

INPLASY PROTOCOL

To cite: Zheng et al. The optimal dose, efficacy and safety of tranexamic acid and aminocaproic acid in intravenous and intra-articular administrations to reduce bleeding for patients after TKA: A systematic review and Bayesian network meta-analysis. Inplasy protocol 202270060. doi: 10.37766/inplasy2022.7.0060

Received: 11 July 2022

Published: 11 July 2022

Corresponding author:
che zheng

zhengchescu@163.com

Author Affiliation:
Department of Orthopaedic Surgery, West China Hospital, Sichuan University, No. 37 Guoxue Road, Chengdu, Sichuan Province, 610041, China.

Support: The Key Project of Sichuan.

Review Stage at time of this submission: The review has not yet started.

Conflicts of interest:
None declared.

The optimal dose, efficacy and safety of tranexamic acid and aminocaproic acid in intravenous and intra-articular administrations to reduce bleeding for patients after TKA: A systematic review and Bayesian network meta-analysis

Zheng, C¹; Xu, JW²; Shen, B³.

Review question / Objective: We aimed to evaluate the optimal dose, efficacy and safety of tranexamic acid (TXA) and aminocaproic acid (EACA) in intravenous and intra-articular administrations for patients after TKA.

Condition being studied: Total knee arthroplasty (TKA), a commonly utilized surgical procedure to alleviate pain and improve function in patients suffering from end stage arthrosis of the knee, is projected to grow 85%, to 1.26 million procedures, from 2014 to 2030. However, patients after TKA may lose a lot of blood during and after the surgery, and therefore may require a large amount of blood transfusion. Blood transfusion has many adverse clinical risks, including transfusions related infection, intravascular hemolysis, kidney damage, immune incompatibility, and even death.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 July 2022 and was last updated on 11 July 2022 (registration number INPLASY202270060).

INTRODUCTION

Review question / Objective: We aimed to evaluate the optimal dose, efficacy and

safety of tranexamic acid (TXA) and aminocaproic acid (EACA) in intravenous and intra-articular administrations for patients after TKA.

Condition being studied: Total knee arthroplasty (TKA), a commonly utilized surgical procedure to alleviate pain and improve function in patients suffering from end stage arthrosis of the knee, is projected to grow 85%, to 1.26 million procedures, from 2014 to 2030. However, patients after TKA may lose a lot of blood during and after the surgery, and therefore may require a large amount of blood transfusion .Blood transfusion has many adverse clinical risks, including transfusions related infection, intravascular hemolysis, kidney damage, immune incompatibility, and even death

METHODS

Search strategy: We initiated our study by searching medical databases including PubMed, Cochrane Library, Embase, Web of Science, CBM and Chinese National Knowledge Infrastructure with the following mesh terms: ('tranexamic acid' or 'AMCHA' or 'AMCA' or 'anvitoff' or 'transamin' or 'amchafibrin' or 'exacyll' or 'aminocaproic acid' or '6 aminohexanoic acid' or 'epsilon aminocaproic acid' or 'capralense' or 'capramol' or 'caproamin' or 'caprocid' or 'epsamon' or 'epsikapron') and 'total' and 'knee' and ('replacement' or 'arthroplasty').

Participant or population: Patients after unilateral total knee arthroplasty.

Intervention: Intravenous tranexamic acid; intravenous epsilon aminocaproic acid; intra-articular tranexamic acid ; intra-articular epsilon aminocaproic acid.

Comparator: Intra-articular administration of 1.0g TXA, intravenous administration of 1g TXA or 10g EACA (30mg/kg TXA or 150mg/kg EACA) are most effective and enough to control bleeding for patients after TKA.

Study designs to be included: Randomized controlled trials and cohort studies.

Eligibility criteria: Studies investigating the efficacy of antifibrinolytic drugs on blood

loss with respect to total blood loss, HB drop, drainage volume, transfusion rates or PE/DVT rates after total knee arthroplasty were included.

Information sources: PubMed, Cochrane Library, Embase, Web of Science, CBM and Chinese National Knowledge Infrastructure.

Main outcome(s): Primary outcomes were the total blood loss, HB drop and transfusion rates afterTKA.

Additional outcome(s): Secondary outcomes included drainage volume and PE/DVT rates.

Quality assessment / Risk of bias analysis: This meta-analysis was guided by the PRISMA guideline (Preferred Reporting Items for Systematic Reviews and Meta-analysis). Characteristics of included studies were collected. The Cochrane Collaboration's tools and Newcastle-Ottawa Score for assessing risk of bias were applied to assess the risk of bias for eligible studies consists of selection bias, performance bias, report bias et al.

Strategy of data synthesis: The OR, standard difference (SD) and 95% CIs were used for evaluating the effect of outcomes. Statistical significance (α) was set at 0.05. According to the three assumptions of network meta-analysis: data homogeneity, transitivity and consistency , we use gemtc (R-Project, Vienna, Austria, version 0.8–2) package of R studio (version February 1, 5019) to decompose this network meta-analysis into two steps: First, we did traditional pairwise meta-analysis with a random-effect model. I^2 metric was used to evaluate the heterogeneity in included studies. Then we carried out sensitivity analysis and eliminated the studies with obviously high heterogeneity. Then, Bayesian Markov chain Monte Carlo method with a random-effect or fixed-effect model after considering the heterogeneity was used and the data were entered into R software in gemtc package, the network meta-analysis of various glucocorticoid regimens was performed.

We separately set 50,000 simulations for 4 chains as the burn-in period and yield 200,000 iterations. The convergence was accessed by Brocks-Gelman-Rubin plots, trace graph and density graph. Meanwhile, the rank probability diagrams were provided by gemtc software package, and the consistency between direct and indirect comparison were assessed by node-splitting method.

Subgroup analysis: Antifibrinolytic drugs were divided into three subgroups: (1) EACA and TXA in intra-articular administration; (2) EACA and TXA in intravenous administration based on total dosage; (3) EACA and TXA in intravenous administration based on patients' weight. Primary outcomes were the total blood loss, HB drop and transfusion rates after TKA. Secondary outcomes included drainage volume and PE/DVT rates.

Sensitivity analysis: Bayesian Markov chain Monte Carlo method with a random-effect or fixed-effect model after considering the heterogeneity was used and the data were entered into R software in gemtc package, the network meta-analysis of various glucocorticoid regimens was performed. We separately set 50,000 simulations for 4 chains as the burn-in period and yield 200,000 iterations. The convergence was accessed by Brocks-Gelman-Rubin plots, trace graph and density graph. Meanwhile, the rank probability diagrams were provided by gemtc software package, and the consistency between direct and indirect comparison were assessed by node-splitting method.

Country(ies) involved: China.

Keywords: TKA, EACA, TXA, blood loss.

Contributions of each author:

Author 1 - che zheng.

Author 2 - jiawen xu.

Author 3 - bin shen.