CASE REPORT

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The Role of Plasmapheresis in Amlodipine Overdose

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Abstract

Amlodipine overdose is scarcely reported from India, though rare but associated with high mortality. It can lead profound refractory hypotension and shock leading to end organ damage. Management involves early and aggressive measures and calcium in large doses to overcome competitive blockade, hyperinsulinemiaeugycemic therapy, along with some rescue therapies tried in anectodal reports. We report one such case of amlodipine overdose and was successfully managed.

Keywords: Amlodipine, calcium channel blocker, hypotension, plasmapheresis.

INTRODUCTION

Calcium channel blockers are the leading cause of cardiovascular drug overdose and are responsible for 48% of death related to cardiovascular drug exposure.[1] Treating patients with overdose of these medications has been challenging. The difficulty arises because patients severely poisoned with CCBs may have profound refractory hypotension, requiring aggressive supportive measures.[1] We present a case of amlodipine overdose with successful treatment.

CASE REPORT

A 37-year-old woman with no significant past history, presented to our hospital with giddiness, sweating, reduced urine output, after 10 hrs of consumption of 100 tablets of amlodipine (500 mg). She was initially rushed to a local hospital near her home within 30 mins of consumption with complaints of giddiness and sweating, found to have hypotension, gastric lavage was given and ionotrope (nor adrenaline) started and 10 hours later was shifted to our hospital. At presentation she had hypotension with systolic of 60mm of Hg, heart rate of 120 per min, respiratory rate of 30 per min with room air saturation of 85% and 97% on 10l/min oxygen with non-breathing mask, on auscultation had basal crepitations. Gastric lavage with water and activated charcoal (1g/kg) 80g was given through nasogastric tube and ionotrope support with nor adrenaline was titrated to maintain MAP 65, 500 ml normal saline bolus was given, arterial blood gas analysis showed severe metabolic acidosis pH 7.02 pO2 57.2 pCO_2 19.8 $HCO3^-$ 5.2 k^+ 2.3 Ca 0.67 mmol/liter, lactate 7.62 base excess -25.6. Bicarbonate and potassium correction was given, calcium gluconate 10ml iv bolus over 10 mins was given and shifted to intensive care unit. In ICU there was persistent hypotension and started on noradrenaline, vasopressin and adrenaline infusions with fluid resuscitation at 200 ml/hr and later reduced due to fluid overload signs, calcium gluconate infusion at 10ml/hr, potassium correction was started, dextrose with insulin infusion started (0.5 U/Kg/hr), glucagon 3mg subcutaneous stat dose was

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given. Investigations revealed Hb 8.8, TC 19180, Platelet 199900, BUN 17, serum creatinine 1.00, Na 142, K 2.4, Ca 4.30, HbA1C 5.2, liver function test and coagulation profile were normal, ECG showed junctional rhythm, chest X-ray revealed pulmonary edema, 2D ECHO showed left ventricular global hypokinesia with ejection fraction 35%, moderate left ventricular dysfunction,severe MR, moderate PAH. She was intubated on mechanical ventilation, as she was anuric for 12 hrs, hemodialysis was initiated with SLED for 6 hrs with nil ultrafiltrate, followed by plasmapheresis with albumin was done. She improved and inotrope was tapered and stopped on day 2. Calcium infusion was continued with serial serum calcium levels monitoring every 12 hrs till day 5 and later thrice a day for 2 days. Insulin infusion was stopped day 2, four sessions of hemodialysis was done once a day and later iv diuretics with intermittent boluses were given. A repeat 2D ECHO on day 3 showed an improvement with ejection fraction 49%. She was weaned and extubated on day 4. After extubation she was tachypneic, managed on non invasive ventilation and later on NRBM with 10l per min oxygen, chest X-ray showed ARDS with pleural effusion,she developed fever with elevated leucocyte count, sputum and blood cultures were sent and empirical broad spectrum antibiotics were started, supplemented with bronchodilator nebulisations and intravenous steroids, along with aggressive chest physiotherapy and incentive spirometry. Culture reports showed no growth. She recovered and discharged on day 9.

Monitored parameters included clinical status, IVC compressibility, urine output, arterial blood gas, serum electrolytes including calcium, magnesium and ECG every 6hrs for first 48hrs, thereafter every 12 hrs. she had acute kidney injury, hemodialysis was initiated and later recovered after 5 days. She was weaned off ventilator after 4 days and later complicated with ARDS. In our case we tried all the conventional treatment modalities like charcoal lavage, calcium infusion and insulin therapy and other supportive measures like inotrope and ventilation support and later after initiating plasmapheresis she improved and avoided ECMO.

DISCUSSION

Amlodipine, a dihydropyridine calcium channel blocker, has a half-life of approximately 30 to 50 hours and a large volume of distribution (21 L/kg). CCBs such as amlodipine reduce calcium flux through voltage gated slow (L-type) calcium channels. The major toxic effect of an overdose is refractory hypotension, due to both vasodilation and impaired cardiac metabolism and contractility. Tissue ischemia and lactic acidosis ensue. Blockade of calcium channels in other tissues, such as pancreatic beta cells, also has other important adverse consequences (*i.e.*, reduced insulin release).[2]

Due to a long elimination half-life and delayed onset of effects, patients with amlodipine overdose should receive aggressive decontamination therapy. Gastric lavage with water or polyethylene glycol and activated charcoal (1g/kg initially and to be continued for 24 through nasogastric tube) can be a useful modalities, especially in long-acting preparations.[3] Though definitive evidence of benefit of gastrointestinal decontamination in CCB overdose is lacking, it is still recommended due to potential lethal nature of CCB overdose and lack of specific antidote.[3]

Treatment includes supportive care including maintenance of airway, breathing and circulation (ABCs). Hypotension is initially managed with volume loading; however, as our patient had signs of fluid overload, we did not continue to administer iv fluids. Inotropes (dopamine, norepinephrine, epinephrine) can be added[4,5] after normalization of CVP. Correction of acid-base disturbances and electrolyte abnormalities optimizes cardiac function. Our patient presented with giddiness caused by hypotension attributable to generalised vasodilation due to direct effect on vascular smooth muscle worsened by negative effect on the cardiac pacemaker and myocardial contractility.

