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Calcium Channel Blocker Toxicity in Post Renal Transplant Patient

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Abstract: Calcium Channel blocker (CCB) poisoning is on rise due to increased use for the number of cardiovascular diseases. CCB poisoning either accidental or intentional can be lethal. Standard approaches for the management of CCB overdose like stomach wash, IV fluids, resuscitation, administration of calcium gluconate, atropine, Hyper insulinimeia–Euglycemia (HIE) therapy are given. We report a case of CCB toxicity who improved after administration of HIE therapy.
Keywords: Hyper insulinimeia-Euglycemia, Calcium Channel Blockers, Poisoning.

INTRODUCTION

Calcium channel blockers protect transplant patients from cyclosporine-induced daily renal hypo perfusion. Renal toxicity, possibly due to vasoconstriction and vascular injury, is the most relevant side-effect of cyclosporine therapy given to prevent graft rejection. Daily renal hypo perfusion induced by cyclosporine in renal transplant patients is completely prevented by the administration of the calcium channel blocker, which did not impair the endothelin synthetic pathway [1, 2].

CASE REPORT:

A 31 year old patient consumed 60 tablets noncardiac retard 20mg under the influence of alcohol with suicidal tendency, was brought to emergency department within four hours, and with complains of giddiness and vomiting with systolic blood pressure of 80mmHg. He had undergone renal transplant six months back, Basic disease was chronic glomerunephirtis, mother was donor with 3 antigen matches, serum creatinine on discharge was 1.2 mg/dl with immunosuppressant drugs sine transplant. Immunosuppression was Prednisolone 30mg once day, Tacrolimus 2mg twice a day and Mycofenolate Mofetil 500mg twice day. On examination patient was drowsy under the alcohol influence with systolic blood pressure of 70mmHg and unrecordable dia-sytolic blood pressure with pulse 60/m. Systemic examination was normal. He was given stomach wash, inotropic support with norepinephrine and dopamine was started, IV calcium gluconate with 30ml stat and 10ml/hr infusion followed by IV Human act rapid insulin 30 units stat, with infusion pump with 30units/hr, blood glucose levels were maintained upto 200mg/dl with glucose infusion. Patient received charcoal hemoperfusion. After initiation of HIE therapy and calcium gluconate within 5-6 hours blood pressure increased to 100/60mmHg and requirement of inotropic support started to reduce which was later weaned off within 24 hours. Patient received 720 units of total Human act rapid insulin and 328 gms of calcium gluconate. He recovered completely and was discharged on the 6th day of admission.

Table-1:Basic Investigations on Admission

HB	10.41gm/dl
Total Leucocyte Count	5400/µl
Random Sugar level	134mg/dl
Serum Sodium	135meq/l
Serum Potassium	2.22mmol/L
Blood Urea	49.40mg/dl
Serum Creatinine	1.31mg/dl
Blood pH	7.316
PCo2	105mmHg
Po2	105mmhg
HCO3	12.4mmol/l

Table-2:Treatment Chart

	1st hour	3rd hour	5rd hour	9th hour	11th hour
Insulin Dose	30ml/hr	30ml/hr	30ml/hr	30ml/hr	30ml/hr
Serum Glucose(mg/dl)	174	256	216	180	161
Serum Sodium (mmol/l)	134	135.9	136	133	137
Serum Potassium (mmol/l)	3.36	2.38	3.2	3.4	3.7
Serum Calcium (mg/dl)	10.51	11.88	15	12	11
Ionic Calcium (mmol/l)	1.76	1.46	1.8	1.4	1.2

DISCUSSION:

CCB were first introduced in 1962 in Germany, which were later on used or frequently prescribed class of medication mainly in cardiovascular diseases [3].

Pharmacology of CCB

CCB are currently divided into mainly dihydropyridine and non di hydro pyridine. Dihydropyridine are mainly Nifedipine, Amlodipine, Nicardipine which mainly acts on the L-type calcium channels in smooth muscle resulting in smooth relaxation and vasodilatation. CCB have effect on pancreas via L-types calcium channels resulting into insulin resistance causing hyperglycemia [4].

Clinical features of Toxicity

Patient with CCB toxicity usually present dizziness, syncope palpitations, flushing, weakness, confusion, nausea vomiting hypotension and bradycardia due blockade of L-type calcium channels in myocardial cells, smooth-muscle cells, and beta cells. Hypotension is usually due to vasodilatation and reduced cardiac output. Due to myocardial depression and depressed contractility patient may result pulmonary edema or with acute kidney injury due to acute tubular necrosis due vasoconstriction. Patient may have impaired mental status due to hyperglycemia [5, 6].

Management of CCB Toxicity

Management of CCB toxicity was done as per standard guidelines. For the restoring cardiac functioning and systemic hypotension supportive care was initiated, stomach wash was done Initial therapy consists of securing the airway for those who have altered mental status. In hypotensive patient intravenous fluid bolus of 1-2 litres can be given, inotrops can be initiated if hypotension persists [7, 8].

Intravenous calcium is used as an agent for CCB toxicity to overcome the antagonism [8]. Calcium can be given either in the form of calcium gluconate or calcium chloride. Calcium gluconate is preferred more over calcium chloride due to irritative effect on veins. Calcium gluconate can be started with bolus dose of 0.6ml/kg followed by infusion of 0.2ml/kg/hr titrated according the hemodynamic status of patient [9, 10].

Sodium bicarbonate is another potentially useful drug used in the CCB toxicity. Treatment of academic environment may improve the hemodynamic status of the patient. Sodium bicarbonate can also be used in the higher doses of CCB toxicity with QRS prolongation of more than 120 milliseconds [11, 12].

Glucagon is also another drug which is usually recommended in CCB toxicity. Glucagon acts via adenyl cyclase through G proteins with increase in cyclic AMP causing muscle contraction which stimulate positive inotropic effect causing improvement in hemodynamic status of the patient [13, 14]. The initial dose of 50-150 microgram/kg bolus repeated in three-five minutes followed by infusion with the dose of 10microgram/kg/hour. Significant side effect of glucagon is vomiting.

Inspite of above supportive care patient may detoriate. However in recent times Hyperinsulinemia–Euglycemia (HIE) therapy has gained the wider acceptance. CCB toxicity results in hyperglycemia from decreased insulin production due to blockage of L-type calcium channels in pancreas. With hypo insulinemia and acquired insulin resistance myocardial cells are unable to use glucose as energy source leading to decreased myocardial contractility and hypotension. HIE therapy leads to reversal of cardiovascular collapse in CCB toxicity by improving myocardial utilization of carbohydrate as well as removing lactic acid [15.16]. Charcoal hemoperfusion –It is one of the preferred method to enhance the elimination of toxin in poisoned patients [15].

CONCLUSION:

As CCB toxicity accidental or intentional is on rise which can be fatal. HIE therapy have shown to be beneficial in majority of studies were more research is warranted .HIE therapy should be initiated early in course of treatment. Close monitoring of serum electrolytes and serum glucose is advisable [14, 15, 16].

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