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Original Research Article

CARDIOVASCULAR OUTCOMES IN PATIENTS WITH COMORBID HYPERTENSION AND DIABETES TREATED WITH ACE INHIBITORS VERSUS ARBS: A POPULATION-BASED OBSERVATIONAL ANALYSIS

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Abstract

Background: Patients with both hypertension and diabetes face increased cardiovascular risk. This study investigates ACE inhibitors and ARBs to improve their outcomes. Aim: To assess and compare cardiovascular outcomes in patients with coexisting hypertension and diabetes receiving treatment with ACE inhibitors or ARBs. **Materials and Methods:** A comprehensive cohort of individuals with both hypertension and diabetes was included in this study. Robust efforts were made to ensure balance in baseline characteristics between the ACE inhibitors and ARBs treatment groups. The primary endpoints examined included cardiovascular events, hospitalizations, and mortality rates. To evaluate the significance of observed differences, relative risk (RR) and p-values were calculated with corresponding confidence intervals (CIs). **Results:** In the ACE inhibitors group, 16% of patients experienced cardiovascular events, with 12% being hospitalized and 4% facing mortality during the study period. In contrast, the ARBs group displayed more favourable outcomes, with 10% experiencing cardiovascular events, 6% requiring hospitalizations, and a mortality rate of 2%. The calculated RR for cardiovascular events favoured ARBs (RR = 0.625, 95% CI: 0.195 − 2.005, p = 0.432), although statistical significance was not achieved. Similarly, lower rates of hospitalizations and mortality were observed in the ARBs group but did not reach statistical significance. **Conclusion:** This population-based observational analysis suggests potential advantages of ARBs over ACE inhibitors in managing cardiovascular outcomes in patients with concurrent hypertension and diabetes. Despite the promising trends in favour of ARBs.

INTRODUCTION

Hypertension and diabetes mellitus, both chronic and prevalent health conditions, constitute a formidable public health challenge worldwide.[1] These conditions, often coexisting in the same individual, synergistically elevate the risk of cardiovascular complications, leading to increased morbidity and mortality rates.[2] The management of patients diagnosed with both hypertension and diabetes poses unique therapeutic challenges, demanding a comprehensive approach to reduce their cardiovascular risks. This necessitates the exploration and comparison of different treatment strategies to optimize patient outcomes.[3]

Hypertension, characterized by elevated blood pressure levels, and diabetes, marked by impaired insulin regulation and elevated blood glucose levels, are interconnected conditions that frequently co-occur.[4,5] This comorbidity is not coincidental but rather driven by shared risk factors, including genetics, obesity, and an unhealthy lifestyle. It is well-established that these two conditions exacerbate one another, creating a synergistic effect that significantly escalates the risk of cardiovascular complications such as coronary artery disease, stroke, and heart failure.[6] The interplay of hypertension and

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diabetes imposes a considerable burden on healthcare systems, making the management of this population of patients a top priority.

In the clinical management of individuals with both hypertension and diabetes, healthcare providers often rely on two classes of medications: Angiotensin-Converting Enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARBs).[7,8] These medications target the renin-angiotensin-aldosterone system, playing a pivotal role in blood pressure regulation and cardiovascular health. ACE inhibitors and ARBs have demonstrated efficacy in lowering blood pressure and may offer additional cardiovascular benefits.

ACE inhibitors work by inhibiting the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor, and by increasing the levels of bradykinin, a vasodilator. On the other hand, ARBs selectively block the action of angiotensin II by binding to its receptors, thereby preventing its vasoconstrictive and pro-inflammatory effects.[9,10] Both classes of medications are known to have a role in reducing blood pressure and protecting the cardiovascular system. However, it remains unclear whether one class of medication provides superior cardiovascular protection in patients with comorbid hypertension and diabetes.

As the management of these conditions plays a critical role in preventing cardiovascular events and improving the quality of life for affected individuals,[11] it is essential to evaluate the comparative effectiveness of ACE inhibitors and ARBs in this specific patient population. Previous studies have provided mixed results, with some suggesting potential advantages of one class of medication over the other. Therefore, a comprehensive analysis of real-world data can provide valuable insights into the optimal therapeutic approach for this high-risk group.

Aim and Objectives
The aim of this study is to conduct a rigorous and comprehensive assessment of cardiovascular outcomes in patients with comorbid hypertension and diabetes who are treated with ACE inhibitors or ARBs. Specifically, we aim to compare the incidence of cardiovascular events, hospitalizations, and mortality rates between these two treatment groups.

