



Myoclonus, Seizure, and Ventricular Fibrillation after Intrathecal Injection of Tranexamic Acid

Feridoun Sabzi, MD^{1*}, Hassan Teimouri, MD², Abdolhamid Zokai, MD¹

¹Imam Ali Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran.

²Khorramabad Heart Center, Khorramabad University of Medical Sciences, Khorramabad, Iran.

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Abstract

Tranexamic acid is generally used in the treatment of disorders that predispose one to bleeding. It is a synthetic lysine analog that has strong antifibrinolytic activity. Plasminogen binds to fibrin to form plasmin, which in turn degrades fibrin into fibrin degradation products. Tranexamic acid blocks the lysine binding site on plasminogen and prevents interaction with fibrin. Tranexamic acid reduces blood loss in open heart surgery, hip replacement, and gynecology procedures. In this first case of inadvertent intrathecal injection of Tranexamic acid in a pregnant woman, we found that a massive intrathecal injection of Tranexamic acid triggered refractory ventricular fibrillation and cardiovascular collapse, which did not respond to full resuscitation.

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Introduction

Coagulopathy remains a common problem after coronary artery bypass grafting (CABG) and some gynecological operations, resulting in significant fibrinolysis as reflected by the increasing concentrations of plasmin and fibrin degradation products, both of which have deleterious effects on platelet function. Fibrinolysis is believed to be responsible for 25-45% of significant post-operative bleeding, and many antifibrinolytic agents have been used to reduce post-operative bleeding; these include Aminocaproic acid, Aprotinin, and Tranexamic acid (TA). TA has been found to bind to the lysine binding sites of plasmin, and plasminogen TA is thought to be effective in controlling bleeding in patients with hemorrhagic diathesis and in patients treated with anticoagulants pre-operatively. TA has also been successfully used in controlling bleeding in gynecological surgeries.¹⁻³

Case Report

A 30-year-old woman was admitted to our hospital for twin pregnancy, one in breech position. She had one previous cesarean section (C/S) due to the mal position of the fetus.

Her medical and surgical history was otherwise not contributory, and the decision was made to proceed with a C/S delivery. Before surgery, her coagulation test and her hemoglobin were normal. The test results were as follows: Hemoglobin=13 mg/dl, glucose=90 mg/dl, Na=135 meq/l, K=4.7meq/l, calcium=4.5 meq/l, and WBC=3000/mm³. The patient's ECG was also normal.

Epidural analgesia was performed with the patient in the sitting position. In the box of the anesthetics, there was a vial of Tranexamic acid (made in Iran) similar in appearance to the vial of Bupivacaine. The anesthesiologist nurse mistakenly prepared this vial of Tranexamic acid instead of Bupivacaine, and the anesthesiologist, consequently, injected the dose of Tranexamic acid into the intrathecal space. Immediately

*Corresponding Author: **Feridoun Sabzi**, Associate Professor of Cardiac Surgery, Kermanshah University of Medical Sciences, Imam Ali Hospital, Shaheed Beheshti Ave, Kermanshah, Iran. Tel: +98 918 1311896. Fax: +98 831 8360043. Email: dr_Sabzi@yahoo.com.

after the injection, the patient complained of severe pain in the back and gluteal region. Spinal analgesia not being successful, C/S was performed via general anesthesia and the two babies were delivered safely with a normal Apgar score. Immediately after the delivery, however, the mother developed generalized convulsions and myoclonus. The seizure abated after an intravenous injection of 15 mg Diazepam, but she suddenly became tachycardic with Bigeminal premature ventricular contractions, followed by ventricular fibrillation and severe hypotension with immeasurable blood pressure. After intubation and closed cardiac massage, the patient went into refractory ventricular fibrillation; and one hour of full cardiopulmonary resuscitation resulted in her reverting to sinus rhythm with a low blood pressure. A subsequent brain CT scan showed brain edema. During the next hour, resuscitative efforts were made for ventricular fibrillation, but there was no response to full resuscitation and direct current electrical shock of 360 J. The drugs used during the resuscitation included Lidocaine, Amiodarone, Epinephrine, and Amrinone. The patient was pronounced dead after 3 hours of resuscitation attempts. The patient had no systemic diseases, and her family refused to sanction an autopsy.

Discussion

Tranexamic acid is generally well tolerated, and its side effects are mainly gastrointestinal such as nausea and diarrhea. There are, however, reports of neurotoxicity in experimental studies;⁴⁻⁶ and when applied topically to the cerebral cortex in animal studies, this drug is known to produce seizures.⁶⁻⁸

The ability to elicit epileptic activity depends on the concentration of the drug and the area of the cortex exposed. In one experimental study, the drug caused intracranial and systemic hypertension and epilepsies.⁹ Furtmuller was able to produce epileptiform discharges by the application of Tranexamic acid to the spinal cord of rats.¹⁰

Our data on the effect of the intrathecal injection of Tranexamic acid in humans are insufficient. For the first time, Wong reported a case of inadvertent intrathecal injection of Tranexamic acid in an 18-year-old man in the ward. The patient experienced myoclonus, convulsions, progressive generalized seizure, and persistent sensory block of both lower extremities but responded to intravenous Diazepam.¹¹

In a case report, Leede-Vander Marig reported a case of an old man who by accident received an intrathecal injection of Tranexamic acid and developed refractory seizure, which had to be treated with Diazepam and Thiopental. His medical course eventually resulted in bilateral peroneal palsy.¹² Yamamura et al.⁴ reported that an intracranial injection of Tranexamic acid in cats caused seizures within 45 to 60 seconds. In the present case, the patient received an intrathecal injection of Tranexamic acid (500mg) which

was far more than the experimental dose of 5mg/Kg in the case report of Yamamura. In the present case, ventricular fibrillation was refractory to all resuscitative efforts. The mechanism of convulsion and ventricular fibrillation by an intrathecal injection of Tranexamic acid is not known. Yeh-Hvei-Ming postulated that high doses of drug would cause massive sympathetic discharge as evidenced by the initial hypertensive response and the subsequent ventricular fibrillation in the patient.¹³

Spinal analgesia is a well-accepted method of C/S. General anesthesia is associated with higher mortality rates in comparison to spinal anesthesia; nonetheless, spinal anesthesia is not without risk. Death in regional anesthesia, primarily related to excessive high regional blocks and toxicity of local anesthetics, reduction in doses, and improvement in techniques to avoid higher block levels and heightened awareness to the toxicity of local anesthetics, have contributed to a reduction in complications related to regional anesthesia.¹⁴ Currently, 0.5% Bupivacaine is used commonly for epidural anesthesia. In the literature, there are rare cases of fatal catastrophes after incidental intrathecal injections of Penicillin,¹⁵ Gallamine,¹⁶ and Vincristine,¹⁷ these patients were treated with anticonvulsants and spinal fluid lavage.¹⁵⁻¹⁷

Conclusion

In this first case of inadvertent intrathecal injection of Tranexamic acid in a pregnant woman, we found that a massive intrathecal injection of Tranexamic acid triggered refractory ventricular fibrillation and cardiovascular collapse, which did not respond to full resuscitation. Recently, an Iranian company produced Tranexamic acid vials that are similar to Bupivacaine vials in appearance and configuration.

We have advised the company to change the configuration of the Tranexamic acid vial, and we have since embarked upon labeling the drugs used in spinal analgesia with different colors so that the intrathecal drug box is clearly identified. We would recommend that anesthesiologists and nurses take this precautionary measure.

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