Late treatment of calcium channel blocker intoxication with Hyperinsulinemia/Euglycemic Therapy (HIET): a case report

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Introduction

Amlodipine is a dihydropyridine calcium channel blocker (CCB) largely used for the treatment of hypertension and angina, owing to its selectivity for both vascular and myocardium calcium channels. Its pharmacokinetic is characterized by slow absorption, large volume of distribution and a relatively long elimination half-life (30-50 hours).[1] CCB overdose may cause bradycardia, sinus and/or AV block, hypotension, heart failure, cardiogenic shock and arrhythmias. Other toxic effects may be nausea, hyperemesis, hyperglycemia, metabolic lactate acidosis and seizures, all associated with high morbidity and mortality.[2]

Case report

A 20-years old female presented to emergency department (ED) with a history of 24-hours hypotension, bradycardia and sluggish bowel sounds. She denied drug abuse and pregnancy.

At presentation, the patient had a Glasgow Coma Scale (GCS) of 15, but her clinical conditions rapidly worsened: her mental status deteriorated to a GCS 7 (intubation was performed); a severe lactic acidosis (pH 7,25, lactate 10) and a hypotensive state rapidly appeared (crystalloid resuscitation and norepinephrine started).

Laboratory findings at admission included WBC 31.51 10^3/L, Hb 11.6 g/dl, Platelets 371000, INR 1.13, aPTT 0.81, Urea 82 U/L, Glucose 410 mg/dl, Creatinine 4.03 mg/dl. Urine and serum toxicology screen, including benzodiazepine, recreational drugs was negative.

Electrocardiogram showed sinus rhythm (77 beats per minute), first degree atrioventricular block, wide QRS (right bundle block), QTc of 450 ms. Trans-thoracic echocardiogram displayed a normal left ventricular function without structural abnormalities.

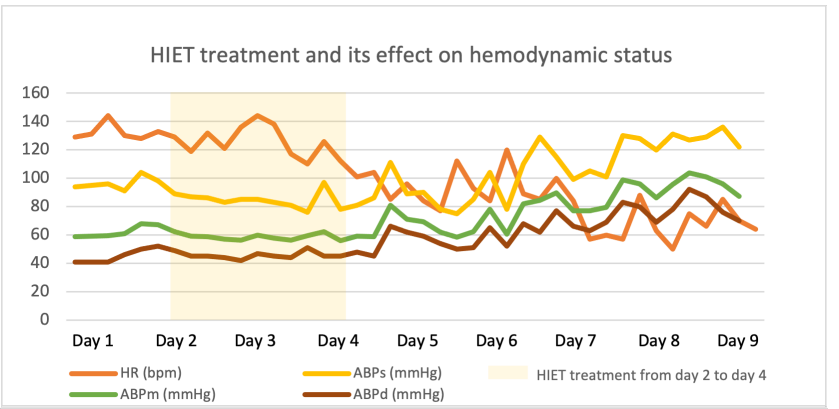
Thus, shock from septic, cardiogenic, hypovolemic and neurogenic sources were excluded by medical history, clinical examination, laboratory and instrumental tests.

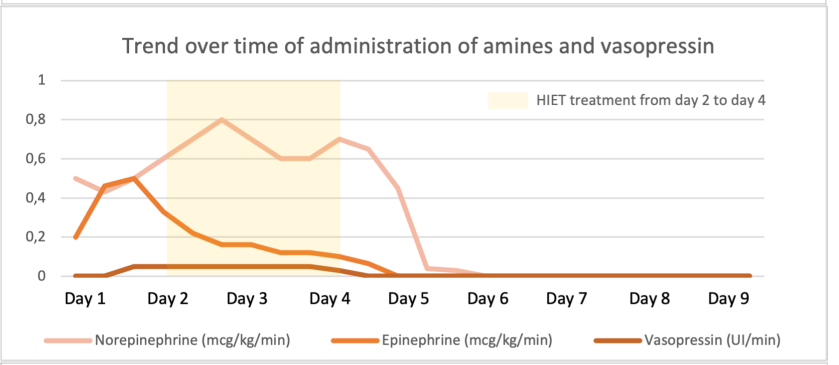
The patient was admitted to the intensive care unit (ICU) where, owing to severe vasoplegic shock with bradycardia, maximal supportive therapy with norepinephrine (0,8 mcg/kg/min), epinephrine (0,5 mcg/kg/min), vasopressin (0,05 UI/min) and hydrocortisone in association with aggressive fluid resuscitation were performed.

