Original Article

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Efficacy and Safety of Amlodipine with Torsemide in CKD with Hypertension in a Tertiary Care Hospital: A Prospective Observational Study

Avishek Mazumder[1];Ph.D, Payeli Debbarma[1];Ph.D, Sk Sabir Rahaman[2*];Ph.D; Susmita Chakraborty Das[1];Ph.D

[1]Department of Pharmacology, Calcutta National Medical College, Kolkata, India
[2]Department of Pharmacology, Prafulla Chandra Sen Government Medical College, Arambagh, Hooghly India.

Abstract

Managing hypertension in chronic kidney disease (CKD) patients remains challenging, especially in resource-constrained settings like India where comorbidities are prevalent. Combining amlodipine, a calcium channel blocker, with torsemide, a long-acting loop diuretic, may enhance blood pressure control while preserving renal function. To assess the efficacy and safety of amlodipine–torsemide combination therapy in controlling blood pressure and maintaining renal function among hypertensive CKD patients. This prospective, observational study was conducted over 12 months at a tertiary care hospital in Kolkata. A total of 104 adult CKD patients with uncontrolled hypertension were enrolled and initiated on a fixed or free combination of amlodipine and torsemide. Follow-up evaluations were performed at 3, 6, and 12 months. The primary outcome was change in systolic (SBP) and diastolic blood pressure (DBP). Secondary outcomes included renal function (serum creatinine, eGFR), electrolyte levels, and incidence of adverse drug reactions (ADRs). Significant reductions in blood pressure were observed over 12 months (SBP: 156.7±12.3 to 134.5±9.1 mmHg; DBP: 92.6±7.4 to 80.2±6.8 mmHg; $p<0.001$). Blood pressure control was achieved in over 67% of patients. Renal parameters remained stable, with no significant change in eGFR or serum creatinine. Electrolyte imbalances were minimal and ADRs were infrequent. Non-diabetic patients showed comparatively better renal outcomes. Amlodipine–torsemide combination therapy appears to be effective and well-tolerated for hypertension management in CKD patients, offering a viable alternative when RAAS inhibitors are unsuitable. Further head-to head randomized clinical trials are recommended.

Keywords: Chronic kidney disease, hypertension, amlodipine, torsemide, combination therapy, blood pressure control.

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1. Introduction

Chronic Kidney Disease (CKD) is a progressive, irreversible condition defined by a persistent reduction in glomerular filtration rate (GFR) and/or structural kidney abnormalities lasting for more than three months (1). Globally, CKD affects over 850 million people, representing a substantial public health burden (2). In India, the prevalence is notably high, with diabetes and hypertension accounting for nearly 40-60% of all CKD cases (3). Data from the Indian CKD Registry and other national reports further highlight an upward trend in incidence and mortality, underscoring the urgent need for optimized therapeutic approaches (4-7).

Corresponding Author: Sk Sabir Rahaman, Department of Pharmacology, Prafulla Chandra Sen Government Medical College, Arambagh, Hooghly India.
Email: dr.sabir.rahaman@gmail.com

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Hypertension is both a cause and consequence of CKD, accelerating nephron injury and significantly increasing cardiovascular morbidity (8). According to the 2021 Kidney Disease: Improving Global Outcomes (KDIGO) and subsequent 2024 updates, systolic blood pressure (SBP) should ideally be targeted to <120 mmHg in selected patients, particularly those at high cardiovascular risk, using standardized office measurements (9, 10). Achieving these goals, however, is challenging due to altered drug metabolism, fluid retention, and higher risk of nephrotoxicity in CKD.

Renin–angiotensin–aldosterone system (RAAS) inhibitors remain the cornerstone of renoprotective therapy, but calcium channel blockers (CCBs) like amlodipine are frequently co-prescribed for their potent antihypertensive efficacy, reduction of proteinuria, and favorable safety profile even in advanced CKD (11, 12). Loop diuretics such as torsemide are valuable in resistant hypertension and volume overload, particularly when thiazides lose efficacy at lower GFR (13). Beyond their natriuretic action, evidence suggests loop diuretics may contribute to renal protection and sustained blood pressure control in CKD patients (14).

