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MULTICENTER STUDY ON INFLUENCE OF TELMISARTAN IN HYPERTENSIVE PATIENTS WITH PRE-DIABETES

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ABSTRACT

An angiotensin II receptor blocker, telmisartan, has a higher affinity for AT_1 receptors and it's recognized as partial agonist of the nuclear hormone receptor PPAR-gamma. The present study was conducted to study the influence of telmisartan in hypertensive patients with pre-diabetes. It is a prospective and randomised study done on 150 hypertensive patients with impaired fasting glycaemia. All the patients underwent following investigations like Fasting plasma glucose, blood pressure and body mass index were also measured. Fasting plasma glucose, blood pressure (Systolic and Diastolic) showed significant decrease after intake of 40 mg Telmisartan for three months. Changes in BMI are not significant. It concludes that the telmisartan is effective in controlling blood-pressure by its AT_1 receptor blocking activity. It is also effective in decreasing fasting blood glucose by its insulin sensitizing activity through partial peroxisome proliferator activated receptor (PPAR) gamma activity.

Keywords: Telmisartan, Hypertensive, Pre-diabetes, PPAR gamma activity.

INTRODUCTION

Burden is rise of non-communicable diseases (NCDs), which is causing increasing morbidity and premature mortality in developing countries. In 1990, cardiovascular diseases (CVD) accounted for 63 per cent of all deaths and India contributed to 17 per cent to the worldwide mortality[1]. Hypertension is one of the leading causes of morbidity and mortality worldwide [2]. The concomitant occurrence of type 2 diabetes mellitus leads to a further significant increase in this risk[3] and reported also that the patients with hypertension have an increased prevalence of type 2 diabetes mellitus or pre-diabetes [4].

Clustering together hypertension, obesity, and diabetes or impaired glucose regulation (impaired fasting glycaemia and impaired glucose tolerance) is recognized as metabolic syndrome[5]. The increasing availability and abundance of high-calorie, low-fiber foods and the adoption of more sedentary lifestyles are all leading to increased prevalence of the metabolic syndrome in developing countries[6]. Not only hypertensive patients with diabetes, but also hypertensive patients without overt diabetes tend to be resistant to insulin stimulated glucose uptake compared with normotensive people [7]. It has been reported that about 20% of patients with hypertension having impaired fasting glycaemia will develop type 2 diabetes in a period of 3 years. Insulin resistance as predicted by impaired fasting glycaemia is also associated with endothelial dysfunction, which is predictive of future cardiovascular events [8, 9].

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Few classes of anti-hypertensives, particularly angiotensin II receptor blockers (ARBs), have been shown to reduce the incidence of new onset diabetes. These antihypertensive agents have differential effects in hypertensive patients with impaired fasting glycaemia. Numerous recent trials involving patients with hypertension have suggested that telmisartan, unlike other ARBs, acts as a partial peroxisome proliferator-activated receptor-gamma (PPARγ) agonist at concentrations that are achievable with oral doses [10-12]. So, it is recommended for the treatment of hypertension with impaired fasting glycaemia, thus suggesting its insulin- sensitizing effect. Therefore, the present study on influence of telmisartan on blood pressure and blood sugar levels in hypertensive patients with impaired fasting glycemia.

METHODOLOGY

Objective of this prospective study, was to observe the effect of 40 mg once daily dose of telmisartan on blood pressure and blood sugar levels in hypertensive patients with pre-diabetes. To carry out the study, required permission was obtained from the centers, viz: (1). KIMS & Research Centre, Bengaluru; (2). Divisional Railway Hospital, Bengaluru, and (3). Bangalore Baptist Hospital, Bengaluru.

Consent was obtained from all the patients. Patients of either sex, aged 25-55 years, who were newly diagnosed mild to moderate essential hypertension (stage-1 JNC-7) with impaired fasting glycemia, attending medical OPD in the respective hospitals were included in this study, after satisfying inclusion and exclusion criteria.

Study was conducted in 150 patients over a period of 6 months; each patient was being followed for 6 months. History, physical examination, clinical findings, vital data recordings and relevant laboratory investigation findings of the studied patients were recorded. Periodic recording of blood pressure was done every two weeks. Periodic fasting blood sugar levels were recorded every month.

BMI was measured at the beginning and end of the study. Laboratory investigations were carried out before initiation of therapy and at the end of the study. Blood pressure was measured in the non-dominant hand, in sitting posture after 5 minutes rest with arm supported at heart level. Sugar levels were measured after 8 hours of overnight fasting.

Inclusion criteria

Age: 25 to 55 years; Sex: both sexes; newly diagnosed essential hypertension (Stage-1 JNC-7) with impaired fasting-glycaemia who was willing to give the consent and normal liver and renal function tests.

Exclusion criteria

Severe hypertension; Secondary hypertension; Patients already on other antihypertensive therapy; Overt diabetes mellitus patients; severe obesity (>35 kg/ m^2); chronic use of NSAIDS, Corticosteroids and Oral contraceptives pills; any acute illness; thyroid disease; Pregnancy and lactation.

Investigations done

Hemoglobin; Total and differential WBC count; Fasting blood sugar; Blood urea; Serum bilirubin; Serum creatinine; Complete urine examination-urine albumin and sugar and microscopic examination; Microalbuminuria tested with strip method with early morning sample of urine.

