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Original Article

Comparison of therapeutic effects between urapidil and nitroglycerin for treatment of acute heart failure with hypertension and atrial fibrillation in elderly patients: a randomized multi-center parallel-control study in China

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Abstract: *Background and objective:* Acute heart failure (AHF) is a complex clinical syndrome and frequently complicated by hypertension and atrial fibrillation (AF). The aim of this study was to evaluate whether urapidil provides additional therapeutic benefits compared to nitroglycerin (NG) in the treatment of AHF with hypertension and AF in elderly patients. *Methods:* 58 elderly patients from 10 hospitals were randomized into 2 groups. Control group (n=30) were treated with NG, while other group (n=28) were treated with urapidil. We monitored systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and carry out echocardiogram before and 24 h, 48 h, 72 h and 7 d after treatment with either NG or urapidil. Lipid profile, liver and kidney function, blood glucose levels in nitroglycerin and urapidil groups were examined before and 24 h, 48 h, and 7 d after treatment. *Results:* Patients receiving urapidil had lower SBP than that in NG group ($P<0.05$). Compared with NG group, patients in urapidil group showed increased LVEF ($P<0.05$), CO, SV and CI ($P<0.05$), but no significant differences in LVEDD and EDV. NT-proBNP was decreased following the treatment of urapidil or nitroglycerin, and the difference of NT-proBNP level was significant between the two groups ($P<0.01$) at 7 d. Urapidil had trend to decrease blood glucose after 7 d. *Conclusions:* Urapidil demonstrated better efficacy and fewer side effects than nitroglycerin on lowering and stabilizing systolic BP, attenuating cardiac afterload and improving cardiac function.

Keywords: Urapidil, hypertension, atrial fibrillation, heart failure

Introduction

Acute heart failure (AHF) is characterized by failing compensatory mechanisms utilized by the body in an attempt to restore the primary deficit in cardiac output. It is also a complex clinical event associated with excess morbidity and mortality [1, 2]. More than 1 in 10 patients died, and approximately twenty percent were readmitted to the hospital within 1 month for AHF [3]. It is well established that hypertension and arrhythmias are the main etiologies of acute heart failure syndrome (AHFS) [4].

Atrial fibrillation (AF) is the most common cardiac arrhythmia with acute or chronic heart failure (HF) with a prevalence of 30% to 45% [5, 6]. In the setting of acute heart failure (AHF), AF is associated with significant morbidity and an increased mortality rate [7, 8]. AF is also associated with worsening in-hospital outcomes among patients hospitalized for AHF and reduced qualityof life [1]. In addition, hypertension is associated with left ventricular remodeling and is a risk factor for incident HF [9].

Guidelines suggest considering a vasodilator for symptoms of congestion, particularly in the setting of acute pulmonary edema or severe hypertension. Nitroglycerin (NG) have long been considered first-line agents for acute HF with

hypertension [10]. It relieves pulmonary congestion primarily through direct venodilation, but may dilate coronary arteries and increase collateral blood flow at higher doses, an effect desirable in patients with ischemia [11, 12]. However, there are some potential shortcomings of use of NG. Adverse effects of nitroglycerin during the first 24 h after the start of therapy have been described in the VMAC study [2]. The most frequently reported side effects are headache, nausea, and hypotension. The hemodynamic and clinical effects of NG wane upon continuous (> several hours) therapy. Elkayam et al. already reported in the year 1987 that tolerance to intravenous infusion of NG in patients with coronary heart disease or heart failure may develop within 24 h [13]. Therefore, it is necessary to explore other new therapeutic strategies for elderly HF patients and optimize the current treatment protocol.

Urapidil an a1-adrenoceptor antagonist and 5-HT1A receptor agonist is a sympatholytic antihypertensive drug [14]. Because of its modulation of the central nervous system, a1-mediated vasodilation does not result in reflex tachycardia [15]. Urapidil is routinely used for acute and chronic treatment of arterial hypertension and acute HF [16]. Several clinical trials have shown that urapidil can effectively reduce heart rate (HR) and improve cardiac function in HF patients [17, 18].

