EM CASE OF THE WEEK.

BROWARD HEALTH MEDICAL CENTER
DEPARTMENT OF EMERGENCY MEDICINE

BROWARD HEALTH
Care Warriors

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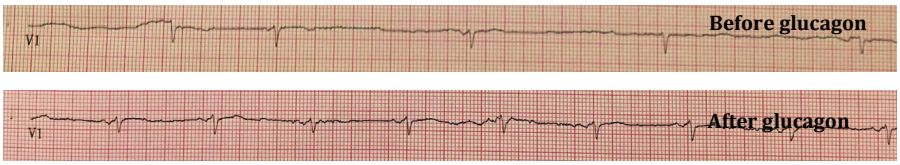
Beta-Blocker Overdose

A 75-year-old female with a past medical history of HTN and CAD is brought in by ambulance with shortness of breath and lethargy x1 day. As per family the patient's primary care physician recently increased her metoprolol. Vital signs reveal a heart rate of 38 beats per minute and blood pressure of 53/30. On physical exam the patient has altered mental status with weak radial pulses. She receives IV fluids, dopamine, and atropine. ECG before and after an initial bolus of 5 mg of glucagon administration is shown below.



Despite subsequent boluses and IV infusion of glucagon, the patient's bradycardia and hypotension returns after 15 minutes of each administration. The hospital pharmacy calls and states that the hospital's remaining glucagon supply is low. Which of the following is the next best step in treatment for this patient's condition?

A. Transfer the patient to a higher level of care

B. Use the remaining glucagon at 1 mg/dose

C. Activated charcoal 1g/kg by mouth or nasogastric tube

D. Insulin bolus of 1 unit/kg followed by continuous infusion

E. Dialyze the patient

Google Image

Beta-blockers have been in clinical use for more than 30 years in the management of a range of disorders, from hypertension to migraine headaches.

Beta-blockers are the fifth most commonly prescribed medication in the US. Although safe for most patients when taken as prescribed, beta-blocker toxicity is associated with significant morbidity and mortality.

EM Case of the Week is a weekly "pop quiz" for ED staff.

The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.

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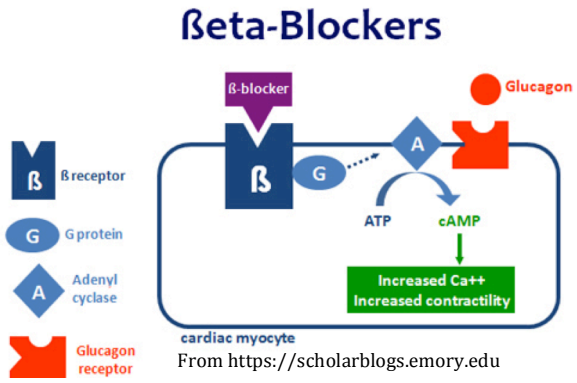
The correct answer is D. Start high dose insulin therapy with bolus of 1 IU/kg.

Beta-blocker overdose is traditionally managed with IV fluids, vasopressors, calcium, atropine, and glucagon. Yet these therapies often fail or are minimally or transiently effective as seen in this patient. High-dose insulin (HDI) therapy is an emerging therapeutic modality for patients who manifest hemodynamic instability refractory to initial interventions. The few HDI clinical trials and existing data are limited to case series or animal models and therefore its popularity is not yet widespread. Regardless, HDI has shown great promise in both existing literature and practice as an effective treatment for beta-blocker toxicity.

Discussion

Beta 1 receptors are found primarily in heart muscle and contribute to heart rate, contractility, and AV conduction. Beta 2 receptors are present in heart muscle but are prominent in bronchial and peripheral vascular smooth muscle. The competitive antagonism of beta-blockers prevents catecholamines from binding to beta receptors and thus decreases levels of cAMP and prevents the intracellular cascade of calcium uptake into the cardiac myocyte. Beta-blocker overdose can present with profound bradycardia and hypotension, as well as altered mental status, seizure, hypoglycemia, and bronchospasm.

Not all beta-blockers are the same. Manifestations of toxicity are observed in varying degrees. In addition to selective and non-selective beta-adrenoreceptor blockade, two properties that affect toxicity include membrane stabilizing activity (MSA) and lipophilicity. MSA agents such as acebutolol can widen the QRS interval and potentiate other dysrhythmias by inhibiting myocardial fast sodium channels. Beta-blockers with high lipid solubility like propranolol rapidly cross the blood brain barrier and cause seizures and delirium. Other beta-blockers are known for their specific toxicities, such as Torsades de Pointes with sotalol, and toxic epidermal necrolysis with carvedilol.



