Amlodipine, a dihydropyridine calcium channel blocker, is commonly prescribed for the treatment of hypertension. Ingestion of an overdose leads to severe hypotension; if the hypotension is not treated, death may be imminent. Conventional and unconventional interventions were used to treat an adolescent who ingested a life-threatening dose of amlodipine. Severe hypotension resistant to conventional treatment with intralipids and hyperinsulinemia-euglycemia therapy led to the use of plasmapheresis and a pneumatic antishock garment as lifesaving measures. Plasmapheresis has been described in only one other case of severe amlodipine overdose, and the use of a pneumatic antishock garment has never been described in the management of a calcium channel blocker overdose. Because short-term use of a pneumatic antishock garment has associated risks, the critical care nurse’s anticipation of side effects and promotion of safe use of the garment were instrumental in the patient’s care and outcome. (Critical Care Nurse. 2016;36[4]:64-69)
Case Report

A 16-year-old girl with a history of multiple suicide attempts came to the emergency department (see Figure). No relevant family medical history was available because the patient was an adopted child. On arrival, she was ambulatory with assistance, had a Glasgow Coma Scale score of 14, and acknowledged taking a handful of amlodipine belonging to a family member. She became progressively obtunded in the emergency department, and the score on the Glasgow Coma Scale decreased to 8. She was intubated and had severe refractory hypotension despite administration of crystalloid fluid boluses and dopamine and norepinephrine infusions.

The patient was transferred to the pediatric intensive care unit (PICU). On arrival, the norepinephrine infusion was increased to 1.8 μg/kg per minute in an effort to improve persistent blood pressures of 52/28 mm Hg with mean arterial pressure between 33 and 35 mm Hg. Within 4 hours, the patient was also given continuous infusions of epinephrine 1.0 μg/kg per minute, phenylephrine hydrochloride 10 μg/kg per minute, norepinephrine 2.5 μg/kg per minute, and dopamine 10 μg/kg per minute. Despite aggressive fluid replacement, aggressive management with vasopressor agents, and a normal ejection fraction, no significant changes occurred in the patient’s blood pressures.

Further investigation revealed that the patient most likely had ingested 400 mg of amlodipine. The PICU team concluded that the patient’s hypotension was due to the amlodipine overdose, and 3 separate infusions of 1 g of calcium chloride were administered in an attempt to outcompete the calcium channel blocker. Although the patient’s serum level of calcium increased rapidly, reaching a maximum of 19.2 mg/dL (to convert to millimoles per liter, multiply by 0.25) and an ionized calcium level of 2.57 mmol/L, her blood pressure remained alarmingly low. Additional management included intralipids and hyperinsulinemia-euglycemia (HIE) therapy. Her response was similar to her response to calcium chloride; although the insulin infusion was increased to a maximum of 65 U/h (1 U/kg per hour), mean arterial pressure remained less than 40 mm Hg.

Six hours after admission to the PICU, the patient began to show signs of cardiogenic shock, including indications of acute kidney failure and an increase in serum lactate level to 12 mmol/L. The serum level of troponin increased to 3.15 ng/mL, indicating a troponin leak most likely associated with persistent tachycardia and low diastolic pressure. An attempt to rapidly reduce circulating drug levels via plasmapheresis was started because of the long half-life of amlodipine and the patient’s resistance to vasoactive agents. Serum levels of amlodipine were checked before, during, and after plasmapheresis, along with levels in plasmapheresis fluid (see Table). Laboratory reports of the levels of the drug were received several hours after completion of the plasmapheresis and indicated a marked reduction in amlodipine concentration with the use of plasmapheresis.

Despite the reduction in the level of circulating amlodipine, the patient’s blood pressure remained critically low with doses of norepinephrine 1.8 μg/kg per minute, epinephrine 1 μg/kg per minute, phenylephrine hydrochloride 20 μg/kg per minute, and an ionized calcium level of 2.57 mmol/L. Even with the persistent hypotension and elevated troponin and lactate levels, echocardiograms continued to show normal ejection fractions, suggesting an overwhelming systemic vascular resistance index. Approximately 12 hours after admission, the decision was made to begin therapy with a military/medical antishock trouser suit, now referred to as a pneumatic antishock garment (PASG).

