Therapeutic Effect of Amlodipine Besylate in Conjunction with Enalapril Maleate Tablets in Diabetic Nephropathy and Hypertension

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To observe the efficacy of benzenesulfonate amlodipine in conjunction with enalapril in treating female patients with diabetic nephropathy and hypertension. From August 2022 to August 2023, a total of 79 female patients diagnosed with both diabetic nephropathy and hypertension were recruited as participants for our study in the outpatient clinic. The patients were assigned randomly to either the control group (40 cases) or the observation group (39 cases). The control group was prescribed oral benzenesulfonate amlodipine tablets to manage their blood pressure, while the observation group received supplementary oral enalapril maleate tablets based on the treatment provided to the control group. The treatment regimen was administered to both groups of patients without interruption for a period of 3 mo. The study aimed to analyze and contrast the variances in blood glucose, blood pressure, and renal function markers between the two groups, while also monitoring and comparing any adverse reactions that occurred during the treatment course. No notable variations in fasting plasma glucose, postprandial 2 h blood glucose, and hemoglobin A1c were observed before and after the treatment in either group of patients, indicating no remarkable differences ($p>0.05$). Before treatment, there were no notable variations identified in diastolic blood pressure and systolic blood pressure between the two patient groups ($p>0.05$). Nevertheless, after the treatment, both groups demonstrated decreased levels of renal function indicators compared to their baseline measurements ($p<0.05$), and the observation group showcased notably lower levels than the control group ($p<0.05$). Throughout the treatment period, no remarkable disparities in the overall occurrence of adverse reactions were found between the two patient groups ($p>0.05$). Benzenesulfonate amlodipine in conjunction with enalapril is effective in lowering blood pressure and improving renal function in female patients with diabetic nephropathy and hypertension, and it is safe to use.

Key words: Amlodipine besylate, enalapril maleate tablets, diabetic nephropathy, hypertension, dihydropyridine

Characterized by a decline in glomerular filtration rate, heightened urinary protein excretion, and renal dysfunction[1,2], Diabetic Nephropathy (DN) is recognized as a common complication of diabetes. Hypertension holds substantial influence as a triggering and hastening element in the progression of DN, leading to its occurrence and advancement[3]. In the clinical management of DN concomitant with hypertension, antihypertensive therapy assumes a central role. This therapeutic approach not only effectively suppresses the progression of DN but also improves patient's quality of life and prolongs their survival[4,5]. A long-acting dihydropyridine calcium channel blocker called amlodipine besylate effectively reduces blood pressure through the inhibition of calcium influx and the relaxation of vascular smooth muscle tension[6,7]. Enalapril, recognized as an angiotensin II receptor blocker, functions to hinder the effects of angiotensin II, which results in the reduction of peripheral vascular

