Evidence based optimization of medical therapy in Chronic Heart Failure

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Abstract

Despite of modern medical treatment heart failure patients suffer frequently. The optimization of medical therapy is an emphasis for these patients. Device therapy has been showed some improvement in prognosis but nonresponder rate is still 30% in many large trails. So, selection of patients for devices is important as these are expensive. Optimization of medical treatment is the priority and device can be used as an additional option.

Introduction

Heart failure is a chronic debilitating disease. Symptomatic improvement has been achieved with pharmacological treatment e.g. use of beta blockers, angiotensin-converting enzyme inhibitors and diuretics. Although the medical management of chronic heart failure patients has improved considerably over recent times, morbidity and mortality remain high and quality of life is poor for many patients.

Chronic heart failure has significant economic impact on health budgets due to the cost of long-term drug treatment and frequent hospitalization of patients. Heart failure will be an increasing burden in the future due to the recent development of health care systems, advanced treatment.[1-2,] With an aging population the prevalence of heart failure is increasing.[3] Modern treatments have improved the prognosis of heart failure.[4]

Currently, the beneficial role of an electromechanical approach (pace maker) has been promoted as an effective adjunct therapy to optimum medical therapy in selected heart failure patients but not as an alternative.

The purpose of this review is to evaluate the role of optimum pharmacological therapy in chronic heart failure patients.

Definition of Heart Failure

It is a difficult to establish a uniform definition of heart failure due to many concepts from different bodies. It differs dependent on epidemiology, clinical finding and treatment. A recent European definition which is mostly accepted by different authorities is as follows: 'Heart failure is a complex syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to function as a pump to support a physiological circulation'·[5]

Prevalence and Incidence of Chronic Heart failure

In Europe, the prevalence of heart failure is approximately 1-3% of the population. The incidence rate is 1 case per 1,000 of population per year.[6] The prevalence in USA is about 5 million people and more than 550,000 new patients are diagnosed to have heart failure each year.[7] The Framingham Heart Study reported no change in the period 1950-1999 for men, but a small fall in the early stage of that period for women.[8] In the developing countries, about 2% of the adult population have heart failure.[9]

Current trends of treatment of heart failure

In the United Kingdom, community management may be carried out by special technology-telemonitoring; called-'Home Care link', by which remote monitoring of heart failure patients is possible. The first sign of clinical deterioration of the patient is noticed by telemonitoring nurse and then the nurse refers the patient to primary care doctor. The Meta analysis found that telemonitoring programmes for patients with chronic heart failure reduced admissions to hospital, improved quality of life and all cause mortality by nearly one fifth.[10]

Classification of Heart failure

1) Acute, 2) Chronic, and 3) Decompensated.

European Society of Cardiology (ESC) described a new classification in 2008

1. New onset- First presentation of heart failure which is acute or slow onset.
2. Transient- Recurrent or episodic.
3. Chronic- Persistent, stable, worsening or decompensated.

Managements of Chronic Heart Failure

In clinical practice heart failure is diagnosed by history, clinical features and investigations.

General measures

1) Weight reduction, 2) Cessation of smoking, 3) Stop alcohol intake, 4) *Diet restriction: Salt restriction :* It is important to restrict salt intake as it promotes heart failure, 5) *Fluid restriction:* Fluid intake will be restricted in 1 to 1.5 L per day but it will vary with weather, 6) Exercise, 7) *Risk factor management:* Patients who have risk factors for the development of the premature coronary artery disease then it lead to heart failure. So control of risk factors is important. Such as, cessation of smoking, weight reduction, control of diabetes, hypertension and hyperlipidemia. It has been shown in recent trail that statin reduces mortality in chronic heart failure patients due to any cause. [11]

Pharmacological treatment

The main aim of pharmacological treatment is to control the symptoms and improve prognosis.

Diuretics

It is the main stay of treatment of acute heart failure. There is no evidence that diuretics affect the prognosis or survival rate of patients with chronic heart failure. But the chronic heart failure patients respond well and get symptomatic relieves to loop diuretics (like frusemide, bumetanide) as well as thiazides or potassium-sparing diuretics: Aldosterone antagonists or amiloride etc.

Beta blocker

Following table demonstrates different trials of beta blockers in heart failure patients:

Table 3: The doses of beta blockers in different trials.

Drug	Initial dose(mg)	Titration steps(mg)	Target dose(mg)	Freque-ncy	Trial
Carvedilol	3.125	6.25,12.5,25,50	25/50	b.d	COPERNICUS
Bisoprolol	1.25	2.5,5,10	10	o.d	CIBIS-II
Metoprolol	12.5/25	25,50,100,200	200	o.d	MERIT-HF
Nebivolol	1.25	2.5,5,10	10	o.d	SENIORS

Many clinical trials have demonstrated that beta blockers have significantly reduced mortality in chronic heart failure patients.[12] Carvedilol was used in severely symptomatic chronic heart failure patient in another trial and showed mortality benefit.[13] It also reduces the risk of sudden cardiac death which have been shown in MERIT-HF and CIBIS-II studies.[14,15] Some physicians are reluctant to start beta blocker as it has potential side effects like worsening of heart failure, hypotension and bradycardia.[15]

ACE inhibitors

Several studies have been shown the importance of ACE inhibitor in the prognosis of heart failure patients, such as enalapril was used in both CONSENSUS trial, SOLVD trial.[16,17]

Table 4: The doses of Angiotensin converting enzyme inhibitors in different trials.

