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Subarachnoid lavage following inadvertent intrathecal injection of tranexamic acid

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Abstract

Tranexamic acid (TXA) is a commonly used antifibrinolytic drug during surgical procedures to reduce blood loss. An Inadvertent intrathecal injection of TXA may lead to serious side effects including seizures and ventricular fibrillation with reported fatalities. We report a case of an inadvertentintrathecal injection of TXA which occurred as a result of similarities in appearance between TXA and heavy bupivacaine ampoules. The patient had subarachnoid lavage after experiencing back pain, systemic hypertension followed by generalized tonic clonic seizures.

Introduction

Medication errors with associated morbidity and mortality can occur while rendering anaesthesia, and this has been reported to be the seventh most common overall cause of death.[1] Identified risk factors for medication error include inadequate experience (16%), inadequate familiarity to equipment or device (9.3%), haste (5.6%) and inattention or carelessness (5.6%). Other factors are appearance of ampoules, fatigue and lack of double checking.[1]

The antifibrinolytic agent, tranexamic acid (TXA) is widely used to reduce bleeding during surgery such as cardiac, obstetric and gynaecological procedures; it is used to overcome the increased fibrinolytic activity associated with these procedures.[2] Subarachnoid block is commonly performed for surgeries below the umbilicus and the commonly used drug is the local anaesthetic agenthyperbaric bupivacaine injected into the intrathecal space. We report a case of an obstetric patient that had inadvertent intrathecal injection of TXA instead of hyperbaric bupivacaine because the ampoules of the 2 drugs were similar.

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Case Report

The patient is a 32 year old gravid woman referred to our facility and scheduled for an elective cesarean section on account of 3 previous cesarean sections and fetal hydrocephalus. A preanaesthesia review revealed a young woman with no comorbid conditions; previous sub arachnoid blocks done for cesarean section were uneventful. General examination revealed no abnormalities with normal chest and cardiovascular findings. Investigation results available were full blood count and differential, urine analysis, fasting blood sugar, urea, electrolytes and creatinine and they were all within reference limit. In the operating theatre, baseline vitals were pulse rate of 103 per minute, blood pressure of 130/79mmHg, oxygen saturation (SpO^2) of 98%. Asepsis was ensured, the interspace between the 3rd and 4th lumbar vertebra was located and a spinal needle inserted until in the subarachnoid space. The anaesthetist asked for a vial of heavy bupivacaine and the assistant brought a

Figure 1: TXA ampoule used was similar to that of heavy bupivacaine

vial from which 2.5 mls was withdrawn and injected into the subarachnoid space, 5 minutes after the injection, there was neither sensory nor motor blockade but the patient complained of back pain which was immediately followed by episodes of generalized tonic clonic seizures. Oxygen therapy via face mask was initiated and general anaesthesia was induced with 500mg of sodium thiopentone. She had tracheal intubation with the aid of suxamethonium, anaesthesia was maintained with isoflurane in oxygen and muscle relaxation achieved with atracurium. There was an initial upsurge in pulse rate and blood pressure but these stabilized and remained within acceptable limits though the surgery which lasted 32 minutes, no further intra operative seizure was seen. A further check of the drug given revealed she had an inadvertent intrathecal injection of 250mg of TXA. The TXA ampoule used was similar to that of heavy bupivacaine (Fig 1). Episodes of seizure continued in the immediate postoperative period which warranted her admission into the intensive care unit (ICU) where she immediately had a subarachnoid lavage with exchange of 10mls of withdrawn cerebrospinal fluid with 10mls of normal saline with a total of 150mls exchanged. Medications given for seizure control included an initial dose of up to 375mg of STP and subsequently maintained on 25mg per hour, and magnesium sulphate of 500mg per hour after an initial dose of 5gms. Break through seizure was treated with 10mg of midazolam.The patient was mechanically ventilated using the synchronized intermittent mechanical ventilation mode. With adequate seizure control 2 days after admission into the ICU, anticonvulsants were tapered down, the patient was weaned off mechanical ventilation and extubated with stable vital signs, no neurological sequelae was seen thereafter.

