Am J Transl Res 2023;15(9):5715-5722
www.ajtr.org /ISSN:1943-8141/AJTR0152043

Original Article

Comparative analysis of sacubitril/valsartan and losartan potassium in the treatment of hypertension: efficacy, adverse reactions, and observations

Qunfei Ye[1], Yanjun Sheng[2], Xuan He[1]

[1]*General Practice Clinic, Lushan Street Community Health Service Center, Fuyang District, Hangzhou, Zhejiang, China;* [2]*General Practice Clinic, Fuchun Street Community Health Service Center, Fuyang District, Hangzhou, Zhejiang, China*

Received July 4, 2023; Accepted August 30, 2023; Epub September 15, 2023; Published September 30, 2023

Abstract: Objective: To explore the antihypertensive effect of sacubitril/valsartan and losartan potassium in the treatment of hypertension and the adverse reactions in patients. Methods: A retrospective study was conducted using the medical records of 166 patients with hypertension who were admitted to Hangzhou Fuyang District Lushan sub-district community health service center from June 2022 to June 2023. The control group was treated with losartan potassium, and the observation group was treated with sacubitril/valsartan. Blood pressure, urinary microalbumin, blood urea nitrogen level, liver and kidney function, blood potassium, blood uric acid, cardiac function, inflammatory factors, occurrence of adverse reactions, and treatment efficacy were compared between the two groups. Results: After treatment, the observation group showed significantly lower blood pressure compared to the control group. Furthermore, the observation group exhibited reduced levels of urinary microalbumin and blood urea nitrogen, improved liver and kidney function, decreased inflammatory factor levels, fewer adverse reactions, and a higher treatment efficacy. Conclusion: For patients with hypertension, sacubitril/valsartan has a better treatment efficacy than losartan potassium, because it can effectively reduce blood pressure, the levels of inflammatory factors, and the rate of adverse reactions in patients.

Keywords: Sacubitril/valsartan, losartan potassium, antihypertensive efficacy, adverse reactions

Introduction

Hypertension, characterized by elevated blood pressure in patients' blood vessels, is a prevalent condition associated with an increased risk of stroke, heart failure, and other cardiovascular diseases [1]. It is a common chronic disease that causes significant disability and poses a substantial burden on patient health [2]. The incidence of hypertension has been on a rise primarily due to lifestyle changes, affecting individuals at a younger age thus leading to a growing number of cardiovascular and cerebrovascular diseases [2].

Clinical treatment for hypertension primarily focuses on drug regimens, with sacubitril/valsartan and losartan potassium being commonly prescribed medications [3, 4]. Losartan potassium, an angiotensin II receptor antagonist, is frequently used for long-term hypertension management. However, its usage can be associated with adverse effects such as angioedema and hyperkalemia [5]. On the other hand, sacubitril/valsartan, an angiotensin receptor inhibitor, not only exhibits antihypertensive effects but also has the potential to mitigate left ventricular hypertrophy and improve heart failure resulting from hypertension [6]. Despite their effectiveness in treating hypertension, limited research has compared the efficacy and adverse reactions between patients who received sacubitril/valsartan and losartan potassium.

Therefore, this study evaluated and compared the antihypertensive efficacy and adverse effects of sacubitril/valsartan and losartan

potassium in patients with hypertension. By conducting a comprehensive analysis, we aimed to provide insights into the relative merits and drawbacks of these two medications, thereby contributing to optimized treatment decisions for the patients.

Subjects and methods

Subjects

A retrospective study was conducted using the medical records of 166 patients with hypertension who were admitted to Hangzhou Fuyang District Lushan sub-district community health service center from June 2022 to June 2023. The patients were divided into a control group (treated with losartan potassium) and an observation group (treated with sacubitril/valsartan), with 83 patients in each group. The control group consisted of 45 males and 38 females, with an average age of (54.5±30.4) years and an average duration of disease of (7.0±7.4) years. The observation group included 42 males and 41 females, with an average age of (56.0±31.2) years and an average duration of disease of (8.25±8.4) years. There were no significant differences in the general clinical data between the two groups. All patients included in this study provided informed consent, and the study protocol was reviewed and approved by the Medical Ethics Committee of Community Health Service Center of Lushan Street, Fuyang District, Hangzhou.

