8

Prescribing in cardiology

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Key learning points:

- Overview of the disease state
- Key issues for prescribing in this clinical area
- Overview of knowledge and skills for safe and effective prescribing
- Clinical case studies to demonstrate issues in non-medical prescribing
- Cardiology covers a wide range of clinical conditions, but the three areas in which non-medical prescribers are most likely to engage are:
  - Hypertension
  - Ischaemic heart disease (IHD)
  - Heart failure.

Hypertension

Hypertension is defined as a 'sustained blood pressure of greater than 140/90 mmHg'. Most patients with hypertension will be asymptomatic, although some patients with very elevated pressures may complain of headaches. Most cases are therefore picked up on routine blood pressure checks, and an initial high reading should be confirmed by repeated readings taken on two further separate occasions before a diagnosis is made.

Hypertension is generally categorised as 'essential' hypertension, which accounts for 95% of cases and for which no known cause can be identified, or 'secondary' hypertension which accounts for the remaining 5% of cases and where a cause can be found. Key risk factors for developing hypertension include increasing age, Black African or Caribbean background and, for early onset hypertension, male gender. Blood pressure control in patients with hypertension is important to protect against the development of target organ damage and other long-term complications (*Box 8.1*).

Box 8.1 *Target organ damage and complications of hypertension*

- Stroke, transient ischaemic attack (TIA), dementia, carotid bruits
- Left ventricular hypertrophy and/or left ventricular strain on ECG, heart failure
- Myocardial infarction, angina, coronary artery bypass graft or angioplasty
- Peripheral vascular disease
- Fundal haemorrhages or exudates, papilloedema
- Proteinuria
- Renal impairment (raised serum creatinine or reduced estimated glomerular filtration rate).

Key interventions to address high blood pressure are lifestyle modification and drug therapies.

Patients with blood pressure above 140/90 mmHg but lower than 160/100 mmHg without additional risk factors (no cardiovascular disease, diabetes, renal disease or at <20% risk of developing cardiovascular disease over the next 10 years) should be managed by addressing lifestyle issues alone.

Lifestyle advice should be given as part of a full discussion with the patient to identify any specific issues and emphasise the relative contribution of each risk factor to the development of hypertension. Areas to cover in discussion are:

- diet, particularly reducing salt intake
- weight reduction
- increasing physical activity
- smoking cessation
- moderating alcohol intake.

It is important not to underestimate how difficult lifestyle change can be, and patients should be encouraged to set realistic goals. Patients are unlikely to stick to an aggressive regimen that requires them to address every area of their lifestyle in one go. It may be appropriate to focus on one or two key areas and progress to other issues, as the patient succeeds in these areas (*Table 8.1*).

Prescribing in hypertension

Drug therapy should be initiated where blood pressure is consistently >160/100 mmHg or in patients with blood pressure >140/90 mmHg where additional risk factors are present, such as established cardiovascular

Table 8.1 Impact of lifestyle change on systolic blood pressure

Intervention	Effect on systolic blood pressure
Weight reduction	5–10 mmHg/10 kg weight loss
Diet rich in fruit and veg, low in dairy, reduced saturated fat	8–14 mmHg
Restricted dietary sodium	2–8 mmHg
Physical activity	4–9 mmHg
Alcohol moderation	2–4 mmHg

From Williams *et al.* (2004).

disease, diabetes, chronic kidney disease, or the patient is at >20% risk of developing cardiovascular disease. Once drug therapy is initiated, the aim is to lower blood pressure to less than 140/90 mmHg, with more aggressive targets for patients with diabetes (aim for blood pressure <140/80 mmHg or <130/80 mmHg if evidence of kidney, eye or cerebrovascular disease) or chronic kidney disease (aim for blood pressure <130/80 mmHg).

Choice of drug in the treatment of hypertension should be determined by the patient's age, ethnicity and co-morbidities. In line with the National Institute for Health and Clinical Excellence (NICE) algorithm, younger (<55 years) non-black patients should be offered treatment with an angiotensin-converting enzyme (ACE) inhibitor in the first instance (or an angiotensin receptor blocker if first-line ACE inhibitor is not tolerated) (NICE, 2006a). Older or black patients should be initiated on a thiazide diuretic or a calcium channel blocker.

Once initiated, drug therapy should be continued for at least four weeks before the efficacy in blood pressure lowering is assessed. Patients should be counselled that on initiation they may experience dizziness or lightheadedness for the first day or two as the blood pressure falls. In addition, common adverse effects should be discussed. For example, the impact of thiazide diuretic therapy on lifestyle should be considered, the possibility of ankle swelling with calcium channel blockers should be raised. Prior to and following initiation of ACE inhibitor, angiotensin receptor blocker and thiazide it is important to order blood tests to check renal function, in particular serum urea and creatinine, and serum potassium levels. ACE inhibitors and angiotensin receptor blockers can increase potassium levels significantly, especially in the setting of reduced renal function, while thiazide diuretics can lead to hypokalaemia. ACE inhibitors and calcium channel blockers should be started at low doses and therefore the dose needs to be titrated if blood pressure remains uncontrolled. There is little dose response in terms of blood pressure control with thiazide diuretics, but evidence of more side-effects at higher doses.

