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Review Article

Efficacy and Safety of Major Antihypertensive Drug Classes in Adults with Hypertension: A Systematic Review

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ABSTRACT

Background: Hypertension (HTN) remained a major global health concern and a leading risk factor for cardiovascular morbidity and mortality, with many patients requiring more than single-drug therapy to achieve optimal blood pressure control.

Objective: This study aimed to evaluate and compare the efficacy and safety of commonly used antihypertensive drug classes, with a focus on different combination therapy strategies.

Methods: A systematic review was conducted using PubMed and Google Scholar to identify relevant clinical trials and supporting studies in adult patients with HTN. Studies were selected based on predefined eligibility criteria using the Population, Intervention, Comparison, Outcome (PICO) framework. Data extraction included systolic blood pressure (SBP), diastolic blood pressure (DBP), overall blood pressure control, nighttime blood pressure control, sustained effects, and safety outcomes such as adverse effects, electrolyte changes, and heart rate (HR). A structured comparative approach was used to analyze monotherapy, dual therapy, and multi-drug combinations.

Results: The included studies showed that all major antihypertensive drug classes contributed to reductions in SBP and DBP; however, combination therapy demonstrated more consistent and effective overall blood pressure control compared to monotherapy. Differences were observed among drug classes in terms of specific effects, including HR reduction and electrolyte changes.

Conclusion: The findings suggested that combination therapy played an important role in achieving better blood pressure control, and a structured comparison of different drug classes and their combinations provided a clearer understanding of their relative efficacy and safety.

Key Words: Antihypertensive Drugs, Hypertension, Monotherapy, clinical practice, renin-angiotensin-aldosterone system, Combination Therapy in Hypertension.

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INTRODUCTION

Hypertension is one of the most common chronic conditions worldwide and a major contributor to cardiovascular morbidity and mortality. A large proportion of adults are affected, many of whom remain undiagnosed or inadequately treated. Persistent elevation of blood pressure is strongly associated with serious complications such as stroke, myocardial infarction, heart failure, and kidney disease, making its effective management a clinical priority [1].

Despite the availability of multiple antihypertensive drug classes, achieving optimal blood pressure control remains challenging in many patients. This underscores the need for better understanding of treatment strategies and their comparative effectiveness in different clinical settings [2].

Overview of hypertension

Hypertension is defined as a sustained elevation of arterial blood pressure and is one of the leading modifiable risk factors for cardiovascular diseases worldwide. Clinically, it is commonly identified when systolic blood pressure is ≥140 mmHg and/or diastolic blood pressure is ≥90 mmHg, based on repeated measurements. The condition is often described as a "silent disease" because many individuals remain asymptomatic for long periods, despite ongoing vascular damage [3].

It affects individuals across all age groups but is more common in middle-aged and elderly populations. If left untreated, hypertension can lead to serious complications including stroke, coronary artery disease, heart failure, and chronic kidney disease, thereby contributing significantly to global disease burden [4].

Early detection and appropriate management of hypertension are therefore essential to reduce long-term complications and improve overall health outcomes. This makes it a major focus area in both clinical practice and public health research [5].

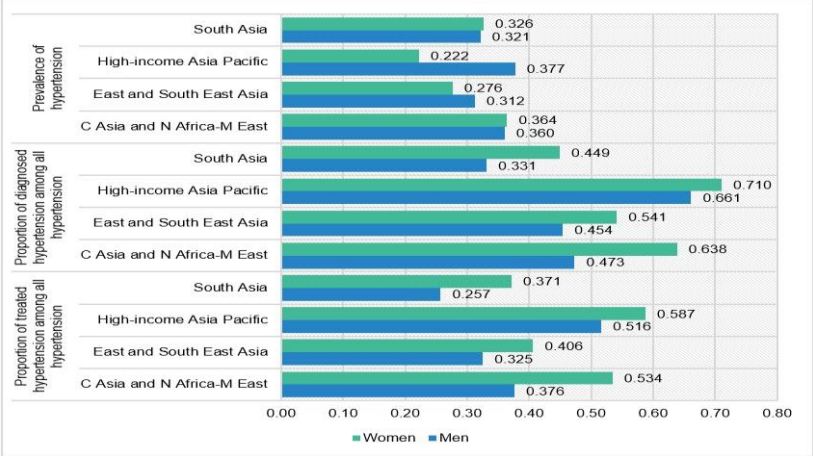

Figure 1: Hypertension Among Men and Women in Asia, 2019

Hypertension, a ticking time bomb that can be stopped to save millions of livesBy Tetsushi Sonobe, Raja Rajendra Timilsina, Dil Rahut

Cause of hypertension

Hypertension is a multifactorial disorder resulting from combined physiological and pathological mechanisms. A major contributor is increased vascular resistance due to persistent vasoconstriction, which reduces lumen diameter and elevates pressure. In contrast, normal vasodilation maintains blood flow, but this balance is often disrupted in hypertension. Overactivation of the renin-angiotensin-aldosterone system (RAAS) further increases blood pressure by promoting sodium and water retention. Increased sympathetic activity also contributes by raising heart rate and causing vasoconstriction. Over time, vascular remodeling and endothelial dysfunction lead to sustained hypertension and related complications [6].

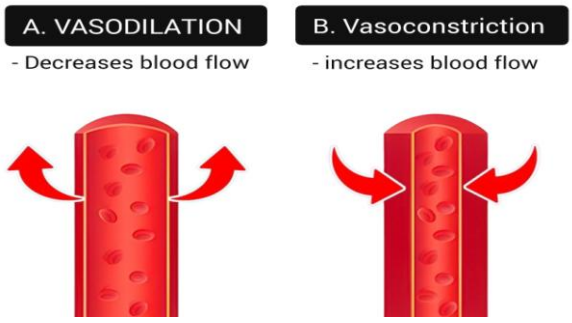

Figure 2: Vasodilation refers to the widening of arteries due to relaxation of the smooth

Muscle in the vessel wall, resulting in an increased lumen diameter and improved blood flow. In contrast, **vasoconstriction** involves the contraction of vascular smooth muscle, leading to narrowing of the arterial lumen and increased resistance to blood flow, which contributes to elevated blood pressure.[7]

Effect of hypertension

Prolonged hypertension affects multiple organs through continuous exposure to elevated vascular pressure, leading to structural and functional damage. In the heart, it increases workload, causing left ventricular hypertrophy and impaired function. In the brain, it damages cerebral vessels, raising the risk of stroke. Blood

vessels also develop stiffness and endothelial dysfunction, worsening blood pressure control. Overall, hypertension causes macrovascular and microvascular damage, affecting organ structure and function if uncontrolled [8].

