BISOPROLOL COMBINED WITH AMIODARONE CAN IMPROVE THE LVEDD, LVDPD AND LVEF IN PATIENTS WITH ARRHYTHMIA

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ABSTRACT

Objective: *To analyse the effects of bisoprolol combined with amiodarone on cardiac function, haemodynamics and inflammatory factors in patients with arrhythmia.*

Methods: *A total of 116 patients with arrhythmia who were treated in our hospital from April 2017 to June 2019 were divided into the control group (n-60) and experimental group (n-56) according to different treatment methods. The control group was treated with bisoprolol. The initial dosage was 1.25-2.5 mg/d. The dosage was doubled 14 days later until the maximum tolerable dose (5-10 mg/d) was achieved. The experimental group was treated with amiodarone on the basis of the control group. The initial amiodarone was 200 mg three times a day for seven days, followed by 200 mg two times a day for seven days and then 200 mg one time a day, thereby gradually decreasing maintenance treatment. The clinical efficacy, adverse reactions and cardiac function indicators in the control and experimental groups [left ventricular ejection fraction (LVEF), left ventricular diastolic diameter (LLVEDD) and left ventricular posterior wall thickness (LVPWD)], haemodynamic parameters (plasma concentration, erythrocyte sedimentation rate, haematocrit and fibrinogen) and inflammatory factors [hypersensitive C-reactive protein (hs-CRP) and serum brain natriuretic peptide (BNP)] levels were compared between the control and experimental groups.*

Results: *The total effective rate was 89.29% in the experimental group and 73.33% in the control group, and there was a significant difference in the total effective rate between the two groups (P<0.05). Before treatment, there was no significant difference in the levels of LVEF, LVEDD and LVPWD between the control and experimental groups (P>0.05); after treatment, the levels of LVEDD and LVPWD in the control and experimental groups were significantly lower than those before treatment, and the levels of LVEF were significantly higher than those before treatment (P<0.05). Prior to treatment, there was no significant difference in haemodynamic parameters between the two groups (P>0.05). After treatment, the levels of fibrinogen, erythrocyte sedimentation rate, haematocrit and plasma viscosity in the two groups were significantly lower than those before treatment, and the levels of fibrinogen, erythrocyte sedimentation rate, haematocrit and plasma viscosity in the experimental group were significantly lower than those in the control group (P<0.05). Prior to treatment, there was no significant difference in the levels of hs-CRP and BNP between the two groups (P>0.05); after treatment, the levels of hs-CRP and BNP in the two groups were lower than those before treatment, and the levels of hs-CRP and BNP in the experimental group were significantly lower than those in the control group (P<0.05). Moreover, the patients had better tolerance to amiodarone, and no thyroid dysfunction occurred after treatment. Further, there was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). Over the course of treatment, there were mild adverse reactions, such as blood pressure drop, nausea, vomiting and dizziness in both groups.*

Conclusion: *Bisoprolol combined with amiodarone can effectively relieve clinical symptoms, reduce adverse reactions, improve haemodynamics, inhibit inflammation and reduce the variability of arrhythmia in patients with arrhythmia while featuring high safety and obvious effects.*

Keywords: *Bisoprolol, amiodarone, arrhythmia, cardiac function indicators, haemodynamics, inflammatory factors.*

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Introduction

Arrhythmia is common in clinical treatment. Cardiovascular diseases mainly refer to abnormal heart impulse conduction, origin, frequency and rhythm[1]. The incidence of arrhythmia is gradually increasing. According to clinical manifestations, patients can be divided into ventricular flutter, fibrillation, premature ventricular beats and ventricular tachycardia[2]. Clinical studies have shown that hypertension, coronary heart disease and other organic diseases can lead to arrhythmia, seriously affecting the daily lives of patients, and even endangering their health[3]. At present, there are many kinds of drugs for arrhythmia in clinical treatment, and although they have certain effects, most have poor compre-

hensive treatment effects[4]. Therefore, finding a method that can effectively improve the therapeutic effect and enhance cardiac function and prognosis of patients is a hot research topic for clinical workers. Bisoprolol is a β1 blocker with high selectivity, definite curative effects, a long half-life and few adverse reactions. It can be used alone or in combination with other drugs. It has been widely employed in clinical treatment[5]. Meanwhile, amiodarone is a common antiarrhythmic drug. It plays an important role in adjusting myocardial ischemia and alleviating cardiac load, and has robust therapeutic effect. However, there are few reports about the combination of the two drugs in the treatment of arrhythmia. Thus, this study applied bisoprolol combined with amiodarone to treat arrhythmia patients in order to explore the impacts of the combination of the two drugs on cardiac function indicators, haemodynamics and inflammatory factors.

