CASE REPORT

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A case of massive atenolol overdose successfully managed with intravenous calcium chloride

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ABSTRACT

Atenolol has been widely used owing to its unique beta-adrenoceptor selectivity and favourable safety profile although overdose cases have been reported associated with its use. We report a 50-year-old man with hypertension who allegedly ingested 1 g of immediate-release atenolol. He presented with hypotension and other clinical manifestations of decreased tissue perfusion such as metabolic acidosis and oliguria in the absence of bradycardia. The patient was given activated charcoal and his hypotension was managed with continuous fluid resuscitation, intravenous inotropes and vasopressors. Despite these, he remained hypotensive until the administration of calcium chloride then which subsequent improvements in hemodynamic and metabolic parameters were observed. The patient recovered without any complications. In conclusion, calcium chloride can be used as an adjunct treatment of beta blocker overdose unresponsive to conventional treatments.

Key Words: Atenolol, beta blocker overdose, calcium chloride, hypotension

Introduction

Atenolol, a β_1-selective adrenoceptor blocker is frequently prescribed for treatment of cardiovascular diseases due to its high selectivity towards β_1-adrenoceptors and favourable safety profile (1). This unique receptor blocking property, however, was lost in overdose resulting in non-selective blockade of β_2- and β_3-adrenoceptors which giving rise to bronchospasm and reduction in inotropy respectively, in addition to the more commonly seen manifestations like hypotension and bradycardia (2). The clinical presentations and management of atenolol overdose reported in the literature vary greatly (3-7). Successful outcomes associated with the use of intravenous calcium salts are even rarely documented (6,7). We describe a case of atenolol overdose presented with hypotension and concomitant metabolic acidosis which was successfully treated with intravenous calcium chloride.

Case report

A 50-year-old, 70-kg Chinese male with hypertension, type 2 diabetes mellitus and anxiety was allegedly ingested 20 tablets of 50-mg immediate-release atenolol (total dose 1 g) along with 6 tablets of 10 mg clobazam. He complains of dizziness, lethargy, palpitations and several episodes of diarrhea after the alleged ingestion. The patient denied taking the medications with alcohol. He was initially resuscitated with intravenous (IV) fluids, 2.0 mg of adrenaline and 1.0 mg of atropine at a private hospital where he developed an episode of syncope prior to the transfer to the government tertiary hospital. On arrival to the emergency department of the government hospital, he was conscious with a blood pressure (BP) of 75/43 mmHg, oxygen saturation of 95% on nasal cannula and was managed with IV infusions of dopamine and noradrenaline along with activated charcoal for decontamination. However, the patient became desaturated later and was admitted to the intensive care unit (ICU) for intubation.

Upon arrival to the ICU, the patient was hemodynamically unstable with a BP of 82/49 mmHg supported by IV infusions of dopamine and noradrenaline. There were no signs of bradycardia (pulse rate of 82 beats per minute) and electrocardiogram abnormalities. Decreased tissue perfusion was evidenced by patient's reduced rate of urine output (<0.5 ml/kg/hour). Arterial blood gas (ABG) showed metabolic acidosis with concomitant lactic acidosis (pH 7.19,

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$PaCO_2$ 31 mmHg, PaO_2 54 mmHg, bicarbonate 11.8 mmol/L and lactate 11 mmol/L). Serum electrolyte analysis showed a persisting elevated potassium level of 5.9 mmol/L despite treatment with IV calcium gluconate, regular insulin and dextrose.

Continuous venovenous hemofiltration (CVVH) was commenced along with IV sodium bicarbonate infusion in view of the patient's unresolved metabolic acidosis and hyperkalemia with ongoing IV fluid resuscitation. IV adrenaline (0.04 mcg/kg/min) and vasopressin (0.04 units per minute) were started due to the patient's persistently low BP (ranged from 69/40 to 93/56 mmHg) despite high dose IV dopamine (38 mcg/kg/min) and noradrenaline (0.76 mcg/kg/min). IV insulin infusion and IV N-acetylcysteine were prescribed for control of plasma glucose level and non-acetaminophen-induced acute liver failure respectively.