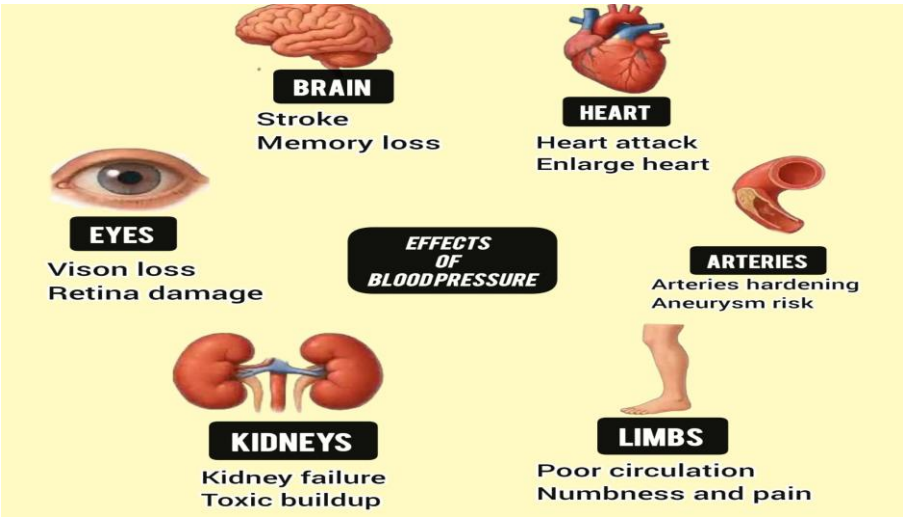

Figure 3: Impact of Hypertension on Multiple Target Organs

Each segment represents a different organ system, including the heart, brain, kidneys, and blood vessels, highlighting how sustained high blood pressure contributes to structural and functional damage.[9]

Pathophysiology and clinical burden

Hypertension results from multiple physiological changes affecting blood pressure regulation. A key mechanism is increased peripheral vascular resistance due to narrowed or less flexible vessels. The renin-angiotensin-aldosterone system (RAAS) also contributes by promoting vasoconstriction and fluid retention, leading to elevated blood pressure.

Clinically, hypertension is significant due to its silent yet progressive nature. Many patients remain asymptomatic until complications such as stroke, myocardial infarction, heart failure, and kidney damage occur, contributing to global morbidity and mortality [10].

Overall, understanding its mechanisms and clinical impact emphasizes the importance of early diagnosis and effective long-term management [11].

Mechanism of hypertensive drugs

RAAS mechanism

The renin-angiotensin-aldosterone system (RAAS) plays a key role in regulating blood pressure and fluid balance. It is activated by reduced renal blood flow, leading to renin release, which converts angiotensinogen to angiotensin I and then to angiotensin II via ACE. Angiotensin II causes vasoconstriction, increasing vascular resistance and blood pressure, and stimulates aldosterone release, promoting sodium and water retention. These effects contribute to the development of hypertension. ACE inhibitors and angiotensin receptor blockers (ARBs) interrupt this pathway by reducing angiotensin II formation or action, leading to vasodilation and decreased fluid retention. This mechanism underlies their therapeutic effect in the present study [12].

Calcium channel blocker mechanism

Calcium channel blockers reduce blood pressure by promoting vasodilation through their action on vascular smooth muscle. They inhibit L-type calcium channels, decreasing calcium influx required for contraction, leading to relaxation of blood vessels and reduced peripheral resistance. Certain subclasses, especially non-dihydropyridines, also reduce heart rate and myocardial contractility, further lowering blood pressure. Due to their effectiveness and compatibility with other agents, they are widely used in hypertension management [13].

Beta blocker mechanism

Beta-blockers reduce blood pressure by acting on the sympathetic nervous system. They block beta-adrenergic receptors, decreasing heart rate and cardiac output, thereby lowering blood pressure. They also reduce renin release from the kidneys, indirectly suppressing the renin-angiotensin-aldosterone system (RAAS). Through effects on both cardiac function and hormonal regulation, they provide a dual mechanism of action and are particularly beneficial in conditions such as heart failure or post-myocardial infarction [14].

Diuretics mechanism

Diuretics lower blood pressure by promoting the excretion of sodium and water through the kidneys. By inhibiting sodium reabsorption in renal tubules, they increase urine output and reduce blood volume, leading to decreased cardiac output. With continued use, they also reduce peripheral vascular resistance. Thiazide diuretics, such as hydrochlorothiazide, are commonly used for long-term control, though they may cause electrolyte disturbances like hypokalemia, requiring monitoring [15].

Combined mechanism

The combined use of antihypertensive drugs targets multiple physiological mechanisms involved in high blood pressure. Unlike monotherapy, combination therapy allows drugs to act simultaneously on pathways such as vascular resistance, fluid balance, and hormonal regulation, resulting in more effective blood pressure reduction. It also enables the use of lower doses, reducing adverse effects, while complementary drug actions may counteract side effects and improve outcomes. Overall, this approach provides greater blood pressure control and better protection against hypertension-related complications compared to monotherapy [16].

Overview of Antihypertensive Drug Combinations and Their Mechanisms

To better understand the therapeutic approach used in this study, a structured overview of commonly used antihypertensive drugs and their combinations along with their mechanisms of action is presented below.

