https://doi.org/10.31925/farmacia.2026.1.15 **ORIGINAL ARTICLE**

VASCULAR REMODELING AND HEMORHEOLOGICAL CHANGES IN THE TREATMENT OF PRIMARY HYPERTENSION WITH IRBESARTAN COMBINED WITH AMLODIPINE BESYLATE TABLETS

JIANJUN WANG, MINGYING XU *, PING LI

Department of Medicine, First People's Hospital of Linping District (Xingqiao Branch), Hangzhou, 311100, Zhejiang, China

**corresponding author: xumingyingmy@163.com*

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Abstract

Primary hypertension is a multifactorial condition without a clearly identifiable etiology, for which pharmacological therapy remains the cornerstone of clinical management. This study evaluated the clinical efficacy and potential mechanisms of irbesartan (IRB) combined with amlodipine besylate (AMB) in patients with primary hypertension. A total of 105 patients treated between June 2022 and December 2023 were randomly allocated into three groups: IRB, AMB, and IRB + AMB, receiving the respective treatments for 10 weeks. Blood pressure levels, vascular remodeling parameters, hemorheological indices, serum inflammatory markers, and adverse reactions were assessed before and after treatment. All groups showed significant post-treatment improvements; however, no significant differences were observed between the IRB and AMB monotherapy groups ($p > 0.05$). In contrast, the IRB + AMB group demonstrated significantly greater reductions in blood pressure, vascular remodeling indices, hemorheological parameters, and inflammatory factors ($p < 0.05$). The total effective rate was highest in the combination group (95.0%), with no significant increase in adverse reactions. These findings indicate that IRB combined with AMB offers superior therapeutic benefits in primary hypertension.

Rezumat

Hipertensiunea primară este o afecțiune multifactorială, fără o etiologie clar identificabilă, pentru care terapia farmacologică reprezintă pilonul principal al managementului clinic. Acest studiu a evaluat eficacitatea clinică și mecanismele potențiale ale asocierii irbesartanului (IRB) cu besilatul de amlodipină (AMB) la pacienți cu hipertensiune primară. Un total de 105 pacienți tratați în perioada iunie 2022 - decembrie 2023 au fost repartizați aleatoriu în trei grupuri: IRB, AMB și IRB + AMB, urmând tratamentele corespunzătoare timp de 10 săptămâni. Au fost evaluate valorile tensiunii arteriale, parametrii remodelării vasculare, indicii hemoreologici, markerii inflamatori serici și reacțiile adverse, înainte și după tratament. Toate grupurile au prezentat îmbunătățiri semnificative post-terapie, însă nu s-au observat diferențe semnificative între grupurile cu monoterapie IRB și AMB ($p > 0,05$). În schimb, grupul IRB + AMB a înregistrat reduceri semnificativ mai mari ale tensiunii arteriale, parametrilor de remodelare vasculară, indicilor hemoreologici și markerilor inflamatori ($p < 0,05$). Rata totală de eficacitate a fost cea mai ridicată în grupul combinat (95,0%), fără o creștere semnificativă a reacțiilor adverse. Aceste rezultate indică faptul că asocierea IRB-AMB oferă beneficii terapeutice superioare în tratamentul hipertensiunii primare.

Keywords: irbesartan, amlodipine besylate tablets, primary hypertension, cardiovascular remodeling, hemorheology, inflammatory response

Introduction

Primary hypertension is a type of hypertension of unknown cause, clinically characterized by elevated systemic arterial pressure. As the disease progresses, symptoms such as palpitations, dizziness, and headaches may develop (1). If primary hypertension is not adequately controlled, it can lead to damage to important target organs and trigger various complications (2). Hypertensive patients typically experience a sustained increase in cardiac afterload, which in turn causes cardiovascular remodeling and increases the risk of cardiovascular events (3,4). The incidence of primary hypertension has gradually risen, along with an increasing number of risk factors. Therefore, effective control of blood pressure is key to the management of primary hypertension.

Hypertension is commonly managed through pharmacological treatment in clinical practice. Angiotensin II is a potent vasoconstrictor that stimulates aldosterone release and promotes the proliferation of cardiomyocytes and vascular smooth muscle cells, making it a key pathogenic factor in hypertension (5). Irbesartan (IRB) is a commonly used antihypertensive drug that belongs to the class of angiotensin II receptor inhibitors. It exerts its effect by blocking the binding of angiotensin II to its receptor, thereby inhibiting its biological effects and ultimately providing blood pressure-lowering and cardiovascular protective effects (6,7). Hao *et al*.

