

Research Progress in the Treatment of Bradyarrhythmia with Traditional Chinese and Western Medicine

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Abstract: Bradyarrhythmia is a prevalent cardiovascular condition characterized by a slow heart rate, has a multifaceted etiology that involves intricate biological mechanisms. The contemporary therapeutic strategies employed in Western medicine primarily consist of the administration of oral medications and the implementation of pacemaker therapy. However, these approaches are often accompanied by adverse drug reactions. Additionally, the high costs associated with pacemaker treatments can be prohibitive for many individuals, leading to reduced patient compliance and acceptance. In light of these reasons, it becomes imperative to explore alternative therapeutic modalities. Traditional Chinese medicine has accumulated rich experience in long-term clinical practice and has many unique advantages, such as fewer adverse reactions and lower cost. Consequently, this article aims to provide a comprehensive review of the research progress made in the field of traditional Chinese medicine as it pertains to the treatment of bradyarrhythmia. The intention is to offer clinicians a broader array of treatment options that may enhance patient outcomes and satisfaction.

1. Introduction

Bradyarrhythmia (BA) refers to a cardiovascular disease in which the formation or conduction of impulses originating from the sinus node is affected by a variety of reasons, and the heart rate is lower than normal due to the impact of atrioventricular conduction. At present, with the development of the aging population, the incidence of BA and the application of pacemakers continue to increase slowly^[1], which gradually attracts more attention and due to treatment. The limitations of the means, it is necessary to find another practical and effective treatment, for BA, although the name of the disease is not recorded in the classics of traditional Chinese medicine, but according to its clinical manifestations, it is not difficult to find. Many doctors in the past dynasties have discussed the disease, and the treatment of Chinese medicine is mainly oral decoction, and can be supplemented by acupuncture, acupuncture and other external treatment methods of traditional Chinese medicine. It has a certain therapeutic effect. Moreover, traditional Chinese medicine has low prices, minimal toxic side effects, and can be used for a long time, making it an effective supplementary treatment for BA.

2. Pathogenesis of BA

2.1. Degenerative changes in the conduction system

As an important component of the cardiac conduction system, the sinus node produces and conducts excitation. Studies have shown that advanced age and a variety of cardiovascular risk factors such as obesity, hypertension, diabetes mellitus and so on affect the function of the cardiac conduction system, especially the infiltration of degenerative idiopathic fibrosis in the sinus node, the increase of collagen fiber connective tissue in the sinus node, and the decrease in the number of cardiac pacemaker cells, resulting in physiological pacing function or conduction dysfunction of the sinus node, resulting in the occurrence of sinus bradyarrhythmia^[2].

2.2. Abnormal autonomic nervous system function

The vagus nerve works with the sympathetic nerve to maintain cardiovascular homeostasis and control cardiac electrophysiological activities, which is closely related to the occurrence of BA. Postganglionic fibers release norepinephrine and β receptors, which, after binding to Gs proteins, promote the conversion of ATP to cAMP, activate protein kinase A and channel proteins, increase Ca^{2+} influx, accelerate atrioventricular conduction velocity, and increase heart rate. In contrast, when the sympathetic nerve is suppressed, norepinephrine release increases, Ca^{2+} influx decreases, and myocardial conduction is blocked, which slows the heart rate^[3]. Acetylcholine, released by postganglionic fibers, mainly binds to M2 receptors on cardiomyocytes and exerts an effect to delay atrioventricular conduction velocity and slow down heart rate^[4]. Therefore, when the vagus nerve is abnormally excited, it can cause sinus bradycardia, atrioventricular block, etc., and cause a drop in blood pressure, cerebral hypoxia, and even vasovagal syncope^[5].

