Clinical Observation on Effects of Xinkeshu Tablets on Patients with Frequent Premature Beats

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ABSTRACT Objective: To investigate the effects of Xinkeshu tablets on patients with frequent premature beats. Methods: Ninety-six patients with frequent premature beats were randomly divided into the experimental group (51 cases) and the control group (45 cases). The patients in control group took Betaloc (Astrazenca Ltd.) 47.5mg per day and the patients in the experimental group took Xinkeshu tablets(Shandong Wohua Pharmaceutical Co., Ltd.) 4 tablets three times a day and Betaloc 47.5mg per day. Holter and general electrocardiogram (ECG) checks were lined before taking the medication and a month after taking it respectively, and its clinical therapeutic effects were observed. Results: It is more effective ($P<0.05$) in the elimination of premature beats and the improvement of the clinical symptoms and HRV in the experimental group compared with the control group. Conclusions: The combination of Xinkeshu tablets and Betaloc can effectively increase the role of Betaloc in treating premature beats, while improving heart rate variability and relieving the side effect of sinus bradycardia caused by Betaloc sustained-release tablets.

Key words: Xinkeshu tablets; Betaloc; Premature beats; HRV

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Introduction

Premature beat is a kind of common arrhythmia clinically, the causes of which are organic or functional. The clinical manifestations include palpitation, chest tightness, shortness of breath and fatigue, etc. If severely, the premature beat can disturb daily work and life, even threaten life. Although the western medicine is effective, there were defects like side effects, poor efficacy and poor patient compliance. Clinically, we observed that the traditional Chinese medicine Xinkeshu tablet is effective on premature beats. To verify the efficacy of Xinkeshu tablets, this study applied Xinkeshu tablets plus Betaloc sustained-release tablets to 96 patients with frequent premature beats.

1 Data and Methods

1.1 General data

96 outpatients with frequent premature beats (including patients with atrial premature beats, ventricular premature beats and some with paroxysmal atrail premature beats) were chosen. There were 54 males and 42 females with the average age of (48.5±12.1). They were randomly divided into the experimental group (51 cases) and the control group (45 cases). Inclusion criteria: the premature beats are more than 30 per hour on the Holter. Exclusion criteria: cases with sick sinus syndrome, high-degreed atrioventricular block, sinus bradycardia, digitalis toxicity, electrolytes imbalance, acute myocardial infarction, unstable angina pectoris and renal damage etc.

1.2 Therapeutic methods

All patients stopped taking antiarrhythmic drugs for 5 half lives. The patients in control group took Betaloc 47.5mg per day and the patients in the experimental group took Xinkeshu 4 tablets three times a day and Betaloc 47.5mg per day. Both of the treatment last for 4 weeks.

1.3 Outcome measures

1.3.1 The effects of the medication on improving premature beats The improvements of premature beats were detected by monitoring the Holter before and after taking the medication. Clinical standards (the guiding lines of clinical researches on the treatment of palpitation with Chinese and new medicines issued by Ministry of Health in 1995[1]): (1) markedly effective: The number of premature beats after treatment reduces more than 90% compared to the number before treatment; (2) effective: The number of premature beats after treatment reduces more than 50% compared to the number before treatment; (3) ineffective: The number of premature beats after treatment reduces less than 50%, remains unchanged or increases compared to the number before treatment.

1.3.2 The analysis of HRV According to the methods set by the National Cooperative Group of HRV of Chinese Medical Association [2], the HRV parameters in the Holter before the treatment and four weeks after the treatment were recorded by the Holter and HRV analysis software. The time-domain parameters (unit: ms) give 24 hours assessment for cardiac autonomic function, including the standard deviation of successive RR intervals (SDNN), the standard deviation of intervals in all-5minute segments (SDANN). The frequency domain analysis of HRV takes 5 minutes parameters, including the high frequency (HF) and low frequency (LF). Frequency domain analysis were done by using Fast Fourier Transform for patients who are required to be in a supine position

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quietly from 9 to 11.

