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Effects of two different angiotensin receptor blockers on blood glucose level and HbA1c in type-2 diabetes mellitus patients with hypertension

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Abstract

Diabetes mellitus is a common metabolic disorder characterized by chronic hyperglycemia and disturbance of carbohydrate, fats, and protein metabolism. Type 2 diabetes mellitus results from reduced insulin secretion, decreased glucose utilization, and increased glucose production, which results in hyperglycemia. Hypertension further increases the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease (PAD). Angiotensin receptor blockers (ARBs) are very effective antihypertensive drugs. This study was done to find the effects of two different angiotensin receptor blockers on various biochemical markers in type-2 diabetes mellitus patients.

Methods

This was a prospective interventional study, comparing two ARBs Azilsartan and telmisartan, involving 76 patients with type 2 diabetes mellitus and hypertension.

Results

Both drugs controlled blood pressure equally. The study showed that improvement in fasting plasma glucose was more with Azilsartan as compared to Telmisartan but their mean difference is not statistically significant ($p > 0.05$). The improvement in post-prandial plasma glucose and HbA1C was more with Telmisartan as compared to Azilsartan but only mean HbA1C was statistically significant ($p < 0.05$).

Conclusions

Telmisartan has a better impact on HbA1c reduction than Azilsartan, as a part of the pleotropic effect of ARBs.

Keywords Pleotropic effect of ARBs, Blood glucose reduction by Telmisartan and Azilsartan, Pleotropic effect of Telmisartan and Azilsartan

Introduction

Diabetes mellitus is a common metabolic disorder described by chronic hyperglycemia and disturbance of carbohydrate, fats, and protein metabolism. Type 2 diabetes mellitus results from reduced insulin secretion, decreased glucose utilization, and increased glucose production, which results in hyperglycemia [1]. It is characterized by defects in insulin secretion, action, or both.

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Bhati *et al. The Egyptian Journal of Internal Medicine*   (2023) 35:72

Page 2 of 5

The International Diabetes Federation (IDF) reported that at present there are 415 million people worldwide affected by T2DM, aged between 20 and 79 years old, the global prevalence being 8.8% and it is anticipated that in 2040 their number will grow up to 642 million with a prevalence of 10.4% [2].

Hypertension is one of the leading causes of the global burden of disease. Raised blood pressure affects more than one billion individuals and causes an estimated 9.4 million deaths per year as per The World Heart Federation. Hypertension further increases the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic stroke, hemorrhagic stroke, renal failure, and peripheral arterial disease (PAD) [3]. Antihypertensive therapy reduces the risks of cardiovascular and renal disease, but a large proportion of the hypertensive population is either untreated or inadequately treated.

Angiotensin receptor blockers (ARBs) are very efficient antihypertensive drugs. ARBs exert their effect through blockage of the type 1 angiotensin II receptor and quite possibly through stimulation by the type 2 angiotensin II receptor [4]. ARBs have been found to be beneficial in the treatment of heart failure and diabetic nephropathy, besides hypertension [5]. ARBs have appeared as being very effective and perhaps superior to other antihypertensive drugs in the prevention of de novo or recurrent stroke [6]. Their stroke-protective effects include their anti-atherogenic, anti-diabetic, anti-platelet aggregating, hypouricemic, and atrial anti-fibrillatory actions. All these actions make the ARBs a true pleotropic class of drugs. There had been a large no of studies in Western literature which have established the pleotropic effect of angiotensin receptor blockers, but very few studies have looked into the new angiotensin receptor blockers like Azilsartan [7, 8].

There is no head-to-head comparison between telmisartan and Azilsartan, to look at their pleotropic effect on diabetes; hence, an attempt was made to compare the pleotropic effect of these two drugs.

Methodology

This study was a prospective, interventional, open-labelled hospital-based study. This study was conducted from November 2017 to July 2019 after getting approval from the Institutional Ethics Committee, J. N. Medical College, and patients were enrolled after getting informed consent. A detailed history and examination were carried out for every patient who entered in study as per a pre-designed proforma.

A total of 62 subjects were recruited and admitted in the wards of the Department of Medicine, and Rajiv Gandhi Center of Diabetes and Endocrinology, J.N. Medical College, AMU. Our inclusion criteria were as follows:

A. Criteria for diagnosing diabetes mellitus: Fasting glucose levels of ≥ 126 mg/dl (7.0 mmol/l) or 2-h PG ≥ 200 mg/dl (11.1 mmol/l) during OGTT (75 g) or random blood glucose ≥ 200 mg/dl or HbA1c ≥ 6.5% (48 mmol/mol) or current treatment with hypoglycemic therapy.
B. Hypertension: SBP/DBP > 140/ 90 mm of Hg

Inclusive criteria were age > 18 years, diagnosed case of type 2 diabetes

Mellitus with hypertension, all patients were on equal dose statin, and equal doses of oral hypoglycemic agents. Exclusion criteria were age < 18 years and patients with unstable angina, secondary hypertension, renal insufficiency/renal artery stenosis, and chronic kidney disease.

