Case Report

Refractory status epilepticus after accidental intrathecal injection of tranexamic acid

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Abstract

Tranexamic acid (TXA) is an antifibrinolytic agent that is commonly used in cardiac, gynecologic, and obstetric surgeries. Inadvertent intrathecal injection of the TXA may lead to serious side effects including myoclonus, seizure, and ventricular fibrillation. So far, the proconvulsive properties of TXA and its mechanism of action are poorly understood. Medical error leads to serious adverse effects that can be attributed to similar appearance of ampoules, location of ampoules, and incorrect labeling of prefilled syringes. We herein report a case of refractory status epilepticus after accidental intrathecal injection of TXA. The patient was treated with thiopentone infusions until achieving a burst suppression pattern on electroencephalogram along with other antiepileptic drugs. Subsequently, the patient recovered completely without any neurological deficit. To the best of our knowledge, this is the first case of refractory status epilepticus after inadvertent intrathecal injection of TXA. Such catastrophic complications can be avoided by vigilance, correct labeling of syringes and ampoules, double checking medications prior to administration, and preventing manufacturing of vials of different drugs with similar appearance.

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1. Introduction

In industrialized countries, the major cause of injury and death in many health centers and hospitals is medication errors. Most of these cases can be prevented by vigilance, correct labeling of syringes and ampoules, double checking medications prior to administration, and preventing manufacturing of vials of different drugs with similar appearance. Tranexamic acid (TXA) is an antifibrinolytic agent that is commonly used in cardiac, gynecologic, and obstetric surgeries. Recently, TXA has been shown to be associated with an increased incidence of postoperative seizures in cardiac patients. Higher frequency of seizures has been reported in patients with preoperative renal failure, open heart surgery, and older age.1 The proconvulsive properties and the underlying pathophysiology of TXA have not been completely understood yet. In this case report, we report a case of refractory status epilepticus due to accidental administration of intrathecal TXA injection instead of bupivacaine for spinal anesthesia.

2. Case Report

A 36-year-old American Society of Anaesthesiologists I physical status male was scheduled for herniorrhaphy for left inguinal hernia in a peripheral hospital in western India. A thorough preanesthetic checkup was done. The patient had no prior history of seizures, neurological illness, exposure to anesthesia, or drug allergy. Baseline monitors (pulse oximetry, noninvasive blood pressure, and electrocardiogram) were
established in the operating room. Spinal anesthesia was administered to the patient in the sitting position at the L3–L4 interspace by a 27-gauge atraumatic spinal needle. An injection of 2.5 mL 0.5% hyperbaric bupivacaine and 25 µg fentanyl was prepared for intrathecal administration. After the intrathecal injection, the patient was placed in the supine position; 1 minute later, the patient complained of pain in the back and in both lower limbs. The partial effect of spinal anesthesia was therefore supplemented with an intravenous injection of fentanyl (100 µg) and midazolam (2 mg) prior to surgery. However, 30 minutes after the administration of intrathecal injection, the patient again complained of pain in the back and in both lower limbs. Within a few minutes, he developed tonic deviation of all four limbs with uprolling of his eyeballs. At that time, his blood pressure was 170/100 mmHg and pulse rate was 115/minute. The patient had oxygen saturation of 100% on air.

Since then, he developed recurrent generalized tonic–clonic seizures (GTCSs). The patient received an injection of lorazepam (4 mg). Despite three repetitive injections of intravenous lorazepam, he had recurrent GTCS. In between seizures, he remained in altered sensorium. A loading dose of phenytoin (20 mg/kg) was intravenously infused over 20 minutes to control the seizures; however, the infusion had no effect. Therefore, a bolus of propofol (60 mg) was administered intravenously, followed by infusion of propofol at a rate of 120 µg/kg/minute. He was intubated with an 8.5-mm cuffed polyvinyl chloride endotracheal tube and put on the mechanical ventilator support. Following intubation, he was shifted to our hospital for further management. Accidental intrathecal administration of a wrong drug was suspected. On inquiry, the used ampoule of TXA was found in the anesthesia tray. Because the patient had recurrent GTCS with altered sensorium in the emergency room, the dose of propofol was increased and he was shifted to the neurointensive care unit. Scalp electroencephalography (EEG) was performed, which showed ongoing status epilepticus. He had refractory status epilepticus as intermittent breakthrough seizures with ongoing seizure activity on EEG. We decided to induce coma with thiopentone. An intravenous bolus of thiopentone injection was given (5 mg/kg over 20 minutes), followed by infusion of the drug at a rate of 2 mg/kg/hour. The dose of infusion was subsequently increased up to 15 mg/kg/hour until a burst suppression pattern was achieved (Fig. 1). The dose of thiopentone was tapered after 6 hours of a clinical and electroencephalographic seizure-free period. Doses of thiopentone and propofol were gradually tapered over 24 hours. The patient was put on a maintenance dose of phenytoin with clobazam. His sensorium started to improve after 72 hours, and he was extubated after 4 days. Magnetic resonance imaging of the brain was performed, and the results were normal (Fig. 1). He was discharged after 7 days without any neurological deficit.

