EM CASES SUMMARY

Episode 90 – Low and Slow Poisoning

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One of the things we need to think about whenever we see a patient who's going low and slow with hypotension and bradycardia is an overdose. B-blockers, calcium channel blockers (CCB) and digoxin are some of the most frequently prescribed cardiovascular drugs. And inevitably we're going to be faced with both intentional and unintentional overdoses from these drugs in the ED. Early recognition and management of these patients will help to prevent mortality.

Differential Diagnosis of Bradycardia and Hypotension (Slow and Low)

Non-toxicological causes:

- MI with cardiogenic shock
- Hyperkalemia
- Myxedema coma
- Spinal cord injury
- Hypothermia

Toxicological causes:

- Calcium channel blockers
- Beta-blockers
- Digoxin
- Opiates
- Alpha-2 antagonists (e.g., clonidine)
- Sodium channel blockers (e.g., TCA, carbamazepine, flexeril, antipsychotics, propranolol, cocaine)

Management of Seizures in the Toxicology Patient

There are several modifications of the usual algorithm for treating adult seizures when it comes to the poisoned patient.

Avoid Sodium Channel Blockers

Benzodiazepines are the first line treatment for treating seizures in patients with an overdose. In toxicological seizures, do **not** treat with antiepileptic drugs that have sodium channel blockade (i.e., phenytoin, fosphenytoin) because

many poisons block sodium channels and additional sodium channel blockade may result in cardiac instability. If seizures persist, even after large doses of benzodiazepines, consider advancing to phenobarbital or propofol.

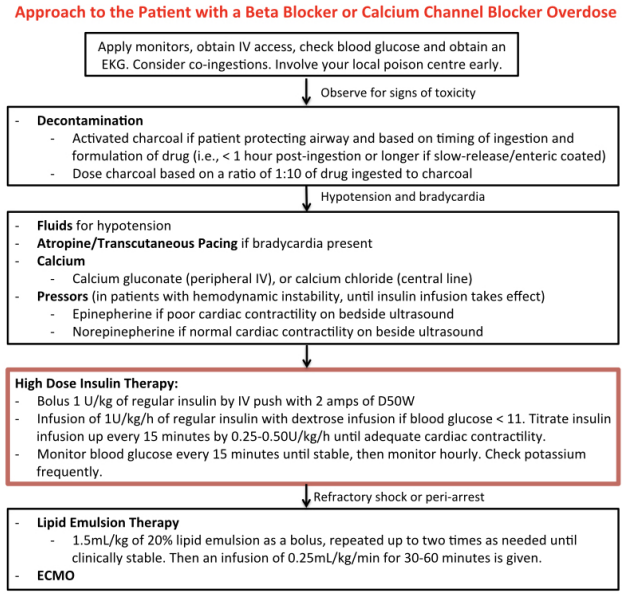
Bicarbonate

In patients with an overdose who are seizing and have evidence of sodium channel blockade (wide QRS on EKG), give sodium bicarbonate.

Naloxone

Consider naloxone in patients who may have an opioid overdose and are seizing. Some opioids can cause seizures (i.e., meperidine). Opioids may also cause hypoperfusion, which can lead to seizures.

General Approach to the Management of Beta Blocker and Calcium Channel Blocker Overdoses



1. Fluids
2. Decontamination
3. Atropine with consideration for transcutaneous pacing
4. Calcium
5. High dose insulin
6. Vasopressors
7. Glucagon
8. Lipid emulsion therapy
9. ECMO

Fluids:

Establish two IVs and give the patient a fluid bolus of normal saline (1-2 liters) to start.

Decontamination:

Consider decontamination with a dose of **activated charcoal.** The dose of activated charcoal is determined by the dose of the drug ingested in a 10:1 ratio of charcoal to drug. For example, a single 240mg tablet of Diltiazem requires only 2.4g of activated charcoal.

Factors to consider in the decision to give activated charcoal:

1. *Does the drug bind to charcoal?*

Charcoal does not bind lithium or iron, therefore, should not be given for overdoses of these drugs.

