Cardiovasc Surg Int 2024;11(3):213-216
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1717
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Case Report Open Access

An interesting case of refractory hypotension and noncardiogenic pulmonary edema after amlodipine overdose

İhsan Alur[1], Gökhan Peker[2], Taner Taşyüz[2], Ahmet Deniz Kaya[3], Osman Kaya[4]

[1]Department of Cardiovascular Surgery, Private Egekent Hospital, Denizli, Türkiye
[2]Department of Anesthesiology and Reanimation, Private Egekent Hospital, Denizli, Türkiye
[3]Department of Cardiovascular Surgery, Ministry of Health, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Türkiye
[4]Department of Anesthesiology and Reanimation, Ministry of Health, Nizip State Hospital, Gaziantep, Türkiye

Received: August 08, 2024 ***Accepted:*** September 16, 2024 ***Published online:*** October 17, 2024

ABSTRACT

Amlodipine is a dihydropyridine calcium channel blocker that acts on intravascular L-type calcium channels. It is most effective on vascular smooth muscle cells and has little effect on cardiac tissue. Its most common use is hypertension, angina, arrhythmias, subarachnoid hemorrhage, migraine, and Raynaud's disease. Amlodipine is preferred because it is used once a day and has minimal side effects on heart rate. However, in case of acute overdose, either accidental or deliberate (e.g., suicide attempts), dangerous side effects may occur and may result in death. Herein, we presented a 34-year-old male patient who ingested 90 tablets of amlodipine 10 mg and was successfully treated.

Keywords: Amlodipine, hemodialysis, hemofiltration, intoxication, overdoze, ultrafiltration.

Amlodipine is a dihydropyridine calcium channel blocker (CCB) that works on intravascular L-type calcium channels. It is most effective on vascular smooth muscle cells and has little impact on cardiac tissue.[1] It is most commonly used to treat hypertension and angina.[2] Amlodipine, unlike other CCBs, has low metabolic clearance and can be administered once daily to maintain an almost constant plasma concentration.[2] However, it has a lengthy half-life of 30 to 60 h and has a protracted impact in acute overdose. It can induce high plasma concentrations that can last for days.[3] Hypotension, acidosis, decreased tissue perfusion, respiratory arrest due to noncardiogenic pulmonary edema, and mortality may ensue in the event of intoxication due to vascular smooth muscle relaxation.[1,2,4] The most frequent therapeutic options for amlodipine acute overdose include gastrointestinal decontamination, fluid resuscitation, intravenous calcium, vasopressor medications, atropine, high-dose insulin euglycemic therapy, and pacemaker implantation.[1-4] Herein, we presented a patient who ingested 90 tablets of amlodipine 10 mg and was effectively treated.

CASE REPORT

A 34-year-old male patient stated taking 90 tablets of amlodipine 10 mg (900 mg in total) over 40 min in an attempt to commit suicide. After ingesting the tablets, he left his house and traveled approximately 2,000 m before passing out. During this time, he noted experiencing dizziness and his pulse slowing down before passing out. The patient was later discovered in a forest on the side of the road and taken to the emergency department. He was monitored at the hospital, and when the patient developed hypotension and anuria 48 h after taking the medications, he was transferred to our hospital due to the absence of a dialysis unit. The patient arrived with signs of pulmonary edema. He appeared

Corresponding author: İhsan Alur, MD. Özel Egekent Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 20125 Merkezefendi, Denizli, Türkiye.
E-mail: alur_i@hotmail.com

Citation:
Alur İ, Peker G, Taşyüz T, Kaya AD, Kaya O. An interesting case of refractory hypotension and noncardiogenic pulmonary edema after amlodipine overdose. Cardiovasc Surg Int 2024;11(3):213-216. doi: 10.5606/e-cvsi.2024.1717.

