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Amlodipine toxicity complicated by concurrent medications

Bhavna Gupta and Sukhyanti Kerai

Department of Anesthesia and Critical Care, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India

Amlodipine is amongst the commonly prescribed medication in patients with hypertension. Cases of amlodipine toxicity have been reported in literature. We report a rare case of 45 year old female with alleged history of suicide with amlodipine, and other medications which included sedatives, anti-hypertensives, oral hypoglycemic agents and thyroid medications. Our patient presented with atypical features of poisoning and hence was managed accordingly. The clinical picture at the time of presentation and management has been described in detail.

Amlodipine is a type of dihydropyridine calcium channel blocker and is used in management of angina pectoris and essential hypertension. It is prescribed as a daily dose of 5–10 mg daily. There are reported cases of amlodipine toxicity in literature, however none described a case of amlodipine toxicity complicated with other concurrent medications. We report a well-managed case of severe amlodipine intoxication complicated by other medications.

A 45-year-old woman with chronic hypertension, diabetes, hypothyroidism, coronary artery disease, and depression had been taking amlodipine 5 mg once daily (OD), telmisartan 40 mg OD, metformin 500 mg twice daily (BID), glimepiride 2 mg BID, levothyroxine 100 μg OD, and alprazolam 0.5 mg at bedtime. She was admitted in an unconscious state, with an alleged suicide attempt by taking ten 5-mg tablets of amlodipine in addition to her usual telmisartan, metformin, alprazolam, and levothyroxine tablets at bedtime. Her history was provided by her son, and an empty tablet container was retrieved.

She was admitted to the emergency department in an unconscious, diaphoretic state, with frothing from the mouth and tongue biting. She was drowsy, with a weak pulse, heart rate of 35 beats/min, systolic blood pressure of 85 mmHg, peripheral oxygen saturation (SpO_2) of 40%–50%, and bilateral basal crepitus. Pupils were equally reactive, and she had oliguria (urine output: 30 ml/h). Relatives reported she had an episode of vomiting, followed by rigidity of limbs and a possible seizure. A 7.5 Fr endotracheal tube was immediately inserted and gastric lavage was performed with activated charcoal via gastric tube. She was also administered a bolus of atropine. Her blood sugar was 60 mg/dl, and she was given 100 ml of 25% dextrose over 20 min. She was subsequently transferred to the intensive care unit (ICU). In the ICU, her pulse rate was 45 /min, with blood pressure of 100/70 mmHg and SpO_2 of 96%. Calcium and magnesium levels, arterial blood gases, an electrocardiogram, creatine phosphokinase (CPK, total and MB) and troponin T levels, and a chest X-ray were obtained. She was empirically given a bolus of calcium gluconate (10%; 30 ml over 10 min), followed by a 10 ml/h infusion, and a loading dose of phenytoin was given. She had a normal blood count, and urea, creatinine, CPK-MB, and troponin T levels were negative. Fig. 1 shows the chest X-ray with a possible right lower lobe infiltrate. Ionized calcium and blood sugar levels were maintained in the reference range and monitored every hour. She was uneventfully extubated 12 h after poisoning and maintained normal consciousness, vital signs, and urine output. Her oliguria responded to fluid boluses. After extubation, she required high-flow nasal oxygen to maintain saturation and had tachypnea of 35 breaths/min, with a resolution after 96 h. Echocardiography and non-contrast brain computed tomography were normal. Over a period of 5 days, her clinical condition improved, and she was moved to a ward and discharged after a few days. She has been followed in the psychiatric clinic for her suicidal behavior.

