The management of atrial fibrillation and stroke prevention

This special cardiovascular section is devoted to atrial fibrillation — a condition that affects up to 1% of the population. The first article, by Gurpreet Virdi and Sotiris Antoniou, is a learning points article looking at the management of atrial fibrillation and prevention of stroke. The second article, by Jyoti Sood, is a medication review article, which runs through the important points to consider when evaluating medicines of a patient with atrial fibrillation.

Introduction

An arrhythmia is an abnormality of the heart's rhythm and can be caused either by an inherited problem or by an acquired condition that disturbs the electrical impulses that regulate the heart. The heart may beat too fast, too slow or in an irregular rhythm.[1]

Cardiac arrhythmias affect more than 700,000 people in England, the most common sustained arrhythmia being atrial fibrillation (AF) affecting up to 1% of the population, and rising to 4% in those aged more than 65 years. It is common, being present in 3–6% of acute medical admissions and accounts for one third of admissions for cardiac arrhythmias.[2] The overall incidence of stroke associated with AF is about 5% per year, hence it is a significant cause of mortality in England. The Framingham Heart Study showed that AF was associated with a 1.5–1.9 fold mortality risk after adjustment for the pre-existing cardiovascular conditions with which AF was related.[3] As a consequence of this, the scope of the *National Service Framework for Coronary Heart Disease* was extended to include cardiac arrhythmias to streamline the way in which the NHS responds to manage patients with cardiac arrhythmias and sudden cardiac death. A great deal of emphasis is now placed upon ensuring people presenting with arrhythmias, receive timely assessment by an appropriate clinician to ensure accurate diagnosis and effective treatment and rehabilitation.[1]

The purpose of this article is to discuss the pharmacological management of patients diagnosed with AF and how to manage and reduce the stroke risk of these patients. After reading this article we anticipate you will be able to:

- ☐ describe the initial treatment strategy for patients presenting with AF
- ☐ describe the rationale of the use of different antiarrhythmic medications and how they work
- ☐ be able to perform a stroke risk assessment on patients with AF and ensure these patients are appropriately anticoagulated
- ☐ describe possible drug interactions seen in AF patients and how to manage them.

The case

Robert Walker is a 76 year-old male (80kg) with preexisting hypertension who presented to hospital with dizziness and troublesome palpitations progressively worsening over the last few weeks. Routine laboratory investigations carried out include a thyroid function test and an electrocardiogram (ECG). The thyroid function test was normal but the ECG showed an absence of P waves, an irregular rhythm and a fast heart rate (up to 200 beats per minute). He was diagnosed with persistent AF.

In this acute setting, he was given 2 doses of metoprolol 5mg IV bolus over 2 minutes to help reduce his heart rate and provide symptom relief and was also anticoagulated with enoxaparin S/C 120mg OD. Once settled a transoesophageal echocardiogram (TOE; ultrasound of the heart — used to examine the valves and to find holes in the heart, blood clots or evidence of infection) was performed. Because this was normal he was electrically cardioverted.

Drug therapy on admission:

Mr. Walker had been taking bendroflumethiazide 2.5mg OM before admission (electrolytes were within the reference ranges).

Drug therapy on discharge:

After his electrical cardioversion Mr Walker felt better. He remained in sinus rhythm and was discharged home taking a beta-blocker for rhythm control and warfarin for anticoagulation. His bendroflumethiazide was stopped.

1. What is AF and what risk factors did Robert have for developing it?

AF is a supraventricular tachyarrhythmia associated with cardiovascular morbidity and mortality. It is a condition where the atria (two upper chambers of the heart) contract irregularly at a very high rate.[4,5]

In a normal heart, ventricular contraction is driven by the sinus node, also known as the body's natural pacemaker, which is an area of specialised cells situated in the atria that emit electrical impulses. These impulses spread through the right and the left atria in a regular and organised way,

and then spread into the ventricles via the atrioventricular (AV) node. This causes the ventricles to contract and pump blood out through the aorta (main artery) and to the rest of the body. A normal heart beats at 60–100 (ventricular) beats per minute.[6]

