Case Report

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Amlodipine-Atenolol Poisioning In ER

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Abstract

We report a case of a young female who ingested large dose of combinations of amlodipine and atenolol. She has taken 90 tabs of Amlodipin-Atenalol combination. she was treated succsesfully. This case highlights how the early and aggressive management in emergency department and intensive care management can result in a favourable clinical outcome.

Keywords: Amlodipine overdose; Atenolol overdose; beta blocker overdose; CCB overdose; combination drug overdose.

Introduction

Beta blockers and CCBs represent the most important classes of cardiovascular drugs. Intentional ingestion of these agents are accociated with high mortality rate. Co-ingestionof Beta blocker and CCB are lethal owing to the similar changes they produce in physiology. We present a patient who intentially consumed 90 tablets of Beta blocker and CCB combination. A total of 450mg of Amlodipin and 4500mg of Atenalol.

Case Report

A 33 Yrs old female patient working as an ECG technician in a govt hospital brought to our ED with a complain of recurrent vomiting , pain Abdomen and decrease urination following ingestion of 90 tabs of combination of amlodipine and atenolol each tablet containing amlodipine 5mg and atenolol 50mg.

She was brought to our ED 24hrs after ingestion, initially she was taken to the govt hospital where gastric lavage has been done approximately 5-6 hrs after ingestion and IV Fluids has been given. At the time of presentation she was conscious but confused her GCS was E4V4M6.BP-70/40mmhg, HR-74/min,RR-24/min, RBS-115mg/dl, axillary body Temp-98.4F, SPO_2-100%@6lit/min with face mask.B /L pupils were 3mm, reactive to light.

On Primary Survey Airway was patent.Lungs were clear to auscultation.there were no heart murmurs or gallop rhythm.Abdominal examination revealed mild epigastric tenderness.Exposure of the patient doesn't showed any signs of physical injury or mark in the body.

Secondary survey and detailed examinations of head to toe were unremarkable.

Her initial ABG showed PH-7.376,PCO_2-29.6mmhg, PO_2-60mmhg, HCO_3-17.4mmol/l, Lactate-2.5mmol/l, Ionised Calcium-0.92mmol/l, Na-128mmol/l, k-3.4mmol/l [Figure 1].

ECG showed Sinus Rhythm with no ST-T changes [Figure 2].

2D echo screening done s/o NO RWMA with EF-62% Initially she was given 1 lit NS IV bolus then by checking the volume status of patient by doing ultrasound of IVC measuring 1cm another 1 litre of NS given. Then she was started in dopamine & nor adrenaline infusion after giving ultrasound guided Right internal jugular central line.

Then patient has given 20ml of 10% calcium gluconate IV over 10mins followed by 20ml/hr to maintain the normal ionised calcium level.

Patient then shifted to MICU with insulin infusion (@0.5unit/kg/hr) along with potassium and dextrose infusion. In the first 5 hrs of admission patient had

decreased urination (15ml/hr) but then her urination improved.Patient started to showing improvement by day 04 and she was completely recovered and was discharged in a good health by day 10 after psychiatry consultation.

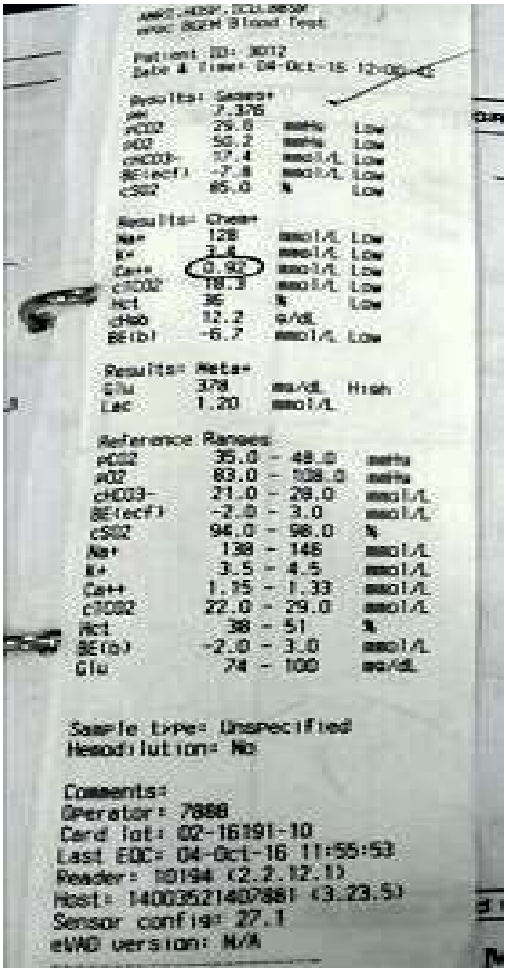

Fig. 1: ABG

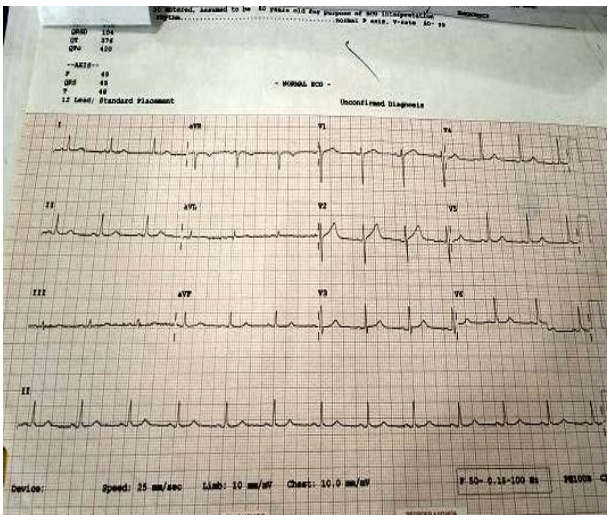

Fig. 2: Normal sinus rhythm

Discussion

Overdoses with cardiovascular drugs are associated with significant morbidity and mortality [6]. Beta adrenergic blockers and calcium channels blockers represent two of the most important classes of cardiovascular drugs.

