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Case Report

Amlodipine Poisoning with Transient Cardiomyopathy and Concurrent Benzodiazepine Overdose

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A 25 year old male with an intentional ingestion of amlodipine and benzodiazepine with suicidal intention, due to peer pressure and psychological distress, had experienced transient cardiomyopathy. This case depicts the improved left ventricular function after the successful management of poisoning with a timely conventional management strategy (i.e. via intravenous fluid, vasopressor and inotropic support and Glucagon and Insulin infusion with 10% Dextrose water, and calcium gluconate administration). Amlodipine is a longer acting dihydropyridine calcium channel blocker that effectively controls blood pressure for 24 hours. It is a commonly used and safe antihypertensive agent.[1] Nevertheless, the overdose can have deleterious side effects.[2-4] Physician should have high index of suspicion of amlodipine poisoning in the patient having refractory shock with the history of drug overdose. As early recognition and timely management of acute amlodipine poisoning will result in successful outcome, like in our case.

Case Report

A 25-year-old male with no Known comorbidities and no addiction history presented in an emergency after ingestion of 15 mg benzodiazepine (bromazepam) and amlodipine 200 mg (Norvasc) in a suicidal attempt one night back with complaints of shortness of breath and cough for one day and drowsiness for few hours. On arrival, vitals were as follows: BP: 97/46, Pulse: 100 beats per minute, respiratory rate: 40 b/min, Oxygen saturation: 95 % on 15-liter oxygen. On examination: Chest: bilateral crackles. CNS: Drowsy but arousable on pain stimulus, bilateral pupils were reactive to light. Other systemic examination was unremarkable i.e. cardiovascular examination showed no added sound or murmur and the abdomen was soft non-tender with no visceromegaly on palpation.

On arrival Chest X-ray, showed bilateral infiltrates in lungs and hilar prominence thus in the relevance of pulmonary edema, his Prohormone of Brain Natriuretic Peptide (Pro-BNP) levels checked i.e. 4275 and echocardiography showed Global hypokinesia and severe Left ventricle [LV] dysfunction with an Ejection fraction of 35%. Electrocardiography showed sinus tachycardia with no ST- T wave changes. Serial troponin checked, which were negative. Urine toxicology was done which showed, raised benzodiazepine levels (561 ng/ml). Serum amlodipine levels were not checked due to the non-availability of the test in our hospital.

The patient had pulmonary edema due to reduce LV function. This was sudden as there was no prior history of shortness of breath, chest pain, or heaviness. Echocardiography showed global hypokinesia with no segmental wall motion abnormality. He had no history of recent viral illness, so myocarditis was least likely. He had never drunk alcohol nor had anemia, hence dilated cardiomyopathy secondary to alcohol and B12 was ruled out. Analyzing the young age and sudden onset of symptoms after intentional overdose contributes towards stress cardiomyopathy to due acute insult by amlodipine poisoning.

The patient got electively intubated in an emergency room for mechanical ventilation due to respiratory distress secondary to benzodiazepine overdose-induced central respiratory suppression and got admitted to the medical intensive care unit [ICU]. For amlodipine poisoning management, he started on Vasopressin, epinephrine, and norepinephrine support. Glucagon 3mg per hour, Insulin infusion with 10% Dextrose water, and calcium gluconate were administered. He got off epinephrine, nor-epinephrine, and vasopressin support after gradual tapering.

On the 7th day of admission, the patient got extubated to non-invasive ventilation support after a successful

spontaneous breathing trial. The next day of extubation, he was hemodynamically stable, with GCS 15/15 and maintaining saturation of 98% on room air, so got shifted to the Special care unit for monitoring. Reviewed echocardiography showed improved LV function with an ejection fraction of 45%. He later shifted to the ward and a psychiatry evaluation was advised to prevent any further attempt of suicide, but the family refused for psychiatry review and Left against Medical Advised (LAMA).

The young male had a meaningful recovery but left against medical advice without psychiatric evaluation and never followed up in the clinic.

Discussion

Amlodipine is a long-acting drug, and its overdosage either intentional or unintentional can be lethal, several cases had been reported in this regard, and others who survived had unconventional management strategy therapy had been utilized.

