Cardiac Pharmacology

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Agents Reviewed

- Thiazides
- Beta- Blockers
- Alpha- Blockers
- Mixed Agents
- Calcium channel blockers
- Angiotensin Converting Enzyme Inhibitors
- Angiotensin Receptor Blockers
- Thrombolytics

Definitions

Preload: Amount of blood that fills the ventricles during diastole

- Reduced by drugs that dilate: Lasix, MS, nitrates
- Increased by drugs that constrict: Dopamine & Epinephrine

Afterload: The force that the ventricles must overcome to eject blood thru the valves

Same as above

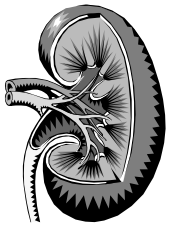
Thiazides

- ***MOA***: Inhibits NA/CL transport pumps in distal tubule of kidney. Initial diuresis & reduction in plasma volume. Over time, plasma volume returns to normal but peripheral resistance decreases.
- ***Use***: Hypertension
- ***Caution***: Hypokalemia, hypomagnesemia, hyperureicemia, hypercalcemia, hyperglycemia

Thiazides

Hydrochlorothiazide

- Dose: 12.5 -50 mg daily
- Maximum 200 mg daily (HTN effects maximal-50mg)
- Notes: less if CrCl < 30 ml/ min

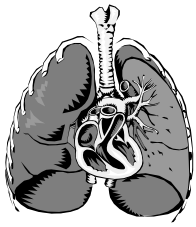


Beta-blockers

- ***MOA***: Antagonize beta-1 receptors in heart. Reduce heart rate & decrease cardiac output
- ***Use***: Hypertension, rate control, MI, ischemic heart disease, CHF
- ***Caution***: Decompensated heart failure, bradycardia, heart block, asthma/ COPD

Normal Physiology

- ***Beta 1 receptors***: found in cardiac muscle, stimulation affects plasma renin & intraocular pressure
- ***Beta 2 receptors***: found in smooth muscle eg. Bronchial tree, vessels
- ***Alpha receptors***: found in vascular smooth muscle & exocrine glands



Normal Physiology

- Stimulation of the Sympathetic Nervous System causes the release of epinephrine & norepinephrine into the blood
- These two neurotransmitters cause stimulation of Beta1, Beta 2, & Alpha receptors
- ***Alpha receptors cause vasoconstriction*** both in periphery & coronary arteries

Normal Physiology

- ***Beta 1 fibers cause increased*** heart rate, increased conduction, increased contractility, increased automaticity, increased BP
- Beta 2 fibers cause bronchodilation & peripheral & venous constriction

Sub classes

- ***1. Cardioselective:*** Mainly B1 receptors with little or no effect on B2 fibers. However, as doses ***increase***, the selectivity ***decreases*** & B 2 fibers may be stimulated
- 2. ***Nonselective***: Blocks both B1 & Alpha
- 3. ***Intrinsic Sympathomemetic Activity (ISA):*** Has ability to block both beta cells & also slightly stimulate them. This ability causes a reduction in resting HR & less of a reduction in contractility

Beta- Blockers

- Atenolol (Tenormin)- ***renal***
- ***Dose:*** 25-50 mg Q 24 Hr (some do better Q 12 Hr)
- ***Maximum***: 100 mg Q 24 Hours

- Metoprolol (Lopressor, Toprol XL)
- Dose: 12.5-50 mg Q 12 Hr (some do better Q 8 Hr)
- Maximum: 200 mg Q 12 Hr

IV to PO conversion is 1 to 2.5
10 mg IV Q 6 Hr = ~ 50 mg PO Q 12 Hr
40 x 2.5 = 100

Alpha- Blockers

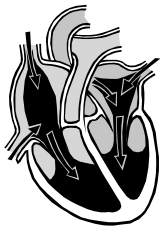
- ***MOA***: Antagonize alpha-1 adrenoreceptors causing relaxation of arterial & venous vessels, reducing peripheral vascular resistance
- ***Use***: Hypertension, BPH
- ***Caution***: Fluid & Na retention, edema, tachycardia, orthostatic hypotension, CNS

Alpha- Blockers

- ***Doxazosin (Cardura)***
Dose: 1-4 mg Q 12 Hr
Maximum: 8 mg Q 12 Hr

- ***Prazosin (Minipress)***
Dose: 2-4 mg Q 12 Hr
Maximum: 10 mg Q 12 Hr

- ***Terazosin (Hytrin)***
Dose: 1-10 mg Q 24 Hr
Maximum: 20 mg Q 24 Hr



Mixed Acting Agents

- ***MOA***: Antagonize Alpha-1 & beta-1 receptors
- ***Use***: Hypertension
- ***Caution***: Like beta- blockers

Mixed Acting Agents

- ***Carvedilol (Coreg)***- *CYP 450*
Dose: 3.125 mg- 12.5 mg Q 12 Hr
Maximum: 25- 50 mg Q 12 Hr

- ***Labetalol (Trandate, Normodyne)***
Dose: 100- 800 mg Q 12 Hr
Maximum: 1200 mg Q 12 Hr

Calcium Channel Blockers

- ***Dihydropyridines:***

Amlodipine
Felodipine
Nifedipine
Nicardipine

Non- Dihydropridines:
Verapamil
Diltiazem

Dihydropyridines- CCB

- ***MOA***: Inhibit calcium ions from entering vascular smooth muscle cells & reduces vascular resistance. Limited effects on cardiac muscle slowing AV node conduction & reducing heart rate & cardiac output
- ***Use***: HTN; Angina
- ***Caution***: Edema, H/A

