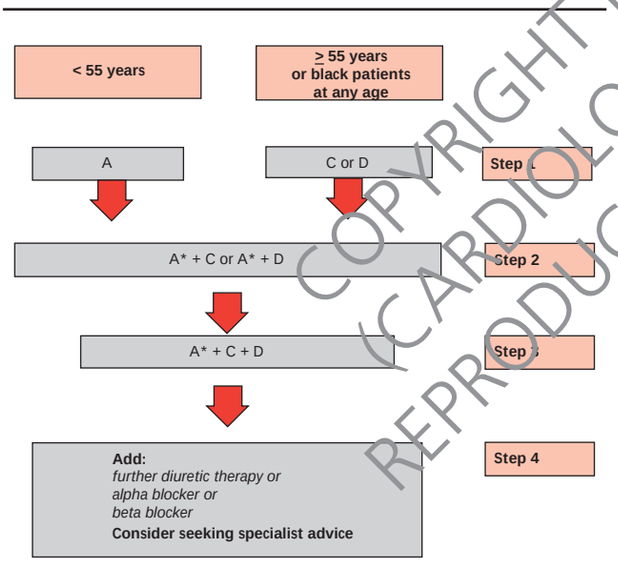
News

NICE updates its hypertension guidance

The National Institute for Health and Clinical Excellence (NICE) in conjunction with the British Hypertension Society (BHS) has updated its clinical guideline on the management of hypertension. Importantly, its recommendations for the pharmacological management of hypertension have been updated since its previous guidance was considerably different from BHS guidance. Consultant cardiologist Adrian Brady and general practitioner Mike Mead report on the new guidance and its implications for the treatment of hypertension in the UK. The full guidance can be found on: http://www.nice.org.uk/CG034guidance

The NICE-BHS Guideline: United Britain shows the way in hypertension

Figure 1. The new NICE-BHS algorithm for hypertension treatment (2006)



Beta blockers are not preferred initial therapy for hypertension but are an alternative to A in patients < 55 years in whom A is not tolerated or contraindicated (including women of childbearing potential)

Black patients are those of Afro-Caribbean descent. There is no evidence in Asian, Chinese or mixed-race patients

Key: NICE = National Institute for Health and Clinical Excellence; BHS = British Hypertension Society; ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker

'It was clear that combination therapy of ACE inhibitor plus calcium channel blocker was well within defined levels of cost-effectiveness'
Adrian Brady

Well, it couldn't go on any longer. For a country to have simultaneously two different national guidelines for hypertension has been a source of confusion and uncertainty for both patients and healthcare professionals. The British Hypertension Society Guideline, BHS IV,[1] was published in 2004, ahead of the NICE Guideline.[2] BHS IV was based on the ABCD algorithm (where A=angiotensin-converting enzyme [ACE] inhibitors [or angiotensin II receptor blockers if ACE-intolerant]; B=beta blockers; C=calcium channel blockers; and D=thiazide diuretics). ACBD was widely adopted by British doctors following its launch. The simplicity of A or B drugs for non-black individuals of less than 55 years of age, and C or D as initial therapy for older patients and black individuals of any age, was straightforward and easy to apply. ABCD was based on the pioneering work of Professor Morris Brown

(Addenbrooke's Hospital, Cambridge), whose rotational drug studies provided confirmatory evidence, together with the emerging mega-trials in hypertension. Brown's work had shown that younger hypertensives generally had high levels of renin driving their hypertension. Older individuals and black patients have low-renin hypertension which responds better to calcium channel blockers and thiazide diuretics.

Later in 2004 NICE released its first guideline for hypertension. The algorithm of drug therapy was influenced substantially by the results of the ALLHAT trial,[3] showing equivalence between C, D and A drugs in an American population with multiple risk factors but rather mild hypertension. The logic of NICE was that if the drugs were equivalent then the cheapest would be satisfactory and thiazides were recommended as first-line therapy.

Publication of ASCOT

In 2005 the ASCOT trial,[4] with over 9,000 UK patients among the >19,000 individuals in the trial, was published with its landmark findings. Combination therapy of the calcium channel blocker amlodipine combined with the ACE inhibitor perindopril offered substantially better therapy than the combination of atenolol-bendroflumethiazide for much more typical British patients. At the same time as the ASCOT trial was published, meta-analyses of beta blockers and, in particular, atenolol,[5] showed that these old favourites offered little or no protection against cardiac events when compared with newer drugs, but were associated with an increased risk of developing diabetes.

