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Fluvastatin combined with benazepril may contribute to the favorable prognosis of patients with atrial fibrillation

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ABSTRACT

The aim of this study was to observe the clinical efficacy of fluvastatin combined with benazepril in the treatment of patients with atrial fibrillation (AF). A total of 92 patients with AF were randomly assigned to the case group (n = 46), in which the patients were treated with fluvastatin (80 mg) plus benazepril (10 mg), or to the control group (n = 46), in which the patients were treated with fluvastatin (80 mg). The conversion rate of sinus rhythm was higher in the case group than in the control group ($P < 0.05$). The case group had more treatment-effective patients than the control group, with fewer treatment-ineffective patients ($P < 0.05$). The LVEDd, LVESd, LAD, and LVEF indexes in the case group were lower than in the control group after 6 months of treatment (all $P < 0.05$). Levels of hs-CRP were also lower in patients in the case group than in patients in the control group after 1 month of treatment ($P < 0.05$). After 12 months, renin and Ang II concentrations were lower in patients in the case group than in the control group (both $P < 0.05$). Significant differences in IL-6 and TNF-α expression were found between the two groups after 1 month, 6 months, and 12 months of treatment (all $P < 0.05$). Compared to patients in the control group, the levels of total cholesterol (TC), triglycerides, and LDL-C in the case group were lower after 6 and 12 months of treatment (all $P < 0.05$), while the HDL level was higher ($P < 0.05$). Treatment with fluvastatin combined with benazepril further increased the conversion rate of sinus rhythm and significantly improved the quality of life and prognosis of AF patients.

1. Introduction

Atrial fibrillation (AF) is a common type of arrhythmia that results from considerably different pathophysiological processes in the atria [1]. It has been reported that the prevalence of AF increases with age, affecting 0.4% to 1% of the general population and 9% of individuals over 80 years of age [2]. Many risk factors can promote the development of AF, including advanced age, obesity, hypertension, valvular heart disease, heart failure and hyperthyroidism [3]. Persistence of AF can lead to changes in atrial structure and function, a serial of processes known as atrial remodeling [4]. AF is consistently associated with decreased quality of life, and increased mortality and morbidity in critically-ill patients [5,6], and can also contribute to an increased risk of stroke, heart failure, dementia and death [7]. Fortunately, there are suggests on AF prophylaxis, including sotalol, β-blockers and amiodarone, and also pharmacological agents for reduction in AF frequency, including angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers combined with inhibition of the renin angiotensin aldosterone system (RAAS), statins, antioxidant agents, magnesium supplementation and antiarrhythmic dedications [8]. Treatment with antiarrhythmic medications has recently become a mainstay in the treatment of AF, and can reduce the frequency and the duration of arrhythmia episodes and hospitalizations and mortality associated with AF [9].

Fluvastatin is a common type of statin that has been established as a treatment for the secondary prevention of atherosclerotic coronary artery disease [10]. Statin treatments have had the greatest impact on reducing the incidence of cardiovascular disease across the world in recent years, and are also potentially beneficial for decreasing the risk of AF in patients with sinus rhythm [11,12]. Satins possess an acceptable safety profile, are not costly, and may function as direct anti-arrhythmic or anti-inflammatory drugs [13]. Benazepril, a type of ACE inhibitors, exhibits favorable pharmacodynamic and pharmacokinetic properties and exhibits good tolerability and antihypertensive effects

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[14]. Although ACE inhibitors are not anti-arrhythmia drugs, they can prevent the synthesis of angiotensin II from angiotensin I [15]. It has been reported that patients who were treated with ACE inhibitors eventually required fewer defibrillation treatments for successful cardioversion than patients receiving other treatments [16]. Therefore, we hypothesize that fluvastatin combined with benazepril in the treatment of atrial fibrillation may have good curative effect. Therefore, this study compares the effect of fluvastatin with benazepril on the treatment of atrial fibrillation and the administration of fluvastatin only to uncover better drug therapies for treating atrial fibrillation.

2. Materials and methods

2.1. Study population

A total of 92 patients diagnosed with AF were admitted to the First Affiliated Hospital of Harbin Medical University between August 2013 and February 2014, including 48 males and 44 females, with a mean age of 63.67 ± 10.30 years. The subject selection was carried out based on strict inclusion and exclusion criteria, as well as the software Power and Sample Size Program. Inclusion criteria: a diagnosis of AF based on electrocardiogram and dynamic electrocardiogram; no renal insufficiency, renal artery stenosis, or hyperkalemia, which are contraindications to angiotensin-converting enzyme inhibitor (ACEI) drugs; patients who provided informed consent and were willing to take part in the clinical observation and follow up. Exclusion criteria: congenital heart disease and rheumatic heart disease; LVEF $<$ 40%; hyperthyroidism; severe valvular disease, such as severe mitral insufficiency and more than moderate aortic valve insufficiency; chronic inflammatory diseases or connective tissue diseases, including chronic obstructive pulmonary disease and rheumatoid arthritis; the presence of an acute infection; hemorrhage in any tissue or organ; trauma and surgery within 3 months; major organ failure, such as lung, liver or kidney failure; or allergy to ACEI and statins. All experimental procedures were conducted following medical ethics standards and were approved by the Institutional Review Board/Ethics Committee of the First Affiliated Hospital of Harbin Medical University. Written informed consent was obtained from all patients.