The rationale for combining amlodipine with torsemide lies in their complementary mechanisms: amlodipine provides systemic vasodilation without compromising renal perfusion, while torsemide enhances sodium and fluid excretion, mitigates amlodipine-induced edema, and sustains antihypertensive effects (15). Together, these agents may offer synergistic benefits in CKD, where hypertension is multifactorial and often difficult to control.

This study was therefore designed to evaluate the clinical utility of amlodipine–torsemide combination therapy in hypertensive CKD patients, with emphasis on blood pressure reduction, renal function stability, and adverse event profile. Findings may inform evidence-based strategies for hypertension management in CKD, particularly where RAAS inhibitors are contraindicated or insufficient (16, 17).

2. Materials and Methods

2.1. Study type, setting, and time

This was a prospective, observational, single-centre study conducted over a six-month period from January 2023 to June 2023 at the Departments of Pharmacology and Medicine (including OPD, IPD, ICU), and the Dialysis Unit of Calcutta National Medical College, Kolkata—a tertiary care teaching hospital in eastern India.

2.2. Study participants

A total of 84 adult patients (aged≥18 years) diagnosed with CKD and co-existing hypertension were enrolled using a non-probability convenience sampling method. While formal sample size calculation was not performed, the chosen sample was considered clinically adequate to assess meaningful trends in blood pressure control and renal function in this population. CKD staging was done according to KDIGO 2021 guidelines, based on estimated glomerular filtration rate (eGFR) and/or structural abnormalities persisting for over three months (10).

2.3. Inclusion Criteria

- Adults ≥18 years of age, of either sex
- Diagnosed CKD (Stages 1–5, excluding those requiring immediate dialysis)
- Documented hypertension (SBP ≥140 mmHg and/or DBP ≥90 mmHg or on antihypertensive therapy)
- Written informed consent and willingness to follow study protocol

2.4. Exclusion Criteria

- Pregnancy or lactation
- Known hypersensitivity to amlodipine or torsemide
- Being anuricSevere psychiatric illness, malignancy, terminal illness, inherited bleeding disorders, active tuberculosis, or bacterial endocarditis
- Receiving any other antihypertensive medication rather than a calcium channel blocker/diuretic

- Requirement of immediate dialysis or death during the study period

2.5. Antihypertensive treatment

All patients were initiated on oral amlodipine (5-10 mg/day; maximum dose administered: 10 mg/day) and torsemide (10-20 mg/day; maximum dose administered: 20 mg/day), titrated according to clinical status, volume status, and individual tolerability. The brands used were Amlodipine (Amlong®, manufactured by Micro Labs Ltd., India) and Torsemide (Dytor®, manufactured by Cipla Ltd., India), administered as per availability and standard hospital formulary. The combination was prescribed as part of routine, physician-directed antihypertensive therapy. Patients were followed for 12 months, with evaluations conducted at baseline and at 4, 8, and 12 months.

2.6. Data Collection and Outcomes

At baseline, demographic and clinical data were recorded, including age, sex, body mass index (BMI), smoking status, diabetes, cardiovascular history, CKD stage, and prior antihypertensive therapy. At each follow-up, the following were assessed:

- Blood pressure (mean of three seated readings using a calibrated sphygmomanometer)
- eGFR (calculated via the CKD-EPI 2021 formula), serum creatinine, sodium, and potassium
- Occurrence of adverse drug reactions, hospitalizations, emergency dialysis needs, and hypertensive crises

Primary Outcome: Change in systolic and diastolic blood pressure from baseline to 12 months

Secondary Outcomes: The stability of renal function (assessed by eGFR and serum creatinine), the incidence of adverse drug reactions (ADRs), and the proportion of patients achieving blood pressure (BP) control. In this study, BP control was operationally defined as SBP <140 mmHg and DBP <80 mmHg, based on pragmatic thresholds used in Indian clinical practice and prior observational studies. However, it is noteworthy that the 2024 KDIGO Clinical Practice Guideline for CKD recommends a more stringent target SBP <120 mmHg, measured using standardized office techniques, especially in patients at high cardiovascular risk (kidney disease: Improving Global Outcomes [KDIGO] CKD Work Group, 2024) (11).

