Profound refractory hypotension following mixed amlodipine, lisinopril and terazosin overdose

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1. INTRODUCTION

This report reflects upon the management of a complex mixed antihypertensive overdose; focusing on calcium channel blocker toxicity due to the prolonged half life of Amlodipine, delivering high dose therapy and adverse interaction between treatments.

Fatalities have been reported following ingestion of 70mg and 140mg of Amlodipine[1 & 2].

2. CASE DESCRIPTION

A 53-year-old male with hypertension and depression presented to the ED following an intentional mixed antihypertensive overdose (280mg Amlodipine, 700mg Lisinopril, 70mg Terazosin) with alcohol.

Initial assessment revealed; a shocked patient, tachycardia and hypotensive. Lactate on arrival 7.4mmol/L. ECG revealed sinus tachycardia.

Fluid resuscitation and peripheral phenylephrine did not elevate his blood pressure or improve his lactic acidaemia, thus noradrenaline was started. Rapidly hydrocortisone, calcium chloride and vasopressin were instigated. Continuous veno-veno haemofiltration was started as his metabolic acidaemia deteriorated and to help clear Lisinopril from his circulation.

3. 'OVERDOSE TO TREAT OVERDOSE'

Amlodipine prevents calcium influx within pancreatic beta cells, preventing insulin release[3]. This results in the patient developing hyperglycaemia (20.9mmol/L). Blockade also results in altered glucose uptake by myocardium and vasculature, producing relative insulin resistance[4].

In the context of poor tissue perfusion, represented by a progressive lactic acidaemia we commenced a treatment recommended by ToxBase of Hyperinsulinaemia and Euglycaemia (HIEG). The exact mechanism is not fully understood; however providing substrate for cellular metabolism with high dose insulin may explain the observed improved inotropy and peripheral vascular resistance.

We commenced an infusion of insulin, initially with a bolus of 80units (1unit/kg) then at 80units/hr (1unit/kg/hr) increased up to 800units/hr over the following 6 hours. We found our patient required no additional glucose for 9 hours during the hyperinsulinaemia therapy. Serum potassium concentration did fall, requiring replacement of KCL up to 60mmol/hr aiming for greater than 3.0mmol/L.

Six hours following admission, profound hypotension continued, despite escalating vasopressors. Point of care echocardiogram showed hyper dynamic left ventricular function, ejecting into low systemic resistance. We therefore continued to increase the dosage of vasoconstrictors and did not use inotropes, intra-aortic balloon pump or extracorporeal membrane oxygenation. At the peak rate of infusion we were delivering Noradrenaline at 140mg/hr (29.2microg/kg/min). In the context of sepsis doses over 3.8microg/kg/min have exclusively been associated with death[5]. In our patient however there was evidence of improvement in mean arterial pressure, once these high doses were administered, and no evidence of excessive vasoconstriction.

4. THERAPY INTERACTION

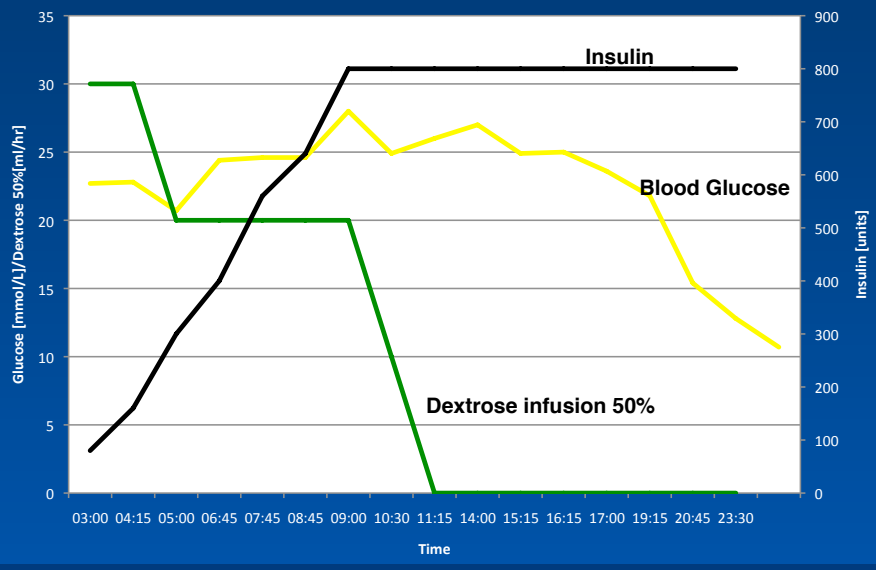
Lipid emulsions have been used in lipophillic medication intoxications, such as amlodipine overdose, and is recommended by Toxbase where cardiovascular collapse exists[4]. We administered a total of 1100ml by bolus followed by infusion. There was no clear improvement in our patients' haemodynamic stability as a result of this intervention.

