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**Overdosage with TXA**

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Regarding the article by Plaster et al., please explain why *JBJS Case Connector* has published a case report of anaphylaxis to TXA in which the dosage administered was 500% of the recommended maximum dosage. The dosage given is a deviation from the standard.

**References**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/019281s041lbl.pdf

Conflict of Interest: None Declared

**Article Author Response**
11 August 2020

**Article Author(s) to Letter Writer(s)**

In response to the reader’s concerns regarding TXA dosing in this case report, we confirm that a 50 mg/kg dosing was the dose administered and that it is in line with current literature. There is much debate on dosing, and while 10 mg/kg is the most common, doses of up to 100 mg/kg have been reported in the spine literature. A high dose of a 50 mg/kg bolus with 5 mg/kg/hr maintenance, the exact same as in our study, has been shown to be more effective at controlling blood loss without increasing the risk of thrombotic event.

Regarding documentation provided by the author of the e-letter, those recommended doses are in reference to patients with poor renal function. As our patient had no clinical evidence of renal impairment, we believe that the administration of high-dose TXA was appropriate.

There is no consensus on the ideal dosing of TXA in spinal surgery in adult or pediatric patients, and most
studies to date have been retrospective. A prospective, randomized, controlled trial comparing high and low doses, which is currently underway, may provide stronger evidence in support of a particular TXA dosing protocol.

Sincerely,

Scott Plaster, MD

References


E-Letter Writer Response

Letter Writer(s) to Article Author(s)

In his response, Dr. Plaster does state, “A high dose of a 50 mg/kg bolus with 5 mg/kg/hr maintenance, the exact same as in our study, has been shown to be more effective at controlling blood loss without increasing the risk of thrombotic event.” This comment is without reference. The references included in his letter involve anecdotal studies or studies that are inherently biased. Indeed, the study by Johnson et al. notes that the decision on dosage was determined by the anesthesiologist at the time of surgery and involved pediatric patients. The study by Verma et al. is a proposed study to clarify this dosage issue. It is to be a randomized and blinded study evaluating different dosages. This future study may help to resolve the issue.

Regarding the dosage for other procedures in orthopaedics, there is less controversy in knee arthroplasty. Shin et al. stated that “The current meta-analysis indicates that IV administration of 10 mg/kg of TXA 20
min before inflation of the tourniquet followed by 10 mg/kg of TXA 15 min before deflation of the tourniquet is effective and safe.”¹ And the guideline as established by the American Academy of Orthopedic Surgeons states that “Network meta-analysis provided the opportunity to perform direct and indirect comparisons between low dose IV (< 20mg/kg or ~ 1g), high dose IV (~ 20mg/kg or > 1g), low dose topical (~ 1.5g), high dose topical (> 1.5g), oral, and combined IV/topical TXA. In terms of the ability to reduce blood loss, no method of TXA administration was found to provide a significantly different outcome.”²

I do accept that anaphylaxis can occur to any substance. And there are other reports of anaphylaxis to TXA. Dr. Plaster has clearly reported such a case of anaphylaxis.

My concerns are that a dosage that has not been supported by any established guideline was used and reported. Case reports are of benefit when they bring to the practicing surgeon events or findings of clinical importance. Many journals no longer publish such cases as they are considered aberrations that may have limited significance and the histories and findings cannot be fully vetted.

I do believe the problems of case reports, as seen in this one involving high dosage TXA, is evident. I appreciate the responses and the references provided.

I thank you for allowing me to review the information on this topic and I do accept that such reactions are rare but of interest.

Regards,

Mark Siegel, MD

References

I appreciate Dr. Siegel’s comments regarding TXA dosing in relation to this case report. I understand the concern and have supplied literature supporting the dose given. As mentioned, anaphylaxis to TXA has been documented, and I have reported such a case. This case report was meant to identify yet another individual who has suffered anaphylactic shock following treatment with TXA so that physicians can be aware of this rare reaction.