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The Influence of Telmisartan on Metabolic Parameters in Hypertensive Patients of Metabolic Syndrome- A Prospective Study.

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ABSTRACT

Background: Telmisartan, an angiotensin II receptor blocker, has a higher affinity for AT1 receptors. It has also been recognized as partial agonist of the nuclear hormone receptor PPAR-gamma. The present study is conducted to study the effect of telmisartan on various metabolic parameters in hypertensive patients who have satisfied the standards of metabolic syndrome. **Methods:** This is a prospective and randomised study done on twenty hypertensive patients suffering from metabolic syndrome. All the patients underwent following investigations like Fasting plasma glucose, post prandial plasma glucose, HbA1c levels, lipid profile including total triglyceride, LDL, total cholesterol and HDL, C-peptide level, blood pressure, body mass index and weight were also measured. All the patients were recommended 40 mg of telmisartan orally every day. The above mentioned investigations were repeated after 4 months. Data was tabulated and compared with the previous readings by using paired t- test and P value < 0.05 was considered significant. **Results:** The change in both weight and body mass index is statistically insignificant. All the three haemodynamic parameters (SBP, DBP, MAP) showed significant decrease after intake of 40 mg telmisartan for four months. All the parameters (Total cholesterol, LDL, Triglycerides) of lipid profile of the patients except HDL demonstrated decrease in value. Regarding glucose metabolism, fasting c- peptide level, glycosylated haemoglobin concentration showed no difference in the value, whereas both fasting and post prandial blood glucose decreased significantly. **Conclusion:** The present study proves that telmisartan has agonistic and modulating action on PPAR Gamma receptor and is thus associated with lipid and glucose metabolism.

Keywords: Hypertension, Metabolic syndrome, Telmisartan.

INTRODUCTION

The angiotensin II receptors are of four types but type 1 are most important. Telmisartan, an angiotensin II receptor blocker, has a higher affinity for AT1 receptors. It is considered as better angiotensin blocker because it has longer half-life of 20-24 hours and better volume of distribution.[1]

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Telmisartan also shows affinity for peroxisome proliferator-activated receptor delta (PPAR-γ) which are present in several tissues of the body. The affinity for these receptors was discovered in 1990. The effects of the drug on PPARs have enhanced our knowledge of differentiation on adipocytes. Besides this, the recent studies suggest that the effect of telmisartan on peroxisomes also plays an important role. Peroxisomes are subcellular organelles which perform varied metabolic functions including β oxidation of fatty acids, H2O2 based respiration and cholesterol metabolism.[2]

PPARs are the proteins which belong to super family called as nuclear hormone factor. These have three sub types alpha, delta and gamma. The gamma subtype mainly effects large variety of fatty acids and mediates the physiological actions on fatty acid derived molecules.[3]

Metabolic syndrome is a constellation of abnormalities in metabolism. The presence of three or more underlying conditions is considered as the metabolic syndrome: 1) Central obesity, 2) Waist circumference > 102 cm (male), > 88 cm (Female), 3) Triglyceride level 150 mg/dL, 4) low HDL < 40 mg/dL (male), < 50 mg/dL (female), 5) BP > 130/85 mm 6) Fasting plasma glucose level > 100 mg/dL and 7) Diagnosed type -2 DM.[4,5]

Telmisartan is a non-peptide, orally active, long acting, angiotensin type 1 (ATI) receptor blocker. In addition to this, it has been recognized as partial agonist of the nuclear hormone receptor PPAR-

gamma. Its mechanism is by relaxing blood vessels, which helps to lower blood pressure. It is mainly used for treating high blood pressure alone or with other medicines. It is also used to reduce the risk of heart attack, stroke, or death due to heart problems in certain patients. The common side effects are back pain; diarrhoea; sinus pain or congestion.[6]

The present study is conducted to study the effect of telmisartan on various metabolic parameters in hypertensive patients who have satisfied the standards of metabolic syndrome.

MATERIALS AND METHODS

This is a prospective and randomised study done in the Department of Medicine, Teerthanker Mahaveer Medical College, Moradabad. Before initiation of the study, approval from Institutional Ethics Committee was acquired. Written consent was taken from patients included in the study. Twenty patients of both sex and age between 20 to 60 yrs. were included in this study. Only those patients who fulfil the following criteria were included in the study. Inclusion criteria are: a) Body mass index >25 kg/m2 b) Blood pressure >130/85 mm of Hg c) Waist circumference >104 cm (male) > 88 cm (female) d) Triglyceride level > 150 mg/dL. Patients with following criteria were excluded from the study: a) Drug hypersensitivity b) diabetes and its complication c) Pregnancy and lactation d) Oral contraceptive pills e) Liver diseases.

All the patients underwent following investigations like Fasting plasma glucose, post prandial plasma glucose, HbA1c levels, lipid profile including total triglyceride, LDL, total cholesterol and HDL, blood pressure, body mass index, weight and height were also measured. Before the initiation of the study, fasting and post prandial C-peptide level were also measured. 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. All the patients were recommended 40 mg of telmisartan orally every day. The above mentioned investigations were repeated after 4 months. Data was tabulated and compared with the previous readings by using paired t- test and P value < 0.05 was considered significant.

