Heart failure pharmacology

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Pathophysiology review

- Heart failure occurs when the cardiac output (CO) is insufficient to meet the metabolic demands of the body
- CO = HR × SV (Cardiac Output = Heart Rate × Stroke Volume)
 - Stroke volume depends on preload, afterload, and myocardial contractility
- HF is divided reduced ejection fraction (HFrEF) and or preserved ejection fraction (HFpEF)
- Pharmacotherapeutics generally involve a combination of three medication classes:
 - o Diuretic
 - o RAAS inhibitor
 - Beta blocker
- Patient education is critical to prevent readmission. This includes education on medication compliance, reduced sodium diet, self-monitoring, and exercise.
- Left-Sided HF Symptoms: Fatigue, exertional dyspnea, orthopnea, cough, and pulmonary rales
- Right-Sided HF Symptoms: Peripheral edema, jugular venous distension (JVD), and ascites.
- BNP (B-type Natriuretic Peptide) or NT-proBNP is a common lab for HF
- Ejection fraction from an echocardiogram is the most used imaging for diagnosing heart failure
- Monitor fluid status in all HF patients

Drug class: Angiotensin Converting Enzyme Inhibitors (ACEI)

- Drugs:
 - Lisinopril (Zestril)
 - Captopril (Capoten)
- MOA: Inhibit the conversion of angiotensin one to angiotensin two
- Indications: HTN, ACS, chronic kidney disease, stroke prevention, and heart failure
- SE/AE: Kidney injury, angioedema, cough, and hyperkalemia
 - o Captopril can cause neutropenia
- Black Box warning: Teratogenic

Drug class: Angiotensin Receptor Blockers (ARB)

- Drugs:
 - Losartan (Cozaar)
 - Valsartan (Diovan)
- MOA: Inhibits angiotensin two receptors
- Indications: HTN and kidney disease
- SE/AE: Kidney injury and hyperkalemia
- Less likely to have a cough and angioedema versus ACEI

Black Box warning: Teratogenic

Drug class: Beta one adrenergic antagonists (Beta blockers)

- Drugs:
 - Nonselective:
 - Propranolol
 - Cardioselective:
 - Metoprolol
 - Atenolol
 - Esmolol
 - Non-selective with vasodilating effects:
 - Labetalol
 - Carvedilol
- MOA: Blocks beta one receptors, reducing cardiac chronotropy and inotropy
- Indications: Angina, HTN, heart failure, AMI, dysrhythmias, migraines prevention, anxiety
- SE/AE: Fatigue, bradycardia, hypoglycemia, sexual dysfunction
- Black Box warning: Abrupt discontinuation can cause adverse cardiac effects
- Caution in using a nonselective with underlying pulmonary conditions,
 - Can cause bronchoconstriction
- Often used option for HTN in pregnancy
- Carvedilol is used primary for heart failure
- Assess HR and BP prior to admin

Drug class: Loop diuretics

- Drugs:
 - Bumetanide (Bumex)
 - Furosemide (Lasix)
 - Torsemide
- MOA: Blocks reabsorption of sodium and chloride in the Loop of Henle (Nephron loop)
- Indications: Edema related to heart failure, liver failure, kidney failure, alternative for hypertension
- SE/AE: Ototoxicity, hypokalemia
- Black Box warning: can cause fluid and electrolyte imbalances
- Most potent class of diuretics
- Patient education: Do not increase your sodium intake
- Reassess based on the route of administration

Drug class: Potassium sparing diuretics (Aldosterone antagonist)

- Drug:
 - Spironolactone
- MOA: Blocks aldosterone (aldosterone increases sodium and water reabsorption)
- Indications: Hypertension, edema and heart failure
- Black box warning: Found to cause tumors in animals

- SE/AE: Hyperkalemia (especially when taking ACEI/ARB)
 - Reproductive / endocrine (i.e. gynecomastia, ED, decreased libido, irregular bleeding)

