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EFFICACY AND SAFETY OF AZILSARTAN IN PATIENTS OF HYPERTENSION WITH DIABETES IN GWALIOR DISTRICT.

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ABSTRACT **Background:** Angiotensin receptor blockers are well established drugs for the treatment of hypertension with or without renal disease. Azilsartan is a new angiotensin receptor blocker being used in the treatment of hypertension. Present study is done to evaluate efficacy and safety of azilsartan in patients of hypertension with diabetes mellitus in Gwalior district.

Methods: The study was conducted in department of pharmacology, Gajra raja medical college, Gwalior Madhya Pradesh during February 2018 to march 2019. It is a longitudinal, prospective, randomized study and total 90 patients of hypertension with diabetes were enrolled out of which 83 patients completed study with a follow up of 1 year period and were divided equally into two groups. Group I received Azilsartan 40- 80 mg once daily and group II received another drug once daily for 12 weeks. Baseline Systolic blood Pressure and diastolic blood pressure were recorded at the start and then at 4th, 8thand 12th weeks after therapy. Fasting and post prandial blood sugar, HDL, LDL-C , total cholesterol values were recorded at start and after 12 weeks of therapy. All the patients were screened for any adverse drug reactions on each visit.

Result: Azilsartan effectively lowered the levels of systolic and diastolic blood pressure from baseline (p=0.00001) confirming the anti-hypertensive efficacy also there was overall significant improvement in HDL values from baseline (p=0.000) and also significant improvement was shown in LDL Total cholesterol levels from baseline (p =0.005). There was significant improvement in FBS and PPBS from baseline (p value 0.00).

Conclusion: Azilsartan effectively lowered the levels of systolic and diastolic blood pressure in patients of hypertension with diabetes and the difference was significant. Azilsartan showed overall improvement in HDL, LDL, TC values with significant difference in hypertensive with diabetes patients.

KEYWORDS : Azilsartan, Hypertension, Diabetes, efficacy, safety

INTRODUCTION

Hypertension (HTN) is the most common cardiovascular disease. It is defined conventionally as sustained increase in blood pressure >140/90 mm of Hg[1]. In recent years, the numbers of patients suffering from both diabetes mellitus (DM) and hypertension have been increasing. Both essential hypertension and DM affect the same major target organs and the common denominator of hypertensive/diabetic target organ-disease is the vascular tree. People with coexisting diabetes and hypertension are at increased risk of developing atherosclerosis, retinopathy, renal failure, and cerebrovascular disease (CVD).[2] Most patients with both disorders have a markedly worsened risk for premature micro vascular and macro vascular complications. The presence of hypertension causes a 7.2-fold increase and a 37-fold increase in mortality in diabetic patients.[3]It has been shown that lowering BP in high risk patients with DM can reduce deaths from strokes and CVD events and can slow down the progression of renal disease in patients with type 2 DM[4]. Hence, in this study, we are undertaking patients of Hypertension with Diabetes.

The renin–angiotensin system participates significantly in the pathophysiology of hypertension, congestive heart failure, myocardial infarction, and diabetic nephropathy[5]. According to JNC-8 guidelines, Angiotensin receptor blockers (ARBs) are now amongst the first line drugs of anti-hypertensive with diabetic treatment. Azilsartan Medoxomil is a prodrug and is rapidly hydrolyzed during its gastrointestinal absorption into azilsartan (TAK-536), the bioactive molecule that selectively and competitively blocks angiotensin II induced activation of AT1 receptors[6].

Due to its Angiotensin receptor blocking (ARBs) property, it has more advantages as compared to other drugs used for treatment in patients of hypertension with diabetes.

MATERIALAND METHODS

The study was conducted in department of Pharmacology in GRMC Gwalior Madhya Pradesh during academic session February 2018 to march 2019. It was longitudinal, prospective, open labelled, comparative study including a total of 90 cases. The study was conducted for a total duration of one year, including the follow up, in Cardiology OPD from February 2018 to March 2019. The follow up was done at every 4, 8 and 12 weeks. Dropout cases were excluded and minimum of 83 patients were included in this manner in the study. Patients already diagnosed as hypertension with diabetes of either sex within the age group of 35-65 years with blood pressure of >140/90 mmHg were included in the study . The upper limit of blood pressure in both groups was 180/110 mmHg. The participants were between 35 to 65 years of age. Patients belonging to hypertension were selected as per JNC VIII report. Undiagnosed cases, patients suffered from CVS, CNS, endocrine disease, pulmonary disease, cancer, pregnancy, fever of unknown etiology, unable to provide informed consent and all HIV or HBs Ag positive patients were excluded from study.

Recording Of Blood Pressure-Systolic and diastolic blood pressure was measured in right arm, in sitting posture by auscultatory method using standard mercury sphygmomanometer. Two recordings of blood pressure were taken at an interval of 15 min by the same physician. Diagnosed cases of hypertension with diabetes were randomly allocated in two groups using random number table having 45 patients in each group. Group I received tablet azilsartan 40-80mg and Group II received another drug once daily for 12 weeks.

Measurement Of Lipid Profile-HDL ,LDL-C ,Total cholesterol levels were measured at the start of therapy and then after 12 weeks.

Measurements Of Blood Sugar-Fasting blood sugar (FBG) and postprandial blood sugar (PPBS) level were measured at the start of therapy and after 12 weeks of therapy.

Recording Of Adverse Effects-Patients were observed at every visit for cough, ankle oedema, nasopharyngitis, headache or any other

adverse effects after start of treatment.

Statistical Analysis -
All the data analysis was performed by using SPSS version 20 software. Quantitative variables were expressed as the mean and standard deviation. P value of< 0.05 is considered as significant.