In essential hypertension, urapidil lowers arterial pressure acutely by a fall in total peripheral resistance with a small compensatory increase in cardiac output. In addition, the acute administration of urapidil increases cardiac index and lowers mean pulmonary artery wedge pressure and systemic vascular resistance by about 30% in patient with heart failure without any sign of toxic or metabolic reactions [19-21].

However, there is general lack of evidence-based data for the application of urapidil in HF patients, especially for the elderly patients with other diseases. The aim of this study was to investigate the effect of urapidil on elderly patients with AHF and compare efficacies of urapidil and NG on treating AHF patients with hypertension and AF in China.

Methods

This was a multi-center, randomized, controlled and open-label study. The study was performed according to the provisions of the Declaration of Helsinki and good clinical practice. All the participants gave written informed consent for our investigation. The study was approved by the Clinical and Animal Research Ethics Committees of Capital Medical University, China.

Patient selection

From August 2011 to November 2013, the study enrolled 58 elderly consecutive patients who had been diagnosed as AHF concurrent with hypertension and AF and were admitted to the following 10 hospitals throughout China: Cardiology and Emergency Department of Xuan Wu Hospital, Beijing Anzhen Hospital, Beijing Tongren Hospital, First Hospital Affiliated with Chongqing University, Ningbo First Hospital, Luhe Hospital of Beijing Tongzhou District, Mentougou Hospital of Beijing, Affiliated Hospital of Tongji University and Heilongjiang People Hospital. Among the enrolled patients, 46 were classified as the New York Heart Association (NYHA) III and 12 were NYHA IV.

As shown in the **Table 1**, there were no significant differences between 2 groups on the gender, age or duration of AF and hypertension in patients on admission.

Inclusion criteria

All patients enrolled met the following criteria: (1) Age >60 years. (2) Satisfied the standard diagnostic criteria for hypertension [22] and diagnosed with AF before or on admission, excluding rheumatic valvular heart disease, valvular heart disease, heart valve replacement surgery, dilated cardiomyopathy. (3) Satisfied the standard diagnostic criteria for AHF (NYHA III and IV).

Exclusion criteria

The exclusion criteria for the candidates were as follows: (1) systolic blood pressure (SBP) ≤ 100 mmHg; (2) evidence of cardiogenic shock or other cardiovascular disorder contradicting intravenous administration of a vasodilator; (3) severe valve stenosis; obstructive hypertrophic

Table 1. Demographic and characteristics of patients

	Urapidil (n=30)	Nitroglycerin (n=28)	t/χ^2	*P* value
Demographic				
Age (year)	76.10±6.73	75.67±6.42	0.20	0.84
Male gender n (%)	17 (56.67%)	16 (57.14%)	0.28	0.60
Smoking	14 (46.67%)	11 (39.29%)	0.27	0.60
Current drink	9 (30.00%)	8 (28.57%)	0.08	0.77
Medical history n (%)				
Diabetes mellitus	11 (36.67%)	12 (42.86%)	0.36	0.52
Stable CHD	22 (73.33%)	22 (78.57%)	0.29	0.59
Stroke/transient ischemic attack	11 (36.67%)	10 (35.71%)	0.07	0.79
Vascular disease	3 (10.00%)	3 (10.71%)	0.12	0.83
Dyslipidemia	8 (26.67%)	9 (32.14%)	0.32	0.57
Chronic respiratory disease	5 (16.67%)	7 (25.00%)	0.86	0.35
Clinical details (mean)				
Scr (μmol/L)	66.23±15.17	67.32±14.88	0.91	0.28
hs-CRP (mg/L)	1.45±4.16	1.41±4.38	0.06	0.85
RDW (%)	14.27±1.43	14.38±1.15	0.07	0.78
LVEF (%)	47.86±6.27	46.86±5.87	0.13	0.68
CI (L/(min·m^2)	2.14±0.95	2.13±0.98	0.08	0.76
LVEDD (mm)	55.70±7.31	54.43±6.59	0.23	0.82
EDV (ml)	189.32±23.14	187.82±23.54	0.21	0.84
E/A ratio	0.76±0.26	0.75±0.32	0.19	0.81
CO (L/m)	3.3±1.1	3.2±1.2	0.98	0.26
SV (ml)	37.6±4.5	38.5±4.1	0.88	0.32
NYHA class n (%)				
III	25 (83.33%)	21 (75.00%)	0.64	0.43
IV	5 (16.67%)	7 (25.00%)	0.35	0.53
Antihypertensivedrugs n (%)				
ACEIs/ARBs	18 (60.00%)	19 (67.85%)	0.22	0.64
Beta blockers	10 (33.33%)	9 (32.14%)	0.36	0.55
CCBs	13 (43.33%)	12 (42.86%)	0.35	0.54
Diuretics	20 (66.67%)	19 (71.42%)	0.42	0.63
Oral anticoagulant drugs n (%)				
None	5 (16.67%)	4 (14.28%)	0.18	0.84
Aspirin	11 (36.67%)	12 (42.86%)	0.14	0.82
Clopidogrel	4 (13.33%)	4 (14.28%)	0.06	0.83
Warfarin	7 (23.33%)	6 (21.43%)	0.08	0.76
Newer oral anticoagulants	3 (10.00%)	2 (7.14%)	0.16	0.82
CHADS2 scores	3.72±1.62	3.68±1.56	0.35	0.52
CHA2DS2-VASc scores	5.35±1.79	5.43±1.82	0.26	0.61

