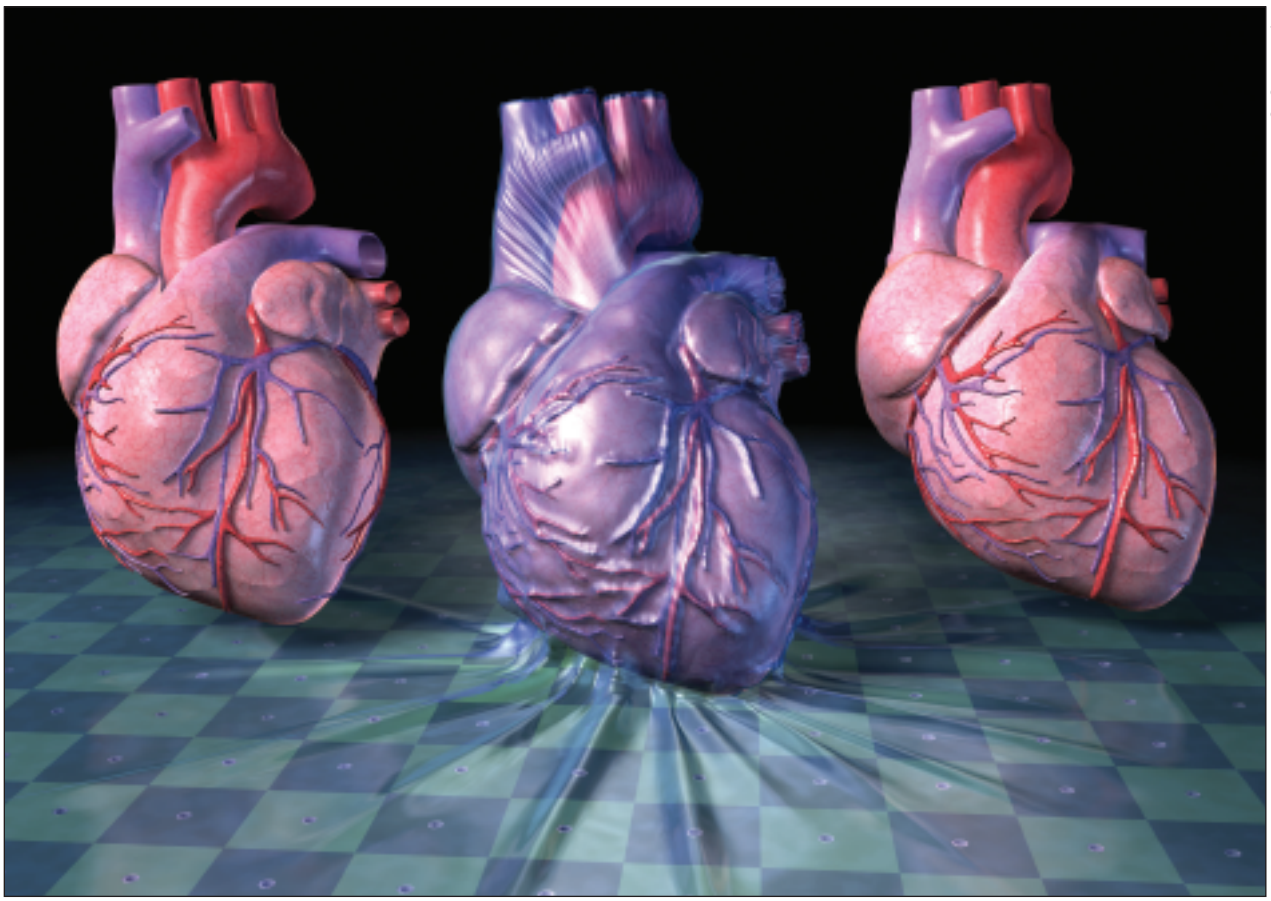
Current drug therapies for the secondary prevention of MI

Ninian Lang *BSc(Hons), MRCP* ***and Keith Fox*** *BSc(Hons), FRCP, FESC*



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Current approaches to the secondary prevention of myocardial infarction include the use of both well-established and newer agents. Our Drug review considers their mode of action and properties and the evidence base for their efficacy, followed by sources of further information and the Datafile.

Ischaemic heart disease presents a huge health burden to UK society – over 1.2 million people currently alive in the UK have had a heart attack. One of the greatest challenges, after primary prevention, rests with the secondary prevention of further ischaemic events and complications. This should involve risk factor management and identification, as well as the introduction of lifestyle measures, drug therapy and cardiac rehabilitation (see Figure 1).