The drugs were administered in the recommended doses: Telmisartan 80 mg once a day and Azilsartan 40 mg once a day. Parametric variables were analyzed by Student's *t* test, non-parametric variables were analyzed by chi-square test. The correlation was analyzed by regression analysis. Complete blood count (CBC), renal function test and serum electrolyte, blood sugar—fasting and post-prandial, HbA1c, lipid profile (total serum cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein) was done in all patients.

The patients were divided into two groups: Group 1 patients on telmisartan and group 2 patients on Azilsartan.

Results

The basic parameters of 62 patients are summarized in Table 1. The mean HbA1c difference (post-treatment - pretreatment) in the Telmisartan group was 1.522%, while in Azilsartan group it was 0.212%. The mean HbA1c difference between the telmisartan and Azilsartan groups was 1.309 and is statistically significant p = 0.000, which is summarized in Table 2.

The mean fasting blood sugar difference (post-treatment-pretreatment) in the telmisartan group was 30.290, while in Azilsartan, it was 15.032. The impact on fasting blood sugar was more with telmisartan in comparison to Azilsartan. The difference between Telmisartan and Azilsartan is 15.258, which is statistically not significant $P = 0.391$.

The mean post-prandial blood sugar difference (post-treatment-pretreatment) in Telmisartan is 49.548, and this difference is statistically significant $P = 0.000$. The mean blood sugar (PP) difference in Azilsartan is 26.838, which is statistically significant with $P = 0.004$. The

Bhati *et al. The Egyptian Journal of Internal Medicine*   (2023) 35:72

Page 3 of 5

Table 1 The basic parameters of 62 patients

Parameters		Telmisartan group	Azilsartan group
Age (years)		59.07	54.71
Gender	Male	19	14
	Female	12	17
Glycemic profile	FBS (mg/dl)	170.7	171.32
	PPBS (mg/dl)	228.1	228.1
	HbA1C (%)	8.9	8.9
Blood pressure	Systolic (mmHg)	136 ± 8	142 ± 6
	Diastolic (mmHg)	88 ± 4	86 ± 10
Medications	Oral hypoglycaemic agent (Metformin)	1 g/d	1 g/d
	Anti-hypertensive	80 mg	40 mg
BMI (kg/m^2)		24.92	25.12

Table 2 The mean HbA1c difference between the telmisartan and Azilsartan groups

	Drugs	Baseline	6 Months	*P* value
Fasting blood sugar (mg/dl)	Telmisartan	170.74 ± 74.41	140.45 ± 75.30	0.091
	Azilsartan	171.32 ± 56.90	156.29 ± 47.51	0.000
Post prandial blood sugar (mg/dl)	Telmisartan	228.13 ± 89.64	178.58 ± 39.82	0.000
	Azilsartan	228.10 ± 78.46	201.58 ± 47.59	0.004
HbA1c (%)	Telmisartan	8.9 ± 1.72	7.4 ± 0.74	0.000
	Azilsartan	8.9 ± 1.99	8.7 ± 1.70	0.212

impact on postprandial blood sugar is more with telmisartan in comparison to Azilsartan. The mean blood sugar (PP) difference between the two study groups is 22.70, and it is not statistically significant $P=0.115$.

Blood pressure was controlled optimally in both groups. The difference between both the groups was not significant, which is shown in Fig. 1.

Discussion

This study revealed that blood sugar (fasting) improves at 6 months follow-up in both the treatment group, more in the Telmisartan group in comparison to the Azilsartan group. There is no significant difference in blood sugar (fasting) between these two drugs (Table 2). Similar results were observed in earlier studies. [6, 9–12] Post-prandial blood sugar improved in both Telmisartan and Azilsartan groups, more in the Telmisartan group (Table 2). HbA1C improves in both Telmisartan as well as Azilsartan after 6 months as compared to baseline. Improvement was more with Telmisartan (Table 2).

They all suggest the beneficial effects of Azilsartan and telmisartan in improving insulin sensitivity. In one of the animal studies, it was found that Azilsartan is very much effective in reducing insulin resistance [11].

One of the studies on diabetic KK-AY mice found that Azilsartan was superior to Candesartan in improving glucose intolerance, insulin sensitivity, and inducing adipocyte differentiation [6].