Dihydropridines- CCB

- ***Amlodipine (Norvasc)***

Dose: 2.5-5 mg Q 24 Hr
Maximum: 10 mg Q 24 Hr

- ***Felodipine (Plendil)***

Dose: 2.5- 5 mg Q 24 Hr
Maximum: 20 mg Q 24 Hr

- ***Nicardipine (Cardene SR)***

Dose: 30 mg Q 12 Hr
Maximum: 60 mg Q 24 Hr

- ***Nifedipine (Adalat CC, Procardia XL)***

Dose 30 mg-120 mg Q 24Hr
Maximum: 180 mg Q 24 Hr

Non- Dihydropyridines- CCB

- ***MOA***: Inhibit calcium ions from entering cardiac muscle slowing AV node conduction reducing heart rate & cardiac output. Limited effects on vascular smooth muscle leading to reduced vascular resistance
- ***Use***: HTN, angina, rate control
- ***Caution***: Bradycardia, AV Block, Edema, CHF, gingival hyperplasia,, constipation

Non-Dihydropyridines- CCB

- ***Both have many CYP 450 drug interactions***
- ***Diltiazem (Cardizem CD, Tiazac, Dilacor XR)***

Dose: 180-360 mg Q 24 Hr
Maximum: 540 mg Q 24 Hr
Cardizem=Q6-8 Hr; VS Cardizem SR= 12 Hr
IV to PO =~ 1:1
5mg/Hr= 30 mg PO Q 6 Hr
15mg/Hr= 90 mg PO Q6 Hr

Non-Dihydroppyridines- CCB

- ***Verapamil (Calan SR, Isoptin SR, Covera HS)***
- Dose: 240-360 mg Q 24 Hr
- Maximum: 360 mg Q 24 Hr (480 mg Q 24 Hr)
- Verapamil= Q 8Hr, Covera HS= Q 24 Hr @ bedtime

ACE Inhibitors

- ***MOA***: Inhibit ACE enzyme that converts angiotensin I to angiotensin II. Reduction in angiotensinII (vasconstriction) leads to decrease inperipheral vascular resistance. Also leads to bradykinin(vasodilator), reduced aldosterone, and reduced sodium and water retention
- ***Use***: HTN, CHF, post- MI
- ***Caution***: Cough, angioedema, acute renal failure, renal artery stenosis,, hyperkalemia,

Ace Inhibitors

- ***Class I***: Captopril
- ***Class II***: Enalapril (Vasotec) & other pril meds
- Class III: Lisinopril(water soluble)

- ***Note: often with CHF: Enalapril, diuretic, & digoxin is ordered (Left ventricular dysfunction = LVEF < 55%)***

ACE Inhibitor

- ***Not given with Aortic Stenosis***
- Risk of renal Failure
- Risk of volume depletion

- Avoid diuretic excess
- Potassium supplements
- Potassium retainers

Angiotensin II receptor Blockers

- MOA: Antagonize the angiotensin II receptor on vascular smooth muscle leading to a decrease in peripheral vascular resistance
- Use: CHF, HTN
- ***Caution: Cough (Less than with ACE I)***

Angiotensin II Receptor Blockers

- ***Candesartan (Atacand)***

Dose: 8- 32 mg Q 24 Hours

- ***Losartan (Cozaar)***

Dose: 25- 100 mg Q 24 Hour (require some 12 Hour)

- Valsartan (Diovan)

Dose: 80-320 mg Q 24 Hours

Natrecor

- B-type naturetic peptide (BNP)
- Given in acutely decompensated CHF
- IV: Bolus of 2/ mcg/ Kg; followed by infusion of 0.01 mcg/ kg/ min
- No titration
- A side effect may be severe hypotension

Low Molecular Weight Heparin

- ***Enoxaparin (Lovenox)*** Binds to antithrombin III & inactivates thrombin
- Onset in 3- 5 hours
- Ordered sc BID 1 mg/ kg
- In system for up to 24 hours

Advantages:
- Improved bioavailability
- Longer plasma life
- Less bleeding (compared to Heparin)
- Less testing

History of Fibrinolytic agents

- ***Stretokinase***: (protein beta hemlytic strep)
- ***Urokinase***: (human renal cells; not available)
- ***Alteplase***: (TPA) Weight based (copy of human template)
- ***Anistreplase***: streptokinase derivative; greater fibrin specificity

- ***Reteplase: newest RPA; longer half life, may administer a double bolus, may use with GPb/ IIIA inhibitors; weight based***

Thromboembolytic Agents

- Used in early course of AMI
- **Must be started within 4-6 hours of onset of SX**
- **Restores blood flow, limits myocardial damage,** preserve left ventricle, prevent death

Action: accelerates natural fibrinolytic process by activating plasminogen
- Plasminogen generates plasmin
- Plasmin is the enzyme that dissolves clots
- Subsequent reperfusion of myocardium

Thrombolytics

- ***Most common complication is bleeding***

Complications:

- Active internal bleeding
- History of CVA
- Intrcranial issues
- Intracranial, spinal, trauma in the past 2 months
- Thoracic, pelvic, abdominal surgery in past 10 days
- Uncontrolled hypertension
- Recent prolonged CPR

Thrombolytics

- Minimize risk of bleeding
- Apply direct pressure over any puncture site for 20/ 30 minutes
- Monitor all secretions for occult blood
- Monitor neuro changes: slurred speech, lethargy, heniparesis
- Monitor for hypotension, tachycardia, gross hematuria

Narcotics

- ***Morphine:*** Reduces O2 demand, releives anxiety, promotes vasodilation, (decreases HR, BP, & respiratory rate

- ***Demerol***: Atropine- like effect, increased HR