INTRODUCTION

Hypertrophic cardiomyopathy, a common cardiovascular disease, is associated with gene mutation. With disease progression, patients suffer from fatigue, dyspnea, dizziness, and even sudden cardiac death. Particularly, the hypertrophic cardiomyopathy patients complicated with malignant ventricular arrhythmias are more prone to sudden cardiac death. Therefore, controlling the symptoms promotes the prognosis. Amiodarone, which is a Class III antiarrhythmic agent, functions by prolonging the effective refractory period of myocardial cells, decreasing the interval between...
action potentials, and eliminating reentry.\textsuperscript{4} Betaloc, a β-receptor blocker, can also treat arrhythmia by exerting antagonist action on excited β-receptor through binding the ectopic pacemaker β1 adrenergic receptor of cardiomyocytes.\textsuperscript{5} Therefore, we herein aimed to study the effects of low-dose amiodarone in combination with Betaloc on hypertrophic cardiomyopathy complicated with malignant ventricular arrhythmias.

**METHODS**

**General Information:** All the studies were approved by the ethics committee of The Fifth Affiliated Hospital of Zhengzhou University, and consent was obtained from all patients. Eighty-two hypertrophic cardiomyopathy complicated with malignant ventricular arrhythmias patients who were treated in our hospital from March 2010 to March 2013 were selected, including 58 males and 24 females aged 24-53 years old, with the average age of (33.63±6.42) years old. All the patients suffered from sudden palpitation, dyspnea and chest tightness, and they were diagnosed as soon as possible after Holter examination, echocardiography and chest radiography. The patients were divided into a treatment group and a control group (n=41) by the random number method. The treatment group consisted of 29 males and 12 females aged 25-53 years old (average: 33.53±6.22), and the control group comprised 29 males and 12 females aged 24-53 years old (average: 33.73±6.62). The patients with ion disorder-induced arrhythmia, as well as abnormal liver, kidney and thyroid functions were excluded. There were no significant differences between the clinical features of the two groups (P>0.05).

**Inclusion Criteria:** According to the Holter examination results and Lown’s grading of premature ventricular contraction (PVC), only Grade 3 and above patients were selected in this study.\textsuperscript{6} “Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy”\textsuperscript{7} was also used for patient selection. The patients with atrial fibrillation, hyperthyroidism and drug-induced arrhythmias were excluded.

**Treatment Methods:** The treatment group was orally administered with low-dose amiodarone and Betaloc ; Amiodarone: 0.2 g, bid; Betaloc: 6.25 mg, bid. After one week, the dose of amiodarone was decreased to 0.1 g (qd) and maintained thereafter. The dose of Betaloc was increased to 12.5 mg (bid) based on the patients’ tolerance and maintained thereafter. The control group was only administered with Betaloc at the same dose. The patients were treated for a period of three months.

**Observation Indices:** The two groups were subjected to Holter examination before and after three treatment courses, during which they were also examined by routine electrocardiography. The longest and shortest QT intervals, QT dispersion, and adverse reaction events were observed.

**Evaluation Standards for Therapeutic Effects:** The therapeutic effects were evaluated according to the Holter examination outcomes. Effective: Absence of sustained ventricular tachycardia, the incidence of non-sustained ventricular tachycardia was decreased by over 90%, and PVCs were decreased by over 75%. Ineffective: Presence of sustained and non-sustained ventricular tachycardia, and unrelieved PVCs.

**Statistical Analysis:** All data were analyzed by SPSS 17.0. The measurement data were expressed as mean ± standard deviation (X±S) and compared by t test. P<0.05 was considered statistically significant.

**RESULTS**

**Comparison between Therapeutic Effects:** The overall effective rate of the treatment group (85.4%) was significantly higher than that of the control group (65.9%) (P<0.05) (Table-I).

