



432



Pharmacology Team

Helpful file for " heart failure drugs"

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Drugs used in the treatment of heart failure

Drugs That Increase Contractility	<u>Drugs that decrease preload</u>	<u>Drugs that decrease afterload</u>	<u>Drugs that decrease preload & afterload</u>
Cardiac glycosides Phosphodiesterase inhibitors β- adrenoceptor agonists	Diuretics Venodilators	Arteriolodilators	- ACEI & ARB - α ₁ -adrenoceptor antagonists -Directly-acting vasodilators

<u>Drugs that increase contractility</u>		CARDIAC GLYCOSIDES Digoxin	β -Adrenoceptor agonists	Phosphodiesterase Inhibitors Bipyridines :(Amrinone ,Milrinone)
PHARMACOKINETICS	<p>Drug has narrow therapeutic index</p> <p>Absorption: orally : 40-80% I.V. : acts within 15 min-3hrs</p> <p>Distribution & Metabolism: 25% protein bound, cumulative, metabolized in liver to cardioactive metabolite</p> <p>Elimination; Slow, mainly renal , $t_{1/2}$ 40 hrs</p>	<p>Dopamine :Acts on: α , β_1 and dopamine receptors. Uses: acute H.F. mainly in patients with impaired renal blood flow.</p>	<p>Dobutamine : More Selective β_1 agonist acute heart failure & Cardiogenic shock</p>	<p>only available in IV form. Half-life 3-6hrs. Excreted in urine.</p>
Mechanism of action	Inhibits Na^+ / K^+ ATP ase			<p>inhibit phosphodiesterase isozyme 3 in cardiac & smooth muscles \rightarrow :\uparrow cAMP</p> <p>In the heart : Increase myocardial contraction</p> <p>In the peripheral vasculature : Dilatation of both arteries & veins \rightarrow \downarrow afterload & preload.</p>
PHARMACOLOGICAL ACTIONS:	<p>CARDIAC:</p> <p>1- Increase the force of myocardial contraction (+ve inotropic)\rightarrow Marked increase in CO</p>			
Therapeutic uses	2- Slow heart rate Mediated through vagal nerve stimulation			
	-Congestive heart failure -Atrial flutter / Atrial fibrillation			For short -term management of heart failure { acute heart failure }
adverse effects	<p>-CARDIAC Arrhythmias</p> <p>- GIT upset : The earliest signs of digoxin toxicity(Anorexia ,nausea)</p> <p>-C.N.S. :Headache, visual disturbances, drowsiness</p>			<p>Nausea ,vomiting</p> <p>Arrhythmias (less than digitalis)</p> <p>Thrombocytopenia</p> <p>Liver toxicity</p> <p>Milrinone less toxic than amrinone</p>
Factors increase digitalis toxicity	<p>Small Lean body mass Renal diseases</p> <p>Hypokalemia</p> <p>Hypomagnesemia</p> <p>Hypercalemia</p>			
Treatment OF ADVERSE EFFECTS	<p>Drugs stop Digoxin</p> <p>Atropine</p> <p>Antiarrhythmics</p> <p>K supplements</p> <p>FAB fragment life saving</p>			
Contraindications	<p>Toxic myocarditis-</p> <p>Constrictive pericarditis</p>			

Drug interactions	Diuretics → hypokalemia (arrhythmia)		
	Quinidine : ↑ plasma level of digitalis		

Drugs used to reduce preload		Reduction of Afterload
Diuretics	Venodilators	Arterioldilators :
<p>-Among First-line therapy of heart failure</p> <p>- Remove the signs and symptoms of volume overload (pulmonary congestion/ peripheral edema)</p> <p>Reduce salt and water retention → ↓ ventricular preload and venous pressure.</p> <p>Reduction of cardiac size → improve cardiac performance</p> <p>e.g. Furosemide , Hydrochlorothiazide , spironolactone</p> <p>.</p>	<p>-Nitroglycerine is used for short term IV treatment of severe heart failure and relief dyspnea due to pulmonary congestion.</p> <p>-Dilate large capacitance veins and reduce preload.</p>	<p>Hydralazine reduce after-load in CHF. Used when the main symptom is rapid fatigue due to low cardiac output.</p>

MECHANISM OF ACTION of	
Angiotensin converting enzyme inhibitors	Angiotensin receptor blockers
<p>slide 42</p> <p>e.g. captopril (ACEI)</p>	<p>Block AT₁ receptors → decreasing the action of angiotensin II</p> <p>e.g. losartan (ARB)</p>

ACE Inhibitors & Angiotensin Receptor Blockers :

Along with digitalis and diuretics are now considered as first –line drugs for heart failure therapy

Effects of converting enzyme inhibitors & angiotensin receptor blockers in heart failure

- ↓Peripheral resistance (Afterload)
- ↓Venous return (Preload)
- ↓sympathetic activity
- ↓cardiac remodeling →↓mortality rate

Direct acting vasodilators:

- **Sodium nitropruside**
 - ❖ given I.V. in acute or severe refractory heart failure, acts immediately and effects lasts for 1-5 minutes.

Uses of β-adrenoceptor blockers in heart failure:

- Reduce catecholamine myocyte toxicity (remodeling)
- Decrease mortality rate
- Decrease heart rate
- Inhibit renin release
- e.g. Carvedilol, Metoprolol ,bisoprolol

Management of	
chronic heart failure	acute heart failure
<ul style="list-style-type: none">➤ Reduce work load of the heart<ul style="list-style-type: none">❖ Limits patient activity❖ Reduce weight❖ Control hypertension➤ Restrict sodium➤ Diuretics➤ ACEI or ARBs➤ Digitalis➤ β- blockers➤ Vasodilators	<ul style="list-style-type: none">● Volume replacement● Diuretics● Positive inotropic drugs● Vasodilators● Antiarrhythmic drugs● Treatment of myocardial infarction

***additional file "thanks modhi"**