Data are presented as mean ± standard deviation or observed number (%) within the group of Urapidil or Nitroglycerin. CHD, coronary heart disease; CVD, cardiovascular disease; CKD, Chronic kidney disease; Scr serum creatinine, hs-CRP highsensitivity C-reactive protein; RDW, red cell distribution width; LVEF, left ventricular ejection fraction; CI, cardiac index; EDV, End diastolic volume; E/A, early diastolic filling to atrial filling velocity ratio of mitral flow; NYHA, New York Heart Association; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers.

cardiomyopathy; restrictive cardiomyopathy or constrictive pericarditis; (4) severe chronic obstructive pulmonary disease; acute phase of some other pulmonary disease; (5) severe liver or kidney insufficiency; (6) history of allergy to nitroglycerin or urapidil; (7) psychiatric or malig-

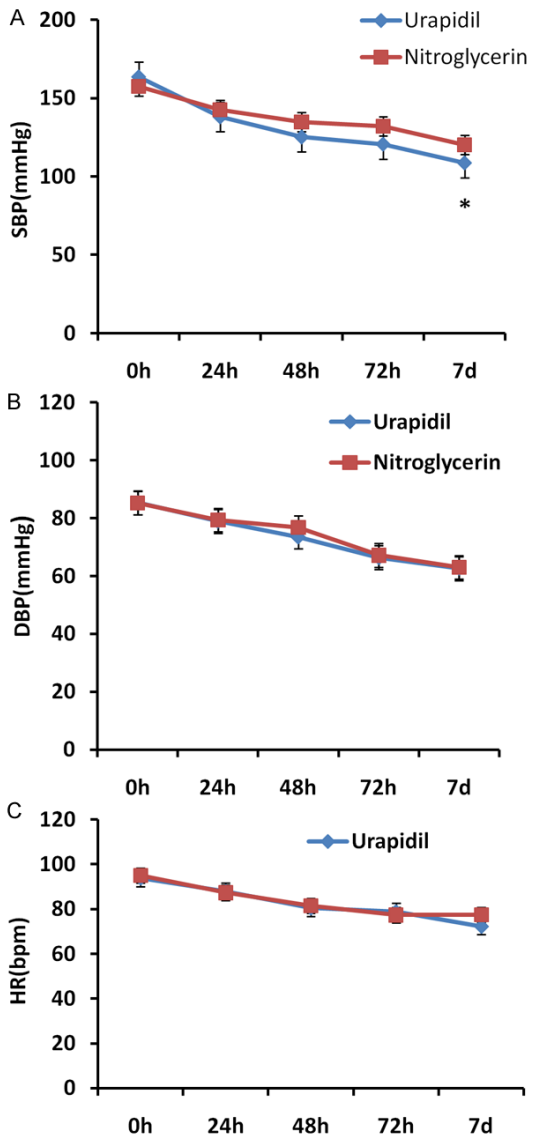

Figure 1. Effects of urapidil and NG on (A) SBP, (B) DBP and (C) HR within 7 days of treatment in elderly patients with hypertension and acute decompensated heart failure. Data are presented as mean±standard deviation within the group of Urapidil or Nitroglycerin.Compared with Nitroglycerin group, *P<0.05. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

nant disease or currently taking other medications or being enrolled in another clinical trial within 60 days.

Each patient provided a signed informed consent prior to enrollment in the study.

Drug delivery

Patients were classified into two groups at random. Doses of urapidil (BykGulden, Leverkusen, Germany) and NG (Beijing Yimin, Beijing, China) were administered to patients on the basis of standard regimes for AHF patients. Urapidil 100 mg and NG 10 mg were diluted in 50 mL of 0.9% normal saline and intravenously delivered to patients within periods of 48 to 140 hours. Patient's blood pressure (BP) was constantly monitored during administration to provide constant information that might warrant adjustment of the dose rate and delivery time. Urapidil was administered at a rate of 50 or 100 mg/min for an initial 6 hours and then adjusted to 300 mg/min for the remaining administration time. Accordingly, nitroglycerin was administered at a rate of 10 mg/min for the initial 6 hours and then adjusted to a maximum rate of 20 mg/min for the remaining administration time.

Parameters for clinical assessment

We monitored systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate HR, NT-proBNP levels and echocardiogram before and 24 h, 48 h, 72 h and 7 d after the treatment with either nitroglycerin or urapidil. Biochemical criterion was examined before and 24 h, 48 h, and 7 d after treatment.

