

Confusion and Lightheadedness Related to Calcium Channel Blocker Toxicity

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ABSTRACT

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Calcium channel blockers are commonly used drugs to control blood pressure and heart rate. These drugs can significantly depress cardiac inotropy and chronotropy at high doses, with adverse effects. We present the case of a woman, recently started on diltiazem for hypertension, who presented with severe hypotension and bradycardia. Electrocardiogram at admission, revealed a junctional rhythm. She was initially resuscitated with intravenous fluids and atropine boluses without any response. Septic workup, cardiac biomarkers, thyroid stimulating hormone and cortisol levels were normal. Hemodynamics gradually improved on glucagon and dopamine drip. She reverted back to normal sinus rhythm in about six hours. This case illustrates the importance of medication reconciliation in patients.

Keywords: Calcium Channel Blocker Toxicity, Diltiazem Toxicity, Bradycardia

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INTRODUCTION

Calcium channel blockers (CCBs) are commonly prescribed anti-hypertensive medications that block the L-type calcium channels in cardiac and smooth muscle cells. There are three classes of CCBs, of which, phenylalkylamines (verapamil) and benzothiazepines (diltiazem) act on the L-type Calcium channels in the myocardium, whereas, dihydropyridines (amlodipine, nifedipine) act on the peripheral vasculature. CCB toxicity can result in excessive blockade of calcium channels, depressing cardiac function and causing peripheral vasodilatation. CCB overdoses resulted in at least 11,764 exposures and 78 deaths in 2011 in the United States, according to the National Poison Data System.¹ Treatment of CCB overdose, involves supportive care, intravenous fluids, atropine, vasopressor agents, calcium, glucagon and recently high dose insulin and intravenous lipid emulsion therapies.

CASE REPORT

A 66-year-old woman with past medical history of hypertension, diabetes and chronic obstructive pulmonary disease presented to the emergency room with complaints of feeling confused and lightheaded for four hours. She was found to be hypotensive with a

blood pressure of 64/44 mm Hg and bradycardia with heart rates in the 50s. Respiratory rate was 14 breaths/min and oxygen saturation of 99% on room air. She denied any chest pain, palpitations, shortness of breath or history of coronary artery disease or cardiac rhythm disturbances. There was no history suggestive of any infection. Physical examination was unremarkable. The initial electrocardiogram revealed a junctional rhythm with retrograde P waves, at a rate of 60 beats per minute. She was fluid resuscitated with two liters of normal saline without any improvement in vital signs. She was given two doses of 0.5 mg of atropine, one dose of 1mg of epinephrine intravenously with minimal improvement in heart rate and was started on a dopamine drip (15µg/kg/min). Blood cultures were sent and patient was started on broad spectrum antibiotics to cover possible sepsis. Stress dose of steroid was also given empirically. Cardiology was consulted, who performed a bedside echocardiogram, which revealed a normal cardiac function. She had a complete blood count, 16,000 WBC/cumm, with 82% neutrophils, 10% lymphocytes, 7% monocytes, platelets 431,000/µL, hemoglobin 11g/dl. Electrolytes and renal function was within normal limits. Blood glucose was 417 mg/dL. Lactate was 0.6 mmol/L. Troponin <0.03 ng/mL. Urinalysis was normal. Serum cortisol was 13. TSH was 2.13 µIU/MI and normal Free T4. Arterial blood gas

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revealed respiratory acidosis with pH-7.25, pCO₂ 56, pO₂ 80 Bicarbonate 25. Chest radiograph revealed no acute abnormalities.

On further inquiry, she reported starting a new medication for hypertension, 240 mg of Extended release Diltiazem twice daily, only 48 hours ago. With concern for calcium channel blocker toxicity, she was given 1000 mg of calcium chloride and two boluses of 5mg of glucagon, with slight improvement in heart rate and blood pressure. The patient was admitted to the medical intensive care unit and the dopamine drip was continued, and the heart rate and blood pressure gradually began to improve. Within six hours electrocardiogram reverted to normal sinus rhythm. Dopamine drip was discontinued after twelve hours. Septic workup and cardiac biomarkers were negative. Diltiazem was discontinued and anti-hypertensive medication regimen was altered prior to discharge.

DISCUSSION

CCB overdose can present with profound cardiotoxic effects as illustrated in this case. Our patient presented with persistent bradycardia, hypotension and rhythm disturbance, concerning for cardiogenic shock. Other presentations described in literature include hyperglycemia, metabolic acidosis, non cardiogenic pulmonary edema and end-organ failure. CCBs antagonize the L-type calcium channels at various levels in the cardiovascular system, depressing sinus node function, atrioventricular conduction, negative inotropy and causing peripheral vasodilatation resulting in severe hypotension and vital organ hypoperfusion. Moreover the extended release preparations, like the one ingested by the above patient, tend to prolong duration of symptoms.

Management of CCB toxicity involves initial resuscitation with intravenous fluids, atropine and vasopressors to maintain circulation. Activated charcoal administration and bowel irrigation, should be considered in patient presenting early (within six hours of ingestion) or ingestion of large amounts is suspected.^{2,3} Alkalinizing urine, hemodialysis and hemofiltration are not very effective, in the case of CCB overdose, as these drugs are lipophilic.³ Conventional management, as described in observational studies, include administration of calcium, atropine and glucagon to improve hemodynamic parameters. Intravenous lipid emulsion therapies have shown some benefit, potentially due to the lipophilic nature of the drugs. Recent literature indicate hyperinsulinemia-euglycemia therapy in CCB toxicity, may be superior to conventional therapy. CCBs block L-type calcium channels that mediate glucose

uptake and insulin release, thereby increasing blood glucose levels and affect insulin resistance. Administration of insulin as a drip (0.5 to 1 IU/kg/hour) increases glucose uptake in cardiac and smooth muscle cells, reducing fatty acid oxidation for energy production, thereby restoring cardiac contractility and peripheral vascular resistance.^{3,4}

CONCLUSION

Calcium channel blocker toxicity should be considered in the differential diagnosis of patients presenting with bradycardia and hypotension, without a clear explanation, and not responding to initial measures. Initial resuscitation include intravenous fluids, atropine and vasopressors. Conventional therapy to improve hemodynamics include calcium and glucagon. Recent literature show hyperinsulinemia-euglycemia and intravenous lipid emulsion to be superior to conventional therapy, though there needs to be further research to confirm this.

END NOTE

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