CARDIOLOGY 2024

Heart Failure Medications

Stacy Reynolds, DNP, RN, CPNP

Friday February 16, 2024

Children's Mercy KANSAS CITY

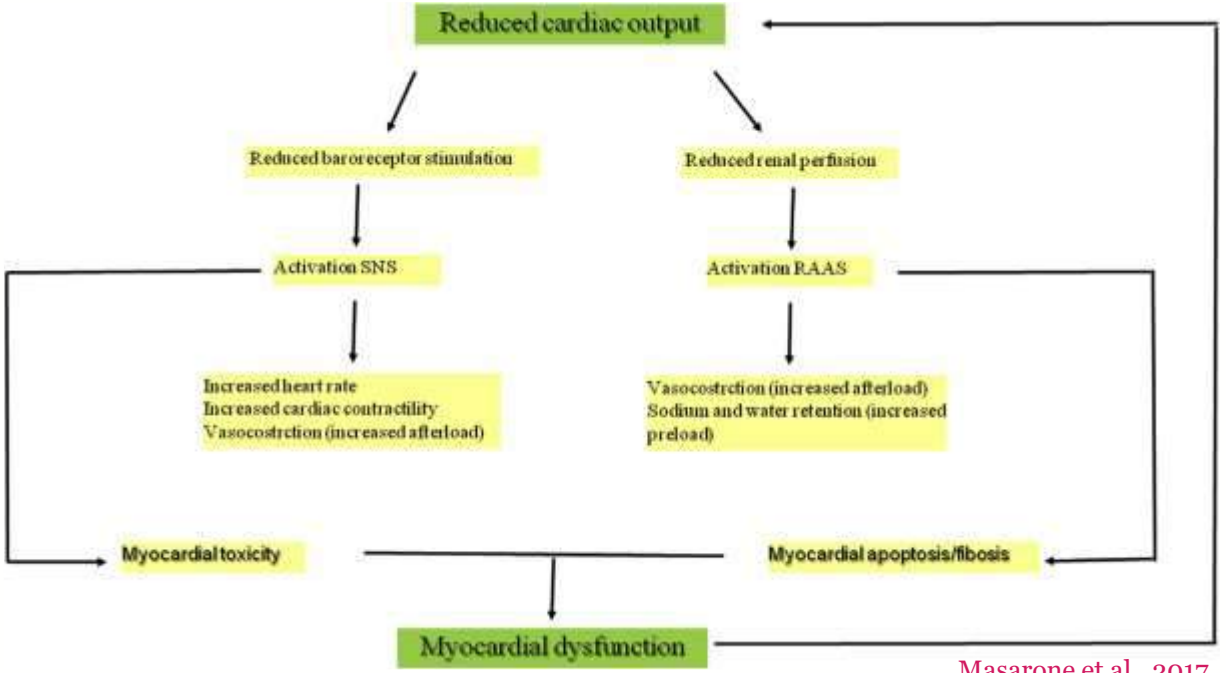
PEDIATRIC HEART FAILURE

- A clinical and pathophysiological syndrome that results from ventricular dysfunction, volume or pressure overload, or both
- Congenital heart disease and cardiomyopathies are the most common causes of pediatric heart failure
- Can be acute, chronic, advanced or end-stage
- Burden is rising in the US
  - Nearly 2-fold increase in ER visits
  - 24-fold increase in hospital charges (Amdani et al., 2022)
- Associated with significant morbidity, hospitalizations and mortality

PEDIATRIC HEART FAILURE

- Limited data
  - 2014 ISHLT guidelines only 8 Class I (strong) guidelines
  - Level of evidence B
- Pediatric guidelines based on expert consensus and mirror adult recs
  - Less certainty d/t lower quality of evidence
- ACEi and BB have not shown to improve transplant free survival or improve symptoms
- Barriers to clinical trials in children
- HF in children differs from HF in adults