Echocardiogram results includes: Left ventricular end diastolic diameter (LVEDD), end diastolic volume (EDV), left ventricular ejection fraction (LVEF), Cardiac index (CI), E/A ratio, Cardiac output (CO), Stroke volume (SV).

For all echocardiography studies, double-blind study was used for the performers and patients during the operation and data collection.

Follow-up

Each enrolled patient will remain in the study throughout the entire study duration, with a minimum follow-up of 1 month after hospital discharge for each patient. The incidence of major adverse cardiac event (MACE) included all-cause death, nonfatal myocardial infarction, malignant arrhythmia, and re-hospitalization due to worsening of heart failure.

Statistical analysis

All data were analyzed using SPSS 16.0 (SPSS Inc, Chicago, IL). The results are given as mean ± standard deviation or percentages, as appropriate. Chi-squared test was used to compare

categorical variables; Analysis of variance and the independent samples t-test were used to analyze repeated-measures data. *P*-values <0.05 and <0.01 were considered as statistically significant and highly significant, respectively.

Results

SBP, DBP, and HR of patients before/after treatment with urapidil or nitroglycerin

We analyzed the effects of urapidil or nitroglycerin on the SBP, DBP, HR of patients at 0 hours, 24 hours, 48 hours, 72 hours and 7 days after treatment (**Figure 1**). NG and urapidil reduced SBP, DBP, and HR time-dependently in the patients. However, urapidil decreased SBP to 108.53 mmHg after 7 days treatment significantly. Urapidil was more effective in lowering BP versus NG.

Cardiac function (echocardiography) and NT-proBNP in patients before/after treatment with urapidil or nitroglycerin

NT-proBNP level might be used as reliable and sensitive markers in the detection of early cardiac impairment especially in heart Failure [23, 24].

In the present study, we monitored cardiac function of patients through detecting NT-proBNP level and echocardiography detection. Study showed that patients in urapidil group showed significantly higher values of LVEF, CO, SV and CI compared to their counterparts in NG group after 7 days treatment. Meanwhile, urapidil significantly decreased left ventricular end-diastolic volume on day 7. The mean E/A ratio showed no difference between the urapidil group and NG group at any time point after treatment.