1.3.3 The analysis of the changes of premature beats The total numbers of premature beats, the numbers of paroxysmal tachycardia and the average heart rates before the treatment and 4 weeks after the treatment were recorded by lining Holter.

1.4 Statistical analysis

All measurement data were represented with ($\overline{X}\pm$ S). The paired t test was used. The measurement data were represented with rate using chi-square test. P<0.05 was considered statistically significant. All data were processed with the statistical software SPSS17.0

2 Results

2.1 The comparison of the clinical treatment in improving premature beats between the two groups

The combination of Xinkeshu tablets and Betaloc sustained-release tablets in the experimental group can improve premature beats than that in the control group. It is statistically significant in comparison with each other(P<0.05)(Table1).

Table1 Comparison of the efficacy between the two groups in the improvement of premature beats

Groups	Cases	Markedly effective(%)	Effective(%)	Ineffective(%)	The total active(%)
Experimental group	51	24(47.1)	16(31.4)	11(21.5)	78.5 *
Control group	45	13(28.9)	9(20.0)	23(51.1)	48.9

P.S.* in comparison with the control group, P<0.05

2.2 The comparison of the parameters of HRV between the two groups

The improvement of HRV in the experimental group was more significant than that in the control group. It was statistically significant(P<0.05)(Table2).

Table 2 The comparison of the parameters of HRV between the two groups before and after the treatment($\overline{X}\pm$ S)

Groups	n		SDNN(ms)	SDANN(ms)	LF(ms^2)	HF(ms^2)
Control group	45	Before treatment	136.1± 41.0	130.9± 44.7	385.3± 188.1	256.6± 150.9
		After treatment	145.1± 54.9	133.9± 29.9	356.8± 145.2	223.1± 117.2
Experimental group	51	Before treatment	172.4± 54.5	136.3± 41.2	299.5± 102.7	259.1± 54.1
		After treatment	194.9± 51.1*△	164.2± 36.9*△	270.9± 98.6*△	278.7± 58.0*△

P.S. * in comparison with the parameter before the treatment P<0.05; in comparison with the control group, P<0.05

2.3 The comparison of the changes of premature beats between the two groups before and after the treatment

The total numbers of premature beats in 24h, the numbers of paroxysmal tachycardia and the average heart rates when premature beats broke out in the experimental group declined compared with those in the control group. It was statistically significant(P<0.05)(Table3).

Table 3 The comparison of the changes of premature beats between the two groups before and after the treatment ($\overline{X}\pm$ S)

Groups beats(/24h)	n		total numbers of premature paroxysmal tachycardia	the numbers of the average heart rates	the average heart rates
control group	45	before treatment	6123.9± 1890.9	9.6± 2.2	97.0± 12.2
		after treatment	5209.5± 1713.6	11.6± 12.3	89.7± 11.9
Experimental group	51	before treatment	6376.4± 3390.4	9.4± 3.4	90.7± 16.9
		after treatment	3552.1± 2814.1*△	4.2± 2.3*△	60.2± 17.8*△

P.S. * in comparison with the parameter before the treatment P<0.05, △ in comparison with the control group, P<0.05

3 Discussions

Premature beat is a kind of common arrhythmia clinically. According to the original site of the premature beat, it can be classified as sinus, atrial, atrioventricular junction and ventricular premature beat. The therapeutic measures of arrhythmia included relieving clinical manifestations improving the long-term prognosis of patients, preventing vicious arrhythmia and sudden cardiac death. In addition to etiological treatment, there were still drug treatment and non-drug treatment. However, anti-arrhythmic drugs react through changing electrophysiological properties such as conducting velocity, refractory periods and the like in the myocar-