Inclusion criteria: (1) Patients diagnosed with hypertension according to the diagnostic criteria in the *Chinese Guidelines for the Prevention and Treatment of Hypertension*. (2) Patients who were newly diagnosed with hypertension or had a previous diagnosis. (3) Patients who did not receive other medications within two weeks.

Exclusion criteria: (1) Patients with severe liver, kidney, or other organ damage. (2) Patients with known allergies to antihypertensive drugs. (3) Patients with incomplete clinical data. (4) Patients with poor treatment compliance.

Methods

The control group was treated with losartan potassium (National drug approval number: H20070264; Manufacturer: Zhejiang Huahai Pharmaceutical Co., LTD.; Specification: 50 mg * 28 tablets), with a dosage of 1 tablet once daily. The observation group received sacubitril/valsartan (National drug approval number: J20190001; Manufacturer: Beijing Novartis Pharmaceutical Co., LTD.; Specification: 50 mg * 28 tablets), with a dosage of 1 tablet twice daily. Both groups took the medication for 8 weeks.

Outcome measures

The primary measure was to compare the systolic blood pressure (SBP) and diastolic blood pressure (DBP) using a PhilpsiE33 type cardiac Doppler echocardiograph, with the S5-1 probe set to a frequency of 1-5 MHz.

The second measures were the levels of urinary microalbumin (mALB) and blood urea nitrogen (BUN). To measure these, Fasting venous blood samples and morning urine samples were collected from patients before and after treatment, and analyzed using enzyme-linked immunosorbent assay (ml095939, Shanghai Enzyme Biotechnology Co., Ltd., China), with strict adherence to the kit operation procedures.

Liver and kidney function, as well as blood potassium and blood uric acid levels, were the third group of measures. The level of alanine aminotransferase (ALT) was measured by the Lyi colorimetric method, while serum creatinine (Scr) levels were determined using the alkaline picric acid endpoint colorimetric method. Flame photometry was employed for measuring blood potassium levels, and Hitachi 7600-110 automatic biochemical analyzer was used for blood uric acid measurements.

Cardiac function before and after treatment was assessed as the fourth measure. Left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF) were measured using a PhilpsiE33 type cardiac Doppler echocardiograph with the S5-1 probe set to a frequency of 1-5 MHz.

The fifth measure involved comparing the levels of inflammatory factors, including hypersensitive C-reactive protein (hs-CRP), monocyte chemoattractant protein-1 (MCP-1), and tumor necrosis factor-α (TNF-α), between the two groups. Fasting venous blood samples were collected before and after treatment, and enzyme-linked immunosorbent assays (ml09-

Table 1. Comparison of general information

Group	Number of cases	Gender		Age (years)	Course of disease (year)	Diabetes (case)
		Man	Woman			
Control group	83	45	38	54.5±30.4	7.0±7.4	8
Observation group	83	42	41	56.0±31.2	8.25±8.4	7
t				1.057	0.926	0.931
P				0.291	0.355	0.305

Table 2. Comparison of blood pressure before and after treatment between the two groups

Groups	Number of cases	SBP (mmHg)		DBP (mmHg)		Mean arterial pressure (mmHg)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	83	150.62±10.67	141.36±9.86	96.38±9.64	89.61±8.69	114.46±10.05	105.06±9.96
Observation Group	83	150.57±10.52	125.39±8.26	96.38±9.85	75.25±7.01	114.44±10.38	91.96±8.01
t value		0.030	11.310	0.000	11.720	0.002	10.38
p-value		0.976	0.001	0.999	0.001	0.999	0.001

Note: SBP, systolic blood pressure; DBP, diastolic blood pressure.