During AF the sinus node loses control of the heart rhythm either because other areas in the atria produce rapid, uncontrolled electrical impulses (ectopic beats) or when cells in the atria do not conduct normal impulses from the sinus node smoothly. (This is explained in more detail in the second part of this article.) The result in either of these situations is rapid and chaotic quivering of the atria where blood cannot be completely pumped out of them. This may pool and clot. The formation of blood clots within the left atrium may embolise to the systemic circulation and cause a stroke or thromboembolism. The absolute risk of stroke is about 4.5% per year with an annual risk 5–6 times higher than patients in sinus rhythm.[7,8] Anticoagulation therefore remains an empirical and essential part of management of this common arrhythmia.[5]

The AV node usually protects the ventricles from pumping too fast but when in AF, it also attempts to keep up with all the extra impulses from the atria. This results in the heart beating rapidly and irregularly between 110 and 130 beats per minute in new onset AF.[6,9] Hence a rhythm or rate control management strategy is also used to manage this arrhythmia.

With each advancing decade from the age of 50 years the prevalence of AF doubles. Other independent risk factors for developing AF include male sex, hypertension, diabetes, smoking, valvular heart disease, hyperthyroidism and myocardial infarction. Mr. Walker's presenting risk factors for AF included being an elderly, hypertensive male.

2. What is the aim of initial management?

The goals of initial management are to stabilize the patient, control the ventricular rate and to prevent embolic complications. At presentation many patients with AF of recent onset convert spontaneously to sinus rhythm. However, when this does not happen the ventricular rate should be treated to slow ventricular response, and if appropriate, efforts should be made to terminate AF and restore sinus rhythm.[2,10]

Acute ventricular rate control is required to improve the haemodynamic status of the patient and to relieve symptoms. The atrial fibrillation follow-up investigation of rhythm management (AFFIRM) and rate control vs electrical cardioversion (RACE) analyses recommend a target resting heart rate of less than 100 beats per minute.[2] This is best achieved with intravenously administered AV nodal blocking drugs like calcium channel blockers (e.g. diltiazem and verapamil) and beta-blockers.[2,10] Amiodarone is also used in practice to manage these patients if beta-blockers or calcium channel blockers are contraindicated or ineffective.[8,11]

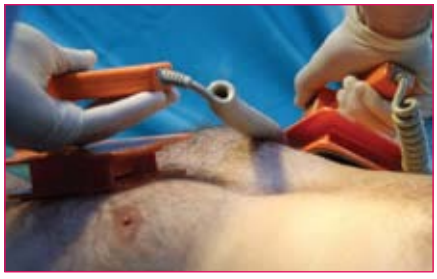
Using TOE up to 30% of patients with AF and embolic stroke are found to have atrial thrombi within 72 hours of a stroke. This demonstrates the importance of starting thromboprophylaxis as early as possible. Either unfractionated heparin (UFH) or low molecular weight heparin (LMWH) can be started at the presentation of acute AF while the international normalised ratio (INR) remains sub-therapeutic during the initiating phase of oral anticoagulation.[8]

3. Was rhythm control for persistent AF an appropriate choice of treatment for Mr Walker?

Alternative diagnoses are paroxysmal, persistent or permanent AF — you may wish to refer to NICE guidelines for a review of these to help you answer this question. Mr Walker was diagnosed with persistent AF because his AF continued for longer than 7 days (see NICE guidelines). This type of AF can be managed either by the rate control or rhythm control strategy.[8]

Several clinical trials have not shown any significant differences between the rhythm and rate control methods for management of AF. The largest trial, AFFIRM, enrolled more than 4000 patients and randomised patients to receive either rate control with digoxin, beta-blockers or calcium channel antagonists or rhythm control with amiodarone, sotalol or propafenone and, if necessary, DC cardioversion.[12] The primary endpoint of all-cause mortality was not significantly different between the two groups and there was no difference in secondary end-points of stroke rate, quality of life and functional status.[12,13]

The treatment method used, therefore, depends upon a number of other factors, such as long-term frequency and hazards of AF, risks of cardioversion and anti-arrhythmic therapy, age of patient, presence of symptoms, coronary artery disease or heart failure.[2,8] Because Mr Walker was symptomatic and presented with his first bout of AF, he was correctly managed by the rhythm control treatment of DC cardioversion.