(2024) (8) developed a spontaneously hypertensive rat model and found that administering 20 mg/kg/day of IRB effectively suppressed the increase in systolic blood pressure and also inhibited oxidative stress, improving cognitive dysfunction caused by hypertension. Zhong *et al*. (2020) (9) discovered that IRB could reduce blood pressure levels in hypertensive renal injury mice and alleviate angiotensin II-induced renal damage by inhibiting Th22 cell chemotaxis and infiltration, thereby mitigating the inflammatory response and fibrosis process associated with renal injury. Theodorakopoulou *et al*. (2021) (10) observed the effect of IRB on blood pressure control in hypertensive patients undergoing dialysis and found that it effectively lowered central systolic blood pressure without affecting the heart rate-corrected augmentation index. Yan *et al*. (2023) (11) also confirmed that IRB, when used for the clinical treatment of non-dipper hypertension patients, effectively reduced blood pressure and improved left ventricular structure while modulating endothelial function. In addition to IRB, amlodipine besylate (AMB) tablets are also commonly used antihypertensive drugs. AMB tablets belong to the dihydropyridine class of calcium channel blockers, and their pharmacological action primarily involves the selective inhibition of calcium ion influx into vascular smooth muscle and cardiomyocytes, thereby reducing intracellular calcium concentrations and affecting cellular contractility (12,13). As a long-acting antihypertensive, AMB maintains a smooth and sustained blood pressure -lowering effect for more than 24 hours, which helps control blood pressure fluctuations in the morning and at night. Lin *et al*. (2023) (14) found that AMB tablets effectively controlled blood pressure in patients with primary hypertension, without causing serious adverse reactions. A meta-analysis also confirmed that the combination of AMB and ACEI provided additional reductions in SBP and DBP compared with AMB monotherapy (SBP reduction: ~5.7 mmHg, DBP reduction: ~3.6 mmHg), with fewer overall adverse effects (15).

In summary, this study included patients with primary hypertension to evaluate the efficacy and safety differences between monotherapy with IRB or AMB tablets and their combination therapy. The study also compared their effects on vascular remodeling, hemorheology, and the inflammatory response. The aim was to provide a reference for the selection of clinical treatment strategies for primary hypertension.

Materials and Methods

Clinical data

In this study, 105 patients with primary hypertension who visited the hospital between June 2022 and December 2023 were selected. All participants agreed to sign informed consent forms with the consent of their family members. This study obtained approval from the ethics committee of First People's Hospital of Linping District (Hangzhou, China).

Inclusion criteria: i) diagnosis of primary hypertension according to the Chinese Hypertension Prevention and Treatment Guidelines (2018 Revision) (16); ii) resting state with no use of any antihypertensive medications, and systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥ 90 mmHg (1 mmHg = 0.133 kPa), classified as stage I or II primary hypertension; iii) no use of antihypertensive medications within the past month; iv) the patient and their family were informed about the study and signed an informed consent form.

Exclusion criteria: i) secondary hypertension, pseudohypertension, and hypertension during pregnancy; ii) history of myocardial infarction, coronary heart disease, or heart failure; iii) presence of heart, liver, or kidney dysfunction, hematologic disorders, immune system dysfunction, metabolic diseases, or severe infectious diseases; iv) concurrent use of other treatments that could affect the study outcomes; v) poor treatment adherence or voluntary withdrawal from the study.

Grouping and treatments

Randomization was performed using a computer-generated random number table. All patients were assigned unique identifiers via the random number function in SPSS 26.0 and then sequentially allocated to the IRB group, AMB group, or IRB + AMB group in ascending order of their random numbers until the target sample sizes for each group were reached (32, 33, and 40 cases, respectively). The entire allocation process was completed before the study initiation, and researchers involved in treatment and outcome assessment remained blinded to the group assignment. IRB group consisted of 15 male and 17 female patients, with ages ranging from 40 to 75 years (mean = 62.7 ± 1.8). Disease duration was 3~15 years (mean = 7.7 ± 0.5). Hypertension was classified as stage I in 12 cases and stage II in 20 cases. AMB group consisted of 14 male and 19 female patients, with ages ranging from 40 to 72 years (mean = 61.6 ± 1.5). Disease duration was 3~12 years (mean = 7.5 ± 0.8). Hypertension was classified as stage I in 13 cases and stage II in 20 cases. IRB + AMB group consisted of 19 male and 21 female patients, with ages ranging from 42 to 75 years (mean = 63.3 ± 2.0). Disease duration was 5~15 years (mean = 8.1 ± 1.2). Hypertension was classified as stage I in 16 cases and stage II in 24 cases. There were no statistically significant differences among the three groups in baseline characteristics, including sex ($\chi^2 = 0.542$, P = 0.762), age (F = 1.374, p = 0.258), disease duration (F = 0.949,

p = 0.392), and hypertension staging (χ^2 = 0.854, p = 0.653), indicating comparability across groups.

The IRB group was treated as IRB. Patients took IRB tablets (XiuZheng Pharmaceutical Group Liuhe Pharmaceutical Co., Ltd., China) with warm water on an empty stomach each morning at a dose of 0.15 g *per* dose, once daily. If the patient's blood pressure was effectively controlled (*i.e.*, systolic blood pressure < 140 mmHg, diastolic blood pressure < 90 mmHg), the dose could be increased to 0.30 g *per* dose. Treatment continued for 10 weeks.

