Cardiac Glycosides and drugs for heart failure

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Treatment of Heart failure

- Systolic dysfunction
  - Coronary artery disease, MI or angina
- Diastolic dysfunction
  - Wall thickened due to long standing hypertension
- NYHA Grade I to IV

Diuretics

- High ceiling diuretics
- IV in acute LVH
- Resistance develops later on, so combined along with metolazone or spironolactone
- Mild cases can be maintained on diuretics with ARBs

ACE inhibitors

- Most commonly used now
- Symptomatic as well as disease modifying benefits
- In all grades of CCF, even in asymptomatic patients

β-blockers

Carvedilol, bisoprolol, metoprolol, nebivolol

Advantages:

1) Reduce cardiac activity

2) Reduce cardiac remodeling due to compensatory sympathetic over activity in heart failure patient

Aldosterone antagonist

- Spironolactone/Eplerenone
- Aldosterone:-
  - Increase ECF (preload)
  - Remodeling
  - Hypokalemia
- Current:- Add-on to ACE inhibitors and other therapy in moderate to severe cases with reduced EF and refractory cases to Diuretic furosemide
  - Only low doses(12.5-25 mg/day) to avoid hyperkalemia

Vasodilators

- IV in acute heart failure that occurs episodically in advanced cases , orally in chronic therapy (Limited role)

1) Venodilators:- IV nitrates, reduces preload
   - Specially in raised CVP and dilated cardiomyopathy in post MI cases
   - Tolerance gradually develops

2) Arteriolar dilators:- hydralazine, minoxidil, nifedipine, reduce afterload
   - Tachycardia and fluid retention

3) Mixed dilators:- ACE inhibitors, ARBs, nitroprusside

Nitroprusside IV + loop diuretics+ inotropic drugs: highly efficacious in severely decompensated patients

*Contraindication to ARBs/ACE inhibitors, A+V

Ivabradine

- Pure bradycardia producing antianginal drug
- Useful in Grade II to Grade IV patients with HR>70/min (C/I to β blockers or HR>75/min after β blockers)
- Add-on therapy
- Does not have cardio-protective property

Inotropic drugs

Dobutamine and dopamine

- 2-8 µg/kg/min IV dobutamine
  - Acute heart failure, decompensated CCF
- 3-10 µg/kg/min IV dopamine
  - Cardiogenic shock

- Low dose leads to improved renal perfusion
- Tolerance & Cardio toxic potential, not useful in long-term CCF

Phosphodiesterase 3 inhibitors

Inodilators (increase cAMP)

- Inamrinone
- PDE-3, located in heart, blood vessels and bronchial muscles
- By IV route, effects start in 5 minutes and remain upto 2-4 hours
- Side effects:- thrombocytopenia(Not used now), nausea, vomiting, diarrhea

Milrinone is preferred due to lesser side effects and more selective and potent

Current:- only short term IV treatment additional to regular treatment in severe and refractory CCF

Myofilament calcium sensitizer

Levosimendan, pimobandan

- Also inodilator, but different mechanism
  - Inotropic: increase sensitivity of Tn C towards Ca2+
  - Dilator: K+ channel opening
  - Also PDE3 inhibitor

Nesiritide

- Recombinant brain natriuretic peptide (BNP)
- Natriuresis + vasodilatation
- Symptomatic improvement
- Approved recently for IV use in refractory cases, but no long term benefits

Angiotensin Receptor/Neprilysin Inhibitor(ARNI)

