Effect of amiodarone hydrochloride tablets combined with potassium magnesium aspartate on hemodynamics and cardiac function in patients with coronary heart disease and arrhythmia

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Abstract

**Purpose:** To investigate the effects of amiodarone hydrochloride tablets combined with potassium magnesium aspartate on hemodynamics and cardiac function in coronary heart disease (CHD) patients with arrhythmia.

**Methods:** In this retrospective research, a total of 110 CHD and arrhythmia patients on admission at Jiaozhou Central Hospital of Qingdao from June 2020 to June 2022 were randomly but equally divided into control group (CG) treated with propafenone hydrochloride tablets, and study group (SG) treated with a combination of amiodarone hydrochloride tablets and potassium magnesium aspartate. Clinical efficacy of the treatment types as well as the number of premature ventricular contractions (PVC), QTc interval and heart rate (HR) of the patients were monitored to determine left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and cardiac index (CI). Fibrinogen levels, plasma viscosity and hematocrit of the patients were also assessed.

**Results:** The total effectiveness/efficacy of treatment in SG was 92.73 %, which was significantly higher than the corresponding CG value of 76.36 % (p < 0.05). Relative to CG, PVC and HR in SG were significantly lower, while QTc interval was significantly higher. The levels of LVED and LVESD were significantly lower in SG than in CG, while CI level was significantly higher. However, fibrinogen, plasma viscosity and hematocrit values were significantly lower in SG than in CG (p < 0.05).

**Conclusion:** When administered along with potassium magnesium aspartate in the treatment of CHD and arrhythmia, amiodarone hydrochloride tablets enhances clinical efficacy and improves electrocardiograph index, hemodynamics and cardiac function. Nonetheless, there is need for expanded clinical trials before the use of this treatment strategy in clinical practice.

**Keywords:** Amiodarone hydrochloride, Potassium magnesium aspartate, Propafenone hydrochloride, Coronary heart disease, Arrhythmia, Hemodynamics, Cardiac function
INTRODUCTION

Coronary heart disease (CHD), a disease associated with high morbidity, presents vascular stenosis or occlusion caused by atherosclerosis lesions in coronary vessels, leading to myocardial ischemia, hypoxia or necrosis. The disease (CHD) occurs mostly in people who are over 40 years old, although the recent years have witnessed an increasing CHD trend among young people [1,2].

Arrhythmia, a common complication of CHD, is manifested as palpitation, accelerated heart rate, chest discomfort and precordial discomfort. It also readily causes increased blood viscosity, aggravated disease conditions, high mortality and poor prognosis. In combination with arrhythmia, CHD affects hemodynamics of patients through impairment of heart pump function. In addition, the combination of arrhythmia and CHD results in cardiovascular events and threatens safety lives of patients if timely treatment is not given [3].

Amiodarone hydrochloride, a broad-spectrum antiarrhythmic agent, eliminates re-entrant excitation and reduces sinus node automaticity through extension of the action potential of myocardial tissues and effective refractory period. Moreover, the drug has the advantages of regulating multiple arrhythmias: it mitigates palpitations, tachycardia and cardiopalp, and it relieves respiratory rapidity, chest discomfort and shortness of breath [4].

Therefore, due to this variety of electrophysiologic effects, amiodarone hydrochloride tablets expand arteries and peripheral vessels, and improve cardiac function in patients [5].

Potassium magnesium aspartate is an electrolyte-regulating drug widely used in the treatment of arrhythmia. The drug maintains normal myocardial contraction force, improves myocardial systolic function, reduces myocardial oxygen consumption, and stabilizes the electrical activity of cardiomyocytes.

A study has shown that amiodarone produces a significant effect on heart failure-related arrhythmia, thereby improving the heart function of patients [6]. However, there are limited studies on the effect of combination of amiodarone hydrochloride tablets and potassium magnesium aspartate on hemodynamics and cardiac function in patients with CHD and arrhythmia. Based on this, 110 CHD patients with arrhythmia were used as subjects in this study.

