Case Report-Amlodipine Toxicity

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ABSTRACT

Amlodipine is a dihydropyridine calcium channel blocker mainly indicated in the treatment of essential hypertension and angina pectoris. Overdose of calcium channel blocker, Amlodipine results in toxicity along with profound hypotension and shock. Here, a 20-year-old female patient was admitted to the MICU with complaints of severe breathing difficulty, and multiple episodes of vomiting one day earlier. After the chest x-ray, ECG, and blood investigations, she was diagnosed as having Amlodipine toxicity, pulmonary edema, circulatory shock, hypocalcemia, hypokalemia, systemic hypotension, and acute kidney injury. She was discharged from the hospital after the symptoms had recovered.

Key words: Calcium channel blockers, Amlodipine, Drug overdose, Dihydropyridine, Hypotension, Toxicity.

INTRODUCTION

Calcium channel blockers are one of the leading causes of a cardiovascular drugs overdose. They are responsible for about 48% of deaths related to exposure to such drugs. Treating patients with the toxicity of these medications can even challenge the physician with more experience. Patients severely poisoned with CCBs may result in profound hypotension and refractory bradycardia.[1] Based on expected physiologic effects, there are two types of CCBs: dihydropyridines and non-dihydropyridines. Dihydropyridine is a potent vasodilator. In terms of improving myocardium conduction and contraction, non-dihydropyridine is more effective; however, it may have a limited impact on vasodilation.[2] Amlodipine is a calcium channel blocker typically used to treat hypertension and angina pectoris and may also have efficacy in treating patients with congestive heart failure.[3] Reports of overdose with calcium channel blockers are very scarce in Indian literature. Here we report the case of a 20-year old female patient with complaints of amlodipine toxicity and had no history of such an adverse event.

CASE REPORT

A 20-year-old female patient presented to the emergency department complaining of breathlessness, vomiting, and chills following an injection of Amlodipine one day earlier. In the beginning, the patient was admitted to her local hospital, where she underwent gastric lavage and received treatment with IV fluids, Inj. Calcium Gluconate, Inj. Insulin infusion and Inj. Dexona. Her SpO_2 was only 60% at room temperature. She underwent intubation in BIPAD mode. The patient received Inj. Amikacin, Inj. Meropenem, Inj. Oseltamivir and Duolin nebulization. Then she was referred to another hospital for more advanced treatment. The patient had no history of any chronic illness and was not administering any medications in the past. She had a history of previous hospitalizations with complaints of fever and tonsillitis in 2014. She had a history of chickenpox in her early childhood. There were no allergies, injuries, accidents, or surgical history in the past. From the subjective and objective data, she was diagnosed as having Amlodipine toxicity, pulmonary edema, circulatory shock, hypocalcemia, hypokalemia, systemic hypotension, and acute kidney injury. She

DOI: 10.5530/ijopp.15.1.9

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sleeps 7 hr daily but has complaints of sleep disturbance after hospitalization. She has a good elimination pattern. They noted that she had a good appetite and had restrictions to food and fluids after hospitalization.

On examination, the patient had tensed posture and uncoordinated gait. The body movement is tremors. On monitoring the vital signs, the pulse is 124 beats/minute while the BP is 80/40mmHg. On examination in the casualty, she was drowsy but arousable on light stimuli. She was pale with cold and clammy extremities. Her temperature was 98.60 F, her heart rate 124 beats/minute, and blood pressure 80/40mmHg. The SpO_2 was 88% in NRBM. The GRBs were 118mg/dl. The abdominal examination reveals mild epigastric tenderness in addition to an initial hemogram, LFT, RFT, ABG, electrolytes, Echocardiography, chest X-ray, and ECG investigations were done. The blood investigations show sodium 133Meq/L, potassium-3mEq/l, total count 16200/million/mm3, ESR -22mm/hr and serum lactate was 2.5mmol/L. The chest X-ray reveals white lungs, which indicates that her lungs are swollen, as having pulmonary edema. The ECG reveals Sinus tachycardia, ST and T wave abnormality, and anterolateral ischemia. In the integumentary system, the skin was pale in colour with a cool temperature. Mild non-pitting edema was present over the lower extremities. The nails were pale, and the capillary refill was >3 sec. The No 16 Ryles tube was present on the right nostrils. The tongue was dry and furry, and difficulty in swallowing was present. In the respiratory system, a productive cough with pinkish frothy sputum was observed. Dullness can be detected on percussion, while crackles are apparent on auscultation. In the cardiovascular system, the S3 gallop is audible on auscultation. In the gastrointestinal system, she had anorexia and gastric upset. During the genitourinary examination, there is a No: 16-foley catheter, no abnormalities of the muscle or nervous system were present.