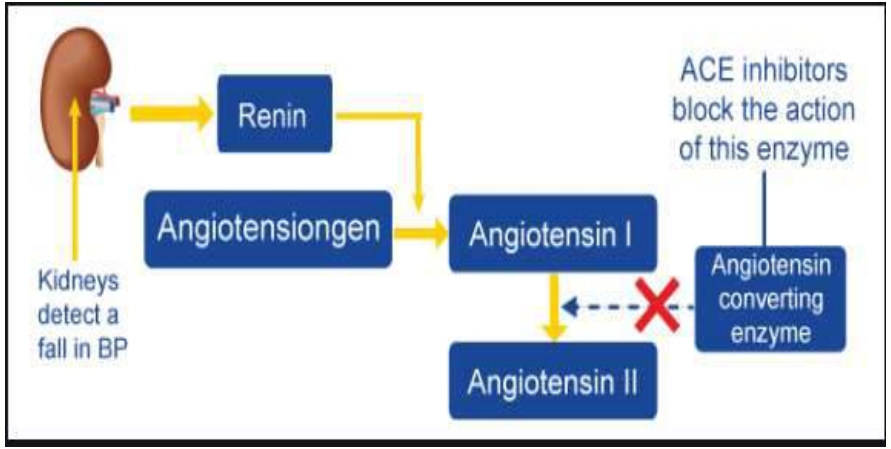
HEART FAILURE



Masarone et al., 2017

ACE INHIBITORS

- Angiotensin converting enzyme inhibitors
  - Blocks the conversion of angiotensin I and II
  - Activates Bradykinin (dry cough SE) and Kallidin
  - Causes vasodilation and naturesis
  - Reduces afterload
  - Helps prevent cardiac remodeling



ACE INHIBITORS

- Used for heart failure and hypertension
  - ISHLT Heart Failure State B-D
- Not recommended for asymptomatic children with mild dysfunction
- No recommended for routine use in single ventricle CHD patients with right ventricle as systemic ventricle
- Limited large randomized controlled trials in pediatrics

ACE INHIBITORS

	Enalapril Epaned/Vasotec	Lisinopril Zestril/Prinvil	Captopril
Infants	0.1mg/kg/day	0.07mg/kg/dose – 5mg	0.01- 0.3mg/kg/dose
Children <6 yrs	0.1mg/kg/day	0.07mg/kg/dose – 5mg	0.3-0.5mg/kg/day
> 6yrs & Adolescents	0.1mg/kg/day	0.07mg/kg/dose – 5mg	0.3-0.5mg/kg/day
Dosing Frequency	Daily or BID	Daily	Infants q6-24 hrs Others q8-12 hrs
Adjustment	Over 2 weeks	Every 1-2 weeks	Every 1-2 weeks
Max Dosage	0.5mg/kg/DAY	0.6mg/kg/day - 40mg	6mg/kg/day

ACE INHIBITORS

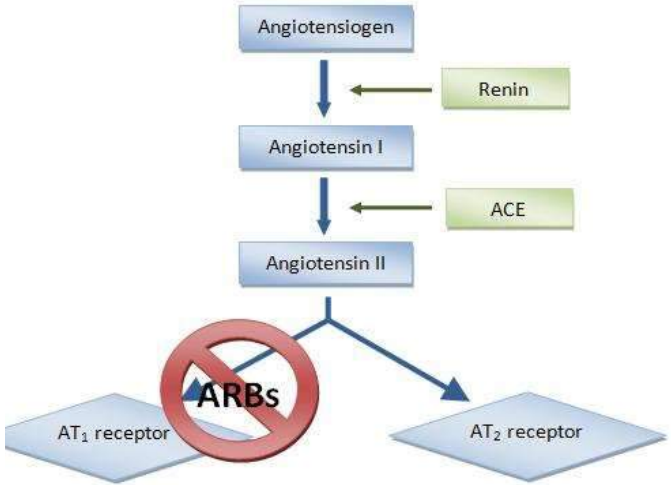
- Caution in renal impairment!
- Can make renal function worse
- Side effects include angioedema, hypotension, proteinuria, hyperkalemia, dry non-productive cough