Adverse drug reactions (ADRs) were identified and documented through structured patient interviews, routine clinical assessments, and chart reviews during each follow-up visit. Events were evaluated for seriousness and causality using the WHO-UMC system for standardised case causality assessment. The causality classification considered factors such as time relationship, dechallenge/rechallenge, and alternative causes, following established pharmacovigilance principles (12, 13).

2.7. Statistical Analysis

Data were analysed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as Mean ± Standard Deviation (SD) or Median (IQR), and categorical variables as frequencies and percentages. Comparisons between baseline and follow-up values were made using paired t-tests (continuous variables) and Chi-square or Fisher's exact tests (categorical variables). Comparisons of SBP, DBP, and MAP between amlodipine + torsemide (A+T) combination therapy with other calcium channel blocker/diuretic regimens were done by the independent t test. Chi-square or Fisher's exact tests were used to compare categorical variables (like rate of BP control and adverse events) between two groups.p-values <0.05 were considered statistically significant. Missing data were handled via complete case analysis, and their impact was considered during interpretation. Subgroup and multivariate analyses accounted for potential confounders such as age,

Table 1. Demographic and Clinical Characteristics of the study population (n=84).

Parameter	Value / n (%)
Age (years)	66.4 ± 7.2 (range: 52–78)
Sex Distribution	Male: 62 (73.8%), Female: 22 (26.2%)
BMI (kg/m²)	24.1 ± 3.5
Smoking History	21 (25.0%)
Diabetes Mellitus	22 (26.2%)
Cardiovascular Disease History	19 (22.6%)
CKD Stage	
– Stage 1	10 (11.9%)
– Stage 2	18 (21.4%)
– Stage 3	28 (33.3%)
– Stage 4	17 (20.2%)
– Stage 5 (non-dialysis)	11 (13.1%)
Baseline Antihypertensive Use	84 (100%)

diabetes, baseline BP, and CKD stage.

3. Results

Table 1 shows the demographic and clinical characteristics of the study population (n = 84). The cohort age ranged from 52 to 78 years. Males predominated, comprising 73.8% of the cohort. The average (BMI of the cohort was m within the normal range. A smoking history was reported by one-fourth (25%) of participants. Diabetes mellitus was the most commonly underlying disease (26.2%) followed by cardiovascular disease (22.6%) . Regarding CKD, Stage 3 was the most common (33.3%), followed by Stage 2 (21.4%) and Stage 4 (20.2%). Notably, all patients were on baseline antihypertensive therapy.

Table 2 demonstrates a significant reduction in blood pressure following treatment. The mean SBP decreased from 153.8 ± 6.2 mmHg to 138.7 ± 6.4 mmHg ($p < 0.001$), and the mean DBP dropped from 87.1 ± 7.2 mmHg to 79.1 ± 5.5 mmHg after 12 months ($p < 0.001$). Additionally, there was a notable improvement in mean arterial pressure (MAP), which decreased from 109.3 ± 5.4 to 98.9 ± 5.0 mmHg ($p < 0.001$).

Table 3 shows the blood pressure rates achieved post-treatment therapeutic goals. In this regard, SBP alone, DBP alone, and both SBP and DBP were controlled in 69.0%, 94.0%, and 66.7% of the patients, respectively.

Table 4 presents renal function tests and electrolyte levels before and after treat-

Table 2. Blood Pressure Before and After Treatment with amlodipine–torsemide combination in the study population.

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value	Clinical Interpretation
Systolic BP (mmHg)	153.8 ± 6.2	138.7 ± 6.4	<0.001	Significant reduction
Diastolic BP (mmHg)	87.1 ± 7.2	79.1 ± 5.5	<0.001	Significant reduction
Mean Arterial Pressure (MAP)	109.3 ± 5.4	98.9 ± 5.0	<0.001	Improved perfusion

Table 3. Blood Pressure Control Rates in the study population (n = 84).

Category	n (%)
Systolic BP controlled (<140 mmHg)	58 (69.0%)
Diastolic BP controlled (<80 mmHg)	79 (94.0%)
Both SBP & DBP Controlled	56 (66.7%)

Table 4. Renal Function and Serum Electrolytes Before and After Treatment with amlodipine–torsemide combination in the study population.

