A STUDY OF HYPERINSULINAEMIA AND DYSLIPIDAEMIA IN HYPERTENSIVE PATIENTS OF ARMED FORCES

Brig AS KASTHURI*, SREEJITH KUMAR⁺,
Dr BL SOMANI[#], Lt Col SK SHARMA^{**}

Abstract

All patients attending the outpatient department were screened for hypertension. An attempt was made to correlate presence of hyperinsulinaemia (HI), dyslipidaemia and anthropometric characteristics in these hypertensives. Effect of angiotensin converting enzyme inhibitor (ACEI) and beta blockers on serum insulin was also studied. 85 patients with blood pressure (BP) $\geq 160/90$ mm Hg and 94 controls with a BP of $< 130/85$ mm Hg were studied. All underwent clinical examination, anthropometric measurements (body mass index (BMI), waist hip ratio (WHR), skin fold thickness (SFT) and laboratory investigation (serum insulin, glucose, lipid profile) and post oral glucose load (POGL) for insulin and glucose. Serum insulin was estimated by I^{125} radio immuno assay. Patients were randomly divided into group A (Tab enalapril) and group B (Tab atenolol). In 51 patients who completed the study, fasting and POGL insulin and fasting lipid profile were estimated two months after treatment. Mean age of cases was 38.91 years. 50% of patients had stage II hypertension. BMI was increased in 36 cases (42.35%) as compared to 9 in (9.57%) controls. Increased WHR was found in 40 cases as compared to 26 in controls. The SFT was more in cases compared to controls. 47 (55.29%) of 85 cases had abnormal lipid profile as compared to 25 (26.60%) in 94 controls. The fasting and POGL insulin levels (13.85 and 60.05 micro u/ml respectively) in cases were significantly higher than in controls (6.87 and 16.16 micro u/ml respectively). The mean POGL insulin values were much higher in obese compared to non-obese hypertensives. The decrease in mean fasting and POGL insulin values in patients taking ACEI and beta blockers were similar. Abnormal lipid profile was significantly more in cases than controls. Increased total cholesterol (TC), Low density lipoprotein cholesterol (LDLC) and total cholesterol (TC)/high density lipoprotein (HDL) ratio were the most frequent abnormality. The mean insulin (both fasting and POGL) levels were higher in obese hypertensives and those with abnormal lipid profile. Both drugs had equal efficacy in reducing the insulin values.

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KEY WORDS : Angiotensin converting enzyme inhibitor ; Beta-blockers; Body mass index; Hyperinsulinaemia.

Introduction

There is a significant increase in prevalence of hypertension (HT) (BP $\geq 140/90$ mm Hg) in both urban (30%) and rural (21.19%) population in India [1]. More than 90% have essential (Primary) HT. Other associated risk factors identified for coronary heart disease (CAD) are HI, dyslipidemia and obesity [2]. HI reflects the presence of insulin resistance and is associated with other risk factors like obesity and dyslipidemia. HI is causally linked to rise in systolic as well as diastolic BP by a variety of mechanisms. Thus, recent evidence calls for the detection of HI in patients of HT [3]. Identification of dyslipidaemia and its association with hyperinsulinaemia in patients of hypertension has also assumed importance. Detection of obesity includes estimation of BMI and WHR. Thus estimation of anthropometric measurements and its correlation with obesity, insulin resistance and hypertension in Indian subjects needs to be studied further [4]. Beta-blockers have well known adverse effects on glucose and lipid metabolism whereas ACEI do not have any adverse effects. The

role of these two drugs in affecting hyperinsulinaemia in patients with HT merits consideration.

It is in this background that this study was undertaken :

(a) To determine the prevalence of hyperinsulinaemia and dyslipidaemia in hypertensive patients.

(b) To correlate the presence of hyperinsulinaemia with dyslipidaemia, anthropometric characteristics (body weight, BMI, generalized or upper body obesity), dietary habits, smoking and alcohol consumption in hypertensives.

(c) To study the effect of beta-blockers (atenolol) or ACEI (enalapril) therapy on serum insulin levels in hypertensives.