Drug class: Cardiac glycosides

- Drug:
 - Digoxin (Lanoxin)
- MOA: Increased effects of calcium resulting in increased contractility
- Indications: Dysrhythmias (atrial fibrillation and flutter) and HF with reduced EF (HFrEF)
- SE/AE: Nausea and vomiting, visual disturbances (notably halos), bradycardia, dysrhythmias
- · Patients should have heart rate, rhythm and digoxin levels monitored when initiating treatment
- Antidote available for digoxin toxicity called digoxin-immune fab

Drug class: Phosphodiesterase inhibitors (PDI)

- Drugs:
 - o Amrinone
 - Milrinone
- MOA: Inhibiting phosphodiesterase resulting in increased contractility and vasodilation
- Indications: Heart failure with reduced EF
- SE/AE: Dysrhythmias and hypotension
- Amrinone is less frequently used due to side effects such as thrombocytopenia

Drug name: Sacubitril-Valsartan (Entresto)

- MOA: Inhibits neprilysin which increases vasodilation plus blocks the RAAS
- Indications: Heart failure
- Also referred to as an ARNI (angiotensin receptor, neprilysin inhibitor)
- Not safe in pregnancy

Drug name: Isosorbide Dinitrate - Hydralazine (Bidil)

- MOA: Isosorbide Dinitrate dilates veins; Hydralazine dilates arteries
- Indications: Heart failure with reduced EF (HFrEF)
- SE/AE: Hypotension, tachycardia, headache
- Avoid with PDE-5 inhibitors
- Often dosed multiple times per day

Drug class: Sodium-glucose co-transporter 2 inhibitors (SGLT-2 inhibitors)

- Drugs:
 - Dapagliflozin (Farxiga)
 - Empagliflozin (Jardiance)
- MOA: Promote urinary glucose excretion; it also reduces cardiac preload and afterload
- Indications: Diabetes, chronic kidney disease, and heart failure
- SE/AE: UTI in females and weight loss

Nitroglycerine is another vasodilator that is used for heart failure. It is discussed in the angina lecture

Mechanical Circulatory Assistive Support (MCAS): Includes devices like LVADs, intra-aortic balloon pumps (IABP), and extracorporeal membrane oxygenation (ECMO) to support circulation in severe heart failure or cardiogenic shock. Heart transplant is also an option for the definitive treatment of heart failure.

Drug class: Vasopressors / Vasoconstrictors

- Drugs:
 - o Epinephrine (Adrenalin)
 - Alpha and beta-adrenergic activation
 - Norepinephrine (Levophed)
 - Alpha and beta-adrenergic activation
 - Phenylephrine (Neo-synephrine) *Does not increase contractility (no "pressor" support)*
 - Alpha adrenergic activation
 - Dopamine
 - Low dose: Dopaminergic activation (increased perfusion to the kidneys)
 - Medium dose: dopaminergic and beta-adrenergic activation
 - High dose: alpha adrenergic activation
 - Isoproterenol Does not cause vasoconstriction
 - Beta adrenergic activation
 - Dobutamine Does not cause vasoconstriction
 - Beta adrenergic activation
- MOA: activates adrenergic and dopaminergic receptors as noted above
- Indication: Shock
- SE/AE: tachycardia and palpitations
- Black Box warning: Can cause extravasation
 - Is treated with phentolamine
 - o Should be given via central line to reduce this risk
- Standard practice is to always infuse through a pump
 - Should ideally be given via a central line to reduce the risks of infiltration
- Doses are titrated to target BP (or MAP)
- Do not stop abruptly, must be tapered down
- Epinephrine and norepinephrine are most commonly dosed in mcg/min starting at 2-5mcg/min
- Dopamine is most commonly dosed in mcg/kg/min starting at 2-5 mcg/kg/min
- Dopamine can cause tachydysrhythmias
- Epinephrine 1:10,000 is the concentration for infusion
 - o Epinephrine 1:1,000 is the concentration for anaphylaxis (i.e. epi pen)
 - Stable allergies may be treated with diphenhydramine, albuterol, steroids, o2
- Does not correct underlying issue in shock related to volume loss

References

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