Inadvertent intrathecal administration of Tranexamic acid in a case of caesarean section: A report of medication error

Amrita Roy[1], Suman Sarkar [2], Subir BasuThakur [3], Pravin Kr Jain[4]

ABSTRACT:

Medication error is a preventable though not uncommon in anaesthesiology practice with some identifiable contributing factors. Here we are presenting a case of accidental intrathecal administration of Tranexamic acid instead of Bupivacaine heavy during spinal anaesthesia in a parturient. After detecting spinal failure, operation started with re administration of subarachnoid block with Bupivacaine heavy. A live baby was delivered. After 15 min the patient became restless and developed myoclonic seizures of lower extremity followed by generalized convulsion within next 5 minutes. Operation was completed in the meantime. Her convulsion was successfully treated with i.v Midazolam and i.v Phenytoin followed by i.v Thiopentone. She suffered from cardiac arrest which was resuscitated successfully. Later she received Thiopentone infusion along with respiratory and haemodynamic support. Full recovery was there after five days of ICU stay. Early detection and prompt management was the cornerstone for having such a better outcome even without neurodeficit in our case.

Key words: bupivacaine heavy, myoclonic seizure, subarachnoid block, Tranexamic acid

[1]Clinical tutor, Department of anaesthesia, [2] Assistant Professor, Department of Paediatric, I.P.G.M.E& R. Kolkata, India.

[3]Head, [4]Consultant, Department of anaesthesia, Calcutta Medical Research Institute, Kolkata, India.

Corresponding author mail: royamrita002@gmail.com

Source of support – None Conflict of interest – None

INTRODUCTION

Medication error is one of the leading causes of injury and death in industrialized countries along with adverse events from drugs[1].Though every anaesthesiologist is very much concerned about patient safety, it happens. The contributing factors are same coloured labels, appearance and location of ampoules and syringes, as well as some human factors[1,2]. Incidence of fatal medication error is 1.5 lakhs annually in USA[3]. In this case report we are reporting an accidental and fatal medication error in a pregnant woman posted for elective caesarean section due to administration of

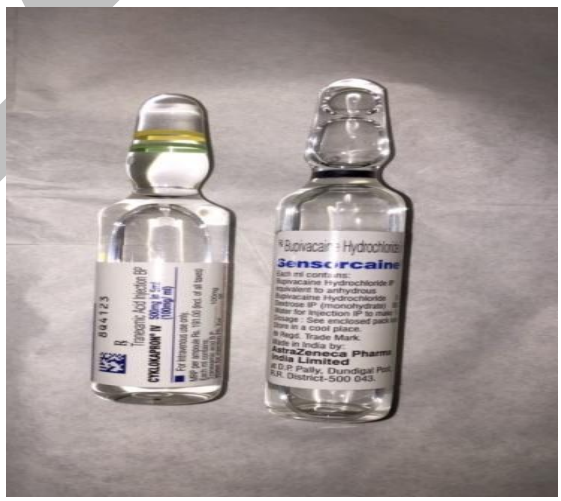
Tranexamic acid instead of hyperbaric bupivacaine intrathecally due to same appearance of both the ampoules.

CASE REPORT

We are presenting this case after obtaining informed consent from a 26 year American Society of Anaesthesiologists physical status I, primigravida (P_{1+0}) who was scheduled for elective caesarean section under subarachnoid block. Both past and present medical history and past surgical history were not significant. She had no history of headache, convulsion, fever, past anaesthetic exposure. She also had no history of allergic reaction to any drugs. Her vital parameters and all investigations were within normal limits.

Subarachnoid block was administered at the level of L3-L4 space by a 27G pencil tipped needle with strict aseptic precaution. 2 mL of drug was administered. Accidental intrathecal administration of wrong drug was suspected after 3 min by checking the motor block and simultaneously looking at the trash tray. It was detected that she received Tranexamic acid injection in subarachnoid space by mistake instead of Bupivacaine heavy which looks like same as Tranexamic acid ampoule.

The ampoule of Bupivacaine heavy (Sensorcaine heavy ,0.5%, 4 mL ampoule, Astra Zeneca Pharma India Limited, India) and Tranexamic acid (Inj. Cyklokapron ,100mg/ml, 5 mL ampoule, Pfizer Medical, U.S)both are same in appearance with same coloured label (Picture 1).



Picture 1: Ampoules of Sensorcaine heavy 0.5% (Bupivacaine heavy 0.5%) and Cyklokapron (Tranexamic acid).

Subarachnoid block was re-administered with the correct drug (2 mL Bupivacaine heavy, 0.5%). Operation started and a male, term, live baby delivered uneventfully and resuscitated. It was uneventful till 15 minutes of intrathecal Tranexamic acid administration. After 15 minutes, the patient became restless; heart rate gradually increased to 150 beats per minute, and within next 5 min myoclonic seizure appeared. Seizure appeared in lower extremity first. Surgery was complete in the meantime. Her blood pressure was 170/110 mm Hg, ECG showing sinus tachycardia, SPO_2 was 90% in room air. She was treated with oxygen, an oropharyngeal airway put in the mouth. Seizure was terminated immediately by Midazolam i.v. But she developed status epilepticus.

