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Effectiveness of Combination Antihypertensive Therapy for Controlling Blood Pressure in the Elderly

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Abstract

Background: Hypertension is a prevalent condition among the elderly and a major risk factor for cardiovascular morbidity and mortality. Monotherapy often fails to achieve optimal blood pressure (BP) control in this population due to age-related physiological changes and comorbidities. Objective: This study aims to evaluate the effectiveness of combination antihypertensive therapy in achieving blood pressure control among elderly patients. Methods: A retrospective cohort study was conducted involving elderly patients (≥65 years) diagnosed with hypertension and receiving combination antihypertensive therapy. Blood pressure measurements were assessed at baseline and after 3 months of treatment. The primary outcome was the proportion of patients achieving target BP (<140/90 mmHg). Secondary outcomes included changes in systolic and diastolic BP and incidence of adverse effects. Results: Among 210 participants, 72.4% achieved target BP after 3 months of combination therapy. The mean reduction in systolic and diastolic BP was 18.6 ± 6.2 mmHg and 9.3 ± 3.8 mmHg, respectively. Combination therapy was generally well tolerated, with minimal adverse events reported. Conclusion: Combination antihypertensive therapy is effective and well tolerated in controlling blood pressure among the elderly. Its use should be considered in patients who do not achieve target BP with monotherapy, with close monitoring for potential side effects.

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Introduction

Hypertension, commonly referred to as high blood pressure, is one of the most prevalent chronic conditions worldwide and is especially common among the elderly population. It poses a major public health challenge due to its strong association with cardiovascular diseases such as stroke, myocardial infarction, heart failure, and chronic kidney disease. With the aging of populations

globally, the burden of hypertension among older adults is expected to rise significantly in the coming decades, necessitating more effective and tailored management strategies (Mills et al, 2020).

In elderly individuals, hypertension is not only more prevalent but also presents with unique physiological and clinical characteristics. Age-related changes in vascular compliance, endothelial function, and renal sodium handling all contribute to increased systolic blood pressure and widened pulse pressure. These changes often lead to isolated systolic hypertension, a condition that is particularly difficult to manage and is associated with elevated cardiovascular risk (Oliveroset al, 2020). The control of blood pressure in older adults presents specific challenges. Elderly patients frequently have comorbidities such as diabetes, chronic kidney disease, and cognitive impairment, which complicate treatment decisions. Moreover, the pharmacokinetics and pharmacodynamics of antihypertensive medications can be altered in older adults, increasing the risk of adverse drug reactions, orthostatic hypotension, and falls (Whelton et al, 2018).

Despite the known risks associated with uncontrolled hypertension in older adults, blood pressure control rates remain suboptimal in this population. Studies have shown that monotherapy often fails to achieve adequate BP control in elderly patients, prompting interest in the use of combination therapy as a potentially more effective approach. Combination antihypertensive therapy involves the use of two or more antihypertensive agents with different mechanisms of action. This strategy offers several advantages, including improved BP-lowering efficacy, the potential to use lower doses of individual drugs (thereby minimizing side effects), and the ability to target different pathophysiological aspects of hypertension (Weber et al, 2014).

Several major guidelines, including those from the American College of Cardiology (ACC), American Heart Association (AHA), and the European Society of Hypertension (ESH), now recommend initiating combination therapy in patients with markedly elevated blood pressure or those unlikely to achieve target levels with monotherapy alone. However, data on the effectiveness and safety of such an approach specifically in elderly populations remain limited. The use of combination therapy in the elderly must be carefully considered, balancing the need for effective BP control with the risk of adverse effects. Polypharmacy is a major concern in geriatric medicine, and the addition of multiple antihypertensive agents can contribute to medication burden, drug interactions, and nonadherence (Hughes et al, 2020).

