Section: Pharmacology

Original Research Article

COMPARATIVE OUTCOMES OF FIRST-LINE ANTIHYPERTENSIVE AGENTS ON RENAL FUNCTION IN HYPERTENSIVE PATIENTS WITH CHRONIC KIDNEY DISEASE: AN OBSERVATIONAL COHORT STUDY

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Abstract

Background: Hypertensive patients with chronic kidney disease (CKD) often require first-line antihypertensive agents**. Aim: To** compare the effects of four primary first-line antihypertensive agents on renal function in hypertensive patients with CKD over a 12-month period. **Materials and Methods:** A balanced cohort of 100 patients, equally divided into four groups, were administered the primary first-line antihypertensive agents: ACE inhibitors (ACEIs), Angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and Beta-blockers. Outcomes assessed over 12 months included changes in estimated glomerular filtration rate (eGFR), incidence of acute kidney injury (AKI) events, and alterations in proteinuria. **Results:** Over the 12-month period: eGFR Changes: The ACEIs group recorded a decrease of 2.5 ml/min/1.73m^2. ARBs patients had a decline of 2.0 ml/min/1.73m^2, suggesting marginally better kidney protection compared to ACEIs. The CCBs and Beta-blockers groups exhibited declines of 3.0 and 3.5 ml/min/1.73m^2, respectively, indicating potential concerns regarding their renal protective capabilities. AKI Incidence: The ARBs group had the lowest AKI incidence at 4%. In comparison, ACEIs, CCBs, and Beta-blockers groups showed AKI incidences of 8%, 12%, and 16%, respectively. Proteinuria Changes: ARBs led with the most substantial proteinuria reduction at 15 mg/g. ACEIs, Beta-blockers, and CCBs observed reductions of 10 mg/g, 8 mg/g, and 5 mg/g, respectively. **Conclusion:** Among the observed antihypertensive agents, ARBs may offer better renal protection in hypertensive CKD patients, as evidenced by lower declines in eGFR, reduced AKI events, and greater proteinuria reduction. Further randomized studies are warranted to confirm these findings.

INTRODUCTION

Hypertension, a prevalent cardiovascular condition, frequently coexists with chronic kidney disease (CKD), posing substantial challenges in patient management.[1] Patients suffering from both conditions require effective antihypertensive therapy to mitigate the risk of cardiovascular events and slow the progression of CKD. The selection of first-line antihypertensive agents in this population is a critical decision, as it can significantly impact renal function and overall patient outcomes.[2,3] This observational cohort study investigates the comparative outcomes of four primary first-line antihypertensive agents—Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Blockers (ARBs), Calcium Channel Blockers (CCBs), and Beta-blockers—on renal function in hypertensive patients with CKD.

Hypertension and CKD are two intertwined medical conditions that share a complex pathophysiological relationship. Hypertension is a well-established risk factor for CKD development and progression. CKD, in turn, exacerbates hypertension, creating a detrimental cycle that requires effective management.[4,5] To address this challenge, clinicians often turn to first-line antihypertensive agents, each

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with unique mechanisms of action and potential impacts on renal function.

ACEIs, by inhibiting the conversion of angiotensin I to angiotensin II, reduce vasoconstriction and aldosterone release, thereby lowering blood pressure and potentially preserving renal function. ARBs, on the other hand, block angiotensin II receptors, leading to similar blood pressure reduction and renoprotective effects.[6,7] CCBs act by dilating blood vessels, decreasing peripheral resistance, and reducing cardiac workload, while Beta-blockers target the sympathetic nervous system, slowing heart rate and reducing cardiac output.

Given these diverse mechanisms, it is crucial to investigate which of these first-line antihypertensive agents provides the most favorable renal outcomes in hypertensive CKD patients.[8] While studies have explored their efficacy in blood pressure control, limited research has focused on their comparative effects on renal function and safety profiles in this specific population.

Rationale

The rationale for this study stems from the need to optimize the management of hypertensive patients with CKD. These patients are particularly vulnerable to progressive kidney damage and cardiovascular events, necessitating meticulous selection of antihypertensive agents. Furthermore, existing guidelines provide recommendations for first-line therapies but lack granularity regarding their differential impact on renal function in CKD patients.

Aim and Objectives

The primary aim of this observational cohort study is to compare the effects of four primary first-line antihypertensive agents—ACEIs, ARBs, CCBs, and Beta-blockers—on renal function in hypertensive patients with CKD over a 12-month period.

The specific objectives are as follows

To assess changes in estimated glomerular filtration rate (eGFR) over the 12-month study period in patients receiving ACEIs, ARBs, CCBs, and Beta-blockers.

To determine the incidence of acute kidney injury (AKI) events among patients taking each of the four antihypertensive agents.

To evaluate alterations in proteinuria levels over 12 months in hypertensive CKD patients treated with ACEIs, ARBs, CCBs, and Beta-blockers.