METHODS

Patients

Basic clinical information on 110 CHD subjects with arrhythmia on hospital admission in Jiaozhou Central Hospital of Qingdao from June 2020 to June 2022 were selected for retrospective research. The subjects were randomly assigned to control group (CG) administered propafenone hydrochloride tablets, and study group (SG) treated with amiodarone hydrochloride tablets and potassium magnesium aspartate, with 55 patients in each group.

Inclusion and exclusion criteria

Patients who were diagnosed with CHD and arrhythmia using electrocardiogram, coronary angiography and echocardiography; patients with complete clinical data, those willing to cooperate to the completion of the study; patients with no acute cardiovascular event in the past half year; patients with no history of myocardial infarction, and patients who had not taken antiarrhythmic drug for nearly one month, were included in this study.

Patients with severe dysfunction in heart, liver and kidney; those with cardiomyopathy and rheumatic heart disease; those who could not communicate with others due to mental illness; patients who were allergic to drugs used in this study; those in gestational period or lactation period; those with thyroid dysfunction, and those with atrioventricular conduction block, were excluded from this study.

Ethical matters

This study received approval from the ethical authority of Jiaozhou Central Hospital of Qingdao (approval no. 20200413), and carried out in line with provisions of the Helsinki Declaration [7]. Patients and their family members agreed to join the study voluntarily and signed informed consent.

Treatments

The CG was given propafenone hydrochloride tablets (manufacturer: Hubei Ouly Pharmaceutical Co. Ltd; NMPA approval no.: H42020511; tablet strength: 50 mg). An oral dose of 150 mg was given three times a day. The SG received amiodarone hydrochloride tablets (Beijing Jialin Pharmaceutical Co. Ltd; NMPA approval no. H20003843; tablet strength: 0.2 g) at an oral dose of 0.2 g given three times a day in the first week, twice a day in the second week.

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and once a day in the third week until the end of treatment, with continuous application for 4 weeks. In addition, two tablets of potassium magnesium aspartate (Shanghai Shyndec Pharmaceutical Co. Ltd; NMPA approval no. H31022534; tablet strength: 0.149 g) were given orally thrice daily for 4 weeks continuously.

**Evaluation of parameters/indices**

**Baseline data**

The baseline data included gender, average age, body mass index (BMI), arrhythmia types, New York Heart Association (NYHA) functional classification, educational level, and place of residence.

**Clinical efficacy**

Clinical efficacy evaluation was based on the Evaluation Criteria of Coronary Heart Disease Arrhythmia in Internal Medicine (7th edition) [8]. If ECG of patients returned to normal and clinical symptoms disappeared completely, the patients were deemed cured. If indicators of arrhythmia such as atrial fibrillation, ventricular vibration and ventricular tachycardia were reduced by > 90 %, and clinical symptoms were reduced by 80 - 90 %, the treatment outcome was obviously effective.

If indicators of arrhythmia such as atrial fibrillation, ventricular vibration and ventricular tachycardia were reduced by ≥ 50 %, the treatment was effective. However, if the arrhythmia indices such as atrial fibrillation, ventricular vibration and ventricular tachycardia were not improved, or were even aggravated, the treatment was deemed ineffective.

\[ TER = CR + OER + ER \]  \( \text{(1)} \)

where \( TER \) = total effectiveness, and \( CR \) and \( OER \) and \( ER \) = number of subjects in cured, obviously effective, and effective treatment categories, respectively.

**24-h Dynamic electrocardiogram**

During treatment, the PVC, QTc interval and HR were determined once a week through 24-h dynamic electrocardiogram.

**Evaluation of cardiac function**

The HP5500 Color Ultrasound (manufacturer: Hewlett-Packard Company, USA) was used to determine LVESD, LVEDD and CI.

