Case Report

Management of life-threatening calcium channel blocker overdose with continuous veno-venous hemodiafiltration with charcoal hemoperfusion

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Abstract

Cases of calcium channel blocker overdose reported from India are few, and although rare, they are associated with high mortality. Management includes fluids, vasopressors, calcium gluconate or chloride, glucagon infusion, and hyperinsulinemia-euglycemia therapy along with some rescue therapies tried in anecdotal reports. We report here a case of life-threatening overdose of amlodipine with shock, refractory to conventional therapies. Salvage therapy with continuous veno-venous hemodiafiltration using charcoal hemoperfusion with prior infusion of intravenous lipid emulsion resulted in a successful outcome.

Keywords: Amlodipine overdose, calcium channel blocker overdose, charcoal hemoperfusion, continuous veno-venous hemodiafiltration

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Introduction

Calcium channel blockers (CCB) are the leading cause of cardiovascular drug overdose.[1] Complications such as hypotension, pulmonary edema, and conduction blocks are responsible for adverse outcomes. Reports of CCB overdose are scarce in Indian literature.[2,3] We describe here a case of life-threatening overdose of amlodipine causing shock refractory to standard management.

Case Report

The case we present here is about a 42-year-old male, who was hypertensive (on amlodipine 5 mg bd), with history of left hemiglossectomy and modified radical neck dissection for carcinoma tongue, a renal transplant recipient (on triple dose immunosuppression), and hepatitis C virus positive status was admitted with an alleged history of consumption of 100 tablets of amlodipine (5 mg each, total dose 500 mg) around 5 h prior to presentation. On admission, he was drowsy but was responding to painful stimuli. His heart rate was 52/min, blood pressure was 40 mmHg systolic, respiratory rate was 8/min and was afebrile. Systemic examination was within the normal limits. He was intubated electively, given fluid boluses and started on dopamine and noradrenaline infusions. His blood gases showed acute respiratory and metabolic acidosis with hyperlactatemia (4.5 mmol/l). A 12-lead electrocardiograph was normal. Gastric lavage was done with 100 g of charcoal. He was given 3 g IV calcium gluconate as a slow bolus followed by 50 mg/h infusion along with 5 mg IV glucagon over 15 min followed by an infusion at 5 mg/h. He was also started on injection insulin and 50% dextrose as hyperinsulinemia-euglycemia therapy.

His condition continued to deteriorate, despite aggressive resuscitation. Terlipressin infusion at 2-3 μg/min was also started along with injection hydrocortisone 100 mg tds as an immunosuppressant as the patient was postrenal transplant recipient. Mean arterial pressure (MAP) could not be maintained more than 50 mmHg despite very high doses of vasopressors (dopamine 20 μg/kg/min, norepinephrine 20 μg/min, epinephrine 20 μg/min and terlipressin 10 μg/min). In view of refractory shock and

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anuria, with severe metabolic acidosis, continuous veno-venous hemodiafiltration (CVVHDF) with charcoal hemoperfusion using HA Resin hemoperfusion cartridge (Model HA 280, Jafron Biomedical Co., Ltd.) along with 250 ml of 20% intravenous (IV) lipid emulsion given prior to CVVHDF was started as rescue therapy [Figure 1].

The patient's condition started improving with increase in MAP around 6 h after starting CVVHDF. Another session of CVVHDF with charcoal hemoperfusion with IV lipid emulsion was given after 24 h. Vasopressors were progressively weaned off in the next 96 h and stopped on day 7. The infusions of glucagon, calcium and insulin-dextrose were continued for 96 h and then gradually stopped. CVVHDF without charcoal hemoperfusion was stopped on day 12 as patient's renal functions started improving. Total dose of glucagon used was 252 mg, calcium gluconate was 64 g and insulin was 2000 IU. The patient was extubated on day 11 and transferred to wards on day 13.

Discussion

Amlodipine is a CCB of dihydropyridine class and is prescribed for the treatment of hypertension, angina pectoris and congestive heart failure.[4] It has predominant effect on vascular smooth muscle cellas and causes marked peripheral vasodilatation and hypotension although it also causes coronary vasodilation.[4] It is fully absorbed from the gastrointestinal tract with peak plasma levels reaching in 6-12 h, has a large volume of distribution and is extensively distributed in tissues and organs. The drug is highly lipophilic with 97.5% being protein bound. It undergoes extensive hepatic metabolism to inactive metabolites with a mean elimination half-life of 35-50 h.[5]

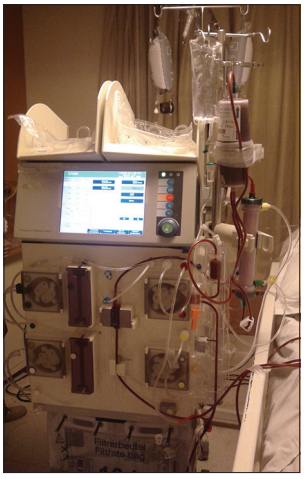

Figure 1: Continuous veno-venous hemodiafiltration using HA Resin Hemoperfusion Cartridge (Model HA 280, Jafron Biomedical Co., Ltd.)

Physical symptoms of amlodipine overdose are nonspecific such as headache, nausea, abdominal pain, and edema, which go unreported. The management of CCB overdose includes gastrointestinal decontamination with activated charcoal and total gut lavage with polyethylene glycol along with IV fluids, vasopressors, glucagon and/or calcium infusions.[6] Specific antidote is calcium gluconate or chloride. Other measures which can be tried include hyperinsulinemia-euglycemia therapy.[7] However, in patients with shock refractory to these therapies, anecdotal therapies have been tried with some success. These include CVVHDF without charcoal hemoperfusion,[8] IV lipid emulsion,[9] levosimendan,[10] methylene blue,[11] intra-aortic balloon pump,[12] and extracorporeal life support.[13,14] All these modalities were used as single rescue therapy as these patients had consumed smaller dose of CCBs and were less seriously ill than our patient.

Theoretically, hemodialysis is ineffective for removal of drugs that are highly protein bound.[6] The shock in our patient was refractory to all other measures, which prompted us to use a combination of IV lipid emulsion, CVVHDF and charcoal hemoperfusion as a rescue therapy. Our case was unique because, to the best of our knowledge, multiple therapeutic modalities had not been combined previously. Our patient showed a dramatic response to this triple therapy.

The limitation of our case report is the absence of drug levels of amlodipine in our institution and hence the effect of IV lipid emulsion and charcoal hemoperfusion on serum concentration of amlodipine could not be ascertained.

Conclusion

Management of massive CCB overdose requires combined use of fluid resuscitation, vasopressors, calcium and glucagon infusions to improve organ perfusion. IV lipid emulsion for binding of CCB's followed by the use of extracorporeal therapies like CVVHDF with charcoal hemoperfusion for removal of CCB from circulation may be tried as rescue therapies in patients with shock refractory to standard measures.

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