

Chapter 2

THE SAFETY AND EFFICACY OF TRANEXAMIC ACID IN TOTAL JOINT ARTHROPLASTY

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INTRODUCTION

Tranexamic acid is a synthetic derivative of the amino acid lysine and competitive inhibitor of plasminogen activation that interferes with fibrinolysis (Yang, Chen and Wu, 2012). Tranexamic acid inhibits fibrinolysis by blockage of lysine binding receptors on plasminogen molecules. It inhibits activation of plasminogen by preventing plasmin from binding fibronogen and fibrin (Dunn and Goa, 1999). Tranexamic acid can decrease extensive delayed bleeding by acting on fibrinolytic system (Dunn and Goa, 1999).

TRANEXAMIC ACID IN ARTHROPLASTIES

Joint arthroplasties are most commonly performed orthopaedic operations. Postoperative anemia is a common problem in these patients. Blood transfusion was required in many patients. Half of these patients require blood product transfusion during perioperative period (Bozic et al, 2005). Immunosuppression, transfusion reaction, cost and also increased risk of periprosthetic joint infection are the negative effects of blood transfusion (Lange, van Aken and Westphal, 2007; Fraser et al, 2008; Ramsey, Smith and Flynn, 2006; Tobias, 2004; Pulido et al, 2008). Variable methods can be used to prevent transfusion risk and transfusion amount. Tranexamic acid can be used in total knee arthroplasties and total hip arthroplasties for these purposes.

American Association of Hip and Knee Surgeons (AAHKS), the American academy of orthopaedic surgeons (AAOS), the Hip society, the Knee society, and the American Society of Regional Anesthesia and Pain Medicine

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In high risk patients for thromboembolic events (Venous thromboembolism history, myocardial infarction history with stent, cerebrovascular occlusive disease) clinicians concern using antifibrinolytic medication which limit the use of tranexamic acid (Dai et al, 2011). Whitining et al studied on high risk patients to address tranexamic acid use in these patients (Whitining et al, 2014). Duncan et al reported that use of tranexamic acid in total knee arthroplasty and total hip arthroplasty could result in greater cost savings and may reduce transfusion related complications in patients with higher morbidity (Duncan et al, 2015). Although high risk patients should be considered individually with multidisciplinary approach for tranexamic acid usage (Fillingham et al, 2018a). Future research must be done to determine the safety of tranexamic acid in high risk patients.

CONCLUSION

Tranexamic acid should be used in total joint arthroplasty to reduce the risk of transfusion and to reduce blood loss. The route of administration doesn't affect the efficacy of tranexamic acid. The dose of tranexamic acid was not found to significantly affect its efficacy. Tranexamic acid administration is safe in patients without a history of venous thromboembolism.

REFERENCES

1. Alshryda S, Mason J, Sarda P, Nargol A, Cooke N, Ahmad H, Tang S, Logishetty R, Vaghela M, McPartlin L, Hungin AP. (2013). Topical (intra-articular) tranexamic acid reduces blood loss and transfusion rates following total hip replacement: a randomized controlled trial (TRANX-H). *The Journal of Bone and Joint Surgery Am*, 95(21), 1969-74.
2. Alvarez JC, Santiveri FX, Ramos I, Vela E, Puig L, Escolano F. (2008). Tranexamic acid reduces blood transfusion in total knee arthroplasty even when a blood conservation program is applied. *Transfusion*, 48(3), 519-25.
3. Barrachina B, Lopez-Picado A, Remon M, Fondarella A, Iriarte I, Bastida R, Rodríguez-Gascón A, Achaerandio MA, Iturricastillo MC, Aizpuru F, Valero CA, Tobalina R, Hernanz R.(2016). Tranexamic Acid Compared with Placebo for Reducing Total Blood Loss in Hip Replacement Surgery: A Randomized Clinical Trial. *Anesth Analg*, 122(4), 986-95.
4. Bozic KJ, Katz P, Cisternas M, Ono L, Ries MD, Showstack J.(2005). Hospital resource utilization for primary and revision total hip arthroplasty. *Journal of Bone and Joint Surgery Am*, 87(3), 570-576.