The AMB group was treated with AMB. Patients took AMB tablets (Jiangxi Pharmaceutical Co., Ltd., China) with warm water on an empty stomach each morning at 5 mg *per* dose, once daily. If the patient's blood pressure was effectively controlled, the dose could be increased to 10 mg *per* dose. Treatment continued for 10 weeks.

The IRB + AMB group was treated with the combination of IRB and AMB. Patients took IRB (0.15 g *per* dose) and AMB tablets (5 mg *per* dose) with warm water on an empty stomach each morning, once daily. If the patient's blood pressure was effectively controlled, the dose of both drugs could be appropriately increased. Treatment continued for 10 weeks.

Outcome measures

Clinical efficacy: (1) Markedly effective: diastolic blood pressure is reduced by at least 10 mmHg and blood pressure is restored to normal levels, or diastolic blood pressure is reduced by at least 20 mmHg; (2) Effective: diastolic blood pressure is reduced by less than 10 mmHg and BP is restored to normal levels, or diastolic blood pressure is reduced by 10-19 mmHg, or systolic blood pressure is reduced by 30 mmHg; (3) Ineffective: blood pressure is not restored to normal levels, or diastolic blood pressure is reduced by less than 10 mmHg, or systolic blood pressure is reduced by less than 30 mmHg. The overall clinical efficacy rate = (markedly effective + effective cases) / total number of cases × 100%.

Blood pressure level: blood pressure levels were measured pre- and post-treatment using the diastolic blood pressure-01H electronic blood pressure monitor (Shenzhen Xingmai Medical Instruments Co., Ltd., China). Diastolic and systolic blood pressures were measured 2 cm above the antecubital fossa on the upper arm. Three measurements were taken, and the average value was recorded. A 2-minute interval was allowed between each measurement.

Vascular remodeling indicators: Pre-treatment and post-treatment, cardiovascular remodeling indicators, including left ventricular end-diastolic (LVED) interventricular septal thickness (IVST), LV posterior wall thickness (LVPWT), and LVED diameter (LVEDD), were measured using the Affiniti70 color Doppler ultrasound diagnostic system (Philips, Netherlands). The ultrasound probe frequency was set between 2.50 and 3.75 MHz. Measurements were taken over three consecutive cardiac cycles along the long axis of the left sternal border, and the average value of each indicator was recorded. The LV mass index (LVMI) was calculated using the Devereux methodology as follows:

$$LVMI = \{1.04\times[(IVST + LVPWT + LVEDD)^3 - LVEDD^3 - 13.6]\}/\{[0.0061\times height + 0.0128\times weight] - 0.1529\}.$$

All echocardiographic examinations were performed by two certified cardiac sonographers (with intermediate or higher professional qualifications) who underwent standardized training and remained blinded to group allocation throughout the study. To assess measurement reproducibility, a random sample of 30 participants was selected for repeated measurements by the same operator at different time points. The intraclass correlation coefficient (ICC) was calculated to evaluate consistency, with all ICC values exceeding 0.90, demonstrating excellent measurement reproducibility.

Hemorheological indicators: Pre- and post-treatment, fasting venous blood samples were extracted. Hemorheological parameters, including whole blood high/low shear viscosity (WBHSV/ WBLSV), plasma viscosity (PV), and erythrocyte aggregation index (EAI), were measured utilizing the SA-6600 fully automatic blood rheology analyzer (Beijing SciTech Technology Co., Ltd., China).

Serum inflammatory cytokine indicators: Pre- and post-treatment, fasting venous blood samples were centrifuged at 3000 rpm for 10 minutes to obtain serum. Subsequently, enzyme-linked immunosorbent assay (ELISA) was used to measure the levels of inflammatory biomarkers, including C-reactive protein (CRP), interleukin (IL)-6, IL-1β, and tumor necrosis factor (TNF)-α) in the serum. All test kits were purchased from Beyotime Biotechnology Research Institute (China).

Adverse reactions: Adverse reactions such as arrhythmias, cough, nausea and vomiting, headache and dizziness, diarrhea, and other side effects occurring during the treatment process should be recorded.

Statistical methods

Data were analyzed and processed employing *SPSS 23.0* and *GraphPad Prism 9.5.0*. Categorical data were presented as frequencies or percentages, and χ^2 test was used for comparisons between groups. Continuous data were denoted as mean ± standard deviation ($\bar{x} \pm s$). One-way analysis of variance compared data among multiple groups, while independent-samples t-test compared data between two groups. A $p < 0.05$ was statistically significant.

Results and Discussion

Object characteristics

One hundred twenty-two patients with primary hypertension visited the hospital between June 2022 and December 2023. After screening according to the inclusion criteria and other requirements, 105 patients were randomly assigned to a 10-week double-blind treatment regimen. They were treated with IRB (n = 32), AMB (n = 33), or IRB + AMB (n = 40), and all patients completed the study (Figure 1).