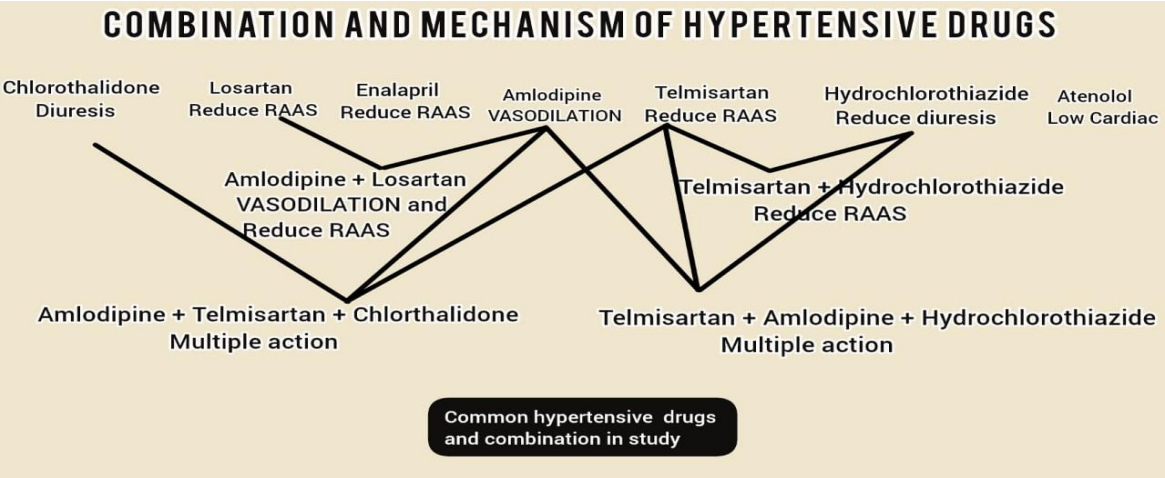

Figure 4: commonly used antihypertensive drugs and their combinations along with their primary mechanisms of action

The upper section includes individual drugs with their key mechanisms such as vasodilation, RAAS inhibition, diuresis, and reduction in cardiac output. The lower section illustrates dual and triple drug combinations, highlighting their combined mechanisms that target multiple pathways simultaneously. The connecting lines demonstrate how different classes of drugs are integrated in combination therapy to achieve more effective and sustained blood pressure control[17].

Knowledge gap in existing literature

Although many studies have evaluated antihypertensive drugs, the evidence is often scattered and focused on individual classes rather than direct comparisons. Most trials assess single drugs or specific combinations, making it difficult to draw consistent conclusions about overall blood pressure control and safety [18].

While combination therapy is widely used, there is limited consolidated evidence comparing the effectiveness of different dual and triple regimens, as most studies report findings in isolation, therefore, a systematic approach is needed to organize available evidence and better understand the comparative performance of antihypertensive drug classes and their combinations to improve treatment strategies and outcomes [19].

Aim of study

The aim of this systematic review is to evaluate and compare the efficacy and safety of commonly used antihypertensive drug classes. It focuses on understanding their performance both individually and in combination, as used in clinical practice, A structured approach was used to compare monotherapy, dual therapy, and triple combinations by grouping treatments based on pharmacological classes and commonly used regimens. This reflects real-world management, where combination therapy is often required to achieve target blood pressure levels [20].

Multiple outcome parameters were analyzed, including systolic and diastolic blood pressure, overall control, nighttime control, sustained effects, and safety outcomes such as adverse effects and electrolyte changes. This helps provide a clearer comparison of different therapies.

Overall, the objective is to present a clinically relevant comparison of antihypertensive therapies, highlighting the role of combination strategies in improving blood pressure control and patient outcomes [21].

Methods

This systematic review evaluated the efficacy and safety of commonly used antihypertensive drug classes, focusing on monotherapy, dual therapy, and triple drug combinations. A structured approach was followed in which selected clinical studies were analyzed and grouped based on drug classes and commonly used combinations to allow practical comparison. Outcome measures included systolic and diastolic blood pressure reduction, overall control, nighttime control, sustained effects, safety profile, and effects in specific populations. Overall, the methodology aimed to provide a clear

comparison of antihypertensive therapies, emphasizing the effectiveness of combination treatment strategies [22].

Eligibility Criteria (PICO Framework)

The eligibility criteria for this review were defined using the PICO (Population, Intervention, Comparison, Outcome) framework. Studies included adult patients with hypertension, including those with comorbid conditions, while pediatric and undefined populations were excluded. Interventions involved common antihypertensive drug classes such as ACE inhibitors, ARBs, calcium channel blockers, beta-blockers, and diuretics, including monotherapy and combination therapies. Comparisons were made between different drug classes and combinations, including monotherapy versus dual and triple regimens. Outcomes assessed included systolic and diastolic blood pressure reduction, overall and nighttime control, sustained effects, safety outcomes, and effects in specific populations. This framework ensured a structured and clinically relevant selection of studies [23].

Information Sources

The literature search was conducted using PubMed and Google Scholar, selected for their wide coverage of peer-reviewed biomedical literature and availability of free full-text articles. The search focused on clinical trials and review articles related to antihypertensive drug classes and their combinations, including only English-language full-text studies. Reference lists of selected articles were also screened to identify additional relevant studies. This approach ensured inclusion of reliable and high-quality literature for the review [24].

Search Strategy

The search strategy was conducted in a stepwise manner to compare antihypertensive drug classes and their combinations. Initially, clinical trials were identified using keywords such as "hypertension," "antihypertensive drugs," "clinical trial," "blood pressure reduction," and "combination therapy" in PubMed and Google Scholar. Emphasis was placed on studies reporting measurable outcomes, particularly systolic and diastolic blood pressure changes, forming the primary dataset. In the second stage, review articles and meta-analyses were included using terms like "dual therapy," "triple therapy," and "combination antihypertensive treatment" to support and validate findings. Manual screening based on commonly used drugs and combinations further refined the selection, ensuring an evidence-based and structured approach [25].