2.3. Abnormal myocardial ion channel function

The proper functioning of the heart depends on the production and distribution of cardiomyocyte action potentials. By regulating the opening and closing of ion channels, myocardial ion channels participate in the exchange of multiple ions on both sides of the membrane, and regulate the concentration of calcium, potassium, sodium and other ions in cells, thereby triggering cardiac electrophysiological responses and maintaining normal cardiac electrical activity. Aberrant expression or dysfunction of myocardial ion channel expression may be a cause of arrhythmias^[6]. Genetic studies have shown that genetic defects or mutations are often the main cause of hereditary BA^[7]; These include sodium channel-related genes, calcium channel-related genes, etc.

3. Study of traditional Chinese medicine in BA

Ancient Chinese medical practitioners did not record the name of bradycardia, but based on specific clinical symptoms and pulse conditions, it can be classified as "palpitations" and "slow pulse syndrome" in traditional Chinese medicine. Traditional Chinese medicine has a long history of treating BA and has significant curative effects^[8], and many doctors in the past generations have discussed the etiology and pathogenesis of BA have their own unique understanding, and the treatment methods and drugs also vary from person to person. Compound preparations are mainly used in TCM treatment, which have the advantages of scientific formulation, clear efficacy and few adverse reactions, but there are still some shortcomings, such as long course of treatment, slow onset of effect and other related problems. Although there are many shortcomings, TCM treatment is still an effective means to treat BA.

There are many causes of BA, but through the induction and analysis of traditional Chinese medicine classics and literature, it is found that its main causes often include congenital deficiencies, post illness body deficiency, and imbalance of work and rest. The main site of the disease is in the heart, followed by close relationships with organs such as the liver, spleen, stomach, and kidneys. Although BA has various causes, its pathological changes always belong to the principle of deficiency and excess syndrome. This deficiency is caused by insufficient yin and yang in the heart, kidney, spleen, qi and blood, loss of nourishment in the heart and pulse, inability to fill the blood vessels, weak agitation, and loss of continuity in the pulse and qi; Evil is actually caused by blood stasis, qi stagnation, phlegm turbidity, cold dampness, and the interweaving of phlegm and blood stasis, as well as the accumulation of turbid and toxic substances, leading to poor circulation of the meridians, blocked heart vessels, and abnormal pulse circulation^[9].

Boli Zhang^[10] proposed that the rise and fall of heart qi is directly related to the circulation of qi and blood and the heartbeat. The main pathogenesis of this disease is insufficient heart qi. Qi deficiency leads to blood stagnation, and poor qi and blood flow, resulting in weak heartbeat and slow arrhythmia. Zhongmin Wei^[11] advocated that this disease should start from three aspects: cold pathogenic factors, deficiency and decline, and blood stasis. Due to innate deficiencies, deficiency of body yang and kidney yang can lead to deficiency caused by cold and blood stasis caused by deficiency, ultimately resulting in phlegm turbidity, water retention, and blood stasis obstruction.

4. Treatment progress

4.1. Western medicine treatment

At present, the treatment of BA mainly includes etiology-specific treatment, anti-arrhythmic therapy and cardiac pacing therapy. Usually, asymptomatic sinus bradycardia does not require special treatment. However, if the patient is bradycardia with significant hemodynamic changes, such as dizziness, blurred vision, and difficulty breathing, drug therapy is indicated. In patients with sinus arrest who do not resolve symptoms and do not return to normal heart rate after the cause has been eliminated, pacemaker implantation may improve quality of life and reduce mortality^[12].

Commonly used drug types include anticholinergic drugs, adenosine receptor antagonists, etc., such as atropine, aminophylline. Atropine increases heart rate by blocking the M2 receptor of the sinus node and eliminating cardiac vagal inhibition, and increases ventricular rate in patients with atrial fibrillation or atrial flutter by inhibiting the effective refractory period of the sinus node^[13]. However, atropine may produce various adverse reactions when used for a long time, such as difficulty urinating, blurred vision, etc.; If taken in excess, irritability, fever and dry mouth, or central symptoms such as delirium, hallucinations, and even more severe bradycardia may occur. Aminophylline enhances the self-regulation function of the sinus node, accelerates conduction, increases heart rate in patients with sick sinus syndrome, and reduces the duration of sinus arrest^[14,15]. Aminophylline also has many adverse reactions such as nausea, vomiting, etc., and even dyspnea and cardiac arrest in severe cases. It is not difficult to find that the Western medicine treatment for BA mainly increases heart rate, but it cannot be used as a long-term medication due to its adverse reactions.

