**Leslie Jackowski**
BSc(Hons), MBBS, Sansom Institute, University of South Australia, for the Department of Veterans Affairs, Veterans' Medicines Advice and Therapeutics Education Services (Veterans' MATES) Writing Group. leslie.jackowski@unisa.edu.au

**Roshmeen Azam**
MBBS, MPH, for the Department of Veterans Affairs, Veterans' Medicines Advice and Therapeutics Education Services (Veterans' MATES) Writing Group.

# Beta blockers in systolic heart failure

■ Heart failure is a common reason for general practice encounters. It affects 4% of Australians aged 45 years or over[1] with the prevalence increasing from about 1% at age 50–59 years to more than 50% at 84 years of age and over.[2] Patients with heart failure are increasingly managed in the primary care setting, and the emphasis of new national programs on early recognition of signs and diagnosis of heart failure suggest that this trend will continue.[3] Beta blockers have been shown to reduce morbidity and mortality in patients with heart failure when used with an angiotensin converting enzyme inhibitor (ACEI) and a diuretic.[2,4]

Although the use of beta blockers in heart failure is increasing, barriers remain to their use. These may include previous learning, initial worsening of symptoms, an expectation that these agents will be initiated by specialists, poor communication between hospitals and general practitioners (eg. discharge summaries not providing adequate information to guide GPs), and a reluctance to titrate upward when medications have been initiated by another doctor.

## Prevention of heart failure

When given early in the postmyocardial infarction (MI) period, beta blockers reduce the development of heart failure in patients with preserved ventricular function (VF). They also slow the progression of the condition in patients with impaired VF.[2] Beta blockers should therefore be commenced early after an MI, irrespective of systolic VF.[2,4]

There is limited data on the use of beta blockers to prevent progression to symptomatic heart failure in patients with asymptomatic left ventricular (LF) dysfunction not associated with MI.[2] Nevertheless, beta blockers are recommended in all patients without a recent history of MI who have asymptomatic LV dysfunction.[4]

## Treatment of symptomatic systolic heart failure

Patients with mild symptoms or who appear clinically stable may not seem to require additional treatment. However, even if a patient improves with an ACEI and diuretic therapy, a beta blocker should be used because these agents favourably influence the long term prognosis of heart failure (improved LV function, reduced disease progression, and reduced hospitalisation and mortality), whereas a diuretic alone does not confer mortality benefit.[2,4,5]

Three beta blockers – carvedilol, bisoprolol and metoprolol (extended release) – have been shown to improve mortality outcomes in patients with mild to moderate heart failure already receiving an ACEI.[2,4] This benefit includes both a reduction in sudden death, and death due to progressive pump failure.[2] A class effect for the use of beta blockers in heart failure has not been definitively demonstrated.[4] Beta blockers can also improve the symptoms of heart failure, particularly in patients with advanced disease.[2,4] Beta blockers are recommended therapy, unless not tolerated or contraindicated, for all patients with systolic heart failure in addition to appropriate doses of ACEIs and loop diuretics.[4,6–8] The benefits of beta blockers in heart failure are also seen in patients with co-existent diabetes mellitus. However, close monitoring of blood glucose levels is required.[4,9]

Gradual up titration of beta blockers improves LV function and reduces risk of death and hospitalisation for patients with all grades of systolic heart failure.[2,4,5] These benefits are in addition to those achieved with ACEIs.[2,4,5]

Beta blockers should not be initiated during a phase of acute heart failure but only after the patient's condition has stabilised.[2] The beta blocker is conventionally added after achieving the recommended or highest tolerated dose of an ACEI. However, a recent study has suggested that major clinical outcomes are similar whether a beta blocker is started before an ACEI, or the conventional order is followed.[2]

Patients already taking a beta blocker for a concomitant condition such as angina or hypertension may be changed to one approved for the treatment of heart failure, or the beta blocker already prescribed may be continued.[7] Individual clinical factors such as comorbidities (eg. atrial fibrillation) and tolerability may influence the decision to continue or change the beta blocker in use.

For patients who have previously tried a beta blocker for another condition, and discontinued it because of adverse effects, consider re-starting therapy with an agent approved for heart failure, unless contraindicated.[4,7]

### Initiating beta blockers

Start low and go slow *Table 1*:
• commence with the low dose specified
• increase the dose gradually to the highest tolerated dose.
*Table 1* outlines minimum recommended titration intervals. The rate of dosage increase may need to be slower. Slow upward titration over weeks minimises adverse effects associated with beta blocker therapy in heart failure (eg. increased tiredness, hypotension).[8]

### Monitoring and review

• Monitor heart rate, blood pressure and clinical signs and symptoms of heart failure on a weekly basis during dose titration
• Advise patients to weigh themselves daily, preferably each morning before dressing. Changes of >1.5 kg in 24 hours may indicate increased fluid retention.[4,7,10]

### Managing adverse effects

Adverse effects are often (but not always) transient and any interventions may only need to be temporary. Adverse effects include increased fatigue, hypotension, bradycardia, increased fluid retention, and bronchospasm.[4,7]

### Low blood pressure

If asymptomatic hypotension is present, usually no change in therapy is required. If hypotension causes dizziness, light headedness or confusion, consider the effects of drugs that may lower blood pressure (eg. antihypertensive agents, alpha blockers and tricyclic antidepressants). Diuretic dose may require adjustment.

