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PREVENTING AND MANAGING CATASTROPHIC DRUG ERRORS IN NEURAXIAL ANAESTHESIA: THE TRANEXAMIC ACID EXPERIENCE

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ABSTRACT **Background:** Accidental intrathecal administration of tranexamic acid (TXA) is a rare but potentially fatal medication error during neuraxial anaesthesia. TXA, an antifibrinolytic agent, inhibits plasminogen activation to reduce bleeding but causes severe neurotoxic and cardiotoxic effects when administered intrathecally (1,2). Neurotoxicity results from competitive antagonism of GABA_A and glycine receptors in the spinal cord and brain, producing neuronal hyper-excitability, seizures, and myoclonus (3,4,5). Ventricular arrhythmias may result from sympathetic overactivity (6,7). **Case Presentation:** We report an ASA grade II patient undergoing haemorrhoidectomy who inadvertently received 300 mg intrathecal TXA instead of 15 mg hyperbaric 0.5% bupivacaine. Lack of anaesthetic effect led to a repeat subarachnoid block within 20 minutes, masking early signs of TXA toxicity. Postoperatively, the patient developed abdominal myoclonic jerks, refractory seizure and ventricular arrhythmias. Lower limb myoclonus was initially unnoticed. Isoflurane anaesthesia was instituted to induce coma and reduce cerebral metabolic demand. A cerebrospinal fluid (CSF) tap was considered but deferred, as the drug had already widely distributed within the CNS. Intensive supportive management and close monitoring enabled full recovery by day 7. **Discussion:** This case emphasises the catastrophic consequences of intrathecal TXA and the importance of stringent verification protocols, segregation of look-alike vials, and careful evaluation of block failure before repeating neuraxial anaesthesia (4,8,9). Symptomatic management includes anticonvulsants, haemodynamic support, sedation, and, in selected cases, CSF lavage to reduce TXA concentration (6,10,11,12). Despite such measures, mortality remains significant in reported cases. Prevention through rigorous anaesthetic safety practices and improved pharmaceutical packaging differentiation is critical. Further research is required to clarify TXA's neurotoxic and cardiotoxic mechanisms and optimise treatment strategies.

KEYWORDS : Tranexamic Acid, Intrathecal Injection, Spinal Anaesthesia, Medication Error, Anaesthesia Safety

INTRODUCTION

Tranexamic acid (TXA) is a synthetic antifibrinolytic agent widely used in surgical, trauma, and medical settings to prevent and control excessive bleeding. (11,12)It acts by competitively inhibiting the activation of plasminogen to plasmin, thereby stabilising fibrin clots and reducing intra operative and postoperative blood loss(11). Although TXA is generally considered safe when administered via the correct intravenous route, serious adverse events have been reported, particularly when there is inadvertent exposure to the central nervous system.(13,14)

The neurotoxic effects of TXA stem from its ability to act as a competitive antagonist at gamma-aminobutyric acid type A (GABA_A) and glycine receptors, key mediators of inhibitory neurotransmission in the central nervous system(15,16). This antagonism results in the disruption of inhibitory currents, increasing neuronal excitability and precipitating seizures and other neurological complications(17,18). Accidental intrathecal or cerebrospinal administration has been linked to severe pain, convulsions, and high mortality rates of around 50%(19). Additionally, TXA has been associated with ventricular arrhythmias of unclear mechanism, which may be fatal or persistent(20).

Given these potential catastrophic neurological and cardiac outcomes, strict adherence to safe handling, correct dosing, and appropriate administration routes is essential. This is particularly important in high-risk environments such as operating theatres, where the risk of medication errors may be increased due to similarities in drug packaging and vial appearance(14,19). The present study aims to highlight the, potential complications related to incorrect TXA administration, emphasising the critical importance of prevention strategies in clinical practice.