2. *Was the drug ingested within one hour?*

For most drugs, activated charcoal is indicated within one hour of ingestion only.

3. *Is the drug likely to stay in the stomach for a prolonged time (beyond the one hour post-ingestion)?*

Some drugs will stay in the stomach or upper intestinal tract for a prolonged period of time. In overdoses that involve drugs with these properties, charcoal should still be considered even if the ingestion occurred more than one hour ago. Examples of such drugs would include medications that are extended release formulations, enteric-coated medications, opioids and anticholinergic medications that delay gastric emptying, ASA, and theophylline.

4. *Is the patient protecting their airway?*

Aspiration pneumonitis is the most common complication of activated charcoal administration. If you suspect that a patient not be able to protect their airway because of altered level of awareness or anticipated seizure, avoid the use of activated charcoal.

Gastric lavage should only be considered for a massive life-threatening ingestion if it can be undertaken within 60 minutes of ingestion, and if the size of the tablets taken is smaller than that of the lavage tube (36-40f). Remember that these patients will need their airway secured prior to placement of the lavage tube. There is no evidence to suggest that gastric lavage reduces mortality from overdose.

Whole bowel irrigation There is no evidence in the literature that whole bowel irrigation improves outcomes in overdoses. Consider whole bowel irrigation in 3 situations:

1. Large drugs not bound by charcoal: iron, lithium, potassium
2. Body packers
3. Massive overdoses of extended release medications

Go to Episode 5 for a discussion on body packer management

Atropine:

Consider a trial of 0.5mg IV atropine in patients with bradycardia.

What about cardiac pacing? In the overdose patient, transcutaneous pacing is unlikely to be successful, but may be attempted. If transcutaneous pacing is unsuccessful, it is generally agreed that transvenous pacing should be avoided in the patient with a slow and low poisoning as it may precipitate dysrhythmias in the overdose patient with an 'irritable' heart.

Calcium:

Calcium Gluconate 3amps IV push *or* **Calcium Chloride** 1amp IV push if a central line is established followed by infusion if an effect is seen.

High Dose Insulin:

High dose insulin is used for both beta blocker and calcium channel blocker overdoses. A bolus of 1U/kg IV push of regular insulin is given with 2 amps D50W IV push.

Follow the bolus with a 1 U/kg/hr insulin infusion with a 0.5 g/kg/hr dextrose infusion if blood glucose is < 11. Titrate the insulin infusion up every 15 minutes by 0.25-0.5 U/kg/hr until cardiac contractility is adequate based on bedside ultrasound findings and vital signs. **One of the biggest pitfalls in the management of B-blocker overdoses is not giving enough insulin. Patients may require up to 8-10U/kg/hr**!

Serum glucose should be monitored every 15 minutes initially, and then can be reduced to hourly once the glucose has stabilized. Remember to monitor the serum potassium.

The insulin takes approximately 30-45 minutes to start to work, therefore, start treatment EARLY!

Pressors:

Norepinepherine or **epinephrine** may be required for hemodynamic support until the insulin takes effect. The choice of medication will depend on cardiac contractility on point of care ultrasound (POCUS). Epinepherine is favored over norepinephrine in patients with evidence of myocardial depression on POCUS. Norepinepherine is favored in patients with normal contractility on POCUS.

Glucagon:

Glucagon may be considered as a last resort. Our experts do not recommend the routine use of glucagon in beta blocker overdoses. It can worsen hypotension and bradycardia, as well as cause vomiting which increases the risk of aspiration.

Lipid emulsion therapy:

Lipid emulsion therapy (intralipid) is a management option for patients who have overdosed on a lipid soluble drug (e.g., lidocaine/bupivacaine, calcium channel blockers, amitriptyline, seroquel, buproprion) who are in refractory shock or peri-arrest.

There are downsides to lipid therapy including complications such as pancreatitis and pulmonary fat emboli. Electrolytes, blood gases etc. cannot be measured in lipemic serum.

