Cardiovascular Meds Intoxication

Zohair Al Aseri MD,FRCPC EM & CCM

Cardiovascular BB & CCB Intoxication

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Principles of Disease Pathophysiology

- Inhibit endogenous catecholamines
- Rapidly absorbed after oral ingestion, and the peak occurs in 1 to 4 hours.
- Volume of distribution for various beta-blockers generally exceeds 1 L/kg, meaning tissue concentrations exceed those of serum.

hemodialysis is not efficacious for most beta-blockers

MANIFESTATIONS AND COMPLICATIONS OF BETA-BLOCKER OVERDOSEIN ORDER OF DECREASING FREQUENCY

1. Bradycardia (65/90 cases)
2. Hypotension (64/90)
3. Unconsciousness (50/90)
4. Respiratory arrest or insufficiency (34/90)
5. Hypoglycemia (uncommon in adults)
6. Seizures (common only with propranolol, 16/90)
7. Symptomatic bronchospasm (uncommon)
8. VT or VF (6/90)
9. Mild hyperkalemia (uncommon)
10. Hepatotoxicity, mesenteric ischemia, renal failure (rare or single case reports)

*Intoxication with beta-sympatholytics.
VF, ventricular fibrillation; VT, ventricular tachycardia.

Management

- IV fluids
- Oxygen
- Monitoring of card for rhythm and respirations.
- Activated charcoal is unproven treatment.
- Multiple-dose charcoal without supporting evidence for an improvement in outcome.

Management

The first step in the treatment of beta-blocker overdose is

- Atropine
- Glucagon
- Crystalloid fluids.

Others

- Catecholamines
- Sodium bicarbonate if Na blockers
- Ca
- Extracorporeal Elimination and Circulatory Assistance

- **High-Dose Insulin Euglycemia (HDIE) Therapy**
- **Insulin**

TREATMENT OF BETA-BLOCKER POISONING

Phase I (Resuscitation)

Boluses of atropine, glucagon, fluids

Phase II (Stabilization)

Infusions of
- Glucagon
- Insulin-glucose
- Catecholamines (epinephrine, norepinephrine, isoproterenol, dobutamine, dopamine, metaraminol)
- Phosphodiesterase inhibitors (amrinone)

Early cardiac pacing if no prompt response to chronotropic or dromotropic drugs

Peripheral arterial and pulmonary artery catheter monitoring if refractory hypotension

Consider hemodialysis of hydrophilic beta-blockers with low protein binding and low V_d

V_d, volume of distribution.

Other Treatment

- High-Dose Insulin Euglycemia (HDIE) Therapy
- Insulin

Disposition

- Patients who remain completely asymptomatic for 6 hours after an oral overdose of normal-release preparations can be safely referred for psychiatric evaluation, with medical consultation for the first 24 hours.

CALCIUM CHANNEL BLOCKERS

Perspective

- Most fatalities occur with verapamil, but severe toxicity and death have been reported for most drugs of this class.

Pathophysiology

Calcium channel antagonists

- block the slow calcium channels in the myocardium and vascular smooth muscle, leading to coronary and peripheral vasodilation.
- reduce cardiac contractility
- depress SA nodal activity
- slow AV conduction.

Pathophysiology

- Both verapamil and diltiazem act on the heart and blood vessels, whereas nifedipine causes primarily vasodilation.
- In the pancreas, calcium channel blockade inhibits insulin release, resulting in hyperglycemia.
- As with beta-blockers, selectivity is lost in cases of overdose

Pathophysiology

- All calcium channel blockers are rapidly absorbed
- Onset of action and toxicity ranges from less than 30 minutes to 60 minutes
- Peak effect of nifedipine can occur as early as 20 minutes after ingestion,

MANIFESTATIONS AND COMPLICATIONS OF CALCIUM CHANNEL BLOCKER POISONING

Cardiovascular: Hypotension, sinus bradycardia, sinus arrest, AV block, AV dissociation, junctional rhythm, asystole; ventricular dysrhythmias uncommon except with bepridil

Pulmonary: Respiratory depression, apnea; pulmonary edema; adult respiratory distress syndrome

Gastrointestinal: Nausea, vomiting, bowel infarction (rare)

Neurologic: Lethargy, confusion, slurred speech, coma; seizures (uncommon); cerebral infarction (rare)

Metabolic: Metabolic (lactic) acidosis; hyperglycemia (mild); hyperkalemia (mild)

Dermatologic: Flushing, diaphoresis, pallor, peripheral cyanosis

AV, atrioventricular.

