Effects of valsartan combined with atorvastatin on cardiac function, myocardial enzymes and thyroxine levels in patients with chronic heart failure

Xiao-Gang Wang\textsuperscript{1,}\* De-Xuan Chen\textsuperscript{2}, Kai Li\textsuperscript{1}

\textsuperscript{1}Department of Geriatrics, Jiading District Community Health Service Center, Shanghai 201800, China
\textsuperscript{2}Department of Geriatrics, Jiading Central Hospital, Shanghai 201800, China

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\textbf{ABSTRACT}

\textbf{Objective:} To observe the effects of valsartan combined with atorvastatin on cardiac function, myocardial enzymes and thyroxine levels in patients with chronic heart failure (CHF).

\textbf{Methods:} 90 cases of CHF cases were divided into observation group and control group according to the order of single and double number, 45 cases each. In the control group, atorvastatin was given on the basis of conventional therapy, and the observation group was given valsartan on the basis of the control group. After 6 months, the differences of cardiac function indexes (LVEF, LVEDD, LVESD, E/A), myocardial enzymes (LDH, AST, CK, CK-MB) and thyroxine (TT3, TT4, FT3, FT4, TSH) in the two groups were observed.

\textbf{Results:} After treatment, LVEF and E/A in both groups increased significantly ($P<0.05$), while LVEDD and LVESD decreased significantly ($P<0.05$), and LVEF (49.05±5.37)% and E/A (1.13±0.19) are higher than the control group, while LVEDD (51.55±5.26) mm and LVESD (38.87±3.61) mm are lower than the control group, the difference was statistically significant ($P<0.05$); After treatment, two groups of LDH, AST, CK, CK-MB were significantly decreased ($P<0.05$), LDH, AST, CK and CK-MB in the observation group were (165.06±29.45) IU/L, (31.51±13.33) IU/L, (96.45±29.58) mmol/L and (19.53±8.75) mmol/L respectively, lower than the control group, the differences were statistically significant ($P<0.05$); After treatment, two groups of TT3 and FT3 increased significantly ($P<0.05$) while TT4, FT4 and TSH levels had no significant changes ($P>0.05$), the observation group TT3 and FT3 were respectively (1.37±0.33) mol/L and (2.61±0.69) pmol/L, higher than the control group, the difference was statistically significant ($P<0.05$). \textbf{Conclusion:} valsartan combined with atorvastatin in the treatment of CHF, can improve cardiac function and myocardial protection effect, and can effectively promote the recovery of thyroid hormone levels, better than the single use of atorvastatin.

1. Introduction

Chronic heart failure (CHF) occurs, the progress of sustained myocardial damage is the key step leading to ventricular remodeling and decreased cardiac pumping function\cite{1}. Therefore, same with the protection of cardiac function and inhibition of ventricular remodeling, the protection of myocardium is also an important part of delaying the progress of CHF disease. In recent years, research\cite{2} found that CHF patients often accompanied by abnormal thyroid hormone levels, which is not only the result of CHF disease progression but also an important factor leading to the exacerbation of CHF, therefore, the regulation of thyroxine levels in recent years has been valued highly. This study was to investigate the effects of valsartan combined with atorvastatin on cardiac function, myocardial enzymes and thyroxine levels in patients with CHF and...
to provide reference for clinical application. The report is as follows.

2. Materials and methods

2.1. General Information

Cases from January 2015 to August 2016, admitted elderly CHF patients in our department and Jiading District Central Hospital, all in line with the CHF diagnostic criteria of "Chinese Heart Failure Diagnosis and Treatment Guidelines"[3], choose cases of cardiac function of grade II–IV NYHA classification into the study. Exclusion criteria: (1) severe liver, brain, lung, kidney disease, cancer and endocrine, severe immune system diseases; (2) acute coronary syndrome, severe infection and trauma, surgery patients; (3) exclude cognitive disorders, mental retardation, neuropathy and allergies; (4) who did not sign informed consent. A total of 90 patients were enrolled, divided into the observation group and the control group according to the order of single and double number, 45 cases each. The observation group of 27 males and 18 females; aged 60 to 75 years; duration of 2 to 13 years; Basic diseases: ischemic cardiomyopathy in 33 cases, 8 cases of hypertensive heart disease, dilated cardiomyopathy in 2 cases; Heart function of NYHA class II 14 cases , III grade 23 cases, IV grade 8 cases. Control group of 25 males and 20 females; aged 60 to 74 years; duration of 3 to 15 years; Basic diseases: ischemic cardiomyopathy in 31 cases, 10 cases of hypertensive heart disease, dilated cardiomyopathy in 3 cases, hypertrophic cardiomyopathy in 1 case; heart function of NYHA class II 15 cases , III grade 24 cases, IV grade 6 cases. There was no significant difference between the two groups ($P>0.05$).

