

Comparative Efficacy and Safety of Telmisartan–Amlodipine versus Amlodipine–Chlorthalidone Combination Therapy in Patients with Uncontrolled Essential Hypertension: A Randomised Controlled Trial

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Abstract

Background: Hypertension uncontrolled on monotherapy represents a common clinical challenge, yet the optimal fixed-dose combination for treatment intensification remains uncertain. We compared the efficacy and safety of telmisartan–amlodipine versus amlodipine–chlorthalidone in patients with uncontrolled hypertension despite stable monotherapy.

Methods: In this 12-week, randomised, open-label, parallel-group trial conducted at a tertiary care centre in India, 186 adults aged 30–70 years with uncontrolled essential hypertension on stable monotherapy were randomised 1:1 to receive fixed-dose telmisartan 40 mg–amlodipine 5 mg (n = 93) or amlodipine 5 mg–chlorthalidone 12.5 mg (n = 93) once daily. The primary outcome was change in mean seated office systolic blood pressure (SBP) from baseline to week 12, analysed using ANCOVA with baseline SBP as a covariate. Secondary outcomes included changes in diastolic blood pressure (DBP), blood pressure control rate, adherence, and adverse events.

Results: Baseline characteristics were well balanced between groups. Mean SBP reduction was 25.8 mmHg with telmisartan–amlodipine and 23.0 mmHg with amlodipine–chlorthalidone (adjusted between-group difference: –2.8 mmHg; 95% CI: –5.6 to –0.1; p = 0.04). DBP reductions were similar between groups (–11.8 vs –9.6 mmHg; adjusted difference: –1.5 mmHg; 95% CI: –3.2 to 0.2; p = 0.08). Blood pressure control was achieved in 68.9% versus 62.5% of participants, respectively (p = 0.37). Hypokalemia occurred exclusively with amlodipine–chlorthalidone (6.5% vs 0%; p = 0.01); peripheral oedema was more frequent with telmisartan–amlodipine (7.5% vs 3.2%; p = 0.19). Adherence exceeded 88% in both groups.

Conclusions: Both fixed-dose combinations provided substantial blood pressure reduction in patients with uncontrolled hypertension on monotherapy. Telmisartan–amlodipine conferred modestly greater systolic blood pressure reduction and a more favourable metabolic profile, supporting its preferential use for treatment intensification.

Keywords: Hypertension, Fixed-dose combination, Telmisartan, Amlodipine, Chlorthalidone.

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Introduction

Hypertension remains the leading modifiable risk factor for premature death and disability worldwide, contributing substantially to the global burden of ischemic heart disease, stroke, and chronic kidney disease [1]. The World Health Organisation estimates that nearly 1.3 billion adults live with hypertension, yet fewer than half achieve adequate blood pressure control [1]. This persistent treatment gap persists despite widespread availability of effective antihypertensive agents and clear, evidence-based guidance from major societies [2]. Even in well-resourced clinical settings, a substantial proportion of patients initiated on monotherapy fail to reach target blood pressure, reflecting the complex and multifactorial pathophysiology of essential hypertension as well as the inherent limitations of targeting a single pressor mechanism [2].

The recognition that most patients will require more than one agent to achieve control has fundamentally reshaped contemporary treatment paradigms. Current guidelines endorse early use of low-dose combination therapy, particularly for patients with grade 2 hypertension or those at high cardiovascular risk [2]. The pharmacological rationale is compelling: agents with complementary mechanisms of action target distinct pathways—renin-angiotensin-aldosterone system activation, sympathetic drive, vascular tone, and sodium retention—while mitigating counter-regulatory responses that blunt monotherapy efficacy. Seminal meta-analytic work by Wald and colleagues showed that combining two agents from different classes produces about fivefold greater blood pressure reduction than doubling the dose of a single drug, while also conferring a favourable adverse effect profile [3]. This evidence has firmly

established combination therapy as a cornerstone of modern hypertension management.

Nevertheless, the clinical decision about which specific combination to select for a patient uncontrolled on initial monotherapy remains genuinely uncertain. Numerous two-drug combinations are guideline-endorsed, but direct comparative evidence in this specific step-up scenario is sparse. Among the most rational and widely prescribed options are combinations of a renin-angiotensin system blocker with a calcium channel blocker, and a calcium channel blocker with a thiazide-type diuretic. The fixed-dose combination of telmisartan and amlodipine offers potent, sustained blood pressure reduction with excellent tolerability and has demonstrated superiority over monotherapy components in randomised trials [4, 5]. Pairing amlodipine with chlorthalidone is a similarly mechanistically sound strategy, leveraging a long-acting dihydropyridine with a thiazide-like diuretic whose benefits were convincingly established in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial and corroborated by large-scale observational analyses [6, 7]. Both combinations are recommended in current guidelines, yet they have not been directly compared in patients with hypertension uncontrolled on monotherapy.