Diagnostic Strategies

- Serum levels are not available
- Glucose and Electrolytes Hyperglycemia secondary to insulin inhibition occurs occasionally
- Lactic acidosis occurs with hypotension and hypoperfusion.

- ECG
- A prolonged QRS or QT interval suggests bepridil or a co-ingested cardiac toxin such as a TCA.

Management

- IV
- O2
- Cardiac monitoring
- Vomiting is a powerful vagal stimulus that can exacerbate bradycardia and heart block.

- No evidence for activated charcoal

Hypotension and Bradycardia

- Atropine
- Intravenous calcium
- Epinephrine, norepinephrine, and dobutamine have also led to successful outcomes.
- Glucagon has also been used for its inotropic and chronotropic effects.
- Insulin

Other Treatment

High-Dose Insulin Euglycemia (HDIE) Therapy

TREATMENT OF CALCIUM CHANNEL BLOCKER INTOXICATION

Phase 1

Boluses of atropine, calcium, fluids

Phase 2

Catecholamine infusions
Calcium infusion
Insulin glucose infusion
Glucagon infusion
Phosphodiesterase infusion
Transcutaneous or transvenous cardiac pacing
Invasive monitoring

Phase 3

Consider intra-aortic balloon counterpulsation, cardiac bypass

NITRATES AND NITRITES

- Widely used as vasodilators in the treatment of heart failure and ischemic heart disease.
- augment coronary blood flow as well as reduce myocardial oxygen consumption by reducing afterload.
- At lower doses nitrates primarily dilate veins
- At higher doses they also dilate arteries.

NITRATES AND NITRITES

- Hypotension is a common complication, but usually responds to supine positioning, IV fluids, and reduction of dose.
- Hypotension is usually transient.
- Low-dose pressors are occasionally needed, but it is best to avoid them in the setting of acute coronary syndromes.

NITRATES AND NITRITES

- Nitrites are also oxidizing agents that convert hemoglobin to methemoglobin, impairing oxygen delivery.

NITRATES AND NITRITES

- When methemoglobin levels exceed 15%, a venous blood sample appears chocolate brown, and the skin appears blue even while patients look remarkably comfortable.

- Unlike most cases of cyanosis, supplemental oxygen does not improve the patient's color.

NITRATES AND NITRITES

- Pulse oximetry is not reliable,

Treatment

- IV methylene blue, but this antidote is usually not needed unless methemoglobinemia approaches 30%

- The usual dose of methylene blue in adults is 1 to 2 mg IV over 5 minutes.

Digitalis Intoxication

Zohair Al Aseri MD,FRCPC EM & CCM

Principles of Disease

Pathophysiology

In therapeutic doses, digitalis has two effects:

(1) increasing the force of myocardial contraction

(2) decreasing atrioventricular (AV) conduction to slow the ventricular rate in atrial fibrillation.

Principles of Disease

Pathophysiology

- It inhibits membrane sodium-potassium adenosine triphosphatase (ATPase), which increases intracellular Na and Ca and increases extracellular K.

- With toxic levels, digitalis paralyzes the Na-K pump, K cannot be transported into cells

Principles of Disease

Pathophysiology

- At therapeutic levels, digitalis indirectly increases vagal activity and decreases sympathetic activity.

- At toxic levels, digitalis can directly halt the generation of impulses in the SA node, depress conduction through the AV node, and increase the sensitivity of the SA and AV nodes to catecholamines.

