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Comparative Analysis of Empagliflozin Plus Valsartan Capsule and Amlodipine in the Treatment of Patients with Diabetes and Hypertension: Efficacy and Cardiovascular Protection

Yuqin Huang[1], Qionglan Zhou[*1], Zixi Zhou[1], Dan Li[1], Qian Huang [1], Linxin Yang[1], Xiaochun Du[1], Yajun Li[1]

[1] Yilong County People's Hospital, Nanchong, Sichuan, 637600, China

Email: hyq15983792535@126.com

Abstract

Objective: To evaluate the therapeutic efficacy of empagliflozin combined with valsartan capsule and amlodipine in patients with diabetes mellitus complicated by hypertension.

Methods: A total of 132 patients with diabetes mellitus and hypertension admitted to our hospital between March 2024 and March 2025 were enrolled. Patients were randomly assigned according to medical record sorting into a dual-therapy group (valsartan capsule plus amlodipine, n = 66) and a triple-therapy group (empagliflozin plus valsartan capsule plus amlodipine, n = 66). Clinical efficacy was compared between the two groups.

Results: No significant differences were observed between groups in baseline levels of blood glucose, blood pressure, blood lipids, cardiac function parameters, or in the incidence of adverse events during treatment (all $P > 0.05$). After treatment, fasting plasma glucose (FPG), 2-hour postprandial glucose (2hPG), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and left ventricular end-diastolic diameter (LVDD) were significantly lower in the triple-therapy group compared with the dual-therapy group ($P < 0.05$). Left ventricular ejection fraction (LVEF), high-density lipoprotein cholesterol (HDL-C), and overall clinical efficacy were significantly higher in the triple-therapy group (all $P < 0.05$).

Conclusion: Empagliflozin combined with valsartan capsule and amlodipine provides superior clinical efficacy in the management of diabetes mellitus with hypertension. This regimen significantly improves blood glucose, blood pressure, and lipid control, offers favorable cardiovascular protection, and demonstrates a high level of clinical safety.

Keywords: Empagliflozin; valsartan capsule; amlodipine; diabetes mellitus with hypertension; cardiovascular protection

Introduction

Diabetes mellitus and hypertension are among the most prevalent chronic diseases in middle-aged and elderly populations and frequently coexist. Both conditions share common pathophysiological mechanisms, including obesity, high-fat dietary patterns, and sedentary lifestyle behaviors [1]. The coexistence of diabetes and hypertension not only exacerbates impairment of cardiac, renal, and peripheral vascular function but also increases the risk of severe complications such as stroke and diabetic retinopathy [2,3]. These comorbidities substantially diminish patients' quality of life and pose a considerable threat to health and survival, underscoring the urgent need to explore safer and more effective therapeutic strategies [4].

Pharmacological therapy remains the cornerstone of management, with combination regimens often preferred over monotherapy to simultaneously achieve glycemic and blood pressure control while minimizing the risks associated with high-dose single-agent use [5]. Among commonly prescribed agents, empagliflozin has demonstrated robust glucose-lowering efficacy along with auxiliary antihypertensive benefits, while the combination of valsartan capsule and amlodipine provides effective blood pressure reduction [6,7]. However, clinical evidence regarding the concomitant use of all three agents remains limited. Given their complementary mechanisms, triple therapy may offer enhanced clinical benefits in patients with diabetes and hypertension [8].

The present study was therefore designed to evaluate the clinical efficacy, metabolic effects, and cardiovascular protective properties of empagliflozin combined with valsartan capsule and amlodipine in this patient population.

1.Materials and Methods

1.1 General Information

A total of 132 patients with diabetes mellitus and hypertension who were admitted to our hospital between March 2024 and March 2025 were enrolled. Patients were randomly assigned into two groups using a medical record–based random sequencing method: the dual-therapy group and the triple-therapy group. No significant differences were observed in baseline characteristics between the two groups ($P > 0.05$). Details are shown in Table 1.