Materials and methods

General information

A total of 116 patients with arrhythmia who came to our hospital from March 2017 to May 2019 were selected.

The criteria for admission were as follows:

• They all met the diagnostic criteria of arrhythmia in the 8th edition of Internal Medicine;

• They all had typical manifestations of arrhythmia, such as panic, precordial discomfort and palpitation;

• They were diagnosed as arrhythmia by routine electrocardiogram examination.

Exclusion criteria:

• Sick sinus syndrome and slow arrhythmia, such as atrioventricular block, sinoatrial block, severe bradycardia, etc. above degree II;

• Organ dysfunction of liver and kidney;

• Chronic pulmonary diseases and acid-base disorders, such as hypothyroidism or hyperthyroidism;

• Ventricular and electrolyte disorders caused by drug poisoning.

According to various treatment methods, they were divided into a control group (n = 60) and an experimental group (n = 56). In the control group, there were 26 females and 34 males, aged 56~78 years, with an average course of disease of (67.58±3.59) years, and 3.01-5.10 years, with an average course of disease of (4.03±0.31) years.

In the experimental group, there were 27 females and 29 males, aged 55-76 years, with an average age of (67.0±3.58) years, and the course of disease was 2.90-5.01 years, with an average age of (4.03±0.34) years. There was no significant difference in gender, age or course of disease between the two groups.

Method

The patients in the control group were treated with bisoprolol (specification: 2.5mg J20170042 produced by German Merck Company), the initial dose was 1.25-2.5mg/d, and the dose was doubled after 14 days until the maximum tolerable dose was 5-10 mg/d. The patients in the experimental group were treated with amiodarone (specification: 0.2 g standard Chinese medicine H19993254 competition) on the basis of the control group. The initial amiodarone load was 200 mg three times a day for seven days, followed by 200 mg two times a day for seven days and then 200 mg one time a day for seven days. Angiotensin-converting enzyme inhibitors, diuretics, cardiac tonics and other commonly used drugs were employed in the two groups at the same time. The patients were followed up for 90 days (5).

Observation indicators

• To compare the clinical efficacy of the two groups after treatment[6] - significant effect: clinical symptoms, such as palpitation and precordial discomfort, disappeared completely, and the number of ventricular arrhythmias decreased by more than 90%; effective: clinical symptoms, such as palpitation and precordial discomfort, were improved, and the number of ventricular arrhythmias decreased by 50%-89%; ineffective: clinical symptoms of patients; the improvement was not obvious, and the number of arrhythmias decreased by less than 50%. Total effective rate = (significant cases + effective cases)/total cases *100%.

• The changes of left ventricular posterior wall thickness (LVPWd), left ventricular ejection fraction (LVEF) and left ventricular end diastolic diameter (LVEDD) were measured by Doppler echocardiography before and after treatment in both groups.

• To compare the changes of haemodynamic indexes between the two groups before and after treatment. Four millilitres of peripheral venous blood were extracted from patients before and 14 days after treatment. Serum was separated after centrifugation and stored in a refrigerator at -45oC for detection. Non-invasive haemodynamic detector was used to detect plasma concentration, erythrocyte sedimentation rate, haematocrit, blood cell specific volume

and blood cell volume. Change in fibrinogen levels and operation methods were in strict accordance with the literature[7].

• The levels of inflammatory factors in the two groups were compared before and after treatment. The levels of hs-CRP and BNP in serum were detected by enzyme-linked immunosorbent assay.

• Observe the incidence of nausea, vomiting, dizziness and other adverse reactions in the two groups.

Statistical method

The Statistical Package for the Social Sciences (SPSS; IBM, Chicago, USA) v.19.0 software was applied to analyse the data, haemodynamics and other measurements were expressed by (x±s; t-testing was used) and counting data was expressed by [n (%)]; χ^2 testing was used). Grade data were compared by Ridit analysis; P<0.05 was considered significant.

Results

Comparison of clinical efficacy between two groups

The total effective rate of the experimental group was 89.29%, and that of the control group was 73.33%. There was a significant difference in the total effective rate of each group (P<0.05), as shown in Table 1.

Group	n	Significant effect (%)	Effective (%)	Ineffective (%)	Total effective rate (%)
Experiment group	60	15 (25.00)	29 (48.33)	16 (23.33)	73.33
Control group	56	13 (23.21)	37 (66.07)	6 (10.71)	89.29
χ^2					4.796
P					0.029

Table 1: Comparison of clinical efficacy between the experimental and control groups [n (%)].