Given the clinical equipoise surrounding optimal second-line therapy, a head-to-head evaluation of these two contemporary fixed-dose combinations is warranted. This study was therefore designed to compare the antihypertensive efficacy and tolerability of telmisartan-amlodipine versus amlodipine-chlorthalidone in adults with uncontrolled essential hypertension on stable monotherapy.

Methods

Study Design and Setting

This prospective, randomised, open-label, parallel-group controlled trial was conducted between January 2024 and June 2025 in the Department of Pharmacology in collaboration with the Department of General Medicine at a tertiary care teaching hospital in North India. Adults with uncontrolled essential hypertension despite stable antihypertensive monotherapy were randomised in a 1:1 ratio to receive fixed-dose telmisartan–amlodipine or amlodipine–chlorthalidone for 12 weeks. Participants and treating clinicians knew the treatment allocation; outcome assessment was blinded where feasible.

Study Population

Adults aged 30–70 years with established essential hypertension were eligible if their office systolic blood pressure (SBP) was ≥ 140 mmHg and/or diastolic blood pressure (DBP) was ≥ 90 mmHg despite at least 4 weeks of stable antihypertensive monotherapy, confirmed by repeated standardised measurements. We assessed medication adherence to the pre-existing treatment before classifying blood pressure as uncontrolled; inadequate control on monotherapy was not considered resistant hypertension for this study. Key exclusions were secondary hypertension, hypertensive emergency, pregnancy or lactation, bilateral renal artery stenosis, severe renal or hepatic impairment, clinically significant heart failure, recent myocardial infarction or stroke, significant arrhythmia or valvular disease likely to affect treatment assessment, known hypersensitivity or contraindication to study medications, clinically relevant baseline electrolyte abnormalities, uncontrolled diabetes, gout requiring active treatment, use of concomitant medications likely to interfere with blood pressure or study treatment, and inability or unwillingness to provide consent or comply with follow-up.

Study Interventions

Participants in the intervention group received fixed-dose telmisartan 40 mg plus amlodipine 5 mg orally once daily. The comparator group received fixed-dose amlodipine 5 mg plus chlorthalidone 12.5 mg orally once daily. Both regimens were continued for 12 weeks at fixed doses, with no protocol-specified dose escalation. Treatment could be interrupted or discontinued when clinically necessary due to intolerance or safety concerns. All participants received standard lifestyle advice, including dietary sodium restriction, regular physical activity, weight management, tobacco avoidance, and moderation of alcohol intake, as background management.

Blood Pressure Measurement

Blood pressure was measured using a validated device with an appropriately sized cuff after at least 5 minutes of seated rest. Participants sat with their back supported, feet flat on the floor, legs uncrossed, and arm supported at heart level; they avoided conversation. Participants were advised to avoid caffeine, smoking, and vigorous physical activity before assessment where applicable. We obtained three readings approximately 1 minute apart and used the average of the second and third readings for analysis. Pulse pressure was calculated as SBP minus DBP.

Outcomes

The primary outcome was the change in mean seated office SBP from baseline to week 12, calculated as week-12 SBP minus baseline SBP. Secondary outcomes included change in DBP, blood pressure control rate, proportion achieving a clinically meaningful systolic response (reduction in SBP ≥ 10 mmHg from baseline), change in pulse pressure, medication adherence, incidence and severity of adverse drug reactions, treatment discontinuation due to adverse

events, and changes in serum sodium, potassium, creatinine, estimated glomerular filtration rate (eGFR), uric acid, and fasting glucose. Blood pressure control was defined as achieving an office BP <[Insert Threshold] mmHg. Medication adherence was assessed by pill counts at follow-up visits and calculated as [(number of tablets dispensed – number returned) / number expected] × 100; adherence ≥80% was considered adequate where prespecified.

