New BHS guidelines: up-to-date hypertension management in diabetes

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ARTICLE POINTS

1 Treatment of hypertensive patients with type 2 diabetes is a particular focus of recently published guidelines from the British Hypertension Society (BHS).

2 The current BHS guidelines recommend that, in diabetes, anti-hypertensive treatment should be initiated if usual systolic BP is 140 mmHg or higher and/or diastolic BP is 90 mmHg or higher.

3 The BHS takes the view that a return to single risk-factor management is a retrogressive step.

4 Implementation of the BHS recommendations by primary care professionals should do much to improve the health, wellbeing and survival of people with diabetes and hypertension.

KEY WORDS

- **Blood pressure**
- **Cardiovascular disease**
- **Lipid lowering**

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Introduction

The recently updated guidelines from the British Hypertension Society (BHS) have incorporated evidence from trials and other sources over the past five years, and have a particular focus on risk factor management in people with hypertension who have type 2 diabetes. This article reviews the evidence from landmark trials that has been incorporated in the guidelines, discussing the benefits of lipid lowering, how low to aim when reducing blood pressure, and how the BHS guidelines tie in with other guidelines, such as those from the National Institute for Clinical Excellence.

The British Hypertension Society (BHS) has recently published updated guidelines (Williams et al, 2004). This followed a review by the Society's fourth working party of important data that has emerged from clinical trials and other sources in the five years since the previous BHS recommendations (Sever et al, 1993). The revision was necessary to encourage transfer of the gains observed in trials to everyday clinical practice.

Treatment of hypertensive patients with type 2 diabetes is a particular focus of these guidelines, since much evidence has accumulated indicating the great benefits of risk factor management in such individuals. Hypertension (blood pressure; BP >140/90 mmHg) is twice as common in people with diabetes as in the non-diabetic population (Williams et al, 2004), with a prevalence of type 2 diabetes approaching 80% of the hypertensive population in many European countries (Williams et al, 2003). While hypertension in type 1 diabetes is closely related to overt or incipient nephropathy (Williams et al, 2004), the much more common type 2 diabetes is associated with acceleration of the age-related changes in blood pressure observed in Western societies. Thus, type 2 diabetes is characterised by earlier onset of systolic hypertension and a high prevalence of isolated systolic hypertension, particularly in women (Williams et al, 2003).

Hypertension and diabetes are each powerful predictors of cardiovascular morbidity and mortality. Together, these conditions have at least additive effects on risk. In diabetes, hypertension increases cardiovascular disease two-fold in men and four-fold in women (Zanchetti et al, 2001). In hypertension, diabetes doubles the risk of nephropathy, cardiovascular complications and mortality (Zanchetti et al, 2001).

It is now abundantly clear that the optimal treatment of diabetes should not focus on glycaemic control in isolation. Many patients with type 2 diabetes are overweight and would benefit from weight reduction, increasing activity, dietary sodium reduction, and smoking cessation. Landmark trials such as the Heart Protection Study, the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) and the Collaborative AtoRvastatin Diabetes Study (CARDS), have emphasised the inter-relationship of cardiovascular risk factors, especially hypertension and lipids, and the importance of addressing these at levels previously considered to present little or no risk (Heart Protection Study Collaborative Group, 2002; Sever et al, 2003; Colhoun et al, 2004).

Targeting lipids in hypertensive patients with diabetes

ASCOT is a primary prevention trial of 19342 high-risk uncontrolled hypertensive

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1 The lipid lowering arm of ASCOT was terminated early as the primary endpoint, myocardial infarction plus fatal coronary heart disease, was reduced by 36% in those taking atorvastatin.

2 CARDS also ended prematurely as in those taking atorvastatin there was a reduction in stroke risk (48%), cardiovascular events (37%) and total mortality 27%, regardless of gender and baseline LDL-cholesterol.

3 Tight blood pressure control is more effective than tight blood sugar control in reducing cardiovascular morbidity and mortality, and progression of retinopathy, albuminuria and nephropathy.

patients, with an average of 3.7 other cardiovascular risk factors. In the study's lipid-lowering arm, over 10 000 patients with non-fasting total cholesterol concentrations below 6.5 mmol/l were randomly assigned to either a statin (10 mg atorvastatin) or placebo in addition to antihypertensive treatment (Sever et al, 2003).