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4. What is cardioversion and was electrical cardioversion the best option for Mr Walker?

Cardioversion is a term given to a process that restores an abnormal heart rhythm to a normal one. This can be done either electrically or pharmacologically depending on the type of AF and the various patient factors.

The chance of spontaneous cardioversion is greatly reduced if the episode of AF lasts for more than 7 days.[2,4] In these patients, restoration of sinus rhythm can be achieved by pharmacological or electrical cardioversion. The advantages and disadvantages of both strategies should be discussed with patients before starting treatment.[8]

Direct comparisons between pharmacological and electrical cardioversion have

To maximize the likelihood of a successful outcome NICE recommends to attempt cardioversion as soon as possible following AF onset.

not been made and although pharmacological approaches appear simpler they may be less efficacious for AF lasting longer than 48 hours.[4] The major risk of this method is related to the toxicity of the antiarrhythmic drugs.[4]

From clinical experience and current practice, episodes of AF lasting longer than 48 hours are best restored by electrical cardioversion.[8] This has an acute success rate of 70–90% but requires sedation or general anaesthesia.[2,14] To maximize the likelihood of a successful outcome NICE recommends to attempt cardioversion as soon as possible following AF onset.[8] It is also worth bearing in mind that after electrical cardioversion many patients will experience a relapse of the arrhythmia.[14]

Because this was Mr. Walker's first episode of AF that had been present for longer than 7 days an electrical cardioversion was the preferred option after the TOE was clear of clots in the atria.

5. Was Mr. Walker's anticoagulation appropriate for him?

It is important to ensure the correct anticoagulant is prescribed for patients with AF. The choice of drug is dependent upon the patient's risk factors rather than the presenting type of AF. Vitamin K antagonists such as warfarin are proven to be superior to antiplatelet agents, especially in patients with a high risk of stroke.[14] In a recent meta-analysis of 29 trials involving 28,044 patients, warfarin and aspirin reduced the risk of stroke by 64% and 22% respectively.[14] The ACTIVE-W study compared the combination of aspirin and clopidogrel with coumarin derivatives and this trial was stopped early because of the superiority of warfarin in preventing vascular events.[14]

Table 1. Components of $CHADS_2$ scoring system[15]

$CHADS_2$ item	Points
Congestive heart failure	1
Hypertension (systolic >160 mmHg)	1
Age greater than 75 years	1
Diabetes	1
Prior cerebral ischaemia (**S**troke)	2

Table 2. Clinical classification of $CHADS_2$ score for predicting stroke risk[17]

$CHADS_2$	Risk	Risk of stroke per year (%)	Anticoagulant of choice
0	Low	1.9	Aspirin
1	Intermediate	2.8	Aspirin or Warfarin
2	High	4.0	Warfarin
3		5.9	
4	Highest	8.5	Warfarin
5		12.5	
6		18.2	

The $CHADS_2$ score is an acronym used to estimate the stroke risk in patients with AF. As shown in Table 1, because of his age and past medical history of hypertension, Mr Walker had a $CHADS_2$ score of 2 and hence an annual stroke risk of 4.0% (Table 2).[15]

Patients with a $CHADS_2$ score of 1 can be given either aspirin or warfarin. Warfarin reduces the absolute risk of stroke by 2.7% per year for primary prevention compared with aspirin, which reduces the risk by 1.5%.[16] However, major extracranial bleeding is increased in those patients who receive warfarin compared to those taking aspirin (absolute risk increase 0.2% per year).[16] The point at which the benefit of warfarin outweighs the risk is seen in those patients with an annual stroke risk of between 3 and 5%.[5] Warfarin was the choice of anticoagulation for Mr Walker over aspirin because his risk of developing of a stroke was high and because he had been electrically cardioverted[8] (see NICE guidelines).