DYSRHYTHMIAS ASSOCIATED WITH DIGITALIS TOXICITY

Nonspecific
PVCs, especially bigeminal and multiform
First-, second- (Wenckebach's), and third-degree AV block
Sinus bradycardia
Sinus tachycardia
Sinoatrial block or arrest
Atrial fibrillation with slow ventricular response
Atrial tachycardia
Junctional (escape) rhythm
AV dissociation
Ventricular bigeminy and trigeminy
Ventricular tachycardia
Torsades de pointes
Ventricular fibrillation

More Specific, but Not Pathognomonic
Atrial fibrillation with slow, regular ventricular rate (AV dissociation)
Nonparoxysmal junctional tachycardia (rate 70–130 beats/min)
Atrial tachycardia with block (atrial rate usually 150–200 beats/min)
Bidirectional ventricular tachycardia

AV, atrioventricular; PVC, premature ventricular contraction.

- Digitalis can produce any dysrhythmia

Principles of Disease Pathophysiology

- The significant protein binding and large volume of distribution suggest that hemodialysis, hemoperfusion, and exchange transfusion are ineffective.

NONCARDIAC SYMPTOMS OF DIGITALIS INTOXICATION IN ADULTS AND CHILDREN

General
Weakness
Fatigue
Malaise

Gastrointestinal
Nausea and vomiting
Anorexia
Abdominal pain
Diarrhea

Ophthalmologic
Blurred or snowy vision
Photophobia
Yellow-green chromatopsia (also red, brown, blue)
Transient amblyopia, diplopia, scotomata, blindness

Neurologic
Dizziness
Headache
Confusion, disorientation, delirium
Visual and auditory hallucinations
Paranoid ideation, acute psychosis
Somnolence
Abnormal dreams
Paresthesias and neuralgia
Aphasia
Seizures

Diagnostic Strategies

- Serum digoxin levels.
- Peak levels after an oral dose of digoxin occur in 1.5 to 2 hours, with a range of 0.5 to 6 hours.

- Steady-state serum concentrations are not achieved until after distribution, or 6 to 8 hours after a dose or overdose, and may be only one fourth to one fifth of the peak level.

Management

There is no evidence to support

- Gastric emptying
- Activated charcoal
- Multidose charcoal has no proven benefit

- Atropine
- Pacing

Cardioversion and defibrillation can cause asystole after attempts to treat tachydysrhythmias.

Lower energy settings, such as 25 to 50 J, may be less hazardous.

Electrolyte Correction

- K
- Raising the serum potassium level to 3.5 to 4 mEq/L is an important early treatment.
- Level greater than 5 mEq/L warrants consideration of digitalis antibody (Fab fragment) treatment.
- Mg For significant magnesium depletion

Fab Fragments (Digibind or Digifab)

RECOMMENDATIONS FOR ADMINISTRATION OF DIGITALIS ANTIBODY FRAGMENTS

Adults

1. Severe ventricular dysrhythmias
2. Progressive and hemodynamically significant bradydysrhythmias unresponsive to atropine
3. Serum potassium greater than 5 mEq/L
4. Rapidly progressive rhythm disturbances or rising serum potassium level
5. Co-ingestion of cardiotoxic drugs such as beta-blockers, calcium channel blockers, or tricyclic antidepressants
6. Ingestion of plant known to contain cardiac glycosides *plus* severe dysrhythmias (rare)
7. Acute ingestion greater than 10 mg *plus* any one of factors 1 through 6 above
8. Steady-state serum digoxin greater than 6 ng/mL *plus* any one of factors 1 through 6 above

Children

1. Ingestion of greater than 0.1–0.3 mg/kg or steady-state digoxin greater than 5 ng/mL *plus* rapidly progressive symptoms or signs of digitalis intoxication *or* potentially life-threatening dysrhythmias or conduction blocks *or* serum potassium greater than 6 mEq/L
2. Co-ingestion of other cardiotoxic drugs with additive or synergistic toxicity
3. Ingestion of plant known to contain cardiac glycosides *plus* severe dysrhythmias (rare)

Main reference is Rosen Text book of EM

Thank you