Calcium gluconate or chloride in continuous infusion (Ca chloride 0.2 ml/kg/hr) or iv boluses (10 ml of 10% calcium chloride/20-30 ml of calcium gluconate, every 15-20 minutes; maximum: 30g over 12 hours) is given to overcome the competitive blockade of calcium channels. We treated our patient with parenteral calcium and monitored with clinical response, ECG and serum calcium levels. Calcium infusion provides a direct antidote and may be helpful; however, the response to calcium is also often inadequate.

In refractory cases, glucagon (5-10 mg iv)[4,5] and hyperinsulinemic – euglycemia using dextrose and insulin infusion (with 0.5 IU/kg/hr) as inotropic agents. [6,7,8]

Glucagon may be infused because it activates myocardial adenylate cyclase and thus increases cardiac cyclic adenosine monophosphate levels, which results in an inotropic effect. High-dose

insulin infusion together with adequate glucose to maintain normal glucose levels so-called "hyperinsulinemia/euglycemia therapy" has been shown to be very effective in experimental models of CCB overdose.[9,10] Insulin has a direct positive cardiac inotropic action and may also improve myocardial carbohydrate oxidation, which is often impaired in these patients.

Oliguric renal failure with features of fluid overload seen in our patient is attributable to prolonged refractory hypotension and hypoperfusion and end organ ischemia. Hemodialysis was initiated for acute renal failure and later after 4 sessions of hemodialysis the kidneys recovered to normal.

Therapeutic plasma exchange is a procedure used to remove pathologic substances from a patient's blood that has proven useful in some cases of drug overdose. Refractory hypotension prompted the use of plasmapheresis in an attempt to lower serum amlodipine levels as knowing that amlodipine is highly protein bound. In the case of drug overdose, the American Society for Apheresis (ASFA) guidelines suggest the use of albumin or fresh-frozen plasma (FFP) based on the specific drug-binding affinities to help draw the medication into the intravascular space.[11] As albumin is responsible for most nonspecific protein binding of drugs,we have used albumin for plasmapheresis. A dramatic improvement of cardiovascular stability was already observed during plasmapheresis, gradually inotropes were tapered. Only a few case reporting has been done on plasmapheresis. In our case doing plasmapheresis early prevented the patient from ECMO. ECMO, intra-aortic balloon pump, ventricular assist device are a few of treatment modalities tried in overdose.

CONCLUSION

Along with conventional therapies including gastric lavage, activated charcoal, Hyperinsulinemia-Euglycemia Therapy, calcium infusion, glucagon, vasopressor, early plasmapheresis can be effective in restoring hemodynamic stability and preventing complications like acute renal failure from hypotension in severe calcium channel blockers toxicity and other invasive modalities of treatment.

REFERENCES

1. DeWitt CR, Walksman JC. Pharmacology, pathophysiology and management of calcium channel blocker and β-blocker toxicity. Toxicol Rev 2004;23:223-38.
2. Tapan Patel, MD, David Tietze, MD, Amlodipine overdose.Proc (BaylUniv Med Cent). 2013 Oct; 26(4): 410–411
3. Kenny J. Treating overdose with calcium channel blockers. BMJ. 1994;308:992–3. [PMC free article] [PubMed] [Google Scholar]
4. Saravu K, Balasubramanian R. Near-Fatal Amlodipine poisoning. J Assoc Physicians India. 2004;52:156–7. [PubMed] [Google Scholar]
5. Russel RP. Side effects of calcium channel blockers. Hypertension. 1988;13:I37–40. [Google Scholar]
6. Yuan TH, Kerns WP, II, Tomaszewski CA, Ford MD, Klinc JA. Insulin glucose as adjunctive therapy for severe calcium channel antagonist poisoning. ClinToxicol. 1999;37:463–74. [PubMed] [Google Scholar]
7. Boyer EW, Shannon M. Treatment of calcium channel blocker intoxication with insulin infusion. N Engl J Med. 2001;344:1721–2. [PubMed] [Google Scholar]
8. Kute VB, Shah PR, Goplani KR, Gumber MR, Vanikar AV, Trivedi HL. Successful treatment of refractory hypotension, noncardiogenic pulmonary edema and acute kidney injury after an overdose of amlodipine. Indian J Crit Care Med. 2011;15:182–4 [PMC free article] [PubMed] [Google Scholar]
9. Lheureux PE, Zahir S, Gris M, Derrey AS, Penaloza A. Bench-to-bedside review: hyperinsulinaemia/euglycaemia therapy in the management of overdose of calcium-channel blockers. Crit Care. 2006;10(3):212. [PMC free article] [PubMed] [Google Scholar]
10. Azendour H, Belyamani L, Atmani M, Balkhi H, Haimeur C. Severe amlodipine intoxication treated by hyperinsulinemia euglycemia therapy. J Emerg Med. 2010;38(1):33–35. [PubMed] [Google Scholar]
11. Schwartz J, Padmanabhan A, Aqui N *et al*. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the writing committee of the American Society for Apheresis: the seventh special issue. J ClinApher. 2016;31:149-162.