If blood pressure remains high on optimal first-line therapy, it is important to check that the patient is adhering to the prescribed medication in the first instance. If concordance is confirmed, then second-line therapy should be considered in line with the NICE algorithm. Most people with hypertension require two or more drugs to control blood pressure adequately. NICE guidance recommends that if a patient was initiated first-line on an ACE inhibitor, then the next step is to add a thiazide diuretic or a calcium channel blocker; or if started on one of the latter agents, then an ACE inhibitor should be added. Again, appropriate monitoring and dose titration should be undertaken. If blood pressure remains uncontrolled after optimising the second agent, then consideration should be given to adding in the missing agent from the group (ACE inhibitor, thiazide or calcium channel blocker, depending which agents have been used at steps 1 and 2). Lifestyle factors should be revisited at each step in the treatment pathway.

After the first three drugs have been initiated and optimised, if blood pressure remains uncontrolled, the clinician can consider adding in other agents such as alpha-blockers, beta-blockers or spironolactone. However, this may also be an appropriate time to consider referral for specialist advice, depending on the competence of the prescriber. Specialist hypertension or vascular risk clinics will focus on identifying underlying reasons for resistance to drug therapy. Certain patients are appropriate for earlier referral for specialist advice, in particular patients with early onset hypertension, such as white patients with hypertension below the age of 40 years old, or black patients with high blood pressure below the age of 30 years old. Hypertension in pregnancy should be referred for specialist management by an obstetrician, due to the risk of pre-eclampsia.

In addition to managing blood pressure, patients with hypertension require full cardiovascular risk assessment using a validated risk assessment tool, such as the Joint British Societies Risk Prediction Charts at the back of the BNF (Joint British Societies, 2005). Patients with a risk of developing cardiovascular disease of more than 20% over the next 10 years should be considered for treatment with a statin and low-dose aspirin (once blood pressure has been controlled to below 150/90 mmHg).

Ischaemic heart disease

The management of ischaemic heart disease encompasses two specific issues:

- control of angina symptoms and
- secondary prevention of cardiovascular disease.

Anginal chest pain occurs when the oxygen demand of the heart exceeds that of supply usually, although not exclusively, as a result of an atheromatous narrowing (stenosis) in one or more of the coronary arteries. Estimated prevalence rates for angina vary significantly from study to study, but a figure of 4% of all adults in the UK has been calculated, equating to over 2 million angina patients across the UK. Patients with angina are at an increased risk of cardiovascular events in the future; hence in addition to managing angina symptoms (*Box 8.2*), secondary prevention of cardiovascular events is essential.

Box 8.2 *Common features of stable angina*

- Central chest pain
- Pain radiating to the lower jaw or arms
- Shortness of breath
- Lack of exercise tolerance
- Provoked by exercise, stress, extremes of temperature
- Relieved by rest, nitrates.

Anti-anginal therapies

The symptoms of stable angina result from an imbalance between the oxygen requirements of the heart muscle and the supply it receives. Treatments are aimed at improving myocardial oxygen supply and/or reducing cardiac workload, hence lowering myocardial oxygen demand.

Acute chest pain should be treated initially with sublingual nitrate therapy, followed by chronic background therapy using beta-blockers, nitrates, calcium channel blockers, nicorandil and/or ivabradine to prevent recurrent episodes, except in those with very minimal and predictable symptoms manageable with sublingual nitrates alone.

There are few outcome data to guide choice of drug class to protect the patient against angina episodes, although most clinicians endorse the use of beta-blockers first-line where possible. This is based on extrapolation of outcomes achieved in post-myocardial infarction patients and the theoretical benefits of heart rate control in the setting of ischaemic heart disease. Choice of beta-blocker should take into account side-effect profile and ease of dosing, but key to protecting patients from ischaemic episodes is dose titration to achieve a resting heart of between 50 and 60 beats per minute. Common adverse effects include bradycardia and hypotension, cold extremities, lethargy/fatigue and impotence. Patients should be counselled to avoid abrupt cessation of beta-blocker therapy which has been associated with increased risk of cardiovascular events.

Where beta-blockers cannot be used due to contraindications or failure to tolerate therapy, rate-controlling calcium channel blockers, such as diltiazem or verapamil should be considered, or the more recently licensed ivabradine, a pure heart rate-lowering agent. If chest pain persists despite optimal first-line therapy, other agents can be added such as dihydropyridine calcium channel blockers (i.e. amlodipine), nitrates or nicorandil. In patients with recurrent episodes of angina, clinicians should have a low threshold for considering referral to a specialist for assessment of suitability for revascularisation (percutaneous coronary intervention or coronary artery bypass graft surgery).

