A PROSPECTIVE STUDY OF EFFECT OF TELMISARTAN (ANGIOTENSIN II RECEPTOR BLOCKER) ON METABOLIC PARAMETERS IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME

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ABSTRACT

BACKGROUND

The metabolic syndrome is currently a major worldwide epidemic. It strongly associates with obesity, insulin resistance, type 2 diabetes, and cardiovascular diseases, which are major pathologies contributing to mortality and morbidity worldwide. The effect of PPAR-y on metabolic syndrome is significant it is critical regulator of adipogenesis the gain in PPAR-y is resulted in obesity but loss of PPAR–y by mutation is associated with loss of weight and insulin resistance. Telmisartan is an orally active, long-acting, non-peptide angiotensin type 1 (ATI) receptor blocker. In addition to this, it has been identified as partial agonist/selective modulator of the nuclear hormone receptor PPAR-y.

MATERIAL AND METHOD

This is a prospective, randomised and open labelled 16 weeks study conducted in the Dept. of General Medicine, Konaseema Institute of Medical Science, Amalapuram. Present study is designed to study the effect of telmisartan on various metabolic parameters in hypertensive patients who fulfilled the criteria of metabolic syndrome.

RESULT

There was statistically significant change in all parameters most important was lipid profile; LDL concentration was decreased from 139.2 mg/dL to 120.2 mg/dL. Baseline triglyceride concentration was 161.0 mg/dL which was changed 152.8 mg/dL Total cholesterol was decreased from 203.2 to 193.8 mg/dL.

CONCLUSION

In our study, we have also found that use of telmisartan is associated with decrease in lipid concentration in addition to its effect on blood pressure regulation. But a long term study with high dose required of this drug is required because safety profile of this drug is better than thiazolidinedione. Financial part of this study is our limitation.

KEYWORDS

Telmisartan, PPAR Gamma Receptor, Metabolic Syndrome

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INTRODUCTION: Peroxisome proliferator activated receptors were discovered in 1990, ending 25 years of uncertainty about molecular mechanisms of peroxisome proliferation subsequently, PPARs have improved our understanding of adipocyte differentiation. But there is more to PPARs than solving a puzzle about an organelle (the peroxisome), long considered an oddity and their medical significance goes beyond obesity too.(1) Peroxisomes are subcellular organelles found in most organisms that perform diverse metabolic functions including H_2O_2 based respiration, β oxidation of fatty acids (FAs) and cholesterol metabolism. PPARs proteins belong to super family, of phylogenetically related proteins termed nuclear hormone factor. They mainly exist in three sub types α, β/delta and Gamma, each of which mediates the physiological actions of large variety of fatty acids and fatty acid derived molecules.(2)

Metabolic syndrome is a term for cluster of metabolic abnormality. As per NCEP: ATP III 2001 and harmonising criteria, central obesity, waist circumference > 102 cm (male), > 88 cm (Female), Triglyceride level 150 mg/dL or specific medication, low HDL < 40 mg/dL (male), < 50 mg/dL female or specific medication BP > 130/85 mm of the or specific medication fasting plasma glucose level > 100 mg/dL or specific medication or diagnosed type -2 DM. If three or more of the these conditions present, then it is considered as metabolic syndrome.(3) All PPAR isoforms have found their value on the treatment of metabolic syndrome PPAR α regulates fatty acid oxidation, transport and lipoprotein generation, PPAR β/delta is the one studied relatively less in metabolic syndrome, its function is largely demonstrated in the other aspects such as concern

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osteogenesis and reproduction. The effect of PPAR-y on metabolic syndrome is significant, it is a critical regulator of adipogenesis, the gain in PPAR-y is resulted in obesity but loss of PPAR–y by mutation is associated with loss of weight and insulin resistance. In the past decades, the rapidly increasing evidences on PPARs proved its value in metabolic syndrome.[4]

Telmisartan is an orally active, long acting, non-peptide angiotensin type 1 (ATI) receptor blocker. In addition to this, it has been identified as partial agonist/selective modulator of the nuclear hormone receptor PPAR-y.[5,6] Present study is designed to study the effect of telmisartan on various metabolic parameters in hypertensive patients who have fulfilled the criteria of metabolic syndrome.

MATERIAL AND METHOD: This is a prospective, randomised and open labelled 16 weeks' study conducted in the Dept. of General Medicine, Konaseema Institute of Medical Science, Amalapuram. Before start of the study, permission from Institutional Ethics Committee was obtained. Written informed consent was taken from patients on predesigned consent form. Twenty patients of both sex and age between 20 to 60 yrs. were included into this study as per inclusion and exclusion criteria.