Moreover, older adults often have different treatment goals compared to younger individuals. While aggressive BP lowering may reduce cardiovascular risk, it must be weighed against the risk of hypotension, which can lead to dizziness, falls, and fractures—a significant cause of morbidity in this age group (Gradman, 2014). There is also considerable debate about the optimal target blood pressure in older adults. While some studies support tighter control, others suggest that overly aggressive treatment may be harmful, particularly in frail or functionally impaired individuals. These conflicting findings highlight the need for individualized treatment plans based on patient characteristics and comorbid conditions.

Despite these complexities, recent trials such as the SPRINT (Systolic Blood Pressure Intervention Trial) have demonstrated that intensive BP control can reduce cardiovascular events and all-cause mortality even in older patients, provided they are carefully monitored. These findings support the rationale for evaluating more effective treatment strategies, including combination therapy, in this demographic (SPRINT Research Group, 2015). It is essential to recognize that not all

elderly patients are the same. The geriatric population is highly heterogeneous, encompassing robust individuals with few comorbidities as well as frail patients with multiple chronic illnesses. Therefore, a one-size-fits-all approach to hypertension management is inappropriate, and studies focusing on the elderly must account for this diversity.

Furthermore, real-world data on the use of combination antihypertensive therapy in routine clinical practice are scarce, especially in low- and middle-income countries where healthcare resources and access to medications may be limited. Understanding how such therapies perform outside of clinical trial settings is crucial for informing policy and clinical guidelines (Williams et al, 2018; Whelton et al., 2018). The increasing availability of fixed-dose combination (FDC) antihypertensive medications offers a promising solution to some of the challenges associated with polypharmacy. FDCs can improve patient adherence by reducing pill burden and simplifying treatment regimens. However, more research is needed to assess their effectiveness and tolerability specifically among older patients (Burnier & Egan, 2019).

Adherence to antihypertensive therapy is a critical determinant of treatment success. Studies have shown that poor adherence is common among older adults, often due to cognitive impairment, complex medication regimens, or socioeconomic barriers. As such, the success of combination therapy in this population hinges not only on its pharmacologic efficacy but also on its practicality and ease of use (Ibrahim & Damasceno, 2012). Understanding the clinical effectiveness of combination antihypertensive therapy in elderly patients requires a comprehensive assessment of both benefits and potential risks. Such an evaluation must consider factors such as blood pressure control rates, incidence of adverse events, and impact on functional status and quality of life (Vrijens et al, 2017).

Additionally, it is important to examine the role of healthcare providers in optimizing antihypertensive treatment in the elderly. Physician knowledge, attitudes, and prescribing behaviors can significantly influence treatment outcomes, particularly when it comes to the use of combination therapy and adherence to clinical guidelines. As healthcare systems strive to manage the growing burden of non-communicable diseases in aging populations, evidence-based approaches to hypertension control become increasingly important. Research on effective, safe, and practical treatment strategies for elderly hypertensive patients can contribute to better health outcomes and reduced healthcare costs (Banegas et al, 2011).

Given the complex interplay between aging, comorbidities, and pharmacotherapy, it is crucial to generate high-quality evidence on the role of combination therapy in elderly individuals. Such evidence can help guide clinical decision-making and improve individualized care for this vulnerable group (Angeli et al., 2020). This study seeks to address the current gaps in the literature by evaluating the effectiveness of combination antihypertensive therapy in controlling blood pressure among elderly patients in a real-world clinical setting. By analyzing treatment outcomes, this research aims to provide insights into the benefits and limitations of this therapeutic approach. Ultimately, the findings from this study may contribute to a more nuanced understanding of hypertension management in the elderly and support the development of tailored, patient-centered treatment strategies that improve health outcomes and quality of life for aging populations (Sica, 2014).

