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CASE REPORTS / CASE SERIES

Accidental administration of tranexamic acid into the epidural space: a case report

Administration accidentelle d'acide tranexamique dans l'espace péridural : une présentation de cas

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Abstract

Purpose *Tranexamic acid administration into the epidural space has not been previously reported. We describe our experience managing and investigating a drug error involving incorrect route of tranexamic acid administration through an epidural catheter.*

Clinical features *A syringe containing tranexamic acid, intended for intravenous bolus and infusion intraoperatively using microbore tubing, was inadvertently attached to an epidural catheter via the Luer-type connector on the microbore tubing and epidural adapter.*

Conclusions *Saline lavage of the epidural space may be considered if tranexamic acid has been administered into the epidural space. Early multidisciplinary team involvement combined with repeated postevent neurologic monitoring is recommended to guide therapy. Adoption of neuraxial route-specific connectors, when available, may be warranted to reduce Luer-type misconnections.*

Résumé

Objectif *L'administration d'acide tranexamique dans l'espace péridural n'a pas été rapportée auparavant. Nous décrivons notre expérience de prise en charge et d'investigation d'une erreur médicamenteuse due à une erreur dans la voie d'administration d'acide tranexamique via un cathéter péridural.*

Caractéristiques cliniques *Une seringue contenant de l'acide tranexamique, destinée à l'administration peropératoire intraveineuse de bolus et de perfusion via des tubulures de microcalibre, a été fixée par inadvertance à un cathéter péridural via un connecteur de type Luer sur la tubulure de microcalibre et l'adaptateur péridural.*

Conclusion *Un lavage salin de l'espace péridural peut être envisagé si de l'acide tranexamique a été administré dans l'espace péridural. La participation rapide d'une équipe multidisciplinaire combinée à un monitorage neurologique répété après l'événement sont recommandés pour guider le traitement. L'adoption de connecteurs spécifiques à la voie neuraxiale, lorsqu'ils sont disponibles, pourrait être utile pour réduire les erreurs de connexion de type Luer.*

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

Tranexamic acid (TXA) is a commonly administered antifibrinolytic drug to minimize hemorrhage. It has relatively few side effects when given intravenously (*iv*). Nevertheless, catastrophic outcomes are frequent following intrathecal (IT) route TXA.[1] We describe a unique case of accidental epidural route administration of TXA and our management. Full disclosure of the drug error was made to the patient. The patient provided informed consent for publication of this case report.

A 70-yr-old woman (weight, 73 kg) with colorectal metastases to the liver was scheduled for an elective right hepatectomy and diaphragmatic nodule resection via subcostal laparotomy. A thoracic (T8/9) epidural catheter (20G, Portex®, Smiths Medical, Keene, NH, USA) was placed and attached to the connector (Portex EpiFuse® Epidural Catheter Connector, Portex, Smiths Medical, Keene, NH, USA). Aspiration from the epidural catheter was negative for blood and cerebrospinal fluid and the test dose (3 mL of 2% lidocaine containing 5 $\mu g \cdot mL^{-1}$

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epinephrine) was also negative. Radial artery catheterization, *iv* induction, central venous catheterization, endotracheal tube intubation, and volatile maintenance of general anesthesia were performed without unintended consequences.

Tranexamic acid administration was planned as an *iv* bolus (10 $mg \cdot kg^{-1}$) before surgical incision and as an infusion throughout the case (1 $mg \cdot kg^{-1} \cdot hr^{-1}$). The TXA (100 $mg \cdot mL^{-1}$) was prepared and labeled in a 10-mL syringe to which portless, microbore infusion tubing (Baxter Healthcare Corporation, Deerfield, IL, USA) was connected. The 10-mL syringe containing the TXA and microbore tubing was then loaded into a syringe pump and programmed to deliver the bolus (10 $mg \cdot kg^{-1}$, 700 mg) over five minutes. Once programmed, the microbore tubing with male Luer connection was inadvertently connected to the female Luer connection of the epidural catheter connector before the start of the surgical procedure. Approximately 5 mL (500 mg) of TXA was administered over a four-minute period before the line misconnection was noted when the resident and staff anesthesiologist reviewed the arrangement of infusion medications and IV lines.

