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EFFECT OF AZILSARTAN ON SERUM LIPID PROFILE AND SERUM CREATININE AMONG PATIENTS OF HYPERTENSION WITH DIABETES.

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ABSTRACT **Background:** Angiotensin receptor blockers are well established drugs for the treatment of hypertension with diabetes patients. Azilasartan is a new angiotensin receptor blocker used in the treatment of hypertension. In present study, the effect of Azilsartan was evaluated on serum lipid profile and serum creatinine in hypertension with diabetic patients.

Material and Method- This is a longitudinal, prospective study was conducted in department of pharmacology and out patient cardiology of J.A.group of hospital, Gajra Raja Medical College Gwalior, M.P. Total 45 patients diagnosed as hypertension with diabetes were enrolled during February 2018 to March 2019. At the end of 12 weeks significant improvement in lipid profile was evaluated apart from its antihypertensive effect but Azilsartan did not produced significant reduction in serum creatinine from baseline at the end of 12th week.

Conclusion- Azilsartan are proved to be effective not only in controlling BP, but had a favorable effect on lipid profile in patients of hypertension with diabetes while Azilsartan did not seemed significant effect on serum creatinine. However Azilasartan has shown significantly better efficacy in lowering lipid profile.

KEYWORDS : Azilsartan , serum creatinine , lipid profile, Enalapril

INTRODUCTION-

Hypertension occurs more commonly in diabetes than in non-diabetics. About 20 to 60% of patients with diabetes , depending on obesity ,dyslipidemia ethnicity , and age develop hypertension(1). Most patients with triple disorders have a markedly worsened risk for premature micro vascular and macro vascular complications. Patients with hypertension are at two to three times higher risk of developing diabetes than patients with normal blood pressure(2,3) .The simultaneous presence of hypertension and diabetes is devastating to the cardiovascular system . In patients with diabetes blood pressure events and can slow down the progression of renal disease(3,4) . In recent years, the numbers of patients suffering from both diabetes mellitus and hypertension have been increasing. Both essential HTN 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 DM and HTN are at increased risk of developing atherosclerosis, retinopathy, renal failure, and CVD(5) . Angiotensin receptor blockers act by blocking action of angiotensin II on AT1 receptors are equally efficacious and devoid of cough and angioedema(6). Azilsartan medoxomil (AZL-M) is a newer angiotensin receptor blocker and is promising drug to control blood pressure . It is a prodrug and is converted into active metabolite in the GIT(7) . Till now, there is no study available regarding its effectiveness in hypertension with diabetes. Therefore, present work is undertaken to seen the effect of Azilsartan on serum lipid profile and serum creatinine in hypertension with diabetic patients .

MATERIALAND METHODS-

The study was conducted in department of pharmacology and out patients department of cardiology in Gajra raja medical collage Gwalior madhyapradesh during February 2018 to March 2019 after the approval institutional ethical committee.

This was prospective , longitudinal, clinical trial. A total of 45 patients were enrolled in the study as per the selection criteria .patients with already diagnosed 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. Patients belonging to hypertension were selected as per JNC VIII report. Only already diagnosed hypertension with diabetes patients were included in our study

The following categories of patients were included and excluded from the study:

INCLUSION CRITERIA-

1) Confirmed Cases of HTN with Diabetes Mellitus (having SBP 140 180 mm of Hg, DBP 90-110 mm of Hg) diagnosed by the physician.
2) The participant could be of either sex.
3) The participant must be 35 years and not more than 65 years old.

EXCLUSION CRITERIA-

1) Undiagnosed cases
2) Patients suffered from CVS, CNS, Endocrine disease, pulmonary disease, cancer
3) Pregnancy
4) Fever of unknown etiology
5) Unable to provide informed consent
6) All HIV or HBsAg positive patients
7) Patients of allergic reaction (drug under study)

The patients were examined by the consultant physician to rule out hypertension with diabetes patients. Systolic and diastolic blood pressure was measured in right arm, sitting posture by auscultatory method using standard mercury sphygmomanometer. The pressure at which the sounds were first heard was taken as the systolic pressure and the pressure at which the sounds disappeared was taken as the diastolic pressure. Two recordings of blood pressure were taken at an interval of 15 min by the same physician. After initial screening, the demographic data,

past medical history, family history, findings of physical examination, and clinical examination were recorded in the case report form. Diagnosed cases of hypertension with diabetes were enrolled and

received Azilsartan 40-80 mg under the supervision physician . All patients were instructed to take the tablet orally once a day with glass of water in the morning.

The patients were advised to report for follow-up every 4, 8, 12week . On each visit, blood pressure was recorded. Renal function test, lipid profile (HDL, LDL, TC, TG) and ECG were assessed before starting the treatment and end of treatment.

Measurements of treatment efficacy- Primary end point was change in lipid profile levels such as serum cholesterol, HDL, LDL, TG, TC and serum creatinine were measured at 3 months as compared to baseline values.

STATISTICALANALYSIS:-
All the data analysis was performed by using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare the Tables. Quantitative variables were expressed as the mean and standard deviation. Categorical data was expressed in actual numbers and percentage. PRISM and Microsoft office was used to prepare the graphs. Student t- test and paired t-test was used to compare the means. Chi Square test was used to compare the categorical data. p-value of < 0.05 is considered as significant.