6. After cardioversion, what medications need to be added or continued — and for how long?

In most patients cardioverted from AF, early and late recurrence of the disorder without antiarrhythmic drug therapy is high.[14] The drugs used commonly in UK practice to maintain sinus rhythm post-cardioversion include beta-blockers, class Ic agents such as flecainide, or class III antiarrhythmic agents, such as amiodarone. The evidence on efficacy of these drugs is in favour of amiodarone, which has been shown to be associated with an increased likelihood of patients remaining in sinus rhythm. However, the adverse effects of amiodarone after long-term use, which include pulmonary, hepatic, ophthalmic and thyroid toxicity, make it a last-line therapy for patients who are intolerant to other antiarrhythmic drugs.[8]

NICE recommends a standard beta-blocker as the first-line treatment option because this has been shown to be as equally effective as sotalol in the maintenance of AF.[8] Risks of side-effects are also lower than other antiarrhythmic drugs. The rationale for their use is that sympathetic activation and resulting catecholamine elevation associated with myocardial ischaemia or stress stimulates cardiac beta-receptors and this is thought to cause arrhythmias through multiple mechanisms. Beta-blockers work

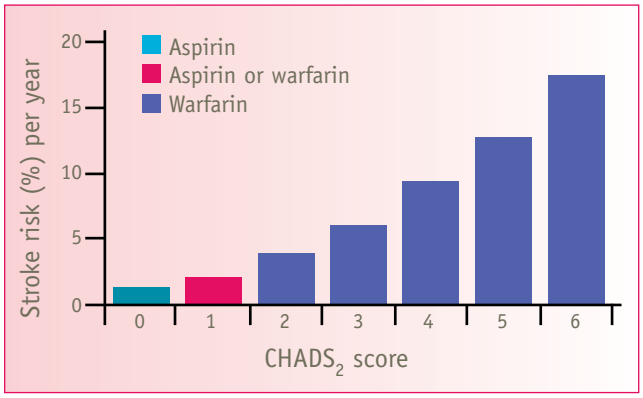

Figure 1. Stroke risk in patients with atrial fibrillation according to the $CHADS_2$ risk index. The colour-coded bar graphs indicate the appropriate antithrombotic treatment strategy, adapted from Blaauw and Crijns[14]

by increasing the effective refractory period, which reduces the abnormal electrical activity.[18] Mr Walker was therefore started on atenolol 25mg OD to help maintain sinus rhythm with the additional aim of lowering his blood pressure because his bendroflumethiazide had been stopped on admission.

Stroke may occur at the time of cardioversion because of possible expulsion of an atrial thrombus and may also occur up to 4–6 weeks after because cardioversion is recognised to be associated with reversible, left atrial mechanical dysfunction. This process is also known as atrial stunning.[5,8,19] Atrial contractility may still be reduced from days to weeks, leading to the formation of new thrombi.[14] Adequate anticoagulation (maintaining INR between 2 and 3) therefore needs to be achieved with warfarin for at least 4 weeks post-cardioversion. Data from the AFFIRM and RACE studies showed that discontinuation of anticoagulation in the rhythm control arm was associated with an excess of strokes.[14] Only in low-risk patients ($CHADS_2$ score of 0 or 1) is it probably safe to discontinue warfarin and start aspirin.[14]

7. What pharmacological treatment options are available for Mr Walker if atenolol was found to be ineffective? How do these drugs work in patients with AF?

Because Mr Walker's electrical cardioversion provided him with symptomatic relief this suggested that rhythm control was an effective option for him. The chances of recurrences post-cardioversion are high with up to 50% after 12 months so administration of other antiarrhythmic drugs to convert Mr Walker's AF to sinus rhythm would be the next option.[8,14] The selection of antiarrhythmic drugs for prevention of AF is dependent on whether the patient has underlying heart disease, such as structural, hypertensive, ischaemic heart disease or congestive heart failure.