Material & Methods

All patients who reported to the medical out patient department (OPD) for various ailments were screened. Asymptomatic individuals in neighbouring units were also screened to detect hypertension. Measurement of BP was done as per Joint National Committee Vth report. Hypertension was defined as systolic blood pressure (SBP) of ≥ 140 mm Hg and / or diastolic blood pressure (DBP) of ≥ 90 mm Hg [5]. The present consensus advocates non

*Commandant, 158 Base Hospital, C/o 99 APO, ⁺Postgraduate student, [#]Scientist F, Department of Biochemistry, Armed Forces Medical College, Pune - 411 040., ^{**}Classified Specialist (Medicine), Military Hospital, Jodhpur.

pharmacological measures for treatment of HT in patients with BP < 160/90 mmHg. Drug treatment is recommended for those with BP $\geq$ 160/90 mmHg. Our study involves effects of drug therapy on insulin levels, hence only those patients whose BP was $\geq$ 160/90 mmHg were included in this study.

The following groups of patients were excluded from the study; known cases of HT, secondary HT, diabetes mellitus and coronary heart disease. After exclusion, 85 patients were included in the study. 94 age and sex (88 males, 6 females) matched normotensive (BP < 130/85 mmHg) individuals were included as controls. The patients were subjected to a detailed clinical and laboratory evaluation. Physical examination included the following :-

(a) Anthropometric measurements [6]:

i) Height

ii) Weight

iii) BMI : Body mass index was calculated using the formula: Weight in kilogram / (height in meter)²

iv) Chest, waist and hip measurement

(aa) Waist to hip ratio = waist in cm/hip in cm.

(bb) Waist to chest ratio = waist in cm/chest in cm.

v) Skin fold thickness : The skin fold thickness was measured at four (triceps, subscapular, biceps and supra-iliac regions) different places in the body using GPM skinfold caliper.

(b) Laboratory tests : Fasting blood sample was collected in the morning after an overnight fast for fourteen hours for estimation of insulin (radio immuno assay), glucose (glucose oxidase peroxidase method) and for urea, creatinine, uric acid, electrolytes, lipid profile and liver function tests. Then the patient was given 75 gm glucose orally and post oral glucose load (POGL) blood sample was collected after two hours. The POGL sample was used for estimation of glucose and insulin. The serum samples for estimation of insulin and triglyceride were stored at -30°C. Insulin assay was done using COAT-A-COUNT kit of Diagnostic Products Corporation, USA, which is a solid phase I¹²⁵ radio immuno assay for estimation of insulin in serum.

(c) Estimation of lipid profile : (as per AUTOPAK by Bayer Diagnostics, Baroda). Estimation of total cholesterol was done by enzymatic method. HDLP estimation was done by the phospho tungstate method. Triglycerides were estimated by enzymatic 3,5-dichloro 2-hydroxy benzene sulfonic acid (DHBS) calorimetric method. LDL-C was calculated using the formula LDL = TC-HDL-(TG/5).

Randomization and follow up : All patients were advised non-pharmacological measures for decreasing BP as per recommenda-

tions of JNC V [5]. On simple random allocation all patients were randomized into two groups (A and B). Tablet enalapril at a dose of 5-mg daily to Group A and tablet atenolol at a dose of 25 mg daily to Group B was given. Patients were reviewed every two weeks for adjustment of drug dose for control of BP and at the end of two months BP was recorded. The post treatment fasting and POGL insulin levels and the fasting lipid profile were estimated. Out of 85 cases 51 qualified for the follow up study. All the observations and findings were tabulated in individual tables and statistical analyses was carried out. These statistical procedures included the calculation of Odds ratio; Chi square test for contingency tables and analysis of variance for the difference between means [7,8].

Results

For statistical purposes the study groups were divided into three age categories as under : Category A age < 40 years (Male 41, Female 2), Category B age 40-59 years (Male 26, Female 9), Category C age $\geq$ 60 years (Male 6 Female 1). Most of the 43 (50.59%) cases and 66 (70.21%) controls belonged to the age category of < 40 years. Mean age of cases was 38.91 years and controls 42.5 years. The staging of hypertension was done as per JNC VI [9]: 21 (24.71%) patients were in stage I, 50 (58.82%) patients in stage II and 14 (16.47%) patients in stage III hypertension.

Majority of our patients (60%) were asymptomatic. The common symptoms in the rest of the patients were headache, giddiness, palpitation, chest pain and edema. Majority (82.4%) of our cases were non-vegetarian. Common addictions noticed were consumption of alcohol and smoking. 27 of our cases had no addictions. Values of mean SBP and DBP were not significantly higher in those having addictions.

It was observed that 24 (28.2%) out of 85 cases had family history of HT as against only 4 (4.25%) out of 94 controls, which was significant ($p < 0.001$). The risk for a person with family history of HT to develop HT was 8.85 times greater than a person without family history of HT (Odds ratio 8:85).