2.2. Groups and treatments

The patients were randomly assigned to one of two groups according to random number table method. The case group had 46 patients, who were treated with a combination of fluvastatin and benazepril. The control group had 46 patients, who were treated with fluvastatin.

Treatment methods: (1) The case group: taking 80 mg of fluvastatin orally (Novartis pharmaceutical Co. Ltd., Beijing, China) once daily before sleeping; taking 10 mg of benazepril orally (Novartis pharmaceutical Co. Ltd., Beijing, China.) once daily in the morning. (2) The control group: taking 80 mg of fluvastatin orally (Novartis pharmaceutical Co. Ltd., Beijing, China.) once daily before sleeping. The patients in these two groups underwent 1 −year of treatment and were maintained on the medicine long term. The patients were excluded from the study if they failed to tolerate treatment or presented with any adverse reactions.

2.3. Efficacy evaluation

The patients received electrocardiogram (MAC1200ST, GE Medical Systems Co. Ltd., USA), dynamic electrocardiogram (Beneware Medical Equipment Co. Ltd., Zhejiang, China), and ultrasonic cardiogram (UCG) (GE Vivid E9, GE Medical Systems Co. Ltd., USA) examinations before and after treatment. Samples of morning fasting venous blood from all patients were obtained to detect blood lipids, routine blood markers, and markers of liver and kidney function. A radioimmunoassay kit (Beijing Beifang Immune Reagent Institute, China) was used to quantify renin and angiotensin levels. An enzyme-linked immunosorbent assay (ELISA) kit (Tianjin Union Medical Technology Co. Ltd., China) was used to detect IL-6 and TNF-α in serum samples. All patients were tested at 1 month, 6 months and 12 months, at which times the fasting venous blood was also obtained. Detection was performed as in previous procedures.

The efficacy criteria were as follows: significantly effective: paroxysmal AF disappears or occasionally occurs; persistent AF is converted into sinus rhythm or paroxysmal AF; effective: paroxysmal AF is decreased by 30% in terms of time and frequency and persistent AF is converted into paroxysmal AF; ineffective: patients fail to meet the effective criteria.

2.4. Statistical analysis

Data were analyzed using the statistical package for the social sciences (SPSS) version 21.0 (SPSS Inc.; Chicago, IL, USA). Continuous data were displayed as the mean $\pm$ standard deviation, all of which were consistent with normal distribution by *k-s* test, and the differences between the two groups were analyzed by *t* test. Categorical data were expressed as ratio or percentage and the Chi-square test was conducted. $P < 0.05$ was regarded as statistically significant.

3. Results

3.1. Clinical characteristics of subjects

A total of 92 AF patients underwent treatment, including 63 patients with persistent AF and 29 patients with paroxysmal AF. All of the subjects in the case group (n = 46) and the control group (n = 46) exhibited no significant differences with respect to age; gender; body mass index (BMI); course of disease; smoking; other diseases such as hypertension, diabetes, coronary disease, or hyperlipidemia; persistent AF ratio; or paroxysmal AF ratio (all $P > 0.05$, Table 1)

3.2. Sinus rhythm conversion and efficacy rate

Among the 92 AF patients, 45 (48.9%) were restored to sinus rhythm. This included 28 patients (60.9%) in the case group, which was a significantly higher number than the 17 patients (37.0%) in the control group ($P < 0.05$, Table 2). Compared with the effective rate of 69.5% in the control group, the case group had an elevated rate of 87.0% ($P < 0.05$), which indicated that the effect of fluvastatin + benazepril surpassed that of fluvastatin alone.

3.3. Changes of cardiac function

No significant differences were found in the LVEDd, LVESd, LAD or LVEF indexes before treatment and 1 month after treatment between the case group and the control group (all $P > 0.05$). The LVEDd, LVESd, LAD and LVEF indexes 6 and 12 months after treatment in the case group were lower than those in the control group (all $P < 0.05$). In the case group, the LVEDd, LVESd and LAD indexes gradually declined (all $P < 0.05$), and LVEF increased ($P < 0.05$). There were no significant differences in terms of the LVEDd, LVESd, LAD and LVEF indexes between 6 months and 12 months after treatment (all $P > 0.05$). Moreover, in the control group, the LVEDd, LVESd and LAD indexes gradually decreased 6 months after treatment with respect to the pre-treatment values