**Assessment of hemodynamics**

After treatment, fasting venous blood (3-mL) samples were collected from patients from the two groups. The samples were subjected to a 15-min centrifugation at 3000 rpm and preserved in a refrigerator at -50 °C. Fibrinogen, plasma viscosity and hematocrit were determined using a non-invasive hemodynamic detector (manufacturer: Nanjing Beideng Medical Co. Ltd; type TCD-2000A), and the operations were in strict accordance with the instructions in the instrument manual.

**Statistics**

Data were processed using SPSS 20.0, while graphs were generated using GraphPad Prism 7. Enumeration data and measured data are presented as \([n (\%)\] and mean ± SD, and were evaluated with \( \chi^2 \) test and t-test, respectively. Statistical significance was assumed at \( p < 0.05 \).

**RESULTS**

**Patients’ baseline data**

Table 1 shows that there were no statistical differences in baseline data between the two groups \((p > 0.05)\).

**Clinical efficacy**

The total effectiveness/efficacy of treatment was significantly higher in SG than in CG \((p < 0.05)\), as shown in Table 2.

**Dynamic electrocardiogram indices**

Figure 1 shows that the values of PVC and HR in SG were markedly lower than those in CG, while QTc interval was significantly higher \((p < 0.05)\).

**Cardiac function indices**

Levels of LVESD and LVEDD were overtly lower in SG, while CI level was markedly higher in SG than in CG \((p < 0.05)\), as shown in Table 3.

**Hemodynamic indices**

Table 4 shows that fibrinogen, plasma viscosity and hematocrit were significantly lower in SG than in CG \((p < 0.05)\).

**DISCUSSION**

The main pathological changes in CHD, a common cardiovascular disease with rapid onset, are atherosclerotic stenosis in coronary vessels,
Table 1: Comparison of baseline data between both groups [n (%)]

<table>
<thead>
<tr>
<th>Variable</th>
<th>CG (n = 55)</th>
<th>SG (n = 55)</th>
<th>χ²/t</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>36 (65.45)</td>
<td>34 (61.82)</td>
<td>0.157</td>
<td>0.692</td>
</tr>
<tr>
<td>Female</td>
<td>19 (34.55)</td>
<td>21 (38.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>54.76 ± 6.89</td>
<td>55.29 ± 8.59</td>
<td>0.355</td>
<td>0.723</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.23 ± 1.43</td>
<td>21.51 ± 1.16</td>
<td>1.151</td>
<td>0.252</td>
</tr>
<tr>
<td>Arrhythmia types</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>25 (45.45)</td>
<td>28 (50.91)</td>
<td>0.328</td>
<td>0.567</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>18 (32.73)</td>
<td>16 (29.09)</td>
<td>0.170</td>
<td>0.680</td>
</tr>
<tr>
<td>Ventricular premature beat</td>
<td>7 (12.73)</td>
<td>5 (9.09)</td>
<td>0.374</td>
<td>0.541</td>
</tr>
<tr>
<td>Premature atrial contraction</td>
<td>5 (9.09)</td>
<td>6 (10.91)</td>
<td>0.101</td>
<td>0.751</td>
</tr>
<tr>
<td>NYHA functional classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>29 (52.73)</td>
<td>26 (47.27)</td>
<td>0.327</td>
<td>0.567</td>
</tr>
<tr>
<td>Grade III</td>
<td>17 (30.91)</td>
<td>18 (32.73)</td>
<td>0.042</td>
<td>0.838</td>
</tr>
<tr>
<td>Grade IV</td>
<td>9 (16.36)</td>
<td>11 (20.00)</td>
<td>0.244</td>
<td>0.621</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>College and above</td>
<td>19 (34.55)</td>
<td>17 (30.91)</td>
<td>0.165</td>
<td>0.684</td>
</tr>
<tr>
<td>Middle school</td>
<td>25 (45.45)</td>
<td>28 (50.91)</td>
<td>0.328</td>
<td>0.567</td>
</tr>
<tr>
<td>Primary school</td>
<td>11 (20.00)</td>
<td>10 (18.18)</td>
<td>0.059</td>
<td>0.808</td>
</tr>
<tr>
<td>Place of residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Urban area</td>
<td>24 (43.64)</td>
<td>22 (40.00)</td>
<td>0.149</td>
<td>0.699</td>
</tr>
<tr>
<td>Rural area</td>
<td>31 (56.36)</td>
<td>33 (60.00)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Comparison of clinical efficacy in both groups [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>Cured</th>
<th>Highly effective</th>
<th>Effective</th>
<th>Ineffective</th>
<th>Total effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>11 (20.00)</td>
<td>21 (38.18)</td>
<td>10 (18.18)</td>
<td>13 (23.64)</td>
<td>42 (76.36)</td>
</tr>
<tr>
<td>SG</td>
<td>16 (29.09)</td>
<td>26 (47.27)</td>
<td>9 (16.36)</td>
<td>4 (7.27)</td>
<td>51 (92.73)</td>
</tr>
</tbody>
</table>

