

Tranexamic acid and total hip arthroplasty: optimizing the administration method

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Total hip arthroplasty (THA) is associated with significant peri-operative bleeding that can cause hematomas and sometimes acute anemia requiring blood transfusion with potential risks and costs. These complications will delay a patient's functional recovery and discharge. Blood-sparing strategies are one element of the rapid recovery protocols used for joint replacement surgery. Tranexamic acid (TXA) has its rightful place in this context.

TXA is a synthetic lysine analog with antifibrinolytic activity—it inhibits the conversion of plasminogen to plasmin, an enzyme that breaks down fibrin-containing blood clots. By stabilizing these clots, TXA reduces active bleeding. TXA is currently being used in orthopedic surgery through the intravenous (IV) route during hip and knee arthroplasty procedures either for primary and revision. Its efficacy has been demonstrated in recent studies (1,2); it reduces total peri-operative blood loss and the need for blood transfusion without increasing the risk of deep vein thrombosis or pulmonary embolism.

However, TXA use is not universal and research continues in order to define the method of administration and doses needed during various surgical procedures, namely THA. The first studies, published in the early 2000s, showed that IV administration of TXA during THA was effective at reducing total blood loss and the transfusion

rate. The recent meta-analysis by Moskal and Capps confirms these findings: 300 to 400 mL less blood was lost relative to a total blood loss of about 1,500 mL in the placebo group, along with a nearly 50% reduction in the transfusion rate, which was about 20% in the placebo group and slightly less than 10% in the IV TXA group (3).

About 10 years later, the efficacy of topical TXA application in the context of THA was explored. These studies found no significant difference in terms of efficacy or complications when compared to IV administration, as shown in the recent meta-analysis by Sun *et al.* (4).

The next logical step was to combine IV administration of TXA with topical administration. Although preliminary studies with this combination have been published, very few have analyzed it in the context of THA procedures.

Yi *et al.* (5) published a study with a high level of evidence on this topic in June 2016. In this single-center, prospective, randomized, placebo-controlled, level I study, 150 patients undergoing primary unilateral THA were included between December 2013 and May 2014. These patients were randomized into three groups of 50 patients: combined TXA (IV 15 mg/kg + topical 1 g/100 mL), IV TXA (15 mg/kg) and placebo. The primary outcomes were the amount of blood loss and transfusion values. The secondary outcomes were the length of the hospital stay, range of hip motion,

Harris Hip Score and the prevalence of thromboembolic complications (deep vein thrombosis and pulmonary embolism). They found significantly less total blood loss and fewer blood transfusions in the combined TXA group relative to the two other groups ($P < 0.05$): 200 mL less blood loss with IV TXA (1,200 mL blood loss in the placebo group *vs.* 1,000 mL in the IV TXA group) and an additional 200 mL less blood loss in the combined TXA group (about 800 mL total blood loss). The IV TXA group had a nearly 50% reduction in the blood transfusion rate relative to the placebo group (19/50 *vs.* 8/50). The need for blood transfusion was almost completely eliminated in the combined TXA group (1/50). They also found no statistically significant differences in any of the secondary outcomes, namely thromboembolic complications. The authors concluded that combined TXA administration during THA was more effective than IV administration or placebo, and did not increase the risk of thromboembolic complications.

A review of literature found only a few other studies performed on THA cases—all of them were consistent with the results of the Yi study (5).

In a 210-patient study published in January 2016, Xie *et al.* compared three different TXA administration groups: combined (1 g IV + 2 g topical), IV only (1.5 g) and topical only (3 g). Combined administration was significantly better at reducing total blood loss, while the thromboembolic complications were similar (6).

Another study published in April 2016 by Wu *et al.* (7) looked into the efficacy of combined TXA administration relative to IV TXA in 84 cases of THA revision randomized into two groups of 42 patients. They reported similar findings: the total blood loss and number of transfusions were significantly lower in the combined TXA group, with no significant differences in terms of thromboembolic complications.

While there is broad consensus on the dose of IV TXA (8), the timing of its preoperative and/or postoperative administration varies between studies. Similarly, the dose used for topical administration can vary three-fold (4,5). Lastly, the timing of the hip joint's exposure to TXA and the duration of this exposure vary between studies. A rigorous protocol incorporating these two aspects still needs to be defined.

It is also interesting to note that this combination has been studied more extensively in total knee arthroplasty surgery. A recent meta-analysis by Yuan *et al.* (9) showed that the combination of IV and topical routes is more effective than placebo, IV alone and topical alone, in terms of total blood

loss and the transfusion rate, without significantly increasing the risk of thromboembolic complications.

Similarly, other kinds of searches relative to blood loss control with antifibrinolytics in THA are underway. One study of note is the recent study by Lee *et al.* (10) that compared pre- and postoperative oral TXA to placebo in the context of THA and found less total blood loss without increasing the thromboembolism risk. Oral administration now needs to be compared to the better known IV route; other combined routes could also be explored.

Other antifibrinolytics have been used in THA procedures: ϵ -aminocaproic acid (EACA) has been compared with TXA using different administration routes. Recent studies have confirmed the efficacy of both IV and topical EACA administration in the context of THA. EACA could have an advantage in terms of cost; however, TXA is not very expensive to use (11,12). The combination of administration routes and the comparison with TXA should be expanded.

In summary, combined IV and topical TXA administration during THA appears to significantly reduce the total blood loss and transfusion rate. In addition, this reduction is significantly greater than when TXA is administered by IV only. Lastly, the risk of thromboembolic complications is not higher in the short and medium term. This makes TXA a simple, low-cost, effective solution for controlling postoperative blood loss. Nevertheless, other studies with a high level of evidence and ones that focus solely on THA must be performed to confirm the superiority of combined TXA administration in the context of this surgical procedure and to achieve consensus as to the administered dose.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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