When recognized, the TXA infusion was immediately stopped and the issue communicated to the surgical team who had completed draping the patient but had not yet incised the skin. The care team consulted other available anesthesiologists to review management options. The anesthesiologists consulted were familiar with the morbidity associated with IT TXA cases;[1] however, no one present, nor a rapid literature search, could identify a report specific to epidural route TXA and its management.

Attempts to aspirate fluid from the epidural catheter were unsuccessful. A sterile, preservative-free saline, 0.9% sodium chloride USP (Pfizer Canada Inc., Kirkland, QC, Canada) epidural lavage was started. A 20-mL syringe bolus of saline was administered over a five-minute period through the epidural catheter. Two additional 20-mL boluses of saline were given over the next 60 min for a total of 60 mL of saline in the epidural space within the first hour of the drug error. An infusion of saline at 20 mL per hour was then initiated through the epidural catheter and continued postoperatively for 48 hr.

The patient's clinical picture and hemodynamics were unremarkable throughout this event. There was no evidence of motor seizure activity or myoclonus, though the patient was under sevoflurane general anesthesia and neuromuscular blockade. Electroencephalography waveforms from the depth-of-anesthesia monitor were consistent with moderate to deep general anesthesia. Somatosensory evoked potential monitoring was not available at the campus where the event occurred. Additional consultations to our hospital's pharmacy, toxicology, and neurology services were requested, seeking any possible additional advice and guidance. None of these specialty colleagues had experience with or training specific to epidural administration of TXA. Supportive measures, as aforementioned with lavage, were felt to be reasonable.

After careful consideration, multidisciplinary discussion, and re-evaluation of the patient's clinical status, the decision to proceed with surgery was made after the saline lavage, 60 mL over 60 min as described above, of the epidural space was completed. The procedure was successfully completed in 3 hr 50 min and with approximately 1,000 mL of blood loss, without the need for blood transfusion. The patient was extubated in the operating room, hemodynamically stable, and transported to the postanesthesia care unit (PACU). Neurologic assessment in the PACU noted a normal motor function exam in all four limbs and no evidence of seizures, myoclonus, or other abnormalities. Given the propensity for seizures following TXA in the intrathecal space, a loading dose of levetiracetam 1,500 mg *po* was given to the patient. To ensure appropriate neurologic monitoring (every hour for the next 24 hr), the patient was transferred to the intensive care unit and started on an *iv* patient-controlled analgesia pump. The epidural catheter was removed after 48 hr of saline infusion.

The patient's recovery was in keeping with convalescence following posthepatic resection with subcostal laparotomy without epidural analgesia. Ongoing neurologic assessments revealed no motor weakness or any change from the initial, postanesthesia emergence exam. The patient was able to sit at the edge of the bed unassisted 24 hr after completion of the surgery. Within 48 hr of surgery, the patient was ambulating with a four-wheeled walker because of incisional, dynamic pain, not from leg or motor weakness. No seizure-like activity was noted at any time postoperatively. Neurologic monitoring was stopped after 48 hr; saline infusion through the epidural catheter was ended 48 hr postoperatively; and the patient was discharged home on postoperative day eight without any neurologic sequelae. Follow-up at three months, six months, and nine months after the event revealed that the patient's neurologic status was unchanged from the preoperative state.

Discussion

Mindful of the significant morbidity and mortality risk associated with intrathecal TXA administration,[1] injection of a recognized neurotoxic drug in the epidural space presented a very concerning clinical challenge without any literature to guide management. The immediate treatment

(e.g., cessation of the infusion and saline lavage of the epidural space) was drawn from other case reports of intrathecal[2, 3] and epidural route drug errors.[4–6]

An initial volume of 20 mL of a saline bolus over five minutes was felt to be a reasonable approach to reduce the concentration of TXA in the epidural space. Venous and lymphatic structures throughout the epidural space may offer a disposal route to further enhance medication removal.[7–9] Nevertheless, despite a lowered concentration, the saline bolus may further cranial spread of TXA. We are unable to confirm how much epidural lavage played a role, if any, in our patient's outcome.

Since our event occurred, a narrative review of cases where potassium chloride (KCl) was administered into the epidural space has been published.[10] Patel and Dexter[10] provide a useful summary of case details where epidural saline lavage therapy was employed in eight of the 25 patients given epidural route KCl. Among these eight patients who developed neurologic symptoms after epidural KCl administration, saline lavage practices varied considerably in the amount, rate, and duration of therapy. Overall, in seven of the eight patients treated with saline lavage after epidural route KCl administration, neurologic symptoms were completely resolved.