Between 7 and 15 per cent of patients who suffer an acute myocardial infarction (MI) die within one year of hospital discharge. Patients who survive the acute phase of MI are, therefore, a group at high risk of future ischaemic events and neither morbidity nor mortality should be underestimated.

Changes in diagnostic criteria have progressively lowered the threshold for the diagnosis of MI and more patients are now considered appropriate targets for secondary prevention. This is justifiable: based on data from the Global Registry of Acute Coronary Events (GRACE), this population of

patients not previously fulfilling diagnostic criteria for MI are still at increased risk of coronary events and death compared with those who are troponin negative. Evidence also confirms a two-fold increase in both one-year and four-year mortality after non-ST elevation MI (NSTEMI) when compared with mortality after ST elevation MI (STEMI).

Efforts aimed at efficiently and effectively directing secondary prevention strategies have been outlined in the government's National Service Framework for coronary heart disease. Furthermore, both the Scottish Intercollegiate Guidelines Network (SIGN) and the National Institute for Health and Clinical Excellence (NICE) have published updated guidelines for secondary prevention after MI. These guidelines provide excellent and timely advice but, while many approaches are well established, progress in this area is rapid and aspects of the evidence base can become quickly outdated.

This review will outline contemporary drugs used in the secondary prevention of MI. It will provide the reader with an insight into the pharmacological action of these agents, give a rationale for their use and guide a sensible post-MI drug regimen. The role of cardiac rehabilitation and lifestyle change is, of course, of the utmost importance but discussion falls outwith the scope of this article, as does any detailed discussion of implantable devices.

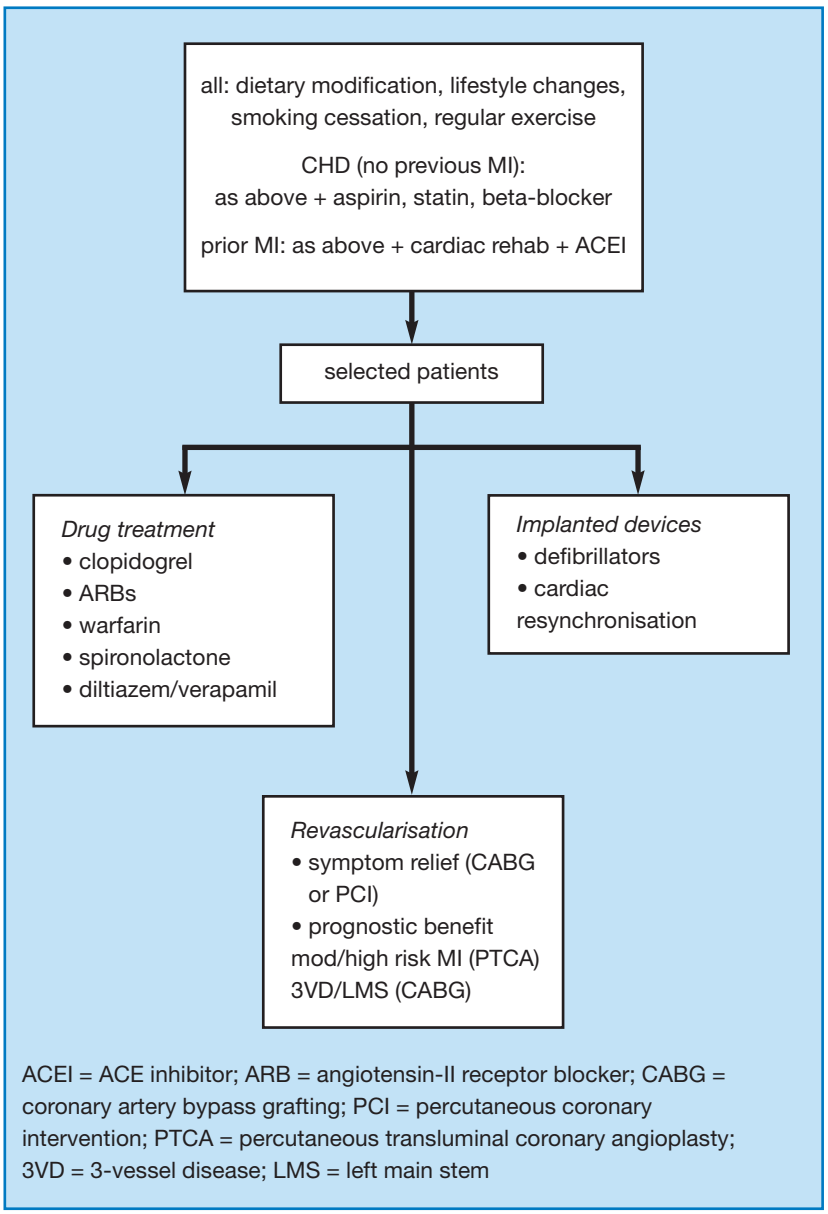

Figure 1. Overview of standard therapies and those for use in selected patients in the secondary prevention of myocardial infarction

