

Chinese Patent medicine to treat a 32-year-old man with sinus bradycardia and cardiac sinus arrests

A case report

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Abstract

Rationale: Sinus bradycardia refers to a sinus heart rate <60 bpm. Cardiac sinus arrests refer to the omission of atrial activation caused by transient cessation of impulse generation at the sinoatrial node. Normally, drugs such as atropine, isoproterenol, dopamine, dobutamine, or epinephrine can be used for the acute treatment of bradycardia. Temporary pacing is used for treating severe symptomatic bradycardia due to a reversible cause. Permanent cardiac pacing is used for chronic therapy of bradycardia. However, for traditional Chinese medicine (TCM), benefiting qi and nourishing yin and activating blood circulation is the general principle in treatment and show remarkable curative effects.

Patient concerns: A 32-year-old man was found to have 1-degree atrioventricular block and sinus bradycardia during a physical examination. He reported suffering from palpitation and shortness of breath occasionally. An ambulatory electrocardiogram showed sinus arrhythmia, sinus bradycardia, and significant sinus arrhythmia. The minimum heart rate was 33 bpm (beats per minute). The number of sinus arrest was 42 and the maximum RR interval was 2216 ms.

Diagnoses: The patient was diagnosed with bradyarrhythmia in Western medicine and "palpitation" in TCM.

Interventions: The patient was treated with methods of benefiting qi and nourishing yin and activating blood circulation along with warming yan for nearly 5 months. CPM (Chinese patent medicine) such as Yixinshu capsule, Bingdouling oral liquid, Zhenyuan capsule, Zhibaidihuang pills were used for treatment. At the same time, he was suggested to change his lifestyles including falling asleep before 10:00 PM and abandoning spicy diets.

Outcomes: The symptoms of palpitation and shortness of breath disappeared. The minimum heart rate increased from 33 to 42 bpm and sinus arrests did not occur. The maximum RR interval decreased from 2216 to 1650 ms and the remarkable sinus arrhythmia had improved obviously.

Lessons: This case report shows that TCM can be an effective alternative therapy for sinus bradycardia and cardiac sinus arrests. CPM may have been a successful intervention in arrhythmias.

Abbreviations: AECG = ambulatory electrocardiogram, bpm = beats per minute, CPM = Chinese patent medicine, ECG = electrocardiogram, SND = sinus node dysfunction, TCM = traditional Chinese medicine.

Keywords: Cardiac sinus arrests, Case report, Chinese patent medicine, Sinus bradycardia, Traditional Chinese Medicine

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Informed written consent was obtained from the patient for publication of this case report and accompanying images.

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1. Introduction

Bradycardia is defined by the National Institutes of Health as a heart rate <60 bpm in adults other than well-trained athletes.^[1] Cardiac sinus arrests refer to the omission of atrial activation caused by transient cessation of impulse generation at the sinoatrial node. It is characterized by a prolonged pause without P wave in an electrocardiogram (ECG). The clinical manifestations of bradycardia can range from occult symptoms to paroxysmal syncope. Mild symptoms include shortness of breath, fatigue, dizziness, and chest distress. Severe symptoms include dizziness, an interval of unconsciousness and convulsions. The symptoms of sinus arrests depend on the time of pause. Several drugs such as atropine, isoproterenol, dopamine, dobutamine, or epinephrine can be used for the acute treatment of bradycardia. Temporary pacing is used to treat severe symptomatic bradycardia due to a reversible cause. Permanent cardiac pacing is used for chronic therapy of bradycardia. Symptomatic SND such as syncope is the most common indication.^[2] However, the therapeutic effects of drugs are limited sometimes and there are many side effects. Moreover, there are procedural complications and death related to the permanent pacemaker, which can increase mental and economic pressure for patients.^[3] Thus, TCM may be an effective alternative therapy for sinus bradycardia and sinus arrests.

