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MULTIFACETED APPROACH TO MANAGEMENT OF LIFE-THREATENING CALCIUM CHANNEL BLOCKERS OVERCONSUMPTION: A CASE REPORT AND REVIEW

Internal Medicine

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ABSTRACT

Amlodipine is commonly prescribed Calcium channel blockers in routine practice. Calcium channel blockers acts by blocking L-type voltage gated calcium channels present in blood vessels and heart. Calcium channels blockade in blood vessels results in vasodilatation -that leads to fall in blood pressure. Calcium channels blockade in heart results in decreased activity of heart (decreased heart rate, AV conduction, contractility). Over consumption of Calcium channels blockers can lead to profound hypotension and shock. Management involves early aggressive management of shock and calcium supplement. We report one such presented with Calcium channel blockers over consumption in shock managed successfully.

KEYWORDS

Amlodipine, Calcium channel blockers,

CASE REPORT

A 38 yr. old Female, staff nurse by profession bought to hospital with h/o consumption of 25 tablets of T amlodipine 5 mg (~ 125 mg amlodipine. Pt reported to local hospital, where gastric lavage given Treated with IV fluids and referred to our hospital in view of non-recordable BP. Patient reported to our hospital, with complaints of giddiness and syncope since last 2 hrs. On examination in ICU on DAY 1 of our hospital pt. was drowsy but arousable on light stimuli, she was pale with cold calmly extremities, Pulse - 54/min regular, ECG s/o - junctional rhythm, low voltage complexes. Bp- 40 mm Hg systolic, No murmur or gallop On auscultation air entry decreased bilaterally, Bilateral minimal crepts +, Per Abdomen examination was normal, ECG on admission to ICU - Junctional rhythm (junctional bradycardia), Patient was started with IV fluids and inotropic supports and IV fluids, Pt had no urine output even after 2 hrs., apart from basic resuscitative measure Pt was started Forced alkaline diuresis cycle, her initial hemogram , LFT , RFT reports were normal (with mild anemia Hb - 9.2), Patient was continued with IV fluids of totaling (4 lit in 24 hr.) and inotropic supports of noradrenaline.

Pt has urine output of around 150 ml next day by 8am with these measures' patient pt. hemodynamic status improved but not up to the mark.

On day 2 patient Started complaining of shortness of breath, BP was 86/50 mm of Hg, Spo2- 86 % on room air, patient developed facial puffiness with periorbital swelling, JVP raised, Urine output was 400 ml in 24 hrs., Repeat hemogram s/o creatinine levels raised to 1.5, Repeat ECG reveal low voltage complexes, 2D echo study reveal normal LV systolic function, HRCT - bilateral mild pleural effusion, clinical and radiological features suggestive of pulmonary edema. Patient was treated with diuretics and O2.

Apart from this patient was started with IV Calcium Gluconate in 100 ml NS TDS f/b BD next day, IVF D25 % + optineuron TDS, cholecalciferol 60000 IU sachet stat, IVF D25 % + 10-unit insulin over 1 hr. BD, ionic calcium of patient was lower, (Ca-1.04)

Table 1.1

	On Admission	12 HRS	24 HRS	36 HRS	48 HRS	60 HRS
PULSE	48 /min	56/min	78/min	112/min	108/min	98/min
BP	40 mm hg systolic	56 mm hg systolic	70 mm Hg	80 mm hg	108/60 mm hg	124/68 mm hg
Electro-cardio-graphic Find-ings	Junc-tional rhythm brady-cardia	Junc-tional rhythm Brady-cardia	Junc-tional rhythm	Sinus Tachy-cardia	Sinus tachy-cardia	Nor-mal
CVP	-	Negative	8-10 cm Of H2O	8-10 cm Of H2O	4-6 cm of H2O	6 cm of H2O
Urine Output	Nil	Nil	100 ml	250ml	400 ml	700 ml
Glucose	122	118	138	189	192	104
Creat-inine	0.8	0.8	1.2	1.5	1.8	0.8
Spo2	Not Record-able	Not Record-able	91% on room air	90% on room air	94% on room air	97% On room air

On DAY 3, patient gradually improved hemodynamically and symptomatically.

