COMMON CARDIOVASCULAR DRUGS
Revised by V'19 cardio group from Dr. Emily Karlin

Introduction

Within this section we will discuss several classes of drugs commonly utilized to treat cardiovascular dysfunction. More detailed info0rmation on the indications, metabolism, dosage, and side effects of individual drugs within these classes can be found in the cardiac drug formulary and other site: **LINK TO DRUG FORMULARY**

I. Angiotensin Converting Enzyme Inhibitors (ACEi) (e.g. enalapril, benazepril, lisinopril)

- **Mechanism of action:** By inhibiting angiotensin converting enzyme, ACE inhibitors interrupt the RAAS system and prevent both the conversion of angiotensin I to angiotensin II and the release of aldosterone. ACEi also increase concentrations of certain vasodilatory substances.
    - Effects: vasodilation, reduced fluid retention, prevention of cardiac remodeling by inhibition of intracardiac RAAS.
- **Indications**
    - Congestive Heart Failure
    - Protein losing nephropathy; glomerulonephritis
    - Systemic hypertension
    - +/- prevention of cardiac remodeling before CHF
- **Side Effects**
    - Hypotension and azotemia (often related to concurrent use of diuretics)
    - Anorexia, depression & GI disturbances

II. Diuretics- Diuretics are the foundation of congestive heart failure therapy. These drugs are routinely used whenever heart disease is accompanied by evidence of congestion (pleural effusion, pulmonary edema, ascites).

A. Loop or "High Ceiling" Diuretics (e.g. furosamide, torsemide)

- **Mechanism of action:** Inhibit the sodium-potassium-chloride cotransporters in the thick ascending limb of the Loop of Henle.
    - Effects: Sodium, potassium, and chloride reabsorption is decreased, so that these ions (and the water that follows) are excreted in urine.
        - Loop diuretics are capable of inducing a natriuresis of 20-25% of the filtered sodium load.
- **Indications**
    - Acute emergency setting or chronic daily use
    - Congestive heart failure (CHF)
        - Left sided CHF: pulmonary edema
        - Right sided CHF: effusions
- **Side effects**
    - Excessive dosage can lead to:

        - Azotemia, weakness, dehydration, lethargy, electrolyte depletion, and hypotension
    - GI disturbances, increased thirst and urination,
    - Ototoxicity when rapidly infused IV

B. Potassium Sparing Diuretics (e.g. spironolactone, eplerenone)

- **Mechanism of action:** Competitively bind receptors in the distal tubule and collecting duct to block the actions of aldosterone. Sodium-Potassium exchange is blocked in this process so that sodium excretion is increased, while potassium is retained.
    - Effects: weak diuretic effect
- **Indications**
    - Congestive heart failure
    - May increase survival in dogs with certain types of heart disease
    - Usually used in combination with a loop diuretic
- **Side effects**
    - GI side effects (vomiting, anorexia)
    - Hyperkalemia

C. Thiazide Diuretics (e.g. hydrochlorothiazide)

- **Mechanism of action:** Inhibit sodium and chloride reabsorption in the renal distal tubule while also promoting potassium and magnesium loss into the urine. As with the other types of diuretics, the loss of these ions promotes water loss by osmotic drag.
    - Effects: moderate diuretic effect
- **Indications**
    - Refractory congestive heart failure
- **Side effects**
    - Azotemia, weakness, dehydration, lethargy, electrolyte depletion, GI effects, and hypotension
    - Less effective in animals with advanced renal failure due to decreased GFR.

III. <u>Pimobendan</u>- Pimobendan is a calcium sensitizing drug.

- **Mechanism of action:** Pimobendan enhances contractile function of cardiomyocytes by enhancing the interactions between troponin C and calcium. It also inhibits phosphodiesterase III, causing peripheral vasodilation.
    - Effects: positive inotrope & vasodilator (“inodilator”)
- **Indications:**
    - CHF in dogs due to DCM and valvular disease
        - Clinical trials have demonstrated improvement of clinical signs, outcome, and survival time in dogs with CHF due to DCM and chronic valvular disease.
    - Asymptomatic dogs with advanced valvular disease
        - A recent clinical trial showed that pimobendan significantly delayed the onset of clinical signs in dogs with asymptomatic chronic valvular disease

    - Often used in cats with CHF, but less research has been done to show the beneficial effects of Pimobendan in felines.
- **Side effects:**
    - Hyperexcitability, possible arrhythmias, and possible GI upset
    - Generally well tolerated

