematomas with postoperative morbidity, including periprosthetic infection [5,6]. While hematomas requiring surgery are uncommon with a reported rate of 0.3% [5], blood transfusions are more common with a reported rate of 4.3% to 6.7%. [3,4,7,8] Besides the costs, allogeneic blood transfusion is associated with rare but serious complications, including allergic and immune-mediated reactions, hemodynamic overload and risk of blood borne infections [9]. In addition, allogeneic blood transfusions may have an immunomodulatory effect [10] that may predispose to increased risk of periprosthetic infection rate, as seen in total hip or total knee arthroplasty [11] as well as in SA [6].

TXA is a synthetic anti-fibrinolytic agent that has been shown to be a successful and cost-effective agent for reducing blood loss and transfusion requirements for patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA) [12]. Two recent meta-analyses [13,14] of TXA use in patients undergoing primary SA found that TXA is an effective intervention to decrease blood loss as measured by drain output, change in hemoglobin (Hb) and total calculated blood loss. Nevertheless, the effectiveness of TXA in reducing transfusion rates after SA has been conflicting. One meta-analysis reported a benefit of TXA [14] in reducing blood transfusion while a second reported no differences in the transfusion rate when TXA was used perioperatively [13]. Possible reasons for conflicting results are (1) the inclusion of non-randomized studies with biased methodology, (2) a high rate of included studies with zero events of transfusion that were excluded from the calculation of the pooling effect and (3) when there are findings that are not conclusive, there is a lack of an additional analysis to further determine the conclusiveness of the results given the low rate of events. As a result, in order to evaluate the effectiveness of TXA to reduce transfusion rates, we performed a new systematic review and meta-analysis that included only randomized controlled trials (RCT), which compared the use of TXA compared to placebo in patients undergoing SA. This meta-analysis considered the primary outcomes to be the effect of TXA upon transfusion rates, formation of hematomas and thromboembolic events. Secondary outcomes included blood loss as measured by drain output, change of Hb and calculated total blood loss.

Methods

The methodology described in the Cochrane Handbook for Systematic Reviews of Interventions [15] was followed to conduct this review and was reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [16]. Cochrane Central Register of Controlled Trials, Embase and Medline were searched up to March 15, 2018. Four RCTs [17–20] involving 375 patients undergoing primary SA were included. The risk of bias of the included studies was assessed and the pooled risk estimates were calculated with random-effect models. For the primary outcomes (transfusion rate and thromboembolic complications), as most of the trials had no events in the tranexamic acid or control group (zero-event studies), a 0.5 continuity correction was used to include data from those RCTs [21]. A trial sequence analysis was conducted to assist in the interpretation of the conclusiveness of the meta-analysis for the effect of TXA in the risk of blood transfusions. The quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results

This meta-analysis confirmed previous meta-analysis results and found that TXA is associated with significantly lower perioperative blood loss compared with placebo and that there is no higher risk of thromboembolic events with TXA (Table 1). However, this meta-analysis found that there was no significant difference for the risk of

