Cardiology: new challenges for the millennium

Hospital Medicine will be holding a major international cardiology conference from 6–9 December to welcome in the millennium and to explore the changing face of cardiology. In spite of enormous strides in the diagnosis and management of ischaemic heart disease, it still remains the single largest cause of death in the UK. As the population ages, and our management of angina and acute myocardial infarction improves, we will see an increase in the number of elderly patients with end-stage heart failure as a result of ischaemic heart disease. What advances have there been and what can we expect?

THROMBOLYSIS AND MYOCARDIAL INFARCTION

In the field of thrombolysis there has been a gradual shift towards the use of tissue plasminogen activator (t-PA) from streptokinase in acute myocardial infarction with its better reperfusion characteristics at 90 minutes, and the recommendation that streptokinase is not used twice. Overall about 30 lives are saved per thousand treated (plus a further 25/1000 with aspirin), but only about 35% of patients ever receive a thrombolytic agent.

In spite of suggestions that prehospital thrombolysis could improve on these figures, little work is being done in the UK in this area. This may be partly because of the logistical difficulties of administration of the thrombolytic agent. It is hoped that newer drugs, modifications of the t-PA molecule which are either double bolus only (e.g. reteplase) or single bolus (e.g. lanoteplase) and easier to administer, might improve the number of patients receiving prehospital thrombolysis. There is little to choose between them in terms of efficacy.

As well as aspirin and thrombolysis, beta-blocking agents and angiotensin-converting enzyme (ACE) inhibitors for patients with left ventricular dysfunction have also been shown to reduce long-term cardiac mortality following myocardial infarction, and their use is increasingly routine.

CORONARY ANGIOPLASTY

Primary angioplasty for acute myocardial infarction is as good as thrombolysis, with some protagonists demonstrating it is better (Grines et al, 1993). Its advantages are a shorter hospital admission and less readmission for further ischaemic events. While this form of treatment is increasingly popular in the USA, in the UK the limited facilities for percutaneous transluminal coronary angioplasty (PTCA) restrict this form of treatment to a few centres. Its role in cardiogenic shock is becoming established.

The use of coronary stents in angioplasty is increasing fast (46% of procedures in 1997), but their use is going to be one of the first techniques to be inspected by the National Institute for Clinical Excellence. The possibility that statins might prove as effective as PTCA in low-risk patients (AVERT trial, Pitt et al, 1999) needs confirming. The present UK PTCA rate in 1997 was 402/million population, still well behind most of Europe and well out of sight of USA rates.

UNSTABLE ANGINA

The use of low molecular weight heparin, aspirin and beta-blockade is established, but the exact timing of further intervention remains controversial. Inhibiting platelet aggregation by using the glycoprotein IIb/IIIa receptor antagonist abciximab has been shown to reduce the risk of coronary angioplasty (EPIC, EPILOG and CAPTURE trials), and stenting (EPISTENT trial). The use of the specific cardiac myocyte marker troponin T has proved useful in risk stratification of patients with chest pain, guiding future management (Hamm et al, 1999).

SHORTFALL IN UK CORONARY PROCEDURES

In spite of these advances there are problems for coronary disease patients in the UK. The waiting times for routine coronary artery bypass grafting (CABG) are too long in spite of a year by year increase in CABG procedures (28 499 in 1997 or 518/million).

The National Service Framework for Coronary Heart Disease, shortly to be published, will recommend an increase to 750/million CABG procedures and 550/million PTCA procedures, or more in areas with high disease prevalence. Achieving this will mean a major investment in both staff and facilities.

CORONARY PREVENTION

There is increasing interest in the prevention of coronary disease (Wood et al, 1998). As well as modification of lifestyle (stopping smoking, moderating alcohol, taking more exercise, reducing saturated fat intake), attention is paid to blood pressure control (ideally <140/85 mmHg), and optimum diabetic control where appropriate.

The use of long-term statins for those with hypercholesterolaemia is known to reduce subsequent cardiac events. This is true in both primary prevention (WOSCOPS trial, Shepherd et al, 1995) and secondary prevention (4S trial, Scandinavian Simvastatin Survival Study Group, 1995; and the CARE study). The cost is enormous and at present a statin is only recommended in primary preven-

tion for patients who carry a greater than 15% risk of developing coronary disease in 10 years.