Secondary prevention strategies

Secondary prevention is defined as the prevention of the progression of a disease in symptomatic patients. In terms of ischaemic heart disease this applies to people who have survived a myocardial infarction and those who present with angina, have had a revascularisation by angioplasty and intracoronary stent insertion or coronary artery bypass graft surgery, or patients with any other manifestation of atherosclerotic disease such as stroke, peripheral vascular disease or diabetes.

There are two aspects of secondary prevention: lifestyle changes and drug treatment. Examples of lifestyle changes to reduce cardiovascular risk include stopping smoking, increasing exercise, losing weight (if obese or overweight), improving diet (e.g. reducing total and saturated fat intake; increasing fruit, vegetable and fibre intake) and moderating alcohol consumption.

Prescribing for secondary prevention

Unless there are contraindications, all patients with ischaemic heart disease should be prescribed a combination of secondary prevention drugs, which will include an antiplatelet agent, usually aspirin, a beta-blocker, a statin and an ACE inhibitor.

- Low-dose aspirin is the first-line antiplatelet agent in the majority of patients because it is effective, generally safe and inexpensive. A dose of 75 mg daily is recommended because it is proven to be equally effective as higher doses and is associated with a lower incidence of side-effects. Patients should be reminded to dissolve soluble aspirin and take it with or after food. Clopidogrel should only be used as an alternative to aspirin where there is evidence of true aspirin allergy.
- Beta-blockers are supported by strong evidence that they reduce the risk of overall mortality, coronary mortality, recurrent non-fatal myocardial infarction and sudden cardiac death in patients post-myocardial

infarction. Beta-blockers have a number of beneficial features including rate control (which may protect against ischaemic events), anti-arrhythmic properties and blood-pressure lowering. Beta-blockers should therefore be given to all patients following myocardial infarction, unless there are contraindications (e.g. uncontrolled heart failure). The benefits of beta-blockers post-myocardial infarction are also extrapolated to those patients with established ischaemic heart disease, and therefore beta-blockers are the first choice anti-anginal in patients with ischaemic symptoms.

- Statins are the only lipid-lowering class with consistent clinical trial data demonstrating a significant reduction in major cardiovascular outcomes, including reduced overall mortality, cardiovascular mortality and non-fatal cardiovascular events. All patients with coronary heart disease should have a full lipid profile performed, receive dietary advice and, if their total cholesterol or low-density lipoprotein (LDL) cholesterol is raised, should be prescribed a statin. Recent NICE guidance has recommended that all patients should be initiated on at least simvastatin 40 mg daily, although those post-acute coronary syndrome should be considered for higher intensity statin treatment such as atorvastatin 80 mg daily or an alternative agent which lowers cholesterol more than simvastatin 40 mg daily (for example, rosuvastatin 20 mg daily). Patients initiated on statin therapy for secondary prevention of cardiovascular disease should be treated with a view to achieving cholesterol targets of total cholesterol <4 mmol/L and LDL cholesterol <2 mmol/L to gain the greatest protection from cardiovascular events.
- ACE inhibitors were initially shown to protect against recurrent cardiovascular events and reduce mortality post-myocardial infarction. However, there is now substantial evidence that they protect patients with any manifestation of cardiovascular disease, except those where risk factors are aggressively controlled (i.e. blood pressure, cholesterol, blood sugar, etc.). Therefore, except where there is a contraindication, ACE inhibitors should be considered for all post-myocardial infarction patients, with or without symptoms of congestive heart failure or known left ventricular disease and all patients with established coronary heart disease.

Heart failure

Despite major advances in the prevention and treatment of cardiac disease, the incidence and prevalence of heart failure continue to rise. Heart failure is associated with a high mortality rate – figures of up to 50% per annum are

quoted. It is also responsible for frequent hospital admission and readmission and poor quality of life. Heart failure is characterised by breathlessness and reduced exercise tolerance, with the main sign being fluid retention, presenting as pulmonary or peripheral oedema.

Drug therapies in heart failure are targeted against two key pathways in disease progression:

- over-activity of the renin–angiotensin–aldosterone system (RAAS), which primarily causes vasoconstriction and sodium and water retention, further overloading the failing heart and
- increased sympathetic activation, which in turn increases blood pressure and heart rate and leads to further decline in left ventricular systolic function over time.

Symptom control in heart failure is achieved through the use of diuretics, mainly loop diuretics which are cheap, easy to use and relatively potent. Diuretic doses are titrated up and down to achieve an appropriate diuresis, sufficient to control heart failure symptoms without causing dehydration. Renal monitoring can be used to guide dosing. Diuretics have little, if any, effect on disease progression and therefore are not suitable for monotherapy in heart failure. All patients must also be started on other agents to improve longer term prognosis.