There were no improvements in BP (90/50 mmHg) and ABG parameters (pH 7.21, bicarbonate 14.4 mmol/L and lactate 10 mmol/L) on the second day of hospital stay despite the above interventions and hypokalemia developed which was corrected with oral potassium chloride 1 g three times daily. These led to the initiation of an IV loading dose of 3.0 g of calcium chloride (followed by a daily maintenance dose of 1.5 g) then which the systolic BP subsequently rose to 101 mmHg and was maintained in the range of 101 to 160 mmHg. IV vasopressin and adrenaline were tapered off later on the same day.

On day 3 of admission, the patient's BP was stabilized (ranged from 112/50 to 161/61 mmHg) and IV dopamine was weaned off successfully. Both metabolic and lactic acidosis were resolved (pH 7.44, bicarbonate 25.1 mmol/L and lactate 1.5 mmol/L) and there was also sign of good tissue perfusion as seen from the patient's urine output rate (more than 1.0 ml/kg/hour). He was extubated on Day 4 and his BP was supported solely by IV noradrenaline. IV calcium chloride was discontinued on Day 5 with the patient's BP within the range of 125/63 to 134/71 mmHg. The patient was subsequently transferred to the general ward and he was discharged on Day 7.

Discussion

An overdose of beta blockers has been shown to block all currently identified beta-adrenoceptors by disabling the coupled G protein complex. This subsequently inhibits the production of cyclic adenosine monophosphate resulting in a reduction in the amount of cytosolic calcium available for muscular contraction (2). These blockades were thought to give rise to a constellation of signs such as hypotension and bradycardia, atrioventricular block and diminished cardiac output, occasional hypoglycemia and bronchospasm (8) from which bradycardia and first degree atrioventricular block appeared to be the early warning signs for the eventual development of symptoms necessitating medical therapy (9). The onset of symptoms was reported to be mostly within four hours post ingestion with immediate-release beta blockers (9). However, the present case illustrated solely the presence of hypotension and its sequelae, that is, metabolic acidosis and oliguria resulting from tissue hypoperfusion in the absence of other signs of cardiovascular compromise.

Beta blocker overdose generally required administration of multiple simultaneous pharmacological interventions to achieve therapeutic goals and the treatment modality usually depends on patient's clinical presentation(s) and the type of beta blocker ingested (10). Functional decontamination with gastric lavage and activated charcoal are recommended only when the presentation took place within an hour of ingestion or in life-threatening situations. IV fluid resuscitation is indicated for most toxicity cases while atropine can be used for symptomatic bradycardia. Vasopressors and inotropes have been employed for hemodynamic support purposes but their efficacies were inconsistent and the use of these agents necessitates large dosages in many cases (11). Phosphodiesterase inhibitors alone can exacerbate pre-existing hypotension due to peripheral vasodilation and therefore limiting their usage (12). Glucagon has been used successfully as an antidote to circumvent beta blockers toxicity (10-12) but there were also reported failures associated with its use primarily in cases of atenolol overdose (5-7) where calcium salts were shown to be more effective in restoration and stabilization of BP (6,7).

Calcium salts improve BP albeit in a short-lived manner (7) via positive inotropic effects (13). O'Grady and colleagues (7) reported a dramatic improvement in systolic BP (from 50 – 60 to 100 – 120 mmHg) in an atenolol overdose hypotensive patient after administration of 1 g of IV calcium chloride with a recurring episode of hypotension 30 minutes later which was corrected with another dose of calcium chloride (7). Similarly, we observed improvement and subsequent

stabilization in BP for our patient when calcium chloride was given but with no episodes of hypotension thereafter. There were no reported complications related with the use of calcium chloride in previous case reports (6,7) and in the present case as well. Other promising approaches to target beta blocker toxicity not responding to conventional resuscitation measures include high dose insulin with supplemental dextrose and potassium (14), intravenous lipid emulsion for elimination of lipophilic beta blockers (15), hemodialysis for clearance of beta blockers which are minimally protein bound and renally excreted (16).

In conclusion; calcium salts may be considered as an adjunct treatment for atenolol overdose unresponsive to conventional therapeutic measures as intravenous fluids, vasopressors and inotropes.

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