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COMPARISON OF ANTIHYPERTENSIVE EFFECT OF AZILSARTAN WITH TELMISARTAN IN DIABETIC PATIENTS- AN OBSERVATIONAL STUDY

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ABSTRACT

Introduction: Despite the availability of effective drugs for hypertension, it remains uncontrolled in majority of patients. Azilsartan, a new antihypertensive drug, has not been studied in diabetic hypertensives. **Objective**: To study the efficacy of azilsartan in patients of T2DM & HT and compare that with telmisartan. **Methods:** Adult patients attending the OPD of Dhanashree Hospital, New Sangavi, Pune; suffering from T2DM and HT were studied. They were treated with usual oral anti-diabetic drugs and received either telmisartan 40mg/d or azilsartan 40 mg/d for hypertension. Clinical examination and laboratory parameters were assessed every three monthsover a period of six months. Data obtained were analysed by Student´s t-test and P value < 0.05 was considered as statistically significant. **Results:** Seventy-one patients were enrolled in the study. Nine were lost during follow-up. Thirty two patients received telmisartan, while 30 were treated with azilsartan. Both the groups were comparable at base-line with respect to clinical & laboratory parameters. Both drugs significantly reduced SBP (152+/-23 vs136 ± 14 mm Hg) and DBP (158+/-25 vs.127 ± 12 mm Hg). Azilsartan was significantly (P<0.05) more effective in reducing the blood pressure than telmisartan. There was no significant difference in the glycaemic and lipid parameters. Both drugs were well tolerated. **Conclusion:** Azilsartan was significantly more effective than telmisartan as an antihypertensive in T2DM patients.

KEYWORDS: T2DM, Hypertension, Telmisartan, Azilsartan.

INTRODUCTION

Hypertension is a primary risk factor for cardiovascular disease, and strict blood pressure (BP) control is critical from the standpoint of prevention of cardiovascular disease.[1] In India, hypertension is the most prevalent chronic disease, with a rate of 20-40% among urban adults & 12-17% among rural adults. For every known case of hypertension, there are 2 cases of undiagnosed hypertension or Pre-hypertension. There is a considerable gap between detection & control of hypertension. In clinical practice, however, it is not infrequent that existing antihypertensive drugs fail to provide an adequate antihypertensive effect that is sustained over 24h.[2]

The renin–angiotensin system (RAS) is an important mediator of blood volume, arterial pressure, cardiac and vascular function.[3,4] Angiotensin II is a key component of the RAS, which acts via the AT1 receptor at every step of the cardiovascular (CV) continuum.[5,6] The angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are two different classes of agents that target the RAS via their effect on the production or action of angiotensin II.[3] Both ACE inhibitors and ARBs prevent CV disease by lowering blood pressure (BP), but also have beyond-BP-lowering benefits, and therefore are now considered first-line treatments for hypertensive target-organ damage and progressive renal disease.[7-10]

ACE inhibitors and ARBs have been shown in head-to-head comparison trials to have comparable CV protective effects. However, ARBs are associated with fewer adverse effects and better patient compliance.[11,12] Their use is recommended in guidelines for the reduction of CV risk in patients with diabetes and hypertension,[13] and in hypertensive patients with microalbuminuria, renal dysfunction, end-stage renal disease, and diabetes mellitus.[14]

Among the recommended first-line anti-hypertensive agents, the ARBs are now widely used as a key component of antihypertensive regimens because of their favourable efficacy/ tolerability profiles.[15] In addition, clinical outcome trials have shown that the ARBs reduce the proportion of hypertensive patients who develop type 2 diabetes mellitus,[16] and improve cardiovascular outcomes in such conditions as high-risk

hypertension,[17,18] heart failure[19,20] and diabetic kidney disease.[21,22]

Despite the availability of effective drugs foe hypertension, it remains uncontrolled in majority of patients. Telmisartan is the most widely used member from the ARBs. Azilsartan, a new ARB has not been studied in diabetic hypertensives. Hence, this study was designed.

AIM

To compare the efficacy of azilsartan with that of telmisartan.

OBJECTIVES

To study the efficacy of azilsartan in patients of Type II DM & HT and compare that with telmisartan.

METHODS

Study design

This was an observational, randomized, open label study comparing the efficacy of azilsartan with telmisartan in patients with Type II Diabetes mellitus and hypertension. The study was carried out on 71 patients in the OPD of Dhanashree Hospital, New Sangavi, Pune from January 2017 to October 2017. Nine were lost during follow-up and out of 62 patients, thirty two patients received telmisartan, while 30 were treated with azilsartan. During the 9 months treatment period, all patients in each group received their usual oral anti-diabetic drugs along with telmisartan 40mg/d or azilsartan 40 mg/d once daily and were followed at three-monthly intervals for minimum six months.

