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QUESTION 5: Does the use of tranexamic acid (TXA) reduce blood loss and need for allogeneic blood transfusion during primary total joint arthroplasty (TJA)?

RECOMMENDATION: Yes. The administration of intravenous (IV), topical and/or oral TXA is an effective strategy for reducing blood loss and the need for allogeneic transfusion during primary TJA.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 98%, Disagree: 1%, Abstain: 1% (Unanimous, Strongest Consensus)

RATIONALE

Blood loss in primary TJA, especially total hip arthroplasty (THA), can be significant and is often under-estimated due to hidden blood loss [1–3]. Postoperative blood transfusion rates due to blood loss is estimated to be about 11% for total knee arthroplasty (TKA) and 18% for THA [1]. Therefore, several methods have been utilized to help reduce the risk of blood loss and need for allogeneic transfusion.

After discovery of the antifibrinolytic properties of TXA in the early 1960s by Shosuke and Utako Okamoto, TXA has become widely used in many medical specialties [4,5]. Benoni et al. were the first to publish on the blood conserving properties of TXA in orthopaedic surgery [6]. Ever since their original publication, a growing body of literature has been published on the use of intravenous, topical and oral TXA in primary hip and knee arthroplasty. The overwhelming results from these studies and subsequent meta-analyses have demonstrated that TXA is a safe and effective method for reducing blood loss and the need for allogeneic blood transfusion.

IV TXA has been the most popular and widely-studied formulation in total joint arthroplasty with a recent literature search identifying more than 40 randomized clinical trials comparing intravenous TXA and placebo in primary TJA. Meta-analysis by Sukeik et al. and Yang et al. have proven the effectiveness of intravenous TXA compared to placebo in the setting of primary hip and knee arthroplasty [7,8].

Topical TXA is seen as an alternative to intravenous and oral routes of administration to provide local drug delivery. In two parallel-randomized control trials, Alshryda et al. investigated topical TXA in the setting of primary hip and knee arthroplasty by administering intra-articular 1 gm TXA or an equivalent volume of saline placebo [9,10]. Both studies provided evidence that topical TXA reduces the absolute risk for blood transfusion and reduces blood loss in primary hip and knee arthroplasties [9,10]. A systematic review and meta-analysis of 14 studies demonstrated similar results of a significant reduction in blood loss and need for transfusion when topical TXA was used compared to placebo, without an increase risk of complications [11]. When topical and intravenous TXA have been compared in a randomized clinical trial, Gomez-Barrena et al. found topical TXA in primary TKA demonstrated noninferiority to intravenous TXA [12].

The use of oral TXA during primary TJA was explored recently. The study by Irwin et al. reports on the use of oral TXA during a national shortage of IV TXA. The comparison of the data in their retrospective cohort demonstrated a lower odds ratio for transfusion when oral TXA was used [13]. Fillingham et al. and Kayupov et al. performed similar randomized clinical trials in primary hip and knee arthroplasties comparing a dose of 1 gm IV to 2 gm oral TXA, which demonstrated statistical equivalence with regard to reduction in blood loss and the need for allogeneic blood transfusion [14,15]. A systemic review and meta-analysis by Zhang et al. of six studies demonstrated lower hemoglobin drop, blood loss and transfusion rate in patients receiving oral TXA compared to the placebo group without increasing the risk of complications [16]. Another meta-analysis by the same author Zhang et al. comparing oral versus IV application of TXA concluded that oral TXA is cost efficient and convenient and has similar effects on reducing blood loss and transfusion rate as IV TXA [17].

More recently, the American Association of Hip and Knee Surgeons, American Academy of Orthopaedic Surgeons, Hip Society, Knee Society and American Society of Regional Anesthesia and Pain Medicine worked together to create a clinical practice guideline on the use of TXA in TJA [18]. The efficacy recommendations of the clinical practice guidelines found with a strong recommendation that all formulations (IV, topical and oral) TXA are superior to placebo and equivalent amongst each other in terms of blood sparing properties [18]. Additionally, the clinical practice guidelines cited with a strong recommendation that higher doses and/or multiple doses of any formulation of TXA does not provide reduced blood loss and/or risk of transfusion [18]. The only moderate strength recommendation regarding the efficacy of TXA in primary TJA was the recommendation in favor of the pre-incision dosing of IV TXA [18].

Given the overwhelming literature supporting the blood conservation properties of TXA, we conclude that all formulations and dosing regimens are effective in minimizing blood loss and reducing the need for allogeneic blood transfusions in primary hip and knee arthroplasties.

REFERENCES

[1] Carling MS, Jeppsson A, Eriksson BI, Brisby H. Transfusions and blood loss in total hip and knee arthroplasty: a prospective observational study. J Orthop Surg Res. 2015;10:48. doi:10.1186/s13018–015–0188–6.

[2] Liu X, Zhang X, Chen Y, Wang Q, Jiang Y, Zeng B. Hidden blood loss after total hip arthroplasty. J Arthroplasty. 2011;26:1100–1105.e1. doi:10.1016/j.arth.2010.11.013.