The results were so strikingly in favour of the statin intervention that the trial was terminated over a year early by the data safety monitoring board. After a median follow-up of just 3.3 years, both placebo-treated and atorvastatin-treated patients had achieved mean BP values of 138.3/80.4 mmHg (Sever et al, 2003). However, the primary endpoint (non fatal myocardial infarction plus fatal coronary heart disease [CHD]) was reduced by 36% in the atorvastatin group. The advantage of lipid lowering was equally marked in the subgroup of 2532 patients with diabetes. The ASCOT findings emphasise the relevance of statin therapy for hypertensive people with type 2 diabetes who have average or below average cholesterol levels.

CARDS focused on patients with type 2 diabetes, two-thirds of whom were also hypertensive (Colhoun et al, 2004). The trial recruited 2838 people with type 2 diabetes aged 40 to 75 who had no prior history of cardiovascular, cerebrovascular or peripheral vascular disease but who had a low-density lipoprotein (LDL) cholesterol level below 4.14 mmol/l and one other cardiovascular risk factor (e.g. hypertension or microalbuminuria). More than half had LDLs below 3.3 mmol/l and a quarter had LDLs of 2.6 mmol/l or less.

Patients were randomised to either atorvastatin 10 mg or placebo for a planned five years. However, the trial ended prematurely after less than four years, when the data safety monitoring board found a significant reduction in prespecified vascular events among patients receiving atorvastatin. Stroke risk was reduced by 48%, cardiovascular events by 37% and total mortality by 27% (Colhoun et al, 2004).

During the trial, the mean LDL cholesterol reduction was 40%. Mean BP in each group at baseline was 144/83 mmHg. Benefits were seen regardless of age, gender and whether baseline LDL was above or below 3 mmol/l.

The impact of such interventions on outcomes has been impressive and may ultimately prove to be equally important in slowing the progression of renal and retinal complications.

The BHS now recommends the routine use of statin therapy in people with diabetes complicated by hypertension (Williams et al, 2004). For type 1 diabetes, there are as yet no data to support statin use but since rates of cardiovascular disease are similar it would seem logical to treat people with type 1 diabetes in the same way. The ASCOT findings suggest that it would be reasonable to prescribe a statin for all patients up to age 80 years with a total cholesterol of >3.5 mmol/l who have a 10-year CVD risk of 20% or more. In effect this means that most hypertensive patients (especially men) aged over 50 years qualify for statin treatment. When resources permit the threshold for intervention could be lowered in line with trial evidence.

BP reduction: how low to aim

Hypertensive people with type 2 diabetes are exquisitely sensitive to BP changes. In the Hypertension Optimal Treatment (HOT) study (Hansson et al, 1998), a difference in diastolic blood pressure of only 4 mmHg (82 mmHg vs 86 mmHg) was associated with a 51% reduction in cardiovascular risk. Tight BP control is more effective than tight blood sugar control in reducing cardiovascular morbidity and mortality, and progression of retinopathy, albuminuria and nephropathy (UK Prospective Diabetes Study Group, 1998).

The current BHS guidelines, like those of other countries, recommend that, in diabetes, antihypertensive treatment should be initiated if usual systolic BP is 140 mmHg or higher and/or diastolic BP is 90 mmHg or higher (Williams et al, 2004). Ideally, BP should be reduced to less than 130/80 mmHg (and <125/75 mmHg if there is proteinuria >1 g per 24 hours). However, it is acknowledged that achieving these targets can be difficult and an audit target of <140/80 mmHg is proposed. The evidence in support of systolic BP is less robust than that for diastolic BP targets, but there is no good evidence that rigorous BP control causes harm.

Almost all hypertensive patients with diabetes will need a combination of drugs to achieve recommended targets; many will

require three or more. Choice of drugs is likely to include a thiazide or thiazide-like diuretic and an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB), particularly if patients already have microalbuminuria or proteinuria. These two drug classes have demonstrated renoprotective effects (Brenner et al, 2001; Lewis et al, 1993; Lewis et al, 2001) and are recommended as initial therapy for patients with, or likely to develop, diabetic nephropathy.

