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Review

Comparison of oral versus intravenous application of tranexamic acid in total knee and hip arthroplasty: A systematic review and meta-analysis

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HIGHLIGHTS

- We made this meta-analysis to compare of oral with IV administrations of TXA following TKA and THA.
- Oral TXA and IV TXA benefit similarly for knee and hip function improvement.
- Oral TXA will not increase the risk of complications.
- Oral TXA is economical and convenient to use compared to IV form.

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ABSTRACT

Background: Tranexamic acid (TXA) is regarded as one of the most important drugs in reducing blood loss and hemoglobin (Hb) drop after total knee arthroplasty (TKA) or total hip arthroplasty (THA). Treatment with tranexamic acid (TXA) by intravenous application has been discussed extensively. Recently, several studies have reported that oral administration has an effect on blood sparing. Therefore, we performed a meta-analysis to investigate the efficacy and safety between oral TXA and intravenous TXA (IV-TXA) for blood sparing in total knee and hip arthroplasty.

Methods: Randomized controlled trials (RCTs) or retrospective cohort studies (RCSs) about relevant research were searched for by using PubMed (1996–April 2017), Embase (1980–April 2017), and the Cochrane Library (CENTRAL, April 2017). Five studies that compared oral with IV administration of TXA were included in our meta-analysis. Meta-analysis results were collected and analyzed by the software Review Manager 5.3 (Copenhagen: The Nordic Cochrane Center, The Collaboration, 2014).

Results: Five studies containing 3474 patients met the inclusion criteria. Our pooled data analysis indicated that oral TXA was as effective as the IV-TXA in terms of the average Hb drop ($P = 0.88$), total Hb loss ($P = 0.57$), total blood loss ($P = 0.42$), transfusion rate ($P = 0.16$), complications ($P = 0.61$), and length of hospital stay ($P = 1.00$).

Conclusions: Compared with the IV-TXA method, oral TXA shows similar blood-sparing efficacy for preventing hemoglobin drop, total hemoglobin loss, and total blood loss following TKA or THA. In addition, no significant differences of transfusion rate, complications, or length of hospital stay were found between the 2 groups. However, because of the limited number of included studies, more studies of high quality are needed to further identify the optimal administration time for oral TXA.

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1. Introduction

Because of the aging of the population, the number of patients who have received total knee arthroplasty (TKA) and total hip arthroplasty (THA) in recent years has increased considerably [1]. It has been estimated that the demand for primary THA will grow by 174% to 572 000 and the demand for primary TKA is expected to grow by 673% to 3.48 million in the United States by 2030 [2]. Total joint arthroplasty has been widely recognized as one of the most important surgeries for relief of pain and improvement of physical function. However, there is concern that TKA and THA are likely to cause substantial perioperative-period blood loss. It has been reported that total calculated blood loss ranged from 500 ml to 1500 ml and 700 ml–2000 ml in primary TKA and THA, respectively, and that transfusions were needed for 10%–38% of patients who received TKA or THA [3–8]. Therefore, several strategies have been employed to minimize blood loss and lower the risks of transfusion in patients who undergo TKA or THA, such as deliberate hypotension, tourniquet use, cell salvage, and the use of antifibrinolytics [6]. Tranexamic acid (TXA) is an antifibrinolytic agent, which inhibits the activation of plasminogen, and TXA has been identified as effectively reducing blood loss and transfusion rate in TKA and THA [9–11].

Patients undergoing TKA or THA can receive TXA intravenously, topically, or orally. However, there remains controversy concerning the optimal administration of TXA [12,13]. There have been many studies comparing the efficacy between IV and topical TXA, and the results showed no statistical differences between these 2 routes of administration [5,14]. Recently, several studies have been published to compare blood-sparing between oral and IV-TXA, while the efficacy and side effects of treatment between oral and IV-TXA are still unknown [5,14].

Thus, we performed a systematic review and meta-analysis to demonstrate the efficacy between oral and IV administration of TXA.