ANGIOTENSIN RECEPTOR BLOCKERS (ARB)

- Used to treat heart failure and hypertension
- Can be used for those who do not tolerate ace inhibitors
- Limited studies in pediatric heart failure

ANGIOTENSIN RECEPTOR BLOCKERS

- Mechanism of action
  - Selective, angiotensin II receptor antagonist
  - Blocks vasoconstrictor & aldosterone-secreting effects of angiotensin II
  - May induce more complete inhibition of renin-angio system than ACE inhibitors
  - No release of bradykinin so no SE of dry cough



Hussey & Weintraub, 2016

ANGIOTENSIN RECEPTOR BLOCKERS

	Losartan Cozaar	Valsartan Diovan
Infants	Not recommended	1mg/kg/dose
Children <6 yrs	Not recommended	1mg/kg/dose
> 6yrs & Adolescents	0.7mg/kg	1mg/kg/dose
Dosing Frequency	Daily or BID	Daily
Adjustment	Every 2 weeks	Every 2 weeks
Max Dosage	1.4mg/kg/dose or 100mg/day	Infants 4mg/kg/day Others 4mg/kg/day not to exceed 160mg/DAY

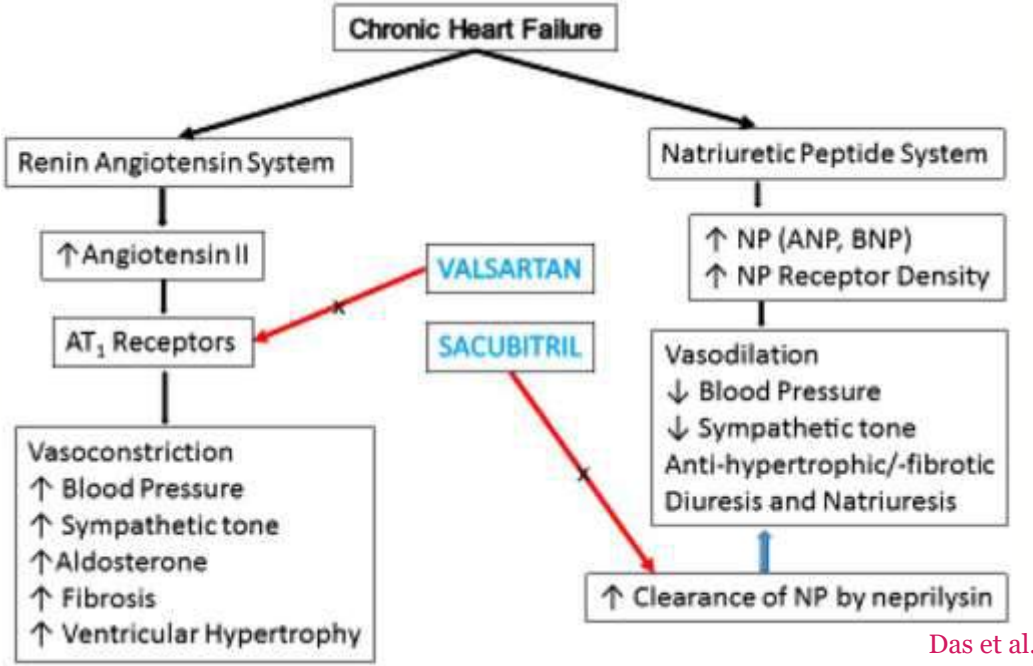
ANGIOTENSIN RECEPTOR BLOCKERS

- Dizziness, hypotension, vertigo, drowsiness, hyperkalemia
- Abdominal pain, back pain, diarrhea, joint pain, dry cough
- Monitor creatinine and potassium
  - Unable to urinate, decreased urine output, weight gain
  - Avoid hyperkalemia
  - May need to adjust diuretics
- Use caution in patients with liver disease
- Losartan not recommended for children <6 yrs