As an initial symptomatic treatment, the physician suggested starting 8 liters of oxygen through an oxygen mask and connecting the cardiac monitor. Along with standard resuscitation measures, the patient received a 10% calcium gluconate infusion at 50ml/hr, Inj. Insulin infusion at 15ml/hr, Inj. Pantocid 40mg IV Stat, Inj. Emeset 4mg IV Stat, Inj. Glucagon 3mg stat, Inj. Lipid Emulsion 20% IV Stat, and Inj. Lasix 4mg/hr IV Infusion. The No16 Ryles tube was inserted. And after that, RT aspiration was carried out. Then the patient was substituted for MICU. As part of MICU treatment, oxygen was administered through face masks, followed by 30 ml of 10% calcium gluconate initially over 10 min, followed by 5 ml of calcium gluconate per hour. Inj. Glucagon 4mg was administered intramuscularly as stat dose and followed by Inj. Glucagon 2mg IV every 2nd hourly for 8 hr. Solution of saline and non-adrenergic medicines of 20ml/hr have been suggested to support blood pressure. With these measures, the patient started showing improvement in her hemodynamics. The other supportive medications include Infusion. Lasix 4mg/hr, Inj. Actrapid 20ml/hr, Inj. Vasopressin 20ml/hr, Inj. Dopamine 10ml/hr and Inj. Phenylephrine 25ml/hr to support the blood pressure. The patient had a No:16 Foley catheter, No:16 Ryles. A right femoral central venous catheter, right subclavian catheter, and right subclavian tube. An arterial in the lower-left arm, the axillae, and the femoral veins were visible. A cannula was used for plasmapheresis under sterile conditions.

The Cardiology, Nephrology, and Pulmonology consultations were done and the pulmonologist suggests BIPAD or mechanical ventilation in the event of chest pain and to repeat Chest x-rays, an ABG, and blood investigations. The Nephrologist advised total plasma volume exchange with 100ml of Human Albumin in 800 ml of Normal Saline. The Cardiologist taught about the complications of Cardiac Arrest, ECMO support, and probable requirement for hemodialysis and invasive ventilation detail to the patient bystander, as the ECHO reveals intact left ventricular systolic function. The treatment had gone on, and the present condition of the client is better.

DISCUSSION

Calcium channel blockers (CCBs) are the most commonly recommended class of medications for a substantial portion of the mortality associated with overdose cases of cardiovascular drugs.[4] A calcium channel blocker such as amlodipine, on the other hand, primarily affects the smooth muscle in the arteries. The half-life of amlodipine is 30–50 hr and had a larger volume of distribution (21 L/Kg).[5] Due to its beneficial features, such as once-daily dosing and minimal effects on heart rate, amlodipine is commonly used in clinical practice.[4] When CCBs are administered in more than the prescribed dosage, and they result in symptoms including bradycardia and hypotension. But DHP intoxication results in arterial vasodilation and reflex tachycardia.[6,7] The selectivity of DHP is lost when it is consumed at excessive doses, and the myocardium and conducting system gets disturbed, resulting in cardiac collapse and bradycardia that eventually results in hypotension.[8]

The common treatment strategies for amlodipine toxicity include crystalloid fluids, atropine, intravenous calcium, preferably calcium chloride, and hemodynamic support with inotropes and vasopressors. Overdoses of amlodipine were also treated with the agents such as adrenaline, noradrenaline, phenylephrine, dopamine, dobutamine, and isoproterenol. Glucagon enhances calcium influx across the cardiac cell membrane and improved cardiac contractility and smooth muscle cells.[9] Hypoinsulinemia and euglycemia treatment is an option to treat CCB overdose patients. As a result, the drug prevents circulatory shock in patients with CCB overdose and is also refractory to "standard" treatment. This therapy also improves the contractility of smooth muscle cells. Amlodipine poisoning can also be cured by methylene blue by reversing vasoplegia. Consequently, cGMP is reduced within the cell, scavenging nitric oxide, and inhibiting the synthesis of nitric oxide.[10] The use of lipid emulsion therapy for treatment for CCB poisoning is currently limited to the selected case reports. Since amlodipine has a high protein binding rate (98%) it cannot be treated by dialysis when it has overdosed.[11]

Among other treatment modalities suggested in patients with refractory cardiac arrest and multiorgan failure, ECMO was demonstrated as effective in many reports. Paediatric patients with bradycardia and high nodal heart block, transcutaneous pacemakers could be used. It may be a beneficial treatment modality when patients are not responding to vasopressors, high-dose insulin, or IV lipid emulsion.[12] In this case report, we believe that amlodipine played a crucial role in contributing to toxicity.

CONCLUSION

Ingestions of calcium channel blockers by children and adolescents result in severe, and even fatal, consequences. A CCB overdose can cause severe refractory hypotension, shock, cardiovascular instability, and metabolic acidosis that may not respond to vasopressor agents with high doses. When significant overdoses occur, treatments such as HIET, glucagon, methylene blue, and calcium chloride may not be effective. So it necessitates either extracorporeal membrane oxygenation or administration of glucagon. Plasmapheresis is another method for removing amlodipine from the body. It is crucial to obtain a careful history, thorough physical examination, and close monitoring of the complications and treat them readily as they occur.

ACKNOWLEDGEMENT

The author would like to thank the staff and the post-graduate students of the Department of pharmacy practice, Nirmala College of Pharmacy, Muvattupuzha and, Dr. Dona Maria Jetto for her support and encouragement.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

CCBs: Calcium channel blockers; **BIPAD:** Bilevel positive airway pressure; **NRBM:** Non-rebreather mask; **ECMO:** Extracorporeal membrane oxygenation; **HIET:** High-dose insulin euglycemic therapy.

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