Both NG and urapidil could reduce NT-proBNP level time-dependently in the patients. However, NT-proBNP level was decreased significantly in urapidil group, compared with NG group (**Table 2**).

Lipid profile, liver and kidney function, blood glucose levels in nitroglycerin and urapidil groups

Biochemical criterion was examined before and 24 h, 48 h, and 7 d after treatment (**Table 3**). Both nitroglycerin and urapidil treatment for 7 days did not affect TCH, TG, LDL cholesterol and HDL cholesterol levels. Both urapidil and NG decreased blood glucose levels in all patients, but there was no significant difference of the decrease between the two groups. Patients in both groups had no effect on ALT, AST, UA and Scr. Liver and kidney function tests showed no differences between the two groups.

Adverse events and clinical outcome

Each enrolled patient remained in the study throughout the entire study duration. During in-hospital treatment, patients of urapidil group without obvious headache, dizziness, nausea, vomiting, sweating, irritability, fatigue, palpitations, or breathing difficulties and other symptoms. The NG group attack signs include headache in 5 cases, hot flashes in 2 cases, and 2 cases of hypotension. Patients in the two groups had no serious adverse events.

The enrolled patients were followed up for 1 month after hospital discharge to evaluate their clinical outcomes (**Table 4**). There were no reported deaths within 1 month after hospital discharge. In the NG group, 1 of 28 patients experienced malignant arrhythmia, although none was found in urapidil group at 1 month after hospital discharge. The rate of re-hospitalization due to HF in NG group is higher than that in urapidil group, but there was no significant difference between the two groups.

The incidence of major adverse cardiac events (MACE) in urapidil group was lower than that in NG group.

Discussion

Prevalent cardiovascular comorbidities in the elderly are arterial hypertension and atrial fibrillation, which contribute to the pathogenesis of acute heart failure (AHF). The goals of therapy for AHF should be not only to improve symptoms, but also to preserve or improve myocardial damage.

In the study, we compared the efficacies between urapidil and NG in the treatment of AHF patients with hypertension and atrial fibrillation. Urapidil demonstrated better efficacy than NG on improving cardiac function and re-hospitalization after 30 days follow-up. While, urapi-

Table 2. Cardiac function (echocardiography and NT-proBNP) in nitroglycerin and urapidil groups

Parameters	Urapidil (n=30)				Nitroglycerin (n=28)			
	0 hr	24 hr	48 hr	7 d	0 hr	24 hr	48 hr	7 d
LVEDD (mm)	55.70±7.31	53.71±7.30	52.17±7.27	48.36±6.83	54.43±6.59	54.34±6.71	52.95±5.90	52.13±5.80
EDV (ml)	189.32±23.14	182.12±23.12	174.23±23.02	151.67±21.56	187.82±23.54	185.32±23.22	180.23±23.12	164.67±21.86
LVEF (%)	47.86±6.27	49.10±5.32	55.78±4.23	62.73±1.45*	46.86±5.87	49.38±5.02	51.58±4.12	53.73±1.55
CI [L/(min·m^2)]	2.24±0.65	2.26±0.78	2.49±0.58	3.68±0.38*	2.23±0.58	2.27±0.65	2.38±0.42	3.02±0.25
E/A ratio	0.76±0.26	0.75±0.23	0.81±0.16	0.91±0.12	0.75±0.22	0.75±0.25	0.79±0.13	0.89±0.11
CO (L/m)	3.29±0.45	3.31±0.56	3.62±0.52	4.88±0.63*	3.26±0.52	3.29±0.54	3.56±0.52	4.13±0.62
SV (ml)	47.61±4.52	48.27±4.64	52.31±5.23	68.45±6.22*	48.55±4.51	48.18±4.40	50.82±5.38	61.62±6.24
NT-proBNP (ng/L)	9396.03±484.31	7205.00±235.22	5837.90±212.32	2424.00±239.24**	9140.13±311.21	8742.60±259.40	6907.77±229.51	4514.33±269.91

