

## Amlodipine Toxicity- A Challenge in Present Day Medical Management

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**Abstract :** Calcium Channel Blockers (Ccbs) Are Prescribed In A Wide Variety Of Cardiovascular Conditions. Nevertheless, They Remain A Major Cause Of Cardiovascular Drug Overdose That Often Leads To A Lethal Outcome. We Report The Case Of Intoxication With Amlodipine, Which Caused Severe Hypotension, In A Middle Aged Man. The Patient Was Initially Treated With Gastric Lavage And Fluids. He Was Given Calcium Gluconate, And Inotropic Support. Patient Was Improved On Fourth Day Without Need Of Glucagon And Hyperinsulinemic Euglycemia. Later The Patient Was Discharged From The Hospital After Psychiatric Consultation.

**Keywords:** Amlodipine Overdose, Calcium, Calcium Channel Blocker(Ccb) Poisoning

### I. Introduction

Calcium Channel Blockers Are The Leading Cause Of Cardiovascular Drug Overdose And Are Responsible For 45% Of Deaths Related To Cardiovascular Drug Exposure<sup>1</sup>. Treating Patients With Overdose Of These Medications Can Produce Challenge To Even The Most Experienced Physicians. The Challenge Arises When Patients Severely Intoxicated With Calcium Channel Blockers May Have Profound Refractory Bradycardia And Hypotension<sup>1</sup>. Reports Of Calcium Channel Blocker Overdose Are Rarely Reported In Indian Literature And Cases Which Have Been Reported Suggest Usage Of Glucagon And Hyperinsulinemic Euglycemia At Fatal Or Toxic Dosage Of Amlodipine<sup>5,6</sup>. Here Is A Case Of Middle Aged Hypertensive Male Presenting With Amlodipine Poisoning In A Tertiary Care Centre Of South Gujarat, Managed Conservatively In Our Icu With Intravenous Fluids, Vaso-Pressors, And Calcium Infusion. Patient Was Improved And Glucagon And Management Via Hyperinsulinemic Euglycemia Was Not Needed.

### II. CASE REPORT

A 44-Year-Old Hypertensive Male Presented To Emergency Department Of New Civil Hospital Surat After Six Hours Of Ingestion Of 100 Mg Of Amlodipine (5mg X 20 Tab) Under The Influence Of Alcohol With Suicidal Intention. He Was A Known Case Of Hypertension For 15 Years, On Regular Medications. On Examination He Was Drowsy But Following Simple Verbal Commands With Normal Sinus Rate Of 104/ Min, Blood Pressure Of 90/64 MmHg. Respiratory, Cardiovascular And Neurological Examinations Were Normal. Electrocardiograph Showed Normal Sinus Rhythm. After Emergency Management With Gastric Lavage And BOLUS IV Fluids, Patient Was Shifted To ICU. Initial Hemogram, Random Blood Sugar, Serum Electrolytes, Arterial Blood Gas And Electrocardiogram Were Unremarkable. Blood Urea And Serum Creatinine Values Were 53 Mg/Dl And 2.3 Mg/Dl Respectively. Echocardiography Revealed Left Ventricular Hypertrophy With Normal LV Systolic And Diastolic Function. The Patient Was Given 30 Ml Of 10 % Calcium Gluconate - Over 5 Mins, Followed By An Infusion Of Calcium Gluconate At A Rate Of 10 Ml/Hr Over The Next Six Hours The Patient Became Hypotensive Not Responding To Volume Resuscitation And Requiring Inotropic Support With Adrenaline And Dopamine Infusion. His Sensorium Gradually Deteriorated And Patient Was Put On 4 L Of Oxygen. Ultrasonography of the Abdomen Showed Normal Kidney Size with Increased Echogenicity. The Next Day the Patient Started Showing Signs of Improvement. His Sensorium Improved But He Remained Oliguric. Over The Next 24 Hours His Condition Stabilised Vially As Well As Neurologically And Inotropic Support, Calcium Infusions Were Tapered Off With Only Supportive Fluids. Lastly Patient Was Discharged With Tablet Enalapril (5 Mg) Once A Day After Psychiatric Counselling.