RESULTS

After 4 months of study on the 20 patients, we found that body weight decreased from 75.4 kg to 71.9 kg and body mass index also decreased from 26.4 kg/m2 to 24.8 kg/m2. But both the changes in parameter were statistically insignificant (>0.05) [Table 1]. The significant decrease in all the three haemodynamic parameters (SBP, DBP, MAP) was noticed after intake of 40 mg telmisartan for four months. The systolic and diastolic blood pressures decreased from 148.2 mmHg to 129.6 mmHg and 94.6 mmHg to 84.8 mmHg respectively. Similarly, mean arterial pressure showed drastic per cent decrease in mean of 10.7 which was statistically significant (<0.05) [Table 2].

Table 1: Changes in BMI after intake of drug.

Parameter	Before	After	% change in mean	P value
Weight (kg)	75.4	71.9	4.64	>0.05
BMI (kg/m^2)	26.4	24.8	6.06	>0.05

Table 2: Changes in haemodynamic parameters after intake of drug.

Parameter	Before	After	% change in mean	P value
Systolic B.P.(mmHg)	148.2	129.6	12.5	<0.05*
Diastolic B.P.(mmHg)	94.6	84.8	10.3	<0.05*
Mean Arterial pressure (mmHg)	112	100	10.7	<0.05*

Table 3: Changes in lipid profile after intake of drug.

Parameter	Before	After	% change in mean	P value
Total cholesterol (mg/dl)	206.8	190.4	7.9	<0.05*
LDL (mg/dl)	142.6	128.2	10.1	<0.05*
HDL (mg/dl)	39.6	40.1	-1.2	>0.05
Triglycerides (mg/dl)	165.8	150.9	8.9	<0.05*

Table 4: Changes in other metabolic parameters after intake of drug.

Parameter	Before	After	% change in mean	P value
Fasting blood glucose (mg/dl)	112.8	100.6	10.8	<0.05*
Post prandial plasma glucose (mg/dl)	144.8	132.1	8.7	<0.05*
HbAIc (%)	6.2	6.2	0	-
C-peptide level (nmol/L)	1.1	1.0	9.1	>0.05*

All the parameters (Total cholesterol, LDL, Triglycerides) of lipid profile of the patients except HDL demonstrated decrease in value in four months. LDL concentration was decreased from 142.6 mg/dL to 128.2 mg/dL, triglyceride concentration from 165.8 mg/dL to 150.9 mg/dL and total cholesterol decreased from 206.8 to 190.4 mg/dL. All these changes in parameters were statistically significant (<0.05) [Table 3, Figure 1].

Regarding glucose metabolism, fasting c- peptide level decreased from 1.1 nmol/L to 1.0 nmol/L which was statistically insignificant (p value >0.05). Glycosylated haemoglobin concentration showed no difference in the value after intake of drug for four months. Although, FPG and PPPG showed significant decrease (p value <0.05) from 112.8 mg/dL to 100.6 mg/dL and 144.8 mg/dL to 132.1 mg/dL respectively [Table 4, Figure 2].

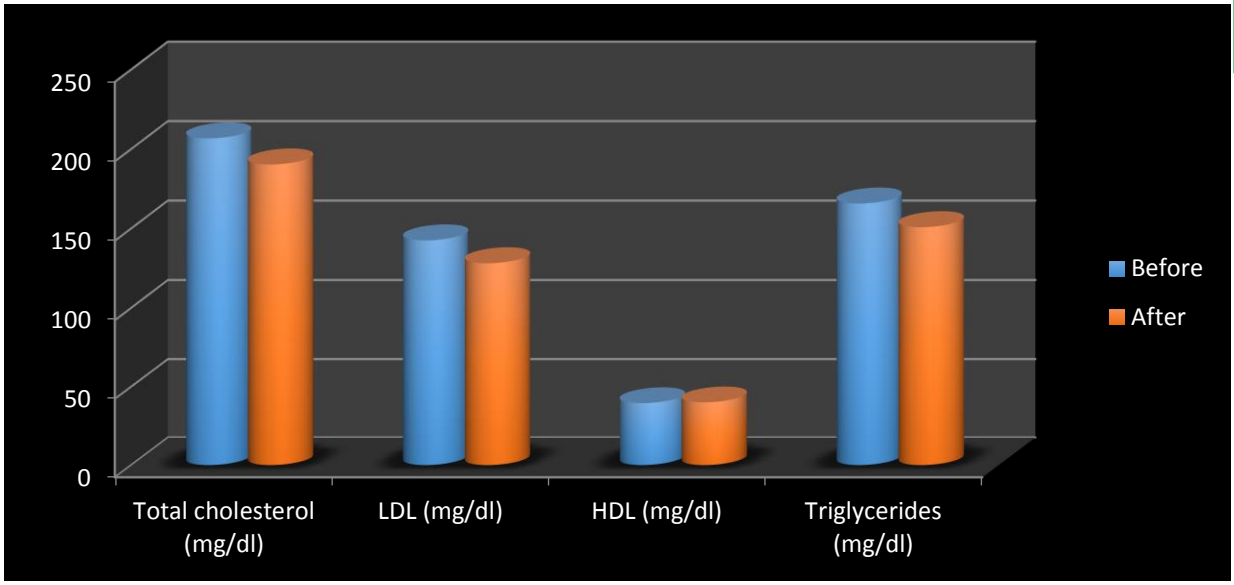

Figure 1: Comparison of lipid profile before and after intake of drug.