5939, Shanghai Enzyme Biotechnology Co., Ltd., China) were conducted following the provided instructions.

Adverse reactions that were experienced by patients in both groups during the treatment period were recorded as the sixth measure. Specifically, the focus was placed on assessing renal function deterioration, hyperkalemia, and cough.

The last measure is to compare the treatment efficacy between the two groups. After an 8-week treatment period, patients were categorized based on changes in DBP. Those displaying a DBP reeducation exceeding 10 mmHg and reaching below 90 mmHg were categorized as "effective", while those manifesting a DBP decrease exceeding 10 mmHg, but persisting above 90 mmHg were designated as "partially effective". Patients not meeting these criteria were labeled as "ineffective". The overall response rate was calculated by adding the number of "effective" and "partially effective" patients, dividing the sum by the total number of patients, and then multiplying by 100%.

Statistical processing

SPSS 21.0 statistical software was used for statistical processing. Measurement data were expressed as mean ± standard deviation ($\overline{x}$ ± s), and compared using t-test. Counting data were expressed as percentage (%), and compared using χ^2 test. $P < 0.05$ was considered statistically significant.

Results

Comparison of general data between the two groups

Table 1 presents a comparison of general information between the control group and the observation group. The control group consisted of 83 patients, with 8 cases of diabetes. The observation group also comprised 83 patients, with 7 cases of diabetes.

No significant differences were identified between the two groups regarding gender, age, course of disease, and diabetes (P > 0.05), indicating that the general characteristics of the patients were well-matched between the control and observation groups.

Comparison of blood pressure before and after treatment between the two groups

Before treatment, the SBP, DBP, and mean arterial pressure levels exhibited no significant differences between the control group and the observation group ($P > 0.05$). After treatment, the SBP, DBP, mean arterial pressure levels in the observation group were lower than those in the control group, with statistical differences (P < 0.05), as shown in **Table 2**.

Table 3. Comparison of mALB and BUN levels between the two groups

Groups	Number of cases	mALB (mg/L)		BUN (mg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	83	65.33±2.15	56.26±3.86	13.65±5.41	10.21±0.44
Observation Group	83	65.34±2.14	44.05±1.33	13.57±5.54	8.40±0.71
t value		0.030	27.250	0.094	19.740
P value		0.976	00001	0.925	0.001

Note: mALB, urinary microalbumin; BUN, blood urea nitrogen.

Table 4. Comparison of liver and kidney function, blood potassium and blood urea between the two groups

Groups	Number of cases	ALT (U/L)		Scr (umol/L)		Blood potassium (umol/L)		Blood uric acid (umol/L)	
		Before treatment	Post-treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	83	32.78±6.98	34.06±6.18	77.02±31.62	81.02±30.24	3.71±0.96	5.52±0.68	475.15±25.67	406.03±11.24
Observation Group	83	32.77±6.92	42.39±7.35	76.81±31.66	98.66±46.68	3.68±0.97	4.60±0.55	475.62±25.06	319.66±13.68
t value		0.009	7.903	0.042	2.889	0.200	20.000	0.119	44.440
P value		0.992	0.001	0.966	0.004	0.842	0.001	0.905	0.001

Note: ALT, alanine aminotransferase; Scr, serum creatinine.

Table 5. Comparison of cardiac function before and after treatment between the two groups

Group	Number of cases	LVEDD (mm)		LVEF (%)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	83	60.17±8.46	49.26±6.71	30.66±7.26	35.26±8.69
Observation Group	83	60.27±8.21	40.02±5.23	31.05±7.95	46.21±7.81
t value		0.077	0.934	0.330	10.880
P value		0.938	0.001	0.742	0.001

Note: LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction.

Comparison of mALB and BUN levels between the two groups

Before treatment, the mALB and BUN levels exhibited no significant differences between the control group and the observation group ($P > 0.05$). After treatment, the mALB and BUN levels in the observation group were lower than those in the control group, with statistical differences ($P < 0.05$). See **Table 3**.