### III. Discussion

Amlodipine Is A Dihydropyridine Group Of Calcium Channel Blocker (Ccbs) Having A Halflife Of 30-60 Hours And A Large Volume Of Distribution (21 L/Kg)<sup>8</sup>. Unlike Nondihydropyridine Ccbs Like Verapamil And Diltiazem, Dihydropyridines As A Group Have Predominant Effect On Vascular Smooth Muscle Cells With No Effect On Cardiac Pacemaker Cells Or Contractility At Therapeutic Doses<sup>9</sup>. In The Case Described, The Effect Of Amlodipine On Vascular Smooth Muscle Was Evident In The Form Of Profound Hypotension Requiring Prolonged Inotropic Support And Refractory Bradycardia Was Due To Blockade Of ‘ L’type Of Channels And Decreased Preload. There Is No Definitive Evidence That Gastrointestinal

Decontamination Either In The Form Of Activated Charcoal/Normal Saline Or The Whole Bowel Irrigation Altering The Clinical Outcome In The Ccb Overdose. However, Gastrointestinal Decontamination Is Still Advocated Because Of The Potential Lethal Nature Of This Overdose And To Avoid Delayed Toxicity By Calcium Channel Blockers Due To Delayed Absorption. Hyperinsulinemic Euglycemia Has Emerged As One Of The **Treatment** Modalities For Ccb Toxicity At Fatal Overdose<sup>7,10</sup>. But Was Not Initiated Due To Persistent Euglycemic Status Of The Patient According To 6 Hourly Rbs Monitoring And To Avoid Life Threatening Hypoglycemia And Hypokalemia. Some Literatures Consider Calcium Gluconate Or Chloride As Specific Antidote. Kenny<sup>3</sup> Et Al Has Suggested 10 Ml Of 10% Calcium Chloride Or 20-30 Ml Of Calcium Gluconate Iv And Depending On Clinical Response To Be Repeated 15-20 Minutes Up To Four Doses With Monitoring Of Serum Calcium. Continuous Calcium Infusion Of Ca Chloride/Gluconate 0.2 Ml/Kg/Hour Is Another Option<sup>4</sup>. However, Buckley Et Al Recommend Higher Doses To Overcome The Competitive Blockade With Ecg Monitoring Rather Than Serum Calcium Levels. Maximum Dose Used By Him Was 30 Gm Over 12 Hours<sup>4</sup>. Treatment With Glucagon<sup>6</sup> Could Not Be Initiated Due Unavailability Of The Drug.

Many Other Treatment Modalities Have Been Described In The Literature. Transvenous Pacing May Be Required In Patients With Severe Symptomatic Bradycardia Not Responding To Atropine Or Isoprenaline Infusion<sup>4</sup>. Standard Cardiopulmonary Bypass Has Been Used In Some Cases To Allow Sufficient Time For Liver Detoxification<sup>11</sup>. Extracorporeal Membrane Oxygenation Was Described In Massive Diltiazem Overdose For Temporary Hemodynamic Support<sup>12</sup>. Therapeutic Plasma Exchange Was Also Utilized In The Management Of Certain Cases Of Amlodipine Overdose<sup>13</sup>. Hemofiltration And Dialysis May Not Be Of Help In Calcium Channel Blocker Overdose Because Of High Protein Binding, Extensive Tissue Distribution And Rapid Rate Of Metabolism Of This Group Of Drugs<sup>4</sup>.

#### **IV Conclusion**

Though Glucagon Infusion And Hyperinsulinemic Euglycemia Are One Of The Treatment Modalities Recommended For Management Of Fatal Dosage Of Amlodipine, But It Can Also Be Managed Conservatively Only By Early Gastric Decontamination, Resuscitation With Calcium And Cautious Use Of Inotropes And Iv Fluids, Even At The Community Health Center Levels Where Treatment Facilities Likewise Tertiary Center Are Unavailable If Aggressive And Careful Monitoring Of The Patient Has Been Taken Into Consideration.

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