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resistance, mitigation of vascular damage, and relief of renal burden. Consequently, this medication achieves a reduction in blood pressure and provides renal protection[8]. Several prior studies have demonstrated the efficacy of amlodipine besylate and enalapril as separate therapeutic options in addressing hypertension or DN[9,10]. Nevertheless, there exists a dearth of clinical data regarding the combined treatment of amlodipine besylate and enalapril for female patients with DN and hypertension. Consequently, additional research is imperative to assess the effectiveness and safety of this therapeutic approach. Accordingly, this study focuses on assessing the clinical effects of combining amlodipine besylate and enalapril in female patients with DN and hypertension. By examining its influence on blood pressure control, renal function improvement, and urinary protein excretion reduction, the study aims to provide scientific evidence guiding clinical treatment decisions and informing personalized approaches for managing this patient group. Over the period spanning from August 2022 to August 2023, a cohort of 79 female patients with coexisting DN and hypertension, undergoing outpatient care at our hospital, were selected as the study participants. Utilizing simple randomization, all patients were grouped into the control (40 cases) and observation (39 cases) groups. Patients within the control group had ages ranging from 61 y to 92 y, with an average of (80.33±7.80) y. The duration of the disease varied from 4 y to 18 y, with an average duration of (9.78±3.47) y. Similarly, the observation group comprised patients aged between 65 y and 90 y, with a mean age of (81.31±7.76) y. The duration of the disease ranged from 3 y to 18 y, with an average duration of (9.58±3.56) y. No remarkable variations were observed in terms of age and disease duration between the two groups ($p>0.05$), indicating comparability. Prior to conducting the study, all participating patients were required to give informed consent, and the research protocol underwent review and approval by the ethics committee of the hospital. Inclusion criteria in accordance with the "Guidelines for the prevention and treatment of type 2 diabetes in China"[11], the diagnosis of DN was made, and the diagnosis of hypertension was based on the "Guidelines for the prevention and treatment of hypertension in China"[12] and patients provided informed consent. In exclusion criteria, the presence of organic diseases; conditions including hyperkalemia, renal artery stenosis, glomerulonephritis, chronic renal failure (stage 4 or later Chronic Kidney Disease (CKD)), ketoacidosis, and urinary tract obstruction; cognitive impairment and allergy to the study drugs were excluded. Prior to the initiation of the treatment, all patients in both groups ceased the usage of any antihypertensive drugs, while keeping their original hypoglycemic plan unchanged. The control group was given oral benzenesulfonate amlodipine tablets (manufactured by Pfizer Inc.; National Drug Approval Number H20093660; dosage 10 mg) to control blood pressure. The dosage was 10 mg per administration, once daily, taken from 6:00 am to 8:00 am. The observation group received additional oral enalapril maleate tablets (Yangtze River Pharmaceutical Group Jiangsu Pharmaceutical Co., Ltd.; National Drug Approval Number H32026568; dosage 10 mg) based on the control group. The dosage was 20 mg per administration. Both patient groups attended regular monthly outpatient follow-up visits and underwent evaluation after 3 mo of uninterrupted treatment. Measurements of blood pressure and blood glucose levels were taken simultaneously for three consecutive days both before initiating treatment and after 3 mo of treatment. Blood pressure, encompassing Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), was assessed utilizing a Yuwell electronic sphygmomanometer (National Medical Products Administration Approval Number: 20202071574, YE620D model). Postprandial 2 h Blood Glucose (P2hBG) and Fasting Plasma Glucose (FPG) were measured using a Yueshi glucometer. Average values of the 3 d measurements were used as the final blood pressure and blood glucose results. Glycosylated Hemoglobin A1c (HbA1c) was measured using a latex immunoturbidimetric assay (Bayer Co., Ltd., Model DCA2000). Meanwhile, 5 ml of venous blood was collected from patients in a fasting state of 8 h, centrifuged at 3500/min for 10 min, and the supernatant was used to measure Serum creatinine (Scr) and Blood Urea Nitrogen (BUN) levels. Urine samples were collected from patients over a 24 h period and analyzed using a Mindray urine analyzer to measure urinary protein levels (National Medical Products Administration Approval Number: 20172220124, Model: OPM-1560A), and Urinary Albumin Excretion Rate (UAER) was calculated. The study involved a comparison of the two groups to assess the variances in blood glucose, blood pressure, and renal function indicators. Moreover, the occurrence of adverse reactions during

the treatment period was meticulously documented. Utilizing the Statistical Package for the Social Sciences (SPSS) 25.0 statistical software, the analysis was performed, and the measurement data were represented as mean±standard deviation. The comparison between the two groups was made using the independent samples t-test, and count data were analyzed utilizing the Chi-square (χ^2) test. Results were deemed to be statistically significant when the $p<0.05$. The FPG, P2hBG, and HbA1c levels did not substantially differ before and after treatment in either group of patients ($p>0.05$) as shown in Table 1. There were no marked variances in DBP and SBP between the two patient groups prior to treatment ($p>0.05$). Subsequently, after the treatment, both groups exhibited a notable reduction in DBP and SBP, with the observation group displaying remarkably lower levels than the control group ($p<0.05$) as shown in Table 2. The levels of renal function indicators did not substantially differ between the two patient groups prior to treatment ($p>0.05$). However, following treatment, both groups exhibited remarkably lower levels of renal function indicators as opposed to their pre-treatment values ($p<0.05$). Notably, the observation group displayed reduced levels of renal function indicators than the control group, with the differences being remarkable ($p<0.05$) as shown in Table 3. Both groups of patients experienced adverse reactions, including dizziness, headache, facial flushing, gastrointestinal symptoms, and foot swelling, during the treatment period. However, no noteworthy variations in the overall incidence of adverse reactions was found between the control group (17.94 %) and the observation group (20.00 %) ($p>0.05$) as show in Table 4. Clinically, the coexistence of DN and hypertension is highly prevalent, and it poses a significant health risk to the population. The present circumstances have witnessed significant transformations in lifestyle habits and dietary patterns, leading to a surge in the number of individuals with concurrent DN and hypertension. Consequently, this presents new challenges to the healthcare system. Hypertension is a crucial factor in the progression of DN, and effective control of Blood Pressure (BP) (BP <180/130 mmHg) in patients can effectively delay the occurrence of end-stage renal disease[13-15]. This study sought to examine the effectiveness of utilizing a combination of amlodipine besylate and enalapril in the management of DN and hypertension in female patients, and to compare its influence on blood glucose, blood pressure, and renal function. Pre- and post-treatment measurements of FPG, P2hBG, and HbA1c revealed similar levels in both patient groups, suggesting that the combination of amlodipine besylate and enalapril may not result in notable enhancements in blood glucose control. Despite this, in terms of blood pressure control, both groups of patients exhibited a notable decrease in DBP and SBP post-treatment, with the reduction being more prominent in the observation group than in the control group. This suggests that the combination of amlodipine besylate and enalapril has a more pronounced effect in managing hypertension. Enalapril may achieve this effect by blocking the action of angiotensin II, reducing peripheral vascular resistance, and lowering blood pressure. In addition, the levels of renal function indicators improved in both groups of patients after treatment, with a more significant improvement observed in the observation group compared to the control group. In this study, the combination of amlodipine besylate and enalapril may protect renal function by reducing blood pressure and reducing the burden on the kidneys. The underlying mechanisms may include amlodipine besylate selectively inhibiting the influx of calcium ions in L-type channels in voltage-gated channels, further reducing the contractile force of the afferent arteriole wall of the renal glomerulus, significantly increasing the glomerular filtration rate, and protecting renal function. Additionally, amlodipine besylate can increase renal blood flow and reduce sodium retention, which has a protective effect on the renal hemodynamics of patients. Enalapril, an Angiotensin-Converting Enzyme (ACE) inhibitor, can inhibit the synthesis of angiotensin II, reduce the filtration rate of plasma macromolecules, thereby reducing the intraglomerular pressure, and have a protective effect on the renal interstitium[16]. During the treatment period, both groups of patients experienced adverse reactions such as dizziness, headache, facial flushing, gastrointestinal reactions, and foot swelling. Nevertheless, the incidence of adverse reactions did not vary remarkably between the two groups. This implies that the safety profile of the two treatment options was alike, and patients demonstrated favorable tolerance towards the adverse reactions. Despite confirming the substantial clinical effectiveness of the combination of amlodipine besylate and enalapril in treating patients with DN and hypertension, this study highlights the necessity for additional research to substantiate and