Intralipid treatment should be reserved for lipophilic drug poisoning with:

1. Hypotension or
2. Dysrhythmias causing hemodynamic instability (not responsive to sodium bicarbonate or lidocaine) or
3. Seizures unresponsive to usual treatments

There is no role for lipid emulsion therapy

- as prophylaxis
- in isolated altered mental status or coma
- as 1st line therapy

How do you give lipid emulsion therapy? Draw up 100mL from a 500mL bag of lipid emulsion and give as an IV bolus, then run the remaining 400mL over 30mins.

ECG Findings in Beta Blocker Overdoses

Bradycardia is the most common ECG finding in beta blocker overdoses. You may see a sinus bradycardia, or any type of heart block (including a complete heart block). A junctional rhythm may be seen.

In *propranolol* overdose, there may be a wide QRS and a tall R wave in aVR due to its sodium channel blocking property.

In *sotolol* overdose, the QTc may be prolonged because of its potassium channel blocking properties.

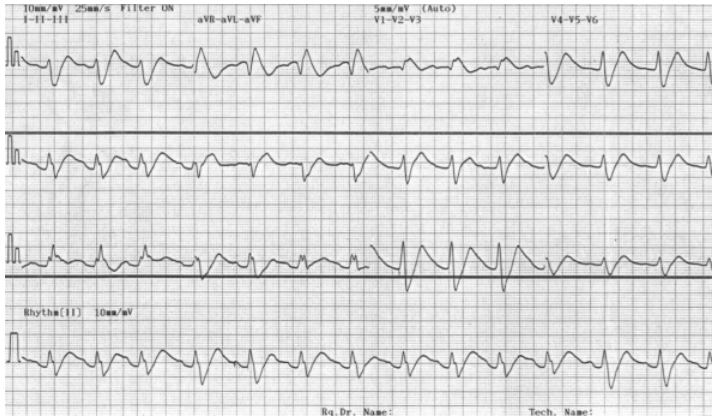


Fig 1. ECG features of propanolol overdose
(image from www.lifeinthefastlane.com)

Which Beta Blocker was used?

Propanolol is one of the most dangerous beta blockers in overdose. It has significant sodium channel blockade and is

lipophilic, therefore, it crosses the blood brain barrier and causes depressed level of consciousness, seizures, and respiratory depression.

Dialyzable Beta Blockers

Not all beta blockers can be dialyzed. Beta blockers that can be dialyzed include: nadolol, acebutolol, and sotalol. There have been case reports of atenolol being dialyzable.

Differentiating Between Calcium Channel Blocker and Beta Blocker Overdoses

There are two key features that may help differentiate a calcium channel blocker overdose from a beta blocker overdose: **Blood glucose** and **level of consciousness**. Calcium channel blocker overdoses tend to cause hyperglycemia, compared to a normal-to-low blood glucose in beta blocker overdoses. Beta blocker overdoses tend to cause a depressed level of consciousness, and calcium channel blocker overdoses, a normal level of consciousness.

Digoxin Poisoning

Chronic digoxin poisoning has a higher mortality, more vague symptomatology, and more low and slow compared to *acute* digoxin poisoning. Ventricular dysrhythmias are more classically associated with acute digoxin poisoning, though can be seen in chronically poisoned patients as well.

The classic patient with digoxin toxicity is the older patient on their usual dose of digoxin who develops vague symptoms such as 'weak and dizzy', altered LOC, nausea and visual symptoms.

Classic triggers for digoxin toxicity in the patient taking their usual daily dose:

- Volume depletion (digoxin is excreted renally)
- Recent medication change (there are many drug-drug interactions with digoxin)

The EKG and Digoxin

First, one must distinguish between digoxin *effect* and digoxin *toxicity.*

Digoxin *effect:* EKG characteristics normally seen in a non-toxic patient taking therapeutic doses of digoxin, displays scooped ST segments, otherwise known as 'The Salvador Dali Moustache' after the great surrealist painter.