Safety Assessment

Participants were actively monitored for adverse events at each visit. For each event, we recorded the type, onset, severity, relationship to study medication, action taken, outcome, and need for treatment discontinuation. We paid particular attention to potential effects of each regimen: dizziness, hypotension, hyperkalemia, and renal function changes with telmisartan; peripheral oedema, headache, flushing, dizziness, and palpitations with amlodipine; and hypokalemia, hyponatremia, volume depletion, muscle cramps, hyperuricemia, and glucose changes with chlorthalidone. We assessed laboratory safety parameters (serum sodium, potassium, creatinine, eGFR, uric acid, and fasting glucose) at baseline and at predefined follow-up visits, and evaluated changes from baseline as safety outcomes.

Data Management and Statistical Analysis

The Institutional Ethics Committee approved the study. All participants provided written informed consent before enrolment. Participants were informed of the study purpose, procedures, confidentiality safeguards, and their right to withdraw at any time without affecting routine medical care.

Participant data were recorded on standardised case report forms and checked for completeness and consistency. Coded identifiers were used to maintain

confidentiality. Analyses were performed using SPSS version 28.0. Continuous variables are presented as mean ± standard deviation or median with interquartile range, depending on distribution; categorical variables are presented as frequencies and percentages. Baseline comparisons used independent-samples t-test or Mann–Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. We analysed the primary endpoint using analysis of covariance (ANCOVA), with week-12 SBP as the dependent variable, treatment group as the main factor, and baseline SBP as a covariate. The adjusted between-group mean difference was reported with a 95% confidence interval and two-sided p-value. Repeated blood pressure measurements were analysed using a linear mixed-effects model with treatment, time, and treatment-by-time interaction. Categorical outcomes were compared using chi-square or Fisher's exact test as appropriate. A two-sided p value <0.05 was considered statistically significant. The intention-to-treat population was used for the primary analysis, with per-protocol analysis as a sensitivity analysis where applicable.

Results

A total of 214 participants were screened; 186 met eligibility criteria and were randomised to receive telmisartan–amlodipine (n = 93) or amlodipine–chlorthalidone (n = 93). At week 12, complete blood pressure data were available for 178 participants (95.7%): 90 in the telmisartan–amlodipine group and 88 in the amlodipine–chlorthalidone group. The intention-to-treat population included all 186 randomised participants, and missing data were handled using the prespecified linear mixed-effects model.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Telmisartan–Amlodipine (n = 93) mean ± SD	Amlodipine–Chlorthalidone (n = 93) mean ± SD
Age, years	54.2 ± 9.8	55.1 ± 10.3
Male sex, n (%)	54 (58.1)	51 (54.8)
BMI, kg/m ²	27.6 ± 4.1	28.0 ± 4.5
Duration of hypertension, years	6.4 ± 4.2	6.8 ± 4.7
Baseline SBP, mmHg	158.4 ± 10.2	157.8 ± 9.6
Baseline DBP, mmHg	94.2 ± 8.1	93.5 ± 7.8
Baseline serum potassium, mEq/L	4.2 ± 0.4	4.1 ± 0.3
Baseline eGFR, ml/min/1.73 m ²	78.5 ± 14.2	76.9 ± 15.1
Baseline fasting glucose, mg/dL	102.4 ± 18.6	104.1 ± 20.3

Table 1 summarises the baseline demographic and clinical characteristics of the two treatment groups. The groups were well balanced with respect to age, sex distribution, body mass index, duration of hypertension, baseline blood pressure, and laboratory parameters, indicating that randomisation achieved adequate comparability between arms. Mean baseline SBP was 158.4 ± 10.2 mmHg in the telmisartan–amlodipine group and 157.8 ± 9.6 mmHg in the amlodipine–chlorthalidone group, reflecting the moderate degree of uncontrolled hypertension targeted by the inclusion criteria. Baseline serum potassium, eGFR, and fasting glucose values were within normal limits in both groups, suggesting that the study population was

relatively free of major metabolic or renal derangements at entry. The mean duration of hypertension exceeded six years in both arms, indicating that participants had a substantial history of prior antihypertensive treatment before enrolment.

Table 2. Primary and Secondary Efficacy Outcomes

Outcome	Telmisartan–Amlodipine (n = 90)	Amlodipine–Chlorthalidone (n = 88)	p value
Baseline SBP, mmHg	158.4 ± 10.2	157.8 ± 9.6	—
Week-12 SBP, mmHg	132.6 ± 9.8	134.8 ± 10.5	—
Change in SBP, mmHg	−25.8 (−28.1 to −23.4)	−23.0 (−25.4 to −20.7)	0.04
Baseline DBP, mmHg	94.2 ± 8.1	93.5 ± 7.8	—
Week-12 DBP, mmHg	82.4 ± 7.2	83.9 ± 7.6	—
Change in DBP, mmHg	−11.8 (−13.4 to −10.1)	−9.6 (−11.3 to −7.8)	0.08
BP control at week 12, n/N (%)	62/90 (68.9)	55/88 (62.5)	0.37

Values are mean $\pm$ SD for baseline and week-12 measurements; changes are reported as adjusted mean change with 95% CI.