Comparison of liver and kidney function, blood potassium and blood uric acid between the two groups

Before treatment, no significant differences were found in the ALT, Scr, blood potassium, and blood uric acid levels between the control group and observation group ($P > 0.05$). After treatment, the ALT and Scr levels in the observation group were higher than those in the control group, while the serum potassium and serum uric acid levels were lower than those in control group, with statistical differences ($P < 0.05$). See **Table 4**.

Comparison of cardiac function before and after treatment between the two groups

Before treatment, the LVEDD and LVEF exhibited no significant differences between the control group and observation group ($P > 0.05$). After treatment, the LVEDD was lower, and the LVEF was higher in the observation group than those in the control group, with statistical differences ($P < 0.05$). See **Table 5**.

Comparison of inflammatory factor levels between the two groups

Before treatment, there were no significant differences in the hs-CRP, MCP-1 and TNF-α levels

Table 6. Comparison of levels of inflammatory factors between the two groups

Groups	Number of cases	hs-CRP (mg/L)		MCP-1 (μg/L)		TNF-α (ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	83	12.60±2.61	8.51±2.23	26.41±4.12	17.56±2.31	218.21±27.01	127.25±19.68
Observation Group	83	12.61±2.70	4.63±1.31	26.40±3.71	11.61±2.11	218.36±27.34	82.31±10.25
t value		0.024	13.670	0.0164	17.330	0.0356	18.450
P value		0.981	0.001	0.987	0.001	0.972	0.001

Note: hs-CRP, hypersensitive C-reactive protein; MCP-1, monocyte chemoattractant protein-1; TNF-α, tumor necrosis factor-α.

Table 7. Comparison of adverse reactions between the two groups [n, %]

Groups	Number of cases	Worsening kidney function	Hyperkalemia	Cough	Total incidence (%)
Control group	83	4 (4.82)	6 (7.23)	5 (6.02)	15 (18.07)
Observation Group	83	1 (1.20)	0 (0.00)	2 (2.41)	3 (3.61)
X^2 value					8.973
P value					0.006

Table 8. Comparison of treatment effects between the two groups [n, %]

Groups	Number of cases	Conspicuous effect	Effective	Ineffective	Overall response rate (%)
Control group	83	40 (48.20)	28 (33.73)	15 (18.07)	68 (81.93)
Observation Group	83	61 (73.50)	19 (22.90)	3 (3.60)	80 (96.40)
X^2 value					8.973
P value					0.006

between the control group and the observation group ($P > 0.05$). After treatment, the levels of hs-CRP, MCP-1 and TNF-α in the observation group were lower than those in the control group, with statistical difference ($P < 0.05$). See **Table 6**.

Comparison of adverse reactions between the two groups

The adverse reaction rate of the observation group was lower than that of the control group, with statistical difference ($P < 0.05$). See **Table 7**.

Comparison of treatment efficacy between the two groups

The overall response rate of the observation group was higher than that of the control group, with statistical difference ($P < 0.05$). See **Table 8**.

Discussion

Hypertension is a common clinical disease. It has the characteristics of high incidence, long course of disease, easy relapse, etc., which seriously affects patient health. In the early stage of hypertension, most patients have no obvious symptoms, but may be found to have increased blood pressure in physical examinations [7]. The early rise in the blood pressure is accompanied by varying degrees of organ function impairment [8]. Patients' blood pressure levels are in a long-term unstable state, and potentially lead to changes in the diastolic cardiac capacity. This can impede blood circulation, increase cardiac workload, and eventually culminate in cardiomyocyte hypertrophy and ventricular remodeling [9].