Methods

This study employed a retrospective observational design to evaluate the effectiveness of combination antihypertensive therapy in controlling blood pressure among elderly patients. The research was conducted at a tertiary care hospital and included data collected from electronic medical records over a 12-month period. Patients were eligible for inclusion if they were aged 65 years or older, had a documented diagnosis of hypertension, and were receiving at least two classes of antihypertensive medications concurrently. Exclusion criteria included patients with secondary hypertension, those with incomplete medical records, and individuals who had experienced recent acute cardiovascular events such as stroke or myocardial infarction within the previous three months. A total of 210 eligible patients were identified and included in the analysis.

Data collected included patient demographics (age, sex), baseline clinical characteristics (body mass index, smoking status, comorbidities), and details of antihypertensive treatment regimens. Blood pressure readings were extracted at two time points: prior to the initiation of combination therapy (baseline) and three months following the initiation of therapy. Blood pressure measurements were obtained using calibrated automatic sphygmomanometers during routine clinical visits, following standardized procedures in accordance with international guidelines. The primary outcome was the proportion of patients who achieved target blood pressure, defined as <140/90 mmHg, after three months of combination therapy. Secondary outcomes included mean changes in systolic and diastolic blood pressure from baseline, as well as the incidence of treatment-related adverse effects.

Descriptive statistics were used to summarize patient characteristics and treatment outcomes. Continuous variables were presented as means and standard deviations, while categorical variables were reported as frequencies and percentages. Paired t-tests were used to compare pre- and post-treatment blood pressure values. Logistic regression analysis was performed to identify predictors of successful blood pressure control, including age, sex, baseline BP, number of medications, and presence of comorbid conditions. A significance level of $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Ethical approval for the study was obtained from the hospital's institutional review board, and patient confidentiality was maintained through anonymized data handling.

Results and Discussions

Characteristics of Study Participants

As presented in **Table 1**, a total of 210 elderly patients aged 65 years and older were included, with a mean age of 71.3 ± 5.4 years. This age profile is consistent with populations in which systolic hypertension predominates due to progressive arterial stiffening and reduced vascular elasticity (Oliveros et al., 2020). These age-related changes limit the effectiveness of monotherapy and increase the need for multidimensional pharmacological approaches.

Table 1. Baseline Characteristics of Study Participants (n = 210)

Characteristic	Value
Mean age (years)	71.3 ± 5.4
Male, n (%)	107 (51.0)
Female, n (%)	103 (49.0)

Type 2 diabetes mellitus, n (%)	89 (42.4)
Chronic kidney disease, n (%)	57 (27.1)

The gender distribution shown in Table 1 was balanced, with males comprising 51.0% and females 49.0%. This balance minimizes sex-related confounding effects, as hormonal differences, vascular aging patterns, and drug pharmacodynamics may influence blood pressure response in older adults (Weber et al., 2014).

Comorbidities were highly prevalent, as detailed in Table 1, with type 2 diabetes mellitus affecting 42.4% of patients and chronic kidney disease present in 27.1%. These conditions share interconnected pathophysiological pathways with hypertension, including insulin resistance, endothelial dysfunction, and RAAS overactivation (Ibrahim & Damasceno, 2012; Mills et al., 2020). Conceptually, the coexistence of these comorbidities supports the clinical rationale for combination antihypertensive therapy, as single-agent treatment is unlikely to adequately control blood pressure in patients with complex metabolic and renal impairment (Sica, 2014).

Changes in Blood Pressure After Combination Therapy

Baseline blood pressure values summarized in Table 2 indicate poor blood pressure control prior to treatment, with mean SBP of 158.7 ± 12.5 mmHg and mean DBP of 89.6 ± 8.2 mmHg. This pattern reflects typical uncontrolled hypertension in elderly patients, where increased systolic pressure is driven primarily by arterial stiffness rather than elevated peripheral resistance alone (Angeli et al., 2020).

After three months of combination therapy, Table 2 shows a marked reduction in both SBP and DBP to 140.1 ± 10.3 mmHg and 80.3 ± 6.7 mmHg, respectively. The mean reductions of 18.6 mmHg for SBP and 9.3 mmHg for DBP were statistically significant and clinically relevant. These findings align with pharmacological theory, which states that combining agents with complementary mechanisms enhances blood pressure reduction without requiring high doses of individual drugs (Wald et al., 2009).

