Evidence-based management of chronic heart failure

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Throughout the past 10 to 15 years, the therapeutic approach to heart failure has undergone considerable change. Current treatment not only concerns symptomatic improvement, but increasingly focuses on the prevention of disease progression and on reducing mortality. The understanding and acceptance of the need to prescribe therapies proven to be effective in large controlled trials is vital for the provision of optimal treatment for heart failure patients.

The use of diuretics in the treatment of heart failure is well established and essential for symptomatic treatment when fluid overload is present. However, there is no evidence that loop and thiazide diuretics improve the prognosis of patients with heart failure.

ACE inhibitors are the mainstay of heart failure treatment. There is good clinical evidence that they improve symptoms and exercise tolerance as well as reduce mortality and hospital admissions in all grades of symptomatic heart failure caused by left ventricular systolic dysfunction (Flather et al, 2000). They also delay progression of asymptomatic left ventricular systolic dysfunction to symptomatic disease (The SOLVD Investigators, 1992). ACE inhibitors are often prescribed at doses lower than those shown to be effective in large controlled clinical trials. Initiation of treatment should be at low doses, but this should be followed by upward titration to the target dose (table1), if tolerated, whether or not there is symptomatic improvement. Monitoring of renal function and electrolytes is recommended after each dose increment. Some rise in urea, creatinine and potassium is to be expected – no action is warranted if the increase is small and asymptomatic, but dosage adjustment is indicated if these parameters rise excessively. It is very rarely necessary, however, to stop the drug altogether. Angiotensin II receptor blockers (candesartan, eprosartan, losartan, telmisartan, valsartan) can be used as an alternative to ACE inhibitors as they have been shown to have similar benefits (Jong et al, 2002; Coletta et al, 2003). These agents can also be considered in combination with ACE inhibitors in patients who remain symptomatic.

Extensive evidence demonstrates the value of beta-blockers (bisoprolol, carvedilol, metoprolol) in addition to ACE inhibitor therapy and diuretics in patients with heart failure due to left ventricular systolic dysfunction (CIBIS-II Investigators and Committees, 1999; Packer et al, 1996; MERIT-HF Study Group, 1999). Particular benefit is gained in patients who have had a myocardial infarction (The Capricorn Investigators, 2001). Long term improvement can be preceded by initial deterioration and therefore beta-blockers should be initiated in patients who are clinically stable at a low dose and increased slowly and progressively over weeks or months. It is evident that even a low dose of a beta-blocker is superior to treatment without beta-blocker administration (Wikstrand et al, 2002; Simon et al, 2003). The introduction of a beta-blocker should therefore be attempted even if the titration period is prolonged.

A major breakthrough has been the recommendation for the inclusion of a low dose of spironolactone (25mg) for patients with advanced heart failure with systolic dysfunction in view of evidence of reduced morbidity and mortality (Pitt et al, 1999). Whether an aldosterone antagonist is of proven benefit in patients with less severe disease remains to be fully established. A recent study using another aldosterone antagonist, eplerenone, has led to this agent being recommended for use as adjunct treatment in all stages of heart failure following myocardial infarction (within 3-14 days of event) (Pitt et al, 2003). The main concern with these agents is the potential for hyperkalaemia thus necessitating monitoring of serum potassium.

Digoxin is one of the oldest known treatments for heart failure. Although it is clearly indicated as a rate controller in patients with concomitant atrial fibrillation, its role in patients with heart failure in sinus rhythm is limited. In this latter case, current guidelines recommend the use of digoxin in patients who remain symptomatic despite optimal doses of ACE inhibitors, beta blockers, diuretics and spironolactone. Digoxin has no effect on reducing mortality but may decrease hospitalizations in these patients.

There is no specific role for direct-acting vasodilator agents. In case of intolerance to ACE inhibitors and angiotensin II receptor blockers, the combination of hydralazine and nitrates can be considered (Taylor et al, 2004).

A summary of the choice of pharmacological therapy in the various stages of heart failure is shown in table 2 (The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology, 2005). Despite longstanding evidence, European surveys on drug therapy of heart failure patients in primary care and in hospital have shown that ACE inhibitors, beta-blockers, and in particular their combination, are not used optimally (Cleland et al, 2002; Cleland et al, 2003). Evidence-based guidelines are now available and should be utilized so as to improve outcomes for heart failure patients (The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology, 2005; Hunt et al, 2001; National Collaborating Centre for Chronic Conditions, 2003).

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Table 1: Recommended ACE inhibitor starting and target doses

Drug	Starting dose	Target dose
enalapril	2.5mg daily	10-20mg twice daily*
lisinopril	2.5mg daily	30-35mg daily*
perindopril	2mg daily	4mg daily**

* doses used in large outcome trials
** manufacturer's recommendation

Table 2: Heart failure – choice of pharmacological therapy in left ventricular systolic dysfunction

	ACE inhibitor	Angiotensin receptor blocker	Diuretic	Beta-blocker	Aldosterone antagonist	Cardiac glycoside
Asymptomatic left ventricular dysfunction	Indicated	If ACE intolerant	Not indicated	Post MI	Recent MI	With atrial fibrillation
Symptomatic HF (NYHA II)	Indicated	Indicated with or without ACE inhibitor	Indicated if fluid retention	Indicated	Recent MI	(a) when atrial fibrillation (b) when improved from more severe HF in sinus rhythm
Worsening HF (NYHA III-IV)	Indicated	Indicated with or without ACE inhibitor	Indicated, combination of diuretics	Indicated (under pecialist care)	Indicated	Indicated
End-stage HF (NYHA IV)	Indicated	Indicated with or without ACE inhibitor	Indicated, combination of diuretics	Indicated (under specialist care)	Indicated	Indicated

NYHA-New York Heart Association, HF-heart failure, MI-myocardial infarction

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