χ² = 5.636, P-value = 0.018

Table 3: Comparison of cardiac function index in both groups (mean ± SD, n = 55)

<table>
<thead>
<tr>
<th>Group</th>
<th>LVESE (mm)</th>
<th>LVEDD (mm)</th>
<th>CI (L·min⁻¹·m⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>43.86 ± 3.67</td>
<td>50.96 ± 4.49</td>
<td>2.82 ± 0.30</td>
</tr>
<tr>
<td>SG</td>
<td>34.91 ± 3.95</td>
<td>46.07 ± 5.63</td>
<td>3.12 ± 0.24</td>
</tr>
<tr>
<td>t</td>
<td>12.318</td>
<td>5.038</td>
<td>5.788</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table 4: Comparison of levels of hemodynamic indices in both groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Fibrinogen (g/L)</th>
<th>Plasma viscosity (mPa·S)</th>
<th>Hematocrit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>4.58 ± 0.62</td>
<td>2.62 ± 0.51</td>
<td>42.76 ± 2.86</td>
</tr>
<tr>
<td>SG</td>
<td>3.32 ± 0.37</td>
<td>1.58 ± 0.30</td>
<td>43.51 ± 3.50</td>
</tr>
<tr>
<td>t</td>
<td>12.834</td>
<td>12.949</td>
<td>7.829</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD, n = 55

thrombosis, coronary artery vasospasm and coronary insufficiency, thereby resulting in myocardial ischemia and hypoxia. In addition, myocardial ischemia, hypoxia and abnormal electrical activity of cardiomyocytes are important pathological basis of CHD arrhythmia [9-11]. A vicious circle formed by CHD and arrhythmia aggravates the condition and increases mortality of patients. A study has found that CHD arrhythmia leads to hemodynamic changes and current fluctuation in myocardial cell membrane due to aggravated myocardial ischemia, resulting in depolarization and repolarization disorders in cardiomyocytes [12]. Moreover, it increases the myocardial dispersion of repolarization, reduces cardiac output, shortens cardiac diastolic time,
and endangers the health of patients, resulting in the occurrence of chest discomfort, shortness of breath, fatigue and palpitations.