ENTRESTO

- Combination pill that contains Sacubritril and Valsartan
- Sacubitril is a neprilysin inhibitor
- Valsartan is an ARB that decreases the effects of the renin-angiotensin-aldosterone system
- Adult data shows Entresto is superior to ACE in managing heart failure and keeping patients out of the hospital
- Clinical trial to evaluate safety in pediatric patients 1 month to < 18 years with LV systolic dysfunction (Shaddy et al., 2023)
  - PANORAMA-HF trial

ENTRESTO



Das et al., 2018

CONVERTING FROM ACE OR ARB TO ENTRESTO

- **Can NOT be given with an ACE inhibitor**
- Need to allow 36-hour washout period when transitioning from ACE
  - Children and Adolescents <40kg
    - Initial: 1.6mg/kg/dose BID
    - Titrate in 2 weeks: 2.3mg/kg/dose BID
    - Titrate in 2 weeks: 3.1mg/kg/dose BID
  - 40 to 50kg
    - Initial: Sacubitril 24mg/Valsartan 26mg BID
    - Titrate in 2 weeks: Sacubitril 49mg/Valsartan 78mg BID
    - Titrate in 2 weeks: Sacubitril 72mg/Valsartan 78mg BID
  - >50kg
    - Initial: Sacubitril 49mg/Valsartan 51mg BID
    - Titrate in 2 weeks: Sacubitril 72mg/Valsartan 78mg BID
    - Titrate in 2 weeks: Sacubitril 97mg/Valsartan 103mg BID

ENTRESTO

- Contraindicated in patients with history of angioedema
- Cannot be given concomitant or within 36 hours of ACE inhibitors
- Common side effects include: symptomatic hypotension, cough, dizziness, syncope, fatigue
- Decrease in renal function: monitor UOP, creatinine, electrolytes
- Hyperkalemia: Use caution or do not use with potassium-sparing diuretics, potassium supplements or potassium containing salts.

BETA BLOCKERS

- Impact neurohormonal pathway by decreasing systemic catecholemines in patients with heart failure
- Improve systolic and diastolic function through afterload and preload reduction, heart rate control and prevention of arrhythmias
- First pediatric RCT using Carvedilol
  - No significant improvement in HF symptoms
  - Did not significantly improve HF outcomes
- Adult studies have shown BB are beneficial in decreasing symptoms, hospitalizations and mortality

BETA BLOCKERS

	Carvedilol Coreg	Metoprolol Lopressor, Toprol
Infants	0.04-0.75mg/kg/dose	Not recommended
Children <6 yrs	0.04-0.75mg/kg/dose	0.1 to 0.2mg/kg/dose
> 6yrs & Adolescents	0.04-0.75mg/kg/dose	0.1 to 0.2mg/kg/dose
Dosing Frequency	Daily or BID	BID
Adjustment	Every 2 weeks	Every 2 weeks
Max Dosage	1mg/kg/day up to 50mg/day	2mg/kg/day up to 200mg/kg/day

CARVEDILOL

- Nonselective but has alpha adrenergic blocking
- Reduce peripheral and coronary vascular resistance
- Benefit of lower dose
- Children can metabolize faster, need close monitoring
- Avoid in bradycardia, asthma or severe liver disease
- Serious SE
  - Dizziness, slow HR, edema, shortness of breath, CP, bronchospasm, hyperglycemia, HA
- Common SE
  - Weakness, diarrhea, dry eyes, FATIGUE, weight gain

