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Original Research Article

Drug-Disease Interactions: Effect of Commonly Prescribed Antihypertensives on Glycemic Control in Diabetic Patients

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Abstract:

Background: Hypertension and diabetes mellitus are two chronic diseases that often coexist, with profound implications for accelerating cardiovascular and renal disease. Antihypertensive drugs are at the heart of managing hypertension, but their effects on glucose metabolism can worsen or enhance glycemic control. It is critical to elucidate the drug–disease interactions between frequently used antihypertensives and diabetes to maximize therapeutic benefits.

Objectives: This research sought to assess the impact of the most frequently prescribed classes of antihypertensive agents—namely, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), beta-blockers, calcium channel blockers (CCBs), and thiazide diuretics—on glycemic status among patients with type 2 diabetes mellitus (T2DM). More specifically, it aimed to determine changes in fasting blood glucose (FBG), glycated hemoglobin (HbA1c), and insulin sensitivity related to chronic use of these drugs.

Materials and Methods: A cross-sectional observational study was done in 300 patients with T2DM and coincidental hypertension who visited a tertiary care hospital. The patients were classified according to their initial antihypertensive treatment. Clinical information, laboratory values such as FBG and HbA1c, and duration of treatment were examined. Statistical analysis was conducted using ANOVA and regression models to establish associations between drug categories and glycemic parameters, while adjusting for confounders such as age, BMI, and lifestyle.

Results: ACEIs and ARBs had a neutral to favorable impact on glycaemic control, with mean HbA1c levels having significant improvement over baseline ($p<0.05$). CCBs had little effect, while small rises in FBG and HbA1c characterized thiazide diuretics. Beta-blockers, especially non-selective ones, had a trend towards worsening insulin resistance, indicated by increased mean glucose ($p<0.05$).

Conclusion: Antihypertensive treatment has mixed influences on glycemic control in diabetic individuals. ACEIs and ARBs are metabolically neutral, whereas thiazide diuretics and beta-blockers can worsen glucose control. Patients with diabetes should be carefully chosen for antihypertensive therapy to avoid adverse metabolic consequences and to improve disease management overall.

Keywords: Antihypertensives, Diabetes Mellitus, Glycemic Control, ACE inhibitors, Beta-blockers, Thiazide Diuretics, Drug–disease interactions.

Introduction

Diabetes mellitus and hypertension are two of the most common chronic conditions globally, commonly found in the same patient. According to epidemiological facts and figures, it has been estimated that approximately 60–80% of T2DM patients will later develop hypertension, incurring a high risk of cardiovascular morbidity, nephropathy, and premature death [1]. It is quite a therapeutic challenge to have these diseases in the same person because both diseases have to be treated for a long time with medications, which can cause complicated drug–disease and drug–drug interactions [2].

Antihypertensive treatment is crucial in the avoidance of vascular disorders and the attainment of the target blood pressure in diabetes patients. Antihypertensives such as ACEIs, ARBs, beta-blockers, CCBs, and thiazide diuretics are frequently used. Although these drugs are potent in lowering blood pressure, their effect on glucose metabolism ranges widely [3]. For example, ACEIs and ARBs are also said to possess beneficial metabolic properties, enhancing insulin sensitivity and retarding the onset of diabetes in those at high risk. Conversely, thiazide diuretics and some beta-blockers have been implicated in the deterioration of

glycemic control through decreased insulin sensitivity and augmented fasting plasma glucose concentrations [4].

The interaction between antihypertensive therapy and glucose control has significant clinical implications. Inappropriately choosing antihypertensive agents can undermine glycemic control, thus exacerbating diabetic complications despite ideal blood pressure control [5]. This emphasizes the importance of a selective and individualized prescription of antihypertensives in diabetic patients. In addition, knowledge of the metabolic effects of various classes of antihypertensive agents can help in designing dual-purpose therapy to reduce blood pressure and preserve glycemic control [6].

In view of the increased global prevalence of diabetes and hypertension, and the trend towards combination pharmacotherapy, the effects of antihypertensives on glycemic measures are of increasing interest [7]. This study was thus set up to examine the impact of frequently prescribed antihypertensive medications on FBG, HbA1c, and insulin sensitivity in T2DM patients. The results are anticipated to offer information on the best treatment modalities for controlling hypertensive diabetic individuals with minimal adverse metabolic consequences.

The current study intends to compare the effect of frequently used antihypertensive drug classes—ACE inhibitors, ARBs, beta-blockers, calcium channel blockers, and thiazide diuretics—on type 2 diabetes mellitus patients' glycemic control. It intends to investigate the change in fasting blood glucose, glycated hemoglobin, and insulin sensitivity with long-term use of these drugs. The study also wants to determine metabolically helpful and harmful antihypertensive options, thus directing clinicians towards optimizing therapy for diabetic hypertensive patients.