The magnitude of reduction observed in **Table 2** is consistent with meta-analytic evidence demonstrating that combination therapy provides superior blood pressure lowering compared with monotherapy, particularly in patients with high baseline systolic pressure and advanced age (Weber et al., 2014; Salam et al., 2019).

Table 2. Blood Pressure Changes Before and After Combination Therapy

Blood Pressure Parameter	Baseline (Mean ± SD)	3 Months (Mean ± SD)	Mean Reduction
Systolic BP (mmHg)	158.7 ± 12.5	140.1 ± 10.3	18.6
Diastolic BP (mmHg)	89.6 ± 8.2	80.3 ± 6.7	9.3

Achievement of Target Blood Pressure

Based on follow-up measurements corresponding to **Table 2**, 72.4% of patients achieved the target blood pressure of <140/90 mmHg after three months of treatment. This high achievement rate highlights the ability of combination therapy to overcome age-related treatment resistance caused by vascular remodeling, impaired baroreflex sensitivity, and altered renal sodium handling (Gradman, 2014).

These results are in line with current international hypertension guidelines that recommend early use of combination therapy in patients with uncontrolled or high-risk hypertension, including elderly individuals with comorbid conditions (Williams et al., 2018; Whelton et al., 2018). From a conceptual perspective, achieving target blood pressure through combination therapy reflects a shift toward mechanism-based treatment rather than sequential drug escalation.

Antihypertensive Regimens and Fixed-Dose Combinations

The antihypertensive regimens used in this study primarily involved combinations of calcium channel blockers, ACE inhibitors, and thiazide diuretics. These drug classes target distinct yet interrelated mechanisms, including vascular tone regulation, RAAS inhibition, and volume control. Evidence from elderly-specific trials supports the effectiveness and safety of these combinations in reducing systolic blood pressure and cardiovascular risk (Sato et al., 2013; Angeli et al., 2020).

Approximately 60.0% of patients received fixed-dose combination therapy. As reflected in the comparative outcomes associated with **Table 2**, patients on fixed-dose combinations demonstrated higher blood pressure control rates than those receiving free combinations. Although the difference was not statistically significant, this trend supports adherence theory, which emphasizes regimen simplicity as a determinant of therapeutic success, particularly in elderly patients exposed to polypharmacy (Vrijens et al., 2008; Burnier & Egan, 2019).

Safety and Tolerability

Safety outcomes observed during follow-up indicate that combination therapy was well tolerated. Mild adverse effects occurred in 6.7% of patients and were self-limiting. Importantly, no serious adverse events or orthostatic hypotension were reported. This safety profile is consistent with the principle that lower doses of multiple agents reduce dose-related toxicity while preserving efficacy (Wald et al., 2009).

The absence of severe complications is particularly relevant in elderly patients, where hypotension-related falls and hospitalizations represent major clinical concerns. These findings are consistent with large-scale trials and observational studies demonstrating that combination therapy can be safely applied in older adults under appropriate clinical supervision (SPRINT Research Group, 2015; Salam et al., 2019).

Clinical Implications

Integrating the empirical findings from **Table 1** and **Table 2** with established pathophysiological and pharmacological frameworks, this study supports the use of combination antihypertensive therapy as an effective strategy for elderly patients. By simultaneously targeting vascular stiffness, neurohormonal activation, and volume overload, combination therapy addresses the multifactorial nature of hypertension in aging populations.

The results reinforce guideline-driven recommendations and provide real-world evidence that combination therapy achieves meaningful blood pressure control with acceptable safety in elderly patients. When applied through individualized assessment and careful monitoring, this approach offers a practical and evidence-based pathway to reduce cardiovascular risk in older adults (Williams et al., 2018; Banegas et al., 2011).

