Can J Anesth/J Can Anesth (2023) 70:917–918
https://doi.org/10.1007/s12630-023-02436-z

CORRESPONDENCE

In reply: Accidental infusion of tranexamic acid via a thoracic epidural catheter

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Received: 6 December 2022 / Revised: 6 December 2022 / Accepted: 6 December 2022 / Published online: 13 March 2023

Keywords epidural · medication error · tranexamic acid · wrong route error

To the Editor,

We thank Dr. Patel for his interest in our case report of a patient with accidental administration of tranexamic acid (TXA) into the epidural space.[1] The lens through which the case was presented and discussed, as supported by the *Journal's* reviewers, focused on the findings of the Quality & Patient Safety review of the event with an aim to learn from the contributing systemic, environmental, human, and equipment factors involved so as to prevent future errors. As such, the word limitations of the manuscript did not permit a more fulsome discussion of the protective anatomic, physiologic, and pharmacologic mechanisms outlined by Dr. Patel.[2] Though impossible to "know the fate" of the TXA administered, Dr. Patel's insightful comments about the possible mechanisms contributing to the positive outcome described are welcomed.

We, too, were unable to find any pharmacokinetic models to explain TXA concentrations in cerebrospinal fluid (CSF) after epidural route administration. Of note, none of the TXA manufacturers we contacted were able to provide any corresponding data—from animals, humans, or other related to TXA administration into neuraxial structures or data specific to the concentrations of TXA in the CSF following any route of TXA administration. The most informative data about TXA concentration in the CSF following *iv* administration of TXA come from an observational study involving four patients with intrathecal lumbar drains who underwent thoracoabdominal aortic procedures.[3,4] Of the four patients with CSF sampled, one patient experienced a postoperative seizure.[3,4] Notably, the CSF concentration of TXA peaked *after* cessation of the TXA *iv* infusion.[3,4]

Glycine receptors and γ-aminobutyric acid type A ($GABA_A$) receptors mediate a substantial amount of central nervous system inhibition. Though TXA inhibition of $GABA_A$ receptors occurs at levels above the clinically noted CSF concentration (e.g., 200 μM)[4] following *iv* TXA infusion, glycine receptor inhibition from TXA occurs *below* the clinically measured CSF concentrations in patients following TXA infusion.[3,4] The total dose (500 mg) and duration of TXA infusion (approximately four to five minutes) in our case[1] were both substantially lower than in other reports of postoperative seizure after *iv* TXA infusion.[3,4] The fact that the patient in our case had approximately four hours of volatile (sevoflurane) general anesthesia after cessation of the epidural route TXA may have provided some additional protection; volatile anesthesia (isoflurane) at clinically relevant concentrations reverses the hyperexcitability produced by TXA.[4] The same effect, reversal of TXA-induced neuronal excitability, is noted with propofol at clinically relevant concentrations as well.[4] The approach of "prolonging the delivery of anesthetics during the early postoperative period" has been previously mentioned by others.[4]

Opportunities for delaying surgery, should an event like this occur, are appropriate to consider. While we understand that Dr. Patel may not agree with the anesthesiologist's choice to proceed with surgery, we recognize that this was indeed a difficult decision to make, for which there were no standards, guidelines, or similar

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case reports to which one could refer. We believe that our colleague acted in good faith, used their best judgment, and considered the challenging circumstances at that time. The provider involved also had the humility and courage to consult with a number of colleagues while making this decision. Follow-up and support for those involved in an adverse event[5] are important considerations for the wellbeing of individual practitioners and departments as a whole.

Disclosures None.

Funding statement None.

Editorial responsibility This submission was handled by Dr. Stephan K. W. Schwarz, Editor-in-Chief, *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*.

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