Comparison of cardiac function between two groups

Before treatment, there was no significant difference in the levels of LVPWD, LVEDD and LVPWD between the control and experimental groups (P>0.05); after treatment, the levels of LVPWD and LVEDD in the control and experimental groups were significantly lower than those in the control group, and the levels of LVEF were significantly higher than those before treatment (P<0.05); and the levels of LVPWD and LVEDD in the experimental group were significantly lower than those in the control group and the level of LVEF. Overall, the experimental group was higher for all measured parameters that the control group (P<0.05; see Table 2).

Group	Time	LVEDD (mm)	LVEF (%)	LVPWD (mm)
Control group (n=60)	Before treatment	69.36±9.69	33.64±5.63	17.16±2.74
	After treatment	61.35±6.63*	37.23±4.61*	13.24±2.13*
Experimental group (n=56)	Before treatment	69.34±10.16	33.43±4.39	17.23±3.09
	After treatment	53.01±5.81*#	43.63±3.76*#	11.31±2.54*#

Table 2: Comparison of cardiac function between the experimental and control groups (x±s).
*Note: Compared with before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.*

Comparison of haemodynamics between two groups

Before treatment, there was no significant difference in haemodynamic parameters between the two groups (P>0.05). After treatment, the levels of fibrinogen, erythrocyte sedimentation rate, haematocrit and plasma viscosity in the two groups were significantly lower than those before treatment, and the levels of fibrinogen, erythrocyte sedimentation rate, haematocrit and plasma viscosity in the experimental group were significantly lower than those before treatment. Overall, the levels of the experimental group were significantly lower than those of the control group (P<0.05; see Table 3).

Group	Cases	Erythrocyte sedimentation rate (mm/h)		Fibrinogen (g/L)		Plasma viscosity (mPa. s)		Haematocrit (fl)	
		BT	AT	BT	AT	BT	AT	BT	AT
Experimental group	56	23.67 ±4.15	13.17 ±2.16*	125.59 ±20.14	23.57 ±4.11*	125.57 ±20.14	13.30 ±2.16*	48.22 ±6.13	30.24 ±4.14*
Control group	60	23.48 ±3.62	16.87 ±2.60*	125.90 ±21.01	35.57 ±3.55*	125.9 ±21.03	16.79 ±2.60*	48.51 ±5.27	37.50 ±5.15*
t		0.166	8.462	0.081	15.624	0.086	7.833	0.279	8.331
p		0.868	<0.001	0.936	<0.001	0.932	<0.001	0.785	<0.001

Table 3: Comparison of haemodynamics between two groups ($\bar{x}$±s).
*Note: BT: Before treatment; AT: After treatment; Compared with before treatment, *P<0.05.*

Comparison of serum inflammatory factors

Before treatment, there was no significant difference in the levels of hs-CRP and BNP between the two groups (P>0.05); after treatment, the levels of hs-CRP and BNP in the two groups were lower than those before treatment, and the levels of hs-CRP and BNP in the experimental group were significantly lower than those in the control group (P<0.05; see Table 4).

Group	n	hs-CRP (md/L)		t	P	BNP (mg/L)		t	P
		BT	AT			BT	AT		
Experimental group	60	20.54 ±2.62	11.43 ±1.52	23.297	0.000	533.84 ±67.56	214.53 ±27.56	33.898	<0.001
Control group	56	19.91 ±2.51	8.36 ±1.12	31.446	0.000	531.62 ±66.89	167.63 ±21.43	38.779	<0.001
t		1.321	12.312			0.178	10.181		
P		0.189	0			0.859	0		

Table 4: Comparison of serum inflammatory factors between the experimental and control groups ($\bar{x}\pm s$).
Note: BT: Before treatment; AT: After treatment.

Comparison of adverse reactions

The patients tolerated amiodarone well, and no thyroid dysfunction occurred after administration. There was no significant differences in the incidence of adverse reactions between the two groups (P>0.05; see Table 5).

Group	Cases	Mild dizziness	Nausea, vomiting	Blood pressure drop	Total
Experimental group	56	3 (5.36)	2 (3.57)	2 (3.57)	7 (12.50)
Control group	60	4 (6.67)	6 (10.00)	5 (8.33)	15 (25.00)
c^2					2.945
P					0.086

Table 5: Comparison of adverse reactions between the experimental and control groups [n (%)].