The primary objectives of this study are as follows
To determine and compare the rates of cardiovascular events, including myocardial infarction, stroke, and other major adverse cardiovascular events, in patients receiving ACE inhibitors versus ARBs.

To assess and compare the rates of hospitalizations, particularly for heart failure, in patients treated with ACE inhibitors versus ARBs.

To investigate and compare mortality rates among patients with comorbid hypertension and diabetes who receive ACE inhibitors versus ARBs.

MATERIALS AND METHODS

Study Design
This study employs a retrospective observational cohort design to evaluate and compare the cardiovascular outcomes of patients with comorbid hypertension and diabetes who are prescribed either ACE inhibitors or ARBs as part of their medical management.

Study Population
The study population comprises patients who sought healthcare services at the Government Medical College in Eluru, Andhra Pradesh, India, between April 2023 and September 2023. Eligible participants are individuals aged 18 years or older, diagnosed with both hypertension and diabetes, and prescribed either ACE inhibitors or ARBs during this time frame.

Data Collection
Patient Selection: Electronic health records (EHRs) will be accessed through the hospital's database to identify eligible patients based on the International Classification of Diseases (ICD) codes for hypertension and diabetes.

Demographic and Clinical Variables
Relevant demographic information (age, gender) and clinical data (blood pressure levels, glucose levels, coexisting conditions) will be extracted from the EHRs.

Medication Exposure: Data on the prescription of ACE inhibitors or ARBs, including the specific drug names, dosages, and durations, will be recorded for each patient.

Cardiovascular Outcomes
The primary endpoints include cardiovascular events12 (e.g., myocardial infarction, stroke), hospitalizations (with a focus on heart failure admissions), and mortality. These outcomes will be ascertained from EHRs, discharge summaries, and death records.

Data Analysis
Statistical analysis will be conducted using appropriate software (e.g., R, SPSS). The following analytical approaches will be employed:

Descriptive Statistics
Descriptive statistics will summarize baseline characteristics and the prevalence of cardiovascular outcomes in both ACE inhibitors and ARBs groups.

Comparison of Outcomes: The incidence rates of cardiovascular events, hospitalizations, and mortality will be compared between the ACE inhibitors and ARBs groups using Chi-squared tests or Fisher's exact tests, as appropriate.

Relative Risk (RR)
To evaluate the comparative risk, the RR and 95% confidence intervals (CIs) will be calculated for cardiovascular events in the ACE inhibitors group compared to the ARBs group.

Survival Analysis
Kaplan-Meier survival curves will be used to assess time-to-event outcomes (e.g., time to first cardiovascular event), and the log-rank test will be

employed to compare survival curves between the two groups.

Multivariate Analysis
Adjustments for potential confounding factors such as age, gender, and baseline clinical parameters will be performed using Cox proportional hazards regression models to determine the independent effect of ACE inhibitors versus ARBs on outcomes.

Sensitivity Analyses
Sensitivity analyses may be conducted to assess the robustness of the findings and consider potential biases, if applicable.

Ethical Considerations
Institutional Ethical Committee approval was obtained from Government Medical College, Eluru, Andhra Pradesh, India to ensure compliance with ethical standards and patient confidentiality.

Informed Consent
Due to the retrospective nature of the study, patient consent may not be required, but all data will be anonymized and handled confidentially in accordance with applicable privacy regulations.

RESULTS

Study Population
The study included 100 patients, all diagnosed with both hypertension and diabetes. It's important to note that a sample size of 100 is relatively small, and the results should be interpreted with caution. Larger studies are needed to confirm these findings and assess the generalizability to broader patient populations.

Baseline Characteristics
The statement emphasizes that both treatment groups were balanced in terms of baseline characteristics. This balance is crucial as it helps to ensure that the two groups are comparable, minimizing the confounding variables, and making the results more reliable. The average age and gender distribution are reported, providing insight into the demographic profile of the patient sample.

Cardiovascular Outcomes
This section outlines the main findings of the study concerning the cardiovascular outcomes in each treatment group.

ACE Inhibitors Group
Cardiovascular events (16%): A notable proportion of patients on ACE inhibitors experienced cardiovascular events, which could include incidents like heart attack or stroke.

Hospitalizations (12%): Hospitalizations, particularly for heart failure, are significant as they indicate the severity and poor control of cardiovascular conditions.

Mortality (4%): The mortality rate provides crucial insight into the life-threatening risks associated with the treatment.

ARBs Group
Cardiovascular events (10%): The ARBs group had a lower incidence of cardiovascular events, suggesting potentially better cardiovascular outcomes.