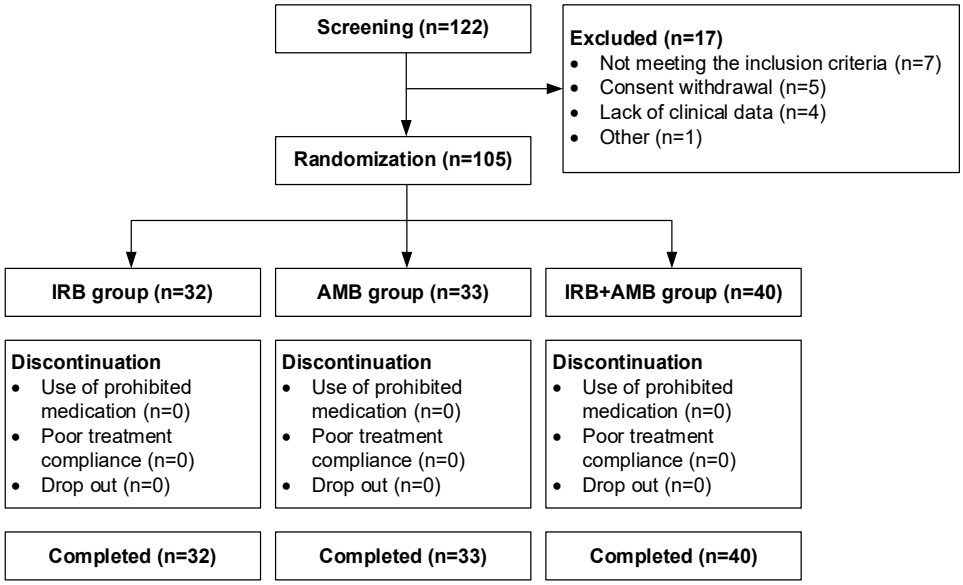

Figure 1.
Research flowchart

Comparison of clinical efficacy

In Table I, the overall clinical efficacy rates post-treatment were 78.1%, 78.8%, and 95.0% for IRB group, AMB group, and IRB + AMB group, respectively. The clinical efficacy rate in the IRB + AMB group markedly surpassed that in the IRB group and AMB group, with the difference being substantial ($p < 0.05$).

Table I
Clinical efficacy among different groups [n (%)]

Group	Case number	Markedly effective	Effective	Ineffective	Total effective rate
IRB group	32	9 (28.1)	16 (50.0)	7 (21.9)	25 (78.1)
AMB group	33	10 (30.3)	16 (48.5)	7 (21.2)	26 (78.8)
IRB + AMB group	40	14 (35.0)	24 (60.0)	2 (5.0)	38 (95.0)

Comparison of blood pressure control effects

In Figure 2, systolic blood pressure, diastolic blood pressure, and pulse pressure differed slightly between the groups before treatment. However, all parameters showed drastic reductions post-treatment. Specifically, the systolic blood pressure, diastolic blood pressure, and pulse pressure in IRB + AMB group were notably inferior to those in IRB group and AMB group, with the differences being marked ($p < 0.05$).

Comparison of cardiovascular remodeling effects

In Figure 3, IVST, LVPWT, LVEDD, and LVMI differed slightly between the groups before treatment. However, all parameters showed significant reductions post-treatment. Specifically, the IVST, LVPWT, LVEDD, and LVMI in the IRB + AMB group were drastically inferior to those in IRB group and AMB group, with the differences being considerable ($p < 0.05$).

Comparison of hemorheological effects

Before treatment, there were negligible differences in WBHSV, WBLSV, PV and EAI between the groups (Figure 4). However, all parameters showed significant reductions post-treatment. Specifically, the WBHSV, WBLSV, PV and EAI in the IRB + AMB group were significantly lower than in the IRB and AMB groups ($p < 0.05$) (see Figure 4).

Comparison of levels of inflammatory cytokines in blood

There were no significant differences in CRP, IL-6, IL-1β and TNF-α levels among groups before treatment (Figure 5). However, all parameters showed significant reductions post-treatment. Specifically, the levels of CRP, IL-6, IL-1β and TNF-α in the IRB + AMB group were significantly lower than in the IRB and AMB groups ($p < 0.05$) (Figure 5).

