FREQUENCY OF RESISTANT HYPERTENSION IN A HYPERTENSIVE POPULATION

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ABSTRACT

Objective: To determine the frequency of resistant hypertension in hypertensive population.

Study Design: Descriptive study.

Place and Duration of Study: CMH Kohat, Pakistan from Aug 2010 to Dec 2010.

Methods: One hundred and fifty patients were selected for the study. All had blood pressure ≥ 140/90 mmHg despite use of 3 antihypertensive drugs including one diuretic. Once admitted, patients were given the same medicines in the doses which they were taking under DOT (direct observed therapy) programme executed by a nursing assistant to exclude non-compliance to treatment. All the data was analyzed using SPSS version 16.

Results: Out of total 150 patients, 96 (64%) patients were males and 54 (36%) were females. Male to female ratio was 1: 1.8. Mean age was 46.93 years (SD ± 16.38). Compliance of patients to anti hypertensive treatment was ensures by DOT. There was no step up treatment. Mean BMI was 25.95 kg/m^2 (SD ± 2.38), patients 71.3% were overweight i.e. BMI ≥ 25 kg/m^2. Out of total 150 patients, 16 (10.7%) patients had resistant hypertension using the cut off value of BP >140/ 90 mmHg.

Conclusion: A significant number of hypertensive patients are suffering from resistant hypertension. Such patients need further evaluation to rule out any genetic, secondary and life style/diet related cause.

Keywords: Adipose tissue, Peudo Resistance, Resistant hypertension.

INTRODUCTION

Hypertension is an overwhelming global challenge which ranks third as a cause of disability-adjusted life-years[1]. Even though the burden of hypertension is currently centered in economically developed countries (37.3%), developing countries will feel a greater impact due to their larger population proportion. Indeed estimates indicate that up to three-quarters of the world's hypertensive population will be in economically developing countries by the year 2025[1]. Pakistan is one of such countries where one in three individuals over the age of 45 years is hypertensive as revealed by the national health survey (NHS)[2-3]. The number of people with uncontrolled blood pressure is also increasing, despite the therapeutic advances[4]. A recent case control study has shown that non adherence to therapy is associated with an increased risk of stroke in patients with hypertension[5]. A study conducted at Shahina Jamil Hospital Abbottabad in 2007 concluded that 48.3% of hypertensive patients were compliant and 51.7% were not compliant to antihypertensive drugs[6]. Despite compliance some patients have resistant hypertension. Resistant, or refractory, hypertension is defined by a blood pressure of at least 140/90 mmHg despite adherence to treatment with full doses of at least three antihypertensive medications, including a diuretic[7] whereas uncontrolled hypertension is blood pressure more than 140/90 mmHg which is secondary to poor drug or dietary compliance although patient is taking full doses of at least three anti hypertensive medications including one diuretic. The term "pseudo-resistance" refers to lack of BP control with appropriate treatment in a patient who does not have resistant hypertension. Several factors contribute to elevated BP readings and produce the perception of resistant hypertension[8]. Such factors include suboptimal BP measurement technique, the white-coat effect, heavily calcified arteries in elderly, poor relation between doctor and patient, inadequate patient education, inadequate doses

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and poor adherence to prescribed therapy[8]. The incidence of resistant hypertension is estimated to be less than 5% of the hypertensive population[9-10]. A careful drug history should be taken that whether medications given to the patient for coexisting medical conditions are causing interference with antihypertensive treatment. Purpose of study was to determine the frequency of resistant hypertension in hypertensive population.

METHODOLOGY

This study was carried out at Combined Military Hospital Kohat from August 2010 to December 2010. We selected a total of 150 patients by consecutive sampling, admitted to medical wards. All of these patients were having blood pressure > 140/90 mmHg. Patients were included in the study if they were known patients of primary hypertension, with duration of hypertension more than 1 year, age >15 and <80 years, both genders and patients taking 3 antihypertensive drugs including 1 diuretic. Exclusion criteria included; individuals with diabetes, ischemic heart disease, chronic kidney disease, valvular heart disease, cardiomyopathy, endocrinopathies and other cases of secondary hypertension: Individuals taking NSAIDs, anabolic steroids, herbal medicines; individuals with dementia and psychiatric illness and individuals on renal replacement therapy.