Table 1. Baseline characteristics of patients in the two groups (n, %, $\bar{x} \pm s$)

Group	n	Male/Female	Age (years)	Duration of diabetes (years)	Duration of hypertension (years)	Body mass index (kg/m²)
Dual-therapy	66	35/31	56.36±5.15	6.89±2.72	5.77±2.26	26.11±2.38
Triple-therapy	66	37/29	56.37±5.17	6.92±2.74	5.79±2.28	26.13±2.42
x^2/t value		0.122	0.011	0.063	0.051	0.048
P value		0.727	0.991	0.950	0.960	0.962

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Patients who met the clinical diagnostic criteria for diabetes mellitus with hypertension; (2) no history of allergy or contraindications to the study medications; (3) ability to comply with medical advice and adhere to prescribed medication schedules; (4) normal hearing and speech ability with good mental status.

Exclusion criteria: (1) presence of cardiovascular or cerebrovascular disease; (2) functional impairment of major organs; (3) failure to provide written informed consent; (4) presence of other metabolic, immune, or systemic disorders.

1.3 Methods

Patients in the dual-therapy group were treated with valsartan capsules and amlodipine. Valsartan capsules (National Drug Approval No. H20103521, Hunan Qianjin Xiangjiang Pharmaceutical Co., Ltd., 80 mg × 7 tablets × 4 blisters) were administered orally at a dose of 1 tablet once daily, preferably after breakfast. After 4 weeks, the dosage could be adjusted to 2 tablets once daily depending on patient tolerance and clinical need. Thirty minutes after valsartan intake, patients were given amlodipine besylate tablets (National Drug Approval No. H20103112, Shanxi Huayuan Pharmaceutical Biotechnology Co., Ltd., 5 mg × 14 tablets × 3 blisters) at 1 tablet once daily.

In the triple-therapy group, empagliflozin was added on top of the dual regimen. Empagliflozin tablets (National Drug Approval No. H20213115, Jiangsu Wanbang Biopharmaceutical Group Co., Ltd., 10 mg × 10 tablets) were taken orally, one tablet once daily, in the morning on an empty stomach.

The treatment duration was 16 weeks for both groups.

1.4 Outcome Measures

1.Clinical efficacy:Markedly effective: fasting plasma glucose (FPG) reduced by >20%, diastolic blood pressure (DBP) decreased by >20 mmHg, or normalization of both blood glucose and blood pressure;Effective: FPG reduction of 10%–19% or DBP reduction of 10–19 mmHg;Ineffective: outcomes not meeting the above criteria.The total effective rate was calculated as (markedly effective + effective) ÷ total cases × 100%.

2. Glycemic and blood pressure parameters: FPG and 2-hour postprandial glucose (2hPG) were measured before and after treatment using a glucometer (Dayou G001, Shanghai Jumu Medical Device Co., Ltd.) with fingertip blood samples obtained in the morning under fasting and 2-hour postprandial conditions. Systolic blood pressure (SBP) and DBP were measured with an automated electronic sphygmomanometer (Omron HBP-9030, Wuhan Hejia Medical Technology Co., Ltd.).

3.Lipid profile: Before and after treatment, 5 mL of fasting venous blood was collected from the cubital vein. After centrifugation at 3000 rpm for 10 min, serum was separated and analyzed with an automated biochemical analyzer (Mindray BS-280, Shenzhen Chuangxing Tianxia Technology Co., Ltd.) for triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

4.Cardiac function parameters: Left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVDD) were assessed before and after treatment using a Doppler echocardiography system (Jiangsu Xinma Medical Equipment Co., Ltd.).

5.Adverse reactions: During treatment, adverse events such as nausea/vomiting, hypoglycemia, dizziness/headache, rash, and edema were recorded. The incidence of adverse events was calculated as (number of adverse events ÷ total cases) × 100%.

1.5 Statistical Analysis

All data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\bar{x}$ ± standard deviation (SD) and compared between groups using the independent samples t-test. Categorical variables were presented as frequencies and percentages, and comparisons between groups were performed using the chi-square (χ^2) test. A two-tailed P value < 0.05 was considered statistically significant.

2. Results

2.1 Comparison of clinical efficacy between the two groups

The triple-therapy group showed a significantly higher overall clinical efficacy compared with the dual-therapy group ($P < 0.05$). Details are presented in Table 2.