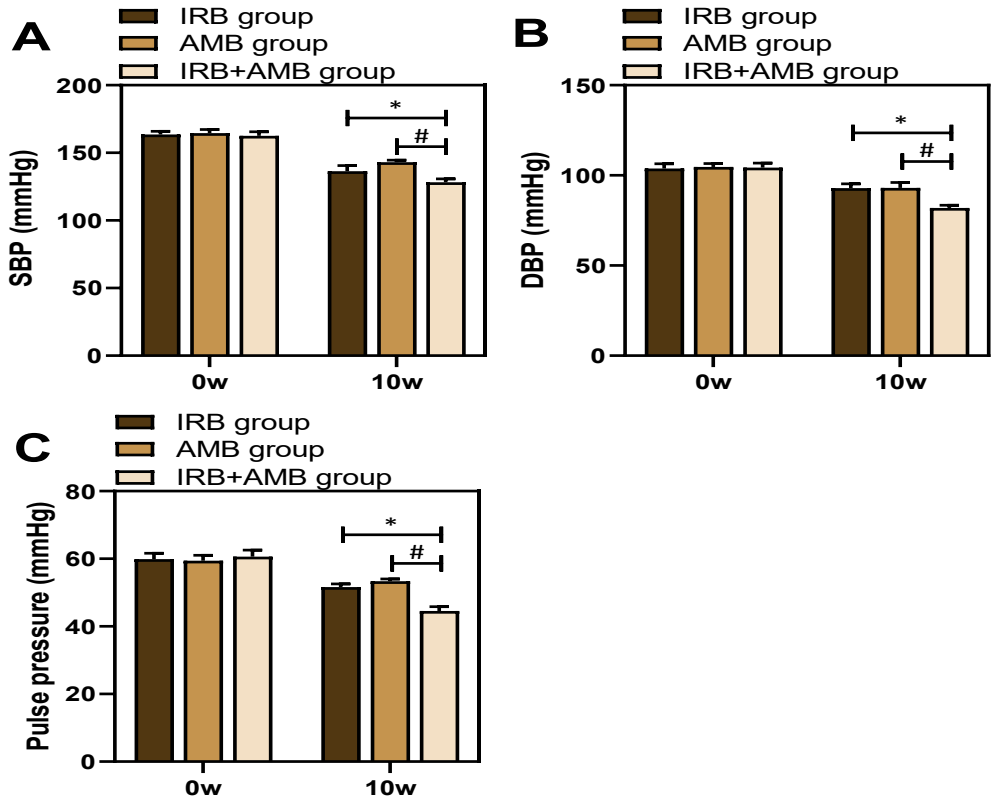

Figure 2.
Comparison of blood pressure indicators pre- and post-treatment in each group. *, $p < 0.05$ compared with IRB group; #, $p < 0.05$ compared with AMB group

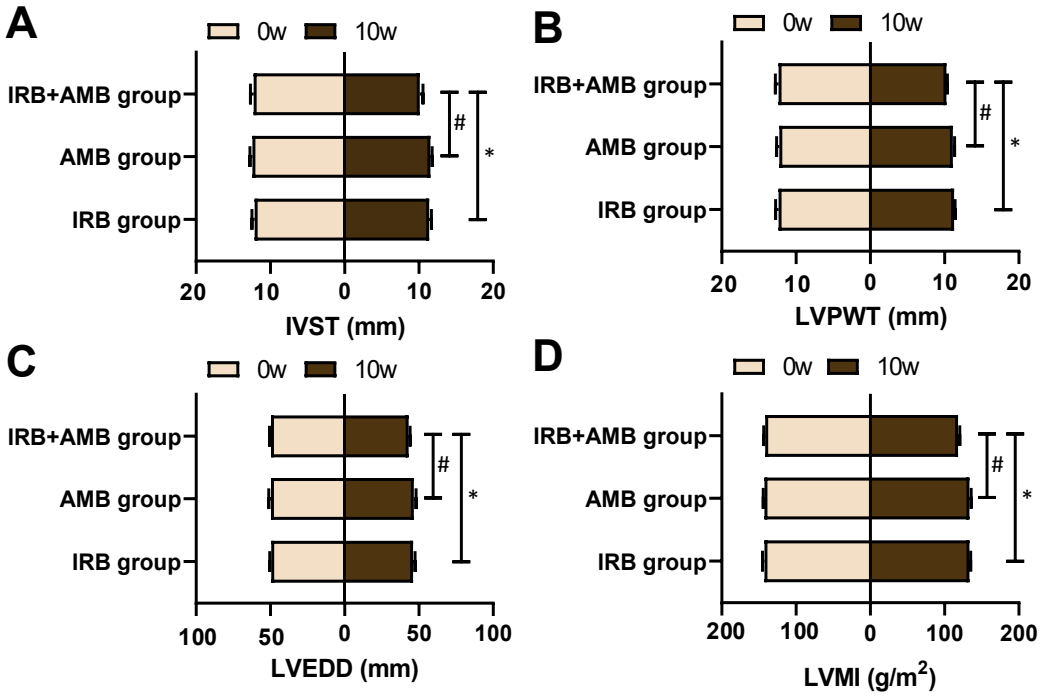

Figure 3.
Comparison of cardiovascular remodeling indicators pre- and post-treatment in different groups. *, $p < 0.05$ compared with IRB group; #, $p < 0.05$ compared with AMB group