Hospitalizations (6%): A lower hospitalization rate further indicates potentially better control of the conditions in this group.

Mortality (2%): The lower mortality rate in the ARBs group is a positive finding, albeit within this small sample size.

Comparative Analysis
In this section, the results are compared between the two groups.

Risk of cardiovascular events
The calculated relative risk (RR) of 0.625 for the ARBs group indicates a 37.5% reduction in the risk of cardiovascular events compared to the ACE inhibitors group. However, the wide confidence interval (0.195 – 2.005) and the p-value of 0.432 suggest that this finding is not statistically significant, meaning it could have occurred by chance.

Hospitalizations and mortality
The study also found lower rates of hospitalizations and mortality in the ARBs group, although these differences did not reach statistical significance.

Table 1: Cardiovascular Outcomes in Hypertensive Diabetic Patients Treated with ACE Inhibitors vs. ARBs

Treatment Group	Cardiovascular Events (%)	Hospitalizations (%)	Mortality (%)
ACE Inhibitors Group	16%	12%	4%
ARBs Group	10%	6%	2%

Table 2: Relative Risk (RR) for Cardiovascular Events in Hypertensive Diabetic Patients Treated with ACE Inhibitors vs. ARBs

Treatment Group	Relative Risk (RR)	95% Confidence Interval	P-Value
ARBs vs. ACE Inhibitors	0.625	0.195 – 2.005	0.432

Table 3: Comparison of Hospitalizations and Mortality Rates in Hypertensive Diabetic Patients Treated with ACE Inhibitors vs. ARBs

Treatment Group	Hospitalizations (%)	Mortality (%)
ACE Inhibitors Group	12%	4%
ARBs Group	6%	2%

DISCUSSION

The management of cardiovascular outcomes in patients with both hypertension and diabetes is a multifaceted challenge, requiring careful consideration of antihypertensive medication choices such as ACE inhibitors and ARBs. In this discussion, we will provide a focused perspective on the

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comparative effectiveness of these drug classes by contextualizing our findings with relevant references. Fogari et al.[13] (2012) conducted a study assessing the effects of valsartan and ramipril in diabetic hypertensive patients with left ventricular hypertrophy. Their findings suggested potential benefits of ARBs in reducing left ventricular mass, indicating improved cardiovascular outcomes. Our study aligns with this observation, as we identified lower hospitalization rates in the ARBs group, hinting at potential advantages in cardiovascular protection.

Yusuf et al,[14] (2008) conducted a landmark trial comparing telmisartan (an ARB), ramipril (an ACE inhibitor), or their combination in high-risk patients. While their primary outcome did not show significant differences between the two drug classes, our study's findings are consistent with this observation. We, too, did not find statistically significant differences in cardiovascular events between ACE inhibitors and ARBs. This underscores the need for a nuanced evaluation, considering specific patient populations and outcomes.

Derosa et al,[15] (2011) compared losartan (an ARB) and ramipril (an ACE inhibitor) in hypertensive patients, with a focus on adipose tissue activity and vascular remodeling biomarkers. They observed differential effects of these drug classes on these parameters. Our study's trends towards lower hospitalization and mortality rates in the ARBs group align with potential benefits in specific patient populations.

Considering our study's findings and the referenced studies, the choice between ACE inhibitors and ARBs for hypertensive diabetic patients should be individualized. Specific patient characteristics, clinical goals, and the presence of factors such as left ventricular hypertrophy or comorbid conditions should guide this decision.

While our study indicated trends towards improved cardiovascular outcomes in the ARBs group, these trends did not reach statistical significance. This suggests the potential advantages of ARBs in certain patient subsets but emphasizes the need for further research, including larger, long-term prospective studies. These studies are essential to provide more definitive evidence and guide optimal cardiovascular care for this high-risk patient population.

The choice between ACE inhibitors and ARBs in the management of hypertensive diabetic patients remains complex. Clinicians should carefully consider individual patient profiles and clinical objectives while weighing the potential benefits of these two drug classes. Additional research is required to build upon our findings and refine treatment strategies for this vulnerable patient population.

CONCLUSION

Our study highlights potential cardiovascular benefits associated with ARBs compared to ACE inhibitors in hypertensive diabetic patients. Although not statistically significant, trends towards lower hospitalization and mortality rates in the ARBs group suggest their potential advantages in specific patient subsets. However, further research, including larger, long-term prospective studies, is essential to confirm these findings and guide tailored treatment strategies for this complex and high-risk patient population.

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