Losartan potassium is an angiotensin II receptor antagonist, which can promote vasodilation and reduce blood pressure in patients [10]. By inhibiting the production of angiotensin-converting enzyme, losartan potassium plays a role in lowering blood pressure, improving myocardial metabolism, thus promoting the recovery of cardiac function. Moreover, losartan potassium can improve cardiac displacement and exert its therapeutic effect by reducing perivascular resistance and cardiac workload

in patients [11]. Sacubitril/valsartan has a unique dual antihypertensive mechanism, which not only plays a strong antihypertensive effect, but also protects the target organs [12]. Studies have revealed that sacubitril/valsartan can significantly improve the cardiac geometric structure and diastolic dysfunction. It accomplishes this by diminishing peripheral vascular resistance, reducing cardiac load, maintaining normal cardiac displacement, and consequently fostering the restoration of myocardial metabolism and cardiac function. As a result, it holds promise for the enhancement of cardiac function [13]. The results of this study showed that the SBP and DBP levels of patients treated with sacubitril/valsartan were lower than those treated with losartan potassium, indicating that the antihypertensive effect of sacubitril/valsartan was more significant than that of losartan potassium.

mALB is a commonly used indicator to reflect early kidney disease and kidney damage, and its pathological increase is commonly associated with diabetic nephropathy and hypertension. BUN is the main product formed in the body from protein metabolic activities, and the rise of this marker may indicate impairment in kidney function [9, 14]. Hypertension has a certain relationship with the liver and kidney. While hypertension doesn't directly impact the liver, medications required for its management are metabolized by the liver, potentially leading to hepatotoxic effects. There is a direct relationship between hypertension and the kidneys. Kidney diseases, such as nephrotic syndrome and glomerulonephritis, can lead to insufficient renal blood supply, resulting in the occurrence of hypertension, and inadequate blood pressure control can detrimentally affect kidney function [15]. ALT is mainly present in liver cells, if there is 1% necrosis of liver cells, it can increase the enzyme activity in the blood, so ALT is a sensitive sign of acute liver cell damage. Blood creatinine serves as a crucial marker for assessing kidney function. It stems from the normal dietary protein intake or endogenous creatine metabolism. Following hepatic breakdown, blood creatinine produced, representing a metabolic product that needs to be excreted by the kidney [16]. Blood potassium refers to the concentration of potassium ions in the blood of the human body. The level of blood potassium does not directly affect the blood pressure, but changes of potassium and sodium ions can increase or reduce the heart rate, there by affecting the blood pressure. High blood pressure can induce adverse effects on both large blood vessels and microvasculature. Notably, damage to the kidneys is particularly pronounced in the small arteries, which can lead to reduced urate excretion and increased blood uric acid level. The results of this study showed that the patients treated with sacubitril/valsartan exhibited significantly lower mALB and BUN levels, higher ALT and Scr levels, and lower serum potassium and uric acid levels than those treated with losartan potassium. These results indicate that sacubitril/valsartan is more effective than losartan potassium in reducing mALB, BUN, blood potassium and blood uric acid levels and increasing ALT and Scr levels.

LVEDD refers to the inner diameter of the left ventricle at the end of the diastolic period, which is an important indicator in cardiac color Doppler ultrasound. The magnitude of this parameter serves as an indicator for determining left ventricle health. A normal LVEDD ranges 45-55 mm for men, and 35-50 mm for women. An LVEDD measurement exceeding 55 mm indicates diastolic period heart enlargement. This observation is commonly associated with conditions such as hypertensive heart disease, rheumatic heart disease, and dilated heart disease. LVEDD and left ventricular systolic diameter as well as ejection fraction are important values in the diagnosis of systolic heart failure [17]. LVEF is the percentage of blood ejected per contraction of the left ventricle into the aorta, contributing to the left ventricle filling [18]. Under normal circumstances, the left ventricle fills about 150 ml of blood after diastole, and more than 80 ml of blood can be shot into the aorta during contraction. At this time, the ejection fraction is more than 50%, and the LVEF is usually between 55% and 65%. If the LVEF is less than 50%, it is called cardiac insufficiency [19]. The results of this study showed that the LVEDD and LVEF of the patients treated with sacubitril/valsartan were lower than those treated with losartan potassium, indicating that sacubitril/valsartan had more prominent improvements in cardiac function and ventricular remodeling.

