Case Report

A Case of Massive Metoprolol Overdose Successfully Managed

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Introduction:

Overdoses with cardiovascular drugs are associated with significant morbidity and mortality. Beta-adrenergic blockers is one of the most important classes of cardiovascular drugs. Overdoses with Beta- blockers typically result from exploratory ingestions by children or intentional ingestions by suicidal adults.

Case report:

A 28 years old, non-hypertensive, non-diabetic lady got admitted into Dhaka Medial Hospital with the complaints of allegedly ingested 98 tablets of 50-mg metoprolol succinate followed by decrease level of consciousness. In that hospital her blood pressure and pulse are non-recordable, GCS 8/15 and ECG shows 2:1 AV block (Fig.-1). Immediately patient got gastric lavage and shock was treated with normal saline, then transferred to ICHRI for the better management. In ICHRI her oxygen saturation suddenly fell to 65%, ABG was done which revealed PaO2 42mmHg, bicarbonate 11.8 mmol/L and lactate 11 mmol/L, serum electrolyte analysis showed a

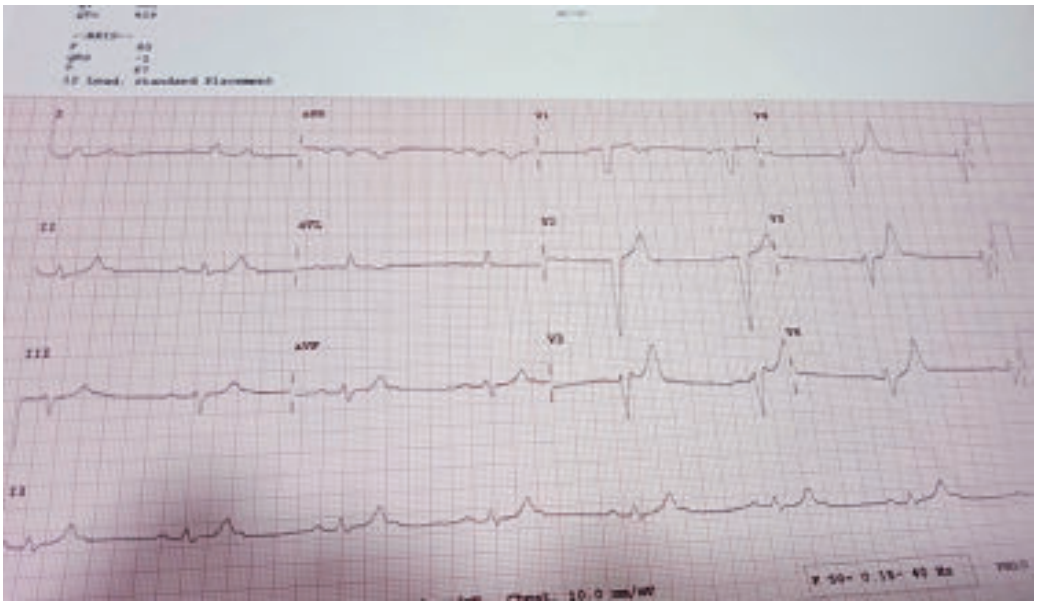

Fig.-1: *12-Lead ECG showing 2:1 AV block.*

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persisting low potassium level of 2.9 mmol/L. She was intubated and put on mechanical ventilator; transferred to Evercare Hospital Dhaka for multidisciplinary care. After admission, she was diagnosed as the case of Metoprolol overdose, 2:1 AV block, hypotension, aspiration pneumonia, AKI with Electrolyte Imbalance. Immediately Infusion Noradrenalin and Normal Saline were started for hypotension. When Inj. Atropine failed to increase the heart rate, Temporary Pace Maker was done. 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 2 ampoule IV loading calcium gluconate followed by a daily maintenance dose which the systolic BP subsequently rose to 110 mmHg. On day 3 of admission, high-dose insulin -euglycemia (HIE) treatment was started @ 1 IU /Kg with 25% DA followed by .5 IU/Kg/hr to augment cardiac contractility. Both metabolic and lactic acidosis were resolved by conservative treatment 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). Inj. Diazepam was administered to prevent seizure. She was extubated on Day 4 and her BP was supported solely by IV noradrenaline. Her junctional bradycardia resolved followed by removal of TPM. IV calcium was discontinued on Day 5 with the patient's BP within the range of 125/63 to 134/71 mmHg. The patient was subsequently discharged on Day 7.