Methodology

Study Design: A cross-sectional observational hospital-based study was done to assess the effect of frequently used antihypertensive medications on the glycemic control in type 2 diabetes mellitus (T2DM) patients.

Study Setting: The study was performed in the Department of Medicine in a tertiary hospital that receives a population of diabetic and hypertensive patients from both rural and urban areas.

Study Population: The population consisted of T2DM patients with concomitant hypertension visiting the hospital's inpatient and outpatient facilities over the study period.

Study Duration: The duration of the study was one year.

Sample Size: 194 patients were included using the proper sampling techniques to acquire adequate statistical power.

Inclusion Criteria

- Adult patients aged 30 years and above diagnosed with T2DM as per ADA standards.
- Patients with a diagnosed history of hypertension, taking antihypertensive drugs for a minimum of 6 months.
- Patients are willing to give informed consent.

Exclusion Criteria

- Patients with type 1 diabetes mellitus or gestational diabetes.
- Patients taking corticosteroids or other medications that interfere with glucose metabolism.
- Patients with acute illness, severe hepatic or renal impairment, or secondary hypertension.
- Pregnant and breastfeeding women.

Sampling Technique: A purposive sampling method was utilized to enroll eligible patients who fulfilled the study criteria and were willing to participate.

Data Collection: The data were gathered through a pretested structured proforma, which entailed demographic information, duration of diabetes and hypertension, type and duration of antihypertensive treatment, and lifestyle. Laboratory tests were carried out for fasting blood glucose (FBG), postprandial glucose (PPG), and glycated hemoglobin (HbA1c).

Study Procedure: Eligible patients were divided into categories according to their antihypertensive regimen: ACE inhibitors, ARBs, beta-blockers, calcium channel blockers, and thiazide diuretics. Combination therapy cases were separately identified. Clinical evaluations and biochemical tests were conducted according to routine protocols. The effect of each class of drugs on the glycemic parameters (FBG and HbA1c) was measured.

Statistical Analysis: Data analysis was performed using SPSS software. Descriptive statistics (standard deviation, mean) were employed to describe patient parameters. ANOVA and Chi-square tests were used to compare glycemic parameters across groups. Multivariate regression analysis was done controlling for confounding variables like age, BMI, duration of diabetes, and lifestyle variables. P-value <0.05 was taken as statistically significant.

Results

Table 1 presents the baseline participant characteristics among the five antihypertensive groups, which were generally comparable. They had

no statistically significant differences in age, gender distribution, BMI, duration of diabetes, or hypertension duration ($p > 0.05$). This shows that the study groups were adequately matched so as not to incur baseline bias, hence enabling an equitable comparison of the impact of antihypertensives on glycemic control.

Table 1: Baseline Characteristics of Study Participants (n=194)

Variable	ACEIs (n=50)	ARBs (n=45)	CCBs (n=40)	Thiazides (n=30)	Beta-blockers (n=29)	p-value
Age (years, mean ± SD)	57.2 ± 8.1	56.8 ± 7.9	58.5 ± 8.4	59.0 ± 7.2	58.3 ± 8.6	0.412
Male (%)	58%	60%	55%	52%	59%	0.537
BMI (kg/m², mean ± SD)	27.1 ± 3.2	26.8 ± 3.1	27.4 ± 3.3	28.0 ± 3.4	27.9 ± 3.1	0.248
Duration of DM (years)	8.1 ± 4.2	8.3 ± 4.5	8.6 ± 4.0	8.9 ± 4.1	9.2 ± 4.4	0.604
Duration of HTN (years)	6.5 ± 3.1	6.3 ± 3.4	6.7 ± 3.2	7.0 ± 3.5	6.9 ± 3.6	0.559

Figure 1 illustrates the differential impact of antihypertensives on glycemic control. ACEIs and ARBs showed a beneficial decrease in HbA1c, whereas CCBs showed a neutral response. However, thiazides and beta-blockers were characterized by an increase in HbA1c, reflecting potential deterioration of glycemic status.