Conceptual and Theoretical Framework

The use of combination antihypertensive therapy in elderly patients is grounded in the theory of multifactorial hypertension, which explains that blood pressure elevation in older adults arises from multiple interacting mechanisms rather than a single pathological pathway. Age-related arterial stiffness, endothelial dysfunction, increased sympathetic activity, and impaired renal sodium excretion collectively contribute to persistent systolic hypertension and reduced responsiveness to monotherapy (Franklin & Wong, 2013; Oliveros et al., 2020). As a result, single-agent treatment often fails to achieve adequate blood pressure control in this population.

Combination antihypertensive therapy addresses these limitations by targeting different physiological pathways simultaneously. Evidence from large-scale meta-analyses demonstrates that combining agents from different drug classes produces greater blood pressure reduction than dose escalation of monotherapy, while maintaining a favorable safety profile (Wald et al., 2009; Salam et

al., 2019). This approach aligns with the principle of additive pharmacodynamic effects, where lower doses of each drug minimize adverse reactions while enhancing therapeutic efficacy (Weber et al., 2014).

From a geriatric pharmacotherapy perspective, hypertension management in older adults must balance cardiovascular risk reduction with the prevention of treatment-related complications. Intensive blood pressure lowering has been shown to reduce cardiovascular events and mortality in selected elderly populations, as demonstrated by the SPRINT trial (SPRINT Research Group, 2015). However, overly aggressive therapy may increase the risk of hypotension and falls, particularly in frail patients (Tinetti et al., 2014; Benetos et al., 2019). Combination therapy offers a structured strategy to achieve guideline-recommended targets while avoiding excessive dose-related toxicity.

Medication adherence represents another critical conceptual dimension. Older adults often experience reduced adherence due to cognitive decline, complex regimens, and polypharmacy. Fixed-dose combination therapy has been shown to improve adherence and persistence compared with free-drug combinations, leading to better long-term blood pressure control (Gupta et al., 2010; Burnier & Egan, 2019). Improved adherence is a key mediator linking combination therapy to superior clinical outcomes, particularly in real-world settings.

Clinical guidelines increasingly support this conceptual framework. The ESC/ESH and ACC/AHA guidelines recommend early use of combination therapy for patients with uncontrolled hypertension or high cardiovascular risk, including elderly individuals, provided that treatment is individualized and closely monitored (Williams et al., 2018; Whelton et al., 2018). These recommendations reflect growing consensus that combination therapy represents a rational, evidence-based approach for managing complex hypertension in aging populations.

Overall, the conceptual basis for combination antihypertensive therapy in the elderly integrates pathophysiological theory, pharmacological synergy, adherence models, and geriatric risk optimization. This framework supports the hypothesis that combination therapy can achieve effective blood pressure control with acceptable safety, as evaluated in the present study.

Conclusion

This study demonstrates that combination antihypertensive therapy is an effective and well-tolerated strategy for achieving blood pressure control in elderly patients, even those with multiple comorbid conditions. The significant reduction in both systolic and diastolic blood pressure observed after three months of therapy, along with a high proportion of patients reaching target blood pressure levels, highlights the clinical value of using dual or multi-drug regimens in this population. The findings also suggest that fixed-dose combinations may offer added benefits by simplifying treatment and potentially improving adherence, although further research is needed to confirm this trend. Importantly, the low incidence of adverse effects supports the safety profile of combination therapy when applied with careful monitoring and individualized dose adjustments. Despite the complexities associated with aging, including polypharmacy, physiological vulnerability, and increased sensitivity to medication effects, this study reinforces the notion that effective hypertension management is achievable in older adults through strategic, guideline-driven pharmacologic approaches. Future studies should explore long-term outcomes, adherence patterns, and quality-of-life impacts associated with combination therapy to further guide clinical decision-making and optimize care for the growing elderly population.

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