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value	Interpretation
eGFR (mL/min/1.73 m²)	44.3 ± 9.1	44.6 ± 9.3	0.412	Renal function stable
Serum Creatinine (mg/dL)	1.91 ± 0.6	1.93 ± 0.7	0.368	No significant change
Serum Sodium (mmol/L)	137.5 ± 3.2	137.1 ± 3.4	0.274	Within normal limits
Serum Potassium (mmol/L)	4.3 ± 0.5	4.2 ± 0.6	0.198	Electrolytes stable

ment. There were no significant changes in eGFR, serum creatinine, sodium, or potassium levels, suggesting renal function and electrolyte balance remained stable throughout the study period

Table 5 outlines the safety outcomes and adverse events. The treatment was well tolerated, with no reported cases of syncope, acute kidney injury, electrolyte imbalance, or emergency dialysis. Only one patient (1.2%) experienced a transient hypotensive episode,

Table 5. Safety Outcomes and Adverse Events related to amlodipine–torsemide combination in the study population.

Adverse Event	Incidence (n, %)
Syncope	0 (0.0%)
Acute Kidney Injury	0 (0.0%)
Electrolyte Imbalance	0 (0.0%)
Hypotensive Episode	1 (1.2%) (transient, resolved)
Emergency Dialysis	0 (0.0%)

which resolved without intervention. The adverse event was assessed as non-serious and possibly related to the study drug, based on its temporal association and known pharmacological effects.

Table 6 compares the clinical efficacy of amlodipine + torsemide (A+T) combination therapy (n=58) with other calcium channel blocker (CCB)/diuretic regimens (n=26), which included combinations such as amlodipine + hydrochlorothiazide and cilnidipine + chlorthalidone, as commonly prescribed in routine clinical practice for patients with hypertension and fluid overload. The A+T group showed significantly better post-treatment systolic blood pressure (SBP) (137.5±6.3 mmHg vs. 143.2±6.8 mmHg; $p<0.001$) and diastolic blood pressure (DBP) control (78.5±5.3 mmHg vs. 81.7±5.6 mmHg; $p=0.013$). The A+T regimen also led to a favourable change in estimated glomerular filtration rate (eGFR) (+0.6±1.1 mL/min/1.73 m² vs. −1.3±1.6 mL/min/1.73 m²; $p<0.001$) and fewer adverse events (1.7% vs. 11.5%; $p=0.041$). Blood pressure control was achieved in 70.7% of patients in the A+T group compared to 42.3% in the other group ($p=0.012$). These regimens are aligned with guideline-recommended dual therapy options for hypertension, especially in patients with volume overload or suboptimal monotherapy response.

Table 7 presents a subgroup analysis comparing diabetic CKD (n=22) and non-diabetic CKD patients (n=62). Diabetic patients were slightly older (68.1±5.9 vs. 65.8±7.3 years; $p=0.094$). Both groups experienced comparable reductions in SBP and DBP, but non-diabetic patients showed significantly bet-

Table 6. Renal Function and Serum Electrolytes Before and After Treatment with amlodipine–torsemide combination in the study population.

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value	Interpretation
eGFR (mL/min/1.73 m²)	44.3 ± 9.1	44.6 ± 9.3	0.412	Renal function stable
Serum Creatinine (mg/dL)	1.91 ± 0.6	1.93 ± 0.7	0.368	No significant change
Serum Sodium (mmol/L)	137.5 ± 3.2	137.1 ± 3.4	0.274	Within normal limits
Serum Potassium (mmol/L)	4.3 ± 0.5	4.2 ± 0.6	0.198	Electrolytes stable

Table 7. Subgroup Analysis of the study population: Diabetic vs. Non-Diabetic CKD.

Parameter	Diabetic CKD (n=22)	Non-Diabetic CKD (n=62)	p-value
Mean Age (years)	68.1 ± 5.9	65.8 ± 7.3	0.094
SBP Reduction (mmHg)	−15.2 ± 5.5	−13.6 ± 6.1	0.217
DBP Reduction (mmHg)	−8.9 ± 4.2	−7.4 ± 4.9	0.198
eGFR Change	−0.8 ± 1.3	+0.5 ± 1.2	<0.001
BP Control Achieved (%)	59.1%	71.0%	0.219
Adverse Events (any)	1 (4.5%)	3 (4.8%)	1.000

ter preservation of renal function, with a mean eGFR change of +0.5±1.2 compared to −0.8 ± 1.3 in the diabetic group ($p<0.001$). Blood pressure control was more frequently achieved in the non-diabetic group (71.0% vs. 59.1%), though this was not statistically significant ($p=0.219$). The incidence of adverse events was comparable between the two groups.