Antiplatelet agents

Aspirin

One of the largest bodies of evidence for any drug used in secondary prevention post-MI exists for aspirin. By irreversibly blocking cyclo-oxygenase, aspirin alters the balance between platelet thromboxane A_2 and prostacyclin to favour the inhibition of both platelet aggregation and arterial thrombus formation.

In a large meta-analysis, aspirin use in patients with a history of MI was associated with large, highly significant reductions in nonfatal reinfarction and vascular death as well as a reduction in nonfatal stroke (see Table 1).[1]

Most of aspirin's unwanted effects are dose related and result from an increased bleeding risk. Cyclo-oxygenase inhibition results in the loss of prostaglandin-mediated mucosal protection and can result in gastritis and peptic ulceration. Coupled with platelet inhibition, upper gastrointestinal bleeding can ensue but aspirin's beneficial cardiovascular effects in secondary prevention have been shown to far outweigh the risk of major bleeding.[1] It is, therefore, recommended that aspirin should be continued indefinitely post-MI at a dose of 75-150mg. Higher doses are no more effective and are associated with a greater incidence of gastrointestinal side-effects.[1] For patients with a history of dyspepsia and those with a history of aspirin-induced bleeding whose ulcers have healed and are *Helicobacter pylori* negative, NICE guidance recommends that aspirin should be co-administered with a proton pump inhibitor.

While the overall population benefit of aspirin use in secondary prevention is large, not all patients benefit to the same extent and 'aspirin resistance' is observed in approximately 25 per cent of patients. While it has been argued that this may, in part, reflect

noncompliance, pharmocodynamic, pharmacokinetic and biochemical factors are likely to be involved. A recent systematic review has confirmed that, in comparison to 'aspirin responders', patients deemed to be 'aspirin resistant' on the basis of laboratory measures are at almost four times greater risk of recurrent cardiovascular events.[2]

Clopidogrel

Clopidogrel (Plavix) exerts its antiplatelet effects via the inhibition of adenosine diphosphate-mediated platelet aggregation and has a firm evidence base to support its use as an adjunct to aspirin in patients with NSTEMI.[3] More recent evidence has shown beneficial effects on artery patency and mortality rates when given with thrombolysis for STEMI.[4,5]

The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial compared outcomes in patients randomly assigned to receive either combined treatment with aspirin plus clopidogrel or aspirin plus placebo shortly after NSTEMI. After 3-12 months' treatment, clopidogrel significantly reduced the primary composite end-point of death from cardiovascular causes, MI and stroke[3] (see Table 1). Based on this evidence, current NICE guidelines recommend that clopidogrel should be continued for one year following NSTEMI.

However, SIGN recommends only three months' treatment in this context. They justify this with the observations from both CURE and CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance)[6] trials. When dual antiplatelet therapy was continued for more than three months following NSTEMI, the beneficial trends for clopidogrel were either absent or restricted to subsets of patients but accompanied by a significant increase in bleeding risk.[7]

Newer trial data examining the use of clopidogrel after STEMI has prompted both SIGN and NICE to recommend its use in addition to aspirin for four weeks following STEMI. This guidance is principally based upon data obtained from COMMIT/CCS-2 (Clopidogrel and Metoprolol in Myocardial Infarction Trial/Second Chinese Cardiac Study) that demonstrated that treatment with clopidogrel (in addition to aspirin) for four weeks following STEMI resulted in a reduction of death, reinfarction and stroke. Importantly, these benefits were seen in the absence

Intervention	Study	Study design	MI	All vascular events	Vascular mortality	All-cause mortality	Study duration
Aspirin	Antithrombotics Trialists Collaboration (1994)	meta-analysis	37	19	71	68	2 years
Clopidogrel	CURE	RCT (addition of clopidogrel to aspirin after NSTEMI)	67	59	250	250	1 year
Beta-blockers	Freemantle *et al* (1999)	meta-analysis	56			48	1 year
ACE inhibitors	HOPE	RCT (ramipril in high-risk patients with normal LV function)	42	27	50	56	4.5 years
	Flather and Yusuf (2000)	meta-analysis (ACEI in patients with LV dysfunction)	43			17	2 years
Statins	Rembold (1996)	meta-analysis	23	15	44	37	5 years
	MRC/BHF Heart Protection Study	RCT	32	19		56	5 years
	4S	RCT		8	31	33	5 years
	CARE	RCT		11	95	133	5 years
Mediterranean diet	De Lorgeril *et al* (1994)	RCT (Mediterranean diet advice *vs* standard dietary advice)				25	27 months
High fish oil diet	DART	RCT				29	2 years
*Smoking cessation**	Daly *et al* (1983)	observational study			21		N/A