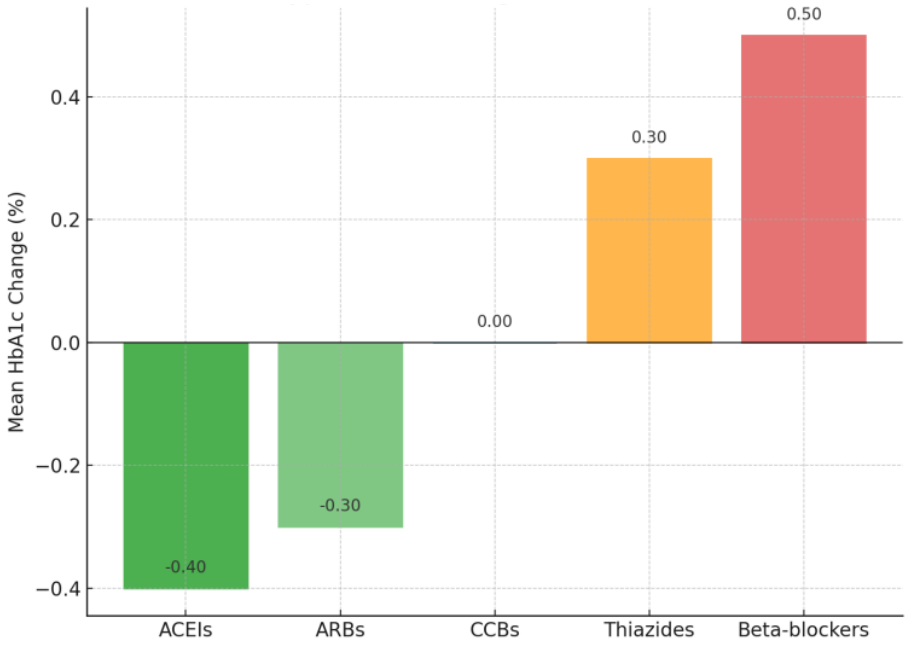

Figure 1: Effect of Antihypertensive Drugs on HbA1c in T2DM Patients

Figure 2 shows the distribution of patients by antihypertensive classes. More patients received ACE inhibitors (25.8%), followed by ARBs (23.2%) and CCBs (20.6%). Thiazides (15.5%) and beta-blockers (14.9%) were used less, indicating the clinicians' choice of metabolically neutral drugs in diabetic patients.

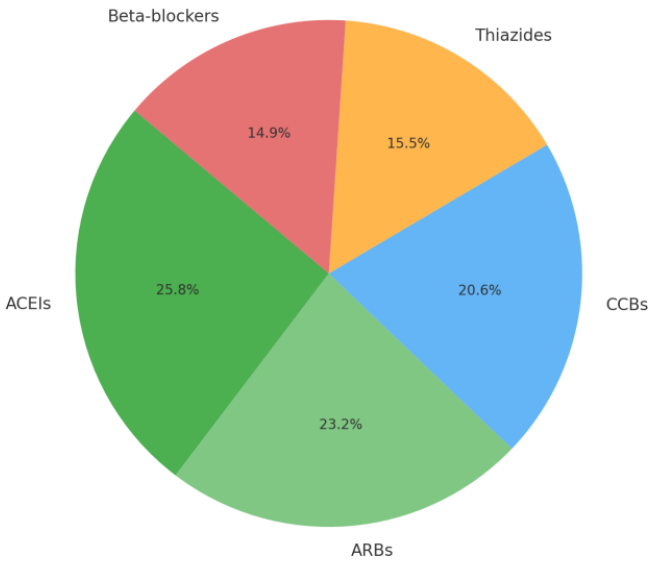

Figure 2: Distribution of Patients by Antihypertensive Drug Class

Table 2 indicates remarkable contrasts in glycemic measures across antihypertensive classes. Fasting blood glucose, postprandial glucose, and HbA1c values were lower in patients receiving ACEIs and ARBs, reflecting improved metabolic control. The CCBs presented intermediate with a neutral effect on glycemic control. Thiazides and beta-blockers were linked with increased glucose concentration and HbA1c, reflecting a detrimental impact on diabetes control.

Table 2: Comparison of Glycemic Parameters across Antihypertensive Groups

Parameter	ACEIs (n=50)	ARBs (n=45)	CCBs (n=40)	Thiazides (n=30)	Beta-blockers (n=29)	p-value
Fasting Blood Glucose (mg/dL)	132 ± 18	134 ± 17	137 ± 20	145 ± 22	149 ± 21	0.018*
Postprandial glucose (mg/dL)	182 ± 25	184 ± 26	187 ± 27	198 ± 28	202 ± 30	0.021*
HbA1c (%)	7.1 ± 0.8	7.2 ± 0.7	7.4 ± 0.9	7.8 ± 1.0	8.0 ± 0.9	0.009*

***Statistically significant at p < 0.05**

Table 3 demonstrates that ACEIs and ARBs had a notable effect on improving insulin sensitivity, as evidenced by the decrease in HOMA-IR scores ($p < 0.05$). CCBs generated a tiny, non-significant change, which indicated an effect on metabolism that was neutral. In contrast, thiazides and beta-blockers significantly increased HOMA-IR, signifying deteriorating insulin resistance. The observations point toward ACEIs and ARBs as being the metabolically safe options for diabetic hypertensive patients.