Table 2. Comparison of clinical efficacy between the two groups (n, %)

Group	n	Markedly effective	Effective	Ineffective	Total effective rate (%)
Dual-therapy	66	31 (46.97)	26 (39.39)	9 (13.64)	57 (86.36)
Triple-therapy	66	36 (54.55)	28 (42.42)	2 (3.03)	64 (96.97)
x^2 value		4.860			
P value		0.027			

2.2 Comparison of blood glucose and blood pressure indices between the two groups

No significant differences were observed in fasting plasma glucose (FPG), 2-hour postprandial glucose (2hPG), systolic blood pressure (SBP), or diastolic blood pressure (DBP) between the two groups before treatment ($P > 0.05$). After treatment, all these parameters were significantly lower in the triple-therapy group compared with the dual-therapy group ($P < 0.05$). Details are shown in Table 3.

Group	n	FPG(mmol/L)		2hPG(mmol/L)		SBP(mmHg)		DBP(mmHg)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Dual-therapy	66	10.17±1.78	7.28±1.47	13.83±2.23	10.79±1.18	103.37±5.77	92.43±5.39	168.23±10.73	153.58±8.39
Triple-therapy	66	10.21±1.81	5.22±1.09	13.85±2.25	6.34±0.93	103.39±5.79	80.88±5.03	168.28±10.89	125.63±5.98
t value		0.128	9.145	0.051	24.062	0.020	12.727	0.027	22.039
P value		0.898	0.000	0.959	0.000	0.984	0.000	0.979	0.000

Table 3. Comparison of blood glucose and blood pressure indices between the two groups ($\bar{x} \pm s$)

2.3 Comparison of lipid profiles between the two groups

No significant differences were observed in lipid parameters between the two groups before treatment ($P > 0.05$). After treatment, total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) levels were significantly lower, whereas high-density lipoprotein cholesterol (HDL-C) was significantly higher in the triple-therapy group compared with the dual-therapy group ($P < 0.05$). Details are presented in Table 4.

Table 4. Intergroup comparison of lipid parameters ($\bar{x} \pm s$, mmol/L)

Group	n	TC		TG		HDL-C		LDL-C	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Dual-therapy	66	7.37±1.54	5.66±1.22	2.21±0.78	1.76±0.57	0.82±0.13	1.09±0.26	4.83±1.19	3.23±0.88
Triple-therapy	66	7.40±1.56	3.67±0.97	2.20±0.77	1.08±0.39	0.83±0.16	2.35±0.37	4.85±1.17	2.14±0.69
t value		0.111	10.373	0.074	7.999	0.394	22.636	0.097	7.919

P value	0.912	0.000	0.941	0.000	0.694	0.000	0.923	0.000

2.4 Comparison of cardiovascular function indices between the two groups

No significant differences were observed in cardiac function parameters between the two groups before treatment ($P > 0.05$). After treatment, left ventricular ejection fraction (LVEF) was significantly higher, and left ventricular end-diastolic diameter (LVDD) was significantly lower in the triple-therapy group compared with the dual-therapy group ($P < 0.05$). Details are shown in Table 5.

Table 5. Comparison of cardiovascular function indices between the two groups ($\bar{x} \pm s$)

Group	n	LVEF(%)		LVDD(mm)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Dual-therapy	66	43.74±1.77	52.85±2.13	62.28±4.16	50.23±3.86
Triple-therapy	66	43.78±1.81	56.98±2.35	62.87±4.24	39.24±3.22
t value		0.128	10.579	0.807	17.762
P value		0.898	0.000	0.421	0.000

2.5 Comparison of adverse events between the two groups

No significant difference was observed in the overall incidence of adverse events between the two groups ($P > 0.05$). Details are presented in Table 6.

Table 6. Comparison of adverse events between the two groups (n, %)

Group	n	Nausea/Vomiting	Hypoglycemia	Dizziness/Headache	Rash	Edema	Total incidence (%)
Dual-therapy	66	1 (1.52)	1 (1.52)	2 (3.03)	0 (0.00)	0 (0.00)	4 (6.07)
Triple-therapy	66	2 (3.03)	1 (1.52)	1 (1.52)	1 (1.52)	2 (3.03)	7 (10.62)
x^2 value							0.893
P value							0.345