Fig. 1. (A) Ongoing epileptiform discharges in the electroencephalography (EEG) recording. (B) Burst suppression in the EEG recording induced by thiopentone. (C) Normalization of the EEG findings after controlling the status epilepticus. (D) Normal magnetic resonance imaging brain (axial cut of the fluid attenuated inversion recovery sequence).
3. Discussion

TXA is a widely used antifibrinolytic agent. It is associated with minor gastrointestinal side effects such as nausea, vomiting, or diarrhea. In experimental studies, topical application of the TXA to the cerebral cortex of the experimental animals is reported to produce seizures.\(^2\),\(^3\) In one experimental study, it has been shown to cause systemic as well as intracranial hypertension and seizures.\(^3\) Its epileptic property is directly proportional to the concentration of the drug and area of the exposed cortex.

Little is known about the direct application of TXA to the human cortex. For the first time in humans, Wong et al.\(^4\) reported a case of inadvertent intrathecal injection of TXA. In their case report, an 18-year-old man developed myoclonus, generalized seizure, and persistent sensory block of both lower extremities after an inadvertent intrathecal injection of TXA. His seizure responded to intravenous administration of diazepam. Since then, many case reports were published on the side effects of inadvertent intrathecal injection of TXA. In another case report, De Leede-van der Maarl et al.\(^5\) reported a case of a 68-year-old male, who inadvertently received 50 mg of TXA intrathecally. Immediately after the intrathecal injection, he developed status epilepticus that was managed with diazepam and thiopental. The patient survived with bilateral peroneal palsy.

Sabzi et al.\(^6\) reported a case of a 30-year-old female who inadvertently received an epidural injection of TXA for epidural analgesia instead of bupivacaine. The patient developed severe pain in the back and gluteal region immediately after the injection. Her cesarean section was performed under general anesthesia because of inappropriate spinal analgesia. Just after the cesarean section, she developed myoclonus and generalized seizure. The seizure responded to intravenous administration of diazepam. Subsequently, she developed refractory ventricular fibrillation and died. The mechanism of convulsion and ventricular fibrillation of intrathecal injection of TXA is not known. It was postulated that high doses of the drug would lead to massive sympathetic surge, which results in the systemic hypertension and ventricular fibrillation.

Our patient developed refractory status epilepticus after an inadvertent intrathecal injection of TXA. The patient required continuous infusion of thiopentone to induce burst suppression pattern. Triggering of seizures may be explained by suppression of the inhibitory gamma-aminobutyric acid (GABA)-A receptors in the cerebral cortex or by direct cerebral ischemia as a result of reduced cerebral blood flow.\(^7\) Activation of GABA-A receptors results in opening of the neuronal chloride channels with subsequent neuronal hyperpolarization and suppression of the neuronal excitability. Blockade of GABA-A receptor by the TXA leads to lower threshold for neuronal depolarization and enhanced neurotoxicity.\(^7\)

In the literature, status epilepticus has been reported because of inadvertent intrathecal injection of the TXA; however, there is no report on refractory status epilepticus secondary to intrathecal injection of the TXA.\(^3\) Treatment of intrathecal injection of the TXA includes administration of the anticonvulsants, intensive hemodynamic monitoring, and if required, cerebrospinal fluid (CSF) lavage.\(^8\) CSF lavage removes and dilutes the injected drug and limits the neuronal excitotoxic damage. In our case, CSF lavage could not be performed as the patient presented after 3 hours of onset of the seizure.

In conclusion, in all the previous case reports, inadvertent intrathecal injection of the TXA instead of hyperbaric bupivacaine was given because of the similarity of appearance of the both ampoules. This is probably the first case report of refractory status epilepticus after inadvertent intrathecal injection of the TXA. Such a catastrophic complication can be avoided by unique manufacturing of the critical drugs such as spinal anesthetic drugs. At the same time, health care professionals should adhere to the double checking concept to prevent such deadly but avoidable complication.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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References