Beta blockers selectively antagonise B-adrenergic receptors that are linked to G proteins. In an overdose situation, receptor selectivity is lost and effects not normally seen at therapeutic doses can occur. Highly lipophilic agents such as propanolol, carvedilol crosses the blood brain barrier and can result in CNS effects.Atenolol has a low lipid solubility[5]. Beta-blocker toxicity can produce clinical manifestations including bradycardia, hypotension, arrhythmias, hypothermia, hypoglycemia, and seizures. The presentation may range from asymptomatic to shock[3][6].

All existing CCBs function by binding to the L-subtype, voltage-sensitive, slow calcium channels in cell membranes.

Amlodipine is a dihydropyridine group of calcium channel blockers (CCBs) having a half life of 30-50 hours and a large volume of distribution (21 L/Kg), act predominantly on peripheral vasculature[1]. This peripheral action reduces afterload and systemic blood pressure. Because dihydropyridine-type CCBs only act peripherally, the vasodilation they cause may induce a compensatory increase in the heart rate. Within the pancreas, calcium channel antagonism results in decreased insulin secretion. Effects on pancreatic tissue and insulin secretion are less well studied but all three subclasses of CCBs appear to have this effect [4,7].

In overdose, β-blockers and CCBs often have similar presentation and there is much overlap in treatment. Cardiotoxicity characterized by hypotension and bradycardia is the common clinical feature, but other effects may help differentiate the exposure. It is important to understand the different features of such poisonings by class and specific agents.

The patient had hypotension that were initially treated with IV Fluids and inotropic agents (dopamine and noradrenaline). In view of persistent hypotension, intravenous insulin along with dextrose and potassium was also administered.insulin increases plasma levels of ionised calcium,improves hyperglycaemic acidotic state and myocardial utilization of carbohydrates and also exerts on inotropic action. Hyperinsulinemic euglycemia therapy should be considered for patients with

calcium channel blocker overdose who are refractory to supportive therapy [2,8,9,12].

Currently all available information on Hyperinsulinemic euglycemia therapy is limited to case reports and series. Probably it should be considered for patients CCB overdose who do not respond to initial supportive therapy. Intravenous calcium supplementation in the forms of calcium gluconate and calcium chloride are also proved to be beneficial as augmenting extracellular calcium overcomes competitive antagonism [10].

Intravenous glucagon as an inotropic agent has been the treatment of choice for massive beta-blocker overdose[11]. However, there is no human studies evaluating the efficacy of glucagon in BB or CCB overdose, multiple case reports has been done reporting clinical improvement following glucagon administration [13].

High-dose glucagon is recommended for Cardiotoxicity produced by β-blocker poisoning. An initial bolus dose of 50–150 μg/kg should be administered i.v. over one to two minutes [12]. This initial dose will have a transient effect that should occur within approximately five minutes. If a benefit is seen, the initial dose should be followed by a continuous i.v. infusion at a rate of 2–5 mg/hr (maximum: 10 mg/hr) diluted in 5% dextrose injection. The infusion rate can then be tapered downward as the patient improves. We have given the 5mg of glucagon to the patient but there was no increase of heart rate and therefore we have not started the infusion of glucagon in fear of the side effects of glucagon like nausea and vomiting which was already there in patient.

There is no definitive evidence that gastrointestinal decontamination either in the form of activated charcoal or the whole bowel irrigation alters the clinical outcome in the CCB & BB overdose. However, GI decontamination is still advocated because of the potential lethal nature of this overdose and lack of specific efficacious antidote. However if its done the patient's airway should be protected and should be done within 1 hour of ingestion of toxic substance/ drugs [14,15].

In our case gastric lavage was done in another hospital 5-6 hrs after ingestion which is questionable. Many other treatment modalities have been described in the literature.Tranvenous pacing may be required in patients with severe symptomatic bradycardia not responding to atropine, dopamine, epinephrine infusion [16].

Surprisingly In our case patient doesn't developed any bradycardia or arrhythmia during the course of stay in hospital.

Hemodialysis is also useful in severe cases of atenolol overdoses because atenolol is less than 5% protein bound and 40-50% is excreted unchanged in urine. Nadolol, sotalol, and atenolol, which have low lipid solubility and low protein binding, reportedly are removed by hemodialysis. Although CCBs are highly protein bound, some physicians believe that hemodialysis may be used as a last resort in severely toxic patients who have no other hope.

In our case patient had oliguria on day 01 which was improved gradually by day 02 by adequate fluid resuscitation and inotropic support.

Extracorporeal membrane oxygenation (ECMO) has also been attempted in patients who have hypotension refractory to all pharmacologic therapies. One case reported by Durward described a massive diltiazem ingestion (12 g Cardura CD) that resulted in prolonged cardiac standstill. However, after 48 hours of ECMO and 15 days in the critical care unit, the patient made a very good recovery and was discharged home "fit and well," showing "no evidence of neurologic dysfunction [17,18].

Conclusion

Overdose of Beta blockers or CCBs or combination of both may present with vague symptoms but usually presented with hypotension and bradyarrhythmia which may be refractory to standard resuscitation measures and prompt treatment should be initiated without delay. High-dose insulin euglycemia is commonly recommended as a first-line treatment in these poisonings, to improve myocardial contractility, and should be instituted early when myocardial dysfunction is suspected. Optimizing serum calcium concentration can confer some benefit to improving myocardial function and vascular tone after CCB poisoning.

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