METOPROLOL

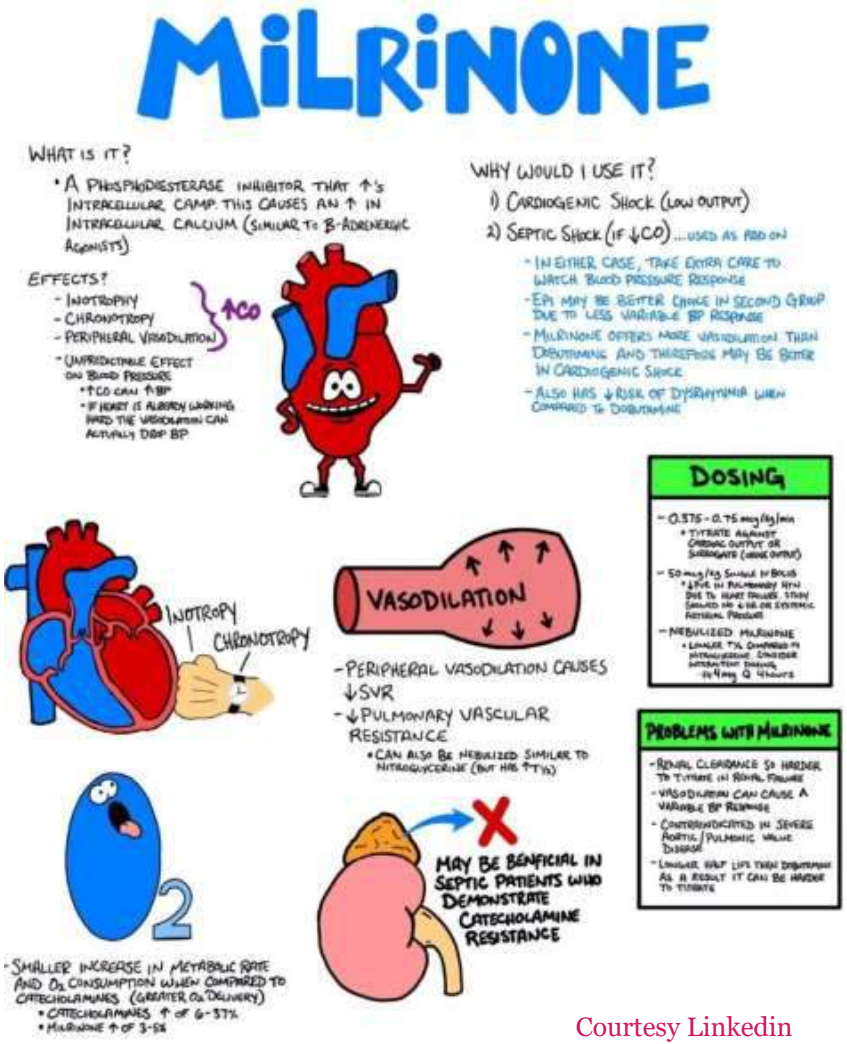
- Beta 1 receptor blocker
- Improvement in left ventricular function
- Abrupt withdrawal can exacerbate underlying conditions
  - Angina pectoris, sinus tachycardia, hypertension, arrhythmias
- Extended-release formula indicated for HF
- Significant drug interactions
- Common SE
  - FATIGUE, dizziness, depression, SOB, hypotension, bradycardia, diarrhea, rash, HA
- Severe SE
  - Edema, CP, bronchospasm, double vision, rapid weight gain, tingling in extremities

MILRINONE

- Phosphodiesterase inhibitor
  - Inhibits PD3 which increases cAMP
  - Alters intracellular and extracellular calcium transport
  - Relaxes arterial and venous smooth muscle
  - Must be given IV

MILRINONE

- Systemic Circulation
  - Vasodilation
  - Increased organ perfusion
  - Decreased SVR
  - Decreased arterial pressure
- Cardiopulmonary
  - Increased contractility and HR
  - Increased SV and EF
  - Decreased preload
  - Decreased PCWP
  - Lusitropy
  - Decreased myocardial oxygen consumption