RESULTS

Table 1 : Age Distribution Of Study Participants (n=48)

Age group (years)	Hypertension with diabetics patient			
	Male patients	Percent	Female patients	Percent
35-45	08	47.05%	09	52.94%
46 -55	18	58.06%	13	41.93%
56-65	22	64.70%	13	38.23%
Total	48		35	

The age of patients ranged from 35 to 65 years with a mean age of essential hypertensive with diabetes patients 52.71 and. Of total 83 patients, most common age group involved was 55-65 years that included 22(64.70%)male and 13 (38.23%) female patients.

Table 2. Efficacy Of Azilsartan Shown In Post-treatment BP Changes In Patients Of Hypertension With Diabetes.

BP in mm Hg	Group I (PRE-Treatment (value)	Group I(Post-Treatment value)	P value
SBP	156.02±10.13	133.26±7.1	<0.0001
BP	94.14±4.5	82.68±3.4	<0.0001

The mean systolic blood pressure of group I significantly decreased from a pre-treatment value of mean of 156.02±10.13 to post-treatment 133.26±7.1, with p value being <0.0001. The diastolic blood pressure value of mean reduced from pre-treatment 94.14±4.5 to post-treatment 82.68±3.4, with p value <0.0001. On statistical analysis, the difference was highly significant with p value being< 0.0001.

Table 3. Comparison Of Pre-treatment And Post-treatment Changes In Lipid Profile Of Patients Taking Azilsartan.

Lipid Profile parameters (MG/DL)	Group I (Pre –treatment values)	Group I (Post –treatment values)	P value
HDL	45.96±8.70	47.61±9.29	P< 0.001
LDL	141.81±19.66	136.51±18.04	p < 0.001
TC	170.51±33.06	160.01±32.97	p < 0.001

Values expressed as mean±SD. P value < 0.05 is considered as significant.

The pre-treatment value of mean of HDL – Cholesterol of patients taking azilsartan was 45.96±8.70 which was increased to 47.61±9.29 at the end of 12th week. On statistical analysis, the P value was found to be p < 0.001 and the difference was statistically significant.

The value of mean of LDL - cholesterol of patients taking azilsartan changed from baseline 141.81±19.66 to 136.51±18.04 at the end of 12th week. The value of mean of LDL – C was found to be lower at the end of 12th week (p < 0.001) and the difference was statistically significant. The pre-treatment value of mean of Total cholesterol (TC) of patients taking azilsartan was 170.51±33.06 which reduced to 160.01±32.97 at the end of 12th week and the difference was found to be statistically significant (p < 0.001).

Table 4. ***Comparison Of Pre-treatment And Post-treatment Values Of Fasting Blood Sugar In Patients Taking Azilsartan.***

Blood sugar	Group I Pre Treatment	Group I Post Treatment	P value
FBS	126.63±25.65	99.75±11.21	P<0.001

Values expressed as mean±SD. P value < 0.05 is considered as significant.

Table 5. ***Comparison Of Pre-treatment And Post-treatment Values Of Postprandial Blood Sugar In Patients Taking Azilsartan.***

Blood Sugar	Group I Pre Treatment	Group I Post Treatment	P value
PPBS	184.75±33.96	152.82±19.74	p < 0.001

Values expressed as mean±SD. P value < 0.05 is considered as significant.

The value of mean of Fasting blood sugar of patients taking azilsartan changed from baseline 126.63±25.65 to 99.75±11.21 at the end of 12th week. The value of mean of Fasting blood sugar was found to be statistically significant at the end of 12th week (p < 0.001).

The value of mean of Postprandial blood sugar of patients taking azilsartan changed from baseline 184.75±33.96 to 152.82±19.74 at the end of 12th week. The value was found to be statistically significant at the end of 12th week (p < 0.001).

DISCUSSION

ARBs are considered as one of the best available therapeutic option for the treatment of hypertension. They act by preventing the binding of angiotensin II on AT1 receptors. Azilsartan is a newer ARB found superior to other sartans such as valsartan, olmesartan and candesartan in lowering blood pressure[7]. It is reported that azilsartan has slow dissociation from AT1 receptor as compared to other sartans[6]. In present study azilsartan at the dose of 40-80 mg once daily for 12 weeks decreased blood pressure by 22.76 mm Hg . An earlier double blind study revealed decrease in blood pressure with azilsartan by 14.3 mm hg after 6 weeks of treatment and was better than valsartan 10 mmHg and olmesartan 11.7 mmHg[7][8]. Our study shows similar results in patients of hypertension with diabetes. In present study azilsartan showed better reduction in SBP and the effect on DBP was found to be more superior. Our study is in accordance with a double blind study where azilsartan showed significant fall in DBP as compared to ramipril[9]. Superior effect of azilsartan on DBP might be its additional role in reduction of vascular inflammation, proliferation and endothelial dysfunction[10][11][12]. Present study revealed that azilsatran treated patients showed better control of fasting and post prandial blood sugar. This might be due to increased sensitivity to insulin by azilsartan as reported earlier in an animal study suggesting a possible role of azilsartan in the treatment of DM [13].In another animal study Azilsartan has shown vascular protection in diabetes induced vascular dysfunction[14][15]. Thus Azilsartan found safe and better tolerated drug. Azilsartan commonly do not cause cough and makes it better alternative to ACEIs in patients of hypertension with or without DM.

CONCLUSION

The present study demonstrated that Azilsartan can be used safely and effectively for the management of hypertensive patients with or without diabetes. However, extensive studies for longer duration and large number of patients are needed to understand mechanism of action and to establish Azilsartan as a new therapeutic strategy for the treatment of hypertension with diabetes mellitus.

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