Neurosurgical Forum
LETTERS TO THE EDITOR**Utility of intravenous tranexamic acid in single-level posterior lumbar interbody fusions**

TO THE EDITOR: We read with great interest the recent article by Kushioka et al.¹ (Kushioka J, Yamashita T, Okuda S, et al: High-dose tranexamic acid reduces intraoperative and postoperative blood loss in posterior lumbar interbody fusion. *J Neurosurg Spine* 26:363–367, March 2017) regarding the use of intravenous tranexamic acid (TXA) for single-level posterior lumbar interbody fusions (PLIFs). The authors conducted a nonrandomized, retrospective, comparative cohort study with 30 patients in each group and found that patients who received intravenous TXA had lower intraoperative and postoperative blood loss without any reported complications. We commend the authors on their effort to investigate the effectiveness and safety of intravenous TXA. There are, however, several issues regarding the methodology and the implications of this article that we wish to discuss.

First, the authors refer to the TXA protocol in this study as “high dose.” Although there is currently no universally accepted definition, in the adult spinal deformity literature a “high-dose” TXA protocol typically implies a loading dose ranging from 50 to 100 mg/kg, followed by a 10–20 mg/kg/hr infusion.^{2,4} In this study, 2 separate doses of 2000 mg of TXA were given 15 minutes prior to the incision and again 16 hours postoperatively. This dosing protocol resulted in patients with higher body mass getting a much lower effective dose of TXA than patients with lower body mass. For example, a patient that weighed 100 kg would be getting a 20 mg/kg dose, whereas a patient weighing 50 kg would be getting 40 mg/kg with the single 2000 mg loading dose. It would have been helpful if the authors included the weight range for the patients in the study to give the readers an idea of the effective dose of TXA patients actually received in the study.

Second, the size and design of the study make it likely that the results overestimate the effect of TXA in this patient population. Estimating intraoperative blood loss is typically an inaccurate process and, in the absence of a description of the specific methods used in this study, one has to assume that precise methods such as weighing sponges and carefully measuring volumes were not employed. In addition, although the authors state that “the

drain was routinely removed 40 hours after the operation,” no data are provided to show that all drains were removed after the same amount of time. A systematic variation in duration of drainage could introduce significant bias to the results. Furthermore, 5 different surgeons performed the procedures in the study. Surgeon-related factors and variation in surgical technique can also influence estimated blood loss (EBL). Finally, the unblinded design of the study introduces the potential for unintentional bias favoring the experimental treatment. A randomized controlled trial conducted by Wang et al.³ in 2013 did not find statistically significant differences in EBL for single-level PLIFs.

In our clinical experience, TXA is an effective agent in reducing blood loss in major spinal surgery such as in deformity correction involving long-segment fusions, osteotomies, or vertebral column resections. Its use in routine single-level degenerative cases, however, must be weighed against the risk of rare complications unlikely to be captured in a small study such as this. The readers should carefully consider the results of this and other studies on TXA before adopting it for routine degenerative cases.

Lee A. Tan, MD

Peter D. Angevine, MD

The Spine Hospital, Columbia University Medical Center, New York, NY

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Disclosures

The authors report no conflict of interest.

Response

Thank you very much for your interest in our study. We will attempt to answer the questions raised by your letter.

First, the average weight of patients in the TXA group was 57.2 ± 8.5 kg (range 44–78 kg). Therefore, the average loading dose was 35.7 ± 5.1 mg/kg (range 25.5–45.5 mg/kg). Wang et al.³ reported the loading dose as 15 mg/kg and Tsutsumimoto et al.² also reported the loading dose as 15 mg/kg. Our loading dose was higher than those in previous studies.

Second, intraoperative blood loss was measured by operating room nurses who were blinded as to whether or not the patients were administered TXA. After the operation, hospital ward nurses who were also blinded as to whether the patients were administered TXA measured postoperative drainage blood loss every 2 hours. We show the postoperative drainage blood loss per hour in Fig. 1. The blood loss per hour was less than 20 ml/hr after 10 hours and less than 10 ml/hr after 32 hours in both groups. We performed a 2-way ANOVA on intraoperative and total blood loss using 2 factors (TXA and surgeon). In both analyses

FIG. 1. Postoperative blood loss per hour. The blood loss per hour was less than 20 ml/hr after 10 hours and less than 10 ml/hr after 32 hours in both groups.

of intraoperative and total blood loss, surgeon-related factors were not significant ($p = 0.768$ and $p = 0.966$, respectively). Furthermore, we all performed exactly the same surgical technique as previously published.¹

Finally, the study design, which was not a double-blind randomized control trial, is a limitation of this study, as we mentioned in the paper. We agree with the opinion that TXA use must be weighed against the risk of rare complications. This study showed TXA administration decreased perioperative blood loss; however, we believe further research is required to examine the incidence of complications.

Junichi Kushioka, MD

Osaka University Graduate School of Medicine, Osaka, Japan

Tomoya Yamashita, MD

Shinya Okuda, MD, PhD

Takafumi Maeno, MD, PhD

Tomiya Matsumoto, MD, PhD

Motoki Iwasaki, MD, PhD

Osaka Rosai Hospital, Osaka, Japan

Ryoji Yamasaki, MD, PhD

Osaka Police Hospital, Osaka, Japan

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INCLUDE WHEN CITING

Published online August 25, 2017; DOI: 10.3171/2017.4.SPINE17388.

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