Prescribing in heart failure

Two drug classes are the cornerstone of chronic heart failure management: ACE inhibitors and beta-blockers. In addition to these agents, spironolactone has a specific use for patients with severe heart failure.

Angiotensin-converting enzyme inhibitors

Large-scale trials of ACE inhibitors in heart failure have demonstrated reductions in mortality, delayed disease progression, improvements in functional class and reduced hospitalisations in ACE-inhibitor-treated patients. These benefits are evident in all grades of heart failure (even asymptomatic heart failure) and have been shown for a number of different agents. ACE inhibitors should be started at a low dose with careful monitoring of blood pressure and renal function. Hypotension should not be considered a contraindication to therapy in this group of patients; ACE inhibitors can successfully be initiated in patients with systolic blood pressures as low as 90 mmHg. The specific diagnosis of bilateral renal artery stenosis is a contraindication to ACE inhibitor therapy, but renal dysfunction in itself is not, although in more severe cases (serum creatinine >250 mmol/L) specialist advice should be sought. Once initiated, ACE inhibitor therapy should be continued indefinitely.

ACE inhibitors should be titrated to achieve the maximum tolerated dose within the licensed dose range; higher doses have been shown to reduce hospital admission rates, when compared with lower doses. The key adverse effect which impacts on patient concordance is the development of an ACE-inhibitor-induced cough. Patients should be advised to persist with ACE inhibitor therapy where possible, but if the cough is troublesome an angiotensin receptor blocker (ARB) can be considered as an alternative. Currently only candesartan and losartan are licensed for this indication. Under specialist supervision, there is also evidence that ACE inhibitor and ARB combination therapy can further improve outcomes over ACE inhibitor therapy alone, although in this circumstance hypotension, renal dysfunction and hyperkalaemia become more problematic.

Beta-blockers

Beta-blockers were established as key to heart failure management in the late 1990s when studies demonstrated significant reductions in mortality, reduced hospitalisations and improved symptom control. The benefits of beta-blocker therapy have been established in all functional classes of heart failure, except asymptomatic disease and are evident in a wide range of patient populations including diabetics, the elderly and those with renal dysfunction. Beta-blockers should therefore be considered for all patients with symptomatic heart failure. Ideally, these agents should be initiated when patients are clinically stable and optimised on first-line therapy (primarily ACE inhibitors and diuretics). Data exist to support the use of bisoprolol, carvedilol, metoprolol and more recently in the elderly population, nebivolol, however metoprolol remains unlicensed for this indication in the UK.

Beta-blocker therapy should be initiated at low doses and titrated slowly over approximately three months to achieve a resting heart rate between 50–60 beats per minute. Low starting doses are necessary to prevent precipitation of an acute episode of heart failure. Due to the effect of beta-blockers on heart rate and force of contraction, patients may experience an exacerbation of symptoms during the dose titration phase. Additional diuretic therapy may aid in the resolution of such symptoms. Beta-blockers are considered to be contraindicated in patients with severe bradycardia, acute heart failure, severe asthma or bronchospasm and peripheral vascular disease. Mild to moderate airways disease is not a contraindication, but prescribers should consider prescribing a cardioselective agent, such as bisoprolol, with careful monitoring of respiratory function.

Spironolactone

Spironolactone, an aldosterone antagonist, has been shown to confer a mortality benefit when prescribed to patients with moderate to severe

heart failure (in addition to ACE inhibitor and beta-blocker). In addition spironolactone-treated patients had fewer hospital admissions for cardiac events. Low-dose spironolactone should be considered for addition to optimised ACE inhibitor therapy in patients with moderate to severe heart failure symptoms following an acute hospitalisation. For this indication, spironolactone should be prescribed at an initial dose of 25 mg daily, titrated to 50 mg daily if symptoms persist after a number of weeks of therapy. Renal function and serum potassium should be monitored carefully throughout therapy. Should hyperkalaemia (serum potassium >5.5 mmol/L) occur, a dosage reduction to 25 mg on alternative days should be considered. Declining renal function, hyperkalaemia and the occurrence of painful gynaecomastia frequently result in withdrawal of spironolactone therapy in clinical practice. Spironolactone is contraindicated in hyperkalaemia, hyponatraemia and Addison's disease.

Other issues

In addition to managing the clinical syndrome of heart failure, it is essential to identify and where possible treat the underlying cause. Common causes of chronic heart failure in the UK are ischaemic heart disease and hypertension (see previous sections), but other causes include excessive alcohol intake, viral infection and valvular heart disease. All patients should be reviewed by a specialist early following diagnosis to assess whether other therapeutic strategies are warranted such as revascularisation for ischaemic patients or the use of implantable devices to manage symptoms. Due to the poor prognosis for heart failure patients, palliative issues should also be considered throughout treatment.