From https://scholarblogs.emory.edu

Treatment

ABC's and contact Poison Control Stabilize the patient and contact Poison Control early to manage treatment.

Atropine For initial treatment of hypotension and bradycardia give atropine 1 mg IV (up to 3 doses).

GI Decontamination This consists of 1g/kg activated charcoal, whole bowel irrigation or gastric lavage. Activated charcoal is recommended within 1-2 hours of ingestion but withheld in sedated patients. Consider whole bowel irrigation for extended release beta-blockers.

Glucagon This is the gold standard at this time. It increases cardiac inotropy by activating cAMP by a secondary mechanism separate from that of catecholamines. Start with 5 mg bolus and re-bolus as needed. Start drip at the effective dose.

HDI When used at doses 10x that of the normal antidiabetic dose, insulin has positive inotropic effects, improves response to vasopressors, and provides lasting effects on hemodynamic stability. Give a bolus of 1 u/kg IV of regular insulin followed by an infusion of 0.5 u/kg/hr. Euglycemia can be maintained by continuous IV infusion of 5-10% dextrose. Keep in mind hemodynamic response to HDI is delayed 30-60 minutes, requiring simultaneous implementation of other therapies.

Vasopressors Use vasopressors when initial therapies are unsuccessful or before HDI takes effect.

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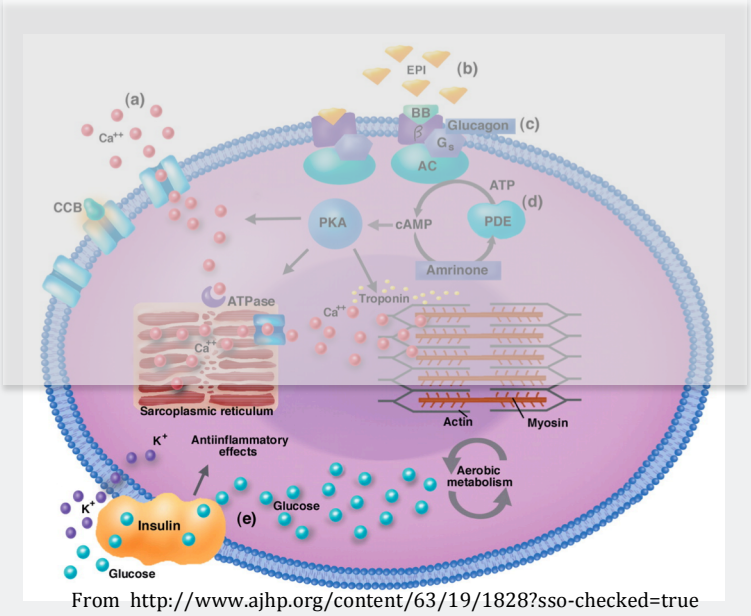
Other treatments to consider Intravenous lipid emulsion can be used for highly lipophilic agents, sodium bicarbonate for prolonged QRS, magnesium for ventricular dysrhythmias, and intraaortic balloon pumps after failure of pharmacologic management. Hemodialysis has a minimal role in treatment of beta-blocker overdose.



From http://www.ajhp.org/content/63/19/1828?sso-checked=true

The above figure portrays the mechanism of action of HDI therapy on the cardiac myocyte. The proposed mechanism of action includes:

1. Strong positive inotropic effect
2. Increases uptake of glucose, the preferred fuel of the heart under stressed conditions, and K+ influx
3. Vascular dilatation by inducing endothelial nitric oxide synthase activity leading to local microcirculation improvement

Take Home Points

- Beta-blocker overdose generally follows a benign clinical course, but patients with significant toxicity require prompt and aggressive medical management.
- Toxicity is based on factors such as MSA and lipophilic agents, while specific beta-blockers have unique toxicities.
- Therapy includes IV fluids, atropine, glucagon, and vasopressors. These therapies often fail or produce transient results.
- In cases of hemodynamic instability refractory to initial treatment, consider HDI. Providers should be aware of this potentially life-saving therapy.

ABOUT THE AUTHOR

This month's case was written by Madeline Fasen. Madeline is a 4th year medical student from NSU-COM. She did her emergency medicine rotation at Broward Health North in October 2017. Madeline plans on pursuing a career in Internal Medicine after graduation.

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