Guest Editorial

Challenges in Resistant Hypertension

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Abstract

Hypertension is the major risk factor for disease and premature death. Although the efficacy of antihypertensive therapy is undisputed, few patients reach target blood pressure. Steps to improve treatment and control include assessment of global cardiovascular risk for the individual patient, improving caregiver support, education and organisation, increasing treatment persistence, using out of office blood pressure monitoring more often, detecting secondary hypertension forms, and referring patients with remaining uncontrolled hypertension to a specialist hypertension centre. In conclusion, there is room for improvement of blood pressure control in hypertensive patients. The clinical benefit of improved blood pressure control may be considerable. This may be particularly true for patients with resistant hypertension.

Keywords

Prognosis, resistant hypertension

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High blood pressure is the major risk factor for disease and premature death worldwide.¹ The associations between blood pressure and fatal coronary artery disease and fatal stroke have been well demonstrated.² Also, associations between blood pressure and morbidity and mortality on specific cardiovascular disease conditions in different age groups, and results concerning the lifetime risk for specific cardiovascular complications associated with hypertension have recently been reported.³ The efficacy of antihypertensive drug therapy is undisputed. However, observational studies show that few patients reach target blood pressure.⁴

We must thus take several steps to improve antihypertensive treatment and control:

- Assessment of global cardiovascular risk is essential to offer the best treatment for the individual patient.
- Improve caregiver support, education and organisation.
- Consider factors that influence drug adherence, reduce drug discontinuation rate and increase treatment persistence to prescribed treatment.
- Increase the use of home blood pressure monitoring and ambulatory blood pressure monitoring to identify patients with a white coat effect, improve risk stratification and increase patient engagement.
- Consider secondary hypertension forms in patients with apparent resistant hypertension.
- Consider referring patients with remaining uncontrolled hypertension to a specialist hypertension centre, as most patients can be well controlled.

Firstly, assessment of global cardiovascular risk is essential to offer the best treatment for the individual patient. Risk assessment can be achieved by taking cardiovascular risk markers, blood pressure level and other risk factors, signs of hypertensive target organ damage, and concomitant cardiovascular and other disease conditions into account.⁵ Secondly, we should consider improving caregiver support and education. Caregivers may think that side effects with antihypertensive drugs treatment are a problem, or that the available evidence to treat high blood pressure in some people is insufficient. However, evidence suggests that quality of life is improved by antihypertensive treatment^{6,7} and there is evidence of the benefit of treating elderly hypertensive patients.⁷ Drugs may be prescribed with an inappropriate dosing or inadequate drug combinations may be used. Recent evidence shows that adding a mineralocorticoid-receptor antagonist to patients with apparent treatment resistant hypertension provides better blood pressure reduction than other drug classes.⁸ Caregiver organisation and systematic follow-up may also need improvement.

Thirdly, key factors to improve drug compliance and treatment persistence must be better understood. We have reported that 35 % of patients attending primary healthcare newly initiated on antihypertensive drug therapy discontinued treatment within 2 years.⁹ Male patients, younger age, mild blood pressure elevation, low income and birth in a foreign country were factors associated with discontinuation. Of note, discontinuation rates were similar for all major antihypertensive drug classes when comorbidity and other potential confounding factors were taken into account (which has

rarely been done in previous studies).¹⁰ Also, in patients referred for apparent treatment resistant hypertension, many do not appear to take their prescribed medication.¹¹ Fourthly, the use of home blood pressure monitoring and ambulatory blood pressure monitoring is important. The use of out of office blood pressure monitoring will identify patients with a white coat effect, improve risk stratification and increase patient engagement. Finally, approximately one out of ten hypertensive patients have secondary forms of hypertension, of which primary aldosteronism, renal hypertension and obstructive sleep apnoea are considered the most common causes. Patients with secondary hypertension can often be offered specific treatment and are thus important to identify, in particular among people with apparent treatment resistant hypertension. Of note, standard screening procedures to assess the aldosterone-to-renin ratio in blood to indicate a diagnosis of primary aldosteronism have been much simplified in recent guidelines, as compared with previous recommendations.¹² Screening for renal hypertension can now largely be performed by non-invasive renal ultrasound and renal artery duplex ultrasound, with no exposure to contrast media or radiation. Screening methods for obstructive sleep apnoea are also simplified with a trend for assessment of fewer variables, computerised air flow evaluation and automated analyses for improved diagnostic accuracy.

Several guidelines and recommendations define resistant hypertension as a blood pressure $\geq 140/90$ mm Hg despite treatment with three different antihypertensive drug classes, appropriately chosen and dosed, and often a thiazide diuretic is mandatory.⁵ Apparent resistant hypertension is prevalent in approximately 10 % of all treated hypertensive patients attending primary healthcare, and is associated with concomitant cardiovascular disease and diabetes mellitus.¹³ More important, apparent resistant hypertension is associated with a worse prognosis, when blood pressure levels and comorbidity are also taken into account. Thus, it is particularly important to identify patients with apparent resistant hypertension, and to bring their blood pressure under control. In this context, the comprehensive overview of the diagnosis and management of resistant hypertension by Tsioufis and colleagues in this issue of *European Cardiology*

Review is of great value.¹⁴ The authors correctly emphasise the importance to recognise the many reasons for apparent resistant hypertension, and how this is best performed in clinical practice. It is important to appreciate that most patients with apparent resistant hypertension can be well controlled when referred to a specialist hypertension centre.¹⁵

However, some patients continue to present true drug treatment resistant hypertension. As described by Tsioufis et al.,¹⁴ other interventional techniques to lower blood pressure can be considered in these patients. The first studies of catheter-based endovascular renal sympathetic denervation in patients with treatment resistant hypertension showed marked and sustained reductions in office blood pressure. However, these initial studies were generally uncontrolled or limited to a non-interventional control arm and included patients based on their office blood pressure values.¹⁶ Indeed, compared with office blood pressure measurements, the effects of renal denervation on ambulatory blood pressure were considerably smaller. More recently, some randomised controlled studies have failed to show reductions in office blood pressure or ambulatory blood pressure by renal denervation.⁶ Current focus on endovascular renal sympathetic denervation is on:

- the development of new devices and procedures to ascertain successful renal nerve ablation;
- identifying the proper target population to offer renal denervation;
- improvement and control of drug persistence; and
- the use of ambulatory blood pressure monitoring for patient selection and evaluation of efficacy.

Interventional techniques other than renal nerve ablation included baroreceptor activation therapy, with promising preliminary results in patients with resistant hypertension.¹⁷

In conclusion, there is room for improvement of blood pressure control in hypertensive patients. The clinical benefit of an improved risk assessment and appropriate treatment may be considerable. This may be particularly true for patients with resistant hypertension. ■

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