Figure 1: Images of Tranexamic Acid and Bupivacaine Vials

Table – 1 Arterial Blood Gas Analysis

Parameters	Day 0	12hrs	24hrs
pH	7.10	7.30	7.40
p CO2	56	29.50	33.90
p O2	55	120	126
SO2	74.3	98.50	99.10

Bicarbonate HCO3	17.5	14.8	21.60
Base excess	-12.40	-11.8	-3.60
Sodium	140	142	134
Pottasium	5.01	4.40	3.14
Chloride	111	117	126.6
Glucose	164	130	135
BUN	21	19	12
Creatinine	1.40	1.40	1.2
Lactate	5.90	1.60	1.0
Osmolality	286	287	271.40

Drug Distribution in Cerebrospinal Fluid:

Local anaesthetic spreads in cerebrospinal fluid mainly by diffusion, moving from high concentration near the injection site to lower concentration areas along the spinal cord. The upward spread within 10 to 20 minutes is linked to CSF circulation, driven by arterial pulsations in the skull.(21)

Case Study

Patient Background

A 64-year-old male with a history of chronic constipation, rectal bleeding, and grade-3 interno-external haemorrhoids was scheduled for haemorrhoidectomy. He had a past history of left tibial fracture (treated by ORIF) and chronic respiratory distress managed with bronchodilators.

Pre-anaesthetic evaluation classified him as ASA II.

Anaesthetic Procedure

After overnight fasting (6 hours NPO), spinal anaesthesia was attempted at L3–L4 with a 27G Quincke tip needle, intending to administer 3 mL of 0.5% hyperbaric bupivacaine (15 mg). No sensory or motor blockade was observed after the first attempt.

Twenty minutes later, spinal anaesthesia was repeated using the same dose and drug vial, achieving T12 level anaesthesia. Surgery proceeded uneventfully.

Intra Operative and Early Postoperative Events

Postoperatively in the recovery room, the patient developed transient abdominal cramps, which resolved spontaneously. This was followed by sudden onset myoclonic jerks, upward eye rolling, and generalised stiffness suggestive of seizure activity.

Emergency Management

- Injection Midazolam 2 mg IV → seizure recurred after 3 min.
- Immediate airway stabilisation and endotracheal intubation with ventilation in volume control mode (TV 450 mL, RR 16/min, FiO_2 100%, PEEP 4 mmHg).
- Seizures managed with IV Levetiracetam 1 g stat, then 500 mg BD.
- Central venous access via right IJV; sodium thiopental loading (700 mg) followed by infusion at 300 mg/hr.
- Sodium valproate bolus (15 mg/kg).
- Isoflurane inhalation for cerebral anaesthesia (MAC 1.2).
- Amiodarone bolus 150 mg and infusion 10 mg/kg/24hrs for arrhythmia prophylaxis.
- Initial ABG: metabolic acidosis with respiratory compensation.

Diagnosis

Retrospective inspection revealed the first injection was not bupivacaine but tranexamic acid, leading to intrathecal TXA exposure.

ICU Course

Day 1:

- Patient maintained on isoflurane at MAC of 1.2 and neuromuscular blockade with vecuronium (0.1 mg/kg bolus, infusion 4 mg/hr).
- Invasive arterial blood pressure monitoring done , patient maintained well with mean arterial pressure (65-75) in the first 4 hours.
- Sedation was gradually tapered.
- MRI brain, EEG, and 2D echocardiography performed → EF 45%, mild LV hypo kinetic.
- Vasopressor support initiated after 4hours with norepinephrine to maintain MAP >70 mmHg due to hypotension (80/60 mmHg).
- Fever 102°F managed with IV paracetamol.
- Urine output monitored hourly.

Day 2:

- Sodium thiopental tapered to 100 mg/hr.
- Muscle relaxants stopped; FiO_2 decreased to 40%.
- Persistent fever; norepinephrine reduced.

Day 3:

- Thiopental infusion stopped; patient conscious (GCS E4VtM6) with spontaneous eye opening.
- Pressure support ventilation initiated (IPAP 12, EPAP 6, FiO_2 21%).
- No recurrence of seizures.

