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Comparison between Oral and Intravenous Tranexamic Acid in Total Hip and Knee Arthroplasty

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***Keywords*— Arthoplasty, Bleeding, Intravenously, Orally, Tranexamic acid.**

***Abstract*—** *Introduction: Total hip and knee arthroplasty is associated with significant perioperative blood loss, increasing the risk of anemia, transfusion, and prolonged hospitalization. Tranexamic acid (TXA) is widely used to minimize surgical bleeding, but the optimal route of administration remains under debate, particularly between oral and intravenous forms. Objective: To compare the efficacy of oral versus intravenous tranexamic acid regarding total blood loss and length of hospital stay in patients undergoing total hip and knee arthroplasty. Methods: This is a narrative literature review. The search was conducted in the PubMed/MEDLINE and SciELO databases using the descriptors "acid tranexamic," "intravenous," "oral," and "total knee/hip arthroplasty," combined with the Boolean operators AND and OR. Randomized clinical trials and meta-analyses published in Portuguese, English, or Spanish from 2020 onwards that directly compared oral and intravenous TXA in total arthroplasty were included. Results: The findings indicate that oral and intravenous TXA have equivalent efficacy in reducing total blood loss. No significant differences were observed in hospital stay duration or complication rates between the administration routes. The oral route demonstrated logistical advantages and lower cost. Conclusion: Oral tranexamic acid is as effective and safe as the intravenous route in hip and knee arthroplasty, representing a viable, accessible alternative with potential to reduce hospital costs.*

I. INTRODUCTION

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) represent some of the most significant advances in modern orthopedics and are currently among the main treatments for end-stage degenerative joint diseases, such as osteoarthritis and femoral head necrosis. These procedures have demonstrated the ability to reduce pain, restore joint function, and substantially improve patients' quality of life, especially in an aging global population (Santos et al., 2023; Zhang et al., 2021). In Brazil, osteoarthritis affects approximately 4% of the population and is associated with important functional limitations, contributing to increased morbidity and

mortality, particularly among older adults, a population group expected to grow significantly in the coming decades (Ferreira et al., 2018).

The growing demand for THA and TKA has relevant clinical, social, and economic impacts. International projections estimate that the need for arthroplasties will increase by more than 600% by 2030, a trend also observed in Brazil, where thousands of hospital admissions are recorded annually, with costs exceeding 700 million reais between 2008 and 2015 (Ferreira et al., 2018; Kurtz et al., 2007). However, despite advances in surgical techniques, perioperative blood loss remains a significant challenge in these procedures, with estimates ranging from 700 to 2,000 mL per surgery and transfusion rates that may exceed 30% of patients (Park et al., 2013; Reale, 2021).

In this context, strategies to minimize bleeding have become essential, given the association of allogeneic transfusions with serious complications such as infections, immune reactions, and increased morbidity and mortality (Vamvakas & Blajchman, 2009; Leverett, 2021). Among pharmacological interventions, tranexamic acid (TXA), a synthetic antifibrinolytic agent that prevents clot degradation and reduces intra- and postoperative blood loss, stands out. TXA is widely used in orthopedic surgeries and has demonstrated effectiveness in reducing transfusion requirements and maintaining hemoglobin levels (Aguilera et al., 2013; Chen Wang et al., 2015; Lu et al., 2021).

The intravenous route is the traditional method of TXA administration, with doses ranging from 10 to 20 mg/kg, usually given before the surgical incision. However, recent studies have shown that oral TXA has similar efficacy to the intravenous route in reducing total blood loss, hemoglobin drop, and transfusion rates, in addition to providing substantial economic advantages—being up to 90% cheaper (Francesco et al., 2016; Erdan et al., 2017; Sun et al., 2020). Furthermore, current evidence indicates no increase in thromboembolic events or additional complications with oral use, supporting this route as a safe alternative in arthroplasty (Defrancesco et al., 2023; Feng, 2025).

Despite this therapeutic equivalence, gaps remain regarding the optimal oral dose, the most appropriate timing of administration, and the efficacy across different patient profiles. The literature also suggests a possible higher incidence of gastrointestinal effects with oral use, although such findings still require more robust studies (McDonald, 2022). Therefore, there is growing scientific interest in systematically comparing the performance of the oral and intravenous routes to support the standardization of protocols and optimize perioperative management of patients undergoing THA and TKA.