In addition to drug therapy, pacemaker therapy is also one of the main ways to treat patients with arrhythmias, pacemakers use microelectronic technology to replicate the natural physiological processes of electrical excitation and conduction of the heart. External cardiomyocytes are stimulated locally for short or continuous purposes by means of low-energy pulses. These stimuli are transmitted to the surrounding myocardium through the gap junction between the myocardial cells and the intercalary disc junction, allowing the atria or ventricles to contract and relax regularly, ensuring adequate blood output for effective treatment of BA. But currently, pacemakers still have

shortcomings such as voltage instability and short-lived battery life.

4.2. Traditional Chinese medicine treatment

4.2.1. Syndrome differentiation and treatment of Chinese decoction medicine

At present, there is no unified standard for the traditional Chinese medicine syndrome differentiation and typing of bradycardia. The book "Integrated Traditional Chinese and Western Medicine Internal Medicine"^[16] divides bradycardia into five types of syndromes, namely heart yang deficiency syndrome, heart kidney yang deficiency syndrome, qi yin deficiency syndrome, phlegm turbidity obstruction syndrome, and heart meridian obstruction syndrome. Xia Li^[17] analyzed multiple traditional Chinese medicine treatment formulas in recent years through statistical methods and found that the main syndrome types of this disease are heart kidney yang deficiency, heart yang deficiency, heart blood stasis, and qi yin deficiency. And the main medicinal formulas include tonifying herbs, warming herbs, promoting blood circulation and removing blood stasis herbs, regulating qi herbs, etc. Commonly used formulas include Shenfu decoction, Mahuang Fuzi Xixin decoction, Shengmai decoction, etc. This study mainly focuses on warming Yang and replenishing qi, treating with syndrome differentiation and flexible use of treatment methods.

4.2.2. Chinese patent drug

Commonly used oral traditional Chinese patent medicines and simple preparations includes Shensong Yangxin Capsule, Xinbao Pill, etc. Shensong Yangxin Capsules are based on Shengmai decoction and can tonify qi, promote blood circulation, unblock meridians, and relieve palpitations. Modern pharmacology believes that Shensong Yangxin Capsules^[18] achieve antiarrhythmic effects by blocking multiple ion channels, and have a wide range of antiarrhythmic effects. Zhiqian Wang et al.^[19] studied the effect of Shensong Yangxin Capsules on KV1.4 potassium current and found that the drug can alter the phase I repolarization action potential of subendocardial myocardial cells, prolong the duration of action potential, which is one of the anti arrhythmic mechanisms. At the same time, studies have shown^[20] that Shensong Yangxin Capsules can increase the excitability of sinoatrial node P cells and accelerate the conduction velocity of the sinoatrial node by regulating non-ionic channels, thereby increasing heart rate. Xinbao Pill is a traditional Chinese medicine compound prepared by extracting and making pills from Chinese medicinal herbs such as goldenrod, deer antler, and artificial musk. It can tonify qi, warm yang, promote blood circulation, and invigorate the meridians. Modern pharmacological research has shown that Xinbao Pill can stimulate sinoatrial pacing cells, inhibit ectopic pacing points, increase myocardial contractility, raise heart rate, and increase coronary circulation blood flow^[21]. Yuanlong Sun et al.^[22] conducted a meta-analysis on the treatment of BA with Xinbao Pill and found that Xinbao Pill can promote cardiac pacing and conduction function, further improve the clinical symptoms and electrocardiogram of BA patients, and increase the 24-hour average heart rate.