Publication of the ASCOT trial prompted urgent meetings between NICE and the Guidelines Working Party of the BHS. The evidence was substantial that the combination of ACE inhibitor plus calcium channel blocker was clearly superior to beta blocker plus thiazide, for so long the mainstay of antihypertensive therapy. The question then addressed by NICE-BHS was whether the cost of this improved therapy fell within acceptable levels of cost per quality-adjusted life year (QALY). The calculations and full guideline[6] can be viewed on the NICE website and it was clear that combination therapy of ACE inhibitor plus calcium channel blocker was well within defined levels of cost-effectiveness. Beta blockers were substantially inferior because of their lack of protection against cardiovascular events and the excess of new-onset diabetes, and so now occupy the position of fourth-line therapy for hypertension (see figure 1).

Beta blockers now fourth-line therapy

Relegating beta blockers from first-line to fourth-line therapy may at first seem astonishing, yet what the guideline really says is that while beta blockers have been good drugs there are now much better drugs available. Therefore, beta blockers should be relegated to a position of inferiority. Once you get used to thinking about this logic, it makes sense, although at first sight the new guideline is dramatically different. The other main message of the guideline is that combination therapy is needed for many, if not most, patients with hypertension. ACE inhibitors (and angiotensin II receptor blockers [ARBs] for those who are intolerant) are first-line therapy for younger individuals, and first added therapy for older patients uncontrolled on thiazide or calcium channel blocker mono-therapy.

What about patients with optimally controlled blood pressure who are on a beta blocker? NICE-BHS says that there is no compelling urgency to alter therapy in the short term. The natural history of hypertension is that blood pressure varies over years, often requiring more therapy. When drugs need to be changed, the opportunity should be taken to introduce modern combination therapy. Beta blockers, of course, remain first-line therapy for individuals post-myocardial infarction and as treatment for angina. They remain first line for women of childbearing potential, in whom ACE inhibitors are contraindicated.

NICE-BHS will certainly cause a storm of protest among traditionalists comfortable with beta blockers for their patients. We must realise that atenolol is now the Ford Cortina of hypertension – brilliant in its day but you wouldn't buy one now. Die-hard beta-blocker Canutes will certainly emerge, refusing to accept the tide of evidence against beta blockers. Yet there is no doubt that combination therapy of A+C will save many lives compared to beta blocker plus diuretic. The BHS is proud of its association with NICE in this brave, bold, yet entirely evidence-based and cost-acceptable guideline. Implementation will without question save many of our hypertensive patients from stroke, MI and premature death.

References

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- An editorial by Professor Bryan Williams on the management of hypertension in the UK, which also discuss the new guidance, can be found on pages 233–7 of this issue.

A general practitioner's view of the new guidance

The new NICE-BHS guideline for the management of hypertension in adults in primary care has profound implications for general practice. The demise of beta blockers can hardly be described as a surprise – we have long had evidence for inferior outcomes with beta blockers and ASCOT clearly demonstrated significant differences between an A plus C compared with a B plus D. Nevertheless, UK GPs are in for a tough time.

The problem, as always, in primary care is one of volume – in this case the sheer volume of the millions of patients on atenolol for hypertension, often in combination with bendroflumethiazide. For many years, of course, this was the perceived best treatment protocol and it was the one chosen by NICE as recently as 2004. With this new guideline effectively removing beta blockers from mainstream antihypertensive use, we have in prospect a significant change in our prescribing pattern for hypertension.

There is, of course, a clear logic and evidence for us to change our regimen of antihypertensive therapy and it is a change that needs to be addressed by every UK practice. We can no longer regard hypertensive patients on beta blockers, particularly in combination with bendroflumethiazide, as on best therapy. We simply can't ignore the need for change.

Managing the change in therapy

Central to the process of change in therapy will be a consistent message for our patients that there is no urgency for a change from their current beta blocker, unless blood pressure is poorly controlled, and discussion with the nurse /GP at the next hypertension review is the appropriate way forward. It must also be emphasised that beta blockers are not to be suddenly stopped and there are still groups of patients in whom beta blockers should continue to be used for cardiovascular benefit (e.g. patients with angina).

The workload involved in changing patients from beta blockers to angiotensin-converting enzyme (ACE) inhibitors (or angiotensin II receptor blockers [ARBs]), the key therapeutic change anticipated as a result of this NICE guideline, is substantial. A change involves not one but several consultations – slowly withdrawing the beta blocker, initiating the ACE inhibitor or ARB, measuring renal function before and after, and monitoring the blood pressure to target. Multiplied by the hundreds of patients on atenolol in each practice, this is a serious increase in consultations at a time when we are already overstretched in trying to meet our new Quality and Outcomes Framework (QOF) targets.