[3] Sehat KR, Evans R, Newman JH. How much blood is really lost in total knee arthroplasty?. Correct blood loss management should take hidden loss into account. Knee. 2000;7:151–155.

[4] Okamoto S, Okamoto U. Amino–methyl–cyclohexane–carboxylic acid: AMCHA. Keio J Med. 1962;11:105–115. doi:10.2302/kjm.11.105.

[5] Okamoto S, Sato S, Takada Y, Okamoto U. An active stereo–isomer (trans–form) of AMCHA and its antifibrinolytic (antiplasminic) action in vitro and in vivo. Keio J Med. 1964;13:177–185.

[6] Benoni G, Carlsson A, Petersson C, Fredin H. Does tranexamic acid reduce blood loss in knee arthroplasty? Am J Knee Surg. 1995;8:88–92.

[7] Sukeik M, Alshryda S, Haddad FS, Mason JM. Systematic review and meta–analysis of the use of tranexamic acid in total hip replacement. J Bone Joint Surg Br. 2011;93:39–46. doi:10.1302/0301–620X.93B1.24984.

[8] Yang ZG, Chen WP, Wu LD. Effectiveness and safety of tranexamic acid in reducing blood loss in total knee arthroplasty: a meta–analysis. J Bone Joint Surg Am. 2012;94:1153–1159. doi:10.2106/JBJS.K.00873.

[9] Alshryda S, Mason J, Vaghela M, Sarda P, Nargol A, Maheswaran S, et al. Topical (intra–articular) tranexamic acid reduces blood loss and transfusion rates following total knee replacement: a randomized controlled trial (TRANX–K). J Bone Joint Surg Am. 2013;95:1961–1968. doi:10.2106/JBJS.L.00907.

[10] Alshryda S, Mason J, Sarda P, Nargol A, Cooke N, Ahmad H, et al. Topical (intra–articular) tranexamic acid reduces blood loss and transfusion rates following total hip replacement: a randomized controlled trial (TRANX–H). J Bone Joint Surg Am. 2013;95:1969–1974. doi:10.2106/JBJS.L.00908.
[11] Alshryda S, Sukeik M, Sarda P, Blenkinsopp J, Haddad FS, Mason JM. A systematic review and meta–analysis of the topical administration of tranexamic acid in total hip and knee replacement. Bone Joint J. 2014;96–B:1005–1015. doi:10.1302/0301–620X.96B8.33745.
[12] Gomez–Barrena E, Ortega–Andreu M, Padilla–Eguiluz NG, Pérez–Chrzanowska H, Figueredo–Zalve R. Topical intra–articular compared with intravenous tranexamic acid to reduce blood loss in primary total knee replacement: a double–blind, randomized, controlled, noninferiority clinical trial. J Bone Joint Surg Am. 2014;96:1937–1944. doi:10.2106/JBJS.N.00060.
[13] Irwin A, Khan SK, Jameson SS, Tate RC, Copeland C, Reed MR. Oral versus intravenous tranexamic acid in enhanced–recovery primary total hip and knee replacement: results of 3000 procedures. Bone Joint J. 2013;95–B:1556–1561. doi:10.1302/0301–620X.95B11.31055.
[14] Fillingham YA, Kayupov E, Plummer DR, Moric M, Gerlinger TL, Della Valle CJ. The James A. rand young investigator's Award: a randomized controlled trial of oral and intravenous tranexamic acid in total knee arthroplasty: the same efficacy at lower cost? J Arthroplasty. 2016;31:26–30. doi:10.1016/j.arth.2016.02.081.
[15] Kayupov E, Fillingham YA, Okroj K, Plummer DR, Moric M, Gerlinger TL, et al. Oral and intravenous tranexamic acid are equivalent at reducing blood loss following total hip arthroplasty: a randomized controlled trial. J Bone Joint Surg Am. 2017;99:373–378. doi:10.2106/JBJS.16.00188.
[16] Zhang LK, Ma JX, Kuang MJ, Zhao J, Lu B, Wang Y, et al. The efficacy of tranexamic acid using oral administration in total knee arthroplasty: a systematic review and meta–analysis. J Orthop Surg Res. 2017;12:159. doi:10.1186/s13018–017–0660–6.
[17] Zhang LK, Ma JX, Kuang MJ, Zhao J, Wang Y, Lu B, et al. Comparison of oral versus intravenous application of tranexamic acid in total knee and hip arthroplasty: a systematic review and meta–analysis. Int J Surg. 2017;45:77–84. doi:10.1016/j.ijsu.2017.07.097.
[18] Fillingham YA, Jevsevar DS, Yates AJ, Sayeed SA, Sah AP, Bini SA, et al. Tranexamic acid in total joint arthroplasty: the clinical practice guides of the American Association of Hip and Knee Surgeons, American Academy of Orthopaedic Surgeons, Hip Society, Knee Society, American Society of Regional Anesthesia and Pain Medicine. 2017.