To compare the safety profiles and adverse events associated with each of the four antihypertensive agents in this patient population.

MATERIALS AND METHODS

Study Design

This study employed a prospective observational cohort design to assess the comparative outcomes of first-line antihypertensive agents on renal function in hypertensive patients with chronic kidney disease (CKD). Data collection and analysis occurred between May 2022 and April 2023.

Study Participants

The study included adult hypertensive patients with a confirmed diagnosis of CKD, aged 18 years and above, who sought care at the Government Medical College and General Hospital Srikakulam during the study period. Patients with other significant coexisting medical conditions that might affect renal function were excluded.

Sample Size Calculation: The sample size was determined using power analysis to ensure statistical significance in detecting differences between the antihypertensive agent groups. A total of 100 patients were recruited, with equal allocation (25 patients each) into four primary first-line antihypertensive agent groups: ACE inhibitors (ACEIs), Angiotensin II Receptor Blockers (ARBs), Calcium Channel Blockers (CCBs), and Beta-blockers.

Data Collection

Patient Demographics: Data on age, gender, and comorbidities were collected.

Medical History

Detailed medical histories, including duration of hypertension and CKD, were obtained.

Medication Information: Information on the type, dose, and duration of antihypertensive medication use was recorded.

Laboratory Tests

Baseline and follow-up measurements of estimated glomerular filtration rate (eGFR), proteinuria levels, and serum creatinine were conducted.

Incidence of Acute Kidney Injury (AKI) Events: AKI events were recorded during the study period.

Outcome Measures: The primary outcome measures included changes in eGFR over 12 months, incidence of AKI events, and alterations in proteinuria levels. eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation.

Statistical Analysis

Descriptive Statistics: Baseline characteristics of the study groups were summarized using means, standard deviations, frequencies, and percentages. Inferential Statistics: Changes in eGFR, incidence of AKI events, and proteinuria levels were analyzed using appropriate statistical tests (e.g., ANOVA, chi-square test). Post-hoc analyses and subgroup analyses were performed as necessary. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Ethical Approval: The study received approval from the Institutional Ethics Committee at Government Medical College Srikakulam, Andhra Pradesh, India

Informed Consent: Informed consent was obtained from all study participants before enrollment, and they were informed about the study's purpose, procedures, and potential risks.

RESULTS

Distribution of Patients Based on Medication: The study comprised an equal distribution of patients across the four primary first-line antihypertensive

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agents. Each group contained 25 patients, ensuring a balanced comparison.

Changes in eGFR over 12 months: eGFR is an essential measure to understand kidney function, with higher values indicating better kidney function and lower values indicating impaired function. A decrease in eGFR over time suggests deteriorating kidney function.

ACEIs: The group taking ACE inhibitors observed an average decrease of 2.5 ml/min/1.73m^2 over the year. This decline suggests that while the ACEIs might have managed blood pressure, they could not completely prevent a decline in renal function in this group.

ARBs: Patients on Angiotensin II receptor blockers displayed a slightly better outcome with only a 2.0 ml/min/1.73m^2 decline. This could indicate that, in this observational set, ARBs were slightly more protective of kidney function compared to ACEIs.

CCBs: The calcium channel blocker group experienced a decline of 3.0 ml/min/1.73m^2, suggesting this group had a slightly more significant deterioration in kidney function compared to the ACEIs and ARBs group.

Beta-blockers: The most significant decline was seen in the Beta-blockers group, with a reduction of 3.5 ml/min/1.73m^2. This suggests that among the observed medications, beta-blockers may have the least renal protective effect for hypertensive CKD patients.

Incidence of Acute Kidney Injury (AKI) Events: AKI is a sudden episode of kidney failure or kidney damage. The incidence rates across the groups were:

ACEIs: 8% of patients on ACEIs experienced AKI.

ARBs: Only 4% of patients on ARBs experienced AKI, making this group the one with the lowest incidence of acute kidney injury, suggesting a potentially better renal safety profile.

CCBs: 12% incidence in the CCB group, which is higher than ACEIs and ARBs, indicating a higher risk of AKI events.

Beta-blockers: The highest incidence was observed in the Beta-blockers group with 16% of patients experiencing AKI.

Changes in Proteinuria Over 12Months: Proteinuria reflects increased amounts of protein in the urine, a sign of kidney damage. A decrease in proteinuria over time is seen as favorable.

ACEIs: Displayed a reduction of 10 mg/g, suggesting a moderate renal protective effect.

ARBs: Showed the most substantial reduction of 15 mg/g, further emphasizing their renal protective nature.

CCBs: Had the smallest reduction at 5 mg/g, indicating a less pronounced effect on decreasing proteinuria.

Beta-blockers: Experienced a reduction of 8 mg/g, which is moderately effective but less than ACEIs and ARBs.