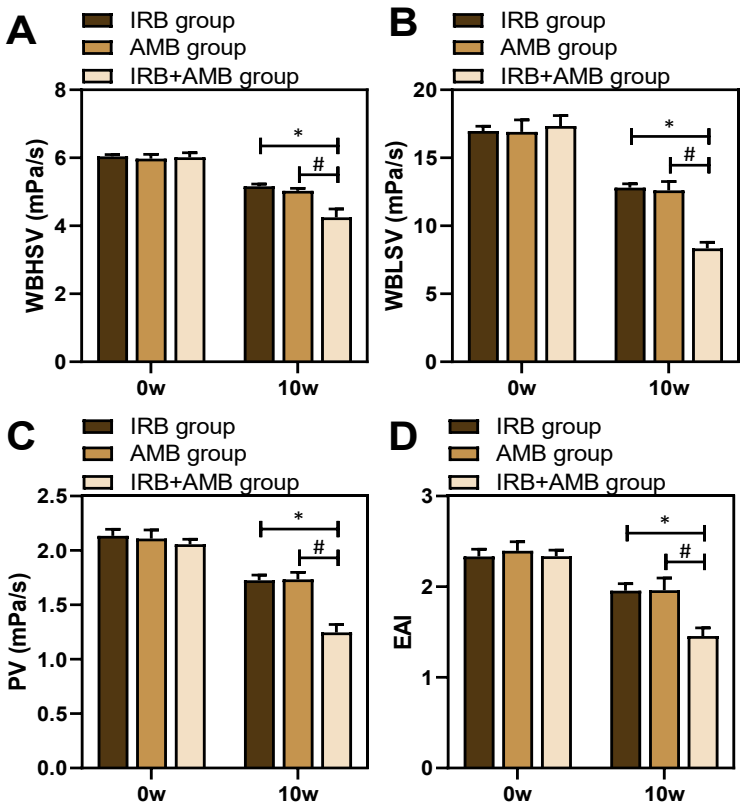

Figure 4.
Comparison of hemorheological indicators pre- and post-treatment in different groups. $^{*}p < 0.05$ compared with IRB group; $^{\#}p < 0.05$ compared with AMB group

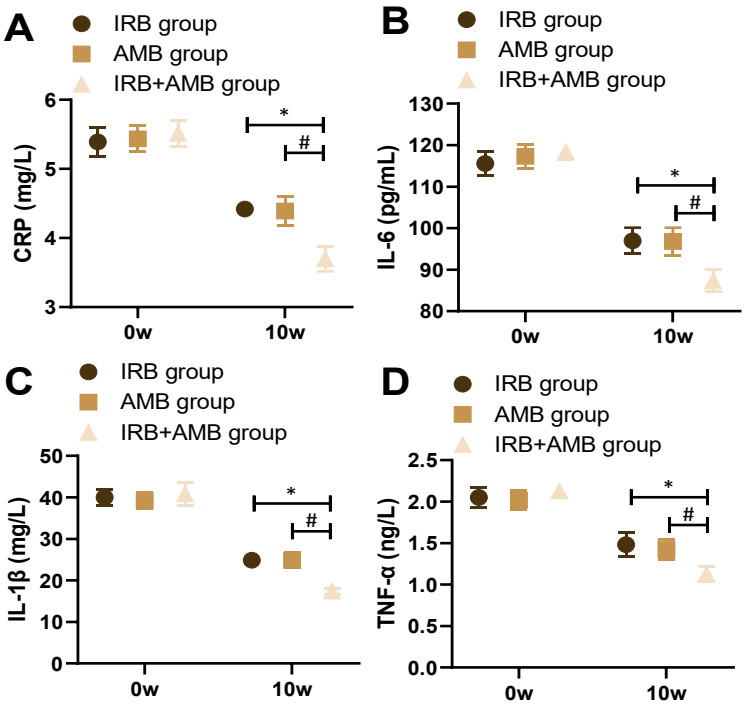

Figure 5.
Contrast of blood inflammatory factor levels pre- and post-treatment in different groups. $^{*}p < 0.05$ compared with IRB group; $^{\#}p < 0.05$ compared with AMB group

Comparison of adverse reactions

The overall incidence of adverse reactions after treatment was 12.5% in the IRB group, 12.1% in the AMB group and 15.0% in the IRB + AMB group (see Table II). There was a slight difference in the overall incidence of adverse reactions between the three groups ($p > 0.05$) (Table II).

Table II

Adverse reactions among different groups [n (%)]

Adverse reactions	IRB group	AMB group	IRB + AMB group
Example number	32	33	40
Arrhythmia	1 (3.1)	1 (3.0)	1 (2.5)
Cough	0 (0.0)	1 (3.0)	2 (5.0)
Diarrhea	1 (3.1)	1 (3.0)	1 (2.5)
Headache and dizziness	1 (3.1)	1 (3.0)	1 (2.5)
Nausea and vomiting	1 (3.1)	0 (0.0)	1 (2.5)
Total adverse reactions	4 (12.5)	4 (12.1)	6 (15.0)