Body mass Index (BMI) calculated with formula, BMI=Weight in Kg / Height in square meters. All patients were given 40 mg telmisartan once daily early in the morning to be taken on empty stomach. All the patients were advised on increasing physical activity, increase in the intake of low salt and high fibre diet. Statistical analysis method employed for analysis of data is paired‘t’ test used for testing the statistical significance. p value <0.01 is taken as statically significant.

RESULTS

Details of the patients

162 patients were enrolled in the study. 12 of them developed diabetes during the study period, hence, they were excluded from the study and 150 patients completed the study period. Out of these 75 patients 54% (n=81) were males and 46% (n=69) were females. Out of 150 patients, 68% (n=102) patients are age group of 45-55yrs, 24% (n=36) of patients were 35-45 years, and 8% (n=12) belonged to 25-35 years of age. Maximum number of patients belonged to 45-55 years.

Systolic BP

153.60±7.49 (Mean±SD) mmHg was at the initiation of study. At the end of 6 months (completion of study), 131.6±8.65 (Mean±SD) mmHg was reported (p <0.001, highly significant).

Diastolic BP

At the initiation of study was 91.40±6.70 (Mean±SD) mmHg. At the end of 6 months (completion of study) was 80.0±4.94 (Mean±SD) mm of Hg (p <0.001, highly significant).

Fasting plasma glucose (FPG)

At the initiation of study was 118.56±3.79 (Mean±SD). At the end of 6 months (completion of study) FPG was 115.04±4.43 (Mean±SD) mg/dl (p <0.001, highly significant).

Body mass index (BMI)

At the initiation of study mean BMI was 29.24±4.34 (Mean±SD) Kg/m^2. At the end of 6 months

(completion of study) was 29.05±4.30 (Mean±SD) Kg/m^2. There is statistically very high significant change ($p<0.001$) found in the levels of both blood pressure and fasting plasma glucose levels in the patients. The difference in the levels of mean BMI before and after the study period is not statistically significant (p value 0.16).

Adverse effects

One patient who developed dry cough was treated with anti-tussives and continued in the study. One patient developed mild rash and was treated with anti-histamines and continued in the study.

Table 1. Patient's Demographics

Patient Particulars	No. of patients (n=150)
Gender Distribution	
Males	81 (54%)
Females	69 (46%)
Age Distribution	
25-35 years	12 (8%)
35-45 years	36 (24%)
45-55 years	102 (68%)
Body Mass index	
18.5-25 Kg/m^2 (Normal)	45 (30%)
25-30 Kg/m^2 (Overweight)	60 (40%)
30-35 Kg/m^2 (Obese)	45 (30%)

Out of these 150 patients 45 patients had BMI between 18.5-25 Kg/m^2 (normal), 60 patients had BMI between 25-30 Kg/m^2 (overweight), 45 had BMI between 30-35 Kg/m^2 (obese class I).

Table 2. Details of investigations done

Particulars of investigations	Before treatment(Mean ± SD)	After treatment (Mean ± SD)
Blood Pressure (mmHg)		
Systolic BP	153.60±7.49	131.60±8.65
Diastolic BP	91.40±6.70	80.0±4.94
Fasting Blood Glucose (mg/dl)	118.56±3.79	115.04±4.43
Body Mass Index (Kg/M^2)	29.24±4.34	29.05±4.30

DISCUSSION

Results suggested that telmisartan 40mg once daily was effective in reducing blood pressure and fasting plasma glucose levels from the base line, in patients with hypertension with pre-diabetes. The results are highly statistically significant ($p <0.001$) in the reduction of both blood pressure and fasting plasma glucose levels in the patients.

Decrease in blood pressure and fasting glycemia are consistent with the results of Cristiana et al. Metabolic effect of telmisartan and losartan in hypertensive patients with metabolic syndrome concludes that besides providing superior 24-hour blood pressure control, telmisartan unlike losartan displays insulin sensitizing activity, which may be explained by its partial PPAR gamma activity[6].

Masaki *et al* found the effect of telmisartan on insulin resistance in Japanese type 2 diabetes mellitus in which it was concluded that blood pressure levels and fasting plasma glucose levels, reduced significantly following treatment with telmisartan[13]. According to Thomas Unger, preclinical effect of RAS inhibition with a focus on telmisartan, that telmisartan is the only ARB that may modulate PPARγ activation at physiological concentration, as an effect that is likely tobe related to telmisartan high lipophilicity and long plasma half-life among all ARBs[14].

Results can also be reinforced with Bahr IN *et al*, high-dose treatment with telmisartan induces monocytic peroxisome proliferators activated receptor-γ target genes in patients with the metabolic syndrome which demonstrates its role in positive actions on lipid and glucose metabolism prevention of new onset of diabetes[15]. No serious adverse effects were observed during the study period. After completion of the study period, patients were advised to continue antihypertensive medication and life style changes like increasing physical activity, intake of low salt and high-fibre diet.

CONCLUSION

Angiotensin receptor blocker, telmisartan is an effective in controlling blood-pressure by its AT_1 receptor blocking activity. It is also effective in decreasing fasting blood glucose by its insulin sensitizing activity through partial peroxisome proliferator activated receptor (PPAR) gamma activity. Patients showed good compliance on treatment with telmisartan, due to its dual beneficial actions and less adverse effects.

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Nil

CONFLICT OF INTEREST

No interest

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