



Resistant Hypertension

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Abstract

According to the American guideline, the office blood pressure of 130/80 mmHg and above in patients taking 3 or more antihypertensive drugs from different classes is uncontrolled resistant hypertension. In patients using 4 or more different classes of antihypertensive drugs, if the office blood pressure is below 130/80 mmHg, controlled resistant hypertension is mentioned. According to the European guideline, resistant hypertension is defined as an office blood pressure of at least 140 / 90mmHg despite the full or highest tolerable dose of at least 3 antihypertensive drugs containing diuretics. The etiology of resistance hypertension is multifactorial. Successful treatment requires identification and reversal of lifestyle factors and to exclude the presence of pseudo resistance. Secondary causes should be treated. Management of resistant hypertension includes maximization of lifestyle interventions, use of thiazide-like diuretics (chlorthalidone or indapamide), addition of a mineralocorticoid receptor antagonist (spironolactone or eplerenone), and, if blood pressure remains elevated, stepwise addition of a beta blocker (bisoprolol, metoprolol succinate), and, if blood pressure remains elevated, stepwise addition of a combined alpha-beta blocker (labetalol, carvedilol), and if blood pressure remains elevated, stepwise addition of antihypertensive drugs with complementary mechanisms of action to lower blood pressure. Device-based treatments are not recommended for routine treatment of hypertension.

Keywords: Resistant hypertension; Pseudo resistance, Secondary causes, Treatment

Introduction

Hypertension is the main risk factor for cardiovascular disease, stroke, and death. According to the American guideline, the office blood pressure of 130/80 mmHg and above in patients taking 3 or more antihypertensive drugs from different classes is uncontrolled resistant hypertension. In patients using 4 or more different classes of antihypertensive drugs, if the office blood pressure is below 130/80 mmHg, controlled resistant hypertension is mentioned [1]. According to the European guideline, resistant hypertension is defined as an office blood pressure of at least 140 / 90mmHg despite the full or highest tolerable dose of at least 3 antihypertensive drugs containing diuretics [2]. While the prevalence of resistant hypertension is 1-5% in all hypertensive, it is 11-15% in reference clinics. Resistant hypertension is one of the leading causes of morbidity and mortality related to cardiovascular diseases. That's why we wrote this mini-review called resistant hypertension.

Causes of Resistant Hypertension

Advanced age, obesity, black race, excessive dietary sodium intake, high basal blood pressure and chronic uncontrolled hypertension are among the demographic characteristics of patients with resistant hypertension. Risk factors contributing to resistant hypertension include obesity, physical inactivity, a high-sodium, excess alcohol intake, obstructive sleep apnea, use of cocaine, amphetamines, no steroidal anti-inflammatory drugs, oral contraceptive hormones, adrenal steroid hormones, sympathomimetic drugs, progressive renal insufficiency. Common causes of secondary hypertension include renal parenchymal disease, atherosclerotic renovascular disease, sleep apnoea, primary hyperaldosteronism, and drug induced hypertension or alcohol induced hypertension. Uncommon causes of secondary hypertension include pheochromocytoma, Cushing's syndrome, hypothyroidism, hyperthyroidism, aortic coarctation,

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primary hyperparathyroidism, acromegaly, fibro muscular dysplasia, and congenital adrenal hyperplasia [3-5].

Diagnosis

Causes of pseudoresistance include incorrect blood pressure measurement, uncompressed calcified in elderly patients atherosclerotic arteries (Pseudohypertension), non-compliance with antihypertensive treatment, suboptimal antihypertensive treatment, non-compliance with lifestyle changes, non-compliance with diet and white coat hypertension [1]. These causes should be excluded in order to make a correct diagnosis of resistant hypertension. In addition, 24-hour blood pressure monitoring should be done to exclude the white coat effect.

Secondary hypertension is one of the causes of resistant hypertension. Secondary hypertension should be suspected if there is new onset or uncontrolled hypertension in adults. There are certain clinical clues that suggest secondary hypertension. Sudden onset and progressive hypertension, papillary edema, oliguria, resistant hypertension, onset of hypertension over the age of 60, recurrent acute pulmonary edema attacks, faster than expected deterioration of renal functions with angiotensin converting enzyme or angiotensin receptor blocker, and systolodiastole in abdominal renal artery tracing on physical examination. In the presence of these symptoms and signs, secondary causes of hypertension should be investigated [6].

Management of Resistant Hypertension

Primarily, the white coat effect, secondary causes and drug incompatibility should be excluded. Lifestyle interventions such as low sodium diet (<2400 mg/d), >6 hours uninterrupted sleep, exercise, overall diet patterns, weight loss should be maximized. Adherence to 3 different classes of antihypertensive drugs ((renin angiotensin aldosterone system blocker, calcium channel blocker and diuretic) should be ensured at the maximum tolerated dose. If blood control is not achieved, an optimal dose of thiazide-like diuretic (chlorthalidone or indapamide) is started. If blood pressure control cannot be achieved despite this added treatment, a mineralocorticoid receptor antagonist (eplerenone 50-100mg/day, aldosterone 25-50 mg daily) is started. Spironolactone has taken its place in resistant hypertension with the PATHWAY study. This study showed that spironolactone showed more significant blood pressure reduction than with placebo, doxazosin, and bisoprolol. The PATHWAY-2 study also evaluated

bisoprolol or doxazosin modified release as alternatives to spironolactone [7]. If blood pressure control cannot be achieved, a beta blocker (metoprolol succinate, bisoprolol) can be added if the heart rate is >70. Again, if blood pressure control is not achieved, combined alpha-beta blocker drugs (labetalol, carvedilol) are started. If beta-blocker is contraindicated central alpha agonist medication (clonidine, guanfacine) is considered. If these drugs are contraindicated, diltiazem is started once a day. If blood pressure is still not controlled with the above-described measures, the addition of hydralazine (25 mg three times daily) should be considered and combined with nitrates (isosorbide mononitrate, 30 mg daily, max dose 90 mg daily) in cases of heart failure. Lastly, minoxidil (2.5 mg two-three times daily) may be tried if hydralazine fails. Several studies have investigated devices that reduce sympathetic nerve activity (carotid body stimulation and renal denervation); however, these studies have not provided sufficient evidence to recommend the use of these device in managing resistant hypertension [8].

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