For pharmacological cardioversion, flecainide and propafenone are the drugs of choice in hypertensive patients.[4] They work primarily by blocking the sodium channels thereby slowing and depressing impulse conduction. Sodium channel blockade in areas of impaired conduction may block the impaired conduction and therefore the arrhythmia entirely.[18] However, these drugs have many side-effects including arrhythmias and should be avoided in patients with structural heart disease.[4,18]

If these agents are ineffective or produce side-effects, then sotalol or amiodarone are an appropriate second choice.[4] The Canadian trial of atrial fibrillation (CTAF), a comparison of amiodarone, sotalol and propafenone demonstrated relapse rates of 35%, 63% and 63% respectively 16 months after cardioversion. These were similar to the findings of the AFFIRM and the SAFE-T trials.

Sotalol works by increasing the action potential duration through inhibition of K^+ channels and slowing repolarisation, and therefore prolonging the effective refractory period (ERP). Drugs that prolong the ERP can prevent re-excitation of myocardial cells that may be the cause of the AF.[18]

Amiodarone is a class III antiarrhythmic drug like sotalol but exerts many other effects; it slows heart rate and atrio-ventricular nodal conduction (via calcium and beta-receptor blockade), prolongs refractoriness (via sodium and potassium channel blockade) and slows intracardiac conduction (via sodium channel blockade). It is highly lipid soluble and stored in high concentrations in fat and muscle, as well as in the liver, lungs and skin. It has therefore been associated with toxicity involving these organs as well as with the eyes, nerves and thyroid gland.[20] Despite the lower efficacy, patients may prefer flecainide or sotalol above amiodarone because they want to avoid these side-effects.[14]

If patients remain symptomatic with heart rate control and antiarrhythmic medication is either not tolerated or ineffective, then non-pharmacological therapies may be considered, such as ablation.[4]

8. What counselling should be given to patients taking warfarin and atenolol?

WARFARINISED is a good acronym used to remember the important counselling points for patients starting therapy with warfarin. WARFARINISED comes from:

- ☐ When to take — same time each day.
- ☐ Alcohol — may increase anticoagulant effect of warfarin.
- ☐ Risk of bleeding — increased risk of bleeding because blood takes longer to clot. If patient experiences bleeding from the nose or gums or blood in urine/stools they should go to A&E.
- ☐ Follow up — ensure anticoagulation appointments are attended to enable INR levels to be checked.
- ☐ Aspirin — avoid taking aspirin unless

Table 3. Selection of antiarrhythmic drugs for prevention of atrial fibrillation in patients with and without underlying heart disease[14]

	First choice	Second choice	Contra-indicated
No structural heart disease	Flecainide, propafenone, sotalol	Amiodarone, *dofetilide	
Hypertensive heart disease without LVH	Flecainide, propafenone, sotalol	Amiodarone, *dofetilide	
Hypertensive heart disease with LVH	Amiodarone		Flecainide, propafenone, *dofetilide, sotalol
Congestive heart failure	Amiodarone, sotalol, *dofetilide		Flecainide, propafenone
Ischaemic heart disease	Sotalol, *dofetilide	Amiodarone	Flecainide, propafenone

*Notes: LVH=left ventricular hypertrophy; *Dofetilide is not available in the UK*

the clinician is aware and prescribes it.

- Reason for taking — started to slow down the rate at which blood clots to reduce risk of stroke.
- Interactions. Drugs and green salads — these can interact with warfarin. Therefore, ensure patient tells the pharmacist they are taking warfarin before they buy any OTC medications. Green leafy vegetables are a good source of vitamin K which oppose the effect of the warfarin. Avoid eating large amounts of these foods while taking warfarin.
- Notify GP, dentist — warfarin may influence any further treatment.
- INR — range recommendation for patients with AF is 2–3, aiming for a target of 2.5. Patients with an INR of 2.5 take 2.5 times longer to start clotting than patients not taking warfarin.
- Skipped dose — advise not to skip any doses. If this does happen, make a note in their yellow anticoagulant book and take the normal dose for that day. Do not double the dose.
- End of course — ensure patient is aware of how long they need to take their warfarin for. Durations can vary.
- Dose — anticoagulation clinic or GP will inform patient of what dose to be taken following an INR check. Look at a copy of the Anticoagulation Therapy Record (yellow book). Colours of tablets will remain the same irrespective of which brand of warfarin. Warfarin 1mg=brown, warfarin 3mg=blue and warfarin 5mg=pink.

