

Drugs used to treat of heart failure with reduced ejection fraction

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Abstract

Heart failure patients need multiple medications to treats a different symptom or contributing factor. Individuals diagnosed with heart failure typically take 5 or more different medications daily. Treatment may help live longer and reduce your chance of dying suddenly. This review describes the main drugs used to treat heart failure with reduced ejection fraction.

Keywords: Heart failure, Drugs, Treatment.

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Introduction

Heart failure (HF) is the common final pathway of most diseases that affect the heart, being one of the most important current clinical challenges in health. HF is characterized by intolerance to exercise, fluid retention and congestive phenomena, and in its later stages has high morbidity and mortality rates. These patients those with preserved systolic function, are referred to as heart failure with preserved ejection fraction (HFpEF). HF is associated with left ventricular dysfunction, and in symptomatic patients with left ventricular ejection fraction (LVEF) $\leq 40\%$, this condition is called heart failure with reduced ejection fraction (HFrEF) or systolic heart failure. In this brief review we will focus on drug treatment of HFrEF (Table 1) [1-7].

Angiotensin-Converting Enzyme (ACE) Inhibitors

All patients with HFrEF should receive ACE inhibitors. It is seen an improved in symptoms between 4-12 weeks, as well as reducing the incidence of hospitalization, and increased patient survival. Blood pressure, renal function and serum potassium levels should be monitored, and also must be used with caution in patients with stenosis bilateral renal artery systolic blood pressure < 80 mmHg, serum creatinine > 3 mg/dl the serum potassium > 5.0 mEq/L. They are contraindicated in patients with a history of angioedema and pregnancy [8,9].

Digitalis Glycoside

Digoxin can reduce the rate of hospitalization and heart failure symptoms, increase exercise tolerance, but has no results on the survival rate. Doses are adjusted according to renal function, age and concomitant medications [10-13].

Vasodilators

It could be beneficial in patients intolerant of an ACE inhibitor or an ARB or those that need additional control of blood pressure, despite the maximum standard dose therapy. It should not be used in conjunction with sildenafil because of the risk of hypotension [2,8].

Aldosterone Antagonists (AA)

It is recommended for patients with heart failure NYHA class II-IV with an LVEF $\leq 35\%$, and has been shown to reduce the risk of hospitalization and death. Renal function and serum creatinine concentrations should be monitored during treatment. AA should be avoided in patients with serum potassium > 5.0 mEq/L and in those with reduced renal function (baseline serum creatinine > 2.0 mg/dl for women or > 2.5 mg/dl for men, or an estimated GFR [2,8,14,15].

Loop Diuretics

Most patients with heart failure have fluid retention. Diuretics in such patients may alleviate pulmonary and peripheral symptoms, but its effect on survival is controversial. Diuretics (furosemide or bumetanide) acting on the loop of Henle, are more effective for the treatment of heart failure than thiazide diuretics (furosemide, bumetanide), acting on the distal tubule [2,8,16,17].

Beta-Adrenergic Blockers (BB)

Its combination with an ACE inhibitor consistently leads to a 30-40% reduction in hospitalization and mortality in adults with heart failure class III-IV (NYHA) class. Should be started at low doses and its increase is gradual, usually at 2-week intervals until the maximum tolerated dose [2,8,18-22].

Table 1. Drugs for Chronic HFrEF.