The haemofilter rapidly filled with lipaemic blood and clotted requiring renewal. A period without haemofiltration resulted in deterioration in our patients acidaemia. Shortened lifespan of the circuit has been described previously in patients with grossly lipaemic serum [6 & 7].

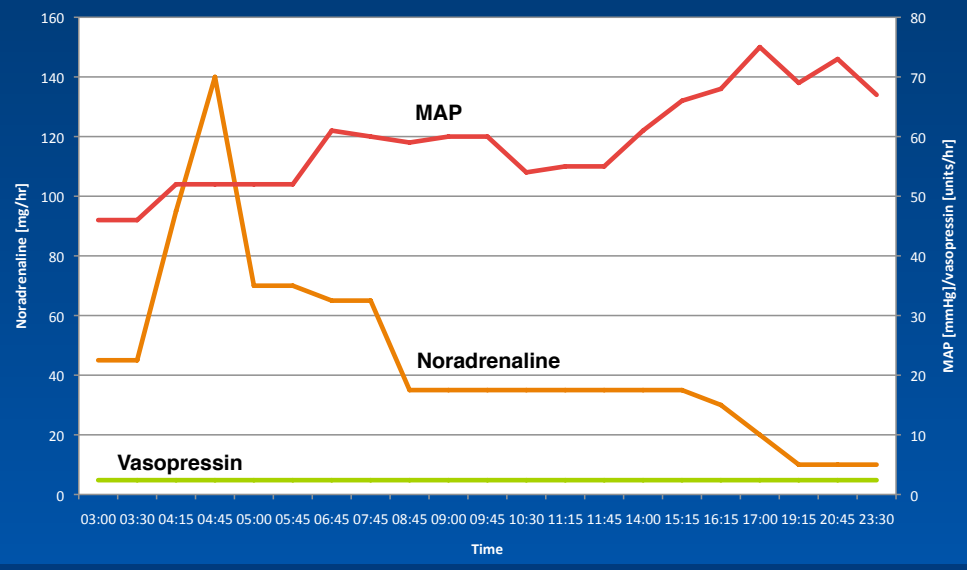
Protracted hypotension posed an increased risk to neurological prognosis, thus we initiated Glucagon therapy, recognising the positive inotropic and chronotropic effects. A 10mg loading dose followed by an infusion 4mg/hr did not clearly offer any haemodynamic benefit. We did encounter a common side effect, of high dose glucagon, of vomiting after 30 minutes of the infusion.

Prior to this we had avoided intubation, judging the risks of exacerbating hypotension too great at both induction and during sedation. Aspiration risk altered this balance and we performed induction with Ketamine and Rocuronium supporting haemodynamics with 1mg Adrenaline and sedation was maintained with midazolam.

Hyperinsulinaemia & Euglycaemia Therapy - Day 1



Vasopressor and MAP during Day 1



5. OUTCOME

We gained haemodynamic stability 7 hours after admission to critical care. The haemofiltration improved his acidaemia and dosage of vasopressors and inotropes reached a plateau. Day two saw his inotropic requirments fall and by day three the high dose insulin infusion was stopped. Renal function recovered and the haemofilter was withdrawn on day 6. A tracheostomy was inserted later the same day to reduce sedation and enable respiratory weaning. He required no further haemodynamic support by day 7. Our patient was discharged to a medical ward 12 days following admission with no neurological or renal impairment.

The patient has provided written consent for the presentation of his case.

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