Table 2 presents the efficacy results. Both treatment strategies produced substantial reductions in systolic blood pressure over the 12-week treatment period. In the telmisartan–amlodipine group, mean SBP decreased from 158.4 ± 10.2 mmHg at baseline to 132.6 ± 9.8 mmHg at week 12, corresponding to an adjusted within-group reduction of 25.8 mmHg. The amlodipine–chlorthalidone group experienced a reduction from 157.8 ± 9.6 mmHg to 134.8 ± 10.5 mmHg, representing an adjusted within-group decrease of 23.0 mmHg. After adjustment for baseline SBP using ANCOVA, the between-group difference in SBP change was -2.8 mmHg (95% CI: -5.6 to -0.1 ; $p = 0.04$), favouring the telmisartan–amlodipine combination. Although the absolute difference between groups was modest, it was statistically significant and suggests a small but consistent advantage for the ARB–CCB combination in this clinical scenario. Diastolic blood pressure reductions paralleled the systolic findings, with adjusted mean decreases of 11.8 mmHg and 9.6 mmHg in the telmisartan–amlodipine and amlodipine–chlorthalidone groups, respectively. The adjusted between-group difference for DBP change was -1.5 mmHg (95% CI: -3.2 to 0.2 ; $p = 0.08$), which did not reach statistical significance. Blood pressure control at week 12 was achieved by 62 of 90 participants (68.9%) in the telmisartan–amlodipine group and 55 of 88 (62.5%) in the amlodipine–chlorthalidone group, representing an absolute difference of 6.4 percentage points that was not statistically significant ($p = 0.37$). These control rates are clinically meaningful, as approximately two-thirds of previously uncontrolled patients achieved target blood pressure with either fixed-dose combination.

Table 3. Comparison of Adverse Events

Adverse Event	Telmisartan–Amlodipine (n = 93)	Amlodipine–Chlorthalidone (n = 93)	p value
Any adverse event, n (%)	38 (40.9)	44 (47.3)	0.38
Dizziness	4 (4.3)	5 (5.4)	0.73
Hypotension	2 (2.2)	3 (3.2)	0.65
Peripheral edema	7 (7.5)	3 (3.2)	0.19
Hypokalemia	0 (0)	6 (6.5)	0.01
Hyperkalemia	0 (0)	0 (0)	—
Hyponatremia	1 (1.1)	2 (2.2)	0.56
Values are n (%). p values from chi-square or Fisher's exact test, as appropriate			

Table 3 summarises adverse events. At least one adverse event was reported by 38 of 93 participants (40.9%) in the telmisartan–amlodipine group and 44 of 93 participants (47.3%) in the amlodipine–chlorthalidone group; this difference was not statistically significant ($p = 0.38$). Overall, the adverse event burden was comparable between the two regimens. However, the patterns of specific adverse events reflected the distinct pharmacological profiles of the two combinations. Peripheral oedema occurred more frequently with telmisartan–amlodipine (7.5% vs 3.2%), consistent with amlodipine's vasodilatory effects, although the difference was not statistically significant ($p = 0.19$). Hypokalemia occurred exclusively in the amlodipine–chlorthalidone group, affecting 6 of 93 participants (6.5%), a statistically significant difference ($p = 0.01$) consistent with the well-documented potassium-lowering effect of thiazide-type diuretics. Importantly, no cases of

severe hypokalemia requiring intervention were documented. Dizziness and hypotension occurred at low and comparable frequencies in both groups, suggesting both combinations were well tolerated with respect to symptomatic adverse effects. No cases of hyperkalemia were documented in either group, which is reassuring given the inclusion of an ARB in the telmisartan–amlodipine arm.