The following counselling points should be discussed with the patient taking atenolol:

- Take it regularly. Do not stop taking unless under doctor's advice.
- Used for maintenance of sinus rhythm.

9. What interactions are commonly seen in patients with AF?

Patients with AF may be taking various combinations of rate and rhythm controlling medications, which may interact, such as:

- Verapamil + beta-blockers: not recommended because patients may be at an increased risk of asystole, hypotension and heart failure.
- Amiodarone + digoxin: amiodarone inhibits digoxin secretion from renal tubules and inhibits the P-glycoprotein membrane transporter system. As a result levels of digoxin are doubled.[20] This interaction occurs in most patients becoming clearly evident within a few days and developing over a course of one to four weeks. On starting amiodarone to digoxin therapy, the recommendation is to halve the dose of digoxin otherwise toxicity may occur.[21]
- Amiodarone + warfarin: amiodarone reduces warfarin clearance and can lead to pronounced increases in the prothrombin time and INR. This peak effect of interaction may occur about 7 weeks after initiation of therapy.[19] The recommendation would be to continue to monitor INR levels and adjust the dose of warfarin as required.
- Amiodarone + simvastatin: there is an increased risk of myopathy. Therefore avoid simvastatin doses of greater than 20mg at night.
- Triple therapy with aspirin, clopidogrel and warfarin: AF patients requiring angioplasty may require triple therapy (see ESC guidance for management of patients with AF and previous article about angioplasty). The use of bare metal stents are preferable and duration of triple clearly stated.

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10. What is the role of the community pharmacist in optimising this patient's care?

Patients have regular access to community pharmacists who can therefore add to the care of a patient medicated for AF. Anticoagulants are one of the classes of medicines most frequently identified as causing preventable harm and admission to hospital.[22] Following the NPSA guidance issued in March 2007 on the safe use of anticoagulant therapy, pharmacists are in a prime position to provide both medication and disease state counselling.[22]

The guidance recommends for patients to receive appropriate verbal and written information if necessary throughout the course of their treatment and to ensure patients' INRs are monitored regularly and are safe before dispensing repeat prescriptions for oral anticoagulation.[22] It also suggests that pharmacists dispensing clinically significant interacting medicines for these patients should check that additional safety precautions have been taken. These include:

- Informing the anticoagulant service that an interacting medicine has been prescribed.
- Ensuring additional INR blood tests have been arranged to monitor any changes.

Pharmacists should educate patients about optimal medication administration, potential adverse events of antiarrhythmics and rate control medications, and when to seek immediate health care. Furthermore, pharmacists must be familiar with the recommendations of the most current clinical practice guidelines to advise health care practitioners concerning drug selection, monitoring and management.

Declarations of interest

The authors have no interests to declare.

Gurpreet Virdi, specialist cardiac pharmacist, and **Sotiris Antoniou,** principal cardiac pharmacist Barts and the London, London

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How best to undertake a review of atrial fibrillation medicines

Introduction

The aim of this article is to look at questions that should be asked when reviewing the management of medications prescribed for atrial fibrillation (AF).

AF is the most common sustained cardiac arrthymia. The recurrence rate remains high after restoration of normal sinus rhythm. AF is a significant risk factor for stroke and other morbidities.[1] The direct annual cost of treating AF in the NHS is £67.6 million. The direct annual cost of stroke is much higher at £985.8 million.[1]

The medical management of AF should have already identified the type of AF and any underlying causes that can be treated, such as hyperthyroidism (see accompanying article p14). At the medication review the following treatment objectives should be addressed:

- ☐ Reach an agreement with the patient on the ongoing management plan.
- ☐ Restoration of the heart to normal sinus rhythm (if applicable).
- ☐ Ventricular rate control.
- ☐ Prevention of thrombosis and stroke.