anxious, restless, agitated, and dyspneic. It was noted that the patient had no history of significant chronic disease or psychiatric disorder and that this was his first suicide attempt. The arterial blood pressure was 80/50 mmHg, and the heart rate was 79 beats per minute. The electrocardiogram revealed sinus rhythm. Bedside transthoracic echocardiography showed a left ventricular systolic function of 60%, with no additional pathological findings. The results of the arterial blood gas examination were as follows: partial pressure of oxygen, 39.4 mmHg; partial pressure of carbon dioxide, 38.1 mmHg; oxygen saturation, 70%; hemoglobin, 11.1 g/dL; hematocrit, 33%; lactate, 7.87 mmol/L; base excess, –13.8 mmol/L. Biochemical analysis revealed a urea of 78 mg/dL, creatinine of 2.44 mg/dL, and blood glucose of 97 mg/dL. A written informed consent was obtained from the patient. The patient was intubated. Due to the hypotensive course, a norepinephrine infusion at 0.4 mcg/kg/min was initiated. Dopamine and dobutamine infusions at 0.5 mcg/kg/min were initiated due to persistent hypotension. The time required for gastrointestinal absorption had passed by the time the patient arrived at the hospital, which was 48 h after ingestion. Therefore, gastric lavage was not performed. Computed tomography of the thorax revealed bilateral lung infiltrates, a ground-glass appearance, and acute respiratory distress syndrome (ARDS) (Figure 1a). Due to low arterial blood pressure, hourly urine output was insufficient; hence, continuous venovenous hemodiafiltration was performed at the bedside. Over six days, a total of 25 L of fluid were taken from the patient. The patient's refractory hypotension persisted for seven days. Later on, respiratory parameters, along with arterial blood pressure and arterial blood gas levels, began to improve. Vasopressors were withdrawn on the eighth day of hospitalization, starting with norepinephrine, followed by dopamine. While oxygen saturation and arterial blood pressure did not change significantly as norepinephrine and dopamine doses were gradually reduced, hemodynamics rapidly deteriorated and oxygen saturation declined when dobutamine dosage was reduced. As a result, dobutamine could only be discontinued on the 12th day due to the patient's hypersensitivity. Furthermore, hourly urine output increased, and venovenous hemodiafiltration was discontinued. After regulated monitoring with continuous positive airway pressure, the patient was extubated on the 10th day of intubation. The ARDS abnormalities were reported to have regressed in the control thorax computed tomography (Figure 1b). On the 13th day of hospitalization, the patient was transferred from the intensive care unit to the general ward. Vital signs were monitored. Arterial blood gas, complete blood count, and biochemistry levels all returned to normal. On the 19th day of his stay, the patient was discharged.

