Can J Anesth/J Can Anesth (2023) 70:915–916
https://doi.org/10.1007/s12630-023-02435-0

CORRESPONDENCE

Accidental infusion of tranexamic acid via a thoracic epidural catheter

Santosh Patel, MD, FRCA, PG Dip (Med Edu)

Received: 26 October 2022 / Revised: 29 October 2022 / Accepted: 31 October 2022 / Published online: 13 March 2023

Keywords drug errors · epidural · medication errors · tranexamic acid

To the Editor,

I read with great interest the recent report of a case of accidental infusion of tranexamic acid (TXA) via a thoracic epidural catheter.[1] Pysyk and Filteau described inadvertent administration of TXA soon after the induction of general anesthesia, before the start of an elective open hepatectomy.[1]

In their discussion, the authors did not explore any potential mechanisms for the lack of neurologic or cardiovascular signs or symptoms following TXA infusion into the epidural space. Although it is impossible to know the fate of TXA in the patient reported, it is likely that TXA did not cross meningeal layers and diffuse in sufficient concentrations to bind to γ-aminobutyric acid type A ($GABA_A$) and glycine receptors because of several factors, including physicochemical properties (e.g., TXA is water soluble), the thickness of the meningeal layers (e.g., thicker in thoracic than lumbar region), and competing processes for removal of TXA from the epidural space.[2,3] Unlike local anesthetics injected into the epidural space, TXA that diffuses via vertebral foramina into the paravertebral space or around nerve roots outside the spinal cord may not bind to $GABA_A$ and glycine receptors located within the gray matter of the spinal cord predominantly in dorsal and ventral horns.[4] Theoretically, normal saline (NS) boluses and infusion into the epidural space might have facilitated the distribution and clearance of unbound (protein binding 3%) and low molecular weight TXA. Nevertheless, it is challenging to understand to what extent.[5]

I am unaware of a pharmacokinetic model to predict cerebrospinal fluid (CSF) concentrations of TXA after epidural bolus or infusion administration. Preclinical studies have shown that applying 200 μM of TXA to neocortical slices *in vitro* markedly increases the frequency of spontaneous epileptiform field potentials.[6] Tranexamic acid inhibits $GABA_A$ receptors, but only at concentrations higher than the concentration detected in the CSF of thoracoabdominal aneurysm repair patients who receive intravenous TXA.[6] More research is required concerning TXA pharmacokinetics within the central nervous system of humans.

The patient in the report by Pysyk and Filteau was described as being asymptomatic under general anesthesia (GA) maintained using sevoflurane and neuromuscular blockade; however, there are reports of refractory seizures occurring in patients who erroneously received intrathecal TXA once GA was lightened or discontinued.[7] Therefore, the decision to proceed with surgery following inadvertent neuraxial administration of TXA demands careful consideration of risks and benefits. The prudent approach would have been to postpone elective surgery and continuous monitoring and decide in a day or two for elective surgery, depending on the clinical course. Exceptions include lower segment Cesarean delivery and any other life-saving emergency surgery.

This article is accompanied by an editorial and reply. Please see Can J Anesth 2023; this issue.

S. Patel, MD, FRCA, PG Dip (Med Edu) (✉) ·
Department of Anaesthesia, Tawam Hospital, Al Ain, UAE
e-mail: skpatel@seha.ae

In a narrative review of neuraxial potassium chloride (KCl) administration errors,[5] the authors mentioned that the tolerability of NS infusion at a high rate (99–100 $mL \cdot hr^{-1}$) into the epidural space is unknown. Nevertheless, patients who received epidural KCl were in severe pain, were para- or tetraplegic, and most needed tracheal intubation.[5] Therefore, conducting any clinical evaluation of high-rate NS infusion into the epidural space was impractical.

Finally, we owe our thanks to Pysyk and Filteau for reporting the first epidural TXA incident in the literature, which occurred under difficult clinical circumstances. The reported case and other recent TXA incidents remind us that there should be no complacency in handling TXA during the execution of neuraxial anesthesia or analgesia or the use of TXA to minimize the blood loss.[8,9]

Disclosures None.

Funding statement No funding received from any sources.

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

References

1. *Pysyk CL, Filteau L.* Accidental administration of tranexamic acid into the epidural space: a case report. Can J Anesth 2022; 69: 1169–73. https://doi.org/10.1007/s12630-022-02276-3
2. *Clément R, Malinovsky JM, Hildgen P, et al.* Spinal disposition and meningeal permeability of local anesthetics. Pharm Res 2004; 21: 706–16. https://doi.org/10.1023/b:pham.0000022419.18144.9e
3. *Kane Z, Picetti R, Wilby A, et al.* Physiologically based modelling of tranexamic acid pharmacokinetics following intravenous, intramuscular, sub-cutaneous and oral administration in healthy volunteers. Eur J of Pharm Sci 2021; 164: 105893. https://doi.org/10.1016/j.ejps.2021.105893
4. *Malcangio M, Bowery NG.* GABA and its receptors in the spinal cord. Trends Pharmacol Sci 1996; 17: 457–62. https://doi.org/10.1016/s0165-6147(96)01013-9
5. *Patel S, Dexter F.* Narrative review of neuraxial potassium chloride administration errors: clinical features, human factors, and prevention measures. Reg Anesth Pain Med 2021; 46: 904–8. https://doi.org/10.1136/rapm-2021-102933
6. *Lecker I, Wang DS, Whissell PD, Avramescu S, Mazer CD, Orser BA.* Tranexamic acid–associated seizures: causes and treatment. Ann Neurol 2016; 79: 18–26. https://doi.org/10.1002/ana.24558
7. *Patel S, Robertson B, McConachie I.* Catastrophic drug errors involving tranexamic acid administered during spinal anaesthesia. Anaesthesia 2019; 74: 904–14. https://doi.org/10.1111/anae.14662
8. *Patel S.* Safe spinal anesthesia practices to prevent intrathecal tranexamic acid incidents. J Clin Anesth 2022; 82: 110889. https://doi.org/10.1016/j.jclinane.2022.110889
9. *Institute for Safe Medication Practices Canada.* Alert: substitution error tranexamic acid during spinal anaesthesia. Available from URL: https://ismpcanada.ca/bulletin/alert-substitution-error-with-tranexamic-acid-during-spinal-anesthesia/ (accessed November 2022).