

Hypertension – a clinical update for physicians

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Introduction

The British Hypertension Society and Royal College of Physicians teamed up to organise a conference aimed at providing physicians with a high-quality, evidence-based update on the diagnosis and management of hypertension. Recent advances such as renal denervation and baroreceptor stimulation were covered during the conference.

The extent of the problem

With more than one billion individuals affected worldwide and a key contribution to global morbidity and mortality (54% of cases of stroke and 47% of ischaemic heart disease), high blood pressure remains a major challenge to healthcare systems in developed and developing countries.¹ In the western world, the prevalence of hypertension will continue to increase as the population ages and the number of people affected by the obesity epidemic soars. The scale of the problem mandates major investment in primary and secondary healthcare, as well as patient education. Early diagnosis and effective blood pressure control should be at the heart of these efforts. The asymptomatic nature of this modifiable yet potent risk factor often delays diagnosis and makes it harder to achieve compliance with medical therapy. These difficulties can be overcome only through active involvement of physicians, especially in primary care, by encouraging routine blood pressure checks in high-risk groups and regular monitoring of response to treatment. When the diagnosis is confirmed, frequent contacts should be maintained with the patient, with a focus on educating them about the consequences of untreated hypertension and the value of lifestyle modifications in reducing cardiovascular risk. The patient should be involved in decision-making regarding treatment and should be encouraged to report any concerns or side effects caused by drug therapy.

Diagnosing hypertension

Establishing and confirming the diagnosis of hypertension was one of the major themes of this conference. The drawbacks of

using blood pressure measurements taken in the clinic as a diagnostic tool – for example, the use of a single measurement to reflect a continuum and the long period of time needed to confirm diagnosis – was reflected in the National Institute for Health and Clinical Excellence (NICE) guidance on hypertension issued in August 2011.² The NICE guidance recommends offering ambulatory blood pressure monitoring (ABPM) to confirm the diagnosis of hypertension for all patients found to have a blood pressure of $\geq 140/90$ mmHg on measurements taken in the clinic. In a large meta-analysis that included more than 7,000 subjects, Hansen *et al* demonstrated the prognostic superiority of daytime ABPM compared with conventional blood pressure measurements.³ In circumstances in which ABPM is not tolerated or available, home blood pressure monitoring (HBPM) is an acceptable alternative. An additional advantage of both ABPM and HBPM is that they aid the diagnosis of white-coat and masked hypertension and also reduce misdiagnosis. Although white-coat hypertension seems to convey no additional cardiovascular risk compared with normotension and so should not be treated, both masked and sustained hypertension result in almost double the risk of cardiovascular disease and can cause significant target organ damage if missed and left untreated.⁴ At first glance, using ABPM to confirm diagnosis in all patients may seem very costly and to require considerable resources. Interestingly, however, when compared to clinic- and HBPM-based confirmation of hypertension, ABPM was shown to be the most cost-effective method. This proved to be the case across all age- and sex-stratified groups within the study population of individuals with suspected hypertension.⁵ If the NHS adopts these guidelines, a high cost will initially be involved to pay for equipment and training, but this ultimately will be offset by the savings predicted in the following years. In fact, NICE estimates savings of around £10 million per year by the fifth year of such a programme.²

When making a diagnosis of hypertension using ABPM, the average of daytime pressure readings should be used. Average blood pressure of $\geq 135/85$ mmHg confirms stage 1 hypertension. Diagnosis of stage 2 hypertension is based on an average daytime blood pressure of $\geq 150/95$ mmHg. The same cut-off points apply to the average of a series of HBPM readings. For clinic blood pressure measurements, $\geq 140/90$ mmHg corresponds to stage 1 hypertension, whereas $\geq 160/100$ mmHg defines stage 2 hypertension.

Once a diagnosis of hypertension has been confirmed, it is crucial to assess the patient's cardiovascular risk formally using a validated risk-score calculator. Furthermore, a careful evaluation of target organ damage should also be performed. This will usually include urine dipstick to check for haematuria and proteinuria, spot urine for urine albumin-to-creatinine ratio (UACR),

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12-lead electrocardiography, fundoscopy for retinopathy, blood electrolytes, glucose, lipids and renal function.

Secondary hypertension

Special attention was given to the importance of considering and diagnosing secondary causes of hypertension during the conference. This is driven by two main reasons: firstly, the prevalence of secondary causes among patients newly diagnosed with hypertension is higher than previously acknowledged. Secondly, a considerable proportion of cases of secondary hypertension is potentially curable and/or mandate specific therapies. If missed, secondary hypertension can present as challenging cases of resistant hypertension and result in irreversible target organ damage and premature death. Work done by Rossi and colleagues on primary aldosteronism neatly illustrates the above concepts.⁶ In this study, 11.2% of 1,125 patients newly diagnosed with hypertension were found to have primary aldosteronism, with 42% of these having a surgically curable subtype of this disease. Hypertension that presents in young people (aged <40 years) and severe and resistant hypertension should raise the suspicion for secondary hypertension. In such circumstances, NICE recommends referral to specialist care for further evaluation and management.

The process of evaluating patients with suspected secondary hypertension should start with screening tests, which are followed by more specialist investigations. The initial screening for all patients should ideally include plasma electrolytes, plasma renin activity and 24-hour urine metanephrines. These tests, combined with the clinical features, will help narrow the differential diagnosis and guide the choice of more specialised investigations. Renal parenchymal disease, renovascular disease, primary aldosteronism, pheochromocytoma, Cushing's syndrome and aortic coarctation are the main causes of secondary hypertension. Specialised investigations such as computed tomography (CT)/magnetic resonance imaging (MRI) renal angiography, renal vein sampling, adrenal CT/MRI and adrenal vein sampling should ideally be performed by a specialist and preferably at a tertiary centre.

