Antidysrhythmic Drugs

Cardiac Arrhythmias result from disorders of impulse formation, conduction, or both.

Causes of arrhythmias

- **Cardiac ischemia**
- **Excessive discharge or sensitivity to autonomic transmitters**
- **Exposure to toxic substances**
- **Unknown etiology**

Antidysrhythmics modify impulse generation and conduction by interacting with various membrane sodium, potassium, and calcium ion channels.

Classification of antiarrhythmics (based on mechanisms of action):

Class I – block the fast Na^+ channels and widen QRS complex

Subclass IA

- **<u>Quinidine</u> – 1st antiarrhythmic used, treat both atrial and ventricular arrhythmias**
- **<u>Procainamide</u>**
- **<u>Disopyramide</u> – extended duration of action, used only for treating ventricular arrthymias**

Toxicity of CLASS IA Antiarrhythmic drugs:

At toxic doses, patients will demonstrate increased Q-T and QRS intervals. Hypotension in type IA intoxication is caused by depressed myocardial contractility from the Na+ channel blockade and peripheral vasodilation from the K+ channel blockade. Class IA

drugs depress rapid action potential upstroke and decrease conduction velocity (Na+ channel blockade). significantly prolong repolarization (K+ channel blockade). Class IA drugs indicated for atrial fibrillation and ventricular tachycardia.

Quinidine

Cinchonism, a syndrome characterized by GI symptoms (abdominal cramping, nausea, vomiting, and diarrhea), tinnitus, and altered mental status may occur in both chronic and acute toxicity. Patients on quinidine may report symptoms of hypoglycemia, as the drug acts on potassium channels in the pancreatic islet cells.

Procainamide

Nausea, vomiting, diarrhea, bitter taste, and light-headedness. Long-term use of procainamide is associated with the development of antinuclear antibodies and drug-induced systemic lupus erythematosus syndrome characterized by arthralgias, myalgias, rash, and fever.

Disopyramide

The anticholinergic property of disopyramide leads to symptoms of urinary retention, constipation, dry mouth, and blurred vision. Patients with preexisting ventricular dysfunction may experience further decline in contractility and report dyspnea, edema, and decreased exercise tolerance.

Subclass IB: Includes

Lidocaine (also acts as local anesthetic) – blocks Na+ channels mostly in ventricular cells, also good for digitalis-associated arrhythmias

Mexiletine - oral lidocaine derivative, similar activity

Phenytoin – anticonvulsant that also works as antiarrhythmic similar to lidocaine

Toxicity of CLASS IB Antiarrhythmic drugs:

Lidocaine

- Symptoms include drowsiness, light-headedness, vision changes, tinnitus, and paresthesias.

Mexiletine

- Nausea and vomiting, neurotoxic adverse effects similar to those that occur with lidocaine.

Phenytoin

- Mouth -Gingival hyperplasia is the most common adverse effect
- Hypotension, bradycardia
- Hirsutism, acne
- Right upper quadrant tenderness, Hepatomegaly
- Fetal hydantoin syndrome if used by pregnant women

Subclass IC: Includes

Flecainide (initially developed as a local anesthetic(Slows conduction in all parts of heart ,Also inhibits abnormal automaticity

Propafenone Also slows conduction**,** Weak β – blocker, Also some Ca^{2+} channel blockade

Toxicity of CLASS IC Antiarrhythmic drugs:

Flecainide

- Worsening congestive heart failure, CNS symptoms that patients may report are headache, irritability, and confusion.

Propafenone

- Alteration in taste, blurred vision, and dizziness. nausea, vomiting, and constipation. Asthmatic patients may report

worsening symptoms, owing to the weak beta-blocking effects of propafenone.

Class II – β–adrenergic blockers

-Based on two major actions

1) blockade of myocardial β–adrenergic receptors

2) Direct membrane-stabilizing effects related to Na^+ channel blockade

-Includes

- **<u>Propranolol</u>**
  - (1) **causes both myocardial β–adrenergic blockade and membrane-stabilizing effects**
  - (2) **Slows SA node and ectopic pacemaking**
  - (3) **Can block arrhythmias induced by exercise.**
  - (4) **Other β–adrenergic blockers have similar therapeutic effect**
- **Metoprolol**
- **Nadolol**
- **Atenolol**
- **Acebutolol**
- **Pindolol**
- **Satolol**
- **Timolol**
- **Esmolol**
- **Class III – K^+ channel blockers**
  - **Includes**
    - **<u>Amiodarone</u>**
    - **<u>Ibutilide</u>**

- **<u>Bretylium</u> – first developed to treat hypertension but found to also suppress ventricular fibrillation associated with myocardial infarction**
- **Dofetilide**

Amiodarone

- **Pulmonary toxicity is the most concerning adverse effect (cough, fever, dyspnea)**
- **Hepatotoxicity leading to cirrhosis is uncommon.**
- **skin changes such as photosensitivity and bluish discoloration.**
- **Patients may also report symptoms suggestive of both hyperthyroidism and hypothyroidism.**
- **Patients on amiodarone long term may report vision loss from corneal deposition, optic neuropathy, or optic neuritis.**

Ibutilide

- **Headache, Light-headedness from hypotension.**

Dofetilide

- **Headache , chest pain, and light-headedness.**

<u>Bretylium</u>

- **Hypotension and postural hypotension have been the most frequently reported adverse reactions**
- **Renal dysfunction, diarrhea , abdominal pain , hiccups**

<u>Sotalol</u> is rapidly and completely absorbed and demonstrates toxicity within an hour of ingestion. In addition to the K+ channel blockade, it also has a significant βadrenergic receptor antagonist effect that explains most of the hemodynamic changes in overdose.

