WeMeReC
Welsh Medicines Resource Centre
Canolfan Adnoddau Moddion Cymru

Bulletin

"Independent prescribing information for NHS Wales"

November 2008

Treatment of chronic heart failure

Background

Heart failure is a common, disabling, complex condition with a poor prognosis.[1] Chronic heart failure (CHF) results from an inability of the heart to respond to the body's demands for increased cardiac output. It is characterised by symptoms and signs such as fatigue, breathlessness, and fluid retention. The most common cause of CHF is myocardial dysfunction, which is commonly systolic and associated with reduced left ventricular contraction and ejection fraction. The prevalence of CHF increases with age and often results from coronary heart disease (CHD) and myocardial infarction (MI).

As the elderly population increases and more people survive MI, the incidence and prevalence of CHF is increasing.[2,3] Based on UK estimates, approximately 45 000 people in Wales aged 45 or over have CHF. The condition is responsible for 1 million inpatient days (2% of all NHS inpatient bed days) and 5% of all emergency admissions to hospital.[2] The prognosis and quality of life of CHF patients are often poor; annual mortality rates range from 10% to over 50% in those patients with severe disease.[2,4]

Despite advances in the management of CHF and evidence for treatments that improve symptoms, reduce hospital admissions, and increase survival, the condition remains under-diagnosed and under-treated.[2,3] To support improvements for patients in Wales, CHF is included in the 1000 Lives Campaign,[2] and the standards of the Cardiac Disease National Service Framework (NSF).[3]

This bulletin discusses the drug treatment of CHF associated with left ventricular systolic dysfunction. It builds on the evidence presented in the previous WeMeReC Bulletin (2001) and focuses on current treatment recommendations.

Summary

- To achieve the benefits possible with treatments for CHF, rigorous follow-up of patients is required. Support is best delivered through organised systems of care – it is recommended that local, multi-disciplinary CHF teams are established in all areas (see page 4).
- Unless contraindicated, an ACE inhibitor and a beta-blocker should be prescribed. Diuretics may be useful for the control of oedema (see page 2). For patients who remain symptomatic, an aldosterone antagonist or an angiotensin II receptor blocker may be considered (see page 3). The use of other medicines needs to be carefully reviewed, especially in elderly and renally impaired patients.
- It is crucial that non-pharmacological measures, including appropriate surgical treatment, should be provided alongside prescribed therapy (pages 2 and 4).

Diagnosis

CHF is difficult to diagnose as the presenting signs and symptoms are often non-specific, especially in elderly patients, and may be attributed to co-morbidities. When CHF is suspected, a detailed history and clinical examination (including precipitating or exacerbating factors and identification of concomitant disease) should be combined with diagnostic tests.[5,6]

Imaging by echocardiography is considered to be the most effective tool in diagnosis.[4] The electrocardiogram (ECG) and plasma B-type natriuretic peptide (BNP) measurement are useful screening tests that can be used to exclude heart failure.[5,6] If an ECG and/or BNP levels are abnormal, a diagnosis of heart failure cannot be excluded and an echocardiogram should be performed.[5]

The extent of CHF is commonly described using the New York Heart Association (NYHA) classification based on symptoms and exercise capacity: NYHA Class I includes patients with asymptomatic left ventricular dysfunction (e.g. post-MI) and Class IV describes those with severe heart failure. Other classifications exist, which are based on structural changes and symptoms.[4]

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Management of CHF

The goal of minimising the impact of CHF on patients, their families, and the health service is reflected in guidance published by various groups.[3-6] These acknowledge the need for rigorous follow-up to achieve the improvements possible with treatments. They also describe the benefits of organised systems of care. The NSF for Wales[3] recommends the establishment of local, multi-disciplinary teams to facilitate the delivery of care to CHF patients. (These teams are discussed on page 4.)

The measures employed to manage a patient's CHF are determined by the extent of their disease, their personal circumstances, and their co-morbidities (and whether any of these are surgically correctable). Important beneficial measures include educating patients about lifestyle changes, appropriate fluid and salt intake, and the importance of reporting sudden changes in daily weight, swelling, or breathing difficulties. Other measures include pneumococcal and annual influenza vaccination.[5]

Pharmacological therapy

Angiotensin Converting Enzyme (ACE) inhibitors should be considered for all patients with CHF associated with left ventricular systolic dysfunction.

ACE inhibitors improve long-term survival in patients with all grades of CHF. They reduce symptoms and hospital admissions and slow the progression of disease. None of the ACE inhibitors studied in large clinical trials (Table 1 lists those most commonly prescribed in Wales) appear to confer any clinical advantages over another; however, the doses used in practice are often comparatively low. ACE inhibitors should be started at low doses and titrated up (doubled at short intervals, e.g. two weeks) to target doses (Table 1) or the highest tolerated dose.