II. METHODOLOGY

This study consists of a narrative literature review aimed at comparing the effectiveness of tranexamic acid (TXA) administered orally and intravenously with respect to total blood loss and length of hospital stay in patients undergoing total hip and knee arthroplasty.

The literature search was conducted in the PubMed/MEDLINE and Scientific Electronic Library Online (SciELO) databases, using the English descriptors “tranexamic acid”, “intravenous”, “oral”, and “total knee/hip arthroplasty”, combined with the Boolean operators AND and OR in order to maximize the sensitivity and specificity of the search.

The methodological process was carried out in sequential steps: delimitation of the topic, definition of eligibility criteria, database searches, study selection, data extraction, and descriptive analysis. Randomized clinical trials and meta-analyses published in Portuguese, English, or Spanish from 2020 onward were included, provided they directly compared oral and intravenous TXA administration in total knee or hip arthroplasty.

Duplicate studies, publications prior to 2020, articles that did not fit the proposed study design (such as narrative reviews, observational studies, or case reports), research addressing other types of surgical procedures, and studies evaluating only one route of administration without direct comparison were excluded.

After initial screening by titles and abstracts, potentially relevant articles were read in full. Eligible studies had their data extracted and organized in a Microsoft Excel® spreadsheet, containing information on authors, year of publication, title, and evaluated outcomes.

Data analysis was conducted descriptively, enabling comparison of the findings related to total blood loss and hospital length of stay between oral and intravenous TXA use, according to the results reported in the selected studies.

III. RESULTS

The initial search identified 270 articles published from 2020 onward. After applying the inclusion criteria—studies that directly compared oral versus intravenous administration of tranexamic acid (TXA) in hip and knee arthroplasty—only eight studies remained eligible for the final analysis. These studies consisted of four randomized

clinical trials and four meta-analyses with high methodological quality.

Table 1. Studies included in the review

AUTHOR	TITLE	YEAR	OUTCOME
Hadi et al.	Comparison of intravenous, oral and intra articular effects of tranexamic acid on reducing postoperative knee replacement bleeding	2020	Randomized clinical trial with 135 patients undergoing total knee arthroplasty. Intraoperative blood loss: intravenous < oral Blood loss at 72 hours postoperatively: intravenous = oral Length of hospital stay: intravenous = oral
Sun et al.	Comparison of oral versus intravenous tranexamic acid in total knee and hip arthroplasty A GRADE analysis and meta-analysis	2020	Meta-analysis including 1,080 patients who underwent total hip or total knee arthroplasty. Total blood loss: intravenous = oral Length of hospital stay: intravenous = oral
Ye et al.	Comparison of efficacy and safety between oral and intravenous administration of tranexamic acid for primary total knee/hip replacement: a meta-analysis of randomized controlled trial	2020	Meta-analysis with 1,140 patients undergoing total hip or knee arthroplasty. Total blood loss: intravenous = oral Hospital length of stay: intravenous = oral
Lu et al.	What is the ideal route of administration of tranexamic acid in total knee arthroplasty? A meta-analysis based on randomized controlled trials	2021	Meta-analysis with 4,200 participants undergoing total knee arthroplasty. Total blood loss: intravenous = oral
DeFrancesco et al.	Effectiveness of oral versus intravenous tranexamic acid in primary total hip and knee arthroplasty: a randomised, non-inferiority trial	2022	Randomized clinical trial with 400 participants undergoing total hip or total knee arthroplasty. Total blood loss in total knee arthroplasty: intravenous = oral Total blood loss in total hip arthroplasty: intravenous = oral
Hootsmans et al.	A randomized trial comparing three routes of tranexamic acid administration in total knee arthroplasty.	2023	Randomized clinical trial with 111 patients undergoing total knee arthroplasty. Total blood loss: intravenous = oral
Piette et al.	Oral as compared to intravenous tranexamic acid to limit peri-operative blood loss associated with primary total hip arthroplasty: A randomised noninferiority trial	2024	Randomized clinical trial with 228 patients undergoing total hip arthroplasty. Total blood loss: intravenous = oral
Feng et al.	A comparison of efficacy and safety of oral versus intravenous applications of tranexamic acid in total hip and knee arthroplasty: an updated systematic review meta-analysis of randomized controlled trials	2025	Meta-analysis with 2,262 patients undergoing total hip or knee arthroplasty. Total blood loss: intravenous = oral Hospital length of stay: intravenous = oral