Status epilepticus was managed by sequential administration of i.v Phenytoin loading dose @20 mg/kg over 15 minutes and put on maintenance dose and Thiopentone @ 5mg/kg i.v as bolus dose followed by maintenance infusion @3mg/kg/hour to produce burst suppression. In the meantime, her airway was secured with ET tube no. 6.5 (cuffed). Simultaneously she suffered from pulseless ventricular tachycardia which was treated by CPR and asynchronized shock of 200 Joule (biphasic). Return of spontaneous circulation happened after 10 min of resuscitation with ventricular tachycardia with pulse. Later infusion of inj. Amiodarone used as 360 mg i.v (1 mg/min) over 6 hours followed by 540 mg i.v (0.5 mg/min) over next 18 hours to manage the ventricular arrhythmia.

Patient was shifted to ICU and put on mechanical ventilator with volume controlled mode. She also received Noradrenaline infusion to maintain the hemodynamic stability. Both the Thiopentone infusion and Noradrenaline infusion dose were adjusted to maintain the haemodynamic stability as well as maintaining perfusion of vital organs. EEG was monitored regularly along with continuous monitoring of HR, BP, SPO_2, ECG, $EtCO_2$, Urine output.

She received Thiopentone infusion for the next 24 hours, and then it was gradually stopped. Noradrenaline infusion was also stopped.

No episode of ventricular arrhythmia occurred since the 2nd postoperative day. Extubation was done on the 3rd postoperative day. She was kept in the ICU for monitoring for next 2 days. It was uneventful. She was discharged from the hospital without any residual

neurological deficit. Her baby was also doing well on breast feeding. She was followed at 1, 3, 6 & 12 month for neurodeficit. Her baby was also followed for the same duration for neuro developmental monitoring which revealed normal.

DISCUSSION

The well known factors which are responsible for medication error are same coloured labels, appearance and location of ampoules and syringes, as well as some human factors that is, lack of double-checking, inattention, poor communication, and fatigue on the part of the anaesthesiologist[1,2]. Wong, et al, reported the first case of accidental intrathecal administration of Tranexamic acid in a 18 yr old male posted for appendicectomy with an uneventful outcome[4]. But the case reported by De Leede, et al, had residual neurodeficit in the form of bilateral peroneal palsy[5]. It was even better than the case reported by Yeh, et al[6]. Here the reported patient died of refractory seizure and ventricular fibrillation after receiving 500mg Tranexamic acid in the subarachnoid space accidentally.

The exact mechanism by which this drug induces convulsions or ventricular arrhythmia is unknown. There is evidence for a dose-related neurotoxicity in animal model, with greater severity and duration of seizure with increasing dose of Tranexamic acid[7]. Potential neurotoxic property of Tranexamic acid in the form of seizure was found when applied topically to the cerebral cortex of animals in one study[8]. In all reports it produce both systemic and intracranial hypertension and convulsion. It may be due to massive sympathetic discharge, as evidenced by the initial hypertensive response and the subsequent ventricular arrhythmia reported in our case report and also in some patient[3,4,5,6,9,10,11,12]. Either direct cerebral ischemia secondary to decrease in regional or global cerebral blood flow, or blockage of inhibitory cortical-aminobutyric acid (GABA)-A receptors is responsible for the seizure[13,14]. Use of high-dose Tranexamic acid in patients undergoing cardiac surgery increased at the incidence of convulsive seizures from 1.3 to 3.8% [15].

Our patient received an intrathecal injection of 200 mg Tranexamic acid with a full recovery unlike three other reported cases of caesarean section [10,11,12].

General anesthesia was administered in almost every case after discovering no motor block. But in our case subarachnoid block was repeated with

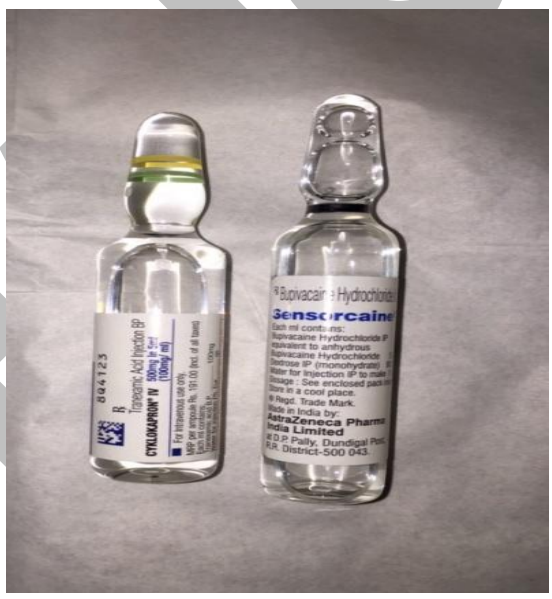
bupivacaine heavy 0.5% 2 ml (10 mg). No CSF lavage was done here[3,6,16]. May be repeat intrathecal injection was the cause that helped the Tranexamic acid to get diluted in the CSF in our case and made the outcome less fatal. Timely resuscitation along with early administration of i.v thiopentone infusion also helped for better outcome.