Contraindications to ACE inhibitors include a history of angioneurotic oedema or bilateral renal artery stenosis. Adverse events include renal impairment, hypotension, hyperkalaemia, and cough. Specialist advice should be sought in patients specifically at risk of these events, including those on high doses of a loop diuretic (e.g. furosemide 80 mg). Blood chemistry (urea, creatinine, and electrolytes) should be checked at baseline, one to two weeks after initiating therapy, and after each dose titration.

Table 1 Target doses of ACE inhibitors in CHF

ACE inhibitor	Target dose
Captopril	50 mg -100 mg three times daily
Enalapril	10 mg - 20 mg twice daily (bd)
Lisinopril	20 mg - 35 mg once daily (od)
Ramipril	5 mg bd or 10 mg od

Beta-blockers should be considered for all patients as soon as their condition is stable, usually following the introduction of an ACE inhibitor (and a diuretic, if necessary).

Beta-blockers reduce mortality, hospital admissions, and the progression of heart failure. However, these effects have not been consistently demonstrated in studies of all beta-blockers. Currently, evidence supports the use of bisoprolol, carvedilol, and nebivolol for CHF. Patients already receiving a beta-blocker for angina and/or hypertension should continue with their current treatment or be switched to one of these agents.[5]

Contraindications to beta-blockers include asthma, hypotension, bradycardia, second or third degree heart block, and sick sinus syndrome. Improvements associated with beta-blockers will not be immediately evident – in the short-term they can produce decompensation with worsening heart failure and hypotension. They should be started in patients with stable CHF. Treatment should be initiated at low doses and titrated slowly (at not less than two weekly intervals) to target doses (Table 2). This can be undertaken in primary care by experienced practitioners. Heart rate, blood pressure, and clinical status should be assessed after each titration. Clinical trials suggest that target doses may not be reached in many patients.

Table 2 Target doses of beta-blockers in CHF

Beta-blocker	Target dose
Bisoprolol	10 mg od
Carvedilol	25 mg bd (50mg bd in heavy patients)
Nebivolol	10 mg od

Diuretics are used in patients with CHF who require relief of congestive symptoms and fluid retention. (Use of aldosterone antagonists is considered separately – see page 3.)

A loop diuretic (e.g. furosemide) is usually the first choice and will be more effective than a thiazide in moderate to severe heart failure. A thiazide (e.g. bendroflumethiazide) might suffice if fluid retention is mild. Optimal dosing to reduce symptoms (but to avoid dehydration or renal dysfunction) will vary widely between individuals and may need to be adjusted following the introduction of other therapies.

In patients with resistant oedema, a combination of a loop diuretic and a thiazide may be effective, but specialist advice should be sought and close monitoring will be required. There is a serious risk of hyperkalaemia when potassium-sparing diuretics are used in combination with ACE inhibitors (or angiotensin II receptor blockers – see page 3).

Further drug treatment options

In patients who remain symptomatic despite optimal treatment with ACE inhibitors, beta-blockers (and diuretics, if necessary), a number of further treatments may be considered. **In most cases these will require careful monitoring and will be initiated by, or in consultation with, a specialist**.

Aldosterone antagonists at low doses should be considered in patients who have advanced heart failure (Class III-IV) despite optimal therapy.

Aldosterone antagonists can reduce morbidity and improve survival.[4,6] The dose of spironolactone used for CHF is 25 mg to 50 mg once daily. If not tolerated, alternate day dosing may be an option. Blood potassium and creatinine concentrations should be monitored closely, especially when starting therapy, for signs of hyperkalaemia and/or deteriorating renal function. For male patients in whom gynaecomastia associated with spironolactone is problematic, eplerenone may be an alternative.[6] Evidence for the use of eplerenone in CHF is limited to one study in patients post-MI who had either diabetes or clinical signs of heart failure.[10]

Angiotensin II receptor blockers (ARBs) may be considered as an alternative for patients who are intolerant of ACE inhibitors (e.g. because of troublesome cough). They may also be beneficial in patients who remain symptomatic despite optimal therapy with ACE inhibitors and beta-blockers unless they are also taking an aldosterone antagonist.

ARBs were not licensed for use in CHF when existing NICE guidance was issued (2003).[5] However, some of these agents are effective at reducing hospital admissions and mortality associated with CHF.[7] Both candesartan (target dose 32 mg od) and valsartan (target dose 160 mg bd) are currently licensed for the treatment of left ventricular failure, although the license for valsartan is in post-MI patients. Therapy should be initiated as for ACE inhibitors with slow titration and close monitoring.