There are several drugs for the treatment of CHD arrhythmia. These include β-blockers and Na⁺, K⁺ and Ca²⁺ channel blockers. Propafenone hydrochloride, an antiarrhythmic drug with broad spectrum, reduces influx rate of extracellular sodium ions in myocardial cells and slows down the speed of myocardial contraction. However, it affects negative myocardial force and decreases cardiac output, with good effect on overall treatment outcome [13]. Amiodarone hydrochloride is a broad-spectrum class III antiarrhythmic drug which prolongs the duration of action potential and QT interval mainly through its inhibitory effect on K⁺ and Ca²⁺ channels. Moreover, this drug weakens the structures and functions of atrioventricular and sinoatrial nodes, increases atrioventricular conduction time, and reduces heart rate, thereby exerting antiarrhythmic effect [14]. In addition, amiodarone hydrochloride reduces cardiac load and myocardial oxygen consumption, increases cardiac output, mitigates the clinical symptoms of patients with CHD and arrhythmia, and enhances clinical efficacy via its dilatory effect on coronary artery and peripheral vessel [15]. Potassium magnesium aspartate, when mixed with magnesium aspartate, forms potassium magnesium aspartate which provides an amino acid transporter with high affinity for cells and increases the concentration of potassium and magnesium ions in cells. Potassium magnesium aspartate promotes depolarization and metabolism in cells, maintains normal function and myocardial conduction force, improves myocardial systolic function, and reduces oxygen consumption and blood viscosity. A study has shown that amiodarone hydrochloride and potassium magnesium aspartate inhibit ventricular tachycardia and reduce cardiac injury, with a synergistic effect in the treatment of arrhythmia [16]. The results of the present study showed that the total effectiveness of treatment was higher in SG than in CG, indicating that coadministration of amiodarone hydrochloride and potassium magnesium aspartate produced a significant effect. The SG had lower levels of PVC, HR, LVESD and LVEDD, and higher QTc interval and CI level, when compared with CG. The reason for these effects is that amiodarone hydrochloride inhibits external fluid of K⁺ and prolongs the duration of myocardial action potential. Furthermore, it prolongs T wave, reduces torsade de pointes, inhibits atrioventricular node, slows down intraventricular conduction, and reduces disease progression. Potassium magnesium aspartate offsets the external fluid of potassium by increasing the concentration of potassium ions, thereby exerting a synergistic role with amiodarone. Besides, potassium magnesium aspartate prevents the excessive prolongation of QT interval and the occurrence of torsade de pointes through its lower degree of damage to liver and kidney. In addition, amiodarone hydrochloride tablets eliminate reentrant excitation, trigger automatically of heart rate, and influences ventricular conduction. Moreover, it does not cause negative inotropy; it produces a significant clinical effect and improves the cardiac function of patients.

The hemodynamics of patients with CHD and arrhythmia is very unstable. After the occurrence of CHD and arrhythmia, pathological changes in tissues and organs are aggravated. This enhances the formation of erythocytes in the kidney, affects hemodynamics, and increases hemoglobin content, number of erythrocytes and hematocrit content. Hematocrit is related to blood viscosity which reduces the effective perfusion of the cardiovascular system, aggravates myocardial ischemia and hypoxia, thereby forming a vicious circle [17]. It has been shown that amiodarone improves hemodynamics in CHD patients with arrhythmia [18]. The results of this study showed that fibrinogen, plasma viscosity and hematocrit were lower in SG than in CG, indicating that concurrent administration of amiodarone hydrochloride tablets and potassium magnesium aspartate improved hemodynamics in patients with CHD and arrhythmia. The reasons for this are that amiodarone hydrochloride tablets expand the coronary arteries, resulting in increased arterial blood flow, blocking of sodium channel, extension of drug half-life, and increased duration of drug action, thereby promoting coronary blood flow.

**CONCLUSION**

The findings of the present investigation show that the combined administration of amiodarone hydrochloride tablets and potassium magnesium aspartate in the treatment of CHD and arrhythmia in patients enhances clinical efficacy and improves electrocardiograph index, hemodynamics and cardiac function. Nonetheless, it is necessary to undertake further large multicenter clinical trials prior to application of this combined regimen in clinical practice.

**DECLARATIONS**

**Acknowledgements**

None provided.
**Funding**

None provided.

**Ethical approval**

This study was approved by the ethical authority of Jiaozhou Central Hospital of Qingdao (approval no. 20200413).

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Conflict of Interest**

No conflict of interest associated with this work.

**Contribution of Authors**

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Gongzhu Han and Yichun Mao designed the study and drafted the manuscript. Gongzhu Han, Hong Qiu and Yichun Mao were responsible for the collection and analysis of the experimental data. Yichun Mao revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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