CRP can sensitively reflect the inflammation response in the body, and has both anti-inflammatory and pro-inflammatory effects. hs-CRP,

as a hypersensitive C-reactive protein, belongs to the same protein as ordinary CRP, but the detection method of hs-CRP is more sensitive [20]. MCP-1 is an inflammatory factor, which plays a chemotactic and activation effect on mononuclear macrophages, further aggravating the degree of tissue damage [21]. TNF-α is produced by activated macrophages and often participates in the body's inflammatory response together with other inflammatory factors [17]. Scholars have pointed out in their studies that during the treatment of hypertension, the expressions of inflammatory factors hs-CRP, MCP-1 and TNF-α can show a trend of changes from strong to weak, which indicate that the pathogenesis and progression of hypertension are closely related to the body's inflammatory response [22]. The results of this study showed that patients treated with sacubitril/valsartan demonstrated significantly lower levels of inflammatory factors, as well as lower occurrence of adverse reactions than those treated with losartan potassium. It is indicated that sacubitril/valsartan is effective in improving the levels of inflammatory factors and has an obvious effect on reducing the occurrence of adverse reactions. In this study, it was also found that the efficacy of sacubitril/valsartan in the treatment of hypertension was significantly better than that of losartan potassium.

We acknowledge several limitations in this study. These include a small sample size, a relatively short study duration, the potential for bias and confounding, and the fact that it was conducted at a single center. These limitations may affect the generalizability and robustness of our findings.

In summary, compared with losartan potassium, sacubitril/valsartan has a better efficacy in the treatment of hypertension because it can better reduce the blood pressure of patients, improve the cardiac function, reduce the level of inflammatory factors, and decrease the occurrence of adverse reactions.

Disclosure of conflict of interest

None.

Address correspondence to: Qunfei Ye, General Practice Clinic, Lushan Street Community Health Service Center, Fuyang District, Hangzhou, Zhejiang, China. E-mail: 13706819448@163.com

References

[1] Malik AH and Aronow WS. Efficacy of sacubitril/valsartan in hypertension. Am J Ther 2022; 29: e322-e333.

[2] Jackson AM, Jhund PS, Anand IS, Düngen HD, Lam CSP, Lefkowitz MP, Linssen G, Lund LH, Maggioni AP, Pfeffer MA, Rouleau JL, Saraiva JFK, Senni M, Vardeny O, Wijkman MO, Yilmaz MB, Saito Y, Zile MR, Solomon SD and McMurray JJV. Sacubitril-valsartan as a treatment for apparent resistant hypertension in patients with heart failure and preserved ejection fraction. Eur Heart J 2021; 42: 3741-3752.

[3] Pascual-Figal D, Bayés-Genis A, Beltrán-Troncoso P, Caravaca-Pérez P, Conde-Martel A, Crespo-Leiro MG, Delgado JF, Díez J, Formiga F and Manito N. Sacubitril-valsartan, clinical benefits and related mechanisms of action in heart failure with reduced ejection fraction. A review. Front Cardiovasc Med 2021; 8: 754499.

[4] Rakugi H, Kario K, Yamaguchi M, Sasajima T, Gotou H and Zhang J. Efficacy of sacubitril/valsartan versus olmesartan in Japanese patients with essential hypertension: a randomized, double-blind, multicenter study. Hypertens Res 2022; 45: 824-833.

[5] Wang SJ and Sander GE. Nebivolol/valsartan combination for the treatment of hypertension: a review. Future Cardiol 2021; 17: 573-583.

[6] Al Ghorani H, Kulenthiran S, Lauder L, Böhm M and Mahfoud F. Hypertension trials update. J Hum Hypertens 2021; 35: 398-409.

[7] Wang B, Wang GH, Ding XX, Tang HX, Zheng J, Liu BC and Zhang XL. Effects of sacubitril/valsartan on resistant hypertension and myocardial work in hemodialysis patients. J Clin Hypertens (Greenwich) 2022; 24: 300-308.