Considerations around the diagnosis

At a medication review, evidence should be sought from the clinical record that a diagnosis of AF was made and any associated co-morbidities or concomitant diseases that could increase the risk of stroke are managed. A check should be made that the patient is taking appropriate anti-thrombotic therapy to reduce the risk of stroke and thromboembolism because these treatments can be underused in AF.[2]

Consideration should be given to how the symptoms are being controlled, ie through a rhythm or rate control strategy. Questions should initially be asked to detect any worsening in control ie breathlessness/dyspnoea, palpitations, syncope/dizziness or chest discomfort.

Reviewing AF medications

A number of drugs used in AF carry a high risk of harm to the patient if not monitored closely. These include digoxin, warfarin and amiodarone. It is important in the medication review to minimise the risk of drug toxicity, ensure adequate monitoring is in place, the patient is adherent with treatment (especially warfarin) and anticipate any clinically significant drug interactions. Some important interactions with drugs used in AF include:[3]

- ☐ Digoxin and verapamil (see p18)
- ☐ Digoxin and amiodarone (see p18)
- ☐ Amiodarone and warfarin (see p18)
- ☐ Grapefruit juice with verapamil[3] or amiodarone[4]
- ☐ Drugs that prolong the QT interval, including quinidine, flecainide, amiodarone, sotalol, erythromycin, certain antihistamines, antipsychotics and antidepressants.[2]

Beta blockers (BBs)[3]

Recommended points to consider include:

- ☐ These are cautioned in diabetics. Check that blood glucose levels are tightly

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controlled because BBs can slightly raise levels and delay the hypoglycaemic response. Cardio-selective BBs such as atenolol and metoprolol may be preferable. Avoid in people who experience frequent hypoglycaemia.

- ☐ Avoid BBs in asthma. If there is no alternative, a cardio-selective BB is used with extreme caution. Check with the patient for any worsening asthmatic symptoms.
- ☐ Verapamil should not be used with BBs, because of the risk of reduced cardiac output and heart failure.
- ☐ BBs are associated with fatigue, coldness of extremities, impotence and sleep disturbances (may be less common with water-soluble BBs, such as atenolol). Remember to ask about these symptoms.

Digoxin[3]

Recommended points to consider include:

- ☐ Digoxin has a narrow therapeutic index (1–2mcg/L). Lower doses should be used in the elderly, renal impairment or if used with medications that significantly increase its plasma concentration.
- ☐ Therapeutic response to digoxin is assessed with a reduction in ventricular rate. This should not drop below 60 beats per minute.
- ☐ Toxicity should be suspected if, nausea, vomiting, diarrhoea, confusion or blurred vision develops. Elderly patients or those with metabolic disturbances, such as hypokalaemia are particularly susceptible.
- ☐ Routine monitoring of plasma concentrations is not indicated unless toxicity or poor compliance is suspected. If required, concentrations are monitored at least eight hours after a dose.

Amiodarone

Recommended points to consider include:

- ☐ It should be checked that the patient has not been left on the loading dose regimen.
- ☐ Amiodarone has a number of non-cardiac side-effects that include:

  Corneal microdeposits. These are not harmful and reversible on withdrawal of treatment. However, patients should be warned that this affects night vision when driving. Check that the patient has not had symptoms of blurred or worsening vision. An annual ophthalmic examination is recommended,[2,4] although the need for this is unclear.[5]

  Liver damage, hypothyroidism or hyperthyroidism. Liver function tests (LFTs) and thyroid function tests are checked every six months.[2,4]

  Phototoxic reactions. Advise patients to limit sunlight exposure and to use a high factor sunscreen.[4]

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- ☐ Consider pulmonary toxicity if there are symptoms of new or progressive shortness of breath or non-productive cough. Also question about symptoms of peripheral neuropathy.[4]

Stroke prevention

All patients with AF should be assessed regularly for their risk of stroke and the need for thromboprophylaxis.[3] Anti-thrombotics primarily used are aspirin and warfarin and should be started without delay, despite whether a rhythm or rate strategy is ultimately applied. The decision should be based on the overall risk of stroke, bleeding risk, preference, and compliance.[6] The overall risk of stroke should take into account concomitant diseases.