**Liver, Kidney, and Cardiac Functions before and after Treatment:** The liver and kidney functions of patients did not differ significantly before and after treatment (P>0.05). The NYHA Class III and IV patients were significantly decreased after treatment (P<0.05). Besides, the heart rate was significantly reduced from (119.99±18.91) bpm to (80.98±12.34) bpm (P<0.05). Moreover, the incidences of PVC and tachycardia were also significantly lowered (P<0.05) (Table-II).

| Group       | Case No. | Markedly effective | Effective | Ineffective | Overall effective rate |
|-------------|----------|--------------------|-----------|-------------|------------------------|
| Treatment group | 41       | 24                 | 11        | 6           | 85.4\textsuperscript{a} |
| Control group    | 41       | 14                 | 13        | 14          | 65.9                   |

Compared with the control group, \textsuperscript{a}P<0.05.
Longest, Shortest QT Intervals and QT Dispersion before and after Treatment: The longest QT intervals after and before treatment were (421±32) ms and (411±35) ms respectively. The shortest QT interval after treatment [(350±36) ms] was significantly longer than that before [(307±31) ms]. The QT dispersion before treatment [(96±29) ms] was significantly higher than after [(64±17) ms] (P<0.05) (Table-III).

Adverse Reactions of the Treatment Group: Four patients in the treatment group were prone to nausea and vomiting which were mitigated without influencing the outcomes. Two patients who suffered from sinus bradycardia claimed tolerance, thus being further treated without special care. The incidence of adverse reactions was 14.63% (6/41).

DISCUSSION

Hypertrophic cardiomyopathy, a cardiovascular disease, is related with the mutation of gene-encoding cardiac sarcomeric genes. The patients are clinically manifested as differently thicked cardiac muscle fibers that results from asymmetric ventricular hypertrophy and disorderedly arranged myocardial cells. Therefore, reentrant excitation is induced owing to different pathways of cardiac electrophysiological conduction. Reentrant excitation may give rise to various ventricular arrhythmia symptoms. With disease progression, patients may die of sudden cardiac death due to hemodynamic instability. Especially, 0.1%-1.0% of the patients may die without early signs. It has previously been reported that malignant arrhythmia was directly associated with sudden cardiac death.

Amiodarone, as a Class III antiarrhythmic agent, can prolong the effective refractory period of myocardial cells, shorten the interval between action potentials, decelerate conduction and terminate reentrant excitation by non-competitively binding α- and β-adrenergic receptors on the myocardial cell membrane. In this study, the patients were also well treated with amiodarone.

Betaloc, which is a β-receptor blocker, can clinically treat hypertension patients who have fast heart rates. Betaloc effectively stabilizes ventricular rate by binding β1 adrenergic receptor, exerting antagonistic effects on its excitation, decreasing the phase-4 depolarization rate and phase-0 action potential rising rate of cardiomyocytes, as well as reducing their self-regulation and conduction rate. Meanwhile, Betaloc can inhibit the proliferation and overoxidation of myocardial cells, prevent them from apoptosis, reverse cardiac remodeling, and alleviate ventricular hypertrophy. Hence, Betaloc not only facilitates the control of ventricular rate and arrhythmia, but also promotes the reversion of hypertrophic cardiomyopathy. In this study, low-dose amiodarone in combination with Betaloc treated hypertrophic cardiomyopathy complicated with malignant ventricular arrhythmias effectively and safely.

Table-III: Longest, shortest QT intervals and QT dispersion before and after treatment.

| Index              | Before      | After       |
|--------------------|-------------|-------------|
| Longest QT interval| 411±35      | 421±32      |
| Shortest QT interval| 307±31     | 350±36*     |
| QT dispersion      | 96±29       | 64±17*      |

Compared with the results before treatment, *P<0.05.
In summary, low-dose amiodarone plus Betaloc can treat hypertrophic cardiomyopathy complicated with malignant ventricular arrhythmias with excellent outcomes, improved prognosis and few adverse reactions, thus being worthy of wider application.

Conflicts of interest: All the coauthors declare that they have no conflicts of interest.