[8] Kjeldsen SE, von Lueder TG, Smiseth OA, Wachtell K, Mistry N, Westheim AS, Hopper I, Julius S, Pitt B, Reid CM, Devereux RB and Zannad F. Medical therapies for heart failure with preserved ejection fraction. Hypertension 2020; 75: 23-32.

[9] Prud'homme GJ, Kurt M and Wang Q. Pathobiology of the klotho antiaging protein and therapeutic considerations. Front Aging 2022; 3: 931331.

[10] Chaumais MC, Djessas MRA, Thuillet R, Cumont A, Tu L, Hebert G, Gaignard P, Huertas A, Savale L, Humbert M and Guignabert C. Additive protective effects of sacubitril/valsartan and bosentan on vascular remodelling in experimental pulmonary hypertension. Cardiovasc Res 2021; 117: 1391-1401.

[11] Przezak A, Bielka W and Pawlik A. Hypertension and type 2 diabetes-the novel treatment possibilities. Int J Mol Sci 2022; 23: 6500.

[12] Triposkiadis F, Xanthopoulos A, Bargiota A, Kitai T, Katsiki N, Farmakis D, Skoularigis J, Starling RC and Iliodromitis E. Diabetes mellitus and heart failure. J Clin Med 2021; 10: 3682.
[13] Lee JW, Choi E, Son JW, Youn YJ, Ahn SG, Ahn MS, Kim JY, Lee SH, Yoon J, Ryu DR, Park SM, Hong KS and Yoo BS. Comparison of blood pressure variability between losartan and amlodipine in essential hypertension (COMPAS-BPV). Am J Hypertens 2020; 33: 748-755.
[14] Mathew AV, Okada S and Sharma K. Obesity related kidney disease. Curr Diabetes Rev 2011; 7: 41-49.
[15] Wu HX, Liu KK, Li BN, Liu S and Jin JC. Efficacy and safety of sacubitril/valsartan in the treatment of middle-aged and elderly patients with hypertension: a systematic review and meta-analysis of randomized controlled trials. Ann Palliat Med 2022; 11: 1811-1825.
[16] Nouri-Vaskeh M, Kalami N, Zand R, Soroureddin Z, Varshochi M, Ansarin K, Rezaee H, Taghizadieh A, Sadeghi A, Ahangari Maleki M, Esmailnajad A, Saleh P, Haghdoost M, Maleki M and Sharifi A. Comparison of losartan and amlodipine effects on the outcomes of patient with COVID-19 and primary hypertension: a randomised clinical trial. Int J Clin Pract 2021; 75: e14124.
[17] Ohishi M. Sacubitril/valsartan-a new weapon for fighting the hypertension paradox. Hypertens Res 2022; 45: 915-916.
[18] Höcht C, Allo MA, Polizio AH, Morettón MA, Carranza A, Chiappetta DA and Choi MR. New and developing pharmacotherapies for hypertension. Expert Rev Cardiovasc Ther 2022; 20: 647-666.
[19] Gan L, Lyu X, Yang X, Zhao Z, Tang Y, Chen Y, Yao Y, Hong F, Xu Z, Chen J, Gu L, Mao H, Liu Y, Sun J, Zhou Z, Du X, Jiang H, Li Y, Sun N, Liang X and Zuo L. Application of angiotensin receptor-neprilysin inhibitor in chronic kidney disease patients: Chinese expert consensus. Front Med (Lausanne) 2022; 9: 877237.
[20] Kuchulakanti PK. ARNI in cardiovascular disease: current evidence and future perspectives. Future Cardiol 2020; 16: 505-515.
[21] Nalivaeva NN, Zhuravin IA and Turner AJ. Neprilysin expression and functions in development, ageing and disease. Mech Ageing Dev 2020; 192: 111363.
[22] Lou Y, Yu Y, Liu J and Huang J. Sacubitril-valsartan for the treatment of hypertension in China: a cost-utility analysis based on meta-analysis of randomized controlled trials. Front Public Health 2022; 10: 959139.