Use of the PASG was started by the nursing team after careful review of the most current available literature and guidance by nurses who had experience with PASGs. Immediately after the lower-extremity cuffs of the PASG were inflated, the patient’s diastolic pressure increased from 33 mm Hg to 45 mm Hg and the mean arterial pressure increased to 55 mm Hg. The PASG was inflated until an audible “crackle” of the hook and loop (Velcro) bindings occurred. Compression of the patient’s legs was released every 30 minutes for a period of 2 to 3 minutes in an effort to maintain adequate perfusion of the lower

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extremities; however, each release of pressure correlated with a 5 to 10 mm Hg decrease in mean arterial pressure. By hospital day 2, the serum level of lactate was 6.9 mmol/L, and the troponin serum level was 3.15 ng/mL with continued maximum vasopressor support and PASG therapy. After 11 hours of PASG support, the team was able to deflate one leg of the suit and then the second leg because the patient’s diastolic blood pressure became increasingly responsive to vasopressor support. The patient was slowly weaned off insulin, and the troponin
Amlodipine overdose is a cause of increased concern because of its long half-life, which leads to prolonged periods of tissue hypoperfusion. 

Calcium channel blockers act by binding to the α-subunit of L-type calcium channels and reducing the influx of extracellular calcium into the cytosol. The relative abundance of the medication in the vascular smooth muscle promotes arterial dilatation, resulting in decreased blood pressure. In addition, the presence of L-type calcium channels in cardiac myocytes and the resultant blockade of calcium influx have a negative inotropic and chronotropic effect on the myocardium. With appropriate doses of amlodipine, these effects are beneficial in the management of hypertension. In excessive amounts, elimination of arterial tone causes severe hypotension and prevents the contraction of vascular smooth muscle, resulting in profound hypotension. In this patient’s case, blood pressures were so severely depressed that reflex tachycardia developed. This effect can be explained by an overdose of amlodipine.

Multiple investigators have described the use of HIE therapy to overcome the effects of overdoses of calcium channel blockers. This therapy is based on the concept that insulin prompts an opening of voltage-sensitive calcium channels, thereby providing a separate method for calcium entry into the cell and resulting in increased arterial smooth muscle contractility and improved blood pressures. In our patient, HIE therapy was ineffective, despite insulin infusion rates as high as 65 U/h and the use of dextrose-containing fluids to maintain normoglycemia. During multimodal therapy, which included HIE, the patient’s blood pressure remained dangerously low. In addition, administration of multiple boluses of calcium chloride provided little benefit. Despite high serum levels of calcium, the patient remained profoundly hypotensive and poorly responsive to vasopressor medications.

Measurements of serum amlodipine levels after toxic amlodipine ingestion have been well documented. In our patient, the measurement of amlodipine levels before and immediately after plasmapheresis indicated a marked reduction in circulating levels of the drug. Serum amlodipine levels decreased by 51% after a single cycle of plasmapheresis, and no adverse side effects occurred. On the basis of the normal half-life of amlodipine, clearance of the amlodipine without treatment would
have required in excess of 2 days. In our patient, amlodipine concentrations were markedly reduced by plasmapheresis in a short time. If the information on serum levels of the drug had been available via a point-of-care test, multiple cycles of plasmapheresis might have been attempted to further reduce the circulating concentration of amlodipine. Multiple cycles might have limited the duration of the patient’s hypoperfusion. Although only a single cycle of plasmapheresis was used, the circulating amlodipine levels measured in this patient suggest that plasmapheresis was a beneficial treatment. Future studies examining the use of plasmapheresis in toxic amlodipine ingestion would better define the role of that treatment.

A PASG is a self-contained inflatable abdominal girdle and/or trouser that provides increased peripheral vascular resistance. Although the garment is used rarely as a therapeutic intervention for shock, in our case it elicited a marked response and allowed maintenance of an improved blood pressure during the initial 24 hours of treatment. Immediately after inflation of the suit’s compressive trousers, a 10 mm Hg increase in diastolic pressures was noted. Because the patient already had a large increase in serum troponin levels, this increase in diastolic pressure and the resultant increase in coronary artery perfusion pressure most likely helped prevent irreversible cardiac damage. Echocardiograms performed on hospital day 2 showed no evidence of wall-motion abnormalities, and the serum troponin level declined steadily during the remainder of the patient’s hospital stay. Although myoglobinuria and neuropathic signs and symptoms developed, which were attributed to the compression of the PASG, these complications resolved before the patient’s transfer out of the PICU. The patient’s renal function returned to baseline and, with physical therapy, the peripheral neuropathies lessened. The transient nature of these side effects, compared with the high probability of demise without PASG application, clearly indicates that this treatment, although extinct in most emergency departments, provided a significant benefit in this case.

