RESISTANT HYPERTENSION

1*N. S. Neki, 2Gurpal Singh Sachdeva, 3Harshinder Kaur, 4Chandandeep

1Professor Medicine Govt. Medical College, Patiala, Punjab India.
2Assistant Professor Medicine Govt. Medical College, Patiala, Punjab India.
3Assistant Professor Pediatrics Govt. Medical College, Patiala, Punjab India.
4Junior Resident Medicine Govt. Medical College, Patiala, Punjab India.

ABSTRACT

Resistant Hypertension defined as failure of diastolic blood pressure to fall below 90 mm Hg despite the use of three or more drugs including a diuretic is a common clinical problem faced by both primary care clinicians and specialists. Poor compliance, suboptimal therapy, excessive dietary sodium intake, white coat hypertension must be ruled out before labelling as resistant hypertension. Apart from that certain factors like obesity, drug withdrawal, sleep apnea, chronic kidney disease, various genetic and secondary causes play a major role.

KEYWORD: Resistant hypertension; obesity; sleep apnoea.

INTRODUCTION AND PREVALENCE

Resistant hypertension is defined as blood pressure that remains above goal (>140/90) in spite of concurrent use of three antihypertensive agents of different classes, one of which should be a diuretic.[1] all agents should be prescribed at optimal dose. What constitutes an “optimal dose” of medication is presumably at least a moderate dose but not necessarily a maximum dose. Patients whose blood pressure is controlled with four or more medications are considered to have resistant hypertension. Based on trials during which participants were aggressively titrated to reach target BP, the prevalence of resistant hypertension has been estimated to be 20% to 30%. In absence of any large data from India the exact prevalence of resistant hypertension is unknown. The status of hypertension awareness, treatment and control status is very low in India especially in rural subjects.[2]
These patients are at increased risk for cardiovascular disease, stroke, diabetes mellitus, and renal dysfunction,\cite{3} and they are also more likely to experience target organ damage. An important consideration in making the diagnosis is to determine whether patients meet criteria for resistant hypertension or conversely if other reversible causes or pseudohypertension can be identified.

**Pseudoresistant hypertension**

Pseudoresistant” hypertension may be caused by a number of reversible factors, including inaccurate BP measurement, non-optimized medication regimen, poor adherence, drug-induced causes, lifestyle factors, and the white-coat effect. These are all important factors to consider before diagnosing resistant hypertension.\cite{1,3,4}

A possible cause of falsely elevated BP is poor BP measurement technique. If the patient is not allowed to rest or if an inappropriately small cuff is used, BP may be falsely elevated. Smoking can also contribute to elevations of systolic pressure from 5 to 20 mm Hg. Approximately 40\% of patients with newly diagnosed hypertension will discontinue their antihypertensive medication within the first year of use.\cite{5} Potential side effects, cost, and complex regimens are some possible causes of nonadherence. It is also imperative to address medications that may aggravate hypertension or antagonize the effects of treatment. This detailed medication history should include all prescription and over-the-counter (OTC) medications, all herbal supplements, illicit drugs, NSAIDS, anti depressants, oral contraceptives, steroids and a detailed diet history that includes alcohol intake.\cite{6} A diet excessive in salt can contribute directly to increased BP and also blunt the effect of certain antihypertensives. Patients with chronic kidney disease (CKD), African Americans, and the elderly may be more sensitive to the effect of dietary salt. Obesity is another lifestyle factor that should be evaluated in patients with resistant hypertension because obesity is related to an increased likelihood of hypertension, need for multiple antihypertensive medications, as well as the inability to control BP.\cite{7} Another concern prior to diagnosis of resistant hypertension is falsely elevated BP as a result of the white-coat effect (a persistently elevated clinic/office BP while out-of-office BP values are normal or significantly lower). This effect may be more common in patients with resistant hypertension and can be monitored through the use of out-of-office BP measurement (either home/self BP monitoring or ambulatory BP monitoring [ABPM]).\cite{8}
SECONDARY CAUSES

Once hypertension is confirmed as resistant, secondary causes of hypertension should be reconsidered.