Case studies

Case study 1

Patient RB is a 46-year-old African man who has had two high blood pressure readings recorded within the GP surgery in the past and has been given appropriate lifestyle advice. He is attending on this occasion for a further blood pressure check to confirm a diagnosis of hypertension. The patient is currently asymptomatic – his high blood pressure was picked up in the gym where he was offered a blood pressure check when he enrolled.

On examination
His blood pressure readings recorded at this visit were:

- initial 180/100 mmHg
- second 168/96 mmHg

- third 166/102 mmHg
- BMI: 32kg/m^2
- abdominal circumference: 107 cm.

His mother died of a stroke at the age of 52 in Ghana. He is a non-smoker. His bloods were ordered following his previous clinic visit, a month ago.

Biochemistry
- Sodium 136 mmol/L
- Potassium 4.6 mmol/L
- Urea 4.2 mmol/L
- Serum creatinine 112 μmol/L
- Estimated glomerular filtration rate (eGFR) 58 mL/min (unadjusted)
- Total cholesterol 5.6 mmol/L
- High-density lipoprotein (HDL) 0.9 mmol/L
- Low-density lipoprotein (LDL) 3.2 mmol/L
- Triglycerides 2.1 mmol/L
- Liver function tests: NAD (nothing abnormal detected)
- Thyroid function tests: NAD (nothing abnormal detected)
- Fasting glucose 4.9 mmol/L.

On discussion, the patient reports being a non-smoker and an occasional drinker (2–4 units per week). He is a bus driver by occupation.

1 What is the diagnosis?
The diagnosis of hypertension is now clear, as high blood pressure readings have been documented on three separate occasions.

2 What information should be given to this patient about the implications of the diagnosis?
It is important to discuss the implications of such a diagnosis with the patient, in particular, highlighting the increased risk of stroke and heart attack, plus the potential damage to the kidneys if this is left untreated. This is an asymptomatic condition and without understanding the long-term adverse effects of high blood pressure, there is little incentive for a patient to make the necessary lifestyle changes to reduce their risk, or comply with any drug therapies prescribed.

Lifestyle factors are important in the management of hypertension and these should be identified and appropriate advice given.

3 What are the prescribing issues?
As this patient had a blood pressure >160/100 mmHg, he met the criteria for initiation of drug therapy. Drug choice should take into account the patient's age and ethnicity, alongside other issues such as co-morbidities. According to NICE guidelines, in a Black African patient first-line treatment

should be a thiazide diuretic, such as bendroflumethiazide, or a calcium channel blocker, such as amlodipine.

However, a thiazide diuretic might be inappropriate here, as the patient is a bus driver and frequent trips to the toilet would be difficult to manage. For this reason the decision was taken to initiate amlodipine at a dose of 5 mg daily. Care was taken when prescribing to ensure the generic amlodipine preparation would be dispensed. The patient was advised that the drug may cause some adverse effects in the first few days, in particular dizziness or lightheadedness as the blood pressure reduced, headaches and flushing. He was advised that these are usually short-lived. In the longer term, the most frequently cited side-effect is ankle swelling and if this occurred and was troublesome, he was advised to seek further advice.

The patient was booked in for a review in one month's time. Bearing in mind his pre-treatment blood pressure, the use of amlodipine at this dose is unlikely to achieve target blood pressure. Most patients require two or more antihypertensives to achieve the blood pressure treatment target of <140/90 mmHg. No specific biochemical monitoring is required following amlodipine initiation, so no blood tests were ordered at this stage.

At the next clinic visit, it will be important to review his blood pressure control, discuss his progress with lifestyle issues, assess the effectiveness and tolerability of the prescribed drug therapy and consider his global cardiovascular risk by undertaking a cardiovascular risk assessment.

Case study 2

Mr AR, a 62-year-old white British man with known hypertension (pretreatment level 170/88 mmHg), was scheduled in for a review of his blood pressure management. He had been seen a number of times before, and had known concordance issues. At the last visit a month ago, his blood pressure was controlled to Quality and Outcomes framework target of 150/90 mmHg for the first time, but was not yet achieving the clinical target of 140/90 mmHg. At the last visit ramipril was added to his drug therapy. Low levels of physical activity. Non-smoker. Alcohol intake ~20 units per week.

Current drug list
- Bendroflumethiazide 2.5 mg daily
- Amlodipine 5 mg daily
- Ramipril 2.5 mg daily.

Bloods from two weeks ago
- Sodium 144 mmol/L
- Potassium 4.1 mmol/L (previously 3.7 mmol/L)
- Urea 5.3 mmol/L

- Serum creatinine 98 μmol/L (previously 93 μmol/L)
- eGFR 62 mL/min (previously 63 mL/min)
- Total cholesterol 5.4 mmol/L
- HDL 0.9 mmol/L
- LDL 3.2 mmol/L
- Triglycerides 2.1 mmol/L
- Liver function tests: NAD (nothing abnormal detected)
- Thyroid function tests: NAD (nothing abnormal detected)
- Fasting glucose 6.1 mmol/L
- BMI 36
- Abdominal girth 112 cm.