### Nurses’ Role

Ingestion emergencies are less common than medical emergencies, and background experience can inform difficult comprehensive care. Priorities in ingestion emergencies typically include assessing the patient, obtaining a history of medications and ingestion, initiating appropriate antidotal therapy, and depending on the patient’s state of consciousness, facilitating a cognitive psychological evaluation. Because critical care nurses may have limited exposure to treating patients who have life-threatening ingestions of amlodipine, understanding the drug’s mechanism of action and conventional treatment options can prepare them to anticipate a patient’s progress. Critical care nurses are experienced in providing and monitoring multimodal therapies and in evaluating best effects of those therapies. However, in instances in which conventional therapies are unsuccessful and unconventional therapies are prescribed, critical care nurses must understand the purpose of the therapies, safely use and monitor them, and evaluate their effectiveness. In our case, PASG was considered unconventional therapy. However, the nurses understood its purpose and quickly determined best practices for its use. They discerned from the literature safe application, inflation/deflation rates, additional monitoring requirements, and assessment of potential adverse effects. Multimodal therapy in patients with amlodipine ingestion has been reported, but primarily in case reports. Therapies include HIE, intralipids, glucagon, methylene blue, and plasmapheresis. Individual responses to the amount of ingested amlodipine vary according to the patient’s previous health status and the timing of interventions to prevent cardiopulmonary collapse. The case reports indicate that critical care teams try to use conventional therapies first and then attempt unconventional therapies when a patient’s response is unfavorable. In each case, critical care nurses participated in the safe use of the therapies and in the monitoring and evaluation. In addition to supporting and educating a patient’s family, critical care nurses also coordinate multiple team members and the delivery of care (eg, coordination of plasmapheresis or continuous venovenous hemodialysis). Multimodal therapy requires constant reassessment and intervention.

Inherent to high-functioning teams are the communication of critical information and the responsiveness to changes in the patient's condition. Critical care nurses play a crucial role in coordinating the delivery of care and ensuring that all team members are well-informed and prepared to respond to any emergent situations.
to interventions. The critical care nurses in this case study promoted and maintained good communication by evaluating all aspects of the therapies delivered and ensured that the therapies were having the intended effect in the patient. The nurses also explained the use of plasmapheresis, HIE, and PASG and provided support to the patient’s family. The nurses’ communication occurred during a particularly uncertain time for survival throughout recovery.

Conclusions

As with overdoses of other calcium channel blockers, amlodipine overdose can induce profound hypotension and shock. This type of shock is a unique challenge because the inciting agent may make standard vasopressor medications ineffective. Specifically, in our case, hypotension did not respond to high-dose vasopressor agents. Moreover, although previously reported as beneficial, both HIE therapy and administration of large doses of intravenous calcium chloride were ineffective in reversing our patient’s signs and symptoms.

In contrast, removal of amlodipine via plasmapheresis and mechanical compression with a PASG were beneficial in our patient. In addition, a single cycle of plasmapheresis reduced circulating drug levels by 51%. Although not attempted in this case, multiple cycles of plasmapheresis might also have been beneficial. In addition, application of the PASG caused an instantaneous, marked increase in blood pressures. Although plasmapheresis and use of a PASG do have side effects, the adverse impact of this therapy was far outweighed by the immediate improvement in organ perfusion obtained in this patient. Caring for patients with life-threatening ingestion requires medication knowledge, anticipation of the patients’ needs, and flexible and creative thinking when a patient is not responding to conventional therapies. In our case, the dedication to detail by the critical care nurses promoted the best possible outcomes with conventional and unconventional therapy.

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None reported.

To learn more about pediatric critical care, read “Complexity Assessment and Monitoring to Ensure Optimal Outcomes Tool for Measuring Pediatric Critical Care Nursing” by Connor et al in the American Journal of Critical Care, July 2015;24:297-308. Available at www.aajcconline.org.

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