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Application of Transexamic Acid in Total Hip Arthroplasty: Review of Current Concepts

Adel Ebrahimpour,[1] Mehrdad Sadighi,[2,*] Mohsen Karami,[1] Mohammad Reza Minator Sajadi,[2] Reza Zandi,[2] and Amin Karimi[2]

[1]Associated Professor of Orthopedic Surgery, Taleghani Hospital, Shahid Beheshti Medical University of Sciences, Tehran, Iran
[2]Assistant Professor of Orthopedic Surgery, Taleghani Hospital, Shahid Beheshti Medical University of Sciences, Tehran, Iran

[*]*Corresponding author*: Mehrdad Sadighi, Taleghani Hospital, Shahid Beheshti Medical University of Sciences, Tehran, Iran. E-mail: mehrdadsadighi92@gmail.com

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Abstract

The purpose of this study was to assess the current concepts of the application of transexamic acid (TXA) in total hip arthroplasty. Perioperative blood loss in patients who undergo hip arthroplasty is a serious problem. Most patients are old and their cardiovascular system cannot easily tolerate hypovolemia. A literature review of 25 papers on TXA use in hip arthroplasty, to assess efficacy and cost-effectiveness of TXA, as well as the risk of thrombotic events may be useful. Our literature review is based on searching TXA and hip arthroplasty related articles in PubMed, Scopus, and Google Scholar. We focused on large meta-analysis articles and randomized clinical trials. Current concepts recommend routine application of TXA in hip arthroplasty, if no contraindications exist.

Keywords: Transexamic Acid, Total Hip Arthroplasty, Blood Loss, Deep Vein Thrombosis

1. Background

Perioperative blood loss is an important concern in patients undergoing total hip arthroplasty (THA); up to 37% of patients require blood transfusion for postoperative anemia (1). The average blood loss during primary THA is between 1,000 and 2,000 mL (2). The purpose of this review article study was to assess the role of TXA in THA and its side effects.

2. Introduction

TXA was discovered in 1962 by 2 independent research groups (3, 4). They found that TXA had antifibrinolytic properties. TXA indirectly blocks the degradation of fibrin by a reversible interaction with plasminogen and plasmin (5, 6). Increased fibrinolytic activity is a contributing factor for increased blood loss during THA (7). TXA prevents the binding of fibrin to the plasminogen-plasmin tissue activator complex, and thus blocks the degradation of fibrin (8, 9). The half-life of intravenous TXA is estimated to be between 80 and 120 minutes (10). TXA rapidly penetrates the synovial fluid and membranes, reaching the same concentration in plasma in just 15 minutes after IV administration (11). Rapid penetration into the synovial membrane and relatively long half-life with reversible temporary effects are among the specifications of TXA that can make it useful in reducing blood loss in hip arthroplasties.

TXA application is contraindicated in active thromboembolic disease, a history of intrinsic risk of thrombosis, and patients with hypersensitivity to tranexamic acid (12).

3. Efficacy of TXA in Total Hip Arthroplasty

We found many articles in our review, especially meta-analysis, which confirmed diminished blood loss with TXA use. In a retrospective cohort study using the US population-based data of 872416 THA and TKA procedures, Poeran et al. determined the effectiveness and safety of different doses of IV administered of TXA (13). Ho, in a meta-analysis of 12 clinical trials, concluded that TXA use in THA and TKA reduced the blood transfusion rate (14). Nicoleta, Stoicea, and Kagoma et al., in 2 different meta-analyses, concluded the same results in patients who received appropriate antithrombotic prophylaxis (15, 16). In another meta-analysis, Sukeik et al. assessed 7 studies (350 patients) that reported reduction of intra-operative blood loss by a mean of 104 mL, postoperative blood loss by a mean of 172 mL, and total blood loss by a mean of 289 ml (17). Henry, who assessed data from 252 RCTs, found that Aprotonin was more effective than TXA, however vascular problems in Aprotinin such as heart attack, DVT, and death were more than TXA (18). It seems that there is currently an agreement regarding TXA use in THA to reduce blood loss and transfusions.