Each patient was asked to sit quietly in a chair with his or her back supported for 5 minutes in a private room before taking the blood pressure measurement. Use of the correct cuff size with the air bladder encircling at least 80% of the arm was ensured. Center of cuff was placed at heart level. Width of cuff was kept equal to at least 40% of arm circumference. Rate of deflation was fixed at 2 mmHg/sec. Systolic BP was measured at first of two regular Korotkoff sounds. Diastolic blood pressure was the point at which the last regular Korotkoff sound is heard. Once admitted patients were asked to produce old prescription of their anti hypertensive medication. DOT (direct observed therapy) was started in the ward in order to minimize pseudo resistance secondary to poor drug compliance. Initially patients were given the same medicines with same doses which they were taking at home and blood pressure was recorded 8 hourly. Mean of three readings was recorded on the proforma daily. Doses were adjusted according to response later on. Subsequently the patients with controlled blood pressure were discharged. The group of patients who remained unresponsive to modified treatment, whose blood pressure was not controlled by at least 03 medicines including a diuretic at their maximum doses during their stay in hospital for 07 days and DOT, were considered to be suffering from resistant hypertension. Data was processed on SPSS version 16. Variables included in study were age, gender, BP recording and BMI. Continuous variables were derived as means and standard deviation while categorical variables were described in percentages/frequencies.

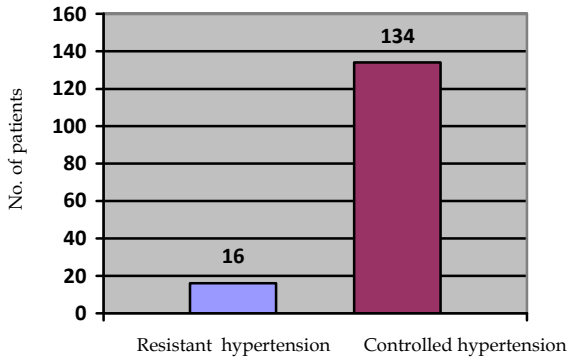

Figure-1: Resistant and controlled hypertension (n=150).

RESULTS

Out of total 150 patients, 96 (64%) patients were males and 54 (36%) were females. Male to female ratio was 1:1.8. The age distribution ranged from 17 – 79 years. Mean age was 46.93 years (SD ± 9.38). BMI of subjects ranged from 18 – 31 kg/m^2. Mean BMI was 25.95 kg/m^2 (SD ± 2.38). Out of total 150 patients, 16 (10.7%) patients had resistant hypertension and 134 (89.3%) had controlled hypertension (Fig-1). Percentage of resistant hypertension was high in females than

in males i.e. 18.5% in females and 6.25% in males (Table-1).

Table-1: Demographic characteristics of study group (n=150).

Demographics	Resistant hypertension	Controlled hypertension	*p*-value
Age (years) mean [SD]	48.62 (±8.84)	45.43 (±9.38)	0.195
Males, n (%)	6 (37.5%)	77 (57%)	0.11
Females. n (%)	10 (62.5%)	57 (43%)	0.0217
BMI (kg/m^2) mean [SD]	27.43 (±2.06)	24.62 (± 3.29)	0.003
Resistant hypertension, n (%)	16 (10.7%)	134 (89.3%)	0.042

DISCUSSION

Resistant hypertension is blood pressure of at least 140/90 mmHg despite adherence to treatment with full doses of at least three antihypertensive medications, including a diuretic. The prevalence of resistant hypertension is increasing because of aging population, increased tendency towards obesity secondary to dietary habits, sleep apnea, and increased prevalence of chronic kidney disease. It is important to rule out pseudo resistance before considering diagnosis of resistant hypertension. A careful drug history should be taken that whether medications given to the patient for coexisting medical conditions are causing interference with antihypertensive treatment. In the elderly, the agents which most commonly cause this are non-steroidal anti-inflammatory drugs (NSAIDs),[11] but sympathomimetics, some immunosuppressants (tacrilimus, cyclosporine)[11], and steroid hormones may also be responsible. White coat hypertension which is present in 20 to 30%[13] cases of mild hypertension can be minimized if blood pressure is measured by a nursing assistant rather than a physician himself. Resistant hypertension is different from uncontrolled hypertension. The later includes patients who lack blood pressure control secondary to poor adherence and/or an inadequate treatment regimen.

