Treatment of Congestive Cardiac Failure

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Congestive cardiac failure, whether due to systolic or diastolic heart failure, is a common cause for hospital admission and the prevalence increases with age. There are many causes of heart failure, such as hypertension, coronary artery disease, cardiomyopathies (including dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, post-partum cardiomyopathy, tachycardia-related cardiomyopathy), toxin-induced cardiomyopathy (e.g. alcoholism, cocaine), chronic rheumatic heart disease, infiltrative or inflammatory heart diseases. However, the aetiology of severe heart failure requiring heart transplantation in our locality is quite different from that in Western population. In contrast to Western countries where coronary artery disease is the major cause of end-stage heart failure, in our locality, valvular heart disease accounts for more than one-third (37%) of our heart transplant recipients, followed by dilated cardiomyopathy (29%) and coronary artery disease (16%). Other causes include congenital heart disease, arrhythmogenic right ventricular dysplasia, hypertrophic cardiomyopathy and sarcoidosis. Patients with heart failure should be educated about dietary salt restriction, fluid restriction, avoidance of toxins (such as tobacco and excess alcohol) and the value of regular exercise. The mainstay of treatment for heart failure is drug therapy. All patients with heart failure should receive at least two neurohormonal antagonists, namely angiotensin-converting enzyme (ACE) inhibitors and beta-blockers and, where appropriate, aldosterone antagonists and angiotensin receptor blockers. These drugs reverse ventricular remodelling, slow the progression of heart failure, improve symptoms and reduce the risk of death. Adjunctive therapy for the underlying or concomitant cardiac disease (e.g. revascularisation for coronary artery disease, valvular surgery for valvular lesions, anti-arrhythmic drugs for arrhythmias) is also important. Recent advances in device therapy and mechanical circulatory support systems have helped in the management of those with symptomatic heart failure not responding to optimal medications and have played an important role as bridge to recovery of the myocardium or to transplantation. In this review, I shall summarise the practical issues related to drug therapy used to treat heart failure and strategies available for treatment of those severe heart failure patients who fail medical therapy.

Drug Treatment for chronic congestive cardiac failure

1) Diuretics

The most rapid and reliable way to improve the symptoms of patients with congestive heart failure is through the judicious use of diuretics. Patients should have their volume status optimised before starting treatment with ACEI or beta-blockers.

2) Angiotensin-converting enzyme (ACE) inhibitors

ACE inhibitors, such as enalapril (CONSENSUS[1], SOLVD[2]), captopril (SAVE[3]), ramipril (HOPE[4]), are proven therapy for patients with ventricular dysfunction, whether symptomatic or not. Major side-effects of ACE inhibitors are hypotension, renal dysfunction and dry cough. Patients at risk for hypotension or renal dysfunction are those with borderline blood pressure (systolic pressure <100mmHg), those with pre-existing renal dysfunction or those with evidence of excessive neurohormonal activation such as hyponatraemia. Patients in high risk categories should be commenced on low doses of ACE inhibitor, for example, captopril 6.25mg thrice a daily or enalapril 2.5mg once or twice daily, and titrated to higher doses as tolerated. ACE inhibitors with longer half-life, such as lisinopril or ramipril, may be less likely to cause dizziness and hypotension because of gradual onset of action and allows once-daily dosing which would improve patient compliance. The combination of hypotension and ACE inhibition may cause deterioration in renal function together with hyperkalaemia, especially in patients with renal vascular disease, diabetes or intrinsic renal disease. Renal function and serum potassium levels should be monitored within one week of initiation of ACE inhibitor. In patients with significant renal dysfunction, fosinopril may be preferable because of dual renal and hepatic excretion. If the creatinine level becomes markedly increased, the diagnosis of renal artery stenosis should be pursued.

Cough is a common side-effect of ACEI and also a common symptom of heart failure. Interestingly, in the Assessment of Treatment with Lisinopril and Survival Study (ATLAS[5]), patients taking higher dose of lisinopril tolerated the drug well and had a lower incidence of cough, perhaps because improved cardiac filling pressure with higher doses reduces the frequency of cough caused by pulmonary hypertension and congestion. Therefore patients who experience cough

while taking an ACE inhibitor should have the dose of ACE inhibitor and diuretics increased to reduce subclinical congestion. If the cough does not improve, it becomes likely that the cough is related to the ACE inhibitor.

3) Beta-blockers

Beta-blockers should be administered to patients with symptomatic heart failure when their condition is stabilized with oral medications. However, not all beta-blockers have the same effect. There are three beta-blockers which have been shown to reduce the risk of death for patients with left ventricular dysfunction after myocardial infarction and those with symptomatic heart failure - carvedilol (US Carvedilol Study[6]), long-acting metoprolol succinate (MERIT-HF[7]) and bisoprolol (CIBIS II[8]). In patients with severe heart failure requiring intravenous inotropic agents or mechanical circulatory support, beta-blockers may be started when the patients are weaned from intravenous medications and stabilised on oral agents. The starting doses of beta-blockers should be as low as possible and increased as tolerated to reach the target doses used in large-scale trials, for example carvedilol at 25mg twice daily. In practice, this is not always possible because of hypotension but low doses are better than none. Benefits of beta-blockers in heart failure are seen even at the low doses, e.g. carvedilol 6.25mg twice daily.