RESULT-
Table No. 1-Demographics and Baseline characteristics

Charecteristics	AZL-M	Total
Number	41	45
Male	25	55.5%
Female	16	35,5%
Age (mean)	52.85	52.85
Marital status(%)	100%	100%
Rural/Urban	23/18	23/18
HDL-C	45.96±8.70	45.39
LDL-C	141.81±19.66	145.19
TC	170.51±33.06	172.80
S.Cr	1.01±0.20	1.03

Patients disposition and demographics- A total of 45 patients were screened in Gajra raja medical collage as per selection criteria. patients with already diagnosed hypertension with type 2 diabetes of either sex within the age group of 35-65 years with blood pressure >140/90 mmHg and upper limit of blood pressure 180/110 mmHg were included in the study. Total 4 out of 45 patients were dropped out from my study, Baseline lipid profile and serum creatinine were recorded and follows at the start and at the end of study.

Safety and tolerability
Azilsartan drug in our study was well tolerated and found to be safe and the only adverse reaction reported was headache and nasopharnyngitis (4.8%) .

Table No. 3- Evaluation of effect of Azilsartan on lipid profile in patients of HTN with DM patients

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

The pre-treatment value of mean of HDL – Cholesterol 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 0.001 ($p < 0.05$). At the end of 12th week, mean value of HDL – C was found to be higher than the baseline values and the difference was statistically significant.

The value of mean of LDL - cholesterol of group I 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 ($p = 0.001$). The pre-treatment value of mean of total cholesterol (TC) of group I was 170.51±33.06 which reduced to 160.01±32.97 at the end of 12th week. Though the post – treatment value of mean at the end was lower than pre-treatment value, the difference was found to be statistically significant ($p = 0.001$).

Table No. 3- Evaluation of effect of Azilsartan on renal function test in patients of HTN with DM patients

RFT parameter in mg/dl	Group I (Pre –treatment values)	Group I (Post –treatment values)	P value
Serum Creatinine	1.01±0.20	1.03±0.22	p = 0.001

The value of mean of serum creatinine of group I changed from baseline 1.01±0.20 to 1.03±0.22 at the end of 12th week. The value of mean of serum creatinine was found to statistically significant at the end of 12th week ($p = 0.001$).

DISCUSSION-
ARBs is well established drugs that inhibit the biological activity of angiotensin II elicit potent blood pressure reduction, are highly protective against end organ damage and may have beneficial metabolic effects such as delaying the onset of Type 2DM. In clinical study like HOPE or The LIFE study, ARB significantly reduced the risk for cardiovascular death, myocardial infarction or stroke as well as the incidence of new onset diabetes, The ONTARGET study demonstrated that in high risk patients with cardiovascular disease or diabetes , an ARB (Azilsartan) was equivalent to an ACE inhibitor (Enalapril) for the reduction in major cardiovascular events and was well tolerated with lower incidence of cough and angioedema. The excellent tolerability of the ARB class translates into high patient adherence to other antihypertensive classes. AZL-M is a new ARB with superior efficacy within the ARB class. In current study, AZL-M on its blood pressure lowering efficacy and its safety and tolerability.. It has expected pleiotropic benefits like improving insulin sensitivity, anti proteinuric effects, anti inflammatory effects, inhibits vascular cell proliferation and endothelial dysfunction and attenuates cardiac remodeling after MI(7,8,9). Research studies pointed out before converge in the stimulation of Peroxisome Proliferating Activated Receptor gamma (PPARγ) pathway from Azilsartan as feasible favorable mechanism of pathophysiology on the vital Angiotensin-1 receptors (AT1) inhibition through improving lipid profile(7,8,9). Similar effect of Azilsartan is observed in our study reducing the lipid levels . In our study we observed that significant reduction in lipid profile as well as serum creatinine levels significantly increased in Hypertension with DM patients.

Azilsartan is commonly prescribed for hypertension with diabetic patients in the medical outpatient department. In the present study, the effect of long term administration of azilsartan on serum lipid profile was evaluated. .The patients who were enrolled into the study had both hypertension and diabetics. In the present study, there was significant effect on serum lipid profile in the patients, who were given azilsartan 40-80 mg/day, for 3 months.

Azilsartan showed significant improvement in HDL – C from baseline, and significant reductions in LDL-C and TC at the end of 12th week .The significant effect of azilsartan on serum lipid profile in the present study is supported by preclinical studies conducted on SHOR(spontaneously hypertensive obese rats) rats BY Khan AH et al[10] (2014) , and other study results were consistent with Mahmood NMA et al[11] (2018) study found that co administration of azilsartan with MTX produced significant decrease in TG and LDL-c concentrations, associated with significant increase in HDL-c levels compared to baseline values;

while serum creatinine level was significantly increased in initial treated hypertensive with diabetic patients at the end of 12th weeks, The significant effect of azilsartan on serum creatinine in the present study is supported by Weber MA et al[12] (2013) in clinical laboratory tests, there were small mean increases in creatinine (0.4–2.2 mmol/l) and other study supported by Cushman WC et al[13] (2017) study found that all serum creatinine elevations that were at least 30% above baseline and greater than the upper limit of normal (ULN) were recorded as an adverse event of special interest.

CONCLUSION-
In our study, Azilsartan proved to be effective and had a favorable effect on lipid profiles apart from BP. azilsartan treatment results in amelioration of cardiovascular risk factors, not only through arterial pressure regulation but also through reduction of serum lipid profile. So, in conclusion, all the patients with uncomplicated hypertension and dyslipidemia without other associated risk factors can be effectively treated with azilsartan. However, the study has its share of limitation. The small number of patients studied over a short period of

time. Thus, a firm conclusion cannot be drawn. More studies for longer duration are needed to seem the effect of Azilsartan on lipid profile and serum creatinine level.

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