BMI was increased (> 25) in 36 (42.35%) cases as compared to only 9 (9.57%) in controls and this was highly significant ($p < 0.001$). The mean BMI also was significantly higher in the cases (24.54 ± 3.91) as compared to controls (22.40 ± 2.23). Increased WHR (> 0.95 in males and > 0.85 in females) was found in 40 (47.06%) of 85 cases as compared to 26 (27.66%) of 94 controls. The mean SBP in those with increased WHR was 158.20 ± 13.33 and DBP 99.7 ± 9.76 mmHg. This was significant ($p < 0.01$). It was seen that increased WHR was more in those with increased BMI than those with normal BMI. The SFT is more in cases compared to controls (Table 1). The difference in mean triceps and triceps + subscapular SFT in cases (both sexes / males

TABLE 1
Mean skin fold thickness

SFT	Cases (SD)			Controls (SD)		
	Males	Females	Both	Males	Females	Both
Triceps	11.21 (4.21)	18.7 (5.25)	12.27	7.6 (4.59)	15.6 (1.50)	8.17
Subscapular	20.5 (6.94)	24.5 (8.21)	21.08	18.8 (9.70)	20.5 (2.80)	18.97
Total	31.73 (10.67)	43.25 (12.97)	33.36	26.53 (13.41)	36.16 (2.22)	27.14

TABLE 2

Lipid profile (cases vs controls)

Status	TC (mg/dl)	LDL-C (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	TC/HDL		Abnormal LP
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	L < 4.5	H > 4.5	No (%)
Cases	179.2 (38.64)	112.3 (31.51)	123.4 (74.45)	42.20 (12.14)	45	40	47 (55.29)
Controls	148.7 (23.24)	84.79 (20.36)	110.8 (52.50)	41.80 (8.55)	80	14	25 (26.60)

alone) was significant ($p < 0.01$). The difference in SFT between female cases and controls was not significant. Increased BMI and WHR also significantly correlate with increased SFT.

The relation between stage of hypertension and lipid profile was studied. The mean levels of cholesterol and lipoproteins as well as the number of abnormal lipid profile did not show any correlation with the stage of HT. Percentage of abnormal lipid profile in cases and controls is given in Table - 2. 47 (55.29%) of 85 cases had abnormal lipid profile as compared to 25 (26.60%) of 94 controls. The relation was significant ($p < 0.001$). The mean total cholesterol (179.2 ± 38.64 mg/dl), LDL cholesterol (112.3 ± 31.51 mg/dl) and triglyceride levels (123.4 ± 74.45 mg/dl) were significantly higher in the cases ($p < 0.001$). The number of cases with increased total cholesterol (TC) and LDL were also significantly ($p < 0.001$) higher than controls. The percentage of cases with increased TG and decreased HDL were also more compared to controls.

The mean insulin levels of cases and controls are given in Fig. 1. The fasting and POGL insulin levels are significantly higher in the cases (13.85 ± 10.41 and 60.05 ± 94.78 respectively) compared to controls (6.87 ± 3.88 and 16.16 ± 18.41 respectively) ($p < 0.001$). This was true for all age groups. The mean fasting insulin values did not show much variation between obese (13.86 ± 8.34) and non-obese (11.39 ± 11.71) patients. However the mean POGL insulin values were much higher (74.00 ± 127.85) in obese compared to non-obese (42.94 ± 51.79) hypertensives (Table-3). The fasting and POGL mean insulin levels in cases (13.19 ± 8.04 and 59.06 ± 8.04 respectively) with abnormal lipid profile were higher than with controls (7.72 and 21.71 respectively) with abnormal profile.

The effect of drug therapy with ACEI and beta-blockers on insulin levels are shown in Table - 4. The mean fasting and POGL insulin values decreased with treatment in both groups. In view of the short duration of therapy and the dose employed no comments

TABLE 3

Obesity vs insulin

Status		Insulin	
		F (SD)	POGL (SD)
BMI	Normal n=49	11.39 (11.71)	42.94 (51.79)
	Increased n=36	13.86 (08.34)	74.00 (127.85)
WHR	Normal n=45	12.53 (12.02)	39.32 (51.42)
	Increased n=40	12.95 (08.38)	74.98 (121.70)

Fig. 1 : Mean insulin levels (micro u/ml) cases vs controls

can be offered.