(RCT = randomised control trial; NSTEMI = non-ST elevation MI; ACEI = ACE inhibitor)
*NNTs for smoking cessation are not strictly comparable with drug NNTs as the treatment is only given once and the events prevented are counted over a lifetime

Table 1. Numbers needed to treat over study duration to prevent myocardial infarction, vascular events and death for the more commonly used strategies in the secondary prevention of myocardial infarction

of an excess of bleeding complications.[5] However, the effects of longer clopidogrel treatment periods after STEMI are as yet unknown.

Clopidogrel has no effect on gastric prostaglandins and theoretically should not induce gastritis or peptic ulceration. In the head-to-head comparison of long-term clopidogrel versus aspirin in patients with vascular disease (CAPRIE Trial) there was a modest reduction in bleeding with clopidogrel.[8] For this reason, clopidogrel has often been used as a substitute for aspirin in patients deemed to be at high risk of gastrointestinal bleeding. However, randomised controlled trial data have shown that in patients with a history of aspirin-induced ulcer bleeding whose ulcers have healed and have negative *H. pylori* status, combined treatment with aspirin and a proton pump inhibitor is superior to clopidogrel alone in the prevention of recurrent ulcer bleeding.[9]

Anticoagulants

New oral anticoagulants are currently under evaluation and include the Factor Xa inhibitor rivaroxiban. However, warfarin remains the cornerstone of oral anticoagulant therapy.

Trials examining the use of warfarin post-MI have yielded inconsistent results but most studies report an excess of haemorrhagic complications. Therefore, warfarin is not recommended for routine use in the post-MI population. However, its use may be considered in patients with intolerance to both aspirin and clopidogrel. Furthermore, warfarin treatment post-MI may be an appropriate first-line therapy in patients who develop atrial fibrillation post-MI. Its use is also appropriate in patients with left ventricular thrombus and potentially in those with a severely dilated left ventricle.

There is very little evidence available to guide recommendations for antiplatelet therapies in patients prescribed warfarin for other indications who subsequently suffer MI. In this group, current NICE guidance suggests that the addition of aspirin should be considered in those at low risk of bleeding but the combination of clopidogrel and warfarin is not routinely recommended. Recent European Society of Cardiology guidelines for the treatment of NSTEMI[10] advise that decisions regarding combined warfarin and antiplatelet therapy should be individualised to each patient and should take into account both thromboembolic and bleeding risk. They also highlight the fact that the warfarin/antiplatelet combination poses a relatively low risk of bleeding in the elderly, providing that tight control of the international normalised ratio (INR) can be achieved.

Rate-limiting agents

Beta-blockers

Although they have fallen from favour as first-line agents for the treatment of hypertension, beta-blockers remain important in the secondary prevention of MI.

The mechanisms by which beta-blockers produce their beneficial cardioprotective effects are diverse and not completely understood. Beta-blockers produce an antihypertensive effect by inhibition of vascular adrenoceptors and by reducing renin and angiotensin production. These drugs mediate further anti-ischaemic actions by decreasing myocardial oxygen demand and cardiac contractility, while a reduction in heart rate allows increased diastolic coronary perfusion. As well as having important antiarrhythmic properties, beta-blockers improve left ventricular structure and function.

In addition to examining the role of clopidogrel after STEMI, another arm of COMMIT/CCS-2 examined the effects of early intravenous beta-blocker therapy in similar patients.[11] It failed to show a mortality benefit when beta-blockers were administered within 24 hours of MI and also found that this regimen was associated with the early development of cardiogenic shock. However, large trials assessing the longer-term effects of beta-blockers have shown that use post-MI can improve survival by 20-25 per cent. This mortality benefit comes through a reduction of cardiac mortality, sudden cardiac death and reinfarction[12,13] and is evident even after the administration of fibrinolysis, aspirin or ACE inhibitors[14] (see Table 1). These benefits have been demonstrated in a very broad population of patients but are most marked in high-risk patients including diabetic patients and those with large or anterior MI or cardiac failure. The beneficial effect of beta-blockade after MI has been demonstrated for up to six years.