Practices will need to sit down together to decide how best to respond to this new clinical challenge. Although

'It is a change that needs to be addressed by every UK practice'

Mike Mead

we are all suffering 'practice meeting fatigue', changing therapy in treating hypertension has to be a key item on any meeting agenda. As any transient observer of general practice will realise, we are all being judged on reaching treatment targets and one of the most richly rewarded targets in our QOF payment system is that for reaching a target blood pressure (the precise target being lower in patients with diabetes than for those with stroke or uncomplicated hypertension). Meeting targets will inevitably involve using drugs in rational combinations, so this guideline will, albeit indirectly, help GPs to meet their payment targets too.

A useable guideline

Probably the greatest relief to GPs will be the fact that at last we have a single guideline to follow rather than the conflicting guidelines of the last two years. ACD looks set to be an eminently useable guideline that all practices can adopt successfully in patient management. The only disappointment in the guideline is that there is still much more to be said on the use of ACE inhibitors/ARBs in specific groups of patients (like those with diabetes or chronic kidney disease).

The greatest beneficiary of all these deliberations and recommendations will be the patient. We have at last identified the treatment choices and combinations most likely to improve cardiovascular outcomes. Apart from being one of the most devastating of personal illnesses, stroke is one of the biggest causes of NHS expenditure and any reduction of the burden of stroke in the community is to be welcomed. Explanation of the new thoughts on blood pressure treatment to patients will already have begun in practices throughout the UK.

Fortunately, patients with a desire to know more

about the whole issue of the NICE guideline and the proposed changes in therapy can be directed to the Blood Pressure Association's website (www.bpassoc.org.uk), which contains a full summary of the changes and their practical implications for the patient. The Blood Pressure Association has welcomed the new guidance and compiled a patient fact sheet to help explain the new guideline and its implications. For a free copy call 0870 770 0600.

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Rimonabant launched for obesity treatment

General practitioners are adopting a new role as 'risk managers' or modifiers, said GP and National Obesity Forum Clinical Director, Dr David Haslam, speaking at Sanofi-Aventis' recent launch of their new anti-obesity drug, rimonabant (Acomplia®). The UK is the first market to have approval for this first-in-class selective, cannabinoid-1 receptor (CB1) blocker, which appears to have the potential to reduce cardiovascular risk significantly.

Rimonabant should be used as an adjunct to diet and exercise for the treatment of obese patients (body mass index [BMI] $\geq$ 30 kg/m^2) or for overweight patients (BMI $\geq$ 27 kg/m^2) who have associated risk factors such as type 2 diabetes or dyslipidaemia.

The endocannabinoid (EC) system is a physiological system present in brain and peripheral tissues, which is involved in energy balance control, metabolism of glucose and lipids as well as regulating body weight. The EC system is highly activated in the presence of excessive food intake, when there is upregulation of CB1 receptors causing fat accumulation. This is particularly characteristic of the overweight or obese patient with increased visceral fat, or central obesity, which is best observed by a large waist circumference (see figures) of more than 101 cm (40 inches) in men and more than 88 cm (35 inches) in women. This is associated with dyslipidaemia, impaired glucose tolerance and increased risk of diabetes. It is estimated that almost 29% of men and 26% of women are abdominally obese.

Blocking central and peripheral CB1 receptors with rimonabant results in loss of between 5–10% of baseline body weight and a reduction in waist circumference of 6–7 cm along with beneficial changes in lipids and glucose metabolism, as shown in a large series of placebo-controlled trials involving some 6,660 patients. In studies in patients without diabetes, a mean weight loss of 6.5 kg from baseline to one year was seen with rimonabant 20 mg versus 1.6 kg weight loss with placebo. This was maintained for two years.

Increases in high-density lipoprotein cholesterol by about 22.3% were observed versus a 13% increase on placebo. Similarly, triglycerides fell by 6.8% versus an increase of 8.3% with placebo. In the RIO-Diabetes study, patients on rimonabant 20 mg achieved an HbA_{1C} reduction of 0.7% versus placebo (only 0.3% of which was attributable to weight loss alone).

The most common adverse reaction seen with rimonabant resulting in discontinuation from trials is nausea, mood alteration with depressive symptoms, anxiety and dizziness. Depressive disorders were reported in 3.2% of patients, which were mild to moderate and which reversed with drug discontinuation. The drug should not be taken by anyone suffering from major depression. It is also not recommended for anyone on antidepressant medication, or patients with severe kidney or liver problems.