Study Selection

The study selection focused on clinical trials with clear and comparable data. Articles from PubMed and Google Scholar were initially screened by title and abstract, followed by full-text review. Only studies reporting measurable outcomes such as systolic and diastolic blood pressure or overall control were included, with preference for those allowing comparison between drug classes or multiple treatment arms. Studies were grouped into monotherapy, dual therapy, and multi-drug combinations for structured comparison. Manual screening further prioritized studies involving commonly used drugs such as atenolol, amlodipine, enalapril, hydrochlorothiazide, and losartan to ensure consistency with the comparative objective [26].

Data Extraction

Data extraction was performed in a structured manner to ensure consistency across studies. Relevant information from each clinical trial was collected, focusing on outcomes usable for comparison. Key data included systolic and diastolic blood pressure reduction, overall control, nighttime control, sustained effects, and safety outcomes such as adverse effects, electrolyte changes, and heart rate. The data were organized based on drug classes and combinations, allowing alignment into a common framework despite differences in study design. Both direct and indirect comparisons were considered, enabling the construction of a comparative table for further analysis of antihypertensive drug combinations [27].

Risk of Bias Assessment

The risk of bias was assessed to ensure reliability of included clinical trials. Factors such as randomization, presence of control groups, and clarity of outcome reporting were considered. Studies with well-described methodology and consistent outcomes were considered lower risk, while those with limited details were interpreted cautiously. Variations in sample size, treatment duration, and patient population were also considered, as they could influence results. Rather than excluding such studies, findings were interpreted within these limitations. Overall, this assessment ensured that comparisons were based on credible evidence while acknowledging study limitations [28].

Data Synthesis

Data synthesis was performed using a structured comparative approach. Extracted data were organized based on parameters such as systolic and diastolic blood pressure, overall control, nighttime control, sustained effects, safety profile, electrolyte changes, and heart rate. Findings were grouped by drug classes and further categorized into monotherapy, dual therapy, and multi-drug combinations. The final synthesis was presented in a comparative table, enabling clear evaluation of efficacy and safety across treatment strategies [29].

Result

Findings from the selected studies are compiled and analyzed to evaluate the comparative efficacy and safety of the interventions. The results are structured in tabular form to facilitate consistency and clarity in interpretation.

Study selection

A total of relevant studies was identified through systematic database searching and screened based on predefined inclusion and exclusion criteria. After removal of duplicates and initial screening of titles and abstracts, potentially eligible studies were assessed for full-text review. Following detailed evaluation, six studies met the

eligibility criteria and were included in the final analysis [30]. The study selection process was conducted in accordance with PRISMA guidelines to ensure transparency and reproducibility [31].

Character of included studies

The studies included in this review consisted of randomized clinical trials along with one pooled analysis, each evaluating different antihypertensive treatment approaches across varied patient populations, Across the studies, a range of treatment strategies were examined, including monotherapy, dual therapy, and triple drug combinations commonly used in the management of hypertension [32].One of the trials focused specifically on the effectiveness of combining amlodipine with losartan in patients diagnosed with stage 2 hypertension.

In addition, a pooled analysis explored the broader effects of hormone therapy on cardiovascular and cancer-related outcomes in postmenopausal women, Another study assessed the long-term safety and sustained efficacy of a triple combination regimen over an extended follow-up period, Furthermore, one study provided a comparative evaluation of multiple antihypertensive drug classes in patients with obstructive sleep apnea, offering insight into drug-specific responses in this subgroup [33].

Risk of bias assessment result

The risk of bias across the included studies was generally acceptable, as most of them were randomized clinical trials with clearly defined methodologies, In several studies, randomization and treatment allocation were appropriately described, which reduces the chances of selection bias. However, a few studies provided limited details regarding blinding and allocation concealment, making it slightly difficult to fully assess performance and detection bias, The pooled analysis study showed some limitations in terms of outcome reporting, as the data were derived from previously published trials rather than a single controlled setting, Overall, the studies demonstrated a moderate level of methodological quality, with some variations in reporting and study design, but none of the limitations were significant enough to exclude them from the analysis [34].

Effect of intervention

The overall findings suggest that combination therapies provide better blood pressure control than monotherapy, especially in moderate to severe hypertension. This highlights the importance of using multiple drug classes to achieve optimal outcomes, One study showed that a low-dose triple combination produced a significant and consistent reduction in both systolic and diastolic blood pressure, indicating that lower doses in combination can be clinically effective [35].

Dual therapy with amlodipine and losartan demonstrated superior blood pressure reduction compared to monotherapy, particularly in stage 2 hypertension, supporting the benefit of combining drugs with different mechanisms, In contrast, a pooled analysis of hormone therapy did not show a clear reduction in cardiovascular events, suggesting limited effectiveness in this context, Long-term data from another study indicated that triple combination therapy maintained its blood pressure-lowering effect over time, highlighting its role in sustained control, Among individual drugs, atenolol showed a greater reduction in diastolic blood pressure compared to amlodipine, enalapril, and losartan, especially during nighttime in patients with obstructive sleep apnea, Overall, while most antihypertensive agents are effective, combination therapies-particularly triple regimens-offer more consistent and sustained control, though effectiveness may vary based on patient characteristics [36].

Comparative table

To enhance clarity, data from the included clinical trials were organized into tables based on therapeutic approach. Due to differences in reporting and treatment strategies, the data were categorized into monotherapy, dual therapy, and triple combination groups based on the number and mechanism of drugs used. A mechanism-based summary table was also included to show how combinations target different pathways. This approach allowed both quantitative comparison and qualitative interpretation of outcomes[37].