Drugs for Chronic HFrEF		
Drug	Initial(I) and maximum(M) dose in adults	
	I	M
Angiotensin-Converting Enzyme (ACE) Inhibitors	Adverse Effects (AE): Cough, angioedema, hypotension, renal insufficiency, hyperkalemia, rash, taste disturbances, and neutropenia.	
Enalapril**	2.5 mg	20 mg
Captopril***	6.25 mg	50 mg
Lisinopril*	2.5-5 mg	40 mg
Perindopril*	2 mg	16 mg
Fosinopril*	5-10 mg	40 mg
Ramipril*	1.25-2.5 mg	10 mg
Trandolapril*	1 mg	4 mg
Quinapril**	5 mg	20 mg
Digitalis Glycoside	AE: Conduction disturbances, cardiac arrhythmias, nausea, vomiting, confusion, and visual disturbances.	
Digoxin *	0.125 mg	0.125-0.25 mg or once every other day
Vasodilators	AE: Tachycardia, peripheral neuritis, lupus-like syndrome, headache and dizziness.	
Isosorbid dinitrate/ hydralazine***	20 mg/37.5 mg	40 mg/75 mg
Aldosterone Antagonists	AE: Hyperkalemia, renal impairment, erectile dysfunction, painful gynecomastia and menstrual irregularities	
Spirolactone*or**	12.5-25 mg	25 mg
Eplerenone*	25 mg	50 mg
Diuretics	AE: hypokalemia, worsening of renal function, gout, hypomagnesemia and renal insufficiency.	
Loop diuretics		
Furosemide *or**	20-40 mg	600 mg
Bumetanide *or**	0.5-1 mg	10 mg
Torsemide *or**	10-20 mg	200 mg
Thiazide diuretics		
Metolazone *or**	2,5mg	10mg
Indapamide *or**	2,5mg	5mg
Hydrochlorothiazide *or**	25mg	100mg
Potassium-sparing diuretics		
Spirolactone *or**	25mg	50mg
Amiloride *or**	2,5mg	20mg
Trianterene *or**	25mg	100mg
Beta-Adrenergic Blockers (BB)	AE: Fatigue, hypotension, bradycardia, asymptomatic fluid retention, dizziness, headache, nausea, stomach pain, trouble sleeping.	

Metoprolol succinate*	12.5-25 mg	200 mg
Bisoprolol*	1.25 mg	10 mg
Carvedilol**	3.125 mg	25 mg/(50 mg for pts>85 kg)
Nebivolol*	1,25mg	10mg
Angiotensin Receptor Blockers (ARBs)	AE: Angioedema, hypotension, renal insufficiency, and hyperkalemia. ARBs: Can be used in patients who cannot tolerate an ACE Inhibitor mainly due to coughing	
Losartan*	25-50 mg	150 mg
Valsartan**	20-40 mg	160 mg
Candesartan cilexetil*	4-8 mg	32 mg
Azilsartan medoxomil *	40-80 mg	80 mg

Once a day *; bid - Twice a day**; tid- Three times a day***; pts- Patient; HFrEF - Heart Failure with reduced Ejection Fraction.

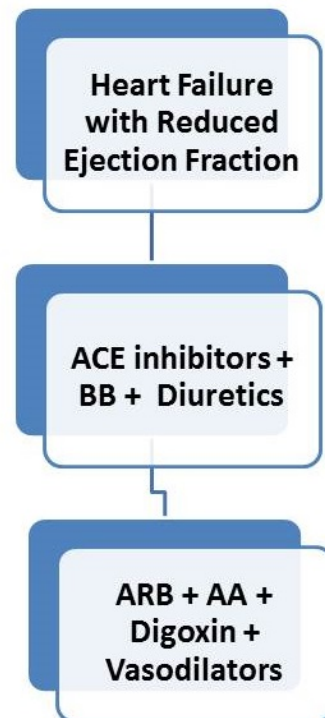


Figure 1. Combinations of the medications used in treating heart failure.

Angiotensin Receptor Blockers (ARBs)

Therapy with an ARB reduces the risk of death in patients with HFrEF; and can be used in patients who cannot tolerate mainly due to coughing an ACE inhibitor. Blood pressure, renal function, and serum potassium concentrations should be monitored [2,8,23].

Serelaxin is a recombinant human relaxin-2 vasoactive peptide that causes systemic and renal vasodilation. The clinical benefits may including improving systemic, cardiac, and renal hemodynamics, and protecting cells and organs from damage

via neurohormonal, anti-remodeling, anti-fibrotic, anti-ischemic, anti-inflammatory, and pro-angiogenic effects [24-26].

Recent studies with the novel agent LCZ696, a dual-acting angiotensin receptor blocker and neprilysin inhibitor (ARNi), with the well established ACE inhibitor enalapril and found significant reduction in mortality among the chronic HFrEF [27-32].

The main combinations of the medications used in treating heart failure are shown in Figure 1.

Drugs used to HFrEF can reduce the rate of hospitalization and heart failure symptoms, increase exercise tolerance and patient survival.

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