2. Materials and methods

2.1. Search strategy

We systematically searched for randomized controlled trials (RCTs)or retrospective cohort studies (RCSs) using PubMed (1996–April 2017), Embase (1980–April 2017), and the Cochrane Library (CENTRAL, April 2017). Trials were also collected from related references to find additional studies. Only English language publications were included in our meta-analysis. The key words used were “total knee arthroplasty”,“total knee replacement”, “total hip replacement”, “total hip arthroplasty”,“oral tranexamic acid”,“oral TXA”, “intravenous tranexamic acid”, “intravenous TXA” in conjunction with Boolean operators “AND” or “OR”. The search results are presented in Fig. 1.

2.2. Inclusion criteria

Trials were identified as qualified to be included in the meta-analysis on condition that they met the PICOS (patients, intervention, comparator, outcome, study design) criteria. These criteria were as follows: 1. Patients had undergone TKA or THA for the first time, 2. The intervention was oral administration of TXA for TKA or THA, 3. The comparator was IV administration of TXA for TKA or THA, 4. the outcomes were Hb drop, total Hb loss, total blood loss, transfusion rate, complications, and length of hospital stay, and 5. The study designs were randomized controlled trials or retrospective cohort studies.

2.3. Data extraction

Two reviewers extracted the available data from the included studies independently. The extracted data from studies included first author, publication date, participants, age, gender, body mass index, patient condition, and study design. The primary outcome consisted of Hb drop, total Hb loss, and total blood loss. Secondary outcomes consisted of transfusion rate, complications, and length of hospital stay. We emailed corresponding authors of the studies which had incomplete data, for further information or used graphical data. Any disagreement between the 2 reviewers was resolved by a third reviewer.

2.4. Quality assessment

We used Jadad scales to evaluate the risk of bias for RCTs, which consisted of the following items: random sequence generation, allocation concealment, masking of participants and personnel, incomplete outcome data, selective reporting, and others [15,16]. We determined that the study was of high quality when the Jadad score was more than 4 points. For non-RCTs, the risk of bias was evaluated by the Newcastle-Ottawa scale, and a high quality study achieved a score of more than 5 points [17].

2.5. Data analysis and statistical methods

Our meta-analysis results were calculated using Review Manager Software Windows 5.3 (Copenhagen: The Nordic Cochrane Center, The Collaboration, 2014). For continuous outcomes, we used mean difference (MD) with 95% confidence intervals (CIs) to weigh the effect interval. For discontinuous outcomes, relative risk (RR), odds ratio (OR) or risk difference (RD) with 95% CIs were used to weigh the effect interval. The statistical heterogeneity was judged by the value of P and I^2 using the standard chi-square test. Values of I^2>50%, $P < 0.1$ were considered to demonstrate significant heterogeneity in our outcomes and the random-effect model was applied for assessment, otherwise the fixed-effect model was used for extracted data.

3. Results

3.1. Search results

A total of 93 studies were identified through the search strategy, and 17 studies were excluded by using Endnote software. Sixty-four studies were excluded after reading the title and abstract. According to the inclusion criteria, 5 studies were included after reading the full text [12,18–21]. Among them, there were 4 RCTs and 1RCS.

3.2. Study characteristics

Among the five included studies, 4 of them evaluated patients' conditions preoperatively using the ASA (American society of anesthesiologists) scale [12,18,20,21]. Almost all patients had similar postoperative conditions, that is, 71.4%–80.0% of the patients of the 4 studies were diagnosed as grade II of the ASA scale. With regard to the dosage of TXA, Kayupov et al. [20] recorded that the oral and IV groups patients each received a total amount of 1950 mg and 1000 mg, respectively. Yuan et al. [21] reported that the oral group patients received 20 mg/kg TXA at 2 h before surgery and the same dose at 12 h postoperatively, and the IV group patients received a dose of 20 mg/kg TXA. Fillingham et al. [12] showed that the oral group received 1950 mg TXA and the IV group received the standard dose of 1000 mg. Zohar et al. [18] reported that a total amount of 4000 mg TXA was administered to each patient in the oral group,