On examination
His blood pressure readings recorded at this visit were:

- initial 141/76 mmHg
- second 136/77 mmHg
- third 135/72 mmHg.

1 How would you assess the patient's cardiovascular risk?
The patient's blood pressure is now well controlled. However, this clinic visit is important in terms of allowing a full assessment of his cardiovascular risk. He has a number of risk factors including male gender, age, known hypertension, adverse lipid profile (raised total cholesterol, LDL and triglycerides and low levels of protective LDL), obesity and raised abdominal girth and low levels of physical activity. The patient's cardiovascular risk should be calculated using a validated risk assessment tool, such as the cardiovascular risk prediction charts issued by the Joint British Societies, which can be found at the back of the BNF. Risk assessment should be performed using untreated blood pressure and lipid levels.

2 What are the implications of this patient's cardiovascular risk?
For this patient, the Joint British Societies risk prediction charts indicate a cardiovascular risk of over 30% over the next 10 years, using pretreatment levels. Patients with cardiovascular risk greater than 20% should be considered high risk and be offered primary prevention. In this case, this would mean initiation of low-dose aspirin and a statin. Aspirin should only be started for primary prevention in hypertensive patients when the blood pressure has been lowered to below 150/90 mmHg to reduce the risk of intracranial haemorrhage. Statin therapy should be started, in line with NICE TA94, using a 'low acquisition cost statin' such as simvastatin (NICE, 2006b).

3 What is the prescribing issue?
The patient is known to have a history of poor compliance with drug therapy. It is therefore important to clearly explain his high risk of developing

cardiovascular disease over the next 10 years, and the benefits afforded by treatment with aspirin and a statin. Care should be taken to advise the patient on potential adverse effects and how to deal with them.

Aspirin should be taken with or after food to reduce the risk of gastrointestinal discomfort. Simvastatin should ideally be taken with the evening meal, but in this case, to aid compliance the patient was advised to take the simvastatin in the morning with all his other medications. For simvastatin, the evidence suggests that a dose taken in the evening lowers cholesterol marginally more than the same dose taken in the morning. This effect may be clinically significant – one study showed a difference in total cholesterol of 0.38 mmol/L and LDL cholesterol of 0.25 mmol/L when comparing morning and evening efficacy. Morning dosing should be considered in patients with compliance problems – better to have a (large) partial effect, than no effect at all because the patient always forgets their evening dose. The patient was also advised to seek medical advice should muscle pain or aches occur.

4 What monitoring and follow-up should there be?
Care was also taken to arrange appropriate monitoring and follow-up. Liver function should be checked at baseline and after one month of therapy, to ensure no adverse effect. The patient should be reviewed in 4–6 weeks to reinforce the need for therapy, check compliance and assess tolerability. Finally, lifestyle advice should not be forgotten; issues for this patient are weight loss and physical activity.

Case study 3

Mrs PH, a 62-year-old white woman, attends your clinic for review and resupply of drug therapy having been discharged from hospital following an acute myocardial infarction (MI) three weeks previously. The scanned discharge summary confirms ST-elevation MI, which was treated by primary angioplasty and bare metal stent insertion. She had an uncomplicated recovery and was discharged on the following drug therapy.

Current drug list
- Aspirin 300 mg daily for one month then 75 mg daily thereafter
- Clopidogrel 75 mg daily for one month then stop
- Ramipril 2.5 mg daily
- Bisoprolol 2.5 mg daily
- Simvastatin 40 mg daily
- Fluoxetine 20 mg daily
- Omeprazole 20 mg daily.

Only fluoxetine and omeprazole were prescribed prior to this hospital admission. Blood pressure today: 110/68 mmHg; heart rate: 67 beats per minute.

The length of hospital stay following an acute MI has reduced significantly in centres performing primary angioplasty – often patients are discharged on day 2 or 3. This leaves very little time to optimise drug therapy and this issue now needs to be addressed in primary care.

1 How should this patient's drug therapy be reviewed?

This patient's drug therapy needs to be reviewed and some agents should be dose titrated to ensure she gets the maximum protection from future cardiovascular events.

As the patient was discharged over three weeks ago, her aspirin dose should soon be reduced to 75 mg daily and clopidogrel therapy should be stopped in a week's time. Most hospitals supply the full duration of clopidogrel therapy, when only one month's treatment is required, so no further prescriptions should be necessary in primary care. Ramipril should be dose titrated over the next few weeks to achieve a target dose of 10 mg daily. However, the dose should not be changed until the patient's renal function has been checked, to ensure no adverse effect since the ACE inhibitor was started in hospital. This will have to be dealt with at a future visit. The bisoprolol dose should similarly be dose titrated, aiming for a target heart rate of 55–60 beats per minute. This could be undertaken today after a check of blood pressure and heart rate. Dose titration can be undertaken provided systolic blood pressure is >90 mmHg and pulse rate is >60 beats per minute.

