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ASSESSMENT OF OLMESARTAN ANTI-HYPERTENSIVE EFFECTS WITH TELMISARTAN IN TYPE II DIABETICS WITH HYPERTENSION ON METFORMIN

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ABSTRACT

Objective: *To compare anti-hypertensive effect and renoprotective effects of Olmesartan and Telmisartan in hypertensive type 2 diabetic patients.* ***Materials and Methods****: 60patients (n=60) of hypertension with type II diabetic mellitus attending the department of general medicine, Prathima institute of medical sciences, nagunur, Karimnagar, between the periods of July 2012 - July 2013. They were divided into two groups- Group I (Olmesartan group) Olmesartan (at a dose of 40mg tab. orally once daily) and Group II (Telmisartan group) Telmisartan were prescribed (at a dose of 40mg tab orally once daily) along with oral hypoglycemic agent (Metformin Dose: 500mg/day) for a period of 12weeks.* ***Results:*** *The antihypertensive effect of both Olmesartan and Telmisartan were satisfactory and statistically significant. Both the drugs have been found to control diastolic blood pressure better than systolic. The target blood pressure was achieved in 43% patients in Telmisartan group and 73% in Olmesartan group(overall 58%). The mean HbA1c % in Telmisartan and Olmesartan groups were found to be 7.53% and 7.36% respectively at first and this reflects poor glycemic control in both groups. After one month there was a 2.1% reduction of HbA1c % in Telmisartan group but in Olmesartan group there was a reduction of 5.2%. Which was found to be statistically significant (p=0.405).* ***Conclusion:*** *Olmesartan is a better choice in patients with type 2 Diabetes Mellitus with hypertension in comparison to Telmisartan*

KEY WORDS

Olmesartan, Telmisartan, Type II diabetes with hypertension, renoprotective

INTRODUCTION

Type II Diabetes with hypertension is associated with pro-atherogenic and inflammatory risk factors that predispose to cardiovascular disease (1). The renin-angiotensin-aldosterone system (RAAS) plays a pivotal role in the pathogenesis of insulin resistance and cardiovascular disease in diabetes (2). Interruption of the RAAS with Angiotensin II type 1(AT1)receptor blockers (ARB) has been shown to prevent or reduce cardiovascular and renal disease progression in diabetic patients with hypertension(3,4). Telmisartan is angiotensin II type 1 (AT1) receptor blocker, which was initially indicated for the treatment of essential hypertension, has already been proven to have other beneficial effects like improved lipid profile, increased insulin sensitivity, regression of left ventricular hypertrophy, reduction of microalbuminuria and amelioration of the associated pro-inflammatory and pro-atherogenic risk profiles(5). Angiotensin receptor blockers appear to exert similar beneficial effects in diabetic patients, but whether clinically significant differences in antihypertensive effect, renoprotection or metabolic effects exist with angiotensin receptor blockers in patients with Hypertension and type 2 diabetes remains to be investigated in

appropriate head- to- head studies. Our present study is an effort to choose the better agent between Olmesartan and Telmisartan in hypertensive type 2 diabetic patients.

The study aims to compare the following claimed benefits, anti-hypertensive effect and renoprotective effects of Olmesartan and Telmisartan in hypertensive type 2 diabetic patients.

MATERIALS AND METHODS

The present study is a randomized, open labeled, comparative clinical study between Olmesartan and Telmisartan in hypertensive type II diabetic patients conducted in single center. The study was conducted on 60 patients of hypertension with type II diabetic mellitus attending the department of general medicine, Prathima institute of medical sciences, nagunur, Karimnagar, between the periods of July 2012 - July 2013. Procedures followed in this study are in accordance with the ethical standard laid down by ICMR's Ethical guidelines for biomedical research on human subjects (2000).

Subjects

60 patients of type II diabetes with hypertension participated. They were divided into two groups by systematic randomization. Informed consent obtained explaining expected advantages and known side effects of Olmesartan / Telmisartan. ICMR's Ethical Guidelines for Biomedical Research on Human subjects (2000) was followed. At the first visit, after clinical evaluation and laboratory investigation, in one group (Olmesartan group) Olmesartan (at a dose of 40mg tab. orally once daily) and in another group (Telmisartan group) Telmisartan was prescribed (at a dose of 40mg tab orally once daily) along with oral hypoglycemic agent (Metformin Dose: 500mg/day) for a period of 12weeks. No medication that could interfere with the clinical evaluations was allowed during the trials. History of Duration of diabetes, risk factors, physical examination - Blood pressure, height, weight, BMI, abdominal circumference was included. 5ml of venous blood was drawn in fasting and 2hr post meal under aseptic precautions, by skilled technician which was immediately sent to lab for analysis of Fasting and post- prandial blood sugar, serum creatinine, blood urea, Glycosylated Hb(Hb $A1_c$%) and lipid profile. At 12 weeks follow-up study, detailed resume of clinical state were made including the hospital investigation and therapy. Follow up of 4 patients of Telmisartan group and 5 of Olmesartan group who were unable to continue trial and was dropped. Hence, Telmisartan group had 26 patients and Olmesartan group 25 patients completed this trial.