IV. <u>Vasodilators</u> (e.g. nitroglycerin, hydralazine, sodium nitroprusside)

- **Mechanism of action:** Vasodilators act on different locations within the cardiovascular system to cause relaxation of vascular smooth muscle. Vasodilators that act on systemic veins (venodilators) reduce preload, while those that act on systemic arteries (arterial dilators) decrease afterload to increase cardiac output. Other vasodilators act on both arterial and venous vessels to induce balanced vasodilation.
    - Effects: decreased blood pressure, and improved cardiac output
- **Indications:**
    - (Emergency) resolution of life threatening pulmonary edema (nitroglycerin, and sodium nitroprusside)
    - Mitral valve disease and hypertension (hydralazine)
- **Side effects:**
    - Hypotension, lethargy, depression, anorexia, nausea, vomiting, pre-renal azotemia

V. <u>Pulmonary Vasodilators</u> (e.g. sildenafil)

- **Mechanism of action:** Inhibition of Phosphodiesterase 5, found primarily in the smooth muscle of the pulmonary vasculature and corpus cavernosum. Prevents degradation of cGMP. This increase in cGMP increases nitric oxide mediated vasodilation in pulmonary vessels.
- **Indications:**
    - Pulmonary hypertension
    - Refractory CHF
- **Side effects:**
    - Inguinal flushing, possible GI upset, weakness, hypotension
    - Do not use concurrently with nitrates: can cause life threatening hypotension

VI. <u>Antiarrhythmic Drugs-</u> Antiarrhythmic drugs can be separated into the following classes:

- Class I - Na+ channel blockers (local anesthetics)
- Class II - β blockers
- Class III - K+ channel blockers (prolong action potential duration)
- Class IV - Ca++ channel blockers

A. Class I Antiarrhythmic drugs (e.g. procainamide, quinidine, lidocaine)

- **Mechanism of Action:** Block fast Na channels found in cardiac myocytes which slows the influx of sodium during the generation of cardiac action potential.

- **Indications:**
    - Ventricular arrhythmias (lidocaine and procainamide)
    - Conversion of atrial fibrillation to sinus rhythm, especially in horses (quinidine)
    - Local anesthesia
- **Side effects:**
    - GI upset (vomiting, colic), tachycardia
    - neurological side effects (seizures, mental depression, etc.) especially in cats and horse

B. Class II Antiarrhythmic drugs (e.g. propranolol, atenolol, metoprolol)

- **Mechanism of action:** Block β adrenergic which slows conduction through the heart. Different drugs within this class exhibit varying degrees of adrenergic receptor specific- some drugs affect β1 receptors alone, while others can also act on β2 and α receptors
    - Effects: negative inotrope (β1 receptors). May also block beneficial bronchodilation and vasodilation (β2)
- **Indications:**
    - Primarily ventricular arrhythmia, sometimes supraventricular
    - Outflow tract obstruction
    - Possibly systemic hypertension
    - Therapy for pheochromocytoma, thyrotoxicosis and certain intoxications (chocolate toxicity, theophylline overdose)
- **Side effects:**
    - Bradycardia, AV block, hypotension, weakness, fatigue, dizziness, bronchospasm, worsening CHF

C. Class III Antiarrhythmic drugs (e.g. sotalol, amiodarone)

- **Mechanism of action:** Block Potassium channels, which prolongs the repolarization phase of the action potential to slow the heart rate. Some drugs in this class also have properties of other antiarrhythmic drug classes.
- **Indications:**
    - Ventricular arrhythmia
    - Supraventricular arrhythmia
- **Side effects:**
    - Could precipitate CHF (negative inotropic effects)
    - Hepatotoxicity and thyroid abnormalities possible (amiodarone)

D. Class IV Antiarrhythmic drugs (e.g. diltiazem, amlodipine)

- **Mechanism of action:** Drugs in this class target calcium channels, however there is some variation within the class as to which calcium channels are targeted. Some drugs block calcium channels at the SA and AV node, slowing conduction (diltiazem), while others selectively block vascular calcium channels, causing vasodilation (amlodipine).
- **Indications:**
    - Supraventricular arrhythmia (diltiazem)
    - Systemic hypertension (amlodipine)
- **Side effects:**
    - Hypotension, bradycardia, AV block, weakness, lethargy, precipitation of CHF

VII. <u>Cardiac Glycosides</u> (e.g. digoxin)

- **Mechanism of action:** Inhibition of the Na/K ATPase causes intracellular sodium concentration to rise. To mitigate this effect, the cell increases Na/Ca exchanger activity, exporting sodium while taking in more calcium. The increased intracellular calcium concentration enhances myocardial contractility. AV node conduction is also slowed via vagomimetic effects.
    - Effects: positive inotrope, negative chronotrope (slows heart rate)
- **Indications:**
    - Supraventricular arrhythmia (atrial fibrillation, SVT)
    - CHF
    - Vasovagal syncope (by restoring baroreceptor function)
- **Side effects:**
    - Anorexia, depression, salivation, vomiting, diarrhea, development of secondary cardiac arrhythmias