The efficacy of simvastatin therapy cannot be assessed at this stage as lipid levels fall naturally for a few weeks post-MI. The lipid levels should be rechecked at least three months after the MI, and dose titration of simvastatin, or use of an alternative agent considered at that point. However, liver function can be checked at this point to ensure no adverse effects.

2 What assessments should be made during the consultation?

In the consultation it was important to assess how the patient had been coping since discharge, both physically and psychologically. The patient was encouraged to attend a cardiac rehabilitation programme to assist with this. In terms of drug therapy, compliance with the new drug therapy regimen was assessed and appeared to be good. The patient was also encouraged to discuss any concerns or adverse effects but had no issues to raise. The importance of secondary prevention to protect against future events was emphasised, and the need for dose titration explained.

The following blood tests were ordered: full blood count and a biochemistry profile (including renal and liver function). A prescription for aspirin 75 mg daily, ramipril 2.5 mg daily, bisoprolol 5 mg daily (dose increased) and simvastatin 40 mg daily was issued, alongside other repeat medications. The patient was counselled that blood pressure may fall following the increase in beta-blocker dose, and as a result she may feel a little dizzy or lightheaded. Other side-effects discussed were increased tiredness and

lethargy, and cold fingers and toes. A further clinic appointment was booked in four weeks with a view to increasing the ramipril dose.

Case study 4

Mr JT, a 52-year-old white man, a builder, was diagnosed with hypertension for many years and more recently developed angina, diagnosed following an exercise tolerance test in a rapid access chest pain clinic. Following diagnosis, the clinic started him on atenolol 50 mg daily, aspirin 75 mg daily, simvastatin 40 mg daily and glyceryl trinitrate (GTN) spray when required to treat acute chest pain. Since it was first identified, his hypertension has been mild at approximately 150/95 mmHg and has therefore not previously warranted drug therapy. He was reviewed in clinic to assess his response to the new agents introduced recently and ensure all his cardiovascular risk factors are being fully addressed.

On examination
His blood pressure was 146/84 mmHg; heart rate 75 bpm; BMI 28; and abdominal girth 86 cm.

The patient reported partial resolution of his angina symptoms, which were entirely exertion related. He was now only experiencing chest pain once or twice a week, compared with almost daily prior to starting atenolol. He had been feeling a little lethargic over the past few weeks, but thought this had improved over time. On discussion it transpires that he is still smoking, although he does express a desire to quit. He has never received any formal smoking cessation advice or nicotine replacement therapy. Also, he has a high alcohol intake of approximately 40 units per week.

1 What are the key issues?
Key issues here were:

- lifestyle issues, in particular smoking and alcohol intake
- blood pressure control – as this patient now has established cardiovascular disease, the threshold for initiating drug therapy falls from 160/100 mmHg to 140/90 mmHg
- optimising anti-anginal therapy to further reduce chest pain frequency
- ensuring secondary prevention strategies are optimised and encourage compliance.

2 What are the treatment options?
The patient was started on atenolol for the treatment of his angina, which had some impact on his blood pressure; but still did not achieve target blood pressure levels. The options now are to increase the atenolol to deal with any residual angina, or initiate another antihypertensive agent. Atenolol dose titration above 50 mg daily has little additional impact on blood pressure

control. Also, the patient had been concerned regarding tiredness since the atenolol was started, which was affecting his work as a builder. In this case, therefore, it seemed appropriate to consider an additional agent. While bendroflumethiazide may be the most cost-effective option here, the combination of beta-blocker and thiazide is known to increase the risk of diabetes. In addition, the use of amlodipine will assist in treating the angina symptoms, as well as the blood pressure. On discussion with the patient, it was decided to add amlodipine 5 mg daily. The patient was warned about the possibility of ankle swelling, headache and flushing with the new treatment.

In terms of secondary prevention, he is already treated with aspirin and a statin. The introduction of an ACE inhibitor for further cardiovascular risk reduction may be warranted in future. He needed blood tests ordering. As he had been newly started on simvastatin and had a history of excess alcohol intake, liver function tests were ordered, alongside a routine full blood count and biochemistry. The patient expressed understanding of his drug therapy and a willingness to comply.

3 What are the counselling points?
It was suggested that he consider seeing the smoking cessation adviser for the practice, with view to the use of nicotine replacement or drug therapy such as varenicline to improve his chance of quitting smoking. Alcohol moderation was advised to within the currently recommended limits of 21 units per week for a male. These issues should be followed up in one month, when the next blood pressure check is due.