Four individual case reports used single-dose bolus volumes of 10 mL,[11] 20 mL,[12] 40 mL,[13] and 50 mL,[14] respectively, with no comment on the time periods over which the boluses were given. Three different reports used higher rates of saline infusion, each for six hours: one case with 100 mL·hr^{-1} [15] and two cases with 99 mL·hr^{-1}.[16, 17] These reports make no comment on patient tolerance or intolerance of these high rates of saline infusion. Interestingly, saline lavage was not used in 15 of the 25 cases with KCl given into the epidural space, and complete recovery was noted. As such, the evidence supporting saline lavage therapy following KCl administration is limited to these few case reports and may not be applicable to TXA.

Following a comprehensive review by the Quality & Patient Safety Committee (led by the authors) within the Department of Anesthesiology and Pain Medicine at our institution,[18] several factors were noted to predispose to the drug error we describe.

Organizationally, the experienced staff anesthesiologist was assigned concomitant clinical and managerial responsibilities, including that of OR coordinator. In this role, interruptions are frequent throughout the day. An anesthesiology resident was also assigned to the case on the day of the event. Prior to and during the start of the case, several requests were made for the OR coordinator to facilitate resources to support clinical care in other areas. In addition to the considerations for major hepatic resection, this patient was enrolled in a study involving complex tasks (randomized trial of phlebotomy for hepatic resection), which required a central line insertion and other administrative undertakings. In anticipation of the multiple case demands, the anesthesiologist planned to administer the TXA bolus using a syringe pump with microbore tubing. This was a departure from their usual practice of connecting the syringe with TXA directly to the IV port and hand pushing the plunger of the syringe. There were some atypical patient factors that required particular perioperative attention by the treating team. Despite instructions to the contrary, the patient self-administered her usual angiotensin receptor blocker on the morning of surgery. As such, the concern for postinduction, preincision hypotension was more acute and demanded additional attention from the anesthesiology team.

The need for TXA was reaffirmed at the "Time Out" for the surgical safety checklist, performed before draping of the patient. The staff anesthesiologist recalls correctly selecting the TXA microbore tubing with the intention of connecting it to an IV port. In the time between picking the TXA microbore tubing and connecting it to the IV port, the anesthesiologist was asked a question by another OR team member. In response to the question, the anesthesiologist paused their action (e.g., held the TXA microbore tubing in their hand), answered the question, then returned to complete the task. It was at this time when the misconnection error transpired: the right action (e.g., connecting the TXA microbore tubing) occurred but on the wrong object (e.g., to the epidural adapter). An observable error of execution, referred to as a "slip,"[19] during performance of a routine task is a skill-based error. Said another way, skill-based errors occur among individuals with the experience, intention, and knowledge to perform a task; however, the action does not turn out as they intended or results in "doing the right thing but on the wrong object" during performance of a familiar task. Reason identifies two conditions "necessary for the occurrence of these slips of action: performance of some largely automatic task in familiar surroundings and a marked degree of attitudinal "capture" by something other than the job in hand."[19] As such, experienced providers familiar with their environment, equipment, and task performance are not protected from committing such slip, skill-based errors. Not surprisingly, the rate of skill-based error increases markedly when an interruption occurs before a task is completed.[20]

Epidural catheter practice patterns and timing cues likely facilitated the slip, or misconnection drug error. A common task performed by anesthesiologists at our institution around the time of surgical draping includes connecting the epidural solution to the epidural adapter. The epidural solution is infused via a syringe pump loaded with a syringe connected to microbore tubing. As such,

connecting microbore tubing to the epidural adapter before incision provided feedback to the anesthesiologist that would be perceived as "normal" task performance in the context of the equipment and situation despite differences in shape, color, size, and design between the choice of epidural connector and IV port (Fig. 1). "Strong but wrong" errors of action manifest because "strong habits can take over when attention to checks is diverted by distractions."[21]