Discussion

Hypertension has emerged as a major health problem worldwide. Various risk factors have been identified which either contribute to development of hyper-

TABLE 4

Insulin levels (Micro U/ML) with treatment

	Before Treatment		Follow up group			
	Fasting (SD) n	POGL (SD)	Before Treatment Fasting n	POGL	After Treatment Fasting	POGL
ACEI	48		27			
	14.78 (12.73)	55.41 (111.30)	13.84 (10.31)	69.06 (144.53)	10.91 (8.44) p .14	51.57 (66.01) p .83
β-Blockers	37		24			
	10.05 (05.29)	57.00 (62.06)	10.50 (04.80)	62.48 (66.21)	9.10 (5.13) p .62	39.06 (40.15) p .57

tension or increase the cumulative cardiovascular risk. The presence of hyperinsulinaemia, dyslipidaemia and central obesity in hypertensives had been recognized by many as an important risk factor. The data on Indian subjects is however scanty [10,11]. In this study, we have attempted to identify the association of various risk factors with hypertension, with special emphasis on anthropometry, hyperinsulinaemia and dyslipidaemia. The effects of two anti hypertensive drugs on the metabolic parameters were also studied.

Blood pressure is known to increase with age. Majority of the cases were in stage II hypertension. The delay in detection may be due to the asymptomatic nature of the illness. Only 40% of cases had symptoms like giddiness, headache, palpitation and chest pain. The study did not include symptom correlation and hence this was not studied further. Obesity is closely correlated with increased BP ($p < 0.001$). Overweight leads to 2-6 fold increase in risk of developing HT. The proportion of HT attributable to obesity is 30-65% in western population. Truncal obesity has been positively correlated with increased BP in most populations, including Indians [9,12]. Present study has confirmed this finding. Increased BMI (≥ 25) and increased WHR were significantly ($p < 0.01$) more in cases than controls. Increased WHR positively correlates with SBP, DBP and the incidence of HT [12,13]. This study correlates with the above observations in that, SBP (158.2 ± 13.33) was significantly higher ($p < 0.01$) in those with increased WHR. The mean DBP also was more in this group. In our study mean SFT was significantly ($p < 0.001$) higher in cases. The increase in SFT was found to be very significant in males but not in females. Mean SFT was significantly more ($p < 0.001$) in those with increased BMI and increased WHR.

Dyslipidaemia frequently co-exists with hypertension. 40% of hypertensives are reported to have abnormal lipid profile (cholesterol ≥ 240 mg/dl). 50% cases had abnormal LP (cholesterol 179.2 ± 38.64 , triglyceride 123.4 ± 74.45), compared to 26% control, which was highly significant ($p < 0.001$). The number of cases with increased total cholesterol and LDL were also significantly ($p < 0.001$) higher than controls. Our results agree with previous studies in Indian population where elevated TC/HDL was seen in 15-47% hypertensives.

Hyperinsulinaemia represents a state of insulin resistance. The normal fasting value for insulin is 6-26 μ u/ml. The normal value for POGL insulin has not been defined. For comparative analysis the average value of insulin in different groups (hypertensive vs.

non-hypertensive) have been compared [11]. Hypertension is known to be associated with hyperinsulinaemia. The study shows the existence of hyperinsulinaemia in hypertensive patients. The mean insulin values were significantly ($p < 0.001$) more in cases than controls. The fasting values in non-obese and obese hypertensives did not show any significant difference. However, the POGL insulin values in obese hypertensives (74.98 μ u/ml) were much higher than in non-obese (39.32 μ u/ml) hypertensives.

Beta-blockers reduce insulin sensitivity. ACEI on the other hand has no adverse effect on insulin sensitivity; however, marginal improvement in insulin sensitivity has been reported [13]. The study compared the effect of both these groups of drugs on insulin levels after treatment for two months. The mean fasting and POGL insulin values decreased in both the groups. No comments can be offered in view of the short duration of study and the different doses employed.

Most of the hypertensives were young and had stage II hypertension. Obesity (increased BMI, increased WHR) was identified as a significant risk factor for developing hypertension. WHR correlated better with hypertension. Mean SFT was significantly more in cases. Abnormal lipid profile was significantly more in cases than controls. Increased TC/HDL ratio, increased TC and increased LDL were the most frequent abnormalities noted. The fasting and POGL insulin levels were found to be significantly higher in cases than controls. POGL values of insulin was higher in obese than non-obese hypertensives. Obesity amplified the effect of hypertension on POGL insulin levels. The fasting and POGL insulin level showed a definite decrease with treatment in both ACEI and beta blocker groups. Mean insulin (both fasting and POGL) levels were higher in obese hypertensives and those with abnormal lipid profiles as compared to those with normal values.

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