The randomized clinical trial by Hadi et al. (2020) included 135 patients undergoing total knee arthroplasty and evaluated three routes of administration: oral, intravenous, and intra-articular. The results showed that all forms significantly reduced bleeding; however, the intravenous route had a greater impact on reducing intraoperative blood loss. Nevertheless, after 72 hours, the total blood loss and the need for transfusion were similar between the oral and intravenous groups.

The meta-analysis by Lu et al. (2021), which synthesized data from 4,200 participants undergoing primary knee arthroplasty, indicated that oral and intravenous TXA demonstrated equivalent effectiveness in reducing total blood loss. The study reinforced that oral TXA can be considered a valid clinical option, offering economic and logistical advantages without compromising clinical outcomes.

Similarly, Sun et al. (2020), evaluating 1,080 patients, and Ye et al. (2020), analyzing 1,140 patients, also found no statistically significant differences between oral and intravenous administration regarding total blood loss or length of hospital stay. In addition, Sun et al. (2020) highlighted that the use of oral tranexamic acid may represent a significant cost saving for healthcare services, with reductions estimated between 70% and 90% compared with intravenous use.

The clinical trial by DeFrancesco et al. (2022), involving 400 patients, reinforced the non-inferiority of oral TXA compared with the intravenous route, demonstrating equivalence in both blood loss and complication rates, including thromboembolic events.

Similarly, in the clinical trial by Hootsmans et al. (2023), blood loss values between the studied routes were comparable, and no patient required blood transfusion. Moreover, the study emphasized that oral TXA offers substantial economic benefit, being approximately ten times cheaper than other formulations. However, the authors noted that the oral route has a slower onset of action due to gastrointestinal absorption, which may influence the optimal timing of perioperative administration.

Finally, the most recent meta-analysis, conducted by Feng et al. (2025) with 2,262 patients, confirmed that oral TXA has comparable efficacy and safety to the intravenous route, with no differences in transfusion rates or length of hospital stay. The study also highlighted that the oral formulation simplifies perioperative management, making it particularly useful in resource-limited settings.

Overall, the eight included studies consistently conclude that oral tranexamic acid is as effective and safe as its intravenous form in total hip and knee arthroplasty, while offering additional advantages such as lower cost, greater practicality, reduced perioperative workflow complexity, and easier implementation across various hospital contexts.

IV. DISCUSSION

The results of this review consistently demonstrate that tranexamic acid plays a key role in controlling perioperative blood loss in total hip and knee arthroplasty. The literature indicates that average blood loss in these procedures can range from 700 to 2000 mL, contributing to significant rates of postoperative anemia and the need for allogeneic transfusions (Park et al., 2011; Reale, 2021). Considering the risks associated with transfusions, such as hemolytic reactions, immunosuppression, and increased morbidity, it is understandable that TXA has become an essential component of modern blood management protocols (Vamvakas & Blajchman, 2009; Leverett, 2021).

The comparison between oral and intravenous TXA, the central focus of this review, reveals a clear trend: both routes are equally effective in reducing total blood loss. High-quality evidence demonstrates that clinical outcomes do not differ significantly between the two routes, supporting the hypothesis of non-inferiority of oral TXA (Feng, 2025; Lu et al., 2021; Sun et al., 2020). Clinical trials such as DeFrancesco et al. (2023) confirm this equivalence by showing that the only transfusion recorded occurred in the intravenous group, suggesting even a marginal potential advantage for the oral route.

Another important finding is that the pharmacodynamics of TXA appear to support multiple administration strategies. The prolonged fibrinolytic activity after surgery, which may persist for up to 18 hours, implies that supplemental doses—whether oral or intravenous—can offer additional benefits in maintaining hemostasis (McDonald, 2022). Kirwan et al. (2024) reinforce this by demonstrating that extended postoperative oral TXA regimens may improve clinical recovery markers such as pain, range of motion, and early ambulation.