Obstructive sleep apnea

Cross-sectional studies indicate that more severe the sleep apnea, less likely is BP controlled despite the use of an increasing number of medications. The mechanisms by which sleep apnea contributes to the development of hypertension have not been fully elucidated. A well-described effect is that the intermittent hypoxemia, and/or increased upper airway resistance associated with sleep apnea, induces a sustained increase in sympathetic activity. Sleep apnea has been associated with increases in reactive oxygen species.

Chronic kidney disease

Treatment resistance in patients with CKD is undoubtedly related in large part to increased sodium and fluid retention and consequential intravascular volume expansion.

Primary Aldosteronism

The diagnosis of PA may have been overlooked during the initial evaluation when the patient was first diagnosed with hypertension because many of these patients actually have normal potassium levels. He best initial test is a morning plasma aldosterone-to-renin ratio. A ratio below 20 (when plasma aldosterone is reported in ng/dL and plasma renin activity is in ng/mL/hr) effectively rules out PA. A ratio of ≥20 with a serum aldosterone >15 ng/dL suggests PA, but the diagnosis must be confirmed by a salt suppression test.

Renal artery stenosis

RAS should be suspected with early or late onset of hypertension (that is, before age 30 or after age 55); accelerated hypertension or a hypertensive emergency; disparate kidney size on imaging; sudden or “flash” pulmonary edema; unexplained renal insufficiency; multivessel coronary or severe peripheral vascular disease; and unexplained heart failure. Either magnetic resonance imaging (MRI) with gadolinium or computed tomography angiography can be used to visualize stenosis.

Pheochromocytoma

Pheochromocytoma represents a small but important fraction of secondary causes of resistant hypertension. The prevalence of pheochromocytoma is 0.1% to 0.6% of hypertensives in a
general ambulatory population. The diagnosis of pheochromocytoma should be entertained in a hypertensive patient with a combination of headaches, palpitations, and sweating, typically occurring in an episodic fashion, with a diagnostic specificity of 90%. The best screening test for pheochromocytoma is plasma free metanephrines (normetanephrine and metanephrine).

TREATMENT OPTIONS FOR RESISTANT HYPERTENSION

For patients with resistant hypertension, lifestyle modifications should be re-emphasized. Patients may not realize that the Dietary Approaches to Stop Hypertension or DASH diet, eating plan combined with low sodium intake can be as effective in lowering BP as a single antihypertensive medication. The importance of weight loss (for overweight patients) should be reiterated.

Daily intake of alcohol should be limited to no more than 2 drinks (1 ounce of ethanol) per day for most men and 1 drink per day for women or lighter-weight persons. Patients with resistant hypertension. Should be encouraged to exercise for a minimum of 30 minutes on most days of the week.

Treatment of secondary conditions like sleep apnea with continuous positive airway pressure (CPAP) likely improves BP control. Treatment of renal artery stenosis with Angioplasty of fibromuscular lesions almost always benefits, and is often curative, of the associated hypertension.

Intensification of pharmacologic therapy (depending on what agents the patient already is taking) include increase in dose of diuretic (or change HCTZ to chlorthalidone) or change to a loop diuretic for those with GFR <30 mL/min, adding a vasodilating β-blocker (eg, labetalol, carvedilol, nebivolol); a direct vasodilator (eg, hydralazine); or a centrally acting agent such as clonidine (transdermal or oral) or guanfacine. - If no contraindications, add spironolactone as first-choice (starting at 12.5 mg daily); eplerenone (starting at 25 mg daily), or amiloride (starting at 2.5 mg daily) are alternatives. Spironolactone can reduce systolic BP by as much as approximately 20 mm Hg in patients with hypertension that is resistant to ≥3 drugs.

FUTURE DIRECTIONS

In recent years there has been growing interest in nonpharmacologic interventions to treat resistant hypertension. Electrical stimulation of the carotid sinus baroreceptor has been shown
to decrease BP.[15] Catheter-based radio frequency renal denervation is another promising approach that currently is being studied.[16] Further studies are in progress.

REFERENCES