Results of study revealed that the overall frequency of resistant hypertension among hypertensive population was 10.7% (16 out of the 150 subjects) which is quite substantial. Interpretations of the results show that a significant number of hypertensive patients are suffering from resistant hypertension. Their BP remains uncontrolled despite three antihypertensive drugs including one diuretic at their maximum doses. Increasing age, female sex and obesity are important risk factors. Such patients need further evaluation to rule out any genetic, secondary and life style/diet related cause. Although only patients of primary HTN were included in study while individuals with diabetes, ischemic heart disease, chronic kidney disease, valvular heart disease, cardiomyopathy and endocrinopathies were excluded, certain genetic causes could not be ruled out for example "Liddle's syndrome". The investigators in Finland screened 347 patients with resistant hypertension for mutations of the β and subunits of the epithelial sodium channel (ENaC) compared with normotensive controls, 2 β ENaC and ENaC gene variants were significantly more prevalent in the patients with resistant hypertension[14]. Similarly glucocorticoid-remediable aldosteronism (GRA) is familial and usually associated with bilateral adrenal hyperplasia and a mild or no hypokalemia. It is a disease of the young usually < 22 years and cannot be ruled out on history and examination. Certain diseases for which patients were themselves unaware and undiagnosed like obstructive sleep apnea (OSA) and metabolic syndrome could be the cause of resistant hypertension. Sleep apnea is particularly common in patients with resistant hypertension[15]. Cause is not well understood but it is postulated that intermittent hypoxia and airway obstruction increase sympathetic flow in body[16]. Our study only included those hypertensive patients who were already on three anti hypertensive drugs

but still having high BP. Thus frequency of resistant hypertension was comparatively higher than previously estimated by other studies[9]. Further research is required for identification of causes contributing to treatment resistance, including secondary causes of hypertension; and documentation of target-organ damage. Young patients should be offered genetic testing to identify Liddle's syndrome and other rare genetic forms of hypertension. All cases of resistant hypertension should be encouraged to lose weight to attain and maintain BMI < 25 kg/m^2 and increase physical activity and adopt dietary approaches to stop hypertension DASH dietary plan. All cases of resistant hypertension should undergo a battery of biochemical tests including urine routine examination, real function texts, and albumin. Aldosterone/renin ratio is an effective screening test for primary aldosteronism, having a high negative predictive value[17]. A ratio > 30 is highly suggestive of primary aldosteronism. Cortisol and dexamethasone suppression test is advised if Cushing syndrome is suspected. Serum calcium level, TSH level, a 24-hour urine collected during ingestion of the patient's normal diet can be helpful in estimating dietary sodium and potassium intake, calculating creatinine clearance, and measuring aldosterone excretion. Measurement of 24-hour urinary metanephrines or plasma metanephrines is an effective screening test for patients in whom pheochromocytoma is suspected[18] and plasma glucose fasting and lipid profile for all patients. The mineralocorticoid receptor antagonists provide appropriate antihypertensive benefit when added to existing multidrug regimens in resistant hypertensive cases. In a study involving 76 patients referred to a hypertension clinic for poorly controlled hypertension, spironolactone (12.5 to 50 mg daily) lowered blood pressure on average by an additional 25 mmHg systolic and 12 mmHg diastolic[19].

CONCLUSION

A significant number (10.7%) of hypertensive patients were suffering from resistant hypertension. Their blood pressure remained uncontrolled despite three anti-hypertensive drugs including one diuretic at their maximum doses. Such patients need further evaluation to rule out any genetic, secondary and life style/diet related cause.

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