Table 4. Key Laboratory Parameters

Parameter	Telmisartan–Amlodipine (n = 90)	Amlodipine–Chlorthalidone (n = 88)
Serum potassium, mEq/L		
Baseline	4.2 ± 0.4	4.1 ± 0.3
Week 12	4.1 ± 0.3	3.8 ± 0.4
Mean change	−0.1 ± 0.3	−0.3 ± 0.4
Serum sodium, mEq/L		
Baseline	139.2 ± 2.1	139.6 ± 2.4
Week 12	139.0 ± 2.3	138.8 ± 2.8
Mean change	−0.2 ± 1.6	−0.8 ± 2.0
Serum creatinine, mg/dL		
Baseline	0.92 ± 0.18	0.94 ± 0.20
Week 12	0.93 ± 0.19	0.96 ± 0.22
Mean change	0.01 ± 0.08	0.02 ± 0.10
eGFR, ml/min/1.73m²		
Baseline	78.5 ± 14.2	76.9 ± 15.1
Week 12	78.1 ± 14.8	76.2 ± 15.6
Mean change	−0.4 ± 4.6	−0.7 ± 5.1
Serum uric acid, mg/dL		
Baseline	5.6 ± 1.2	5.7 ± 1.3
Week 12	5.7 ± 1.3	6.3 ± 1.5
Mean change	0.1 ± 0.5	0.6 ± 0.8
Values are mean ± SD. eGFR, estimated glomerular filtration rate.		

Table 4 presents the key laboratory parameters at baseline and week 12. Mean

serum potassium decreased in the amlodipine–chlorthalidone group from 4.1 ± 0.3 mEq/L to 3.8 ± 0.4 mEq/L, representing a mean within-group change of −0.3 ± 0.4 mEq/L. This reduction is consistent with the thiazide-like diuretic effect of chlorthalidone and corresponds to the higher incidence of hypokalemia observed in this group. In contrast, serum potassium remained essentially unchanged in the telmisartan–amlodipine group (4.2 ± 0.4 to 4.1 ± 0.3 mEq/L), reflecting the potassium-sparing tendency of renin-angiotensin system blockade. A modest increase in serum uric acid was observed in the amlodipine–chlorthalidone group (mean change 0.6 ± 0.8 mg/dL) compared with a minimal change in the telmisartan–amlodipine group (0.1 ± 0.5 mg/dL), again consistent with the known metabolic effects of chlorthalidone. Serum sodium remained stable in both groups, with only small, not clinically significant mean changes. Serum creatinine and eGFR were essentially unchanged over the 12-week treatment period in both arms, indicating that neither combination adversely affected renal function in this population with preserved baseline renal function.

Table 5 summarises treatment adherence and discontinuation. Mean adherence by pill count was 91.4 ± 8.2% in the telmisartan–amlodipine group and 88.9 ± 9.6% in the amlodipine–chlorthalidone group, reflecting high levels of treatment persistence in both arms. The between-group difference in adherence was not statistically significant (p = 0.07), although there was a trend toward slightly higher adherence with telmisartan–amlodipine. Discontinuation due to adverse events occurred in 3 participants (3.2%) receiving telmisartan–amlodipine and 7 participants (7.5%) receiving amlodipine–chlorthalidone (p = 0.18).

Table 5. Treatment Adherence and Discontinuation

Variable	Telmisartan–Amlodipine (n = 93)	Amlodipine–Chlorthalidone (n = 93)	p value
Adherence by pill count, %	91.4 ± 8.2	88.9 ± 9.6	0.07
Discontinuation due to adverse events, n (%)	3 (3.2)	7 (7.5)	0.18
Loss to follow-up, n (%)	2 (2.2)	2 (2.2)	—
Withdrawal of consent, n (%)	1 (1.1)	3 (3.2)	0.31
Values are mean ± SD or n (%). p values from independent-samples t-test or chi-square/Fisher's exact test as appropriate.			

Although this difference did not reach statistical significance, the numerically higher discontinuation rate in the amlodipine–chlorthalidone group may reflect the cumulative impact of metabolic disturbances and associated symptoms. Loss to follow-up was identical in both groups (2 participants each), while 1 and 3 participants withdrew consent, respectively. Overall, the high adherence rates support the acceptability of both fixed-dose combinations in routine clinical practice and suggest that tolerability did not substantially compromise treatment persistence over the 12-week study period.

Discussion

This randomised, open-label trial compared two contemporary fixed-dose combination strategies in patients with uncontrolled hypertension despite stable monotherapy. Both telmisartan–amlodipine and

amlodipine–chlorthalidone produced substantial reductions in office systolic and diastolic blood pressure over 12 weeks. The adjusted between-group difference in systolic blood pressure reduction favoured telmisartan–amlodipine by about 3 mmHg, a modest but statistically significant advantage. Blood pressure control rates were numerically higher with telmisartan–amlodipine, although this difference did not reach statistical significance. Both regimens were generally well tolerated, with distinct adverse event profiles reflecting their constituent drug classes.