The study was approved by ethics committee, and was conducted in accordance with the ethical provisions set out in the Declaration of Helsinki, the International Conference on Harmonisation, Harmonised Tripartite Guideline for GCP (Good Clinical Practice) and all applicable local laws and regulations

Patients

Clinical examination (BW, sitting BP etc.) and laboratory parameters (BSL, GHb, Lipids etc.) were assessed at each visit, i.e. at baseline, three months and six months. Mean of three readings were taken as systolic and diastolic BP reading.

Inclusion Criteria

1. Age>18 years,
2. Newly diagnosed Type II Diabetes Mellitus
3. Either sex
4. Newly diagnosed hypertensives (according to AHA guidelines)

Exclusion Criteria

1. Age > 70 yrs
2. Severe Renal/Hepatic/Cardiac disease
3. Pregnant women
4. Patients on SGLT2-inhibitors/other ARB's.

Primary end point was the changes in BP from the baseline in sitting position in both the groups. And then comparison was done between the efficacy of azilsartan and telmisartan.

Secondary end points were change in BSL (fasting and post prandial), other clinical parameters (eg. serum cholesterol, triglycerides, UACR etc.), adverse events from the baseline in both the groups.

Statistical analysis

Data obtained were analyzed by Student's unpaired "t" test & Chi squared testand P value < 0.05 was considered as statistically significant.

RESULTS

71 patients were enrolled in the study, among which 9 were lost during follow-up. 32 patients received telmisartan, while 30 were treated with azilsartan. Both groups were comparable at base-line with respect to clinical & laboratory parameters. (Table 1 & 2).

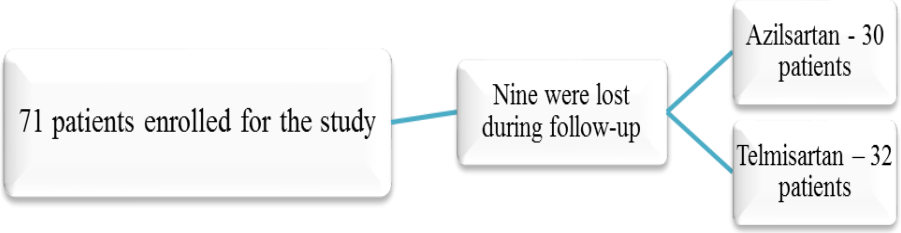

Fig. 1: Flowchart of Patient recruitment.

Table 1: Demographic profile of patients at base-line.

Variables	Telmisartan (n = 32)	Azilsartan (n = 30)
Age (years)	54.0 ± 6.9	54.9 ± 4.5

Female, n (%)	14 (43.75))	13 (43.33)
BMI, kg/m^2	30.4 ± 3.5	29.8 ± 4.0
Smoking, n (%)	8 (25)	7 (23.33)
Dyslipidemia, n (%)	25 (78.13)	23 (76.67)
Gliptin use,n(%)	14 (43.75)	12 (40.0)
Statin use, n (%)	24(75)	22(73.33)
Statin +Fibrate use,n (%)	6(18.75)	5(20)
Saroglitazaruse,n (%)	2 (6.25)	3 (10)
ASA use, n (%)	7 (33.3)	7 (33.3)
Metformin use, n (%)	28 (87.5)	26 (86.67)
Sulfonylurea use, n (%)	15 (46.88)	14 (46.67)

Table 2: Laboratory profile of the study population at baseline.

Variables	Telmisartan (n = 32)	Azilsartan(n = 30)
Serum Creatinine, mg/dl	0.77 ± 0.20	0.79 ± 0.21
Fasting Blood glucose, mg/dl	131.7 ± 43.0	134.0 ± 47.3
Post-prandial Blood glucose, mg/dl	181.7 ± 52.1	192.0 ± 57.5
HbA1c, % total Hb	8.2 ± 0.7	8.4 ± 0.8
Total cholesterol, mg/dl	196.4 ± 35.6	191.9 ± 30.0
HDL cholesterol, mg/dl	45.5 ± 13.5	45.0 ± 12.1
LDL cholesterol, mg/dl	145.9 ± 24.8	141.6 ± 22.1
Triglycerides, mg/dl	217.4 ± 48.0	227.7 ± 56.3
GFR_{MDRD}, ml/min/1, 73 m^2	91.7 ± 21.4	100.0 ± 34.7
UACR, mg/g creatinine	30.5 ± 22.3	34.8 ± 24.8

Table 3: Sitting Clinic Blood Pressure at base-line.

Variables	Telmisartan (n=32)	Azilsartan (n=30)
SBP mmHg	152+/-23	158+/-25
DBP mmHg	95+/-16	92 +/- 14
MAP mmHg	114 +/- 18	115 +/-17

Table 4: Sitting Clinic Blood Pressure at 6 months.