With regard to safety, existing evidence strongly suggests that TXA, regardless of route, does not increase the risk of thromboembolic events, a historical concern in the procoagulant perioperative environment (Feng, 2025; Leverett, 2021). Rates of deep vein thrombosis (DVT) and muscular thrombosis did not differ between oral and intravenous groups across several meta-analyses, supporting the safety profile of the oral formulation (Feng, 2025; Sun et al., 2020). This is especially relevant for high-risk populations such as older adults and patients with multiple comorbidities.

From an economic perspective, the oral route offers substantial advantages. Several studies report that oral TXA costs 70% to 90% less than the intravenous formulation, with significant implications for healthcare sustainability, particularly in resource-limited settings (Feng, 2025; Erdan et al., 2017; Sun et al., 2020). Furthermore, oral administration reduces the need for additional venous access and simplifies perioperative workflows, potentially decreasing dosage errors and logistical demands (DeFrancesco et al., 2023).

Despite these benefits, some limitations must be noted. McDonald (2022) highlights possible gastrointestinal symptoms associated with oral TXA use, although such effects have not been widely documented in orthopedic literature. Additionally, no consensus has been reached regarding the optimal oral dose or timing of administration, as significant heterogeneity exists among study protocols (Sun et al., 2020). These factors underscore the need for future standardized studies with larger samples and specific subgroup analyses.

Regarding hospital length of stay, the studies analyzed consistently showed no significant difference between oral and intravenous routes. Meta-analyses by Sun et al. (2020) and Lu et al. (2021) demonstrated comparable hospitalization periods across groups, indicating equivalent effectiveness in preventing bleeding-related complications. Similar findings were reported by Feng et al. (2025), who confirmed that the oral route does not prolong hospital stay and therefore does not hinder postoperative recovery. Likewise, the clinical trial by DeFrancesco et al. (2023) found no significant differences between routes, indicating that the choice of TXA administration does not influence the clinical course during hospitalization.

Overall, the findings of this review reinforce that oral TXA is an effective, safe, and economically attractive alternative to intravenous TXA in total hip and knee arthroplasty. In the context of increasing demand for arthroplasty driven by population aging and rising prevalence of degenerative joint disease, the adoption of the oral route may not only optimize perioperative management but also enhance healthcare system efficiency (Ferreira et al., 2018; Zhang et al., 2021). Therefore, current evidence supports the consideration of oral TXA as a viable and widely applicable therapeutic approach in modern orthopedic practice.

Although the findings are consistent, this review has notable limitations, primarily due to its narrative design, which does not follow strict bias assessment protocols typical of systematic reviews. Furthermore, the included studies exhibited significant heterogeneity in their protocols, particularly regarding dosage, number of administrations, timing of TXA delivery, and patient characteristics. These differences hinder direct comparisons and may influence outcomes, limiting the generalizability of the conclusions. Thus, while the reviewed evidence supports equivalence between oral and intravenous routes, these results should be interpreted with caution and highlight the need for more homogeneous and methodologically robust clinical trials.

V. CONCLUSION

The review demonstrated that tranexamic acid, regardless of the route of administration, is effective in reducing blood loss and the need for transfusions in total hip and knee arthroplasty. The studies analyzed indicate that the oral route performs equivalently to the intravenous route regarding key clinical outcomes, such as total blood loss and length of hospital stay.

In addition to therapeutic equivalence, the oral route offers important logistical and economic advantages, including lower hospital costs, simplified perioperative management, and easier implementation across different healthcare settings. The findings also suggest that oral TXA maintains a safety profile comparable to that of the intravenous formulation, with no increase in thromboembolic complications.

Thus, it can be concluded that orally administered tranexamic acid is a viable alternative that may be incorporated into clinical protocols as an option equivalent to intravenous administration. However, it is recommended that future studies explore dose standardization, optimal timing of administration, and its effectiveness in specific patient subgroups, aiming for greater precision and consistency in clinical practice.

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