Provided there is no cost disadvantage, it is preferable to administer drugs as fixed-dose combinations so as to minimise the number of medications and improve adherence. Where other drugs need to be added, long-acting formulations make life easier for patients.

Tying in with advice from other guidelines

National Institute for Clinical Excellence (NICE) guidelines on essential hypertension have recently been published (North of England Guidelines Development Group, 2004). These differ from the new BHS guidelines in that they focus on the treatment of essential hypertension in uncomplicated patients. They do not, therefore, advise on when to use statin therapy to reduce total cardiovascular disease (CVD) risk. The BHS takes the view that a return to single risk-factor management is a retrogressive step. Any patient identified as having elevated BP is at increased risk of CVD not only from their BP elevation but also from an aggregate of other risk factors which might include dyslipidaemia, impaired glucose tolerance and concomitant target organ damage. The BHS believes that optimal management means assessing the totality of risk and intervening accordingly to reduce it.

In previous guidelines the BHS endorsed use of the Joint British Societies' computerised Cardiac Risk Assessor and its CHD risk chart, based on Framingham data (BCS et al, 1998). The chart had two drawbacks. It predicted the 10-year absolute risk, which meant it risked under-treating young people at high relative risk, e.g. a 35-year-old woman smoker with diabetes, total cholesterol/high density lipoprotein cholesterol ratio of 9 and systolic BP 180 mmHg would not reach the 10-year 30% risk of CHD threshold. It also risks over-treating older people with a lower relative risk, e.g. most elderly men who qualified on grounds of age and gender. Secondly, it focused on CHD rather than CVD risk, thus failing to include risk of stroke, a major consequence of hypertension.

The latest Joint British Societies' chart has also been modified to assess people for a threshold 10-year CVD risk (including both risk of fatal or non-fatal stroke as well as CHD) of 20%. A separate chart for people with diabetes is not provided since the Joint British Societies considered most people with diabetes as having risk of CVD equivalent to someone with established coronary disease. People with type 2 diabetes of 10 years duration and who are aged over 50 years are thus categorised as CHD risk equivalents and should be considered for lipid-lowering treatment according to secondary preventive criteria.

Guidelines from the BHS and the Joint British Societies

PAGE POINTS

1 Of the 550 clinical indicator points available in the new GMS contract quality framework, 158 relate directly to hypertension.

2 Systolic BP is identified as one of the world's most preventable causes of premature morbidity and mortality by a recent World Health Organization report.

3 Systolic BP as a determinant of CVD risk in people with diabetes is of particular importance.

4 Implementing new recommendations from the BHS should do much to improve the health, wellbeing and survival of people with diabetes and hypertension.

informed recommendations made by the National Service Frameworks (NSFs) for coronary heart disease, diabetes, and older people. The NSF for CHD set an intervention threshold at a 10-year CVD risk of 30% or greater for pragmatic reasons. As care systems mature and once patients at highest risk have been identified and treated, the NSF suggests primary care physicians should intervene at lower risk levels.

The new General Medical Services contract for primary care sets out a quality framework to reward practices delivering care to higher standards. Among the clinical standards, providing the greatest financial rewards, CVD is covered by standards including those related to hypertension and diabetes. Of 550 clinical indicator points available, 158 relate directly to hypertension. For example, a score of 20 points is awarded where 90% of hypertensive patients have had their BP recorded in the past nine months. A further 56 points can be obtained if 70% of hypertensive patients have their last BP recorded as being 150/90 mmHg or less. Rewards for measuring and lowering BP in patients with diabetes are less generous; reducing BP to 145/85 mmHg or less in 55% of patients with diabetes qualifies for 17 points.

The overwhelming importance of systolic BP as a determinant of cardiovascular risk has been demonstrated in a recent epidemiological survey and identified in a World Health Organization report as one of the world's most preventable causes of premature morbidity and mortality (Lewington et al, 2002; Ezzati et al, 2002). Systolic BP as a determinant of CVD risk in people with diabetes is of particular importance. The new BHS guidelines acknowledge this and implementation of its recommendations by primary care professionals should do much to improve the health, wellbeing and survival of people with diabetes and hypertension. ■

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