### Heart rate

If the heart rate is <50 bpm an electrocardiogram (ECG) should be performed even if the patient is asymptomatic. The dose of beta blocker should be reduced if there is symptomatic bradycardia. Review the need to continue treatment with other drugs that may slow heart rate (eg. verapamil, diltiazem, digoxin and amiodarone). If unsure, consult a specialist.

### Increased fluid retention

Increase the dose of loop diuretic, monitoring carefully for volume depletion and electrolyte disturbances. If the response is unsatisfactory, consider reducing the dose of beta blocker. Review the need to continue treatment with drugs that may exacerbate fluid retention (eg. nonsteroidal anti-inflammatory drugs [NSAIDs], both traditional NSAIDs and COX-2 selective agents).

### Severe fatigue

Exclude conditions such as anaemia, depression or hypothyroidism. If persistent consider reducing the dose of beta blocker.

### Bronchospasm

Beta blockers can aggravate bronchospasm in patients with asthma and/or chronic obstructive pulmonary disease (COPD). However, many patients with mild asthma tolerate beta blockers well. Patients with COPD who do not have a bronchospasm component to their illness may also tolerate beta blockers. Monitor for deterioration and

Table 1. Dosage recommendations for beta blockers approved to treat heart failure in Australia[8] (these agents are PBS listed for moderate to severe heart failure in patients stabilised on conventional therapy which must include an ACEI if tolerated)

| Beta blocker | Starting dose | Up titration | Target dose |
|---|---|---|---|
| Bisoprolol (Bicor®) | 1.25 mg once daily for 1 week | Increase dose if tolerated: 2.5 mg once daily for 1 week, then 3.75 mg once daily for 1 week, then 5 mg once daily for 4 weeks, then 7.5 mg once daily for 4 weeks, then to target maintenance dose | 10 mg once daily |
| Carvedilol (Dilatrend®, Kredex®) | 3.125 mg twice daily for 2 weeks | Increase dose if tolerated: at intervals of at least 2 weeks to 6.25 mg twice daily, then 12.5 mg twice daily, then to target maintenance dose | 25 mg twice daily (in patients <85 kg with mild to moderate heart failure and in all patients with severe heart failure) or 50 mg twice daily (in patients >85 kg) |
| Metoprolol succinate controlled release (Toprol-XL®) | 23.75 mg once daily* for 2 weeks | Increase dose if tolerated: at intervals of at least 2 weeks to 47.5 mg daily, then 95 mg daily, then to target maintenance dose | 190 mg once daily |

* If NYHA Class III-IV initiate at half 23.75 mg tablet once daily for 1 week then a full 23.75 mg tablet once daily for second week

counsel patients to report increasing breathlessness and wheeze. Beta blockers may be contraindicated in patients with fully or partially reversible airways disease, where inhaled beta agonists provide functional or symptomatic benefit.

## Cessation

Beta blockers should not be stopped abruptly unless absolutely necessary; ideally seek specialist advice before discontinuation.

## Pre-existing conditions where specialist management may be indicated

- Uncontrolled heart failure, valvular heart disease particularly aortic stenosis/incompetence and mitral regurgitation
- Severe heart failure requiring hospitalisation and/or intravenous diuretics
- Reversible airways disease, asthma
- Bradycardia, ie. <50 bpm
- Symptomatic hypotension
- Second or third degree heart block (unless managed with a pace maker)
- Severe ischaemic heart disease requiring other specialist intervention.[4,10]

For drug information including precautions, adverse effects, interactions and contraindications, please refer to the *Australian Medicines Handbook* 2007 and approved product information.[8]

Conflict of interest: none.

## References
1. Australian Institute of Health and Welfare. Heart failure... what of the future? June 2003. Available at www.aihw.gov.au/publications/aus/bulletin06/bulletin06.pdf.
2. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. Available at www.heartfoundation.com.au/downloads/CHF_2006_Guidelines_NHFA-CSANZ_WEB_PDF-1.2MB.pdf.
3. Phillips SM, Marton RL, Tofler GH. Barriers to diagnosing and managing heart failure in primary care. Med J Aust 2004;181:78–81.
4. American College of Cardiology and the American Heart Association. ACC/AHA Guidelines for the evaluation and management of chronic heart failure in the adult, 2005. Available at content.onlinejacc.org/cgi/reprint/46/6/e1.
5. National Heart Foundation of New Zealand. A guideline for the management of heart failure – health professionals guide, 2001. Available at www.nhf.org.nz/files/Cardiac_Care/heart_failure_guidelines.pdf.
6. Therapeutic Guidelines. Cardiovascular. Version 4. 4 edn. Melbourne: Therapeutic Guidelines Limited, 2003.
7. The National Collaborating Centre for Chronic Conditions. Chronic heart failure: national clinical guideline for diagnosis and management in primary and secondary care. Royal College of Physicians of London. 2003. Available at www.nice.org.uk/pdf/Full_HF_Guideline.pdf.
8. Rossi S, et al, editors. Australian Medicines Handbook. Adelaide: Australian Medicines Handbook, 2007.
9. Haas SJ, Gilbert RE, Krum H. Are beta-blockers as efficacious in patients with diabetes mellitus as in patients without diabetes mellitus who have chronic heart failure? A meta-analysis of large-scale clinical trials. Am Heart J 2003;146:848–53.
10. Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. [Erratum appears in Eur Heart J 2001 Dec;22:2217–8]. Eur Heart J 2001;22:1527–60.

**AFP** CORRESPONDENCE afp@racgp.org.au