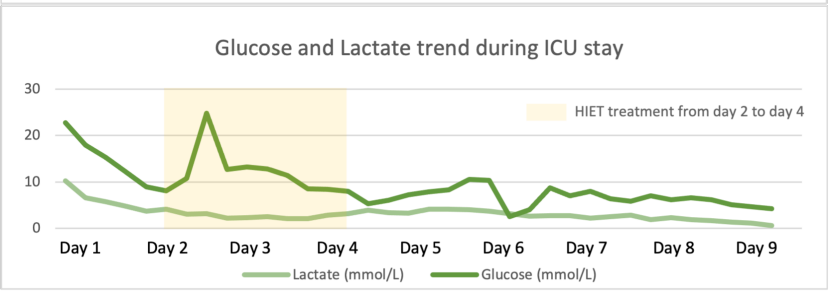
Calcium gluconate (12 mg/hr) and methylprednisolone (100 mg every 8 h) were also administered.

Pleural effusion appearance, probably due to the fluid challenge, required a pleural drainage, and a continuous veno-venous hemodialysis (CVVHDF) started due to severe metabolic acidosis and anuria.

Although the patient denied inappropriate drug intake and the toxicology test in the ED was negative, the anamnestic data of a recent interest in Amlodipine arose the clinical suspicion of vasoplegic shock from drug intoxication.[3] The diagnosis was confirmed the day after by the discovery of Amlodipine serum levels 50 times higher than therapeutic range and of two empty packs of olmesartan/amlodipine in the girl's room.







However, given also the clinical evolution compatible with CCB intoxication, targeted therapy with methylene blue and calcium replacement was already started. As hypotension persistence, high-dose insulin/euglycemic (HIET) therapy started too. Insulin has three mechanism of action: direct inotropic effect on cardiomyocytes, stimulate glucose-uptake in cardiomyocytes and, finally, it is a peripheral vasodilator. While administering insulin, 50% dextrose should be given and strict glucose monitoring is recommended to maintain a glucose blood target of 150-180 mmol/L.[4] Although 48 hours elapsed since medication intake, activated charcoal and bowel irrigation with polyethylene glycol started too. Lipid solution was not introduced, due to an unclear pancreatitis, showed by CT scan.[5,6]

Within three days of maximal targeted therapy, vasoplegic shock resolved and renal function slowly recovered. Patient was transferred to the internal medicine ward on 9th day and discharged from the hospital on 13th day. At one year follow up, the patient is alive and in health.

Conclusion

The diagnosis and treatment of CCB intoxication is often challenging, because amlodipine has prolonged gut absorption, associated with persisting toxic symptoms poorly responsive to standard supportive therapy, so patients may appear well at presentation, but their clinical conditions may deteriorate rapidly and disastrously. Severely symptomatic patients should be managed through a multiple approach, including stabilization of the airway, gut decontamination procedures, additional i.v. boluses of isotonic crystalloids, i.v. vasopressors, i.v. calcium salts, i.v. glucagon, i.v. high-dose insulin and glucose (HIET).

In our case, the treatment of CCB intoxication was also challenging due to late ED presentation, drug assumption denial and the absence of CCB dosage in ED toxicological test. Nevertheless, HIET played a key role in improving hemodynamic conditions.

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