

## Bupivacaine-Induced Cardiac Arrest during Epidural Anesthesia

Muhammad Azharuddin\* ; Rishi Raj; Radhika Annam; Mattina Charles J; Lubna Bashir Munshi

### \*Muhammad Azharuddin

Department of Internal Medicine, Monmouth Medical Center, USA

Email: azhar\_uddin203@yahoo.com

### Abstract

Local anesthetic-induced cardiac arrest is a type of rare and potentially fatal complication of regional anesthesia. Bupivacaine is a long lasting amide local anesthetic used clinically, and is known to improve analgesia after surgery. It has use in cutaneous infiltration, regional nerve blocks, epidural anesthesia, and spinal anesthesia. We hereby report a case of a 57-year old male (co-morbidities) was admitted to the hospital for an elective left knee arthroplasty. On the day of his procedure, epidural anesthesia was initiated, in which (how much) bupivacaine was injected into the epidural cavity. Almost 20 minutes later, the monitor started showing widening of the QRS complex followed by bradycardia and eventually asystole. Code blue was called and ACLS protocol was started with CPR and one dose of epinephrine, intravenous lipid emulsion was given and patient regained pulse within five minutes. The patient was intubated. Lab workups including EKG, chest x-ray exams were all normal. The patient was extubated successfully the following day and then discharged to home.

### Keywords

local anesthetics; epinephrine; spinal; epidural; bupivacaine

### Abbreviations

ACLS: advanced cardiac life support; CPR: cardiopulmonary resuscitation; EKG: electrocardiogram; ICU: intensive care unit; ECHO: echocardiogram; NSR: normal sinus rhythm; HR: heart rate; RCA: root cause analysis; LVEPD: left ventricular end-diastolic pressure; LVEF: left ventricular ejection fraction; CNS: central nervous system; CVS: cardiovascular system;  $\text{NaHCO}_3$ : sodium bicarbonate; ROSC: return of spontaneous circulation

### Introduction

Sometimes bradycardia and asystole may occur while administering spinal anesthesia in healthy and young patients. Although cardiac arrests during spinal anesthesia are known to be rare, it is actually quite common. Reports of cardiac arrests are  $6.4 \pm 1.2$  in 1,000,000 patients [1]. Sudden and unanticipated cardiac arrests have been previously reported. One of the many mechanisms involved in cardiac arrest after spinal anesthesia is through administering excessive doses of local anesthetics (LAs), or drugs that reversibly block nerve impulse transmission without affecting consciousness [1,2].

Bupivacaine is a long lasting amide LA used clinically, and has been used for postoperative analgesia by providing cutaneous infiltration, regional nerve blocks, epidural anesthesia, and spinal anesthesia [2]. Several years ago, George Albright alerted anesthesia practitioners of six concurrent cases

of seizures and cardiovascular failures after unintentionally injecting intravascular etidocaine and bupivacaine, resulting in most patients failing to recover. This report suggested that bupivacaine had smaller therapeutic margin for heart conduction system block compared to the standards at that time (ex. lidocaine or mepivacaine). Bupivacaine is able to rapidly block sodium channels during systole, but with slower dissociation as compared to lidocaine. Subsequent electric conduction depression would induce return of ventricular arrhythmias. In addition, high blood concentrations of bupivacaine could support ventricular arrhythmias by directly acting on the brain stem [3,4].

## Case Presentation

57 year old male was admitted to the hospital for an elective left knee arthroplasty, having a past medical history of hyperlipidemia, hypertension, gout, rheumatoid arthritis & alcohol abuse. On the day of the elective surgery, he was taken to the operative room and pre-medicated with IV midazolam & propofol. After this the patient was made to sit and epidural anesthesia was started and Bupivacaine was injected into the epidural cavity. Almost 20 minutes after the initiation of the epidural anesthesia, the monitor started showing widening of the QRS complex followed by bradycardia and eventually asystole. Code blue was called and ACLS protocol was started with CPR and one dose of epinephrine and 20% Lipid emulsion was given after which within five minutes the patient regained pulse and went back into Normal Sinus rhythm. The patient was intubated and the operative procedure was aborted then transferred to the ICU.

On examination patient was intubated on the ventilator and the physical exam was essentially benign. The lab work was all within normal limits. The EKG showed a NSR with no ST segment or T wave changes and a HR of 82 bpm. Serial troponins were negative. The chest X-ray was normal. His TSH was normal and alcohol level <10. The patient did well as was extubated the following day. ECHO was normal. The patient was started on aspirin, metoprolol & atorvastatin. Cardiac catheterization was done which showed 30-40 % mid RCA lesion & elevated LVEDP-180/32 & Normal LVEF. After the cardiac catheterization, lasix was added to his medications. The patient was discharged to home, and order to follow-up with cardiology. Two months later during follow-up, he was completely normal.

## Discussion

Spinal anesthesia is known to be a safe procedure. However, there are a few complications including cardiopulmonary arrest. Although it is still unknown exactly how spinal anesthesia causes bradycardia or asystole, the final pathway is certain to be the increased activity of the parasympathetic nervous system [1]. Mistakenly injecting into the subarachnoid space can cause apnea or under-ventilation through the cephalad extension of anesthesia in the motor level, leading to cardiac arrest. Sympathetic blockade can cause hypotension or myocardial depression with decreased cardiac output [1].