In their review article on TXA drug errors during the conduct of spinal anesthesia, Patel *et al.* remark that "no reports of accidental epidural administration of tranexamic acid" exist given that TXA vials or ampoules "are not so readily confused with the normal local anesthetic preparations used for epidural analgesia."[1] Among spinal anesthesia drug errors involving TXA, the wrong vial is selected and TXA is inadvertently aspirated from the vial before intrathecal injection.[1] In our case, the final, prepared appearance of the TXA syringe on the syringe pump with microbore tubing was a factor. The environmental review highlighted that a syringe pump with microbore tubing is commonly used to administer both *iv* and epidural route medications at our institution (Fig. 2). Consequently, the equipment appearance may have conferred a look-a-like, perceptual error based on utility of the same equipment set-up for both *iv* and epidural medications. As such, a lesson from our report includes reviewing the syringe shape and size, as well as equipment (e.g., syringe pump and microbore tubing) used to administer epidural solutions in the perioperative environment.

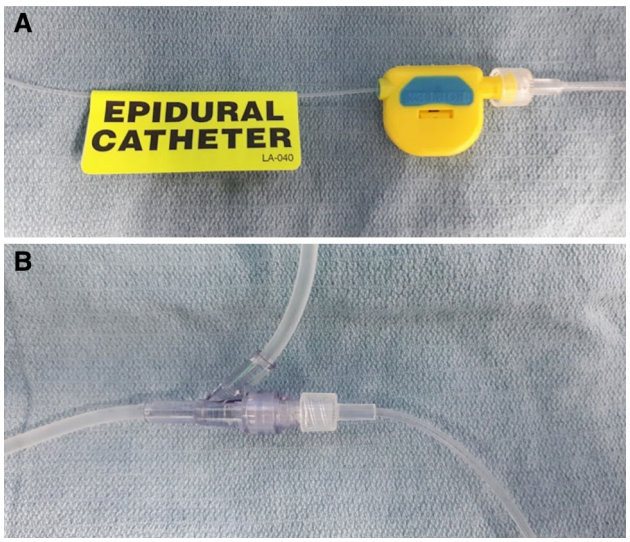

Fig. 1 Appearance of microbore tubing (entering from right hand side of each panel) in the unintended state (Panel A) and the intended state (Panel B) of connection. Panel A: Microbore tubing attached to epidural catheter connector. Panel B: Microbore tubing attached to the intravenous port.

Fig. 2 Replicated set-up of syringe infusion pumps with tranexamic acid in a 10-mL syringe (top) and epidural solution in a 20-mL syringe (bottom).

Consideration to providing epidural route-exclusive equipment for infusion of medication is another worthwhile prevention strategy.[6] Additionally, obtaining a preprepared, *iv*-ready TXA infusion alternative, removing the potential for preparation of a look-a-like equipment scenario, is another possible solution. Our findings are in keeping with previously reported causes of nonepidural medications administered into the epidural space—syringe swap and epidural and epidural/*iv* line misconnections are common.[4–6] Furthermore, as reported by others, skill-based and perceptual errors, like we describe here, account for the majority of epidural route medication errors.[6, 10]

System-focused solutions, such as equipment and environmental redesign making inadvertent misconnections far less likely or impossible, are more effective at improving safety than person-focused efforts (such as messaging, warnings, recommendations for labeling, and generation of operational policies) are.[22] Given the aforementioned case details, the *iv*-intended microbore tubing with a Luer connection would have been incompatible with the epidural catheter if a neuraxial route-specific adapter (as described by ISO 80369-6:2018—Small bore connectors for neuraxial application[23] such as NRFit connectors) had been available for clinical use in this case.

It is our understanding that these connectors will soon become available in Canada. Nevertheless, adoption of this new system can complicate other aspects of care. For example, availability of mission-critical, "stand alone" equipment, like a neuraxial route syringe to top up an epidural catheter in advance of Cesarean delivery, is paramount to facilitate an appropriate and timely workflow and care paradigm. In addition, neuraxial route-specific

adaptors will only prevent misconnection of the intended route, as described in this case report. If a syringe with a neuraxial route-specific connection is filled with an *iv*-intended medication, like TXA, the wrong drug can still be administered into the neuraxial space.

Planning for implementation of this new equipment will require coordination among many stakeholders in the healthcare system. Harmonized local, regional, and national strategies to facilitate roll out of neuraxial route-specific equipment will be essential to provide timely and sufficient access to this safety-enhancing equipment for all patients undergoing neuraxial procedures.

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