Some CHF patients may benefit from the addition of an ARB to ACE inhibitor and beta-blocker therapy.[4,6] The CHARM-Added trial found that adding candesartan to therapy for CHF patients who were already taking an ACE inhibitor (55% were also taking a beta-blocker and 17% spironolactone) led to a significant reduction in the composite endpoint of cardiovascular death or hospital admission for CHF.[8] All-cause mortality was not affected. In another trial (Val-HEFT)[9] the addition of valsartan to standard therapy for CHF (93% of patients were also receiving an ACE inhibitor and 35% a beta-blocker) also led to a reduction in the combined endpoint of mortality and morbidity. However, a post-hoc analysis of this trial found an adverse effect on mortality in the subgroup of patients (30% of the total) who were receiving a combination of all three agents. ARBs in both trials were associated with higher rates of discontinuations. The safety of combining an ARB with an ACE inhibitor and an aldosterone antagonist is not established and this is not recommended.

Digoxin may improve symptoms and reduce hospital admissions in CHF patients.[4] However, much of the evidence for its use in CHF patients is drawn from one large trial (the DIG trial)[11] that pre-dates the routine use of beta-blockers.[4,6] Digoxin plays a more important role in CHF patients with atrial fibrillation (AF).[5] Digoxin can be used to control ventricular rate before a beta-blocker is initiated or when a beta-blocker alone fails to control heart rate.[4,6]

The combination of **isosorbide dinitrate** and **hydralazine** may be employed in patients who are unable to tolerate either an ACE inhibitor or an ARB.[4] There is some evidence that the combination may be beneficial when added to standard therapy.[4,6]

Concomitant therapy

It is important that CHF patients with AF receive appropriate anticoagulant therapy.[2] If an anti-arrhythmic drug is required, amiodarone is preferred. Other anti-arrhythmic drugs should be avoided.[4]

For CHD patients, the use of aspirin and statins is generally appropriate. If beta-blockers are not being taken, patients with angina may require treatment with nitrates. If a calcium channel blocker is being considered, amlodipine or felodipine would be the agents of choice.[5,6] Verapamil, diltiazem, and short-acting dihydropyridine agents (e.g. nifedipine) should be avoided.

Other medicines that should be avoided whenever possible in patients with CHF include:[12]

- nonsteroidal anti-inflammatory drugs
- corticosteroids
- glitazones
- tricyclic antidepressants
- clozapine
- itraconazole
- oncology agents
- tumour necrosis factor antagonists.

It is important to be vigilant for potentially serious adverse effects and interactions associated with medicines in patients with CHF, especially in the elderly and those with renal impairment.

The Summaries of Product Characteristics should be consulted for full prescribing information.

Heart failure management – multidisciplinary clinics

Numerous studies have confirmed that multi-disciplinary support, involving collaborative working between doctors, nurses, and pharmacists, can improve clinical outcomes for CHF patients.[4-6,9] However, there is evidence from recent studies of hospital admissions that the care of many CHF patients is suboptimal.[13]

A multidisciplinary team brings together the necessary competencies for managing the complex needs of CHF patients. Ideally it includes specialist nurses and pharmacists with supplementary and independent prescribing qualifications who work with the guidance of cardiologists and the support of local general practitioners (GPs). Input from physiotherapists, occupational therapists, and dieticians is also desirable.

Clinics for CHF patients are typically based in primary care settings with links to specialist services. Regardless of location, it is essential that clinic staff liaise with staff from both primary care practices and secondary or tertiary treatment centres, who may be involved with diagnostic services or with the hospital admission and discharge of patients. Processes that facilitate the flow of information across the primary/secondary care interface, especially around the discharge of patients are vital. Examples of other processes that can improve services include electronic referral systems that enable GPs to have rapid access to echocardiography and cardiology review.

All CHF patients should be offered information about their condition and prognosis, have a management plan, and a named person they can contact for advice and support.[3] Local clinics provide the opportunity for communication with patients and can facilitate timely and convenient access to monitoring services. Healthcare professionals working in these settings can educate and encourage patients to manage their CHF as independently as possible. Patients can be observed and examined and their blood test results checked – their condition can be assessed and any deterioration detected early. Clinicians can help identify those patients who may be suitable for advanced interventions such as cardiac resynchronisation therapy (CRT) or implantable cardioverter defibrillator (ICD) therapy, and may also recognise and respond to conditions commonly associated with CHF such as AF, anaemia, renal impairment, and depression. Patients' functional performance and quality of life may be enhanced by referral to cardiac rehabilitation programmes.[3]

Medication reviews and appropriate adjustment of drug therapy are important components of clinic services. Effective use of medications is essential to the effective management of CHF and the often substantial burden of co-existing disease. In addition to the initiation of suitable medications, optimal dosing is important.

Clinics can also promote a proactive and integrated approach to other problems and often provide a link with social services and voluntary sector support services. For many patients with CHF, home visits and telephone support may be necessary.

Finally, while severe CHF is a terminal illness associated with distressing symptoms, the need for palliative care is often overlooked. In many cases, clinic personnel can facilitate referrals to appropriate services. Guidelines for managing end-stage CHF and criteria for referral to specialist palliative care services are being developed by cardiac and cancer networks in Wales.

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