delve into the long-term effects and safety of this treatment regimen. Additionally, the study solely enrolled female patients, thus leaving the treatment effects on male patients uncertain. Future investigations have the potential to enhance the sample size and incorporate male patients to further explore this matter. Overall, the combined administration of amlodipine besylate and enalapril yields beneficial effects in lowering blood pressure and enhancing renal function in female individuals diagnosed with both DN and hypertension. It is plausible to regard this combination therapy as a viable option in clinical practice. Nevertheless, it is essential to continually monitor and evaluate patients to ensure the safety and efficacy of the treatment.

TABLE 1: BLOOD GLUCOSE LEVELS

Group (n)	FPG		P2hBG		HbA1c	
	Before	After	Before	After	Before	After
Observation (39)	5.38±1.34	5.79±1.35	8.62±3.51	8.41±3.32	6.20±1.47	5.30±1.49
Control (40)	5.75±1.33	5.43±1.24	9.02±2.84	8.41±3.76	5.83±1.24	5.43±1.58
t	1.214	-1.210	0.560	0.009	-1.199	0.372
p	0.228	0.230	0.577	0.993	0.234	0.711

TABLE 2: BLOOD PRESSURE LEVEL

Group (n)	DBP (mmHg)		SBP (mmHg)	
	Before	After	Before	After
Observation (39)	155.62±13.64	128.82±9.34*	99.05±7.83	72.33±7.4*
Control (40)	151.60±12.62	134.78±10.84*	101.03±8.56	86.28±6.64*
t	-1.358	2.613	1.069	8.823
p	0.178	0.011	0.289	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 3: SERUM CYTOKINE LEVELS

Group (n)	Scr (μmol/l)		BUN (mmol/l)		UAER (μg/min)	
	Before	After	Before	After	Before	After
Observation (39)	123.46±13.75	86.05±9.07*	5.74±0.92	4.04±0.49*	161.03±18.75	98.20±13.51*
Control (40)	119.92±14.73	94.22±9.12*	5.86±0.81	5.13±0.77*	149.31±22.88	121.59±16.54*
t	-1.100	3.993	0.615	7.498	-1.431	6.874
p	0.275	0.000	0.540	0.000	0.156	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 4: ADVERSE REACTIONS n (%)

Group (n)	Dizziness and headache	Flushed face	Gastrointestinal complications	Foot edema	Overall incidence
Observation (39)	2 (5.13)	1 (2.56)	2 (5.13)	2 (5.13)	7 (17.94)
Control (40)	1 (2.50)	2 (5.00)	3 (7.50)	2 (5.00)	8 (20.00)
χ^2					0.054
p					0.816

Conflict of interests:

The authors declared no conflict of interests.

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This article was originally published in a special issue, "Recent Progression in Pharmacological and Health Sciences" Indian J Pharm Sci 2024:86(2) Spl Issue "269-273"