Drugs for Heart Failure

* Heart failure is a serious, progressive disorder characterized by ventricular dysfunction, reduced cardiac output, insufficient tissue perfusion, and signs of fluid retention (e.g., peripheral edema, shortness of breath).
* Of the estimated 4.8 million Americans who have heart failure, 10% are likely to die within 1 year, and 50% within 5years.
* Heart failure is commonly referred to as congestive heart failure. This term has been used because heart failure frequently causes fluid accumulation (congestion) in the lungs and peripheral tissues.
* However, since many patients do not have signs of pulmonary or systemic congestion, the term heart failure seems more appropriate.
* The principle drugs employed for treatment are angiotensin-converting enzyme (ACE) inhibitors, diuretics, beta blockers, and digoxin.
* A new drug for heart failure- spironolactone-may also be used.

Treatment goals and Strategies

* Therapy of heart failure has three major goals;
1. Relief of pulmonary and peripheral congestive symptoms,
2. Improvement of functional capacity and quality of life, and
3. Prolongation of life expectancy.
4. To achieve these goals, three strategies are employed.
5. First, we need to treat correctable underlying causes of heart failure, such as hypertension, dysrhythmias, and aortic stenosis.
6. Second , we need to implement nondrug measures.
7. Third, if the first two strategies prove inadequate, drug therapy should be employed.

Nondrug Therapy of Heart Failure

* Nondrug measures are an essential component of treatment.
* Salt intake should be limited to 2 gm/day.
* Excessive fluids must be avoided.
* Obese patients should be encouraged to adopt a reduced-calorie diet.

In the past, bed rest was recommended. However, regular mild exercise (e.g., walking, cycling) is now advised: Being active helps avoid atrophy of skeletal muscle, and there are no data indicating that activity is harmful.

* Alcohol ingestion should be discouraged.
* Excessive, chronic consumption of alcohol is a leading cause of cardiomyopathy.
* In patients with heart failure, acute consumption of alcohol can suppress contractility.
* Accordingly, patients who drink alcohol should be advised to consume no more than one drink a day.

Overview of Drugs Used to Treat Heart Failure

* Heart failure is treated with four major classes of drugs:
1. vasodilators,
2. Diuretics,
3. Beta blockers, and
4. Inotropic agents.
* In addition, spironolactone, an aldosterone antagonist, can offer significant benefits.

ACE Inhibitors and Other Vasodilatiors

* Vasodilators-especially ACE inhibitors- are important drugs for treatment of heart failure.
* In addition to improving symptoms, some vasodilators can prolong life.
* Vasodilators differ with respect to route of administration (oral versus intravenous) and site action (arterioles, veins, or both).
* Route of administration determines whether a drug is used acutely (IV agents) or long term (oral angents).
* Site of action determines specific hemodynamic benefits.
* Drugs that dilate veins increase venous capacitance, and thereby decrease venous pressure.
* As a result, venodilators reduce venous returns and cardiac filling, which in turn decrease excessive ventricular stretching and cardiac oxygen demand.
* In addition to their beneficial effects on the heart, venodilators decrease pulmonary congestion and peripheral edema.
* Drugs that dilate arterioles have tree beneficial effects:
1. Arteriolar dilation reduces cardiac afterload, and thereby allows stroke volume and cardiac output to increase;
2. By increasing cardiac output and dilating arterioles in the kidney, these drugs increase renal perfusion, and thereby promote loss of fluid; and
3. In skeletal muscle, arteriolar dilation increase local perfusion.

These drugs block production if angiotensin II, and thereby dilate arterioles and veins and decrease release of aldosterone.

Arteriolar dilation improves regional blood flow and, by reducing afterload, increases stroke volume and cardiac output.

Venous dilation reduces venous pressure, and thereby reduces pulmonary congestion, peripheral edema, and cardiac dilation.

By dilating renal blood vessels, ACE inhibitors improve renal blood flow, and thereby enhance excretion of sodium and water.

Suppression of aldosterone release further enhances excretion of sodium, while causing retention of potassium.

 From the foregoing, we can see that giving an ACE inhibitor is much like giving three different drugs: an arteriolar dilator, a venodilator, and a diuretic.

ACE inhibitors are especially useful for patients with heart failure plus hypertension, angina, or elevated plasma renin activity.

Isosorbide Dinitrate Plus Hydralazine

* For treatment of heart failure, isosorbide dinitrate (ISDN) and hydralazine are usually combined.
* The combination is an alternative to ACE inhibitors for patients who cannot tolerate them.
* Isosorbide dinitrate [Isordil, Sorbitrate] belongs to the same drug family as nitroglycerin. Like nitroglycerin, ISDN causes selective dilation of veins.
* In patients with severe, refractory heart failure, the drug can reduce congestive symptoms and improve exercise capacity.
* Principal adverse effects are orthostatic hypertension and reflex tachycardia.
* Hydralazine [Apresoline] causes selective dilation of arterioles.
* By doing so, the drug can improve cardiac output and renal blood flow.
* For treatment of heart failure, hydralazine is always used in combination with ISDN, since hydralazine by itself is not very effective.
* Principal adverse effects are hypotension, tachycardia, and a syndrome that resemble systemic lupus erythematosus.