This study found that, compared with monotherapy involving either IRB or AMB, combination therapy involving both drugs resulted in higher overall clinical efficacy (78.1%, 78.8% and 95.0%), with no significant difference in the incidence of adverse reactions (12.5%, 12.1% and 15.0%). Primary hypertension refers to a clinical condition where, without the use of antihypertensive drugs, the patient's systolic blood pressure is ≥140 mmHg and/or diastolic blood pressure is ≥90 mmHg. Primary hypertension develops gradually, and the clinical presentation varies in severity among patients. Early symptoms are often subtle, but as the disease progresses, patients may exhibit a range of neurological dysfunction symptoms such as headache, dizziness, tinnitus, and palpitations. The pathogenesis of primary hypertension is complex, involving multiple factors, including genetic, neural, renal, hormonal, vascular, and insulin resistance mechanisms (17,18). Both IRB and AMB have demonstrated favorable clinical efficacy in the treatment of hypertension. This study found that IRB monotherapy, AMB monotherapy, and their combination all effectively reduced diastolic blood pressure, systolic blood pressure, and pulse pressure in patients with primary hypertension, with the combination therapy showing superior blood pressure control. This can be attributed to the ability of IRB to inhibit the production of angiotensin II, thereby facilitating vasodilation and lowering blood pressure (19). Additionally, IRB reduces aldosterone secretion, further decreasing blood volume and blood pressure. AMB works by inhibiting calcium ion entry into cells through calcium channels in the cell membrane, which lowers intracellular calcium concentration, weakens the contractile force of vascular smooth muscle cells, promotes vasodilation, and reduces peripheral vascular resistance (20). Cui *et al*. (2023) demonstrated that the combination of olmesartan and AMB effectively controlled blood pressure in elderly patients with primary hypertension, with approximately 78.0% of patients achieving their target blood pressure after 8 weeks of treatment (21). Notably, the aforementioned study exclusively enrolled elderly patients (≥ 65 years) with a longer mean disease duration (10.2 ± 2.1 years) and a higher prevalence of atherosclerosis (42%). In contrast, our study encompassed a broader age range (40 - 75 years) with relatively shorter disease duration (mean 7.5 - 8.1 years). Although both studies demonstrated the antihypertensive superiority of combination therapy, the more pronounced vascular remodeling in elderly populations may have amplified the therapeutic differences. Future studies should refine treatment strategies by targeting specific patient subgroups.

Hypertension is the leading risk factor for cardiovascular diseases, and the mechanisms of cardiovascular remodeling induced by hypertension are highly complex. Hypertension causes hypertrophy of large artery smooth muscle cells and, following endothelial cell damage, leads to abnormal collagen fiber proliferation, contributing to atherosclerosis (22). Additionally, hypertension increases peripheral vascular resistance, promoting the secretion of angiotensin and subsequently increasing cardiac load. This alters the hemodynamic state, disrupts endocrine metabolism, and ultimately leads to adaptive changes in cardiovascular anatomical structures (23,24). An increase in the lumen-to-wall ratio or wall-to-lumen ratio in microvessels is a hallmark of hypertension, which may impair organ blood flow reserve. This is related to the maintenance and progressive deterioration of hypertension, as well as the development of organ damage and cardiovascular events mediated by hypertension (25). Furthermore, there exists a vicious cycle between hypertension and vascular remodeling. Hypertension causes vascular remodeling, which, in turn, exacerbates hypertension. This cycle leads to continuous deterioration of vascular structure, ultimately resulting in organ damage. IVST, LVPWT, LVEDD, and EAI are important parameters for assessing changes in left ventricular structure, with an increase in EAI being one of the key manifestations of cardiovascular remodeling

(26). In this study, we found that both monotherapy with IRB and AMB, as well as their combination, effectively reduced vascular remodeling indicators such as IVST, LVPWT, LVEDD, and LVMI in patients with primary hypertension. The combination therapy showed superior effects in reducing these parameters. IRB not only lowers blood pressure but also protects the cardiovascular system, prevents ventricular remodeling, reverses ventricular hypertrophy, and reduces the risk of cardiovascular diseases. Pai *et al*. (2022) demonstrated that IRB can influence the mitochondrial-mediated apoptotic pathway via the cardiac Fas/FasL signaling pathway, thus preventing cardiac cell apoptosis induced by elevated hypertension levels (27). This is because IRB inhibits the proliferation of cardiomyocytes, improves cardiovascular structure and function, prevents ventricular remodeling, and has a mild effect in reversing ventricular hypertrophy. Endothelial dysfunction is a key pathological and physiological basis for target organ damage associated with hypertension and is also an initiating factor in vascular remodeling. AMB can improve endothelial dysfunction caused by hypertension by influencing nitric oxide and prostaglandin levels (28).