Courtesy Linkedin

MILRINONE

- Used as inotropic support in neonatal and pediatric heart failure
- Limited studies in pediatrics
  - Most research focuses on use after cardiac surgery
  - Likely shows positive impact of Milrinone use in pediatric heart failure compared to adult data
- Largely replaced dobutamine
- Potential use for home inotropic therapy
- Can also be used as bridge to transplant

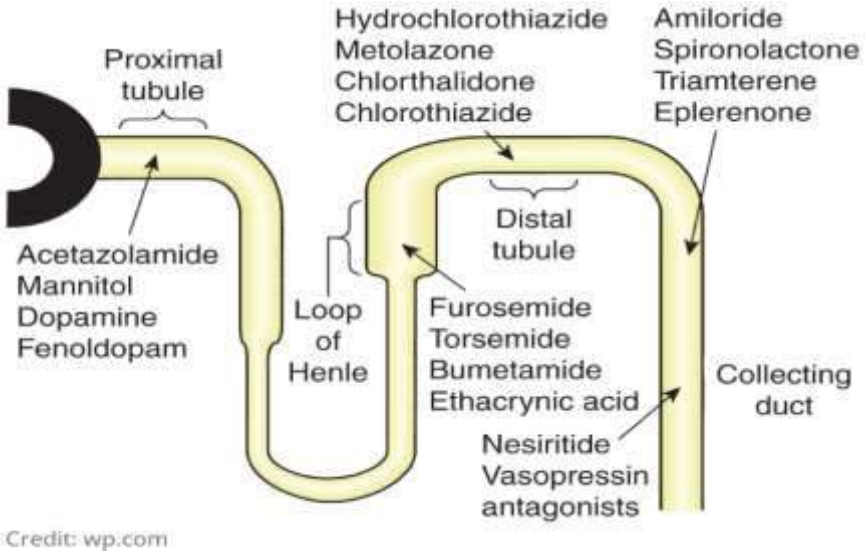
Weisert et al., 2022, Masarone et al., 2017; Deshpande et al., 2016; Hussey & Weintraub, 2016; Birnbaum et al., 2014

MILRINONE

- Bolus is not recommended in heart failure patients
- Usual starting dose 0.25mcg/kg/min up to 1mcg/kg/min
- Can be given peripherally and centrally
- Monitoring parameters include blood pressure, heart rate, ECG; platelet count, electrolytes and fluid status, renal function; infusion site
- Side effects include tachycardia, ventricular arrhythmias, headache, hypotension, cutaneous flushing, nausea and abdominal pain
- Vasodilator

SPIRONOLACTONE

- Mineralocorticoid antagonist
  - Distal tubule
  - Aldosterone antagonist
  - Inhibits Na reabsorption
  - Inhibits K secretion
- Can improve myocardial relaxation
- Helps prevent fibrosis and remodeling
- Decreases mortality associated with ventricular dysfunction and arrhythmias



SPIRONOLACTONE

- Promotes magnesium and potassium retention
- Common SE include nausea/vomiting, stomach cramps, diarrhea, leg cramps
- Serious SE include slow/irregular heartbeat, tingling in extremities, muscle weakness, shortness of breath
  - Think hyperkalemia

DIGOXIN-WHAT IS OLD IS NEW AGAIN!

- Digitalizing dose not usually needed in HF
- Dosages based on normal renal function
- Common SE – dizziness, rash, abdominal pain, N/V, decreased appetite
- Severe SE – bloody emesis, bloody stools, vision changes (halos), fast or slow heartrate, lethargy, confusion.
- Monitor for toxicity – esp with yellow/green tinted vision

	Digoxin
Infants up to 24 months	10-15mcg/kg/day
2-5 years	8-10mcg/kg/day
5-10 years	5-10mcg/kg/day
>10 years	2.5mcg/kg/day
Dosing Frequency	BID
Adjustment	As needed
Max Dosage	1mg/kg/day up to 50mg/day

QUESTIONS?