Table-I

Metoprolol pharmacologic profiles

Bioavailability	50%
Protein binding	12%
Metabolism	Liver via CYP2D6, CYP3A4
Elimination half-life	3–7 hours
Excretion	Kidney
Adrenergic Receptor Blocking Activity	β1
Lipid Solubility	Moderate
Intrinsic Sympathomimetic Activity	No
Sodium Channel Blocking	No
Threshold Dose	
• Adult	• 400 mg
• Child	• 5 mg/kg
Lowest Reported Toxic Dose·	
Adult	• 7500 mg
• Child	• N/C

Table-II

Clinical Manifestation of overdose:

- Bradycardia
- Hypotension and shock
- Hypoglycemia
- Hypoglycemia
- Hypothermia
- Seizure
- Altered mental status
- QTc prolongation
- QRS widening

Discussion:

Metoprolol selectively antagonize â 1-adrenergic receptors that are linked to G proteins. Beta-1 receptors primarily regulate myocardial tissue and affect the rate of contraction via impulse conduction. In an overdose situation, receptor selectivity is lost, and effects not normally seen at therapeutic doses can occur. (1) In addition, some â-blockers may antagonize cardiac sodium channels, producing quinidine-like effects that will increase toxicity in overdose. An important determinant of adverse effects with â-blockers is lipid solubility. Highly lipophilic agents can cross the blood–brain barrier which result in unwanted central nervous system (CNS) effects. Table 1 and 2 displays Metoprolol's pharmacologic profiles (2) and clinical manifestation of overdose subsequently (1).

Due to intrinsic lipophilicity, beta blockers may cause CNS depression. Prompt management of airway is, therefore crucial. Gastrointestinal decontamination with gastric lavage may be necessary for patients who present shortly after massive ingestions and/or with serious symptoms. Administer activated charcoal to limit drug absorption to patients with minor symptoms who present later than an hour after ingestion. Benzodiazepines are the first line of treatment for seizures that may occur due to high lipophilicity of certain beta blockers. Administer sodium bicarbonate for QRS widening and magnesium sulfate for QTc prolongation. Although there have been no controlled trials, glucagon is considered as a first treatment of choice in poisoning beta-blocker overdose. Premedication with antiemetic may be considered since treatment with glucagon may induce vomiting.

Epinephrine & Norepinephrine are the first line medications for hypotension, other options are fluid, Isoprinosine and Dopamine. Treatment with calcium salts may provide benefit for hypotensive patients who

overdosed. High-dose insulin with euglycemia is a safe and simple way to augment cardiac contractility and does not need invasive monitoring[3]. High-dose insulin with euglycemia can cause profound hypokalemia and hypoglycemia that can potentiate the cardiotoxicity. So Potassium and glucose should, therefore, be checked before initiation of high-dose insulin.

IV Atropine and TPM can be done in case of symptomatic Bradycardia. Now a days Intralipid emulsion also can be given @ 1.5 ml/Kg bolus as a binding agent. Hemodialysis is no help in case of Metoprolol overdose because it's not a water soluble drug.

Conclusion:

The outcomes after Metoprolol depend on when the patient presents and the amount ingested. Overall, this lipid soluble beta blockers are more toxic than the water-soluble agents because of their quinidine-like effects. Individuals with underlying heart and lung disease are most susceptible to the toxic effects. Poisoning by â-blockers usually produces hypotension and bradycardia, which may be refractory to standard resuscitation measures. When symptomatic bradycardia and hypotension are present, high-dose glucagon is considered the first-line antidote. Calcium salts improve BP albeit in a short-lived manner[4] via positive inotropic effects[5]. Over the years, the numbers of beta blocker associated toxicity have slightly increased, but the fatalities have decreased because of prompt diagnosis and treatment. When patients present with suspected beta-blocker toxicity, the patients should be admitted to the ICU. Any patient with an intentional overdose should be referred to a mental health counselor prior to discharge.

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