4. Topical Versus Intravenous Administration of TXA

The efficacy of topical TXA in THA has been assessed only in a small number of studies. Wei, in a widespread meta-analysis of 39 RCTs', suggested that regardless of the method of TXA administration in THA (intravenous, intra-articular, topical or oral), TXA can significantly reduce blood loss and the need for allogeneic blood transfusion without apparent increase in the risk of DVT or thromboembolic complications (19). Recently, there has been interest in applying TXA topically before closure of the wound. This has the advantages of easy application and maximum concentration at the site of bleeding, minimizing systemic absorption and consequently, decreasing concerns of possible side effects. Two separate meta -analyses by Xu and Wang were done assessing RCTs' on topical TXA administration; they found that topical administration of TXA significantly reduce blood loss and transfusion requirements in primary THA, without increased thromboembolic complications or wound infection (20, 21). Sukeik, in a meta-analysis, found that topical administration was superior to the intravenous route; however Mehran recommended the IV form for ease of use (17, 22). Gao and Sun evaluated the efficacy and safety of topical application of tranexamic acid (TXA) plus diluted epinephrine (DEP), its effect on perioperative occult blood loss, as well as transfusion requirements in primary unilateral THA. Topical TXA plus DEP, or combined (IV and topical) TXA regimens, are more effective than intravenous or local administration alone (23, 24). It seems that there is debate regarding IV, topical, or combined administration of TXA, however all methods reduce blood loss and transfusions.

5. TXA and Thrombotic Events

As discussed earlier, TXA does not increase thrombotic events such as cardiovascular attacks or DVT. Several studies have reported that TXA does not increase the prevalence of deep vein thrombosis (DVT); however, most used routine chemical thromboprophylaxis, thereby masking the potential risk of TXA on VTE. Nishihara et al. performed THA without routine chemical thromboprophylaxis and they used IV TXA (1 g given pre-operatively) as well as a control group comparison. All patients had mechanical but no chemical thomboprophylaxes. Each patient was examined for DVT by bilateral ultrasonography both pre-operatively and post-operatively on days 1 and 7.

TXA was found to increase the incidence of total DVT significantly on post-operative day 7 compared with controls; however, most cases of DVT were isolated in the distal of the limb (with exception of one patient with proximal DVT) in each group. One patient in the control group developed a non-fatal symptomatic pulmonary embolism (PE). They found use of TXA did not appear to affect the prevalence of either proximal DVT or PE (25). Tranexamic acid did not increase the risk of thromboembolic complications such as deep vein thrombosis, pulmonary embolism, thrombotic cerebral vascular accident, or myocardial infarction (14, 17).

6. Cost-Effectiveness of Tranexamic Acid

Harris et al. reported a study assessing cost effectiveness of TXA use. Before using TXA in primary THA, facility costs were $286.90/THA for blood transfusion and required 0.45 man-hours/THA (transfusion rate 19.87%). After incorporating TXA, the cost for intravenous use was $123.38/THA for blood transfusion and TXA medication as well as 0.07 man-hours/THA (transfusion rate 4.39%). The cost for topical application was $132.41/THA for blood transfusion and TXA as well as 0.14 man-hours/THA (transfusion rate 12.86%) (26). North and Mehran found that there was a significant financial incentive for the use of TXA in THA with a saving of $314 per patient (22). TXA is cost-effective drug, which reduces cost per THA and the man-hours/ of THA while decreasing blood loss.

7. Current Concept

It seems that current concepts recommend routine application of TXA in hip arthroplasty due to of safety, efficacy in decreasing blood loss, and cost-effectiveness.

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Table 1. Summary of Articles About TXA Use in Minimizing Blood Loss in Hip Arthroplasties

Authors	Publication Year	Journal	Research Method	Conclusion
Poeran et al	2014	BMJ	retrospective cohort	Efficient
Ho et al	2003	Anaesthesia and intensive care.	Meta-analysis	Efficient
Kagoma et al	2009	Thrombosis research	Meta-analysis	Efficient
Stoicea et al	2015	Frontiers in surgery	Meta-analysis	Efficient
Sukeik et al	2011	Bone and joint journal	Meta-analysis	Efficient
Henry et al	2011	The cochrane library	Meta-analysis	Efficient

Table 2. Summary of Articles About Topical Versus Intra-Venous(IV) Use of TXA

Authors	Publication Year	Journal	Research Method	Conclusion
Wei	2015	Transfusion medicine	meta-analysis	All methods are efficient
Xu	2015	Drug discoveries and therapeutics	meta-analysis	Topical is efficient without major complication
Wang	2015	International journal of surgery	meta-analysis	Topical is efficient without major complication
North	2016	Journal of arthroplasty	randomized controlled trial	IV form is superior to topical use
Gao	2015	The journal of arthroplasty	randomized controlled trial	Topical with epinephrin
Xie	2016	The journal of clinical and experimental research on hip pathology and therapy	randomized controlled trial	Combined use
Sukeik et al	2011	Bone and joint journal	meta-analysis	Topical form superior to IV

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