Drug	Dose	Study
ramipril	5mg twice daily	AIRE
ramipril	10mg daily	HOPE
captopril	50mg twice daily	ISIS-4
enalapril	20mg twice daily	CONSENSUS
enalapril	10mg twice daily	SOLVD
captopril	25mg 3 times daily	SAVE

Table 2. ACE inhibitor dosages used in trials

Both SIGN and NICE advocate that all patients who have had an MI should be treated with beta-blockers as early as possible, providing that the patient is haemodynamically stable and in the absence of other contraindications. The guidelines extrapolate the data to advocate lifelong treatment and highlight the appropriateness of their use in patients with co-existing hypertension, left ventricular systolic dysfunction or angina. It should be noted, however, that the majority of the trials that underpin the guidance predate the current practice of a more frequent early invasive strategy following MI. Therefore, the benefits of beta-blockade may be less marked in those who have undergone early invasive treatment. In the light of the COMMIT/CCS-2 trial these agents should not be initiated until acute heart failure (NYHA grade III or IV) and/or hypotension have resolved.

In terms of side-effect profile, but not necessarily event rates, there are advantages in the use of cardioselective beta-blockers. However, beta-blockers with intrinsic sympathomimetic activity (an ability to simultaneously act as agonist and blocker at the beta receptor) may be associated with an adverse prognosis after MI and should not be used in this setting. When used in the context of left ventricular dysfunction, beta-blockers with associated vasodilator properties, *eg* carvedilol, are particularly appropriate and an agent licensed for use in heart failure should be preferred.

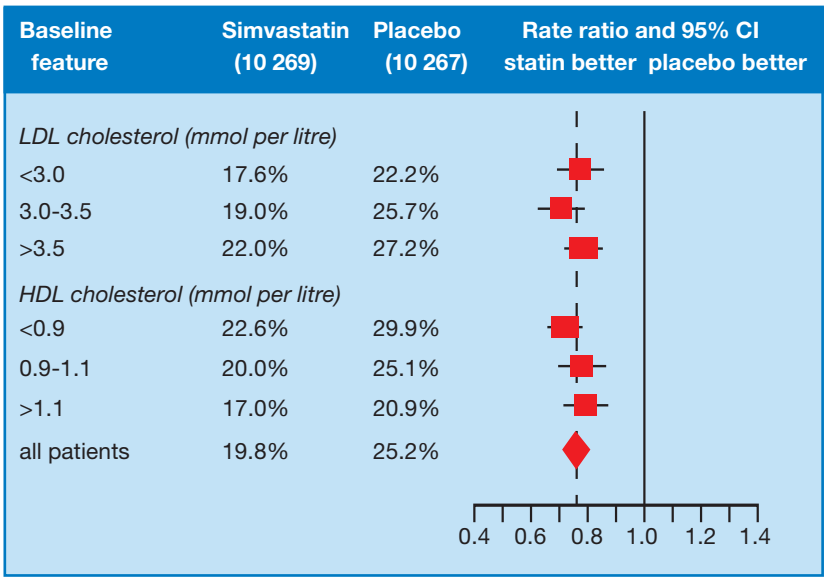

Figure 2. Similar relative reduction in first major vascular event was shown to be independent of baseline LDL and HDL in the MRC/BHF Heart Protection Study comparing simvastatin 40mg once daily *vs* placebo in patients with coronary disease, other occlusive arterial disease or diabetes (41 per cent had had a prior MI)[12]

The side-effect profile for beta-blockers is long but, arguably, its overstatement has contributed to their underuse in secondary prevention. In general, beta-blockers are well tolerated but beta-blockade can cause fatigue and can exacerbate symptoms of cold extremities, Raynaud's phenomenon and severe peripheral vascular disease. Bradycardia and atrioventricular block can occur and caution should be exercised when co-prescribing beta-blockers with other rate-limiting agents. While beta-blockers may mask some of the warning symptoms of hypoglycaemia, other symptoms are maintained and their clinical benefit in diabetic patients after MI far outweighs their risks. Asthma is an absolute contraindication to beta-blockade but use should be attempted in patients with COPD where their benefits outweigh the risks. While some beta-blockers are excreted via the renal tract, others are hepatically metabolised and care should be taken when prescribing these drugs for patients with renal or hepatic dysfunction respectively.