Data are presented as mean ± standard deviation within the group of Urapidil or Nitroglycerin. Compared with Nitroglycerin group, *P<0.05, **P<0.01. LVEDD, left ventricular end diastolic diameter; EDV, end diastolic volume; EF, ejection fraction; CI, cardiac index; E/A ratio, early diastolic filling to atrial filling velocity ratio of mitral flow; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Table 3. Lipid profile, liver and kidney function, blood glucose levels in nitroglycerin and urapidil groups

Parameters	Urapidil (n=30)				Nitroglycerin (n=28)			
	0 hr	24 hr	48 hr	7 d	0 hr	24 hr	48 hr	7 d
ALT (IU/L)	28.83±1.35	24.32±1.37	24.82±1.46	23.96±1.32	26.37±2.72	24.37±1.72	25.37±1.85	25.77±1.23
AST (IU/L)	22.27±1.64	25.28±1.67	22.67±2.01	26.06±1.63	21.23±1.15	23.15±1.03	25.18±1.46	26.66±1.48
UA (μmol/L)	401.47±131.51	400.61±129.50	373.47±116.22	332.67±89.53	415.53±109.16	393.98±105.15	375.88±103.06	326.03±91.55
GLU (mmol/L)	6.74±2.82	6.62±2.02	6.43±1.67	5.88±1.05	6.95±2.75	6.67±1.87	6.60±1.54	6.22±1.16
Scr (μmol/L)	101.33±5.01	102.23±5.76	108.19±4.75	107.58±4.85	106.10±4.51	105.76±5.69	103.53±4.40	106.61±5.50
TCH (mmol/L)	4.15±1.07	3.84±0.88	3.65±0.84	3.18±0.54	4.16±0.95	3.87±0.88	3.80±0.85	3.40±0.57
TG (mmol/L)	1.54±0.49	1.53±0.58	1.47±0.38	1.42±0.27	1.51±0.46	1.49±0.45	1.52±0.40	1.44±0.31
HDL-C (mmol/L)	1.38±0.39	1.31±0.35	1.30±0.37	1.13±0.24	1.33±0.36	1.26±0.35	1.31±0.36	1.12±0.28
LDL-C (mmol/L)	2.45±1.07	2.48±1.08	2.35±0.73	2.27±0.84	2.35±0.75	2.36±0.73	2.32±0.63	2.21±0.71

Data are presented as mean ± standard deviation within the group of Urapidil or Nitroglycerin. ALT, Alanine aminotransferase; AST, Aspartate transaminase; UA, Uric acid; GLU, Glucose; CRE, Serum creatinine; TCH, Total cholesterol; TG, Triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 4. 30-day MACE events between the two groups

	Urapidi (n=30)	Nitroglycerin (n=28)	*P* values
30 days-MACE	3.33% (1)	10.71% (3)	0.26
All-cause death	0 (0)	0 (0)	
Nonfatal MI	0 (0)	0 (0)	
Malignant arrhythmia	0 (0)	3.57% (1)	0.28
Re-hospitalization due to heart failure, n (%)	3.33% (1)	7.14% (2)	0.94

Data are presented as observed number (%) within the group of Urapidil or Nitroglycerin.

dil also had the trend to better the blood glucose metabolism during the treatment [25, 26].

Drawbacks of NG include not only side effects such as headache, resistance, and development of tolerability to nitrates but also free radical production. However, Urapidil has a dual mechanism of action and properties of combining α-blocker and a centrally acting drug, has a high efficiency, comparable to that of the other groups of drugs, and a good tolerability [2, 27].

AHF is particularly accompanied by elevated blood pressure (BP). We found the patients with AHF enrolled in this study present with high blood pressure. Either NG or urapidil could reduce systolic and diastolic blood pressure to normal level without hypotension reaction. It indicated that the two drugs have good antihypertensive effect. However, urapidil could persistently decreased systolic blood pressure within 7 days.