Statistical analysis

Paired t-test, T-test, unpaired t-test, Fisher's exact test was performed with SPSS-18. Interval data has been expressed as mean ±SD and categorical data in percentage. P value <0.05 was considered statistically significant.

RESULTS

Baseline demographic data and clinical characteristics (Table 1) of the 60 patients of type 2 diabetes mellitus with hypertension showed a mean age group of 53yrs and 48yrs with duration accounting to 7.7yrs and 6.9yrs in Telmisartan and olmesartan group respectively.

Characteristics	Telmisartan group	Olmesartan group	P value
Number of the patients recruited	30	30	
Number of the patients at follow up	26	25	
Female patients (%)	46.6	43.4	
Age (years)	53.5 ± 9.26	48.8 ± 9.9	0.06
Duration of diabetes (years)	7.73 ± 3.78	6.97 ± 3.3	0.409
Height(meters)	1.5840±.09633	1.5940± .09141	0.68
Weight(kg)	67.33± 10.077	67.67± 13.476	0.91
BMI (Kg/m2)	27.05±4.23	26.32±5.24	0.56
Waist circumference (Inch.) ABC	38.25±5.30	36.75±3.91	0.21
Meters	3.57± 1.006	3.37± .999	0.44
Systolic blood pressure (mm Hg.)	154.07±8.31	151.53±9.51	0.27
Diastolic blood pressure (mm Hg)	94.47±4.59	92.73±3.38	0.10
HbA1c%	7.50±1.73	7.29±1.59	0.61
Fasting blood sugar (mg/dl)	164.40±38.0	159.73±35.1	0.62
Post-prandial blood sugar(mg/dl)	246.6±53.4	243.6±47.8	0.82
Triglyceride (mg/dl)	146.06±63.933	157.07± 71.430	0.53
Total cholesterol (mg/dl)	178.03±37.0	180.29±32.9	0.80
LDL cholesterol (mg/dl)	111.15±31.9	115.41±32.2	0.60
HDL cholesterol (mg/dl)	41.10± 7.976	41.17± 5.484	0.97
VLDL (mg/dl)	25.00± 13.409	23.73± 12.446	0.70
Serum urea (mg/dl)	55.30± 12.393	58.60± 13.174	0.32
Serum creatinine (mg/dl)	1.307± .5199	1.547± .5224	0.08
Number of patient with micro albuminuria (%)	144.27±76.792	149.17± 89.678	0.82

TABLE 1: Baseline demographic data and clinical characteristics of the 60 patients of type 2 diabetes mellitus with hypertension participated in the study in the first visit

There was a 16 mean decrease in systolic blood pressure and 7.69 mean decrease in diastolic blood pressure in Telmisartan group. Similarly 19.8 mean decrease in systolic blood pressure and 10 mean decrease in diastolic blood pressures in Olmesartan group. The changes in both groups were statistically significant. But when the mean of two groups were compared by t-test the changes in Olmesartan group was found significant.(Table 2)

BP	Telmisartan group				Olmesartan group				Difference between groups ψ
	1ST visit	2nd visit	Mean Δ	P value	1ST visit	2nd visit	Mean Δ	P value	
SBP(mm of Hg)	153.69 ± 8.01	137.69 ± 6.63	16	0.003$	150.8 ± 10.24	131.04 ± 10.2	19.8	<0.001$	0.008*
DBP(mm of Hg)	94.15 ± 4.07	86.46 ± 4.53	7.69	0.004$	93.04 ± 3.5	83.04 ± 3.5	10	0.027$	0.004*

Table:2 Changes in systolic and diastolic blood pressure in study groups.

There was a 0.16 mean decrease in HbA1c in Telmisartan group.(Table-3). Similarly 0.35 mean decreases HbA1c in Olmesartan group. The changes in both groups were statistically significant. But when the mean of two groups were compared by t-test the changes in Olmesartan group was found not significant.

parameters	Telmisartan group				Olmesartan group				Difference Between groups ψ
	1st visit	2nd visit	Mean Δ	P value$	1st visit	2nd visit	Mean Δ	P values$	
HbA1c%	7.52 ± 1.74	7.36 ± 1.58	0.16	<0.001$	7.35 ± 1.57	7 ± 1.55	0.35	<0.001$	0.405

Table:3 Changes in glycosylated hemoglobin in study groups.

There was a 4.19 mean decrease in serum urea, and 0.05 mean decrease in serum creatinine in Telmisartan group. Similarly 4.44 mean decrease in serum urea, and 0.13 mean decrease in serum creatinine in Olmesartan group.(Table 4) The changes in both groups were statistically significant. But when the mean of two groups were compared by t-test the changes in Olmesartan group was found not significant.