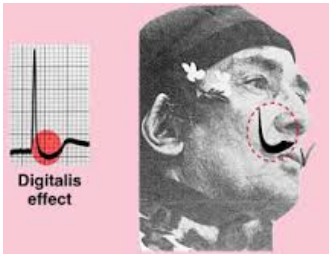


Fig 2: Digoxin effect showing ST scooping on EKG
(image from www.lifeinthefastlane.com)

Digoxin *toxicity:* can cause almost any dysrhythmia *except* rapid atrial fibrillation. As acute digoxin toxicity often causes hyperkalemia, EKG findings may reflect those of hyperkalemia. (Go to *Episode 86 Emergency Management of Hyperkalemia* for EKG examples)

Classic digoxin toxicity EKG findings are a result of *myocardial irritability* or *blockade at the AV node* and include:

Myocardial irritability:

- Slow atrial fibrillation
- Bidirectional ventricular tachycardia
- Frequent PVCs

AV blockade:

- Junctional rhythm
- AV dissociation
- Heart block

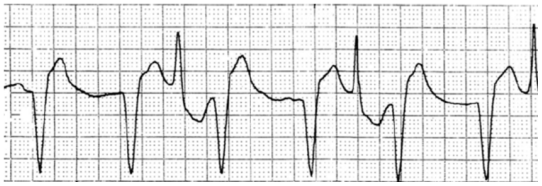


Fig 3: Bidirectional ventricular tachycardia in digoxin poisoning
(image from: Piccini J, Zaas A. Images of Osler: Cases from the Osler Medical Service at Johns Hopkins University. Am J Med 2003 Jul;115(1):70–1)

Pitfalls in Interpreting Digoxin Levels

False positives

- Digoxin levels will always be falsely elevated if taken within 6 hours of ingestion, so you must wait >6 hours to draw the first digoxin level.
- After DigiFab administration

False negatives

- Patients can be digoxin toxic with therapeutic digoxin levels

Treatment of the slow and low digoxin poisoned patient

1. Fluid bolus
2. Trial of atropine 0.5mg IV
3. DigiFab

There is little role for pacing in the slow and low digoxin toxic patient because of increased myocardial irritability and the risk of deterioration into a malignant dysrhythmia. Transcutaneous pacing may be considered in the unstable slow and low digoxin toxic patient if there is a delay to administration of DigiFab when atropine has failed. Transcutaneous pacing should occur at the lowest possible voltage at a rate of no more than 50-60bpm. Transvenous pacing should NOT be attempted.

For *acute* digoxin poisoning with ventricular dysrhythmias, consider IV lidocaine and/or IV esmolol.

Indications for DigiFab antidote

The indications for DigiFab include the following in the setting of suspected digoxin poisoning:

- History of 10mg digoxin ingestion in an adult or 4mg in a child (or 0.1mg/kg)
- Hyperkalemia (serum potassium >5)
- High digoxin serum level
- Renal Failure
- Ventricular or unstable atrial dysrhythmias
- Multiple drug ingestions

Dosing DigiFab - A new regimen

In cardiac arrest due to digoxin poisoning, give 10 vials of DigiFab and repeat in 15 mins prn x 1 for a total of 20 vials.

In *chronic* digoxin poisoning give 1 vial and repeat prn based on clinical condition, ECG and serum potassium (usually requires approximately 5 vials total)

In *acute* digoxin poisoning give 2 vials and repeat prn based on clinical condition, ECG and serum potassium (usually requires approximately 10 vials total)

Once you have given a dose of DigiFab, the digoxin level is rendered useless because it will be high. Monitors these patients based on their serum potassium, EKG and clinical findings.

Is calcium safe in hyperkalemic digoxin toxic patients?

Chronic digoxin toxicity typically causes *hypokalemia*. If a chronic digoxin toxic patient is *hyperkalemic* it is likely due to acute renal failure and those patients giving calcium is likely safe (unlikely to cause 'stone heart').

Acute digoxin toxicity typically causes *hyperkalemia* due to blockage of Na-K ATPase. These patients do not need anything to stabilize their cardiac membranes or shift potassium. These patients need DigiFab.

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FOAMed Resources

1. http://www.thepoisonreview.com/2014/11/06/there-is-no-real-evidence-on-treating-calcium-channel-blocker-overdose/
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