Case study 5

Mr DS, a 72-year-old white man with alcoholic heart failure and ischaemic heart disease, was listed for review in clinic. He was diagnosed with heart failure on echocardiogram 3 years ago (ejection fraction 28%).

Current drug list
- Ramipril 5 mg daily (reduced from 5 mg twice daily two months ago)
- Nebivolol 10 mg once daily
- Furosemide 80 mg daily
- Spironolactone 12.5 mg daily (reduced from 25 mg daily four weeks ago)
- Aspirin 75 mg daily
- Simvastatin 20 mg daily
- Salbutamol inhaler 1 or 2 puffs four times daily
- Seretide 250 inhaler 1 puff twice daily
- Omeprazole 20 mg daily
- Senna 1 or 2 tablets at night as required.

His symptoms have been well controlled for the past six months, since his last admission to hospital with decompensated heart failure.

At this visit, Mr DS is asymptomatic, able to walk for over 20 minutes on the flat without symptoms of breathlessness or chest pain; and climb a flight of stairs without stopping. He reports that he is still drinking an average of 3 pints of draft lager each day. His blood pressure is well controlled at 110/68 mmHg sitting, but there is a significant postural drop, with a blood pressure of 96/54 mmHg on standing associated with dizziness/lightheadedness.

Bloods from a week ago

- Sodium 129 mmol/L (down) (previously in normal range)
- Potassium 5.4 mmol/L (up) (reduced from 5.6 mmol/L one month ago)
- Urea: 12.9 mmol/L (up) (reduced from 14.1 mmol/L one month ago)
- Serum creatinine 197 micromol/L (up) (increased from 164 mmol/L one month ago)
- eGFR: 28 mL/min (down) (reduced from 36 mL/min one month ago)
- Liver function tests: bilirubin 5 μmol/L
- Albumin 38 g/L (down)
- Alanine aminotransferase (ALT) 8 iu/L
- Alkaline phosphatase 80 iu/L
- Gamma-glutamyl transferase (GGT) 136 iu/L (up)
- Thyroid function tests: NAD (nothing abnormal detected).

Lipids were controlled on current statin therapy.

1 What do the blood test results suggest?

The bloods demonstrate a deterioration in renal function, with raised serum creatinine and urea, hyperkalaemia and hyponatraemia with a significantly reduced eGFR. This, together with the postural blood pressure drop, suggests that the patient is dehydrated. The case highlights the difficult balance between optimal heart failure management to improve prognosis and quality of life (ACE inhibitor, spironolactone, diuretic therapy) and the risk of adverse drug effects if the doses are pushed too high.

2 What are the key issues?

Key issues to address here are:

- balancing diuretic use to control symptoms but avoid dehydration
- management of hyponatraemia and hyperkalaemia
- protection of renal function in view of evidence of increased serum urea and creatinine
- counselling on the risks of continuing to drink in the setting of alcoholic heart failure.

3 What are the drug treatment review options?

In this case, the most important therapies to maintain at optimal doses are the ACE inhibitor and beta-blocker as these are known to improve symptom control and prolong life. Reducing the furosemide dose in the first instance would seem a logical step forward, as the patient appears to be dehydrated. This will also assist in correcting the hyponatraemia, but may further exacerbate the hyperkalaemia as the diuresis falls. Spironolactone in the setting of dehydration will contribute to the hyponatraemia and hyperkalaemia and may also adversely affect the renal function. Whether to withdraw the spironolactone at this point depends on a balance of risks. As the patient is relatively stable from a heart failure point of view, it may be considered safer to withdraw the spironolactone therapy in the short term to reduce the pressure on the kidneys and minimise the risk of hyperkalaemia. Careful follow-up is important here to ensure renal function improves, no worsening of hyperkaleamia and, of course, to ensure that heart failure symptoms do not worsen.

In the clinic, the patient's furosemide was reduced to 40 mg daily and the spironolactone withdrawn. Repeat blood tests were ordered for 10 days' time and review in clinic booked for two weeks time with a view to reintroducing the spironolactone for its prognostic benefits if renal function has improved and sodium and potassium levels have normalised. The patient was advised to reduce, or ideally stop, his alcohol intake, and reminded to keep active.

This is a complex case with a high risk of destabilising heart failure control or precipitating renal failure. Non-medical prescribers should consider whether the management of this patient is within their scope of practice, or whether further advice should be sought from the GP or specialist heart failure service.

Further reading

Hypertension

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Ischaemic heart disease

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Williams B, Poulter N R, Brown M J, Davis M, McInnes G T, Potter J P, Sever P S and Thom S McG (2004). The BHS Guidelines Working Party Guidelines for Management of Hypertension: Report of the Fourth Working Party of the British Hypertension Society, BHS IV. *J Human Hypertens* 18: 139–185.