Elevated SBP was found to be associated with improved short and long-term mortality of patients with acute heart failure [28]. In addition, at the early stages of AHF, systolic blood pressure is an important indicator to assess the suitability of the vasodilator. Urapidil is a new selective alpha 1-adrenergic antagonist with strong vasodilating properties and additional central serotonin receptor-mediated antihypertensive activity [29]. The study showed urapidil is more suitable for the treatment of acute heart failure in patients with hypertension.

In this study, there appeared to be no significant difference between urapidil and NG in reduction of heart rate. However, compared with nitroglycerin, urapidil decreased heart rate more stable. The alpha-blocker urapidil might not increase heart rate due to its additional effect on 5-HT1A receptors, decreasing the sympathetic tone and increasing the vagal tone, which may imply less tachycardia with vasodilatation or decreasing blood pressure [30].

Study on heart function evaluated by N-terminal pro-Brain Natriuretic Peptide and left ventricular ejection fraction (LVEF) in acute coronary syndrome patients with heart failure. Patients who present with elevated systolic blood pressure usually have a relatively preserved LVEF, which is a good indication to evaluate cardiac function [31].

Echocardiography results showed that patients in urapidil group not only had better effects on increasing LVEF but also on CI, CO, SV and EDV after 7 days of treatment, compared with NG. Urapidil is also a moderate pre-synaptic alpha 2-adrenoceptor agonist with a weak beta 1-blocking effect. It can reduce the pre- and after-load of the heart and increase EF by reducing the venous blood return and blocking the release of catecholamine [32].

Natriuretic peptides (N-terminal pro-BNP [NT-proBNP]) are recommended in the current HFSA guidelines to aid in the diagnosis of heart failure in patients [33]. NT-proBNP is a sensitive marker in the detection of cardiac function. In the study, both urapidil and nitroglycerin could decrease NT-proBNP level. However, urapidil reduced NT-proBNP level more drastically [34].

The above-mentioned studies indicated that urapidil could improve cardiac function. The mechanism may be related with that urapidil can regulate the balance between calcitonin gene related peptide (CGRP) and endothelin (ET) to increase cardiac index (CI) and EF. The calcitonin gene-related peptide in patients with congestive heart failure, CGRP and ET increase cardiac output and cardiac index, in favor of left ventricular systolic function improved to ease the AHF symptom. None of these adverse effects were observed in the patients treated with urapidil in this study [32].

α-blockers have been shown to improve insulin sensitivity and to decrease serum triglycerides

(TG) and cholesterol. Urapidil treatment was characterized by neutral or favorable effects on several variables associated with the metabolic syndrome [20].

Compared with nitroglycerin, urapidil treatment did not affect TCH, TG, LDL cholesterol and HDL cholesterol levels. The mechanism may be that it is not enough to influence the metabolic system with the short-term administration (7 days) of urapidil.

Long-term administration with urapidil decreases blood glucose level in diabetic patients. Urapidil could not impair glucose metabolism and lipid metabolism and had no adverse effect on liver and renal function [35]. In the present study, both urapidil and NG caused obvious decrease in blood glucose levels in all patients and there was no significant difference of the decrease between the two groups.

The incidence of major adverse cardiac events (MACE) in urapidil group was lower 1 month after hospital discharge. It showed that urapidil had no obvious side effect on AHF patients.

The limitations in this study had to be acknowledged. Firstly, the sample size was less and the time course of this analysis was limited to 7 days of hospitalization. Secondly, it was a short-term evaluationon hemodynamic effect, safety and the curative effect of urapidil. Therefore, the influence on prognosis needs to make further large sample, randomized, controlled clinical validation.In any case, the advantage of our study is the unselected population of patients which reflects real-life clinical practice.

In conclusion, Urapidil was as safe and effective as NG on the treatment of AHF patients with hypertension and atrial fibrillation. However, the present study showed statistically significant differences between the effects of urapidil and NG on blood pressure and cardiac function. Urapidil could more persistently decreased systolic blood pressure and enhanced cardiac function by regulating the systolic and diastolic capacities of the left ventricle without inducing tachycardia. Finding more differences between urapidil and NG on treatment of AHFis needed to carry out the large-scale experiment.

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Disclosure of conflict of interest

None.

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