

Accidental Injection Of Tranexamic Acid Into Subarachnoid Space Leading To Fatal Outcome: Case Report And Review

U Srivastava, K Joshi, V Gupta, A Gupta, N Chauhan, A Dupargude, A Saxena, A Saxena

Citation

U Srivastava, K Joshi, V Gupta, A Gupta, N Chauhan, A Dupargude, A Saxena, A Saxena. *Accidental Injection Of Tranexamic Acid Into Subarachnoid Space Leading To Fatal Outcome: Case Report And Review*. The Internet Journal of Anesthesiology. 2012 Volume 30 Number 2.

Abstract

Medication error leading to significant morbidity and mortality is a cause of great concern. We are reporting a case where a patient received spinal anaesthesia with tranexamic acid by mistake due to similarity between ampoules of bupivacaine and tranexamic acid and had fatal outcome.

CASE REPORT

A 35 year old female patient of ASA status I was scheduled to undergo cholecystectomy. Her medical history was unremarkable and she was non-alcoholic, non-smoker and all the laboratory investigations were within normal range. She received spinal anaesthesia at L2-3 interspace in right lateral position with 3.5 ml of 0.5% hyperbaric bupivacaine which was drawn from the ampoule handed over by the operation room assistant to the anaesthetist. Immediately after turning supine the patients complained of severe pain in the back radiating to both lower limbs and became extremely restless. The BP increased to 170/95 mmHg and heart rate to 124 bpm (Baseline BP 126/84 mm Hg and heart rate 87 bpm). She was given 2 mg of midazolam and 75 µg of fentanyl but without any effect. Few minutes later she developed myoclonic movements of feet followed by generalized convulsions which were controlled by intravenous 10 mg of diazepam. This unusual response aroused suspicion of wrong injection and no broken ampoule of bupivacaine was recovered, instead a broken ampoule of tranexamic acid, [Trenaxa, Macleod's Pharmaceuticals Mumbai, India] was found. Literature was searched but no definite management strategies or antidote could be found. Mean while laboratory investigations including serum electrolytes, glucose, creatinine, urea etc were normal. About five minutes after seizures were abated ,the patient rapidly deteriorated to complete cardiovascular collapse. External cardiac massage, endotracheal intubation, manual ventilation with 100% O₂ ,intravenous adrenaline 1 mg and

IV fluids were instituted and there was return of spontaneous circulation after three minutes. Intra arterial and central venous access were secured. Norepinephrine infusion at the rate of 4µg/min was started . But the arterial pressure remained low ranging between 60 to 75 mm Hg. The patient was immediately shifted to Intensive Care Unit and put on mechanical ventilation with SIMV mode .Vasopressin infusion was added at a rate of 0.03IU/min.The Arterial blood gas analysis on FiO₂ of 1.0 was pH -7.34,pCO₂ 34 mmHg, HCO₃ 22 m Eq pO₂ 385 .ECG showed multifocal premature ventricular contractions (10-12/minute) with a heart rate of 86/min. Treatment with lignocaine, amiodarone failed to revert the rhythm and the patient again had cardiac arrest which could not be revived. The patient died about 5 hours after spinal injection. The patient's relatives denied post-mortem.

Figure 1

Look- alike ampoules of Tranexamic acid and Bupivacaine



DISCUSSION

In therapeutic doses adverse effects of tranexamic acid (TXA) are generally minor and are related to gastrointestinal tract such as nausea, vomiting and diarrhea etc. However, neurotoxic effects have been reported in experimental studies after direct application of TXA to central nervous system of animals in the form of powerful seizures^[1,2]. But there are some reports of non-ischaemic seizures in cardiac surgical patients who received TXA in high doses^[3].

The knowledge of neurotoxic effects in humans is through the sporadic case reports when the patients undergoing surgery accidentally received TXA intrathecally. The first such case was published in 1988 by Wong et al^[4] when a young patient received 75 mg of TA intrathecally and developed generalized seizures four hours after spinal injection. The patient recovered completely without any sequelae. In another case,⁽⁵⁾ a sixty years old man received 50 mg of TXA for spinal anaesthesia by mistake and developed generalized epileptiform seizures immediately after injection. Subsequently other reports of accidental

spinal injection of TXA were published and all the patients presented with myoclonus and convulsions^[6,7,8,9,10]. Some also had hypertension, ventricular fibrillation or arrhythmias that failed to respond to treatment^[9,10]. The exact mechanism by which TXA initiates seizure activity is not clearly known. A proposed mechanism is marked structural similarity of TXA to gamma aminobutyric acid and convulsions could result due to inhibitory action of TXA on GABA receptors^[11]. As GABA-A receptors control the opening of neuronal chloride channels resulting in neuronal hyperpolarization and reduced excitability, blockage of receptors by TXA results in lowering of depolarization threshold and increase in cerebral excitatory phenomenon⁽¹¹⁾. Convulsions could also be due to cerebral ischaemia secondary to reduction in regional or global cerebral blood flow^[12]. Yeh et al (2003) speculated that intrathecal TXA initiates massive sympathetic discharge thus causing hypertension, tachycardia, arrhythmias, myoclonus and generalized seizures.

In the present case we observed myoclonus and seizure activity within minutes of intrathecal injection of TXA. After intravenous injection of 1 gm of TXA, the plasma level is 5-20mg/L and CSF level is 2-5mg/L⁽¹³⁾. Our patient received 350mg of TXA directly into CSF. Extrapolating from animal studies⁽¹⁾ and assuming that the drug was mixed with 500ml of CSF, the CSF level of TXA would have been 700mg /L. The manifold increase in CSF concentration above therapeutic level (2-5 mg mg/ L) caused convulsions. There is clear evidence from animal studies for a dose related neurotoxicity, both in severity and duration⁽²⁾.

The medication errors are due to some recognized factors such as hurry, fatigue, inattention, carelessness or poor communication on the part of anaesthetist or due to look alike ampoules, location of ampoules or syringes^(14,15). This patient received wrong drug due to similarity between the ampoules of bupivacaine and tranexamic acid (Fig 1). Also, traditionally, tranexamic acid is not a part of anaesthesiologist armamentarium. Despite this all reported patients received spinal anaesthesia with this drug. This calls for regular organization of drug drawers in operation rooms. Jensen et al (2004) recommended a 12 point strategy to check medication errors in anaesthesia and critical care⁽¹⁶⁾. We have made it mandatory to identify the label of drug by the anaesthetist personally and label it before injection. To control medication errors, we are introducing a medication safety programme specific for ORs in our hospital which will identify risk factors for errors and then make

recommendations to minimize errors and enhance safety of patients.

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Author Information

Uma Srivastava

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Komal Joshi

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Vishal Gupta

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Amrita Gupta

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Nidhi Chauhan

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Abhishyand Dupargude

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Arpita Saxena

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College

Avanish Saxena

Department Of Anaesthesia And Critical Care And Department Of Surgery, S.N. Medical College