Other than few case reports, there is no information regarding intrathecal administration of Tranexamic acid [3,4,5,6,9,10,11,12,15]. So, we managed the case symptomatically. First, managed the convulsion, later on managed the cardiac arrest as per Advanced Cardiac Life Support protocol.

Jensen L.S, et al, suggested evidence based strategies for preventing drug administration error in their article[17]. Though it was developed for intravenous drugs, it may be equally applicable for every type of drug administration errors.

CONCLUSION

All theses case reports were due to confusion between hyperbaric Bupivacaine and Tranexamic acid. The ampoules were similar in appearance (Picture 1).



Picture 1: Ampoules of Sensorcaine heavy 0.5% (Bupivacaine heavy 0.5%) and Cyklokapron (Tranexamic acid).

This type of fatal medication errors may be minimized by a standardized arrangement of drugs in the operating room, reading the drug label prior to drawing up the drug, drug companies creating different (size, colour, shape) drug labels and vials, continuous review of medication errors in hospitals to identify causative associated

factors and develop systematic interventions for prevention. Early detection and timely resuscitation can reduce morbidity like neurodeficit and morbidity.

REFERENCES

1. Currie M, Mackay P, Morgan C, Runciman WB, Russell WJ, Sellen A, et al. The "wrong drug" problem in anesthesia: An analysis of 2000 incident reports. Anaesth Intensive Care.1993;21:596–601.
2. Cooper JB, Newbower RS, Kitz RJ. An analysis of major errors and equipment failures in anesthesia management: Considerations for prevention and detection.Anesthesiology.1984;60: 34–42.
3. Butala BP, Shah VR, Bhosale GP, Shah RB. Medication error: Subarachnoid injection of tranexamic acid. Indian J Anaesth.2012;56:168-70.
4. Wong J, Yang S, Tsai M. Accidental injection of tranexamic acid (Transamin) during spinal anaesthesia. Ma Zui Xue Za Zhi.1988;26:249–52.
5. de Leede-van der, Maarl MG, Hilkens P, Bosch F. The epileptogenic effects of tranexamic acid. J Neurol.1999;246:843–5.
6. Yeh HM, Lau HP, Lin PL, Sun WZ, Mok MS. Convulsion and refractory ventricular fibrillation after intrathecal administration of a massive dose of tranexamic acid.Anesthesiology.2003;98:270–272.
7. Yamaura A, Nakamura T, Makino H, Hagihara Y. Cerebral complication of antifibrinolytic therapy in the treatment of ruptured intracranial aneurysm: animal experiment and a review of literature. Eur Neurol,1980;19:77-84.
8. Schlag MG, Hopf R, Zifko U, Redl H. Epileptic seizures following cortical application of fibrin sealants containing tranexamic acid in rats. Acta Neurochir (Wien)2002;144:63–9.
9. Kaabachi O, Eddhif M, Rais K, Zabaar M A. Inadvertent intrathecal injection of tranexamic acid. SJA.2011;5:90-92.
10. Sabzi F, Teimouri H, Zokai A. Myoclonus, seizure, and ventricular fibrillation after intrathecal injection of tranexamic

acid. J Teh Univ Heart Ctr 4.2009;4:253-255.

11. Veisi F, Salimi B, Mohseni G, Golfam P, Kolyaei A. Accidental Intrathecal Injection of Tranexamic Acid in Cesarean Section: A Fatal Medication Error. APSF Newsletter, Spring.2010;25(1):1-20.
12. K Raghu, Shrevanni P, Haneef M, Ramyakumar, Rao M.Chenna .Accidental intrathecal injection of tranexamic acid in a term gestation. International Journal of Neuro and Spinal Sciences.2013(Oct-Dec);1(1):1-3.
13. Tsementzis SA, Meyer CH, Hitchcock ER. Cerebral blood flow in patients with a subarachnoid haemorrhage during treatment with tranexamic acid. Neurochirurgia (Stuttg)1992;35:74–8.
14. Furtmuller R, Schlag MG, Berger M, Hopf R, Huck S, Sieghart W, et al. Tranexamic acid, a widely used antifibrinolytic agent, causes convulsions by a gamma-aminobutyric acid(A) receptor antagonistic effect. J Pharmacol Exp Ther.2002;301:168–73.
15. Murkin JM, Falter F, Granton J, Young B, Burt C, Chu M. High-dose tranexamic acid is associated with nonischemic clinical seizures in cardiac surgical patients. Anesth Analg.2010;110:350–3.
16. Tsui B C, Malherbe S, Koller J, Aronyk K. Reversal of an unintentional spinal anesthetic by cerebrospinal lavage. Anesth Analg.2004;98:434-6
17. Jensen L S, Merry A F, Webster C S, Weller J, Larsson L. Evidence based strategies for preventing drug administration errors during anesthesia. Anaesthesia.2004;59:493-504.