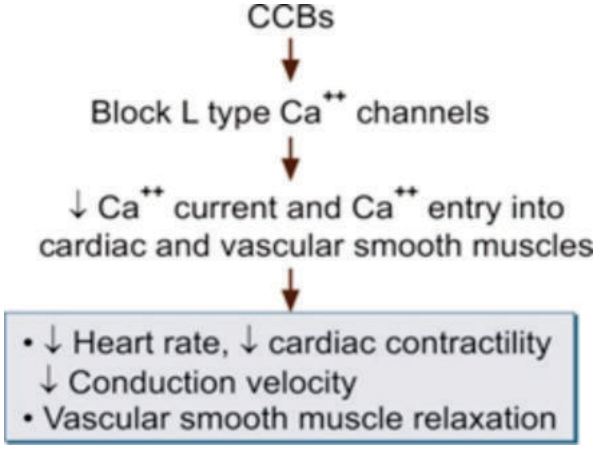
BP improved to 108/60 mm of HG, CVP decreased to normal range (4 cm Hg), ECG- low voltage complexes normal sinus rhythm, Urine output improved to 700 ml in 24 hrs.

Over next 48 hours calcium dose and ionotropic support gradually tapered.

Monitored parameters are: Blood pressure, ECG every 4 hourly for 48 hrs. and 12 hourly later, Serum electrolytes and Ionic calcium levels, Central venous pressure, Urine output

DISCUSSION

Calcium channel blockers. These are the drugs that block L-type of voltage gated calcium channels present in blood vessels and heart. Three groups of CCBs include, phenylalkylamines - verapamil nor-verapamil, benzothiazepines - diltiazem) dihydropyridines - amlodipine, nifedipine, nicardipine, nimodipine, misoldipine, nitrendipine, nicardipine, CCB acts by blocking L type voltage gated calcium channels present in blood vessels and heart Ca channels blockade in blood vessels - vasodilation - fall in BP Ca channels blockade in heart - decreased activity of heart (decreased heart rate, AV conduction, contractility)



Flow Chart 1.1

ECG changes in CCB overdose: Sinus bradycardia 1st degree, 2nd degree and 3rd degree AV block Junctional bradycardia Ventricular bradycardia. A prolonged PR interval is an early sign of, beta-blocker or calcium-channel blocker, toxicity - even in the absence of significant bradycardia.

Amlodipine is a dihydropyridine group of calcium channel blockers (CCBs) half-life of 30-50 hours large volume of distribution (21 L/Kg).

Unlike non-dihydropyridine CCBs like Verapamil and Diltiazem, dihydropyridines as a group have predominant effect on vascular smooth muscle cells with little effect on cardiac pacemaker cells or contractility. But in significant overdose some of this pharmacological selectivity may be lost.

In this case the effect of Amlodipine on vascular smooth muscle was evident. The patient developed profound hypotension requiring prolonged inotropic support with significant effect on cardiac pacemaker or conduction system resulting in bradyarrhythmia on admission and preserved systolic function of the heart case was complicated by transient pulmonary edema which might have resulted from the combined effects of the drug itself, prolonged hypotension and fluid resuscitation during the initial phase of therapy.

Hyperinsulinemia euglycemia has emerged as possible adjuvant therapy for CCB toxicity. Several possible roles of Insulin are described. Insulin increases plasma levels of ionized calcium, improves hyperglycemic acidotic state, improves myocardial utilization of carbohydrates and exerts its own independent inotropic effect.[1] Pulmonary edema in CCB over dose may be due to Pre-capillary vasodilatation resulting in excessive pulmonary capillary transudation was suggested as the possible mechanism of non-cardiogenic pulmonary edema by Humbert et al [2]

HDI (high dose insulin) effectively reverses CS induced by CCBs and BBs due to its inotropic effects, uptake of glucose into cardiac muscle, and peripheral vasodilatation. ILE is theorized to sequester agent's dependent on lipid solubility from the plasma, preventing further toxicity [3]

If the patient is not demonstrating hemodynamic improvement with adrenaline, high-dose insulin euglycemic therapy (HIET) should be initiated while the vasopressor infusion is continued. Delayed HIET has been associated with increased mortality.[4][5]

There are no randomized controlled studies in humans comparing adrenergic agents with HIET, but animal studies and case studies in humans consistently show high-dose insulin euglycemic therapy to be superior to adrenergic agents in terms of hemodynamic effects in severe CCB OD and shock.[6][7]

Hyperinsulinemia-euglycemia therapy [HIE] is a first line therapy recommended in symptomatic calcium channel blocker overdose patients. HIE, particularly if administered in concentrations typically used for glycemic control, would result in a substantial amount of hypotonic fluid administration, which places patients at risk of volume overload. Therefore, it may be beneficial to utilize a concentrated insulin as a strategy to mitigate fluid overload risks .[8][9]

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