4) Angiotensin receptor blockers (ARB)

In contrast to ACE inhibitors which prevent the adverse effects of angiotensin II by blocking its synthesis though ACE, angiotensin receptor blockers prevent angiotensin II from acting on the cell by selectively blocking angiotensin II type 1 (AT1) receptors and may be a more direct way to block the effects of activation of the RAAS in heart failure. ARB such as losartan[9] or valsartan[10] may be used for treatment of chronic heart failure in patients who are intolerant of ACE inhibitors. The benefit of adding an ARB to the treatment of a patient already receiving ACE inhibitor and beta-blocker is not seen across the entire class of ARB. In one study, valsartan was associated with a trend toward increased risk of death or hospitalisation[10]. However, in another study with candesartan[11], this ARB in combination with ACE inhibitors and beta-blockers improved the outcome of patients with heart failure. Therefore, for heart failure patients who remain symptomatic despite ACE inhibitor and beta-blocker therapy, candesartan should be standard treatment.

5) Aldosterone antagonist

Aldosterone antagonists, including spironolactone[12] and eplerenone[13], have been shown to reduce the risk of death in patients with advanced heart failure. Monitoring of serum potassium level is crucial because of the risk of hyperkalaemia. Gynaecomastia which occurs in patients taking spironolactone does not appear to be a side-effect of eplerenone.

6) Digoxin

Digoxin is useful in treating heart failure patients with atrial fibrillation because of positive inotropy, negative chronotropy and digoxin's ability to favourably modulate neurohormonal factors in heart failure. However, the role of digoxin in heart failure patients with normal sinus rhythm is more contentious.

Although addition of digoxin to background therapy of ACE inhibition and diuretic therapy has a neutral effect on mortality, it can reduce hospitalisation due to worsening heart failure. Certainly withdrawal of digoxin in stable heart failure patients is associated with higher adverse event rates[14] and stopping digoxin should be avoided. However, care must be taken to avoid digoxin toxicity, which can result in nausea, vomiting and arrhythmias.

Device therapy

Those patients with severe heart failure and reduced left ventricular ejection fraction (<35%) despite optimal medical therapy should be considered for cardiac resynchronisation therapy (CRT) or implantation of a biventricular pacemaker[15,16]. Although the current selection criteria for CRT includes wide QRS complex (>120ms), it is recognised that a high proportion of patients with narrow QRS complex may demonstrate left ventricular dyssynchrony on tissue Doppler imaging and may benefit from CRT. In view of risk of sudden death in heart failure, implantation of a biventricular implantable cardiovertor defibrillator (ICD) may be indicated to provide both CRT and ICD back-up. Device therapy for heart failure is becoming more and more sophisticated and provides not only pacing and defibrillation therapies but also monitoring specially designed for heart failure. Some CRT+ICD devices include the intrathoracic impedance technology which detects subclinical fluid overload in heart failure patients. A reduction in the intrathoracic impedance may precede clinical manifestation of heart failure by one to three weeks and provide early warning for the need to adjust medications e.g. increasing the dosage of the diuretic. Another investigational treatment for patients with normal QRS duration is cardiac contractility modulation (CCM), which can enhance the strength of left ventricular contraction by delivering non-excitatory signals during the refractory period. It is possible that in the future all these features can be incorporated into a single device which provides a combination of CRT, ICD and CCM.

Acute decompensation of heart failure

Acute decompensation of heart failure necessitates hospital admission and its management requires both rapid identification of the underlying factors precipitating the low-output state and interventions designed to improve the circulatory haemodynamics. When acute pulmonary oedema is the presenting problem, intravenous diuretics and nitrates (e.g. intravenous nitroglycerin) should be given. However, in patients with persistent hypotension and low-output syndrome, haemodynamic monitoring with a flow-directed thermodilution pulmonary artery catheter provides essential information to guide the usage of more aggressive pharmacologic support with intravenous inotropic or vasopressor agents, such as dopamine, dobutamine, milrinone, adrenaline. Cardiac monitoring is imperative when intravenous inotropic agents are given because of the risk of ventricular arrhythmias. Some newer agents, e.g. levosimendan[17] (a calcium sensitizer), nesiritide[18] (the human B-type natriuretic peptide), are electrophysiologically neutral and may prove to be useful in treatment of acutely

decompensated heart failure because of reduced incidence of serious ventricular arrhythmias.

Mechanical circulatory support

In circumstances where a potentially reversible cause of acute heart failure has been identified or where cardiac transplantation is considered an option for refractory end-stage heart failure, mechanical circulatory support systems are available which can maintain the patient until definitive treatment is instituted. Mechanical circulatory support can be life-saving in acute cardiogenic shock and particularly useful as a bridge to recovery in cases of fulminant myocarditis. Time from onset of illness to recovery of ventricular function in fulminant myocarditis usually takes 2 to 3 weeks and those patients who survive this initial period tend to have good long-term prognosis[19]. Mechanical circulatory support includes placement of intra-aortic counterpulsation balloon pumps (IABP), extracorporeal membrane oxygenation systems (ECMO), and left ventricular assist devices (LVAD). In our experience, IABP has been used successfully as bridge to heart transplant in 15% of our local heart transplant population and the longest duration of IABP augmentation is over 4 months. At our centre, ECMO and LVAD have also been used with some success as bridge to recovery in several cases of acute myocarditis but the problems of these devices include limitation to short-term use and high complication rates. The use of LVAD and axial flow pumps as destination therapy for severe heart failure is gaining popularity but unfortunately the technology is not yet available locally.

Cardiac transplantation

Cardiac transplantation is the ultimate treatment for end-stage heart failure which fails to respond to medical and device therapy. Since 1992, a total of 73 cases of heart transplantation (including 2 cases of combined heart-lung transplantation) have been performed at our centre. The 1-year, 3-year and 5-year survival rates for orthotopic heart transplantation are 83%, 81% and 80% respectively. However, heart transplantation is limited by the small number of suitable donors, rejection of allograft and side-effects of long-term immunosuppression.

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