Table 3: Effect on Insulin Sensitivity Index (HOMA-IR)

Drug Class	Baseline HOMA-IR (mean ± SD)	Follow-up HOMA-IR (mean ± SD)	Mean Change	p-value
ACEIs (n=50)	3.5 ± 1.0	3.2 ± 0.9	-0.3	0.042*
ARBs (n=45)	3.6 ± 1.1	3.3 ± 1.0	-0.3	0.038*
CCBs (n=40)	3.7 ± 1.2	3.6 ± 1.1	-0.1	0.251
Thiazides (n=30)	3.8 ± 1.3	4.1 ± 1.4	+0.3	0.033*
Beta-blockers (n=29)	3.9 ± 1.2	4.3 ± 1.3	+0.4	0.029*

***Statistically significant at p < 0.05**

Discussion

This study is brought to light to detail the differing metabolic effects of routinely prescribed antihypertensive drugs in patients with type 2 diabetes mellitus (T2DM). Our findings showed that ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) had a favorable or no effect on

glycemic parameters such as fasting blood glucose, HbA1c, and insulin sensitivity. These results are in line with previous large-scale studies like the HOPE study and the LIFE study, which reported that ACEIs and ARBs not only better control blood pressure but also increase insulin sensitivity and decrease the development of new-onset diabetes [8,9]. Mechanistically, these agents are thought to increase glucose uptake in peripheral tissues and maintain pancreatic beta-cell function by decreasing angiotensin II-mediated oxidative stress and inflammation. Therefore, the findings of the present study contribute to the increasing body of evidence favoring ACEIs and ARBs as first-line treatment for diabetic hypertensive patients due to their dual therapeutic efficacy in both cardiovascular and metabolic areas.

Calcium channel blockers (CCBs), in our analysis, had a predominantly neutral impact on glycemic status, with no altering effect on fasting glucose, HbA1c, or insulin resistance. Consistent with previous observational and intervention studies, these have consistently described that CCBs lower blood pressure well but have minimal effects on glucose metabolism. The ASCOT-BPLA trial, for example, has suggested that regimens of CCBs are metabolically neutral compared to beta-blocker–thiazide combinations [10,11]. Although CCBs are unlikely to be metabolically beneficial, their neutrality is clinically valuable, most notably when selecting add-on treatments in patients where metabolic stability is an issue. Therefore, their place continues to be vital in diabetics, most notably where contraindications to renin–angiotensin blockers are present [12].

On the other hand, thiazide diuretics and beta-blockers were linked with worsening glycemic control in this study, as previously documented. Previous studies, such as the ALLHAT trial, have described how thiazides can increase fasting glucose and HbA1c, primarily due to decreased insulin sensitivity and also potassium loss [13,14]. Likewise, beta-blockers—particularly non-selective ones—have been linked with reduced glucose tolerance and a rise in insulin resistance, as documented in the UKPDS study [15]. Our results echo these findings, as both medication classes were associated with worsening glycemic parameters and rising HOMA-IR scores. Although these drugs continue to be helpful in the management of blood pressure and cardiovascular risk, their adverse effect on glucose metabolism highlights the importance of balancing their use in diabetic patients [16]. In general, the current study highlights the importance of individualized choice of antihypertensives, where ACEIs and ARBs are given first preference due to their metabolic effects. CCBs are regarded as having no prejudicial impact, and thiazides and beta-blockers are used with caution in high-risk patients with adverse glycemic control.

Conclusion

This study concludes that antihypertensive medications have differing impacts on glycemic control in type 2 diabetes mellitus patients. ARBs and ACE inhibitors had favorable or neutral metabolic effects, enhancing HbA1c and insulin sensitivity, whereas calcium channel blockers had mainly neutral effects on these parameters. Thiazide diuretics and beta-blockers were linked to deteriorating glycemic indices, such as increased fasting glucose, HbA1c, and decreased insulin sensitivity. These results are consistent with the literature, supporting judicious selection of antihypertensive therapy in diabetic patients. Agents like ACEIs and ARBs should be given priority for their dual cardiovascular and metabolic protection. At the same time, thiazides and beta-blockers must be used cautiously to avoid undesirable metabolic effects and maximize long-term disease control.

Limitations

The design of the study was cross-sectional, which constrained its potential to demonstrate causal relationships between antihypertensive medication and glycemic change. The sample was moderate in size and from one tertiary hospital, which could limit generalizability. Lifestyle and dietary variables, although accounted for, could not have been strictly controlled for, so they could have had an impact on glycemic endpoints.

Recommendations

Future studies should employ multicenter, longitudinal cohort studies with larger sample sizes to confirm these observations. Randomized controlled trials are required to determine causality and more accurately quantify long-term metabolic impacts of antihypertensives. Clinicians should individualize antihypertensive treatment in diabetic patients by favoring metabolically neutral medications such as ACEIs and ARBs, and carefully monitoring glycemic factors when prescribing thiazides or beta-blockers.

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