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Review

Comparison of topical versus intravenous tranexamic acid in primary total knee arthroplasty: A meta-analysis of randomized controlled and prospective cohort trials

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ABSTRACT

Background: There has been much debate and controversy about the optimal regimen of tranexamic acid in primary total knee arthroplasty. The purpose of this study was to undertake a meta-analysis to compare the efficacy of topical and intravenous regimen of tranexamic acid in primary total knee arthroplasty.
Methods: A systematic review of the electronic databases PubMed, CENTRAL, Web of Science, and Embase was undertaken. All randomized controlled trials and prospective cohort studies evaluating the effectiveness of topical and intravenous tranexamic acid during primary total knee arthroplasty were included. The focus of the analysis was on the outcomes of blood loss, transfusion rate, and thromboembolic complications. Subgroup analysis was performed when possible.
Results: Of 328 papers identified, six trials were eligible for data extraction and meta-analysis comprising 679 patients (739 knees). We found no statistically significant difference between topical and intravenous administration of tranexamic acid in terms of blood loss, transfusion requirements and thromboembolic complications.
Conclusions: Topical tranexamic acid has a similar efficacy to intravenous tranexamic acid in reducing both blood loss and transfusion rate without sacrificing safety in primary total knee arthroplasty.
Level of Evidence: II

Contents

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1. Introduction

Total knee arthroplasty (TKA) is one of the most common operations in orthopedic practice, associated with large amounts of postoperative blood loss and significant rates of transfusion. The reported amounts of blood loss have ranged from 1450 to 1790 mL [1–3], necessitating allogeneic blood transfusion in 10% to 38% of patients [4,5]. However, blood transfusion is certainly not a zero-risk procedure. On the contrary, it has potential hazards including hemolysis, infection, immunosuppression, transfusion-related acute lung injury and even death [6,7].

Tranexamic acid (TXA) is a synthetic antifibrinolytic agent that binds to the lysine binding site of plasminogen and blocks the binding of plasminogen to the fibrin surface. Thus, plasminogen activation is prevented and fibrinolysis is delayed [8]. By this process, TXA is believed to be able to help the body retain blood clots more effectively and therefore reduces bleeding.

Large clinical studies [9,10] and several meta-analyses [11,12] have confirmed that intravenous (IV) administration of TXA could effectively reduce blood loss and transfusions in TKA without increasing the risk of DVT. However, concerns remain over the risk of thromboembolic complications after systemic administration [13].

In light of the safety concerns with the IV-TXA, there has been a growing interest in the topical use of TXA for prevention of bleeding in major orthopedic procedures. Compared with IV-TXA, the topical application leads to 70% lower systemic absorption, and therefore may be a safer alternative to giving it systemically [14]. Besides, the topical application has the advantages of being easy to administer, providing a maximum concentration of TXA at the bleeding site, and inducing partial microvascular hemostasis by stopping fibrin clot dissolution in the affected area.

Cumulative studies of topical administration of TXA [15–17], showed reliable evidence that it was effective in reducing total blood loss and blood transfusion rate compared with the placebo. However, it is still controversial whether topical TXA could attain similarly good results in reducing bleeding and transfusions as IV-TXA. Thus, we carried out a meta-analysis to investigate whether there were any differences when comparing topical TXA and IV-TXA in terms of: 1) blood loss results including total drain output, total blood loss and maximum postoperative hemoglobin (Hb) drop; 2) blood units transfused per patient and transfusion requirements; and 3) thromboembolic complications including deep venous thrombosis (DVT) and pulmonary embolism (PE).

2. Materials and methods

The methods adopted for this review were based on the recommended PRISMA checklist guidelines [18].

2.1. Search strategy

We searched electronic databases including PubMed, CENTRAL (Cochrane Controlled Trials Register), Web of Science, and Embase for relevant studies published between the time of the establishment of these databases and 21 July 2014. The following search strategy was used to maximize search specificity and sensitivity: (total knee arthroplasty OR total knee replacement OR TKA OR TKR) AND tranexamic acid. The bibliographies of identified articles, including relevant reviews and meta-analyses were manually searched for potential eligible reports. In addition, the Google database was used to look for additional trials. There were no restrictions in terms of the date or language of publication.

2.2. Eligibility criteria

Study selection was performed according to the following inclusive criteria: (1) randomized controlled trials (RCTs) or prospective cohort studies (PCSs); (2) participants underwent primary TKA; (3) interventions including topical (intra-articular) and IV-TXA; and (4) reported outcomes, including postoperative total drain output, total blood loss, maximum postoperative Hb drop, blood units transfused per patient, the number of patients receiving blood transfusion, the incidence of DVT and PE. Studies with cadaver and artificial models were excluded, or if patients were with bleeding disorders.

2.3. Data extraction

After exclusion of duplicates, two reviewers (HW and YZ) independently screened the titles and abstracts of identified papers. Most citations could be excluded on the basis of information provided by their respective title or abstract. Otherwise, the full article was obtained and carefully scrutinized by the two reviewers. If necessary, we attempted to contact the author of the original reports to obtain further details. Any disagreement between them was resolved by consensus.

The following data were extracted: (1) demographic data of participants including age, gender, indication for TKA, location of study, length of follow-up and whether they underwent unilateral or bilateral TKA; (2) general surgical information including the surgical approach, method of administration, transfusion criteria and whether it was conventional TKA (Con-TKA) or computer-assisted TKA (CAS-TKA); and (3) the number of patients receiving blood transfusion, blood units transfused per patient, blood loss results including total drain output, total blood loss, maximum postoperative Hb drop, thromboembolic complications including DVT and PE.

2.4. Outcome measures

The primary outcome was the proportion of patients who were transfused with allogeneic blood, autologous blood or both. The secondary outcomes were the amount of blood loss. Thromboembolic complications were also reviewed to check the safety of topical and IV-TXA. Subgroup analysis was performed based on the study type (RCT or PCS), surgical protocol (CAS-TKA or Con-TKA), and timing of drain clamping (short-time, <2 h or long-time, ≥ 2 h).

2.5. Study quality

Two reviewers (HW, YZ) rated the quality of the eligible studies independently. Study quality was judged by using the Jadad five point scale for RCTs and the NEWCASTLE–OTTAWA quality assessment scale for other studies. The Jadad five point scale contained two questions