2.2. Treatment

The cases included are given the relevant health education, urge low-salt, low-fat diet and more rest, and given conventional treatment, including; cardiac glycosides, diuretics, vasodilators, aspirin and other drugs. Sudden angina given nitrates treatment, abnormal blood glucose and blood pressure, control their blood sugar and blood pressure standards. On the basis of conventional treatment, the control group was given atorvastatin tablets (trade name: Lipitor Manufacturer: Pfizer Pharmaceutical Co., Ltd. J20120050), the usage: 20 mg/time, 1 times a day, night meal. The observation group was given the valsartan capsule on the basis of the control group (trade name: Proven manufacturer: Beijing Novartis Pharmaceutical Co., Ltd., Zhunzi H20040217), usage: 80 mg/time, 1 times a day, evening meal. Both groups were continuous treatment for 6 months.

2.3. Observation index

Mainly include: (1) the heart function index: left ventricular ejection fraction (LVEF), left ventricular diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD) and mitral E peak and A peak ratio (E/A). The SIEMENS acuso-nS2000 color Doppler ultrasound diagnostic apparatus (probe frequency: 2.0MHz) applied; (2) Myocardial zymogram parameters including the myocardial enzyme creatine kinase isoenzyme (CK-MB), creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate aminotransferase (AST). Apply the American Backman AU5800 automatic biochemical analyze for detection after take fasting venous blood ; (3) thyroid function index including: three triiodothyronine (TT3), total thyroxine (TT4), thyroid stimulating hormone (TSH), free thyroxine (FT3), three iodine free thyroxine (FT4) were detected by radioimmunoassay and thyroid function tester (Shanghai also Instrument Co., Ltd.) detection after take fasting venous blood by MN-6110. Before and after treatment, each index was examined 1 times.

2.4. Statistical analysis

All data were analyzed by SPSS 17.0. Measurement data using $t$ test. $P<0.05$ considered the difference was statistically significant.

3. Results

3.1. Study completion

In the observation group, 2 cases were lost in the middle of the course, and 43 cases were completed. In the control group, 1 case lost and 2 cases of acute exacerbations, a total of 42 cases completed.

3.2. Comparison of cardiac function in two groups before and after treatment

There was no significant difference in LVEF, LVEDD, LVESD and E/A between the two groups ($P>0.05$). After treatment, the levels of LVEF and E/A were significantly increased ($P<0.05$), while LVEDD and LVESD decreased significantly ($P<0.05$), and the observation group LVEF (49.05±5.37)% and E/A (1.13±0.19) were higher than that of control group LVEDD (51.55±5.26) mm and LVESD (38.87±3.61) mm ,lower than the control group, significant difference ($P<0.05$) (Table 1).
Compared with the same period of control group after treatment; ▲P<0.05; compared with the same group before treatment, △P<0.05.

### 3.3. Comparison of myocardial enzyme levels between the two groups before and after treatment

Before treatment, no significant difference was found between the two groups of AST, CK, LDH, CK-MB (P>0.05); After treatment, two groups of LDH, AST, CK, CK-MB were significantly decreased (P<0.05), LDH, AST, CK and CK-MB in the observation group were respectively (165.06±29.45) IU/L, (31.51±13.33) IU/L, (96.45±29.58) mmol/L and (19.53±8.75) mmol/L, significantly lower than the control group (P<0.05) (Table 2).

### 3.4. Comparison of thyroid hormone levels between the two groups before and after treatment

Before treatment, the TT3, TT4, FT3, FT4 and TSH levels of the two groups had no statistically significant difference (P>0.05); After treatment, two groups of TT3 and FT3 increased significantly (P<0.05), but there was no significant difference in TT4, FT4, TSH levels (P>0.05), the observation group TT3 and FT3 were (1.37±0.33) mol/L and (2.61±0.69) pmol/L, higher than the control group, the difference was significant (P<0.05) (Table 3).

### 3.5. Adverse reaction observation

No obvious discomfort was found in the two groups during treatment, and no abnormal changes were found in liver and kidney function.