dial lesion, not damaging the pathological tissues causing arrhythmia. There were so many side effects to different degrees, even severe arrhythmia as ventricular arrhythmia and heart block which endanger people's lives [3], if anti-arrhythmic drugs are used for a long time. At the present time, Betaloc, a kind of β -receptor blocker, which has a direct role in myocardial electrophysiology is usually used to treat the disease, through slowing heart rates, inhibiting the automaticity of ectopic pacemakers, decreasing conductivity and extending the refractory periods of atrioventricular node. Betaloc can increase the threshold of ventricular fibrillation and improve baroreflex to prevent the incidence of hypokalemia led by catecholamines through decreasing the activity of sympathetic nerves and resisting myocardial ischemia. At the same time, it is unsatisfied to treat premature beats by using western medicine Betaloc alone. If combined with Xinkeshu, Betaloc is more effective in treating the disease. This study indicated that the total effective of the experimental group was better than that in the control. Moreover, the numbers of total premature beats in 24h, the numbers of paroxysmal tachycardia and the average heart rates when premature beats broke out decreased. It is statistically significant ($P<0.05$), indicating that Xinkeshu had a better efficacy in treating premature beats.

HRV analysis is presently recognized as a good method of checking and evacuating cardiac autonomous nerve function and the dynamic activities of heart noninvasively [4-6]. The time-domain parameters of HRV, SDNN, SDANN, reflect the tension of sympathetic nerve. The frequency-domain parameters LF is both influenced by sympathetic nerves and vagus nerves [7,8], and HF is only affected by vagus nerves [9]. Currently, it is commonly considered that the increasing of QT dispersion (QTd) is due to the heterogeneity of ventricular repolarization caused by various reasons[10,11]. It has been verified in clinical and animal experiments that the increase of ventricular repolarization dispersion is the basis of certain ventricular arrhythmia [12]. Most scholars consider that the extension of QTd is related to vicious ventricular arrhythmias. Autonomic nervous system disorders are key factors to inducing ventricular arrhythmias, even leading sudden death [13]. Xinkeshu is a kind of pure Chinese medicine used to prompt blood circulation and heart nutrition which is composed of Salia[14], Panax[15], puerarin, wood, hawthorn [16] and so on. Salvia, Panax are effective in prompting blood circulation and relieving pain. Puerarin helps to supplement Qi, promote the production of body fluids and invigorate heart. Wood can rationalize Qi and break out the congestion. Hawthorn is beneficial to protect the spleen, promote blood circulation and lower lipids. All of these Chinese medicines play a role in prompting Qi, eliminate congestion and invigorate heart. It is evident that puerarin can improve the long-time parameters of HRV comprehensively. Chinese medicine basic research also proved that Panax had an effect on inhibiting the electrical restructuring of the damaged myocardium of rats. The results of the research indicated that the parameters of HRV, SDNN, SDANN, HF and average sinus heart rates increased in the experimental group and that LF, QTd and QTcd decreased. It is statistically significant ($P<0.05$). The research suggests Xinkeshu can regulate autonomic nerves in a two-way adjustment, improve the HRV of the patients, decrease QT dispersion and further lower the incidence of vicious arrhythmias[17].

In conclusion, Xinkeshu[18-20] has a good effect on treating patients with frequent premature beats. It can regulate autonomic nerves in a two-way adjustment, correct the imbalance of autonomic nerves, and improve HRV. And there are fewer side effects, so it is a good way in treating the disease and worth popularization.

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心可舒治疗频发早搏疗效观察

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摘要 **目的**:应用心率变异性的方法观察心可舒片对早搏的治疗效果及其影响。**方法**:将 96 例频发早搏患者随机分成治疗组(51例)和对照组(45 例)。对照组给予倍他乐克缓释片口服,47.5mg/ 次,1 次 / 日,治疗组在口服倍他乐克缓释片基础上加用心可舒片 4 片 / 次,3 次 / 日。在服药前及服药后 1 个月各行 1 次动态心电图及普通心电图检查,并进行临床观察。**结果**:治疗组在消除早搏,改善临床症状方面较对照组明显有效(P<0.05),治疗组较对照组心率变异性改善有明显差异(P<0.05)。**结论**:心可舒片与倍他乐克合用可有效增加其治疗早搏的作用,同时改善心率变异性和改善倍他乐克引起的窦性心动过缓副作用,有较好的临床疗效。

关键词:心可舒;倍他乐克;早搏;心率变异性
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