Local anesthetics are widely used in modern medical procedures [1]. Local anesthetic-induced cardiac arrest is a type of rare and potentially fatal complication of regional anesthesia [5]. Though low adverse effects of local anesthetics have not been often reported, there have been a few severe toxicity and death reports. In cases of seizure during cardiac arrest, benzodiazepines are the preferred drug of choice other drugs like propofol can increase cardiovascular toxicity. Refractory seizures may require

neuromuscular blockade. Anesthetic toxicity symptoms include tinnitus, circumoral tingling, bad taste in the mouth, dizziness, dysarthria, severely changed mental status, anxiety or unconsciousness and arrhythmia [5].

Among all local anesthetics, bupivacaine is considered to be 4-16 times more cardio-toxic than shorter-acting lignocaine, with smaller doses often leading to cardio-toxic symptoms without prior CNS effects [1,2]. CNS symptoms usually occur earlier in toxicity cases as compared to CVS symptoms, but is vice versa in bupivacaine. Experimentally, bupivacaine causes a more severe block in A delta and C fibers (sensory fibers). Motor block has been known to be less severe and shorter compared to bupivacaine [3]. IV bupivacaine is known to have a longer elimination half-life of 3.5 hours, which is longer than all currently known local anesthetics [6]. Bupivacaine often causes unusual conduction and arrhythmias, resulting in cardiac arrest. It lowers venous return, and decreases right atrial pressure, which was observed in 36% of cases below T4 level anesthesia and 53% of cases above T4 level blockade [1]. Lowering the preload causes the bezold-Jarisch reflex, which results in severe bradycardia. Blockade of T8-L1 fibers/suprarenal glands causes lower catecholamine secretions, which can result in refractory cardiac arrest [1]. Toxicity can be reduced by using the lowest effective dosage, and injecting slowly with frequent aspirations. In addition, doses should be tested to verify placement of epidural and nerve block catheter. If possible, local anesthetics should not be re-dosed [7].

In 7% of a study's population, resting bradycardia AV block or complete AV dissociation (presently known as Vagotonia) has higher chances of vagolytic activity during procedure [1]. Patient's physiological factors also influence the LA toxicity threshold. A study on the effects of lignocaine and bupivacaine in anesthetized sheep found that acidosis, hypoxia, and hypercarbia increased cardiotoxicity which leads to increased cerebral blood flow so more anesthetic would reach the cerebral circulation. However, cardiac arrest may be prevented by treating hypoxemia and acidosis with quick control of seizures and management of aggressive airways. NaHCO<sub>3</sub> may be used to treat severe acidosis [7].

Intravenous lipid emulsion was demonstrated to be effective in treating local anesthetic-induced cardiac arrest. Recent case reports have verified the use of lipid rescue from LA toxicity in humans. Initially, lipid emulsion is administered as treatment for bupivacaine-induced cardiac toxicity, concurrent with the administration of ACLS drugs [5]. Recently, epinephrine alone proved ineffective, as it contributed to severe pulmonary edema [8]. Therefore, combining of lipid emulsion with epinephrine was preferred for successful resuscitation. Combining epinephrine is most likely effective since it shortens the time to successful resuscitation by increasing the coronary perfusion pressure, lowering the cardiac concentration of bupivacaine, and accelerating the return of spontaneous circulation (ROSC) [8]. Furthermore, epinephrine is advised to be given early when treating sudden bradycardia, especially if atropine or ephedrine is ineffective [1]. In addition, calcium channel blockers should be avoided, as they could be additive with bupivacaine. In our patient, test dose of 0.5% concentrated 3ml of bupivacaine was given at the level of L2 to detect any toxicity or wrongly placed into the intrathecal or intravascular site. After few minutes, 100mg of 15ml Bupivacaine was injected into epidural space, and maximum dose of bupivacaine was 400mg/24 hours. He developed cardiac arrest after 5min of injection [7].

Epinephrine is the major first-line rescue drug for ROSC and survival after bupivacaine-induced circulatory arrest [7]. Previous studies showed that epinephrine immediately after a lipid emulsion bolus

had the highest recovery and survival rates, the lowest pulmonary hemorrhage rates, the lowest cardiac bupivacaine concentrations, and less pH change when compared with epinephrine alone immediately after cardiac arrest [8].

## Conclusion

This is a case of bupivacaine-induced cardiac arrest in a patient having epidural. Cardiac arrest during anesthesia and operation is a serious concern. Although the incidence of reported adverse effects of local anesthetics is low, occasional severe toxicity and deaths have been reported. Among all, bupivacaine is considered to be more cardio-toxic than lignocaine. For treatment, epinephrine is the major first-line rescue drug for ROSC and survival after bupivacaine-induced circulatory arrest. Combination of lipid emulsion with epinephrine is the preferred treatment method for successful resuscitation. Toxicity can be reduced by using the lowest effective dosage, and injecting slowly with frequent aspirations.

## Acknowledgements

We would like to thank the Department of Internal Medicine for supporting and encouraging us to pursue this study.

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**Manuscript Information:** Received: September 09, 2016; Accepted: November 16, 2016; Published: November 21, 2016

**Authors Information:** Muhammad Azharuddin<sup>1\*</sup>; Rishi Raj<sup>1</sup>; Radhika Annam<sup>1</sup>; Mattina Charles J<sup>1</sup>; Lubna Bashir Munshi<sup>1,2</sup>

<sup>1</sup>Department of Internal Medicine, Monmouth Medical Center, USA

<sup>2</sup>Department of Endocrinology, Mount Sinai Beth Israel, USA

**Citation:** Azharuddin M, Raj R, Annam R, Charles JM, Munshi LB. Bupivacaine-induced cardiac arrest during epidural anesthesia. *Open J Clin Med Case Rep.* 2016; 1188

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