Hemorheology refers to the rheological properties between blood and blood vessels, but when these properties are altered, particularly with increased blood viscosity, it can affect blood flow velocity, leading to elevated blood pressure. In hypertensive patients, increased blood viscosity, enhanced erythrocyte aggregation, and decreased erythrocyte deformability can contribute to impaired circulation and microcirculatory disturbances (29). These changes further exacerbate the condition of hypertensive patients and increase the risk of hypertension-related complications (30). In this study, we found that both IRB monotherapy, AMB monotherapy, and their combination therapy effectively reduced hemo-rheological parameters such as WBHSV, WBLSV, PV, and EAI in patients with primary hypertension, with combination therapy showing superior effects in reducing these parameters. Villano *et al*. (2020) confirmed that cysteine protease inhibitors can improve hemodynamic parameters by inhibiting angiotensin II type 1 receptors (31). IRB can reduce both whole blood and plasma viscosity, which may be related to its ability to improve the structure and function of the vascular walls and promote blood flow. Additionally, IRB may improve the properties and structure of the erythrocyte membrane, reducing erythrocyte aggregation and enhancing erythrocyte deformability, thereby improving blood flow (32). While no studies have directly confirmed the effects of AMB on erythrocytes, it is likely that it indirectly influences erythrocyte deformability by improving the structure and function of the vascular walls, facilitating the passage of erythrocytes through small vessels. In light of the results of this study, the combination of IRB and AMB may complement each other in improving the hemorheological properties of patients with primary hypertension, further enhancing their blood flow characteristics.

Chronic inflammation plays a pivotal role in the progression of hypertension. Proinflammatory cytokines can induce structural and functional damage to the vascular endothelium, promoting vascular remodeling. C-reactive protein (CRP), an acute-phase reactant, is elevated during vascular injury and facilitates leukocyte adhesion and vascular smooth muscle cell proliferation, thereby accelerating atherosclerosis and vascular remodeling (33-35). Interleukin-6 (IL-6) stimulates the migration and proliferation of endothelial progenitor cells, promoting angiogenesis (36), while interleukin-1β (IL-1β) contributes to vascular remodeling by regulating smooth muscle cell proliferation and migration (37). Tumor necrosis factor-α (TNF-α) is a key proinflammatory mediator of endothelial dysfunction and intimal thickening, modulating extracellular matrix metabolism through multiple pathways to exacerbate vascular remodeling (38). Extensive evidence indicates that angiotensin II (Ang II) activates downstream NF-κB and MAPK signaling pathways via binding to its type 1 receptor (AT1R), promoting the expression and release of proinflammatory cytokines and aggravating vascular inflammation and remodeling (39,40). As an AT1R antagonist, IRB effectively blocks Ang II binding, suppressing NF-κB-mediated inflammatory responses, thereby reducing the expression of CRP, TNF-α, and other inflammatory factors, and ameliorating endothelial dysfunction and vascular remodeling (41,42). Meanwhile, AMB modulates intracellular calcium concentration, influencing calcium-dependent MAPK pathway activity to inhibit inflammatory signaling and improve endothelial function (43). Our study demonstrated that IRB monotherapy, AMB monotherapy, and their combination significantly reduced serum levels of CRP, IL-6, IL-1β, and TNF-α in patients with essential hypertension, with the most pronounced reductions observed following combination therapy. These findings suggest that the two drugs act synergistically through distinct yet complementary molecular mechanisms to attenuate vascular inflammation, thereby effectively mitigating hypertension-induced vascular remodeling. In summary, by analyzing changes in inflammatory biomarkers, this study provides preliminary mechanistic insights into how IRB and AMB inhibit proinflammatory cytokine expression by blocking Ang II receptor-associated signaling pathways, thereby intervening in hypertensive vascular remodeling at the molecular level.

This study evaluated the short-term efficacy of IRB and AMB (both as monotherapy and in combination) on blood pressure control, vascular remodeling, and

inflammatory cytokine levels in patients with essential hypertension, demonstrating superior clinical benefits with combination therapy. However, the lack of long-term follow-up data limits the assessment of sustained therapeutic effects and target organ protection. Short-term blood pressure control may not fully reflect long-term blood pressure variability and vascular functional changes, introducing potential biases such as blood pressure rebound and delayed organ protection. Future investigations should focus on longitudinal dynamic monitoring, with particular emphasis on elucidating the mechanistic effects of combination therapy on vascular endothelial function, oxidative stress, and gut microbiota modulation. Additionally, in-depth exploration of related inflammatory and apoptotic signaling pathways is warranted to comprehensively decipher the underlying molecular mechanisms and advance the development of precision medicine for hypertension management.

Conclusions

Compared to monotherapy, the combination of IRB and AMB significantly improves the clinical treatment outcomes in patients with primary hypertension. This combination therapy also helps to enhance vascular remodeling and blood rheological conditions by inhibiting the release of inflammatory cytokines, which is beneficial for reducing the incidence of hypertension-related cardiovascular events. Nevertheless, there is a lack of follow-up data to analyze the long-term effects of the combination therapy on blood pressure control and prognosis in patients with primary hypertension. In conclusion, further multi-center, large-sample clinical studies are required to verify the effectiveness and safety of the combination of IRB and AMB in treating primary hypertension and to explore its underlying mechanisms.

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Funding

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Ethics approval and consent to participate

This study obtained approval from the ethics committee of First People's Hospital of Linping District (Hangzhou, China).

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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