Rate-limiting calcium channel blockers

Trials of the use of rate-limiting calcium channel blockers have shown that these drugs may marginally decrease rates of recurrent infarction post-MI. However, beneficial effects have only been seen in patients without evidence of left ventricular dysfunction, and in patients with left ventricular dysfunction treatment with these drugs caused a trend towards harm.[15,16] SIGN advises that, other than for the treatment of hypertension post-MI, there is insufficient evidence to recommend their routine use in secondary prevention. NICE recommends that rate-limiting calcium channel blockers should not routinely be used post-MI but may be considered in patients with normal left ventricular function in whom beta-blockers are contraindicated or need to be discontinued.

Inhibition of the renin-angiotensin-aldosterone axis

ACE inhibitors

ACE inhibitors have a very strong evidence base for their use in the secondary prevention of MI. Although their antihypertensive action could account for some of the observed treatment effects, this is unlikely to account for all the benefit derived from their use. By preventing the formation of the active peptide, angiotensin II, ACE inhibitors reduce cardiac preload and afterload without causing reflex tachycardia. They exhibit positive effects on postinfarct remodelling and endothelial function and can block local mediators of thrombosis.

The Heart Outcomes Prevention Evaluation (HOPE) study provided evidence for their use in patients post-MI, regardless of left ventricular function (see Table 1).[17] Current guidelines advocate that ACE inhibitors be started in all patients as soon as possible after MI and continued indefinitely in the absence of contraindications.

ACE inhibitors should be used cautiously in patients with aortic stenosis. These drugs are contraindicated in patients with severe bilateral renal artery stenosis and may cause acute renal failure in patients with pre-existing renal disease or dehydration. Renal function should be checked before starting an ACE inhibitor and should be checked again one to two weeks after starting treatment. It should also be checked before and after dose increases, and if additional diuretics are added. Although ACE inhibitors predispose to hyperkalaemia in patients with co-existing heart failure, the co-prescription of low-dose potassium-sparing diuretic is not contraindicated provided patient selection is judicious and potassium levels monitored carefully.

By causing an accumulation of bradykinin, ACE inhibitors can provoke angioedema in susceptible individuals and can be associated with a dry cough.

Angiotensin-II receptor blockers

Angiotensin-II receptor blockers (ARBs) act by blocking the action of angiotensin II at its receptor. As they do not block the synthesis of angiotensin II, accumu-

Drug	Indication	Contraindication	Special precaution	Comments
Beta-blockers	all ischaemic heart disease (IHD)	asthma	COAD, peripheral vascular disease	rate-limiting calcium-channel blocker if contraindicated
ACE inhibitors	prior MI with or without LV dysfunction	renal artery stenosis	hypotension	titrate to target doses
Antiplatelets	all IHD	peptic ulceration		
Statins	all IHD	liver failure		use high dose

Table 3. Indications and contraindications of drugs used in ischaemic heart disease

lation of bradykinin does not occur and cough and angioedema are not common side-effects.

The Valsartan in Acute Myocardial Infarction Trial (VALIANT) demonstrated noninferiority of the ARB valsartan (Diovan) when compared head-to-head with an ACE inhibitor in the treatment of patients with heart failure post-MI.[18] However, trials have failed to show superiority of ARBs over ACE inhibitors in the treatment of this group. ACE inhibitors should therefore continue to be used as a first-line treatment in patients post-MI, but if side-effects such as cough or angioedema are encountered ARBs provide a suitable, although less evidence-based, alternative. Evidence for the benefits of co-prescribing an ACE inhibitor with an ARB is not considered to be strong enough to recommend this strategy at this stage.

Aldosterone antagonists

The aldosterone antagonist eplerenone (Inspra) has recently been licensed for secondary prevention in patients with heart failure post-MI.

Aldosterone antagonists exert vascular protective effects via a variety of mechanisms. As well as a potassium-sparing diuretic effect, they have favourable effects upon vascular inflammation and ventricular remodelling and improve indices of endothelial function.

The Eplerenone Post Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) examined its use in patients post-MI with an ejection fraction of less than 40 per cent and either diabetes mellitus or clinical signs of heart failure.[19] In addition to standard medical therapy, its use resulted in a 2.3 per cent absolute risk reduction (14 per cent relative risk reduction) in all-cause mortality. Based upon these results, both SIGN and NICE guidelines state that it should be initiated in similar patients within 3-14 days of MI and continued indefinitely.

Serum electrolytes should be measured prior to commencing treatment with eplerenone and during treatment. It should be used more cautiously in patients at risk of developing hyperkalaemia and should not be co-prescribed with potassium supplements or other potassium-sparing diuretics, such as spironolactone. In contrast to spironolactone, eplerenone use at recommended doses is not associated with gynaecomastia in men or menstrual irregularities in women. Both aldosterone antagonists can be associated with gastrointestinal upset.