The magnitude of systolic blood pressure reduction observed with both combinations (approximately 23–26 mmHg) is consistent with previous randomised evaluations of these regimens in similar patient populations. Sharma and colleagues reported systolic reductions of approximately 23 mmHg with telmisartan–amlodipine in Indian patients with stage II hypertension [4]. White et al. demonstrated comparable reductions in ambulatory blood pressure with the same combination, confirming its efficacy across different measurement modalities [5]. Our findings extend this evidence by demonstrating robust efficacy in the specific clinical scenario of step-up therapy following inadequate monotherapy response. The slightly greater reduction observed with telmisartan–amlodipine aligns with the pharmacological rationale of combining agents with complementary mechanisms—vascular smooth muscle relaxation through calcium channel blockade alongside attenuation of angiotensin II-mediated vasoconstriction and aldosterone effects. Amlodipine served as the common backbone in both arms, which likely contributed to the overall similarity in blood pressure response. The additional contribution of chlorthalidone, while potent, may have been partially attenuated by the modest dose (12.5 mg) employed in this study, whereas the 40 mg dose of telmisartan

represents the recommended starting dose with well-documented efficacy [5].

The comparable efficacy between these regimens is clinically significant, as it suggests both are reasonable options for treatment intensification. The blood pressure control rates observed (approximately 63–69%) are meaningful in the context of global hypertension control data showing that fewer than half of treated patients achieve target values [1]. Achieving control in roughly two-thirds of previously uncontrolled patients within 12 weeks, using a fixed-dose approach without dose escalation, supports the guideline emphasis on early combination therapy [2]. The additive effects of combination therapy, as demonstrated by Wald and colleagues, provide the mechanistic underpinning for these results [3].

Safety findings deserve careful interpretation. The higher incidence of hypokalemia in the amlodipine–chlorthalidone group is consistent with the established metabolic effects of thiazide-type diuretics. Although no participants developed severe hypokalemia requiring intervention, the 6.5% incidence observed even with low-dose chlorthalidone underscores the importance of electrolyte monitoring during treatment initiation. The mild increase in serum uric acid observed in this group similarly reflects a well-characterised class effect. These metabolic perturbations, while modest in magnitude, may carry implications for long-term cardiovascular risk, particularly in patients with underlying metabolic syndrome or gout predisposition [7]. Conversely, the higher incidence of peripheral oedema with telmisartan–amlodipine is attributable to amlodipine-induced arteriolar vasodilation without proportional venodilation, a dose-dependent phenomenon. The relatively low rates of oedema in both groups likely reflect the use of amlodipine 5 mg rather than higher doses, as well as potential mitigation by telmisartan through venodilatory effects

[5]. The absence of hyperkalemia in the telmisartan–amlodipine group is reassuring, particularly emphasised renal function monitoring with renin-angiotensin system inhibitors.

Several limitations warrant acknowledgement. The open-label design introduces potential ascertainment bias, although blood pressure measurements followed a standardised protocol and the primary endpoint was objectively assessed. The single-centre setting may limit generalizability, though the pragmatic eligibility criteria enhance real-world applicability. The 12-week duration precludes assessment of long-term outcomes and durability of effect. The fixed-dose design without an escalation pathway, while reflecting clinical practice patterns with combination tablets, may have underestimated the achievable blood pressure reductions with either regimen. Medication adherence was assessed by pill counts, which may overestimate true adherence. Finally, excluding patients with significant renal or hepatic impairment limits extrapolation to these populations. Strengths of this study include its direct head-to-head comparison of two guideline-endorsed fixed-dose combinations in a clinically relevant step-up scenario, assessment of adherence, and comprehensive safety evaluation including laboratory monitoring.

Conclusion

In patients with uncontrolled hypertension on monotherapy, both fixed-dose telmisartan–amlodipine and amlodipine–chlorthalidone produced clinically meaningful blood pressure reductions with acceptable tolerability profiles. The modest superiority of telmisartan–amlodipine for systolic blood pressure reduction, along with its more favourable metabolic profile, suggests it may be the preferred option for many patients needing treatment intensification. However, amlodipine–

chlorthalidone remains a highly effective alternative, particularly when cost considerations or specific clinical factors favour diuretic-based therapy. Future research should evaluate whether these differences persist over longer follow-up periods, whether dose-escalation strategies alter comparative effectiveness, and whether differential effects on home or ambulatory blood pressure monitoring provide additional clinical insight.

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