Telmisartan has been found to increase insulin sensitivity in non-diabetic patients with essential hypertension [13]. Telmisartan, an angiotensin II receptor antagonist, is also a partial PPARγ agonist. In male Sprague Dawley rats, fed a high-fat and high-carbohydrate diet for 3 months, telmisartan given along with the diet reduced weight gain as well as glucose, insulin, and triglyceride levels [7, 13]. Adiponectin has been shown to have insulin-sensitizing properties in murine models and studies have shown that some of the beneficial effects of peroxisome proliferator–activated receptor γ (PPAR γ) activation are mediated by the increase in adiponectin levels [14, 15].

Telmisartan, an angiotensin II type 1 (AT1) receptor antagonist, is a partial PPARγ nuclear receptor agonist [13] It is also established that telmisartan reduces insulin resistance in Hypertensive patients with metabolic syndrome [8] Telmisartan significantly reduces plasma glucose in a double-blind, parallel-group, randomized study on patients with metabolic syndrome [13].

Bhati *et al. The Egyptian Journal of Internal Medicine* (2023) 35:72

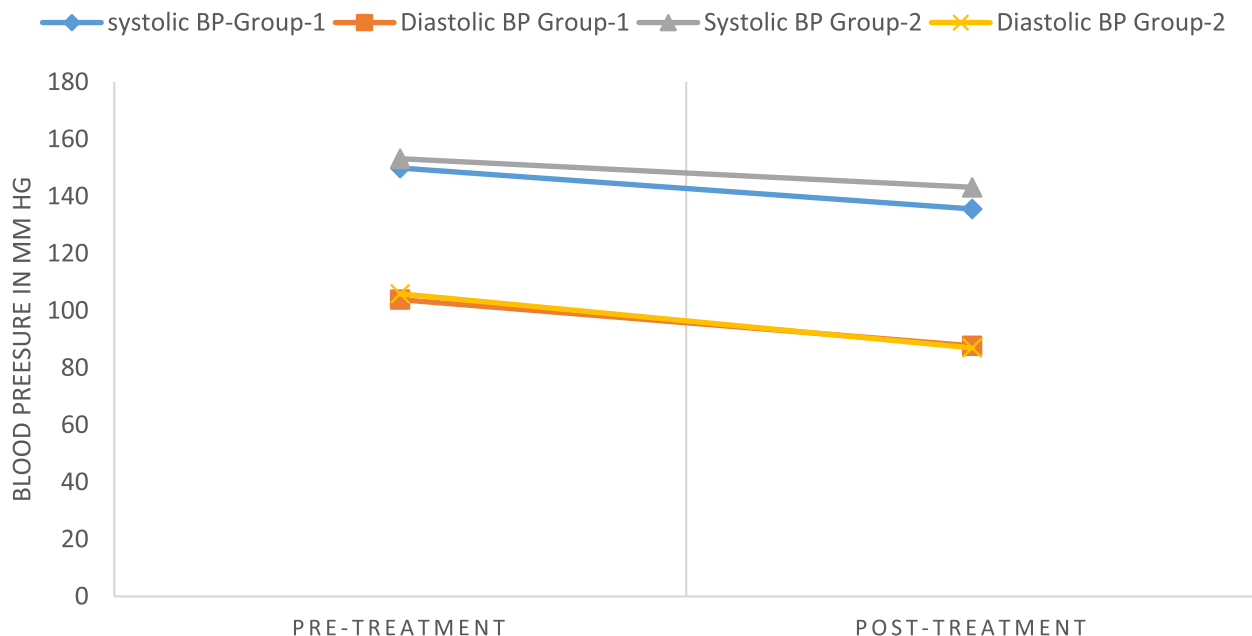Page 4 of 5

BLOOD PRESSURE IN BOTH GROUP

Fig. 1 Blood pressure in both groups

Another study showed improvement in all the three indices of glucose and insulin metabolism like fasting plasma glucose, OGTT, and HbA1C [13]. Similar results were found in another study of telmisartan [14].

This study had a few limitations. The number of patients in our study is small, compared to various studies across the globe. Because our study was conducted at a single center, a tertiary care hospital, hence our results cannot be generalized to the general population, necessitating the need for further large-scale studies.

Conclusion

Telmisartan has a better impact on the glycemic profile in diabetic patients, in comparison to Azilsartan, as a part of its pleotropic effects.

Abbreviations

CHD	Coronary heart disease
CHF	Congestive heart failure
PAD	Peripheral arterial disease
ARBs	Angiotensin receptor blockers
IDF	International diabetes federation
T2DM	Type 2 diabetes mellitus
OGTT	Oral glucose tolerance test
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
CBC	Complete blood count
PPARγ	Peroxisome proliferator-activated receptor gamma

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was started after getting the ethical clearance from the institutional ethical committee of Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, UP, India. Proper consent was also obtained from every patient before enrolment in study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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