There are many unanswered questions in coronary prevention, including the role of dietary vitamin E and other antioxidant supplements, folic acid for possible hyperhomocysteinaemia, and possibly L-arginine to increase nitric oxide production in the vascular endothelium. In addition the positive cardiac benefits of hormone replacement therapy in postmenopausal women have led to the development of selective oestrogen receptor modulators (e.g. raloxifene) and it remains to be seen if this drug will help prevent the development of coronary disease in older women (The RUTH trial).

END-STAGE HEART FAILURE

The pharmaceutical industry, the cardiologist and the cardiac surgeon battle to improve the prognosis in end-stage heart failure, which remains a depressingly relentless downhill condition. On the drug side we have been through a failure of the chronic use of all inotropes. Digoxin is valuable for atrial fibrillation (AF) but does not reduce mortality, although it does reduce hospital readmissions.

Several trials have confirmed the value of ACE inhibitors in prolonging life. We await the results of trials of angiotensin II receptor antagonists in heart failure (e.g. ELITE II, the Losartan in heart failure study). The remarkable finding that 25 mg of spironolactone reduced cardiac mortality by 31% when given in addition to an ACE inhibitor in patients with severe heart failure was a real bonus (RALES trial, *New England Journal of Medicine*, in press). Low dose beta-blockade is now of confirmed value in grades II and III heart failure. Many other drug trials are in the pipeline including the use of neutral endopeptidase inhibitors, and endothelin receptor antagonists.

Perhaps the answer to the problem lies with the cardiac surgeon. Unfortunately so far operations such as cardiomyoplasty (latissimus dorsi muscle wrap) or the Batista procedure (partial ventriculectomy) have not been of value. The artificial heart remains tantalisingly close but we are still stuck with an external power supply. Left ventricular assist devices of various forms have proved valuable as a bridge to transplantation or in tiding over a period of acute myocarditis. Cardiac transplantation cannot cope with the problem unless the Government introduces an obligatory scheme (with a card-carrying opt-out system) for potential donors. The possibility of virus transfer from animal to man seems to have threatened xenotransplantation for the moment.

PACING AND ELECTROPHYSIOLOGY

Permanent pacing has long been established as one of the most cost-effective forms of treatment in the whole of medicine, as judged by the cost of quality-adjusted life years (QALYs) gained. At present 170 centres in the UK are implanting pacemakers with 22 000 implanted in 1997 (400/million population). These numbers are increasing annually. The argument regarding dual *vs* single chamber pacing in the elderly continues and may be answered by the UKPACE trial.

The last 10 years have seen enormous advances in electrophysiology. The implantable cardioverter defibrillator (ICD) has proved to be better than drug therapy in the management of recurrent malignant ventricular arrhythmias, but again the cost of the unit (approx £19 000) limits the UK implant rate to about 7/million per year. It is hoped that the price will continue to fall and, as the units get cheaper and smaller, implantation of ICDs will be come a routine part of a pacing service throughout the UK.

The management and prevention of AF continues to be a challenge, but there are some exciting developments. Some new class III drugs will soon be available (ibutilide, dofetilide). They are effective at preventing AF in paroxysmal cases and in improving the success rate of DC cardioversion. These drugs are pure IK_r blockers, prolonging the QT interval, and there is concern about the possibility of induction of early polymorphic ventricular tachycardia (torsades de pointes). This will require inpatient initiation of drug treatment under careful monitoring.

Catheter ablation of AF is now becoming a reality. Focal AF can be ablated (foci around the ostia of the pulmonary veins in the left atrium). The catheter maze procedure using linear ablation scars in the atria is a possible future direction. An atrial defibrillator is available for patients with recurrent disabling AF not responding to drug treatment. An alternative is AV node ablation with dual chamber rate responsive pacing.

CONCLUSION

Cardiology is a highly evidence-based specialty. The evidence for the advances outlined above and many others will be covered in the forthcoming conference (see p. 650). We hope to see you there to discuss what has been achieved so far and the challenges ahead. HM

Howard Swanton

Consultant Cardiologist

University College London Hospitals

London W1N 8AA

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