Table 1: Monotherapy

Sr No	Drug	SBP ↓ (mmHg)	DBP ↓ (mmHg)	Overall Control	Night-time BP Control	Population	Adverse Effects	Electrolyte Change	Heart Rate	Interpretation
1	Atenolol	13.4 ↓	12.1 ↓	Good	Strong ↓	OSA patients	Fatigue, dyspepsia	No significant change	↓ Significant (~17 bpm)	Strong effect on HR and night BP
2	Amlodipine	14.0 ↓	6.8 ↓	Moderate	Less effective	General HTN	Mild	No significant change	No major effect	Strong SBP reduction
3	Enalapril	7.3 ↓	4.6 ↓	Moderate	Less effective	General HTN	Cough, headache	No significant change	No major effect	Moderate overall effect
4	Hydrochlorothiazide	8.8 ↓	7.4 ↓	Moderate	Comparable	General HTN	Mild	↓ Potassium (~0.32 mmol/L)	No major effect	Volume-based control
5	Losartan	10.7 ↓	5.2 ↓	Moderate	Less effective	General HTN	Mild	No significant change	No major effect	RAAS-targeted effect

Table 1: The monotherapy table presents the effects of individual antihypertensive drugs on blood pressure and related parameters. Amlodipine showed greater reduction in systolic blood pressure, while atenolol had a stronger effect on heart rate and nighttime control. Diuretics reduced blood pressure by decreasing fluid volume, whereas ACE inhibitors and AR

Table 2: Dual combination therapy

Sr No	Drug Combination	SBP ↓	DBP ↓	Overall Control	Population	Adverse Effects	Electrolyte Change	Interpretation
1	Telmisartan + Hydrochlorothiazide	NR	NR	Better than monotherapy	Moderate-Severe HTN	Mild	Possible ↓ Potassium	RAAS + volume control improves efficacy
2	Amlodipine + Losartan	NR	NR	Better than monotherapy	Stage 2 HTN	Well tolerated	No significant change	Vasodilation + RAAS blockade

Table 2: The dual therapy table shows the benefit of combining two drugs for improved blood pressure control. Combinations such as telmisartan with hydrochlorothiazide and amlodipine with losartan were more effective than monotherapy, as they act through different mechanisms to control vascular resistance and fluid balance. These combinations were generally well tolerated with minimal side effects, making them suitable when monotherapy is insufficient.

Table 3: Triple combination therapy

Sr No	Drug Combination	SBP ↓	DBP ↓	Overall Control	Sustained Effect	Population	Adverse Effects	Electrolyte Change	Interpretation
1	Amlodipine + Telmisartan + Chlorthalidone	Significant ↓	Significant ↓	Highly effective	Short-term	Essential HTN	Well tolerated	Possible ↓ Potassium	Multi-pathway targeting
2	Telmisartan + Amlodipine + Hydrochlorothiazide	Strong ↓	Strong ↓	Very high control	Long-term	General HTN	Mild	Possible ↓ Potassium	Sustained multi-drug synergy

Table 3: The triple therapy table represents an intensive approach using three drugs together. These combinations showed the highest blood pressure control, particularly in severe or resistant hypertension. By targeting multiple pathways such as vascular tone, fluid volume, and hormonal regulation, they produced stronger and sustained effects. Despite multiple drugs, tolerability remained acceptable, supporting their use in patients requiring stricter control.

Table 4: Mechanism based comparing

Combination Type	Mechanism Targeted	Example	Clinical Benefit	Suggestion
Beta-blocker based	↓ Cardiac output	Atenolol	HR control, night BP reduction	Useful in OSA patients
RAAS + Diuretic	↓ Volume + ↓ RAAS	Telmisartan + HCTZ	Better BP reduction	Ideal in fluid overload
RAAS + CCB	↓ Resistance + ↓ RAAS	Amlodipine + Losartan	Improved vascular relaxation	Suitable for stage 2 HTN
Triple Therapy	Multi-pathway	Telmisartan + Amlodipine + Diuretic	Maximum BP control	For resistant HTN

Table 4: The mechanism-based table provides a simplified understanding of how drug combinations work. It explains how each combination targets key aspects of blood pressure regulation, including heart activity, vascular resistance, and fluid balance. This highlights why combination therapy is more effective than monotherapy, as multiple contributing factors are addressed simultaneously.

Discussion

The findings of this systematic review suggest that combination therapies, particularly dual and triple regimens, are more effective in controlling blood pressure than monotherapy. These treatments showed greater reductions in both systolic and diastolic blood pressure, resulting in improved overall control, Evidence from individual studies supports this trend. Atenolol showed reductions of about 13.4 mmHg systolic and 12.1 mmHg diastolic, indicating moderate efficacy as monotherapy. In contrast, combination therapies, especially triple regimens, demonstrated more consistent and pronounced reductions.

Dual therapies were also more effective than monotherapy, particularly in advanced hypertension, due to complementary mechanisms, Variations in response were observed in specific populations, such as greater diastolic reduction with beta-blockers in patients with obstructive sleep apnea, Overall, while monotherapy remains useful, combination therapies provide more consistent and clinically meaningful blood pressure control, supporting their role in managing hypertension across diverse patient groups [38].

Principal findings

The principal findings indicate that combination antihypertensive therapies, particularly dual and triple regimens, provide greater blood pressure reduction than monotherapy. Triple therapies showed the most pronounced effects, with significant reductions in both systolic and diastolic blood pressure and improved overall control, Dual therapies were also more effective than monotherapy, especially in moderate to severe

hypertension, supporting the use of drugs with complementary mechanisms to enhance outcomes [39].

Among individual drug classes, moderate reductions were observed, with variations based on class and patient population. Beta-blockers showed a stronger effect on diastolic blood pressure and heart rate, particularly in patients with obstructive sleep apnea, In terms of safety, most therapies were well tolerated with mild adverse effects. However, diuretic-containing regimens were associated with electrolyte imbalances, particularly reduced potassium levels, requiring monitoring, Overall, while all drug classes are effective, combination therapies-especially triple regimens-provide more consistent and clinically meaningful blood pressure control [40].

Interpretation of result

The findings suggest that the improved effectiveness of combination therapies is due to their ability to target multiple pathways involved in blood pressure regulation. By acting on vascular resistance, fluid balance, and hormonal activity, these therapies provide more comprehensive control compared to single mechanisms, Combinations such as ARBs, calcium channel blockers, and diuretics act synergistically on different physiological processes, explaining the stronger and more consistent reductions in systolic and diastolic blood pressure seen with triple therapies. Dual therapies also showed better outcomes than monotherapy, especially in patients with higher baseline blood pressure [41].