5. Camarasa MA, Ollé G, Serra-Prat M, Martín A, Sánchez M, Ricós P, Pérez A, Opisso L.(2006). Efficacy of aminocaproic, tranexamic acids in the control of bleeding during total knee replacement: a randomized clinical trial. *Br J Anaest*, 96(5), 576-82.
6. Carvalho LH Jr, Frois Temponi E, Machado Soares LF, Gonçalves MB, Paiva Costa L, Tavares de Souza ML. (2015). Bleeding reduction after topical application of tranexamic acid together with Betadine solution in total knee arthroplasty. A randomised controlled study. *Orthop Traumatol Surg Res*, 101(1), 83-7.
7. Dai L, Bevan D, Rangarajan S, Sørensen B, Mitchell M.(2011). Stabilization of fibrin clots by activated prothrombin complex concentrate and tranexamic acid in FVIII inhibitor plasma. *Haemophilia*, 17(5), 944-8.
8. Duncan CM, Gillette BP, Jacob AK, Sierra RJ, Sanchez-Sotelo J, Smith HM.(2015). Venous thromboembolism and mortality associated with tranexamic acid use during total hip and knee arthroplasty. *The Journal of Arthroplasty*, 30(2), 272-6.
9. Dunn CJ, Goa KL. (1999). Tranexamic acid: a review of its use in surgery and other indications. *Drugs*, 57(6), 1005-1032.
10. Fraser IS, Porte RJ, Kouides PA, Lukes AS. (2008). A benefit-risk review of systemic haemostatic agents: part 2: in excessive or heavy menstrual bleeding. *Drug Saf*, 31(3), 217.
11. Fillingham YA, Ramkumar DB, Jevsevar DS, Yates AJ, Bini SA, Clarke HD, Schemitsch E, Johnson RL, Memtsoudis SG, Sayeed SA, Sah AP, Della Valle CJ. (2018a). Tranexamic Acid Use in Total Joint Arthroplasty: The Clinical Practice Guidelines Endorsed by the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society. *The Journal of Arthroplasty*,33(10), 3065-3069.
12. Fillingham YA, Ramkumar DB, Jevsevar DS, Yates AJ, Shores P, Mullen K, Bini SA, Clarke HD, Schemitsch E, Johnson RL, Memtsoudis SG, Sayeed SA, Sah AP, Della Valle CJ. (2018b). The Efficacy of Tranexamic Acid in Total Knee Arthroplasty: A Network Meta-Analysis. *The Journal of Arthroplasty*,33(10), 3090-3098.
13. Fillingham YA, Ramkumar DB, Jevsevar DS, Yates AJ, Shores P, Mullen K, Bini SA, Clarke HD, Schemitsch E, Johnson RL, Memtsoudis SG, Sayeed SA, Sah AP, Della Valle CJ. (2018c). The Efficacy of Tranexamic Acid in Total Hip Arthroplasty: A Network Meta-analysis. *The Journal of Arthroplasty*,33(10), 3083-3089.
14. George DA, Sarraf KM, Nwaboku H. (2015). Single perioperative dose of tranexamic acid in primary hip and knee arthroplasty. *Eur J Orthop Surg Traumatol*, 25(1), 129-33.
15. Gilbody J, Dhotar HS, Perruccio AV, Davey JR. (2014). Topical tranexamic acid reduces transfusion rates in total hip and knee arthroplasty. *The Journal of Arthroplasty*, 29 (4), 681-684.
16. Good L, Peterson E, Lisander B. (2003). Tranexamic acid decreases external blood loss but not hidden blood loss in total knee replacement. *British Journal of Anaesthesia*, 90, 596-9.
17. Hourlier H, Fennema P.(2014). Single tranexamic acid dose to reduce perioperative morbidity in primary total hip replacement: a randomised clinical trial. *Hip Int*, 24(1), 63-8.
18. Imai N, Dohmae Y, Suda K, Miyasaka D, Ito T, Endo N.(2012). Tranexamic acid for reduction of blood loss during total hip arthroplasty. *The Journal of Arthroplasty*, 27(10), 1838-43.