Drug	Initial dose(mg)	Titration steps(mg)	Target dose(mg)	Freque-ncy	Trial
Captopril	6.25	12.5,25,50	50	t.d.s.	SAVE
Enalapril	2.5	5,10,20	20	b.d.	SOLVD
Lisinopril	5	10,20,30,40	35-40	o.d.	ATLAS
Ramipril	2.5	5,10	10	o.d.	HOPE
Trandolopril	0.5	1,2,4	4	o.d.	TRACE

Angiotensin-II receptor blockers

The CHARM trial has shown that Cardesartan has a beneficial effect on prognosis, as it reduces both mortality and morbidity.[18] Cohn et al. used Valsartan in their trial which showed improvement of quality of life in chronic heart failure patients.[19]

Aldosterone inhibitors

Spironolactone has been shown survival benefit in chronic heart failure patients in one large placebo- controlled study: RALES Trial. The risk of death was 30% lower in Spironolactone group than the placebo (P<0.001).[20]

Vasodilators

Mortality benefit has been shown in a trial in the treatment of chronic heart failure with hydralazine and isosorbide dinitrate.[21,22]

Calcium-channel blockers

There is no evidence in extra survival benefit of Calcium-channel blocker in heart failure.

Positive inotropic agents

Digitalis is used in chronic heart failure patients with atrial fibrillation for rate control.

There is evidence that it reduces symptoms but has no effect on mortality.[23] Other positive inotropic agents (such as dobutamine, dopamine, and milrinone) are used in patients for short period for their clinical improvement.

Anticoagulation

Anticoagulation is also an important consideration as chronic heart failure patients with atrial fibrillation have risk of systemic embolism. Anticoagulation therapy reduces the incidence of embolism.[24]

Antiarrhythmic agents

Amiodarone is the drug of choice to maintain sinus rhythm in patients with heart failure and atrial fibrillation. Sotalol is also used.

Device therapy

Cardiac resynchronization therapy (CRT)

If patients with advanced heart failure that is NYHA class III and IV who are in optimal medical treatment, have a broad QRS duration >120 ms or left bundle branch block with myocardial dysfunction (EF <35%) may be suitable for cardiac resynchronization therapy (CRT).[5] CRT has been shown to reduce hospital admission and mortality in comparison with conventional treatment.[25.] But nonresponder rate to CRT was 30% in this trial.

Implantable cardioverter-defibrillator (ICD)

Fatal ventricular arrhythmia is the common cause of sudden cardiac death in chronic heart failure patients.

The UK guidelines laid down by the National Institute of Clinical Excellence (NICE) relating to patients with sustained ventricular tachycardia advice implanting a defibrillator in two groups of patients.[5] In one group patients presenting with haemodynamically compromising VT causing collapse, hypotension, left ventricular failure or angina. And the other group was patients presenting with sustained VT without the above features but with an ejection fraction < 35%.

Left ventricular assist device (L-VAD)

Ventricular assist devices were implanted as bride to recovery, bride to transplant and destination therapy in 107 patients with end stage heart failure. The data suggested that Post-VAD survival rate has significantly improved.[26] About 52% of survival improvement has been demonstrated in a trial with young patients with rapidly failing hearts with LVAD.[27]

Cost of heart failure

Approximately 2% of total health budget has been spent on heart failure patients in United Kingdom.5% of acute hospital admissions and 10% bed occupancy and 40% readmission rate in one year. As chronic heart failure is a chronic disease so long term drug therapy is a burden for health budget.[6]

Prognosis

About 50% mortality in 3 years which is worse than cancer.[s] Median survival after diagnosis is 1.7 years for men and 3.2 years for women. The risk of sudden death is 10 times higher in heart failure patients.

Quality of life questionnaire

The 'Minnesota Living with Heart Failure Questionnaire' is used to assess the prognosis of patients with heart failure. This is used commonly in most trials.

The 'Karolinska Questionnaire' is also used in a trial 'MUSTIC' which measures all broad spectrum of quality of life.

Conclusions

The prevalence of heart failure is increasing. Despite improvement of pharmacological therapy some heart failure patients present to the physician repeatedly for their symptoms and poor quality of life. Optimization of pharmacological therapy may be helpful for some heart failure patients. Many trials have shown that CRT reduces morbidity and mortality in certain refractory heart failure patients.

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