Variables	Telmisartan (n = 32)	Azilsartan (n = 30)
SBP mmHg	136 ± 14*	127 ± 12*†
DBP mmHg	81 ± 11*	72 ± 9*†
MAP mmHg	100 ± 12	101 ± 10

Figures are Mean +/- SD * P <0.05 – Comparison within group
† P <0.05-Comparison between the groups

Table 5: Creatinine levels at 6 months.

Variables	Telmisartan (n = 32)	Azilsartan (n = 30)
UACR mg/g Creatinine	24.8 +/- 17.6	25.7 +/- 18.5

Both drugs significantly reduced SBP (152+/-23 vs136 ± 14 mm Hg) and DBP (158+/-25 vs.127 ± 12 mm Hg). Azilsartan was significantly (P<0.05) more effective in reducing the blood pressure than telmisartan. UACR decreased in both the groups, more so in azilsartan treated patients. However, this did not attain statistical significance. There was no significant difference in the glycemic and lipid parameters. Both drugs were tolerated.

Table 6: Comparison of side effects between the groups.

	Telmisartan (N = 32)	Azilsartan (N=30)
Incidence (%)	6 (18.75)	5 (16.67)
Cough	2	1
Fainting / Dizziness	3	4
Palpitations	4	3
Itching /Rash	3	2

The side effects were noted through a questionnaire as following.

2. In the last three months did you feel any of the following symptoms?
2.1. On a 1 to 5 scale, how these symptoms affect your well-being?

			Never affect	Almost never	Some times	Many times	Always affect
1 Tiredness	□ No	□ Yes	1	2	3	4	5
2 Feeling faint	□ No	□ Yes	1	2	3	4	5
3 Sweats	□ No	□ Yes	1	2	3	4	5
4 Gripes	□ No	□ Yes	1	2	3	4	5
5 Nausea	□ No	□ Yes	1	2	3	4	5
6 Diarrhea	□ No	□ Yes	1	2	3	4	5
7 Constipation	□ No	□ Yes	1	2	3	4	5
8 Palpitations	□ No	□ Yes	1	2	3	4	5
9 Swollen feet or legs	□ No	□ Yes	1	2	3	4	5
10 Cold hands or feet	□ No	□ Yes	1	2	3	4	5
11 Muscle pain	□ No	□ Yes	1	2	3	4	5
12 Cramps	□ No	□ Yes	1	2	3	4	5
13 Headaches	□ No	□ Yes	1	2	3	4	5
14 Dizziness	□ No	□ Yes	1	2	3	4	5
15 Anxiety	□ No	□ Yes	1	2	3	4	5
16 Sadness	□ No	□ Yes	1	2	3	4	5
17 Sleep poorly	□ No	□ Yes	1	2	3	4	5
18 Shortness of breath or breathing difficulty	□ No	□ Yes	1	2	3	4	5
19 Persistent dry cough	□ No	□ Yes	1	2	3	4	5
20 Itching	□ No	□ Yes	1	2	3	4	5
21 Skin rash	□ No	□ Yes	1	2	3	4	5
22 Swollen or red face	□ No	□ Yes	1	2	3	4	5
23 Dry mouth	□ No	□ Yes	1	2	3	4	5
24 Frequent urination	□ No	□ Yes	1	2	3	4	5
25 Decreased sexual desire or ability sexual	□ No	□ Yes	1	2	3	4	5

Others symptoms: _____

DISCUSSION

Azilsartan and telmisartan, both were effective in reducing the BP in diabetic hypertensives but azilsartan was significantly more effective in reducing the clinic blood pressure.

Significantly more number of patients achieved target blood pressure with azilsartan. In a meta analysis, Takagi H et al (2014) have found azilsartan to be more effective than other commonly used antihypertensive agents.

Another double-blind, randomized, placebo-controlled trial by White WB et al (2011), compared azilsartan with olmesartan and valsartan. A total of 1,285 patients were randomized to placebo, azilsartan 40–80 mg daily, olmesartan 40 mg daily or valsartan 320 mg daily for 6 weeks. Placebo-adjusted ABPM-SBP was lowered by azilsartan (−14.3 mmHg) was significantly more than by valsartan (−10.0 mmHg; P,0.001) and olmesartan (−11.7 mmHg; P=0.009).

In this small, single centre, observational study azilsartan - the new ARB was found to be more effective in reducing clinic blood pressure, more effective in achieving target blood pressure, equally well tolerated as compared with telmisartanin Type II DM patients with hypertension Hence, it can be considered as an effective & safe anti-hypertensive agent in diabetic hypertensive adults.

CONCLUSION

Azilsartan and telmisartan were effective in reducing the blood pressure in diabetic hypertensives. Both drugs were tolerated. However, azilsartan was significantly more effective than telmisartan in this short study.

There was no conflict of interest
There was no funding agency
Ethics committee approval was taken

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