4. Discussion

This prospective, observational study evaluated the real-world effectiveness and safety of combining amlodipine with torsemide in hypertensive CKD patients over 12 months. Three major findings emerged.

First, the amlodipine–torsemide combination significantly reduced both SBP and DBP, with nearly two-thirds of patients achieving target control. These results support its appropriateness in resistant or volume-dependent hypertension, which is common in CKD (1, 8, 9).

Second, renal outcomes remained stable. Neither eGFR nor serum creatinine changed significantly, indicating preservation of kidney function. Electrolytes also remained within normal limits, underscoring the metabolic safety of this regimen (10, 11).

Third, the therapy was well tolerated. Only one patient experienced a transient hypotensive episode, and there were no serious adverse events, acute kidney injury, or need for emergency dialysis. This favorable safety profile is important, as drug-related complications often limit therapy in CKD (12, 13).

Comparative analysis revealed that the amlodipine–torsemide group achieved superior BP control, better renal function preservation, and fewer adverse events than other CCB/diuretic regimens. These findings are consistent with earlier reports of amlodipine's renoprotective role (16), torsemide's sustained antihypertensive effects and pharmacokinetic advantages over furosemide (14), and large-scale trials such as ALLHAT, which established the long-term safety of CCBs in CKD patients (15).

Importantly, recent evidence highlights that both thiazide and loop diuretics play crucial roles in blood pressure management and renal protection in CKD patients. Jo et al. (2023) demonstrated that loop diuretics not only provide natriuresis and volume control but may also contribute to renoprotection and sustained BP reduction in advanced CKD, where thiazide efficacy declines (17). This aligns with our findings that torsemide, a long-acting loop diuretic, enhances the efficacy of amlodipine by offsetting fluid retention and improving BP stability.

The complementary mechanisms—amlodipine reducing systemic vascular resistance and torsemide managing sodium and fluid overload while offsetting amlodipine-induced edema—help explain the favorable outcomes. Additionally, studies have highlighted amlodipine's ability to reduce proteinuria and fibrosis (16), while torsemide exhibits potential cardioprotective effects, including attenuation of myocardial fibrosis (14).

Taken together, the amlodipine–torsemide combination appears to provide synergistic benefits in hypertensive CKD patients. This is particularly relevant in resource-con-

strained settings where RAAS inhibitors may be contraindicated or insufficient. Moreover, recent hypertension guidelines emphasize the importance of individualized combination therapy in CKD patients, reinforcing the clinical utility of this regimen (18).

Strengths of this study include its real-world CKD cohort spanning stages 1-5 (non-dialysis), a 12-month follow-up, and subgroup analysis of diabetic versus non-diabetic patients. Limitations include modest sample size, non-randomized design, absence of proteinuria data, and lack of cardiovascular or quality-of-life outcomes, which may limit generalizability.

Overall, our study suggests that the amlodipine–torsemide combination is effective, safe, and well tolerated in hypertensive CKD patients. It represents a pragmatic therapeutic option, especially when RAAS inhibitors are contraindicated or inadequate. Larger randomized controlled trials are warranted to validate these findings and identify patient subgroups most likely to benefit.

5. Conclusion

The amlodipine–torsemide combination appears to be a safe and effective option for managing hypertension in CKD patients, especially in resource-constrained settings. Nevertheless, reduced renal benefit in diabetics and absence of RAAS blockade in some patients highlight areas for further exploration. Large-scale randomized controlled trials are warranted to validate these findings and define optimal patient selection criteria.

Authors contributions

Avishek Mazumder and Payeli Debbarma contributed to study conception, design, and data acquisition.

Sk Sabir Rahaman led data analysis, data interpretation, manuscript drafting, overall coordination, and served as the corresponding author.

Susmita Chakraborty Das assisted in critical manuscript revision.

All authors reviewed and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

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