Lipid management

HMG-CoA reductase inhibitors (statins)

The use of statins in the secondary prevention of heart disease has been the focus of many randomised controlled trials.

Inhibition of the hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase enzyme prevents hepatic cholesterol synthesis and enhances the elimination of LDL-cholesterol from the blood. Furthermore, it is becoming clearer that the beneficial effects of statins are likely to be related to their additional cardioprotective anti-inflammatory properties.

The Heart Protection Study demonstrated large and significant reductions in the rate of vascular deaths and major vascular events in high-risk patients (41 per cent of whom had suffered a prior MI) treated with simvastatin 40mg daily versus placebo.[20] Reductions in risk were not dependent upon pretreatment LDL-cholesterol levels (see Table 1 and Figure 2), but influenced by overall risk of the patients. Therefore, SIGN guidance advocates statin therapy for all patients who have suffered a MI, regardless of baseline lipid levels. NICE guidelines propose similar measures but emphasise that the decision to prescribe a statin should take into account additional factors such as co-morbidities and life expectancy.

Side-effects from statin use are most often dose dependent, but may also be associated with the

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Figure 3. Lifestyle changes should not be overlooked in the secondary prevention of myocardial infarction

preparation prescribed. They can cause liver enzyme abnormalities and should be used with caution in patients with a history of liver disease or high alcohol intake. The *BNF* advises that liver function should be checked before commencing treatment and one to three months after starting a statin and, during the following year, checks should be made at intervals of six months unless indicated sooner. Treatment should be discontinued if serum transaminase concentration rises to three times the upper limit of normal. While NICE advocates that baseline liver function tests are checked, they advise that patients with raised liver enzymes should not routinely be excluded from statin therapy.

All patients treated with statins should be advised to seek medical advice if they develop symptoms of muscular pain, tenderness or weakness in order for creatine kinase to be checked. It should be noted that co-administration of a statin with a fibrate, high-dose nicotinic acid or immunosuppressants such as ciclosporin increases the risk of myalgia, myositis and rhabdomyolysis.

Patients who are intolerant of statins should be considered for treatment with alternative lipid-lowering agents such as fibrates, nicotinic acid or ezetimibe (Ezetrol). These drugs may also be used in combination with a statin if lipid control is inadequate.

Conclusion

It is important not to overlook lifestyle changes and cardiac rehabilitation as mainstays of secondary prevention of morbidity and mortality after MI. In the past, insufficient emphasis has been placed on the importance of smoking cessation as well as dietary changes and exercise compared with secondary prevention using drug therapies.

The modern pharmacological means by which secondary prevention is achieved rests upon the use of both well-established and newer treatments. Furthermore, accumulating observational evidence suggests that compliance with evidence-based therapies for acute and chronic coronary disease contributes to the decline in coronary events, including deaths and the development of new heart failure.[21] The clinical impact of these medications on risk reduction may, however, be underestimated because of the high risk of events following ST and non-ST elevation acute coronary syndromes. A pharmacological intervention with a modest relative risk reduction may nevertheless have a clinically important impact upon morbidity and mortality.

As guidelines and evidence for the use of these treatments is applied to larger subgroups, it remains a task for the attending physician to tailor an ever-increasing range of treatments to his or her own individual patients. However, wider appreciation of the impact that these therapies have upon both morbidity and mortality should stimulate the more efficient and effective usage of secondary prevention strategies in the future.

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Dr Lang is a research fellow and Keith Fox is Duke of Edinburgh Professor of Cardiology at the Centre for Cardiovascular Science, University of Edinburgh

Resources

Guidelines

SIGN Guideline 97. *Risk estimation and the prevention of cardiovascular disease.* February 2007. (www.sign.ac.uk/guidelines/fulltext/97/index.html)

NICE Clinical Guideline 48. *MI: Secondary prevention in primary and secondary care for patients following a myocardial infarction*. May 2007. (www.nice.org.uk/guidance/index.jsp?action=byID&r=true&o=11008)

Department of Health. *National service framework for coronary heart disease.* March 2000. (www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4094275)

Groups and organisations

British Heart Foundation, 14 Fitzhardinge Street, London W1H 6DH. Tel: 020 7935 0185, website: www.bhf.org.uk. Charity providing information on all aspects of heart disease for patients and health professionals.