Table 1: Distribution of Patients Based on Medication

Medication	Number of Patients
ACEIs	25
ARBs	25
CCBs	25
Beta-blockers	25

Table 2: Changes in eGFR Over 12 Months (ml/min/1.73m^2)

Medication	eGFR Decrease
ACEIs	-2.5
ARBs	-2.0
CCBs	-3.0
Beta-blockers	-3.5

Table 3: Incidence of Acute Kidney Injury (AKI) Events

Medication	AKI Incidence (%)
ACEIs	8
ARBs	4
CCBs	12
Beta-blockers	16

Table 4: Changes in Proteinuria Over 12 Months (mg/g)

Medication	Proteinuria Reduction
ACEIs	-10
ARBs	-15
CCBs	-5
Beta-blockers	-8

DISCUSSION

The comparative outcomes of first-line antihypertensive agents on renal function in hypertensive patients with chronic kidney disease (CKD) have significant clinical implications. This study's findings shed light on the renal effects of Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Blockers (ARBs), Calcium Channel Blockers (CCBs), and Beta-blockers in this specific patient population. To place these results in context, we will compare them with previous valid

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studies and references, highlighting the clinical relevance and potential implications.

ACEIs and ARBs

Our study observed that ACEIs and ARBs exhibited distinct effects on renal function. ACEIs were associated with a decrease in estimated glomerular filtration rate (eGFR) of 2.5 ml/min/1.73m^2 over 12 months, while ARBs demonstrated a more modest decline of 2.0 ml/min/1.73m^2. These findings align with several previous studies that have investigated the renoprotective effects of ACEIs and ARBs in hypertensive CKD patients.

For example, the REIN-2 trial (Remission Evaluation in Nephropathy 2) Ruggenenti P et al.[9] found that ACEIs were effective in slowing the progression of CKD and reducing proteinuria. Similarly, the IDNT study (Irbesartan Diabetic Nephropathy Trial) Brenner BM et al,[10] demonstrated the renoprotective effects of ARBs in diabetic nephropathy, which shares similarities with hypertensive CKD.

CCBs and Beta-blockers

In contrast to ACEIs and ARBs, our study revealed that patients treated with Calcium Channel Blockers (CCBs) and Beta-blockers experienced more significant declines in eGFR, with reductions of 3.0 ml/min/1.73m^2 and 3.5 ml/min/1.73m^2, respectively. These findings are consistent with the limited existing evidence suggesting that CCBs and Beta-blockers may have less favorable effects on renal function in hypertensive patients with CKD.

A study by Mann et al,[11] reported that CCBs may lead to a greater decrease in eGFR compared to ACEIs or ARBs in hypertensive patients with CKD. Additionally, Coca et al,[12] found that Beta-blockers were associated with a higher risk of adverse renal outcomes in CKD patients.

Acute Kidney Injury (AKI) Events

Our study's findings regarding the incidence of AKI events align with previous evidence. ARBs exhibited the lowest AKI incidence at 4%, suggesting a potentially better renal safety profile. This is consistent with studies like the VALIANT trial (Valsartan in Acute Myocardial Infarction Trial) Pfeffer MA et al,[13] which showed a reduced risk of renal dysfunction with ARBs compared to other antihypertensive agents in high-risk cardiovascular patients.

Proteinuria Reduction

Our study's results on proteinuria reduction further emphasize the renoprotective nature of ARBs, with a substantial reduction of 15 mg/g. This aligns with numerous trials, such as the RENAAL study (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) Makani H et al,[14] which demonstrated significant reductions in proteinuria and slower CKD progression in patients treated with ARBs.

In contrast, CCBs showed the smallest reduction in proteinuria at 5 mg/g, consistent with evidence suggesting their limited efficacy in proteinuria reduction in CKD patients Parving HH et al.[15]

Clinical Implications

The findings of this study have critical clinical implications. ARBs appear to offer better renal protection and a lower risk of AKI events in hypertensive CKD patients compared to ACEIs, CCBs, and Beta-blockers. These results emphasize the importance of personalized treatment decisions for hypertensive patients with CKD, taking into account both blood pressure control and renal outcomes.

It's worth noting that our study has limitations, including its observational nature and relatively small sample size. Larger, randomized controlled trials are needed to confirm these findings. Nevertheless, the results of this study contribute to the growing body of evidence regarding the choice of antihypertensive agents in this vulnerable patient population, guiding clinicians in optimizing treatment strategies to preserve renal function and improve long-term outcomes.

CONCLUSION

The comparative outcomes of first-line antihypertensive agents on renal function in hypertensive CKD patients suggest that ARBs may offer superior renal protection and a lower risk of AKI events compared to other agents. These findings underscore the importance of evidence-based decision-making in the management of hypertensive patients with CKD, with a focus on individualized treatment plans to optimize both blood pressure control and renal health.

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