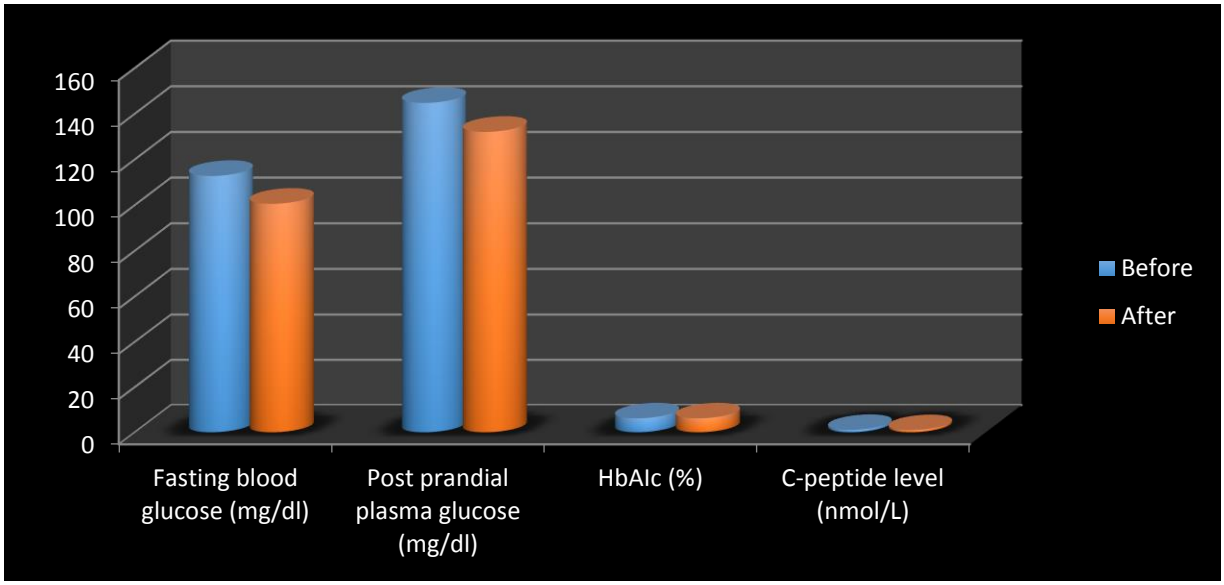

Figure 2: Comparison of glucose metabolism before and after intake of drug.

DISCUSSION

This study conducted on the hypertensive patients suffering from metabolic syndrome showed drastic decrease in different metabolic parameters after intake of 40 mg of telmisartan orally for 16 weeks.

In this study, we have found 4.64% decrease in weight and 6.06% decrease in body mass index which was statistically insignificant (>0.05). This decrease in weight and body mass index might be due to awareness of the patients and increase in their physical activity. Similar findings were also seen in the studies done by Kakuma T et al[7] and Murakami et al[8].

Hueh et al[9] in his study suggested that there is statistically significant reduction in fasting c- peptide

level that is 7.41% of the mean. Glycosylated haemoglobin also showed decreased of about 1.5% which was also statistically significant. In contrast to these findings, the present study showed no significant difference in the values of C-peptide level and glycosylated haemoglobin concentration after intake of drug. Similar to our study, Hueh et al[9] and Jull M Nagel et al[10] found significant decrease in FPG and PPPG.

In the present study various changes in the parameters of lipid profile were studied, and compared after ingestion of telmisartan orally for four months. Regarding effect on lipid profile we have found that HDL concentration showed no significant change in the value. In contrast to our findings Jutta M Nagel et al.[10] found the increase in concentration of HDL by 7.9% of the mean with the t value 5.25 and P value <0.001. Dongxiu Zu et al[11] suggested that there is significant difference in other parameters of lipid profile except HDL, which supports our findings. Similarly, Jayapriya et al[12] and Jutta M Nagel et al.[10] found statistical decrease in the LDL (13.6%), Triglycerides (6.8%) and total cholesterol (4.9%) after intake of drug orally. All these findings support our recent study.

The metabolic syndrome is presently a foremost worldwide epidemic. It sturdily associates with insulin resistance, obesity, type 2 diabetes, and other cardiovascular diseases.[7] All these pathologies are considered as the major factors contributing to cardiovascular mortality and morbidity. Numerous studies[1,8] 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.

CONCLUSION

The present study proves that telmisartan has agonistic and modulating action on PPAR Gamma receptor and is thus associated with lipid and glucose metabolism. The oral intake of drug causes decrease in lipid concentration in addition to its effect on blood pressure regulation. It also plays an important role in controlling the blood glucose level. The limitation of this study is that the drug is given for a short duration and the sample size is also small.

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