Variations among drug classes highlight the role of patient-specific factors. For example, beta-blockers showed greater effects on diastolic blood pressure and heart rate in patients with obstructive sleep apnea, likely due to their action on the sympathetic nervous system, In terms of safety, most treatments were well tolerated, though diuretic-containing regimens were associated with electrolyte changes, emphasizing the need for monitoring, Overall, these findings reflect how combining different mechanisms improves outcomes, supporting the use of individualized and multi-targeted treatment strategies in hypertension management [42].

Comparison with clinical guidelines

The findings of this review are consistent with World Health Organization (WHO) recommendations, which emphasize combination therapy for managing hypertension, especially in moderate to severe cases. WHO suggests initiating treatment with two agents, preferably as a single-pill combination, to improve control and adherence, This aligns with the included studies, where dual and triple therapies showed greater reductions in systolic and diastolic blood pressure compared to monotherapy. The strong and sustained effects of triple regimens further support the use of multiple agents for optimal control [43].

Strength of study

One of the main strengths of this study is its structured comparison of commonly used antihypertensive drug classes and their combinations, making the findings clinically relevant. By integrating evidence from multiple studies, it provides a practical understanding of how different therapies perform in real-world settings, Another strength is the inclusion of both monotherapy and combination therapy, allowing comparison of single, dual, and triple regimens within the same framework, which adds depth and improves the interpretation of effectiveness, Overall, the study offers a clear, structured, and clinically relevant overview of antihypertensive treatment strategies [44].

Limitations

Despite useful insights, this study has several limitations. A major limitation is variability among included studies in terms of design, patient populations, and outcome reporting, making direct comparison challenging, another limitation is the lack of uniform numerical data. While some studies reported clear blood pressure reductions, others were descriptive, preventing quantitative meta-analysis and limiting findings to qualitative synthesis.

Overall, these limitations highlight the need for more standardized and large-scale studies to strengthen the evidence base [45].

Clinical application

The findings of this review have important implications for clinical practice, particularly in managing moderate to severe hypertension. They suggest that monotherapy may not always achieve optimal control, while combination therapies, especially dual and triple regimens, provide more consistent and effective results, Overall, early use of combination therapy with appropriate drug selection can improve blood pressure control and treatment outcomes in hypertension [46].

Limitations of Monotherapy and Its Clinical Implications in Hypertension Management

Monotherapy has traditionally been used as the initial approach in the management of hypertension; however, its effectiveness is often limited in achieving optimal blood pressure control. This is primarily due to the multifactorial nature of hypertension, where multiple physiological pathways contribute to elevated blood pressure, while a single drug targets only one mechanism. From a clinical perspective, inadequate control with monotherapy can delay optimal treatment, increasing the risk of long-term complications such as cardiovascular and renal damage. These findings strongly support the need for early consideration of combination therapy, particularly in patients with moderate to severe hypertension, aligning with the outcomes observed in the present study.[47]

Advantages of Combination Therapy in Hypertension Management

Combination therapy is a more effective approach in managing hypertension, especially in patients not adequately controlled with monotherapy. By targeting multiple pathways such as vascular resistance, fluid balance, and hormonal activity, it provides more consistent blood pressure reduction. It also allows lower

doses of individual drugs, reducing adverse effects while maintaining efficacy. Clinical studies show faster control and improved outcomes, including reduced cardiovascular and renal risks. Fixed-dose combinations may further improve adherence by simplifying treatment, supporting combination therapy as a preferred strategy [48].

CONCLUSION

In summary, this review integrates evidence from multiple studies to evaluate antihypertensive therapies in real-world settings. While individual drug classes are effective, their impact varies across patient populations and clinical conditions. In contrast, combination therapies provide more consistent blood pressure control, particularly in advanced hypertension.

These findings are supported by existing literature, which highlights the limitations of monotherapy and the increasing role of combination strategies in achieving optimal targets, Overall, the review emphasizes the importance of a tailored, multi-drug approach in hypertension management.

Summary of findings

This systematic review provides an overview of the effectiveness of commonly used antihypertensive drug classes and their combinations. All major classes contribute to blood pressure reduction, though the degree varies by drug and patient population. Monotherapy generally produced moderate reductions in systolic and diastolic blood pressure. For example, atenolol reduced systolic pressure by about 13.4 mmHg and diastolic by 12.1 mmHg, indicating meaningful but limited efficacy. Similar moderate effects were observed with calcium channel blockers, ACE inhibitors, ARBs, and diuretics, these findings are supported by previous literature showing that many patients do not achieve optimal control with monotherapy and require combination therapy. Most treatments were well tolerated, although diuretics were associated with electrolyte imbalances, requiring monitoring, Overall, while monotherapy remains useful in some cases, combination therapy-particularly dual and triple regimens-provides more consistent and clinically meaningful blood pressure control in hypertension[49].

Summary of comparative effectiveness

When comparing treatment approaches, monotherapy provides only moderate blood pressure reduction and may be insufficient for many patients, especially those with higher baseline levels or advanced hypertension, Overall, while monotherapy remains useful in selected cases, combination therapy-particularly dual and triple regimens-offers better and more consistent blood pressure control.

Recommendation of clinical practice

Based on these findings, combination therapy appears to be a more practical approach for many patients with hypertension, especially when monotherapy fails to achieve adequate control. While single-drug therapy may be suitable for mild cases, adding additional agents can improve outcomes when needed, Treatment should remain individualized, considering factors such as baseline blood pressure, comorbidities, and patient tolerance. Certain drug classes may offer specific benefits, while others require closer monitoring due to potential side effects, Safety is also important, as most therapies are well tolerated, though diuretic-containing regimens may cause electrolyte changes, requiring periodic monitoring, Overall, a flexible, patient-centered approach is recommended, where combination therapy is used appropriately alongside careful clinical judgment and follow-up [50].