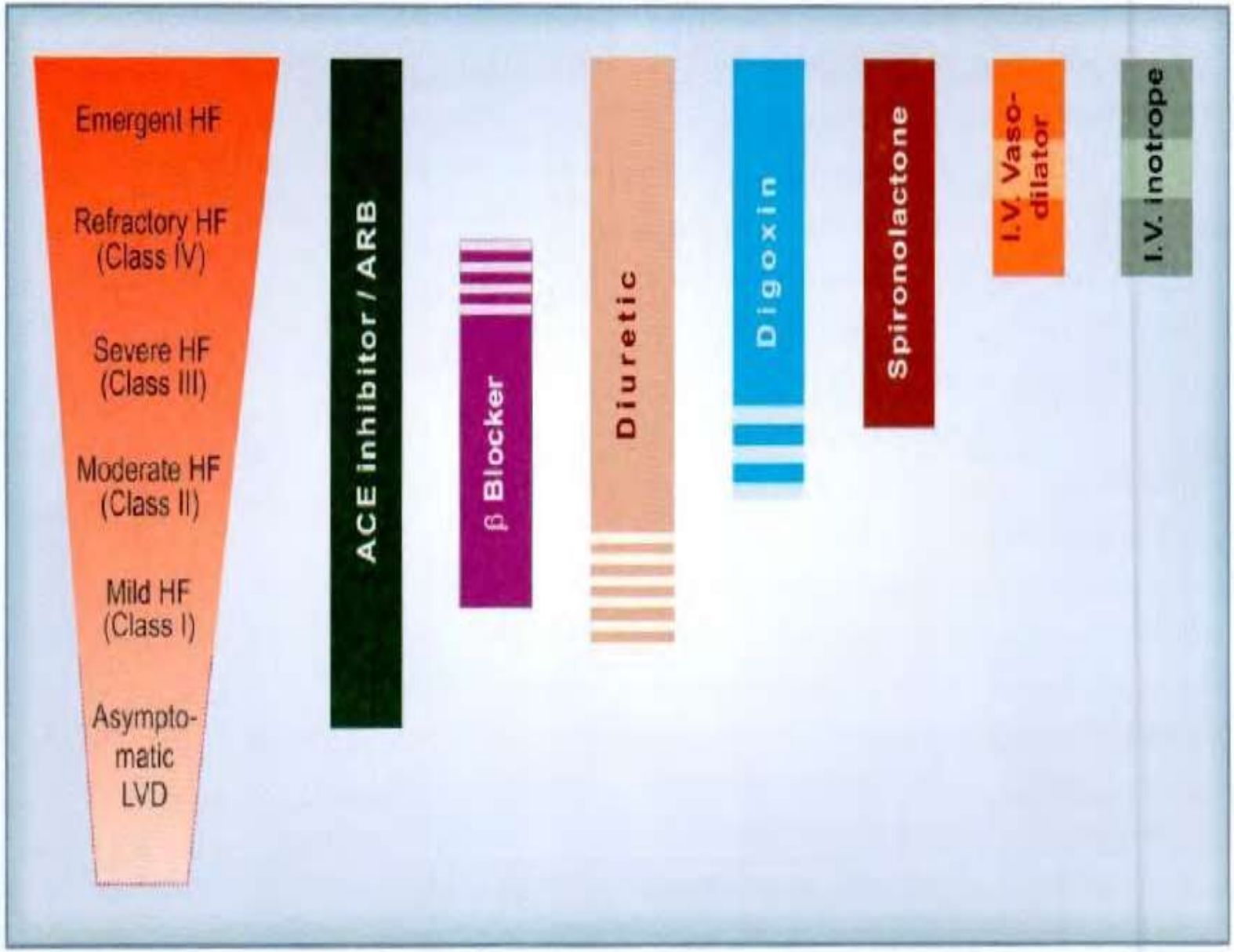
Sacubitril/Valsartan

- Neprilysin degrades ANP,BNP and other vasodilator peptides
- Produces: vasodilatation, natriuresis and diuresis
- Current: Advance decompensated heart failure combined along with Valsartan

Tolvaptan:

V2 Receptor antagonist

Useful in SIADH and advanced CHF


Emergent HF
Refractory HF (Class IV)
Severe HF (Class III)
Moderate HF (Class II)
Mild HF (Class I)
Asympto-matic LVD
ACE inhibitor / ARB
β Blocker
Diuretic
Digoxin
Spironolactone
I.V. Vaso-dilator
I.V. inotrope

Reference

Author	Results	Journal	Level
Claudio borghi, Stefano omboni	As per current guidelines ACE inhibitors are preferred in CHF	Advances in Therapy	Level I

Thank you