Parameters	Telmisartan group				Olmesartan				Difference between groups ψ
	1st visit	2nd visit	MeanΔ	P value	1st visit	2nd visit	MeanΔ	P value	
Serum Urea (mg/dl)	56.23 ± 11.99	52.04 ± 8.5	4.19	<0.001$	58.84 ± 12.39	54.4 ± 8	4.44	<0.001$	0.315
Serum Creatinine (mg/dl)	1.32 ± 0.51	1.27 ± 0.46	0.05	<0.001$	1.54 ± 0.49	1.41 ± 0.44	0.13	<0.001$	0.276

Table 4:Changes in renal parameters in study groups

DISCUSSION

Diabetes Mellitus is one of the most burdensome chronic diseases that is increasing in epidemic proportion throughout the world. Uncontrolled DM may lead to complications like nephropathy, end stage renal disease and cardiovascular events. We have compared antihypertensive, renoprotective, metabolic changes and tolerability of Olmesartan and Telmisartan in type 2 diabetes mellitus with hypertension. Most of the patients were from the district of Karimnagar and few from Warangal and Adilabad. So the study population is homogenous in nature with minimum ethnic variation. The baseline data shows that there is no statistically significant difference between the study groups in respect to demographic and clinical parameters. This strengthens the proof of homogeneity of our study subjects in two groups. Following the inclusion criteria, patients aged more than 30 years were included. In this study group one third (15.0%) of the patients were found to belong to the age group of 31-40 years, (37.7%) patients in the age group of 41-50 years, followed by (33.3%) in 51-60 years age group and only (11.7%) in 61-70 years age group. In our study most of the

patients are in the age group of 31-40 years which is also very much vulnerable to develop cardiovascular morbidity and mortality. The mean duration of suffering was 7 years in Telmisartan group and 6.6 years in Olmesartan group. These values also confirm that there was no significant difference between the study groups and they were homogenous. More than 75% of the patients have given history of suffering for ≥ 5 years. As most of the patients were suffering for a considerably long period, they are definitely at risk for developing renal and cardiovascular complications. To estimate the prevalence of obesity we followed both WHO and Asia Pacific guidelines. According to WHO classification (1997), 57% patients of our study group were found to be having BMI > 25 and classified as overweight(6). According to Asia Pacific Guidelines (2000), 78% patients were found to be overweight in India, National Family Health Survey and study by IHE, DV in collaboration with ICMR found a steady growth in number of obese Indians towards epidemic proportions and it was found that obesity is a major problem in urban women (D.I.) Bansal and R.K. Boupari, 2003. According to Asia Pacific guidelines, 81.5% (22 / 27) of females in our study group were found to be obese.The antihypertensive effect of both Olmesartan and Telmisartan were satisfactory and statistically significant. Both the drugs have been found to control diastolic blood pressure better than systolic. The previous study by [Brunner et al. 2006.] showed the same finding of better control of DBP by Olmesartan. The target blood pressure was achieved in 43% patients in Telmisartan group and 73% in Olmesartan (overall 58%). Our study results support the previous study by [Nakayama S, Watada H, et al. Hypertens Res.2008(7). where in 54% patients target blood pressure was achieved and maintained. To assess the long-term glycemic control, Glycosylated hemoglobin (HbA1c %) has been estimated. The mean HbA1c % in Telmisartan and Olmesartan groups were found to be 7.53% and 7.36% respectively at first and this reflects poor glycemic control in both groups. After one month there was 2.1% reduction of HbA1c % in Telmisartan group but in Olmesartan group there was a reduction of 5.2%. Which was found to be statistically significant (p=0.405).There was no significant change in any of the parameters of lipid profile in Telmisartan group but Olmesartan showed a significant decrease in Total cholesterol, LDL, VLDL and triglyceride levels. In our study it was found that the effect of Olmesartan is maximum on triglyceride and VLDL. [DA.de Luies et al.2010]. Both the drugs were found to be renoprotective as there were significant decrease in serum urea. The renoprotective effect of both the drugs is due to increase in renal blood flow and improved insulin sensitivity. [Nej MED 364; 10 mar 10.20111, WeinbergAS, Zappe DH et al.2006](8). Both the drugs were found to control the diastolic blood pressure better than systolic. Olmesartan was found to be better antihypertensive than Telmisartan with a greater achievement of target level blood pressure in diabetic hypertensive patients.The effect on metabolic parameters was assessed by blood sugar and lipid profile estimation. In both the groups glycemic control was satisfactory with a better control of post-prandial blood sugar. Fasting, post-prandial and long term glycemic control (HbA1c %) were better with Olmesartan than Telmisartan. There was no significant change in any of the parameters of lipid profile in Telmisartan group but Olmesartan though statistically not significant showed a good improvement in total cholesterol, LDL, VLDL and Triglyceride levels with the maximum effect on triglyceride and VLDL.The renoprotective effect of both the drugs was eminent from the improvement of serum urea, serum Creatinine. The comparative study has again proved when

compared with Telmisartan, Olmesartan has got a good renoprotective effect in diabetic hypertension patients due to its varied effects like increase in renal blood flow. There was no-report of serious or new side effects in either group. thus Olmesartan and Telmisartan have again proved their good tolerability. However due to small sample size and time constrain, further studies are needed to asses long-term effects.

CONCLUSION

Olmesartan is a better choice in patients with type 2 Diabetes Mellitus with hypertension in comparison to Telmisartan has more antihypertensive effect with achievement of target level blood pressure with improved glycemic control (both short term and long term) and a better renoprotective effect.

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