TABLE 1. Summary of findings

Outcome No. of Participants (Studies)	Relative Effect (95% CI)	Anticipated Absolute Effects (95% CI)			Certainty
		Without TXA	With TXA	Difference	
Rate of blood transfusion (Transfusion) assessed with: Number of patients who received a postoperative transfusion of packed red blood cells No. of participants: 375 (4 RCTs)	**RR 0.53** (0.17 to 1.64)	**Study population**			⊕⊕ O O LOW [a,b]
		3.7%	**2.0%** (0.6% to 6.1%)	**1.8% fewer** (3.1% fewer to 2.4% more)	
		Low-risk transfusion patients*			
		1.0%	**0.5%** (0.2% to 1.6%)	**0.5% fewer** (0.8% fewer to 0.6% more)	
		High-risk transfusion patients*			
		15.0%	**8.0%** (2.6% to 24.6%)	**7.0% fewer** (12.4% fewer to 9.6% more)	
Thromboembolic complications (TEC) assessed with: Number of patients that developed a thromboembolic complication during follow-up (DVT, PE, Stroke) No. of participants: 375 (4 RCTs)	**RR 0.70** (0.11 to 4.38)	0.5%	**0.4%** (0.1% to 2.3%)	**0.2% fewer** (0.5% fewer to 1.8% more)	⊕⊕⊕O MODERATE
Total blood loss (TBL) assessed with: Estimation of total blood loss with Good's and Nadler's formula No. of participants: 264 (3 RCTs)	-	The mean total blood loss was **1344** ml	-	MD **279.5 ml lower** (411.7 ml lower to 147.3 ml lower)	⊕⊕⊕⊕ HIGH
Postoperative blood loss (PBL) assessed with: Drain output in milliliters (first 24 hours) follow up: mean 1 days No. of participants: 267 (3 RCTs)	-	The mean postoperative blood loss was **216** ml	-	MD **105.4 ml lower** (161.4 ml lower to 49.4 ml lower)	⊕⊕⊕⊕ HIGH
Decrease in hemoglobin (Hemoglobin change) assessed with: Change of preoperative versus lower postoperative hemoglobin (g/dL) No. of participants: 267 (3 RCTs)	-	The mean decrease in hemoglobin was **3.32** g/dL	-	MD **0.7 g/dL lower** (1 g/dL lower to 0.39 g/dL lower)	⊕⊕⊕⊕ HIGH

CI, confidence interval; RCT, randomized control trials; TXA, tranexamic acid

* These numbers were estimated from the literature, considering the rate of transfusion along with a low and high risk of transfusion.

a. The confidence interval crosses the clinical decision threshold between recommending and not recommending tranexamic acid (RR=1 meaning no difference in the rate of transfusion between tranexamic acid and placebo).

b. The accrued sample size of the meta-analysis is underpowered. The estimated optimal sample size with an alpha error of 5%, 80% of power and RRR of 57.4% with a basal risk of 3.7%, was 1555 patients.

Hematoma formation was assessed as an outcome, but it was not included in this table as there were only one trial that reported results.

blood transfusion after SA when comparing TXA with placebo (risk rate 0.53, 95% confidence interval 0.17 to 1.64). Due to the fact that the rate of transfusion after SA is low, the current data is too sparse to provide conclusive evidence for the effect of TXA on blood transfusions. In addition, there is insufficient evidence for the effect of TXA upon hematoma formation or other clinical outcomes after SA.

Conclusion

While this meta-analysis confirmed the effect of TXA in decreasing blood loss, the evidence for its effects on direct clinically important outcomes like rate of transfusions or hematoma formation was inconclusive. Blood loss is a surrogate outcome and there are no defined thresholds to associate a determined amount of blood loss to those clinically important outcomes.

The use of TXA in patients at high risk for transfusion or patients undergoing complex revision arthroplasty has not been adequately studied. Patients at high risk for transfusions include those with low preoperative Hb and hematocrit levels (Hb < 13 g/dL and hematocrit < 39.6%) [3,7,8,22,23], operative time longer than 5 hours [24], surgery with a diagnosis of posttraumatic or rheumatoid arthritis [2,3], and patients with diabetes or ischemic heart disease [8,24]. The use of TXA in these at-risk populations might be justified given the higher baseline risk of transfusion and the greater impact of blood loss. However, this is a recommendation that is weak and limited by the lack of direct evidence. Further study of TXA in these higher risk patients is warranted.

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1.3. PREVENTION: PATIENT CHARACTERISTICS

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QUESTION 1: What is the role of medical comorbidities as potential risk factors for periprosthetic joint infection (PJI) following primary or revision total shoulder arthroplasty (TSA)?

RECOMMENDATION: Specific patient medical comorbidities and demographic factors are potential risk factors for shoulder PJI and appropriate preoperative evaluation and perioperative management should be standard practice.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)