In addition to oral traditional Chinese patent medicines and simple preparations, there are a variety of injections that can be used to treat BA, such as Shenfu Injection and Shenmai Injection. Shenfu Injection is composed of active ingredients such as red ginseng and black aconite tablets. Its efficacy is to restore yang and reverse qi, and to nourish qi and promote detoxification^[23]. It is mainly used to treat patients with bradycardia of heart yang deficiency type, and can significantly improve symptoms such as palpitations, fatigue, and dizziness caused by yang qi deficiency^[24]. Professor Yueping Wu^[25] clinically used this drug to treat patients with bradycardia. The treatment group added 40ml of Shenfu Injection on top of conventional nutritional myocardial therapy for 45 days. The total effective rate of the treatment group was 87.5%, which was stronger than the control

group's 50%. This confirms that Shenfu Injection has a significant therapeutic effect on BA and is superior to conventional treatment. Shenmai Injection is composed of two medicinal herbs, red ginseng and *Ophiopogon japonicus*, which have the effects of nourishing qi, solidifying detoxification, nourishing yin and promoting pulse generation. Chun Wang et al.^[26] found that Shenmai Injection has better therapeutic effects on sinus bradycardia and first-degree atrioventricular block caused by various factors. Based on its pharmacological characteristics, it is considered that Shenmai Injection mainly stimulates the sympathetic nervous system, inhibits the vagus nerve, enhances the sinus conduction function of the heart, and thus treats bradycardia; At the same time, by regulating the concentration of sodium, potassium, and calcium ions inside and outside the myocardium, the contractility of the myocardium can be increased, thereby accelerating the conduction speed of the heart and increasing heart rate.

4.2.3. External treatment of traditional Chinese medicine

In addition to the above mentioned decoction and traditional Chinese patent medicines, the external treatment of traditional Chinese medicine also has a good effect on BA. Acupuncture and moxibustion has been widely used in the treatment of BA. Weidong Zhao et al.^[27] performed acupuncture on Neiguan, Guanyuan, and Zusanli points in patients with sinus bradycardia after modified maze surgery, and used moxa sticks to suspend moxibustion on Guanyuan and Shenque points. The results showed that the total effective rate of the treatment group using the Wenyang Tongmai acupuncture method was 89.66%, with significant therapeutic effects. Haiyan Cheng^[28] used acupuncture and moxibustion combined with traditional Chinese medicine to treat BA. By combining acupuncture at Neiguan and Shenmen on the basis of the control group, she found that the total effective rate of the observation group was higher than that of the control group, and the heart rate and ejection fraction after treatment were also better than those of the control group.

Acupoint application therapy is based on the theory of traditional Chinese medicine meridians. Jiayue Xu et al.^[29] conducted an observational study on the combination of acupoint application and traditional Chinese medicine decoction pieces in the treatment of bradycardia. The results showed that the combination of *evodia rutaecarpa* acupoint application and traditional Chinese medicine decoction pieces can to some extent increase the 24-hour average heart rate of BA patients and improve their clinical symptoms. Feize Li et al.^[30] found that using Wenyang Tongmai Tie to apply to Neiguan, Danzhong, and Geshu points, combined with oral administration of Tongluo Wendou Granules, can improve the average heart rate of BA patients with Yang deficiency and blood stasis type bradycardia, and the slowest heart rate is better than the control group using aminophylline. Yanfei Xia et al.^[31] used a combination of herbal medicine and Zhenxin ointment to apply to Neiguan and Danzhong acupoints in the treatment of BA, which can effectively alleviate patients' clinical symptoms, improve heart function, alleviate inflammatory reactions, and have high safety.

5. Conclusions

At present, there are many adverse reactions in the treatment of BA and cannot be used as a long-term treatment, and the most effective pacemaker treatment also has problems such as high cost and regular battery replacement. Many studies have found that TCM has unique advantages in the treatment of BA, which can not only be used as a supplementary treatment, but also can be used for a long time to improve clinical symptoms and improve quality of life, while not producing more adverse reactions. However, there are still some problems, such as the lack of multi-center and large-sample studies, and relatively few experimental studies have been published, and there is insufficient research on the changes of myocardial potential and ion channels in the treatment of BA by traditional Chinese medicine. It is hoped that future researchers can conduct deeper research.

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