Class IV – Ca^{2+} channel blockers

slow rate of AV-conduction in patients with atrial fibrillation which Includes

1. **Verapamil – blocks Na^{+} channels in addition to $Ca^{2+;}$ also slows SA node in tachycardia**
2. **Diltiazem**

UNCLASSIFIED: ADENOSINE

Adenosine, a nucleoside found in all cells, is released from myocardial cells under physiologic and pathophysiologic conditions. It is administered as a rapid IV bolus to terminate reentrant supraventricular tachycardia. The resultant hyperpolarization of adenosine reduces the rate of cellular firing. The adverse effects of adenosine : Transient asystole, dyspnea, chest tightness, flushing, hypotension, and atrial fibrillation and headache.

Diagnosis

- The most important diagnostic test for patients with acute antidysrhythmic toxicity is electrocardiography.
- Serum electrolytes should be obtained.
- Serum drug levels are not likely to be helpful, but levels of quinidine, lidocaine, and propafenone can be measured in the acute care setting.
- Chest radiographs it should be obtained in patients taking amiodarone and presenting with pulmonary symptoms.
- Thyroid function tests should be obtained in patients taking amiodarone who present with signs and symptoms of hypothyroidism or hyperthyroidism.

Management of Class IA Antidysrhythmic

- **Assessment and correction of cardiovascular dysfunction. Following airway evaluation and IV line placement, continuous ECG monitoring. Appropriate gastrointestinal decontamination is recommended when the patient is sufficiently stabilized and should include whole-bowel irrigation if a sustained-release preparation is involved.**
- **Cardiac Conduction Delays: $NaHCO_3$ 1–2 mEq/kg IV boluses. Maintain arterial pH at 7.4 to 7.5.**
- **Hypotension: 0.9% NaCl 200–500 mL bolus infusions to correct hypovolemia. $NaHCO_3$ 1–2 mEq/kg IV boluses. If still hypotensive, consider a pressor agent (Dopamine, norepinephrine, or epinephrine).**
- **Dysrhythmias:**

1) **Bradydysrhythmias—isoproterenol or epinephrine infusion.**
2) **Polymorphic ventricular tachycardia (torsades de pointes): Magnesium, 2 g IV bolus. May repeat in 5–15 minutes. Isoproterenol or overdrive cardiac pacing For patients who have widening of the QRS complex duration, bolus administration of IV hypertonic sodium bicarbonate is indicated.**

- **Other: Consider hemodialysis or hemoperfusion in patients with procainamide intoxication and large ingestions, high plasma concentrations, presence of circulatory collapse, or renal insufficiency.**

Management of Class IB Antidysrhythmic Toxicity

- **The initial management for IV lidocaine-induced cardiac arrest is continuous cardiopulmonary resuscitation to allow lidocaine to redistribute away from the heart.**

Apart from this setting, management of hemodynamic compromise includes fluid replacement and other conventional strategies. Hypotension should be treated first with a normal saline bolus. Resistant hypotension may require vasopressor (dopamine or norepinephrine) administration.

- **Bradydysrhythmias typically do not respond to atropine, requiring the administration of a chronotrope such as dopamine, norepinephrine, or isoproterenol.**
- **Lidocaine-induced seizures and those related to lidocaine analogs are generally brief in nature and do not require specific therapy. Repetitive seizures should be controlled with IV doses of lorazepam generally used; rarely, a barbiturate is required.**
- **Enhanced elimination techniques are limited after IV poisoning because of the rapid time course of poisoning.**
- **After oral poisoning by a class IB drug, activated charcoal should be administered.**

Management of Class IC Antidysrhythmic Toxicity

- **Initial stabilization should include standard management strategies for hypotension and seizures. Additionally, therapy for hypotension and the electrocardiographic manifestations of class IC poisoning includes IV hypertonic sodium bicarbonate to overcome the Na + channel blockade.**
- **Amiodarone has been benefecial in the setting of flecainide-induced ventricular fibrillation refractory to other therapy.**
- **hemodialysis is successful in removing propafenone after overdose.**

Management of Class III Antidysrhythmic Toxicity

- **The slow absorption of amiodarone allows for late GIT cleaning. Activated charcoal is effective in binding amiodarone . Cholestyramine binds amiodarone in the gastrointestinal tract as well as reduces the elimination half-life of absorbed drug, but its role in this ingestion is currently unclear.**
- **Intravenous potassium should be given slowly to increase the serum potassium to greater than 4.5 mmol/L.**
- **Isoproterenol has been used successfully to treat patients with amiodarone-induced torsades de pointes.**
- **Hemodialysis is not expected to be beneficial in general, either because of extensive protein binding or because of large volumes of distribution**
- **Sotalol ingestions resemble β-blocker intoxications. The initial treatment includes appropriate GIT cleaning, cardiac monitoring, and K+ repletion. Hypotension has been successfully treated with isoproterenol (to increase myocardial rate), dopamine, and cardiac pacing. Glucagon, commonly employed in β-blocker intoxications, is a logical choice in a patient refractory to other pressors.**
- **The treatment of bretylium intoxication includes airway management and other supportive measures. Coma may be prolonged and can resemble brain death. In addition, hypotension may require vasopressors.**

Management of adenosine toxicity

- **Overdose of adenosine has not been reported. Treatment is supportive because of the rapid elimination of the drug.**