REFERENCES

1. Zhu D, Bays H, Gao P, Mattheus M, Voelker B, Ruilope LM. Efficacy and tolerability of a single-pill combination of telmisartan 80 mg and hydrochlorothiazide 25 mg according to age, gender, race, hypertension severity, and previous antihypertensive use: planned analyses of a randomized trial. Integr Blood Press Control. 2013;6:1-14. doi:10.2147/IBPC.S33104.
2. Sung KC, Sung JH, Cho EJ, Ahn JC, Han SH, Kim W, et al. Efficacy and safety of low-dose antihypertensive combination of amlodipine, telmisartan, and chlorthalidone: a randomized, double-blind, parallel, phase II trial. J Clin Hypertens. 2022. doi:10.1111/1750-3841.16020.
3. Kim SH, Ryu KH, Lee NH, Kang JH, Kim WS, Park SW, et al. Efficacy of fixed-dose amlodipine and losartan combination compared with amlodipine monotherapy in stage 2 hypertension: a randomized, double-blind, multicenter study. BMC Res Notes. 2011;4:461. doi:10.1186/1756-0500-4-461.
4. Hemminki E, McPherson K. Impact of postmenopausal hormone therapy on cardiovascular events and cancer: pooled data from clinical trials. BMJ. 1997;315(7101):149-153. doi:10.1136/bmj.315.7101.149.
5. Higaki J, Komuro I, Shiki K, Ugai H, Taniguchi A, Ikeda H, et al. The efficacy and long-term safety of a triple combination of telmisartan, amlodipine, and hydrochlorothiazide in Japanese patients with essential hypertension: a randomized, double-blind study with open-label extension. Hypertens Res. 2016. doi:10.1038/hr.2015.142.
6. Kraiczi H, Hedner J, Peker Y, Grote L. Comparison of atenolol, amlodipine, enalapril, hydrochlorothiazide, and losartan for antihypertensive treatment in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 2000;161(5):1423-1430. doi:10.1164/ajrccm.161.5.9904063.
7. World Health Organization. WHO guideline for the pharmacological treatment of hypertension in adults. Geneva: World Health Organization; 2021.
8. Kalra S, Kalra B, Agrawal N. Combination therapy in hypertension: an update. DiabetolMetab Syndr. 2010;2:44. doi:10.1186/1758-5996-2-44.
9. Magvanjav O, Cooper-DeHoff RM, McDonough CW, Gong Y, Hogan WR, Johnson JA. Combination antihypertensive therapy prescribing and blood pressure control in a real-world setting. Am J Hypertens. 2020;33(11):1047-1055. doi:10.1093/ajh/hpaa093.
10. Mallat SG, Tanios BY, Itani HS, Akl EA. Free versus fixed combination antihypertensive therapy for essential arterial hypertension: a systematic review and meta-analysis. PLoS One. 2016;11(8):e0161285. doi:10.1371/journal.pone.0161285.
11. Oparil S, Acelajado MC, Bakris GL, Berlowitz DR, Cífková R, Dominiczak AF, et al. Hypertension. Nat Rev Dis Primers. 2018;4:18014. doi:10.1038/nrdp.2018.14.
12. Wang JG, Kario K, Park JB, Hoshide S, Chen CH, Huo Y, et al. Management of morning hypertension: a consensus statement of an Asian expert panel. J Hypertens. 2018;36(7):1506-1517. doi:10.1097/HJH.0000000000001701.
13. Pradhan A, Vohra S, Sethi R. A "20/20" match: ACC/AHA 2017 versus ESC/ESH 2018 guidelines for management of hypertension. Indian Heart J. 2019;71(2):151-157. doi:10.1016/j.ihj.2019.03.004.
14. Memon HA, Park MH. Pulmonary arterial hypertension in women. Methodist Debakey Cardiovasc J. 2017;13(4):224-229. doi:10.14797/mdcj-13-4-224.