Inclusion Criteria	Exclusion Criteria
BMI > 25 kg/m2	Hypersensitivity to drug
BP > 130/85 mm of Hg	Diabetes and its complication
Waist circumference > 104 cm Male > 88 cm Female	On any other medication Pregnancy and lactation
TG level > 150 mg/dL	OC Pills, Liver Diseases

Before start, all the parameters were measured like FPG, post prandial plasma glucose, HbA1c, lipid profile like serum triglyceride, LDL, total cholesterol and HDL, blood pressure was measured every 15 days, body mass index and weight was also measured. Fasting and post prandial c-peptide level was measured before start of the study, patients were given 40 mg telmisartan every day in the morning and all the parameters were repeated after 16 weeks. Plasma glucose was measured by hexokinase method, c- peptide was measured by radio immunoassay, glycosylated haemoglobin was measured by spectrophotometer, total cholesterol was estimated by ZAK modified method. HDL was estimated by precipitation method, LDL was estimated by W.T. Friedewald, R.I. levy and D.C. Fredrickson and serum triglyceride was estimated by method of Neri and Frienge. Data was calculated by using paired t- test and P value < 0.05 was considered significant.

RESULT: After 16 weeks of continuous followup of the 20 patients, we found that mean body weight decreased from 79.6 kg to 77.6 kg and body mass index was also changed from 27.5 kg/m^2 to 26.8 kg/m^2. Systolic blood pressure was significantly decreased from mean value 146.8 to 131.8 and similarly diastolic blood pressure was also decreased from 92.2 mm of Hg to 81.8 mm of Hg.

Regarding glucose metabolism, fasting c- peptide level was decreased from 1.076 nmol/L to 0.996 nmol/L, Glycosylated haemoglobin concentration also decreased. Although their FPG and PPPG was little higher side of the normal range that also decreased from 106.2 mg/dL to 100.2 mg/dL FPG, and 149.2 mg/dL to 139.6 mg/dL PPPG.

Character	Baseline	Study end mean	% change mean	t value	p value
Body weight	79.6	77.6	2.5%		
BMI	27.5	26.8	2.5%		
SBP (mm of Hg)	146.8	131.8	10.21	7.02	<0.001
DBP (mm of Hg)	92.2	81.8	11.27	9.75	<0.001
C-peptide level.	1.076	0.996	7.4%	2.95	<0.05
HbAIc (%)	6.51	6.41	1.5%	3.898	<.05
FPG(mg/dL)	106.2	100.2	5.6%	4.61	<0.001
PPPG(mg/dL)	149.2	138.6	7.3%	5.29	<0.0001
HDL(mg/dL)	40.4	43.2	7.9	5.25	<0.001
LDL (mg/dL)	139.6	120.2	13.6%	75.74	<0.05
TG (mg/dL)	161	152.8	6.8%	4.828	<0.001
Total chol.(mg/dL)	203.2	193.8	4.90%	3.615	<0.01

Table 1: Changes in Metabolic Parameters Baseline and at the end of the study

Lipid profile of all the patients also changed, HDL level was increased from 40.4 to 43.2; LDL concentration was decreased from 139.2 mg/dL to 120.2 mg/dL. Baseline triglyceride concentration was 161.0 mg/dL which was changed 152.8 mg/dL. Total cholesterol was decreased from 203.2 to 193.8 mg/dL.

DISCUSSION: In our study, we have found that there was decrease in the body weight by 2.5% and body mass index also by 2.5% which may also be due to awareness of the patients, increase in their physical activity, as per Kakuma T et al. There is decrease in both but Murakami et al found that there is no change in body weight.[7,8]

The present study demonstrates that there is statistically significant reduction in fasting c- peptide level that is 7.41% of the mean. Glycosylated haemoglobin was also decreased but only 1.5% which was also statistically significant. FPG and PPPG was decreased by 5.6% and 7.6%

respectively which is similar to the study of Hueh et al and Jull M Nagel et al. [9,10] Telmisartan is a well-established drug for the treatment of hypertension, so as usual that also significantly decreased, with t value 7.02 and 9.75 and P value <0.001.

Regarding effect on lipid profile, in our study, we have found that HDL concentration was increased by 7.9% of the mean with the t value 5.25 and P value <0.001, which is similar to the study of Jutta M Nagel et al.[10,11], but some authors found that there is no significant change in other lipid parameters that is Ilse – Nirmala Bahr et al and Dongxiu Zu et al[5,11], but in our study, we found statistically significant decrease in LDL, TG and total cholesterol that is 13.6%, 6.8% and 4.9% which is similar to the study of Jayapriya et al and Jutta M Nagel et al.[10,12]

CONCLUSION: The metabolic syndrome is currently a major worldwide epidemic. It strongly associates with obesity, insulin resistance, type 2 diabetes, and cardiovascular diseases, which are major pathologies contributing to mortality and morbidity worldwide. Numerous studies have demonstrated that the peroxisome proliferator–activated receptor (PPAR) plays an important role in regulating carbohydrate and lipid metabolism and those ligands for PPAR can improve insulin sensitivity, reduce triglyceride levels, and decrease the risk for atherosclerosis. Various agonists like thiazolidinedione, fibrates are used clinically for treatment of dyslipidaemia and diabetes. Recent studies have proved that telmisartan has also agonistic and modulating action on PPAR Gamma receptor. In our study, we have also found that use of telmisartan is associated with decrease in lipid concentration in addition to its effect on blood pressure regulation. But a longterm study with high dose required of this drug is required because safety profile of this drug is better than thiazolidinedione. Financial part of this study is our limitation.

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