Amlodipine is typically known to produce fewer side ef-

Corresponding author: Bhavna Gupta, MBBS, DA, DNB
Department of Anesthesia and Critical Care, Maulana Azad Medical College and Lok Nayak Hospital, Bahadur Shah Zafar Marg, Balmiki Basti, New Delhi 110002, India
Tel: 91-8527686660, Fax: 91-8527686660
Email: bhavna.kakkar@gmail.com
ORCID: https://orcid.org/0000-0002-3108-0408

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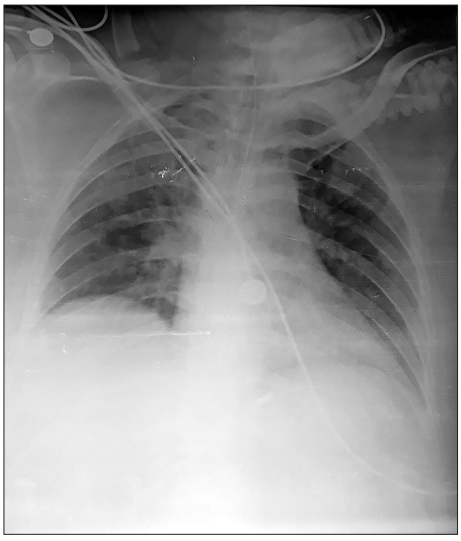

Fig. 1. Chest X-ray suggestive of right side infiltrates/haze in lung bases.

fects compared with other calcium channel blockers, such as diltiazem and verapamil, because of a relative lack of negative inotropic effects. However, a few fatal cases of amlodipine overdosing have been reported [1,2]. Signs and symptoms of amlodipine toxicity may include dizziness, light-headedness, syncope, chest pain, dyspnea, seizure, headache, nausea, vomiting, confusion, palpitations, headache, and flushing. Our patient was admitted in an unconscious state, with bradycardia and bradypnea. Specific management is symptomatic, as in any case of poisoning. The management of the airway, breathing, and circulation is recommended, followed by decontamination. Although there is no definitive literature evidence for gastrointestinal decontamination, this is still advocated because of the potentially lethal nature of an overdose and absence of a specific antidote. An overdose of a calcium channel blocker can result in binding to the alpha-1 subunit of L-type calcium channels, found in cardiac myocytes, smooth muscle cells, and beta islet cells, preventing the influx of calcium. Receptor sensitivity may be lost in overdosage, and amlodipine can cause cardiotoxicity along with vasodilatation in large doses. Cardiac manifestations of overdosage include bradycardia, myocardial depression, and sino-atrioventricular nodal blockade. Systemic manifestations include hypotension, coronary vasodilation, and decreased afterload. Metabolic effects include hyperglycemia owing to decrease in insulin release, which is dependent on calcium influx into beta islet cells [3]. However, our patient had low blood sugar, possibly because of concurrent medications (metformin and glimepiride), in addition to prolonged fasting.

The initial management of amlodipine toxicity includes fluid resuscitation (at a rate of 20 ml/kg), intubation for airway protection, and laboratory and imaging studies to rule out infection or polysubstance abuse. Intravenous calcium is recommended in early management to improve blood pressure and myocardial contractility [4]. Several authors have suggested a role of high-dose insulin in calcium channel blocker toxicity [4]. However, because our patient had already ingested her oral hypoglycemic, insulin was not started. Euglycemia was maintained at all times. Seizures are rare in cases of amlodipine toxicity and may be attributed to hypoglycemia and hypotension at the time of presentation. Our patient had a single seizure episode with vomiting, which could have resulted in microaspiration in the lungs, leading to bilateral crepitus. Amlodipine toxicity is also known to cause pulmonary edema owing to excessive transudation because of precapillary vasodilation, with increased transcapillary pulmonary pressure, and ultimately interstitial edema [5]. Crepitus resolved with diuretics and fluid overload was ruled out by echocardiographic findings. Pulmonary microaspiration could not be ruled out, and management was symptomatic.

Our case was unique as it involved the management of amlodipine toxicity complicated by the presence of concurrent antihypertensive, diabetic, thyroid, and sedative medications. The outcome was good with timely intervention, aggressive fluid management, early mechanical ventilation, early gastric decontamination, seizure control, and management of calcium and blood glucose levels, as well as timely extubation and intervention.

ORCID

Bhavna Gupta, https://orcid.org/0000-0002-3108-0408
Sukhyanti Kerai, https://orcid.org/0000-0002-7771-0786

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