Morini et al. reported a case of fatal amlodipine poisoning in which autopsy showed a relatively low level (0.17 mg/L)of amlodipine in peripheral blood, hence it showed that even the low-level overdosage of amlodipine can lead to death.[2] Zahed et al. reported another fatal amlodipine case of a young 25-year-old male with adult polycystic kidney disease presented after ingestion of 450 mg of amlodipine.[3]

Amlodipine can cause prolonged and refractory hypotension while taken in overdose. Chudow et al. reported a fatal case of a 53-year-old male with an intentional ingestion of eight tablets of 10 mg amlodipine which lead to persistent hypotension, refractory to multiple therapeutic approaches.[4] Similarly, Kapelios et al. reported a case 72-year-old male with sustained hypotension refractory to crystalloid and vasoconstrictor infusions. An extensive diagnostic workup was done to evaluate the cause but it was unfruitful. After a toxicological investigation, it was found to be a case of unintentional amlodipine intoxication.[5] The prolonged hypotension after acute amlodipine overdose was attributed to the prolonged elimination half-life of amlodipine due to a decrease in hepatic clearance secondary to saturation of metabolism, as postulated by the case report of Chudoku et al. They presented a case of a 75-year-old elderly female with acute amlodipine poisoning. The serum Amlodipine concentration checked on the 1st hospital day was 355.6 ng/ml. The subsequent analysis of serum Amlodipine concentration showed delayed elimination half-life in the early period as compared to the later period.[6] Cortical blindness secondary to bilateral optic atrophy from prolonged hypotension can be a consequence of amlodipine poisoning, as reported by Kao et.al. They reported a case of a 49-year-old female with known ingestion of 150 mg of amlodipine who recovered successfully but suffered from cortical blindness.[7] There is a paucity of literature regarding Left Ventricular [LV] function in amlodipine poisoning, one of the case reports showed normal LV function.[8] However, our case of the young male is the first to report reduced left ventricular function with pulmonary edema on presentation and had improved left ventricular function after successful management of acute poisoning.

There have been various therapeutic measures that are now recognized to deal with amlodipine poisoning or overdose. Seegobin et al reported a case of successful management of a 54-year-old female, presented with combined ingestion of hydrochlorothiazide, doxazocin, atenolol, and amlodipine. She was initially refractory to treatment with conventional therapy i.e. (intravenous fluids, activated charcoal, glucagon 5 mg followed with glucagon drip, calcium gluconate 10%, and atropine) and insulin at 4 U/kg. Shortly after high dose insulin was achieved with 10 U/kg, there was a dramatic improvement in hemodynamics, and got off all vasopressor support in less than 24 hours. Thus High dose insulin has shown promising results and it can be beneficial if initiated as early as possible for a better outcome.[9] Intravenous lipid emulsion (ILE) is reported as a potentially novel antidote for the treatment of acute poisoning caused by Calcium channel blockers with refractory shock.[10] However, Jović et al. reported a fatal case of, a 24-year-old woman who ingested multiple drugs i.e. amlodipine, metformin, and gliclazide for self-poisoning. Along with conventional treatment which included fluid resuscitation, vasopressors, intravenous calcium, and glucagon, ILE also had been administered but circulatory shock persists, and ultimately died due to cardiac arrest refractory to cardiopulmonary resuscitation. Thus Intravenous lipid emulsion may be ineffective in acute poisonings of combined multiple drug ingestion.[11] Methylene blue, is another beneficial therapeutic measure in drug-induced vasodilatory shock as reported by Laes et al. They reported the case of refractory shock caused after combined ingestion of atenolol, amlodipine, and valsartan. Shock persisted after multiple therapies including vasopressors, high-dose insulin, hemodialysis, and 20% intravenous fat emulsion. But there was a dramatic improvement in hemodynamics after Methylene blue (2 mg/kg IV over 30 min) was administered.[12] Extracorporeal Membrane Oxygenation (ECMO) either venous–venous (VV ECMO) or venous-arterial (VA ECMO) is recognized as a viable treatment strategy in refractory cases that failed all other therapeutic measures in case of severe amlodipine poisoning.[13] Laes et al. reported a case in which a percutaneous left ventricular assist device (Impella) is used in vasodilatory poison-induced shock. Interestingly, in our case, the young

male responded well to conventional therapeutic measurement and successfully recovered.

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