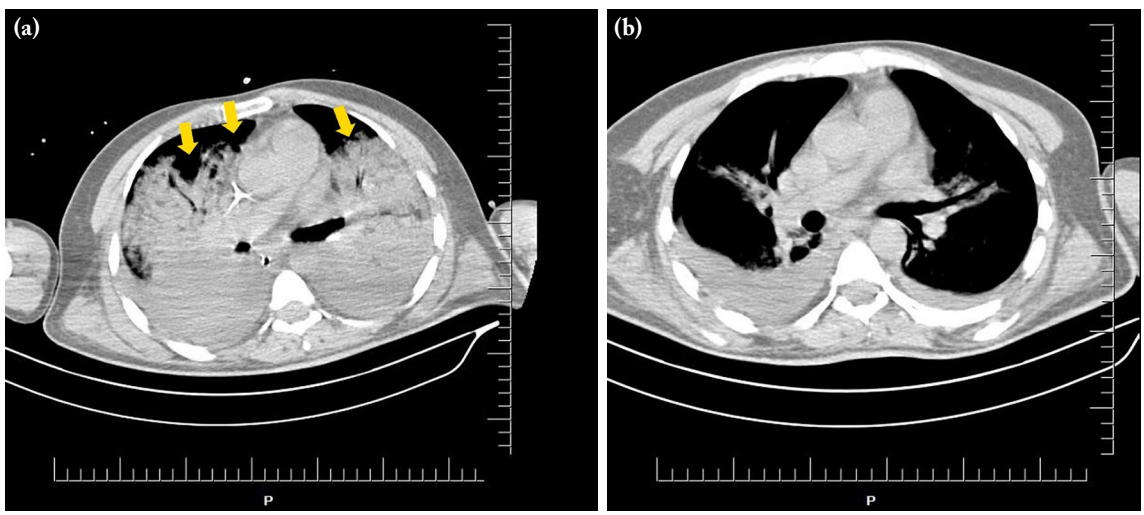

Figure 1. **(a)** Bilateral lung infiltration, ground glass appearance, and ARDS on thorax computed tomography (yellow arrows). **(b)** Control thorax computed tomography shows regression of ARDS findings.
ARDS: Acute respiratory distress syndrome; CT: Computed tomographic.

DISCUSSION

The patient arrived at our hospital 48 h after ingesting the tablets, was extubated after 10 days of intubation, recovered hemodynamically without the need for extracorporeal membrane oxygenation (ECMO), and was discharged, distinguishing this case from similar reports in the literature.

Calcium channels are present in numerous cells throughout the body, including cardiac myocytes, smooth muscle cells, and pancreatic β-cells. Calcium channel blockers inhibit calcium mobilization through each of these channels.[1] The effects of this vascular smooth muscle blockade comprise a drop in blood pressure, dilation of the coronary vascular system, and a decrease in afterload. Impaired inotropy emerges from calcium channel blockade in the cardiac muscles, and heart rate decreases owing to channel blockade in the sinoatrial and atrioventricular nodes.[1] Under normal physiological circumstances, amlodipine is selective for peripheral calcium channels. However, this selectivity is lost in acute overdose, leading to negative cardiac effects such as hypotension and bradycardia.[1] Inotropic support with isoproterenol is beneficial in the treatment of amlodipine-associated bradycardia.[5] Calcium administration and hemodynamic support with vasopressors and inotropes are standard treatments for amlodipine intoxication. Calcium is delivered at supratherapeutic levels as boluses or continuous infusions to overcome calcium channel antagonism.[1] Our patient did not have bradycardia, so isoproterenol was not started; however, intravenous bolus calcium replacement was initiated for its vasopressor effect.

Due to peripheral vasodilation in patients with amlodipine overdose, maintaining intravascular volume balance is critical. Excessive fluid administration to an anuric patient may lead to pulmonary edema. Vasopressor support must be initiated concurrently with volume support.[1-3] In our case, the hypotension proved resistant to inotropic medications. With a maximum blood pressure of 80/50 mmHg, the patient was observed for seven days with high-dose inotropic support and intravenous volume replacement. Due to anuria, continuous venovenous hemodiafiltration was also used at the bedside. As a result, we tried to maintain the arterial blood pressure and avoid hypervolemia to prevent the recurrence of pulmonary edema. Subcutaneous insulin was used to control the patient's blood glucose levels. Patel et al.[6] emphasized that glucagon has an inotropic effect by activating the cardiovascular adenylate cycle and that glucagon therapy and hyperinsulinemia/euglycemia therapy may enhance the direct cardiotropic effect of insulin and improve cardiovascular carbohydrate oxidation, which is often impaired in these patients. Another treatment modality for lipid-soluble drug overdose is intravenous lipid infusions.[6] Since our patients was not hypoglycemic, we did not administer glucagon.