19. Jansen AJ, Andreica S, Claeys M, D'Haese J, Camu F, Jochmans K.(1999). Use of tranexamic acid for an effective blood conservation strategy after total knee arthroplasty. *Br J Anaesth*. 1999, 83(4), 596-601.
20. Konig G, Hamlin BR, Waters JH.(2013). Topical tranexamic acid reduces blood loss and transfusion rates in total hip and total knee arthroplasty. *The Journal of Arthroplasty*, 28(9), 1473-6.
21. Lange M, Van Aken H, Westphal M. (2007). Prevention and treatment of major blood loss. *New England Journal of Medicine*, 357(12), 1260.
22. Lin PC, Hsu CH, Chen WS, Wang JW.(2011). Does tranexamic acid save blood in minimally invasive total knee arthroplasty?. *Clinical Orthopaedics and Related Research*, 469(7), 1995-2002.
23. Maniar RN, Kumar G, Singhi T, Nayak RM, Maniar PR. (2012). Most effective regimen of tranexamic acid in knee arthroplasty: a prospective randomized controlled study in 240 patients. *Clinical Orthopaedics and Related Research*, 470(9), 2605-12.
24. Martin JG, Cassatt KB, Kincaid-Cinnamon KA, Westendorf DS, Garton AS, Lemke JH.(2014). Topical administration of tranexamic acid in primary total hip and total knee arthroplasty. *The Journal of Arthroplasty*, 29(5), 889-94.
25. Nadler SB, Hidalgo JH, Bloch T. (1962). Prediction of blood volume in normal human adults. *Surgery*, 51, 224-232.
26. Nilsson IM. (1980). Clinical pharmacology of aminocaproic and tranexamic acids. *J Clin Pathol Suppl (R Coll Pathol)*, 14, 41-7.
27. Orpen NM, Little C, Walker G, Crawford EJ. Tranexamic acid reduces early post-operative blood loss after total knee arthroplasty: a prospective randomised controlled trial of 29 patients. *Knee*, 13(2):106-10.
28. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. (2008). Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clinical Orthopaedics and Related Research*, 466(7), 1710.
29. Ramsey EZ, Smith KM, Flynn JD.(2006). Prophylaxis of perioperative blood loss. *Orthopedics*, 29(8), 689.
30. Roy SP, Tanki UF, Dutta A, Jain SK, Nagi ON.(2012). Efficacy of intra-articular tranexamic acid in blood loss reduction following primary unilateral total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc*, 20(12), 2494-501.
31. Sarzaem MM, Razi M, Kazemian G, Moghaddam ME, Rasi AM, Karimi M. (2014). Comparing efficacy of three methods of tranexamic acid administration in reducing hemoglobin drop following total knee arthroplasty. *The Journal of Arthroplasty*, 29(8), 1521-4.
32. Surgeons AAoO. *AAOS clinical practice guideline and systematic review methodology*. https://www.aaos.org/uploadedFiles/PreProduction/Quality/Guidelines_and_Reviews/guidelines/Guideline%20and%20Systematic%20Review%20Processes_v2.0_Final.pdf
33. Tobias JD. (2004). Strategies for minimizing blood loss in orthopedic surgery. *Semin Hematol*. 41(1), 145.
34. Whiting DR, Gillette BP, Duncan C, Smith H, Pagnano MW, Sierra RJ.(2014). Preliminary results suggest tranexamic acid is safe and effective in arthroplasty patients with severe comorbidities. *Clinical Orthopaedics and Related Research*, 472(1), 66-72.
35. Wind TC, Barfield WR, Moskal JT. (2014). The effect of tranexamic acid on transfusion rate in primary total hip arthroplasty. *The Journal of Arthroplasty*, 29(2), 387-9.

36. Wong J, Abrishami A, El Beheiry H, Mahomed NN, Roderick Davey J, Gandhi R, Syed KA, Muhammad Ovais Hasan S, De Silva Y, Chung F.(2010). Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. *Journal of Bone and Joint Surgery Am*, 92(15), 2503-13.
37. Yang ZG, Chen WP, Wu LD. (2012). Effectiveness and safety of tranexamic acid in reducing blood loss in total knee arthroplasty: a meta-analysis. *The Journal of Bone and Joint Surgery Am*, 94,1153-9.
38. Yue C, Kang P, Yang P, Xie J, Pei F.(2014). Topical application of tranexamic acid in primary total hip arthroplasty: a randomized double-blind controlled trial. *The Journal of Arthroplasty*, 29(12), 2452-6.