3. Discussion

The coexistence of diabetes mellitus and hypertension amplifies organ damage and increases clinical risk, with each condition potentially exacerbating the progression of the other [9]. Chronic hyperglycemia, dyslipidemia, insulin resistance, and renal dysfunction in diabetic patients contribute to endothelial injury and sodium-water retention, which in turn reduce vascular elasticity, accelerate atherosclerosis, increase blood volume, and predispose to the development of hypertension [10,11]. Conversely, the onset of hypertension in diabetic patients further aggravates endothelial and renal injury, exacerbates atherosclerosis, and increases insulin resistance, thereby establishing a deleterious feedback loop that amplifies systemic damage and elevates the risk of cardiovascular and cerebrovascular events [12,13]. These observations underscore the importance of providing safe, comprehensive, and effective therapeutic strategies to preserve patient health and reduce morbidity and mortality [14].

Current management of diabetes with hypertension focuses primarily on glycemic and blood pressure control, often necessitating combination therapy to achieve optimal outcomes. Among available agents, empagliflozin, valsartan, and amlodipine have demonstrated notable efficacy. Empagliflozin primarily lowers blood glucose while providing auxiliary blood pressure reduction, whereas valsartan and amlodipine exert potent antihypertensive effects [15,16].

In this study, the triple-therapy group demonstrated superior clinical efficacy compared with the dual-therapy group, indicating a synergistic therapeutic advantage. Mechanistically, empagliflozin inhibits renal glucose reabsorption, increasing urinary glucose excretion and lowering blood glucose. It also promotes natriuresis and diuresis, thereby reducing blood volume and contributing to blood pressure control [17]. Valsartan blocks angiotensin II–mediated vasoconstriction and suppresses aldosterone release, reducing sodium and water retention and lowering blood pressure [18]. Amlodipine, a calcium channel blocker, relaxes vascular smooth muscle by inhibiting calcium influx, further reducing blood pressure. These three agents act through complementary pathways, resulting in enhanced clinical efficacy [19].

Post-treatment, the triple-therapy group showed significantly lower FPG, 2hPG, SBP, and DBP compared with the dual-therapy group, reflecting the superior glycemic and blood pressure control afforded by the combined regimen. While valsartan and amlodipine contribute primarily to blood pressure reduction and have limited glycemic effects, empagliflozin plays a central role in glucose regulation by both reducing renal glucose reabsorption and promoting urinary glucose excretion. Its natriuretic effect also synergizes with antihypertensive therapy, achieving simultaneous glycemic and blood pressure stabilization [20].

Similarly, post-treatment lipid profiles in the triple-therapy group indicated lower TC, TG, and LDL-C levels and higher HDL-C compared with the dual-therapy group, demonstrating improved lipid metabolism. Empagliflozin, as a sodium-glucose cotransporter 2 inhibitor, indirectly modulates triglyceride synthesis through metabolic improvement. Valsartan and amlodipine, by controlling sodium-water retention and mitigating endothelial injury, complement empagliflozin's metabolic effects, thereby improving insulin sensitivity and optimizing lipid parameters [21].

Cardiovascular function indices also favored the triple-therapy group, with higher LVEF and lower LVDD values, indicating enhanced cardioprotective effects. Increased LVEF reflects improved myocardial contractility, partly attributable to reduced myocardial lipid accumulation and enhanced cellular metabolic efficiency mediated by empagliflozin. Valsartan mitigates angiotensin II–induced myocardial stress, inhibiting hypertrophic remodeling, while amlodipine enhances coronary perfusion via vasodilation. The combined effects on blood pressure and ventricular remodeling contribute to decreased LVDD, reflecting improved cardiac structure and function [22].

No significant difference in adverse event incidence was observed between groups, indicating that the triple-therapy regimen is clinically safe. This safety profile is likely due to the distinct mechanisms of action of the three agents, which minimize overlapping toxicity and adverse interactions. Reduced side effects support treatment adherence and the maintenance of long-term glycemic, blood pressure, and metabolic stability.

In conclusion, the combination of empagliflozin, valsartan, and amlodipine provides superior clinical efficacy in patients with diabetes mellitus and hypertension. The regimen effectively stabilizes glycemia, blood pressure, and lipid profiles, confers cardioprotective benefits, and demonstrates a high level of clinical safety, making it a promising strategy for comprehensive disease management.

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