Discussion

The drug ampoule of TXA used for this patient was similar to that of hyperbaric bupivacaine which resulted in drug error. Although TXA often used to reduce bleeding in obstetric patients may cause side effects like nausea, diarrhea, fever, headache, its use is generally well tolerated and itis frequently stored in close proximity with other medications including injectable local anaesthetic agents.

Tranexamic acid when injected into the intrathecal space is a potent neurotoxin and neurological sequelae can manifest, with refractory seizures, this has also been shown to result in systemic hypertension and a reported mortality of up to 50%.[3] Our patient had seizures shortly after an inadvertent intrathecal TXA administration which persisted post operatively. Subarachnoid lavage which was carried out was aimed at reducing the concentration of TXA thus providing for a better outcome. Subsequent treatment for control of seizure was with a combination of sodium thiopentone, magnesium sulphate and midazolam. Wong et al[4] first reported an inadvertent intrathecal injection of TXA in an 18 years old man scheduled for appendectomy, their patient similarly developed generalized seizures which responded to intravenous diazepam. In a case report by Olfaet al[5], a 30 year old man who was scheduled for knee ligament reconstruction surgery also had inadvertent intrathecal injection of 80 mg of TXA. Like in our patient, he also complained of severe back pain with elevated blood pressure and subsequentmyoclonic movements in the lower extremities which did not respond to midazolam (3mg) and Fentanyl (100ug). Following general anaesthesia, the patient developed tonic-clonic convulsions postoperatively in the upper extremities and the face, which were treated with an infusion of sodium thiopental (3–5mg/kg/h). Gastric administration of Phenobarbital 200mg

daily was initiated. He had tracheal extubation on the 3rd day of ICU admission following mechanical ventilation and subsequently discharged on the 6th day with no neurological sequelae.

Although the exact mechanism by which TXA induces these seizures isn't completely understood, it has been reported that high doses of TXA cause massive sympathetic discharge, as was seen in our patient with an initial hypertensive response. Seizures may be induced either from direct cerebral ischemiaor from neuronal hyperexcitability from blockade of inhibitory cortical-gamma aminobutyric acid (GABA)-Areceptors.[6]

Our patient made good recovery with no neurological sequelae following interventions taken. Previous reports have recorded fatalities as a result of intrathecal injection of TXA. Reham et al[7] reported the case of a 21 year old primigravida scheduled for an elective caesarean section that had an inadvertent injection of 160mg of TXA. She developed burning sensation at the site of injection, back pain and gluteal pain 50 seconds following injection; this was followed by recurrent polymyoclonus and seizures which were controlled with intravenous sodium thiopentone, also seen were elevated pulse rate, blood pressure and respiratory rates. Seizures recurred following general anaesthesia and delivery of a live fetus, clonazepam (1 mg) and phenobarbital (800 mg) with continuous sedation using midazolam and Fentanyl were instituted. Thepatient was admitted in ICU where mechanical ventilation continued. Results of arterial blood gases (ABG), brain CT and blood analysis done were normal. Fourteen hours after admission, the patient suffered hypotension, tachyarrythmias, ventricular fibrillation which could not be reversed after cardiopulmonary resuscitation. Al Tael et al[8] in USA also reported mortality after an inadvertent intrathecal injection of TXA in a 76 year old man scheduled for knee replacement surgery. Their patient developed myoclonic seizures, tachycardia, hypertension and tachypnea. He was treated with intravenous levetiracetam (1000mg), midazolam infusion; he was intubated, admitted into ICU and mechanically ventilated. His ICU stay was however complicated by aspiration pneumonitis, he eventually passed away due to respiratory failure.

Conclusion

We emphasize that all cited case reports of erroneous intrathecal TXA administration was a resulted of similarity in drug ampoules of TXA and hyperbaric bupivacaine. A subarachnoid lavage following inadvertent intrathecal injection of TXA reduces drug concentration thus may improve patient outcome. It is recommended that critical drugs like the drugs used for spinal anesthesia have unique appearance and package to avoid mistakes. Anaesthesia providers should also endeavor to double check drug labels before administration.

Conflict of Interest

We declare no conflict of interest

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