An overdose of CCBs can be fatal, leading to noncardiogenic pulmonary edema and shock. Conventional therapy is insufficient for a severe CCBs overdose. The primary course of therapy for CCB overdose is supportive care, which includes fluid resuscitation. Since the mechanism underlying noncardiogenic pulmonary edema is unclear, mechanical ventilation is typically employed. In patients with severe poisoning, circulatory shock may not react to atropine, glucagon, or calcium, necessitating the use of vasopressors. For CCB poisoning, hyperinsulinemia/euglycemia therapy is preferable over other treatments because it actively transports glucose via insulin, counteracting the intracellular carbohydrate deficiency caused by CCBs. Although there is little use of intravenous lipid emulsion in treating lipophilic drug overdose, intravascular sequestration may enhance cardiac inotropy.[4] If oxygenation values do not improve despite intubation due to ARDS, ECMO support might be initiated. Extracorporeal membrane oxygenation has been shown to be effective until the lung parenchyma tissue recovers functionally.[4] In the study by Yusuke et al.,[7] a 46-year-old male patient intoxicated with 1,210 mg of amlodipine and 936 mg of candesartan was treated with vasopressors, calcium gluconate, and hyperinsulinemia/euglycemia therapy as an intubation and therapeutic protocol. However, the patient's hemodynamic condition deteriorated, and venoarterial ECMO support was initiated on the fifth day. The patient died on the 18th day. Initiating ECMO support earlier may have resulted in a better outcome. Although success was achieved in our case, it can be argued that ECMO support should be rapidly considered for poisoning with 1,000 mg or more.[7] In our case, ECMO support was not required because placing the patient in prone position improved oxygen saturation to roughly 80 to 90%, and respiratory parameters were adequate following intubation. One notable aspect of this case was the

patient's relative sensitivity to dobutamine compared to other vasopressor medications. Although there were no changes in oxygen saturation and arterial blood pressure during the progressive reduction of norepinephrine and dopamine doses, a rapid deterioration in hemodynamics was observed when the dobutamine dose was reduced. Additionally, arterial blood pressure began to decrease, and oxygen saturation dropped below 70%. Consequently, due to the patient's hypersensitivity to dobutamine, it could only be terminated on the 12th day.

In conclusion, the occurrence of refractory hypotension, leading to anuria and subsequent acute renal failure, is a significant issue in cases of amlodipine intoxication. In these patients, it is imperative to initiate vasopressor treatment in conjunction with volume support to rectify the blood pressure. Simultaneously, pulmonary edema may develop in these cases. In the event of the development of pulmonary edema, it is recommended to administer continuous venovenous hemodiafiltration, conventional hemodialysis, or ultrafiltration at the bedside while also ensuring careful monitoring of volume balance.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, writing, control/supervision: İ.A.; Design, data collection and/or processing: G.P.; Literature review: T.T.; Design/analysis and/or interpretation: A.D.K.; Data collection/design: O.K.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Chudow M, Ferguson K. A case of severe, refractory hypotension after amlodipine overdose. Cardiovasc Toxicol 2018;18:192-7. doi: 10.1007/s12012-017-9419-x.
2. Osman AF, Prasad RM, Marein S, O'Brien C. Multi-organ dysfunction as a presentation of calcium channel blocker intoxication. BMJ Case Rep 2022;15:e245711. doi: 10.1136/bcr-2021-245711.
3. Jang DH, Nelson LS, Hoffman RS. Methylene blue in the treatment of refractory shock from an amlodipine overdose. Ann Emerg Med 2011;58:565-7. doi: 10.1016/j.annemergmed.2011.02.025.
4. Siddiqi TA, Hill J, Huckleberry Y, Parthasarathy S. Non-cardiogenic pulmonary edema and life-threatening shock due to calcium channel blocker overdose: A case report and clinical review. Respir Care 2014;59:e15-21. doi: 10.4187/respcare.02244.
5. Ebihara T, Morita M, Kawada M, Amano K, Kato F, Nakata Y. Efficacy of isoproterenol for treating amlodipine overdose resulting in bradycardia. Acute Med Surg 2017;4:353-7. doi: 10.1002/ams2.284.
6. Patel T, Tietze D, Mehta AN. Amlodipine overdose. Proc (Bayl Univ Med Cent) 2013;26:410-1. doi: 10.1080/08998280.2013.11929022.
7. Yusuke M, Hidetoshi Y, Yusuke T, Koji I, Masahito T, Susumu Y, et al. Intoxication with massive doses of amlodipine and candesartan requiring venoarterial extracorporeal membrane oxygenation. Acute Med Surg 2023;10:e878. doi: 10.1002/ams2.878.