Chest, Heart & Stroke Scotland, 65 North Castle Street, Edinburgh. Tel: 0131 225 6963, fax: 0131 225 6313, website: www.chss.org.uk. Charity aiming to improve the quality of life for people in Scotland affected by chest, heart and stroke illness through medical research, advice and information, and support in the community.

Other useful resources

BMJ Collected Resources. All articles published in the *BMJ* since January 1998. (bmj.bmjjournals. com/collections)

Coronary heart disease statistics: factsheet. British Heart Foundation Statistics, 2007 Available from: www.heartstats.org.

Drugs used in the secondary prevention of MI

Drug	Available as	Form/strength	Dosage	Cost[1]
Antiplatelet drugs				
aspirin	Angettes Nu-Seals aspirin	75mg tabs 75mg tabs 75mg soluble tabs	75-150mg once daily 75mg daily 75-150mg once daily 75mg gastro-resistant tabs	87p-£1.74 £1.30 29-58p 51-86p
clopidogrel	Plavix	75mg tabs	75mg daily	£35.31
ACE inhibitors				
captopril	Acepril Capoten captopril	12.5mg, 25mg, 50mg tabs 12.5mg, 25mg, 50mg tabs 12.5mg, 25mg, 50mg tabs	75-150mg daily in divided doses	£16.78-£28.60 £16.78-£28.60 £1.41-£2.05
lisinopril	Carace Zestril lisinopril	5mg, 10mg, 20mg tabs 2.5mg, 5mg, 10mg, 20mg tabs 2.5mg, 5mg, 10mg, 20mg tabs	5mg once daily for 2 days, then 10mg once daily	£10.51 £9.70 74p
perindopril	Coversyl perindopril	2mg, 4mg, 8mg tabs 2mg, 4mg, 8mg tabs	4mg once daily for 2 weeks, then 8mg once daily	£10.60 £10.29
ramipril	Tritace ramipril	1.25mg, 2.5mg, 5mg, 10mg tabs 1.25mg, 2.5mg, 5mg, 10mg tabs/caps	2.5-5mg twice daily	£15.02-£20.92 tabs: £4.00-£5.76 caps: £1.60-£2.06
trandolapril	Gopten	0.5mg, 1mg, 2mg, 4mg caps	4mg once daily	£11.64
Angiotensin-II receptor blocker				
valsartan	Diovan	40mg (caps and tabs), 80mg, 160mg caps	160mg twice daily	£43.32
Aldosterone antagonist				
eplerenone	Inspra	25mg, 50mg tabs	50mg once daily	£42.72

[1]NHS cost of 28 days' treatment at the usual maintenance dosage. Prices *MIMS/Drug Tariff* November 2007

Drugs used in the secondary prevention of MI (cont.)

Drug	Available as	Form/strength	Dosage	Cost[1]
Noncardioselective beta-blockers				
timolol	Betim	10mg tabs	5mg twice daily for 2 days, then 10mg twice daily	£3.88
propranolol	Syprol	5mg, 10mg, 50mg per 5ml oral soln	40mg 4 times daily for 2-3 days, then 80mg twice daily	£55.94
	propranolol	10mg, 40mg, 80mg, 160mg tabs	5-21 days post-MI	£2.14
Cardioselective beta-blockers				
atenolol	Tenormin	25mg, 50mg (LS), 100mg tabs	50-100mg daily	£5.11-£6.50
	Tenormin Syrup	25mg per 5ml		£7.98-£15.96
	atenolol	25mg, 50mg, 100mg tabs		29p
metoprolol	Lopresor	50mg, 100mg tabs	200mg daily	£6.68
	metoprolol	50mg, 100mg tabs		£2.60
Class I calcium-channel blocker				
verapamil	Securon SR	120mg (Half Securon SR), 240mg sust-rel tabs	360mg daily in divided doses	£14.07 (240mg + 120mg) or £24.54 (3 x 120mg)
Omega-3 acid ethyl ester				
EPA/DHA[2]	Omacor	1000mg gelatin caps (EPA 460mg, DHA 380mg)	1 daily with food	£13.89
Statins				
pravastatin	Lipostat	10mg, 20mg, 40mg tabs	40mg once daily at night	£27.61
	pravastatin	10mg, 20mg, 40mg tabs		£7.54
simvastatin	Zocor	10mg, 20mg, 40mg, 80mg tabs	20-40mg once daily in the evening	£29.69
	simvastatin	10mg, 20mg, 40mg, 80mg tabs		54p-£1.31

[1]NHS cost of 28 days' treatment at the usual maintenance dosage. Prices *MIMS/Drug Tariff* November 2007
[2]eicosapentaenoic acid and docosahexaenoic acid