Tranexamic acid for reducing intra- and postoperative blood loss in posterior lumbar interbody fusion: Is it safe enough?

TO THE EDITOR: We read with great interest the recent article by Kushkioka et al.2 (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), which described the use of intravenous tranexamic acid (TXA) during single-level posterior lumbar interbody fusions. The authors conducted a nonrandomized, retrospective, comparative cohort study with 30 patients in each group (TXA vs no TXA) and found that patients who had received intravenous TXA had lower intraoperative and postoperative blood loss and that TXA administration did not result in any complications. We would like to congratulate the authors for their exciting results, which have helped to clearly outline useful treatment strategies to clinically manage patients undergoing spine surgery with TXA for reducing postoperative blood loss. Nonetheless, we wish to draw attention to the potential complications associated with TXA use by describing our experience.

We encountered a 56-year-old male who was otherwise healthy with no history of seizures and who had undergone an L3–5 transforaminal lumbar interbody fusion for spinal stenosis at our facility. We had intravenously administered 3000 mg of TXA (7 mg/kg/hr) and had also applied 2000 mg of TXA on the lumbar spinal wound before closing the wound and placing a drainage tube, which was clamped for 4 hours. Postoperative recovery was unremarkable, and the anesthesiologist confirmed that the patient’s condition remained stable. However, the patient experienced one episode of tonic-clonus epilepsy at 5 hours postsurgery, which was managed by administering intravenous single-dose midazolam. A brain CT showed no intracranial lesion, and the final diagnosis of epilepsy was confirmed by a neurologist.

In agreement with our experience, a recent meta-analysis by Lin and Xiaoyi3 reported that the cumulative incidence rate of TXA-associated seizures was 2.7% and that the incidence rate increased with increasing dosage. Leckler et al.4 have reported the occurrence of TXA-associated seizures during the early postsurgical period after cardiac and non-cardiac surgery and in patients receiving other medical treatments. Such seizures usually occur within the first 5–8 hours after surgery, which corresponds to the period of weaning from intravenous sedation. Further, such events tend to persist for a few minutes but do not progress to status epilepticus. Data from the current literature show the occurrence of sporadic seizures after TXA administration during cardiac surgery, particularly with valve replacement or coronary artery bypass grafting because high doses of TXA are used during these procedures to reduce blood loss. Because TXA and glycine are structural analogs, TXA can bind to glycine receptors as a competitive antagonist and inhibit glycine-activated inhibitory signals, which increases muscle excitability and results in seizures. However, anesthetics, such as propofol, isoflurane, sevoflurane, and desflurane, act as positive allosteric modulators of glycine receptors that can reverse such TXA-mediated inhibition of glycine receptors or midazolam binding to GABA_{\alpha} receptor and thereby compensating for the reduction in glycinergic inhibition.4 Therefore, seizure episodes occur during the first 5–8 hours postsurgery because while anesthetic levels are rapidly declining in the CNS during this time, TXA levels are either peaking or only slowly declining.4 In orthopedic surgery, TXA is usually used as an intravenous infusion or topical application during total knee or total hip arthroplasty.1,5 Based on the above mechanism, we cannot exclude the possibility of epilepsy due to TXA use during spine surgery, and surgeons must be aware of the possibility of TXA-related seizures. Such seizures can be easily managed by administering intravenous propofol or midazolam to reverse TXA-induced inhibition of glycinergic receptors.

Yi-Syuan Li, MD
Chun-Yu Chen, MD
Chi-Hui Chen, MD
Zhi-Kang Yao, MD
Yu-Hsiang Sung, MD
Kai-Cheng Lin, MD
Chien-Jen Hsu, MD
Jenn-Huei Renn, MD

Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan
Tetrad issues exist regarding spinal fusion with pedicle screws and adjacent-segment disease

TO THE EDITOR: We read the elaborate clinical review article by Agarwal and colleagues1 regarding adjacent-segment disease (ASD) following thoracic fusion with pedicle screws (Agarwal N, Heary RF, Agarwal P: Adjacent-segment disease after thoracic pedicle screw fixation. J Neurosurg Spine 28:280–286, March 2018). Indeed, it has been noted that ASD with clinical manifestations might occur as a long-term adverse event for both cervical and lumbar spine fusion. If diagnostic imaging indicates adjacent-segment stenosis or degeneration without clinical symptoms, it is called adjacent-segment degeneration.2 Even in lumbar fusion without pedicle screws, ASD occurred in more than 42% patients with 33 years of follow-up on average.3 The current article sheds novel light on ASD following thoracic fusion.

There might be tetrad issues regarding spinal fusion with metal implants. First, the best treatment strategies for ASD remain undefined. Currently, there are several treatment options for ASD, i.e., simple decompression, and fusion with instrumentation extension with or without removal of primary implants. In fact, the underlying mechanisms of ASD remain unclear, yet several hypotheses exist, including increased stress and compression of adjacent segments, the splitting of paraspinal muscles, and the natural degeneration/aging of adjacent discs.4

Second, the criteria for pedicle screw implant removal have not reached a consensus. Literature is scant regarding the issue of implant removal, including the timing for removal, the healing of the pedicle after implant removal, and the indications for removal. There were several reports addressing pedicle stress fractures after implant removal, including extension of fusion for the treatment of ASD.5,6

Third, serum metal iron levels should be appreciated as systemic reactions to spinal metal implants. Accumulating evidence indicates spinal metal implants, including pedicle screws and metal artificial discs, will cause systemic and local reactions in the human body. For instrumented spinal fusion, serum titanium, niobium, and aluminum levels were significantly elevated, in addition to local metal debris.7–9 This potentially harmful issue should be addressed, particularly for children and adolescents undergoing spinal fusion for scoliosis due to the long implant retention time during their remaining lifetime.

Fourth, and most importantly, we propose that the harmful radiation exposure and effective dose reduction of radiographic imaging should be noted. Overwhelming evidence indicates that the cumulative radiation dose from multiple diagnostic radiographies for adolescents with scoliosis increases cancer risks, particularly breast cancer.10 With an average of 16 radiographs, 170 patients with adolescent idiopathic scoliosis had a relative risk of 4.8 for developing cancer compared to the age-matched normal Danish population. We noted that Agarwal and colleagues were still adopting traditional spine radiographic imaging, as seen in Fig. 1. To reduce the radiation dose,