Day 4:

- GCS E4V5M6; following commands, full spontaneous ventilation.
- Successful extubation; neurological exam normal; oral feeding resumed.
- Shifted to ward, recovered without deficits.

Outcome

The patient was discharged on postoperative day 7 with complete neurological recovery and was advised regular neuropsychiatric follow-up.

CONCLUSIONS

This case underscores the grave dangers posed by accidental intrathecal administration of tranexamic acid—an error that may result in catastrophic neurological and cardiovascular outcomes. While timely recognition and aggressive multidisciplinary intervention can be life-saving, this event highlights broader, system-level vulnerabilities that require urgent attention.

To effectively prevent such incidents, healthcare teams must move beyond reliance on individual vigilance and embrace robust, multi-layered safety strategies in the operating theatre (OT):

- **Colour-coded, Tall Man Lettering, and Clearly Differentiated Drug Labels:** Manufacturers should be mandated to design distinctly coloured, tactilely and visually unique ampoules for high-risk drugs like tranexamic acid and local anaesthetics. Incorporating Tall Man lettering (e.g., TRAneXAMIC vs. BUPivacaine) enhances label readability and reduces mix-ups.
- **Barcode Scanning and Digital Double-Checks:** The adoption of barcode-based drug verification systems in OTs—where every medication must be scanned and digitally verified before administration—creates an additional electronic barrier against drug errors.
- **Dedicated Drug Preparation Zones:** Segregate areas within the OT for the preparation of anaesthesia drugs, ensuring high-alert medications are clearly separated from routine ones, with controlled access and standardised protocols.
- **Team-Based 'Read Aloud' Protocols:** Reinforce a culture of collaborative authentication, where two licensed practitioners jointly read drug labels, dose, and route aloud before administration. This practice should be non-negotiable for all spinal or epidural injections.
- **Periodic Simulation-Based Training:** Conduct regular OT drills simulating drug error scenarios, focusing on rapid identification, communication, and management—including mock drills for accidental intrathecal injection scenarios.
- **No Interchangeable Storage:** Never store non-anaesthetic drugs (such as tranexamic acid, potassium chloride) anywhere near spinal drugs or in the anaesthesia work area. Employ locked, dedicated storage for high-risk agents.
- **Audit and Feedback:** Maintain a 'zero harm' dashboard with routine OT audits, near-miss reporting, and feedback loops to both detect vulnerabilities and cultivate continuous improvement in medication safety.

Prevention is not only about learning from errors but also about system redesign rooted in human factors engineering. By weaving these high-reliability strategies into OT practice, we can move closer towards making catastrophic drug errors in anaesthesia a 'never event' in modern peri operative care.

Table2: Drug Doses and Uses

Drug/ Intervention	Dose/Use	Rationale in Intrathecal TXA Toxicity
Midazolam (IV)	2 mg bolus	First-line anticonvulsant; enhances GABA-A activity to counter TXA-induced GABA antagonism

Levetiracetam (IV)	1 g stat → 500 mg BD	Broad-spectrum anticonvulsant; useful adjunct in refractory seizures
Sodium Thiopental (IV)	700 mg bolus → 300 mg/hr infusion	Potentiates GABAergic inhibition, provides cerebral protection
Sodium Valproate (IV)	15 mg/kg bolus	Inhibits GABA transaminase, succinic semi aldehyde dehydrogenase which elevates brain GABA levels, useful in counteracting TXA activity.
Isoflurane (Inhalation)	MAC 1.2	Provides burst suppression, reduces cerebral metabolic rate.
Vecuronium (IV)	0.1 mg/kg bolus → 4 mg/hr infusion	Provides muscle relaxation revents muscle injury and ventilator dyssynchrony during prolonged seizures; facilitates ventilation
Amiodarone (IV)	150 mg bolus → 10 mg/kg/24 h infusion	Prevents ventricular arrhythmias. Amiodarone stabilizes cardiac membranes
Paracetamol (IV)	For fever management (>102°F)	Antipyretic; decreases fever exacerbation and neuronal injury

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