Management of hypertension

Management of hypertension was addressed during the conference, with an emphasis on the new changes included in the most recent NICE guidance.² Lifestyle advice should be offered to all patients with hypertension, as many simple lifestyle interventions have been shown to be effective in reducing blood pressure in patients with hypertension and those with pre-hypertension. Reducing dietary intake of salt (sodium chloride, NaCl), losing weight, moderating alcohol consumption and taking regular physical activity are among the beneficial lifestyle modifications. The scarcity of evidence on optimal blood pressure targets and the fact that aggressive blood pressure lowering is not supported by results from recent trials was acknowledged at the meeting.^{7,8} The current guidelines recommend the use of clinic blood pressure to monitor control, with a general aim of blood pressure

<140/90 mmHg.² Uncertainty remains about more intensive control (target <130/80 mmHg) in subgroups of patients with cardiovascular disease, chronic kidney disease or diabetes. In patients with a white-coat element, monitoring of response to treatment must be guided by ABPM or HBPM.

Only a few changes to the hypertension pharmacotherapy algorithm were included in the NICE guidance published in 2011,² some of which were highlighted during the conference sessions. One of the important changes is the downgrading of thiazide-like diuretics from step 1 therapy in patients aged ≥ 55 years and black patients of African or Caribbean origin to step 3. According to the new guidelines, the first-choice therapy in this group – as long as they have no evidence of heart failure and are not at high risk of heart failure (that is, aged >75 years) – is calcium channel blockers (CCBs). This change was driven by a number of proven clinical merits of CCBs. The metabolic neutrality of CCBs makes them easy to use without the need for any special monitoring such as renal or liver function tests. In the cost-effectiveness analysis carried out by NICE,² CCBs were shown to be the most cost-effective first-line antihypertensive therapy. The ability to reduce blood pressure variability, an independent predictor of stroke, is another favourable attribute of CCBs.⁹ Surprisingly, the use of 2.5 mg of bendroflumethiazide once daily – a drug and dose that is still widely prescribed in the UK to treat hypertension – is not justified by any evidence in the literature. When a drug from the thiazide group is indicated, the preference now is therefore for thiazide-like diuretics such as indapamide and chlortalidone over standard thiazides.

Resistant hypertension

When clinic blood pressure is persistently >140/90 mmHg despite optimal doses of three of the antihypertensive drugs recommended at step 3 of the treatment algorithm (usually this will be angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker + CCB + thiazide-like diuretic), a diagnosis of resistant hypertension is suspected. This should be confirmed by ABPM. It is worth pointing out that a secondary cause for hypertension should be ruled out before making this diagnosis, as the contribution of undetected secondary causes to suspected resistant hypertension cases is much more substantial than previously believed. One of the key take-home messages from the conference regarding resistant hypertension was the need for awareness of issues around compliance with medication. A significant number of patients referred because of resistant hypertension are likely to be non-compliant with their existing medications.

Specialist advice should be sought when managing patients with resistant hypertension. The next step in the treatment algorithm would be adding another diuretic. This will normally be low-dose spironolactone (that is, 25 mg once daily) if serum potassium is <4.5 mmol/l. However, when serum potassium is >4.5 mmol/l, an increase in the dose of the thiazide-like diuretic should be considered. If blood pressure

control is still suboptimal, or the patient is unable to tolerate the higher dose of diuretic, an alpha blocker or beta blocker can be added.

Novel therapies

Despite the use of optimum regimens of several antihypertensive medications, blood pressure remains uncontrolled in a subset of patients with resistant hypertension. A new treatment option for those patients may come from novel non-pharmacological interventions, namely renal sympathetic denervation and carotid baroreceptor stimulation. Renal sympathetic denervation involves using a specialised catheter to perform radiofrequency ablation of renal sympathetic nerves in both renal arteries. The catheter is delivered to the renal arteries percutaneously and connected to a radiofrequency generator. For carotid baroreceptor stimulation, the stimulator is usually implanted through a mini-surgical procedure that involves placing the pulse generator subcutaneously. Two leads connected to the pulse generator are attached to the carotid sinuses after being tunnelled under the skin.

Both treatments are invasive and aimed at disrupting the sympathetic overactivity that is one of the neural mechanisms underlying hypertension. Initial results regarding safety and efficacy are promising for both techniques; however, it is important to take into account the small size of the studies from which the evidence has emerged and the relatively short follow-up periods involved.^{10,11} Larger and better-designed studies are currently underway.

Both of these interventions could play a significant role in the management of resistant hypertension in the future. In addition, improved and better tolerated blood-pressure monitoring devices and honed clinical skills will hopefully lead to better outcomes.

Conclusion

Hypertension remains a major cause of morbidity and mortality worldwide. Making and confirming the diagnosis early and achieving and maintaining good blood pressure control are key to tackling the hypertension epidemic. Joint efforts are needed to implement the guidelines in clinical practice and major research endeavours are needed to fill the gaps in evidence. Although a lot of excitement surrounds the new non-pharmacological inter-

ventional therapies for hypertension, enthusiasm for their deployment should be matched by enthusiasm to undertake rigorous evaluation of their longer term safety and efficacy.

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