Resistant Hypertension

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Hypertension is a major risk factor for cardiovascular disease [1,2]. Hypertension is present in approximately 69% of patients with a first myocardial infarction, in approximately 77% of patients with a first stroke, in approximately 74% of patients with congestive heart failure, and in approximately 60% of patients with peripheral arterial disease [3,4]. Hypertension is also a major risk factor for a dissecting aortic aneurysm, sudden cardiac death, angina pectoris, atrial fibrillation, diabetes mellitus, the metabolic syndrome, chronic kidney disease, thoracic and abdominal aortic aneurysms, left ventricular hypertrophy, vascular dementia, Alzheimer's disease, and ophthalmologic disorders [2].

The American College of Cardiology Foundation/American Heart Association 2011 expert consensus document on hypertension in the elderly recommended that the blood pressure should be lowered to less than 140/90 mm Hg in adults younger than 80 years at high risk for cardiovascular events [2]. On the basis of data from the Hypertension in the Very Elderly trial, these guidelines recommended that the systolic blood pressure should be reduced to 140 to 145 mm Hg if tolerated in adults aged 80 years and older [5].

A statement from the American Heart Association defined resistant hypertension as a blood pressure remaining above goal despite the use of 3 optimally dosed antihypertensive drugs from different classes, with one of the drugs being a diuretic [6]. The National Institute for Health and Clinical Excellence guideline suggests that the 3 drugs should be an angiotensin-converting enzyme inhibitor or angiotensin blocker plus a calcium channel blocker plus a thiazide-type diuretic [7].

Pseudo hypertension in the elderly is a falsely high systolic blood pressure which results from markedly sclerotic arteries which do not collapse under the blood pressure cuff [2]. Pseudo hypertension can be confirmed by measuring intra-arterial pressure. White coat hypertension is diagnosed in persons with persistently elevated office blood pressures but normal daytime ambulatory blood pressures. Ambulatory blood pressure monitoring is recommended to confirm white coat hypertension in persons with office hypertension but no target organ damage [2]. Home recordings of blood pressure should also be obtained to avoid excessive blood pressure reduction in patients.

Before a patient is considered to have resistant hypertension, pseudo-resistant hypertension must be excluded [7]. White coatresistant hypertension which is an elevated office blood pressure greater than 140 mm Hg but a normal home blood pressure or 24 hour ambulatory blood pressure must be excluded [7,8]. Poor patient compliance, inadequate doses of antihypertensive drugs, inadequate choice of combinations of antihypertensive drugs, poor office blood pressure measurement technique, and having to pay for costs of drugs are factors associated with pseudo-resistant hypertension [7,9].

Factors contributing to resistant hypertension include obesity, excess dietary sodium, excess alcohol intake, use of cocaine, amphetamines, non-steroidal anti-inflammatory drugs, contraceptive hormones, adrenal steroid hormones, sympathomimetic drugs (nasal decongestants and diet pills), erythropoietin, licorice, herbal supplements such as ephedra, progressive renal insufficiency, and inadequate diuretic therapy [7]. Secondary causes of resistant hypertension include primary hyperaldosteronism, renal artery stenosis, renal parenchymal disease, obstructive sleep apnea, coarctation of the aorta, Cushing's syndrome, pheochromocytoma, hyperthyroidism, hypothyroidism, and intracranial tumors [7,10].

Using data from the National Health and Nutrition Examination Survey database from 2003 through 2008, it has been estimated that the prevalence of resistant hypertension was 8.9% of all United States adults with hypertension [11]. Of 614 patients with hypertension followed in a university cardiology or general medicine clinic, 40 patients (7%) were receiving 4 antihypertensive drugs, and 9 patients (1%) were receiving 5 antihypertensive drugs [9]. In 53,380 patients with hypertension and atherothrombotic disease in the International Reduction of Atherothrombosis for Continued Health (REACH) registry, the prevalence of resistant hypertension was 12.7% with 4.6% receiving 4 drugs and 1.9% receiving 5 or more drugs [12].

However, the best study on the incidence of resistant hypertension found that among 205, 750 patients with incident hypertension, 1.9% developed resistant hypertension within a median of 1.5 years from initial therapy [13].

Patients with resistant hypertension have an increased incidence of cardiovascular events [12,13]. Therefore, more effort is needed to improve clinical outcomes in these patients.

Some data support the use of spironolactone as a fourth drug in the treatment of resistant hypertension if the serum potassium level is $\leq 4.5 \text{ mmol/L}$ [7,14]. New drugs and device therapy with percutaneous transluminal radiofrequency sympathetic denervation of the renal arteries and carotid baroreflex activation are currently under investigation for treatment of resistant hypertension [15]. At 24 month follow-up after catheter-based renal sympathetic denervation of 153 patients with resistant hypertension, post procedure office blood pressure was 32/14 mm Hg lower without significant adverse events in the Symplicity HTN-1 study [16]. The European Society of Hypertension position paper summarizes current evidence, unmet needs, and practical recommendations on use of renal denervation to treat resistant hypertension in hypertension excellence centers [17].

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