The $CHADS_2$ scoring system can help decide to use either aspirin or warfarin (see Table 1, p16). The total score can be used to predict the expected stroke rate for a patient. If the total score is ≥2, anti-coagulation with warfarin is recommended. If the score is <2 aspirin should be considered (see Table 2, p16).

Warfarin

Systematic reviews have shown warfarin to be more effective than aspirin for reducing stroke risk, but it is more likely to cause bleeding.[2]

- ☐ The prothrombin time, activated partial thromboplastin time, LFT's and platelet count need to be checked before starting warfarin.
- ☐ Monitor the INR weekly until stable, then every 12 weeks.[3] The risk of major bleeding remains low as long as the INR is well controlled and remains below 4.0.[7]
- ☐ Aim for an INR of 2.5 (range 2.0–3.0).[7]
- ☐ Check that the INR is being regularly monitored by the GP or hospital clinic.
- ☐ Check dosage recommendations[8]:

  Use the least number of tablets each day.

  Use constant daily dosing and not alternate day dosing.

  Don't use half tablets. Patients find it difficult to break tablets and instead, when necessary, would rather use 0.5mg tablets.
- ☐ Check that anticoagulants are not added to monitored dosage systems (for example in the case of community or care home patients) without caution[8] (because these may result in inadvertent administration of incorrect doses).
- ☐ Make sure instructions on prescriptions (and therefore labels are meaningful. For instance: 'take dose shown in anticoagulant book'). Avoid set dosage instructions such as take 'one daily'

because the dose recommended from the anticoagulant clinic may change.

- ☐ Discuss the benefits and risks of treatment. Remind the patient to take warfarin at the same time each day and discuss any dietary restrictions. Ensure they have an anticoagulant monitoring booklet and are aware they should let any health care professional treating them know that they are taking warfarin. Also remind patients to present their booklet with all warfarin prescriptions.

Aspirin

Recommended points to consider include:

- ☐ Prescribe aspirin if the $CHAD_2$ score is less than or equal to 1, and there are no contraindications.
- ☐ Consider clopidogrel if aspirin is contraindicated. Consider gastro-protection with aspirin if there is an increased bleeding risk.

Patient discussion points

Each patient should have an individual assessment of their risk of stroke in relation to any other concomitant diseases. The review should open-up discussion on whether the high risk medications are being monitored appropriately and if any adverse effects or significant interactions are present. This includes some OTC medicines, such as pseudoephedrine, which can precipitate arrthymias.

Patients should also be asked about lifestyle and given advice accordingly. Some examples include minimising salt intake for hypertension control, stopping smoking for reducing stroke risk and ensuring their diet is balanced.

Summary

Pharmacological treatment of AF involves controlling the ventricular rate, restoring sinus rhythm with anti-arrthymics and using anti-thrombotics to reduce the risk of stroke and thromboembolism. The review should identify whether thrombophylaxis has been used and the INR is monitored appropriately. It is important that these medications are reviewed because some have a narrow therapeutic index and can cause potentially serious side-effects as well as significant drug interactions. ✣

Declarations of interest

The author has no interests to declare.

Jyoti Sood, pharmacist manager, Sainsburys, New Barnet

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Academic excellence awards: The Royal Pharmaceutical Society calls for 2009 applications

The Royal Pharmaceutical Society of Great Britain is calling for applications from accredited schools of pharmacy for its 2009 Academic Excellence Awards — a programme of PhD studentships to help develop the next generation of academic pharmacists.

The scheme aims to help exceptional pharmacists and pharmacy graduates who are registered with the Society and interested in pursuing an academic career in pharmacy to undertake PhD training. It has been designed to try and help increase the number of pharmacists working in academia and research to foster the important role played by members of the academic workforce in developing and leading the profession. The Society provides funding for two annual awards and is open to all accredited pharmacy schools throughout the UK.

Successful applicants will be chosen following external peer review and by an external judging and awarding panel. Decisions are based on innovation of research, quality of training and support environment.

Deadline for applications: 3 April 2009. The Society will announce the successful applicants in September 2009.

Guidance notes and a revised application form for interested schools are available on the Society's website http//:www. www.rpsgb.org or by contacting 020 572 2466.