15. Bidani AK, Griffin KA. Pathophysiology of hypertensive renal damage: implications for therapy. Hypertension. 2015;65(5):1001-1007. doi:10.1161/Hypertensionaha.115.04260.
16. MacDonald TM, Williams B, Webb DJ, Morant S, Caulfield M, Cruickshank JK, et al. Combination therapy is superior to sequential monotherapy for the initial treatment of hypertension: a double-blind randomized controlled trial. J Am Heart Assoc. 2017;6(11):e006986. doi:10.1161/JAHA.117.006986.
17. Guerrero-García C, Rubio-Guerra AF. Combination therapy in the treatment of hypertension. Drugs Context. 2018;7:212531. doi:10.7573/dic.212531.
18. Natarajan A, Jose PA. Renal modulation: the renin-angiotensin-aldosterone system (RAAS). In: Comprehensive Clinical Nephrology. Elsevier; 2019.
19. Takahashi H, Yoshika M, Komiyama Y, Nishimura M. The central mechanism underlying hypertension: roles of sodium ions, epithelial sodium channels, the renin-angiotensin-aldosterone system, oxidative stress and endogenous digitalis in the brain. Hypertens Res. 2011;34(11):1147-1152. doi:10.1038/hr.2011.100.
20. Mallat SG, Itani HS, Tanios BY. Current perspectives on combination therapy in the management of hypertension. Integr Blood Press Control. 2013;6:69-78. doi:10.2147/IBPC.S33940.
21. Sonobe T, Timilsina RR, Rahut DB. Hypertension among men and women in Asia: a review of the burden and risk factors. Int J Environ Res Public Health. 2019;16(20):3875. doi:10.3390/ijerph16203875.
22. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020;75(6):1334-1357. doi:10.1161/Hypertensionaha.120.15026.
23. Garjón J, Saiz LC, Azparren A, Gaminde I, Ariz MJ, Erviti J. First-line combination therapy versus first-line monotherapy for primary hypertension. Cochrane Database Syst Rev. 2020;2:CD010316. doi:10.1002/14651858.CD010316.pub2.
24. Parati G, Kjeldsen S, Coca A, Cushman WC, Wang J. Adherence to single-pill versus free-equivalent combination therapy in hypertension: a systematic review and meta-analysis. Hypertension. 2021;77(2):692-705. doi:10.1161/Hypertensionaha.120.15781.
25. Ott C, Schmieder RE. Diagnosis and treatment of arterial hypertension 2021. Kidney Int. 2021;100(6):1243-1255. doi:10.1016/j.kint.2021.09.026.
26. Smith DK, Lennon RP, Carlsgaard PB. Managing hypertension using combination therapy. Am Fam Physician. 2020;101(6):341-349.
27. Molina de Salazar DI, Coca A, Alcocer L, Piskorz D. The rationale for using fixed-dose combination therapy in the management of hypertension in Colombia: a narrative review. Adv Ther. 2024;41(4):1523-1537. doi:10.1007/s40256-024-00634-8.
28. Messerli FH, Bangalore S, Bavishi C, Rimoldi SF. Angiotensin-converting enzyme inhibitors in hypertension: to use or not to use? J Am Coll Cardiol. 2018;71(13):1474-1482. doi:10.1016/j.jacc.2018.01.058.
29. Morales-Olivas FJ. Diuretics use in the management of hypertension. Hipertens Riesgo Vasc. 2024;41(2):73-78. doi:10.1016/j.hipert.2024.03.004.
30. Griffin M, Trow TK. The evolving landscape of combination therapy for pulmonary arterial hypertension. Ther Adv Respir Dis. 2017;11(2):139-153. doi:10.1177/1753465816677485.
31. Giles TD. Rationale for combination therapy as initial treatment for hypertension. J Clin Hypertens. 2003;5(5):368-374. doi:10.1111/j.1524-6175.2003.02673.x.
32. Patel PS, Raval AM, Patel AAAK, Patel PDK, Prajapati TG, Patel PB. A comprehensive review of antibiotic resistance: mechanisms, causes, and novel therapeutic approaches. Asian J Pharm Res Dev. 2026;14(2):117-128.
33. Raval AM, Bhavsar PR, Pandya FU, Patel D. Co-processed excipients in pharmaceutical formulation: advances, characterization, and applications. Asian J Pharm Res Dev. 2026;14(1):105-113. doi:10.22270/ajprd.v14i01.1705.
34. Patel PBK, Raval AM, Patel HB, Patel KH, Patel P, Vaidya PAK, Kahar KH. A comprehensive review of polycystic ovary syndrome (PCOS): pathophysiology, diagnosis and management. *Asian J Pharm Res Dev*. 2026;14(2):32-41. doi:10.22270/ajprd.v14i2.1716.
35. Thakor AD, Dharajiya RM, Shaikh MZ, Raval AM. A review on neuropharmacology: mechanisms, drug classes, and clinical applications. *Asian J Pharm Res Dev*. 2026;14(1):114-121. doi:10.22270/ajprd.v14i01.1709.
36. Raval AM, Rana T, Joshi SY, Buch S, Arora B, Patel VS. Artificial intelligence in pharmacy and healthcare: applications in drug discovery, precision medicine, clinical practice, and future perspectives. *Asian J Pharm Res Dev*. 2026;14(2):62-69. doi:10.22270/ajprd.v14i2.1721.
37. Senjaliya T, Patel M, Raval AM. Strategies for combating the global health threat of antibiotic resistance: novel therapeutics and combination approaches. Asian J Pharm Res Dev. 2026;14(1):122-130. doi:10.22270/ajprd.v14i01.1707.
38. Mevada J, Patel K, Raval AM. Materiovigilance: From device failure to safety reform, the growing importance of materiovigilance systems. Int J Pharm Sci. 2026;4(1):962-74.
39. Falwariya R, Jethva T, Raval AM, Lokhande D. Comprehensive review: Microneedle patches–A painless revolution in transdermal drug delivery. World J Pharm Med Res. 2026;12(1):199-207.
40. Mevada J, Patel K, Raval AM. Role of pharmacovigilance in drug safety monitoring. World J Pharm Med Res. 2025;11(11):235-40.
41. Patel N, Raval AM. Gastro-retentive drug delivery system: A review. Int J Pharm Sci. 2026;4(1):734-42.
42. Zankhwala MF, Raval MA, Kushkiwala MA, Sarvaiya MS, Raval MK, Thakar MN, Barjod MS. Formulation And Evaluation Of Optimized Polymer Blends For Diclofenac Diethylamine Transdermal System. The Review of Diabetic Studies. 2025 Sep 14:701-8.
43. Kushkiwala AM, Zankhwala FM, Patel MD, Raval AM. Flurbiprofen loaded ethosomal gel: Design, optimization, and anti-inflammatory activity. Int J Res Anal Rev. 2024;11(4):709-42.
44. Raval MA, Suthar MA, Durani MB, Thakar MN, Zankhwala MF, Kushkiwala MA, Rathod MS. Smart Co-Processed Excipient Platforms: A Novel Strategy for Multifunctional Optimization of Ibuprofen Tablet Formulations. practice.;1:2.
45. Tripathi KD. Essentials of medical pharmacology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers; 2019.
46. Ritter JM, Flower RJ, Henderson G, Loke YK, MacEwan DJ. Antihypertensive drugs. In: Rang and Dale's pharmacology. 10th ed. London: Elsevier; 2023.
47. Raval AM, Zankhwala FS. *Disease & treatment (बीमारियांऔरउनकाउपचार)*.Testbook Edu Solutions Pvt Ltd; 2023. ISBN: 978-81-966977-7-8
48. Raval AM, Rathod SR. *Medicine review*. Raval Amarkumar Maheshbhai; 2026. ISBN: 978-93-5890-644-8
49. Dimmitt SB, Stampfer HG, Martin JH, Ferner RE. Efficacy and toxicity of antihypertensive pharmacotherapy relative to effective dose 50. *Br J Clin Pharmacol*. 2019;85(10):2218-2227. doi:10.1111/bcp.14033.
50. Jussil H, Chaimani A, Carlberg B, et al. Comparative efficacy and acceptability of different antihypertensive drug classes for cardiovascular disease prevention: protocol for a systematic review and network meta-analysis. *BMJ Open*. 2021;11:e044302. doi:10.1136/bmjopen-2020-044302.