Discussion

Studies have shown that arrhythmia is a common cardiovascular disease[8]. The main causes include chronic functional failure, coronary heart disease and acute myocardial infarction, which can lead to chest tightness, palpitation and dizziness, seriously affecting the normal quality of life of patients and threatening their health[9]. Research surveys have shown that the incidence of arrhythmia is increasing year by year. Although the clinical key can improve the patient's condition to a certain extent, treatment effects have not achieved the expected impact[10]. Therefore, it is crucial to choose a safe and effective antiarrhythmic drug that can stabilize the heart rate and improve the clinical symptoms of patients.

Clinical studies have indicated that β blockers can effectively regulate heart rhythm, and about 70% of patients achieve the desired results[11]. Bisoprolol is a highly selective receptor blocker of the β1 adrenal gland. The cardiac β1 receptor inhibits agonism, maintains robust adhesion in vascular tissue, improves heart function, lowers heart rate and regulates β receptor density. In addition, bisoprolol can also diminish damage to the heart caused by catecholamines in the systemic circulation, and myocardial ischemia can be improved. The β receptor can be blocked by amiodarone, does not cause negative inotropic effects and plays an important role in accelerating heart rate self-discipline, triggering activity and reentry agonism. At the same time, ventricular conduction will not be eliminated. It can also play an effective role in anti-fibrillation, improve the clinical therapeutic effect, improve patients' cardiac function and reduce the incidence of adverse reactions. The combined use of drugs can increase myocardial oxygen tolerance, inhibit platelet aggregation, improve hypoxic capacity and myocardial metabolism, reduce blood lipid levels, inhibit Ca^{2+} influx of myocardial cells, regulate autonomic nervous function, reduce cell autonomy, improve microcirculation and so on. It also has a strong regulating effect on the arrhythmia of each group.

Amiodarone is an antiarrhythmic drug that can prolong the action potential and effective refractory period of atrial muscle, ventricular muscle and the atrioventricular node. Its antagonism to α and β receptors is non-competitive. With this, amiodarone can inhibit calcium influx in slow-response cells, regulate energy metabolism in ischemic myocardium cells, reduce phospholipid damage in ischemic myocardium, and protect organelles and cells. It features prominently in abolishing oxygen free radicals, resisting lipid peroxidation and myocardial ischemia[12]. However, amiodarone has many characteristics, such as high dosage and slow onset, leading to unsatisfactory effects. The results showed that the total effective rate of the experimental group was 89.29%, while that of the control group was 73.33%. There was a significant difference in the total effective rate of each group (P<0.05). It is suggested that the combination of the two drugs can effectively decrease ventricular tachycardia, ventricular premature and paired ventricular premature, while also reducing the probability of arrhythmia, and the effect is better than that of bisoprolol alone.

Studies have found that the severity of arrhythmia is related to the expression level of inflammatory factors. The higher the expression level of inflammatory factors, the more serious the arrhythmia is[13]. Hs-CRP is one of the most common inflammatory factors. Its importance index can reflect the activity and existence of inflammatory reactions, induce the secretion of inflammatory transmitters on the surface

of vascular endothelial cells, cause local thrombosis, raise the incidence of adverse cardiovascular events and then lead to plaque rupture. BNP is a cardiovascular regulatory peptide with the function of diuresis and sodium excretion. Clinical studies have shown that the abnormal increase of BNP levels can be caused by the damage of cardiac function[14]. The results showed that the levels of hs-CRP and BNP in the experimental group were significantly lower than those in the control group ($P<0.05$). It is suggested that the combination of the two drugs can diminish the inflammatory reactions of patients.

Arrhythmia can lead to the difficulty of simultaneous contraction of ventricular muscles and an abnormal contraction sequence of atrioventricles, leading to changes in haemodynamics. Elevated plasma-specific viscosity results in aggregation of plasma macromolecules around erythrocytes, which can synthesize network structure, increase haematocrit, cause stagnation of blood perfusion and ultimately result in insufficient blood supply[15]. The high concentration of plasma fibrinogen can accelerate the development of atherosclerotic plaques and narrowing of the lumen while increasing the risk of coronary heart disease and cerebrovascular disease. The results showed that the levels of fibrinogen, erythrocyte sedimentation rate, haematocrit and plasma viscosity in the experimental group were significantly lower than those in the control group ($P<0.05$). It is suggested that the combination of the two drugs can improve the haemodynamic indexes of patients with arrhythmia. In conclusion, bisoprolol combined with amiodarone can effectively alleviate clinical symptoms, reduce adverse reactions, improve haemodynamics, inhibit inflammation and reduce the variability of arrhythmia in patients with arrhythmia. Moreover, the combination is safe and obviously effective.

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