### 4. Discussion

Myocardial injury is the pathogenesis of CHF and the key to progress[1]. Such as ischemia and hypoxia, inflammation, stress response and mechanical traction and other factors will lead to myocardial cell apoptosis, necrosis and loss of function, leading to ventricular remodeling, cardiac pump function decline, then caused CHF. The occurrence of myocardial damage after CHF still exists, resulting in sustained reduction of myocardial cells and CHF condition continued to deteriorate[4]. In this study, the myocardial enzymes spectrum indexes including LDH, AST, CK, and CK-MB, which are released into the blood after myocardial injury, their elevated levels can reflect the severity of myocardial injury, recognized as the landmark indicators in the diagnosis and treatment of CHF[5]. Research shows that atorvastatin can inhibit inflammation, stress response and protect vascular endothelial cells, regulate blood lipid and improve myocardial metabolism to alleviate the myocardial injury[6,7]; Valsartan has obvious protective effects on myocardial ischemia, the effective mechanism is related to increasing the myocardium on norepinephrine tolerance, activation of protein kinase C and the promotion of myocardial cells using adenosine triphosphate (ATP)[8,9]. The results of this study show that the myocardial enzyme indexes of LDH, AST, CK and CK-MB in
the observation group after treatment were significantly lower than the control group, suggesting that the effect of valsartan combined with atorvastatin can better reduce myocardial injury, which is beneficial to inhibit the progression of CHF.

Decreased cardiac function is the main manifestation of CHF, improving cardiac function is one of the main therapeutic targets of CHF\[10\]. Cardiac function decreased caused insufficient cardiac pump function, the body tissues and organs affect the physiological function due to lack of effective circulation, such as effect of respiratory function leads to difficulty in breathing, shortness of breath, night not supine\[11\]; Effect of skeletal muscle leads to exercise endurance effects, resulting in daily life and social activities limited\[12\]. There are many reports about valsartan and atorvastatin in treating CHF, reported show that: valsartan can block the excitement of the sympathetic nervous then cause heart rate slowed down and decreased myocardial oxygen consumption, combine with angiotensin II block the vasoconstriction and indirectly play a role in vasodilatation, reduce water and sodium storage by inhibiting the secretion of aldosterone to reduce cardiac load, inhibit the inflammatory response, play a role in inhibiting ventricular remodeling and protection of cardiac function through a variety of roles\[13\]; In addition to lipid-lowering, anti-inflammatory, atorvastatin can also inhibit myocardial fibrosis and the progress of myocardial hypertrophy\[14\], the role of inhibiting ventricular remodeling and protecting cardiac function is also very positive. At present, the effects of valsartan and atorvastatin on cardiac function are still relatively rare. This study observed heart function indexes including: LVEF, LVEDD, LVESD and E/A, the improvement of LVEDD and LVESD can reflect the corrective effect of ventricular remodeling to varying degrees\[15\], the results showed that the indexes of the observation group after treatment improved significantly better than the control group, suggesting that valsartan combined with atorvastatin can improve the CHF patients with heart function.

Thyroxine levels reflect the severity of CHF and have potential as a prognostic indicator for assessment CHF\[16\]. The relationship between CHF and thyroid hormone is a research hotspot in recent years, the study\[17\] showed that patients with CHF often associated with normal thyroid dysfunction syndrome, manifested as, T3, FT3 levels decreased while T4, TT4 and TSH levels stay normal, namely: low T3 syndrome. The mechanism of pathophysiology may be: (1) In CHF stress state, the synthetic and increased release of catecholamines, cortisol, glucocorticoids will inhibit T4 transform to T3; (2) The clearance rate of T3 in CHF increased; (3) In the hypoxic state of the body, peripheral T4 deiodination at 5 to form a small anti-iodine anti-T3 ,leaving the formation of normal T3 reduction\[18\]. Low T3, FT3 state, ventricular systolic / diastolic function weakened, peripheral vascular resistance increased, myocardial tissue on adrenergic nerve stimulation decreased sensitivity, thus play a negative regulatory role on ventricular remodeling and cardiac function\[19\]. At the same time, low T3 and FT3 levels, abnormal glucose and lipid metabolism, increased inflammatory response, increased vascular endothelial damage are considered important risk factors for atherosclerosis, also promoted the progress of CHF course. In addition, there has been reported that the tissue blood supply is relatively insufficient in CHF, the impact of thyroid function showed decreased levels of thyroxine\[20\]. Recent researches\[21,22\] show that, TT3, FT3 levels was negatively correlated with CHF risk, and the two form a vicious cycle to aggravate the disease, and with CHF remission, the TT3 and FT3 levels can be gradually restored. The results of this study show that the observation group after treatment, TT3 and FT3 increased more significantly than that of control group, suggesting that valsartan combined with atorvastatin have better effect on low T3 syndrome, and CHF disease eased to a greater extent. So how does valsartan and atorvastine affect TT3, FT3 levels? I believe that the main stress response with the decreased CHF after treatment and the stability blood supply of thyroid, but the direct impact of drugs on the role of the thyroid cannot rule out.

In summary, valsartan combined with atorvastatin in the treatment of CHF, can improve cardiac function and myocardial protection effect, and effectively promote the recovery of thyroid hormone levels in patients with CHF. Better than single atorvastatin treatment.

References