The correct way to measure waist circumference

Smoking cessation potential

Although not specifically licensed for this indication, rimonabant also has smoking cessation potential, which as diabetologist, Professor Tony Barnett from Birmingham Heartlands Hospital describes as "icing on the cake" when it comes to cardiovascular risk reduction. Obesity is associated with a nine-year reduction in life expectancy which is markedly amplified in smokers. The condition is associated with multiple co-morbidities and it increases risk of cancer as well as cardiovascular and other diseases.

Rimonabant treatment costs £55.20 per month. While this may cause some PCTs to wait until NICE issues guidance on the drug, Professor Barnett said that the real question is "can we afford not to treat selected patients?". With one in five adults in the UK being obese (roughly about 10 million people), the economic costs of overweight and obesity in the UK are estimated to be about £7.4 billion annually, with an untold burden of premature death and morbidity.

New home monitoring technology gives greater control to chronic heart failure patients

A pioneering new home monitoring system for chronic heart failure patients has started trials in the UK to help empower patients to be more actively involved in their treatment and care. This study is a radical new way of looking at how diseases, such as chronic heart failure, can be more effectively managed and treated using modern technology in the home.

The research project, funded by Honeywell HomMed, is being co-ordinated at the Royal Brompton Hospital and will take place at three hospitals across London; Ealing, Hillingdon and West Middlesex University hospitals in collaboration with academic partner, Imperial College London.

The study aims to evaluate whether the new home monitoring system can help prevent heart failure admissions to hospital. It will also assess patients' anxiety levels and whether the home monitoring system improves their quality of life following hospital discharge. This careful monitoring should act as an early-warning system so patients can be effectively treated before their condition requires further, and often more serious and complex, treatment.

Using telemonitoring, the system is easy to use and ensures accurate transfer of information (such as blood pressure, pulse rate, blood oxygen levels and weight) from the patient's home to a heart failure nurse specialist at the hospital (figure 1). The information is then screened and if important changes are picked up, the patient will be contacted by the nurse who will offer advice, arrange a clinic visit or suggest changes in the patient's medication.

Principal investigator for the trial, Professor Martin Cowie (Imperial College London), said: "There are at least 750,000 people with heart failure in the UK, and their symptoms of breathlessness, fatigue and fluid retention are often poorly monitored. The signs of deterioration are often not picked up early enough, leading to unnecessary admissions to hospital. This innovative research study will test for the first time whether a home monitoring approach can revolutionise the quality of care that patients receive. If it proves successful it could be the first step in radically changing the way the NHS delivers care to people living with heart failure."

Patients with heart failure who are ready to be sent home from hospital will be enlisted to this trial, with half being allocated to the home monitoring system and the other half to their 'usual' care. Each patient will be followed up for six months, with the results of the trail available by Autumn 2007.

Studies in the US began in 1999; there are 35,000 telemonitors in daily use. One study conducted by the Ochsner Clinic Foundation in New Orleans shows that the use of HomMed® telemonitoring substantially reduces utilisation of health care resources and morbidity in heart failure. There was a 41% relative reduction in hospitalisations with acute decompensated heart failure and emergency department visits ($p<0.05$) in a study evaluating 115 adult heart failure patients compared to a parallel control population of 158 patients who declined participation.

Figure 1. The telemonitoring system is able to transfer information from the patient's home to a heart failure nurse specialist at the hospital

Cordis scholarships for clinical cardiology research

The 2006 Cordis Clinical Cardiology Research Scholarships have been awarded to the following:

- **Dr William van Gaal, John Radcliffe Hospital, Oxford (supervised by Dr Adrian Banning), for 'Myocardial injury following coronary artery surgery versus angioplasty'.**
- **Dr Billal Patel, Royal Liverpool University Hospital (supervised by Dr Mike Fisher), for 'The contribution of inflammatory mechanisms to myocardial and vascular injury'.**
- **Dr Andrew Worrall, New Cross Hospital, Wolverhampton (supervised by Dr James Cotton), for 'The impact of platelet resistance to aspirin and clopidogrel on clinical outcomes'.**

Scholarship applicants were encouraged to propose projects that reached beyond the laboratory and into clinical practice. Each scholarship provides a grant of £60,000 for the pursuit of clinical research in the field of cardiovascular medicine over the coming year. Each recipient is a UK-based specialist registrar pursuing a career in clinical care.