REFERENCES
1. Girolami F, Ho CY, Semmansian C, Baldi M, Will ML, Baldini K, et al. Clinical features and outcome of hypertrophic cardiomyopathy associated with triple sarcomere protein gene mutations. J Am Coll Cardiol. 2010;55(14):1444-1453.
2. Thiene G, Cordaro D, Rigato I, Basso C. Why and how to support screening strategies to prevent sudden death in athletes. Cell Tissue Res. 2012;348(2):315-318.
3. Spöhr F, Wenzel V, Böttiger BW. Drug treatment and thrombolitics during cardiopulmonary resuscitation. Curr Opin Anaesthesiol. 2009;19(2):157-165.
4. Haverkamp W, Rolf S, Stockburger M, Dietz R. Acute treatment of stable hemodynamically tolerable ventricular tachycardia. Anaesthes Intensivmed Nothallmed Schmerzther. 2011;40(4):207-212.
5. Rathore SS, Berger AK, Weinfurt KP, Schulman KA, Oetgen WJ, Gersh BJ, et al. Acute myocardial infarction complicated by atrial fibrillation in the elderly: prevalence and outcomes. Circulation. 2000;101(9):969-974.
6. Kishi T, Yamada A, Okamatsu S, Sunagawa K. Atorvastatin might improve ventricular electrostability and decelerate the deterioration of renal function in patients with heart failure and diabetes mellitus. J Cardiol. 2009;53(3):341-348.
7. Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, et al. 2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;58(25):e212-260.
8. Correia E, Rodrigues B, Santos LF, Moreira D, Gama P, Cabral C, et al. Longitudinal left ventricular strain in hypertrophic cardiomyopathy: correlation with nonsustained ventricular tachycardia. Echocardiography. 2011;28(7):709-714.
9. Morita H, Nagai R, Seidman JG, Seidman CE. Sarcomere gene mutations in hypertrophy and heart failure. J Cardiovasc Transl Res. 2010;3(4):297-303.
10. ten Cate FJ, Soliman OI, Michels M, Theuns DA, de Jong PL, Geleijnse ML, et al. Long-term outcome of alcohol septal ablation in patients with obstructive hypertrophic cardiomyopathy: a word of caution. Circ Heart Fail. 2010;3(3):362-369.
11. Ho CY, Lopez B, Coelho-Filho OR, Lakdawala NK, Cirino AL, Jarolim P, et al. Myocardial fibrosis as an early manifestation of hypertrophic cardiomyopathy. N Engl J Med. 2010;363(6):552-563.
12. Willems R, Sipido KR, Holemans P, Ector H, Van de Werf F, Heidbüchel H. Different patterns of angiotensin II and atrial natriuretic peptide secretion in a sheep model of atrial fibrillation. J Cardiovasc Electrophysiol. 2001;12(12):1387-1392.
13. Babouth F, Mutlak D, Furman M, Musallam A, Hammerman H, Lessick J, et al. Relationship of functional mitral regurgitation to new-onset atrial fibrillation in acute myocardial infarction. Heart. 2010;96(9):683-688.
14. Cairns JA, Connolly SJ, Roberts R, Gent M. Randomised trial of outcome after myocardial infarction in patients with frequent or repetitive ventricular premature depolarisations: CAMIAT. Canadian Amiodarone Myocardial Infarction Arrhythmia Trial Investigators. Lancet. 1997;349(9053):675-682.
15. Chen YJ, Chen YC, Tai CT, Yeh HI, Lin CI, Chen SA. Angiotensin II and Angiotensin II receptor blocker modulate the arrhythmogenic activity of pulmonary veins. Br J Pharmacol. 2006;147(1):12-22.
16. Porter KE, Turner NA. Cardiac fibroblasts: at the heart of myocardial remodeling. Pharmacol Ther. 2009;123(2):255-278.
17. Healey JS, Baranchuk A, Crystal E, Morillo CA, Garfinkle M, Yusuf S, et al. Prevention of atrial fibrillation with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: A meta-analysis. J Am Coll Cardiol. 2005;45(11):1832-1839.
18. Wachtell K, Lehto M, Gerdtz E, Olsen MH, Hornestam B, Dahlöf B, et al. Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study. J Am Coll Cardiol. 2005;45(9):712-719.