Sinus bradycardia and cardiac sinus arrests belong to the category of "palpitation" in TCM. Arrhythmia caused by different causes can be classified into palpitation. It refers to a paroxysmal self-feeling of heart rapid flopping, which cannot be self-controlled. Patients can also feel alarmed and restless. Deficiency and excess are 2 aspects of the pathogenesis of palpitation. Deficiency includes deficiency of gi, blood, yin, and yang leading to the heart losing nourishment. Excess includes all pathogenic factors disturbing the heart. But actually, deficiency and excess intermingling are more common to see. On the basis of clinical practice, the syndrome of Qi-Yin deficiency with blood stasis was recognized as the most common type of syndrome. A randomized study about Shensong Yangxin capsule shows that benefiting gi and nourishing vin and activating blood circulation can significantly increase the heart rate without side effects.^[4] Therefore, benefiting qi, nourishing yin, and activating blood circulation are called the general principle in treatment. It is the most common method of clinical treatment and shows remarkable curative effects.^[5,6] Here, we present a case of a 32-year-old man with sinus bradycardia and cardiac sinus arrests. He was treated only by Chinese patent medicine (CPM). After treatment for nearly 5 months, not only the symptoms were relieved but also the heart rate got increased and sinus arrests did not occur anymore.

2. Case presentation

A 32-year-old man went to our cardiac clinic on June 22, 2018. He reported that he was found to have 1 degree atrioventricular block and sinus bradycardia during a physical examination. He presented with palpitation and shortness of breath occasionally. He had stayed up continuously in the last 2 months and he had difficulty falling asleep at present. Then, his symptoms became worse so he went to our outpatient clinic for treatment. He denied neither taking antiarrhythmic or psychoactive drugs nor snoring in sleep. There was no family history related to hypertension and bradycardia. Neither ECG nor echocardiography showed abnormal manifestations. He was recommended to perform an

ambulatory ECG (AECG) to evaluate the condition. One week later, the patient came with the AECG report showing a minimum heart rate of 33 bpm, a maximum RR interval of 2216 ms, and a maximum heart rate of 127 bpm. The number of sinus pause (>2000 ms) was 42. On physical examination, his tongue was puffy-red with cracks and the tongue fur was thin and vellow. His pulse was weak and deep. He was diagnosed with bradyarrhythmia in Western medicine and "palpitation" in TCM. The patient was prescribed Yixinshu capsule 1.2g 3 times/ day, Bingdouling oral liquid 10 mL 3 times/day, and Zhenyuan capsule 50 mg 3 times/day. At the same time, the patient was suggested to change his lifestyle. He should fall asleep before 10:00 PM to gain adequate rests and abandon spicy diets such as chili, pepper, cinnamon, anise, garlic, soy sauce, and vinegar. After taking the medicine for nearly 2 months, the patient can fall asleep at night. The symptoms of palpitation and shortness of breath did not occur, but the patient got constipation. So, Zhibaidihuang pills 8 pills 3 times/day were added into the prescription. After 1 month of treatment, the patient's symptom of constipation disappeared. The color of his tongue turned palepuffy and his tongue fur became thin and white. The pulse was thready. The patient was advised to take drugs continuously to consolidate the efficacy. One month later, all the symptoms had disappeared and the repeat AECG showed a minimum heart rate of 42 bpm, a maximum RR interval of 1650 ms, and a maximum heart rate of 128 bpm. There was no sinus pause (>2000 ms).

3. Discussion

According to 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay, a sinus rate <50 bpm and/or a sinus pause >3 seconds are chosen as the definition of SND (sinus node dysfunction).^[2] SND is most often related to age. Older individuals are more common to suffer from this disease.^[7] In this case, the AECG shows a minimum heart rate of 33 bpm and a maximum RR interval of 2216 ms. However, the patient is a 32-year-old young man. Thus, the presence of bradycardia and sinus arrests should not be diagnosed with SND. Sleep-related bradycardia is common in clinic and continuous positive airway pressure can decrease the frequency of episodes. For this patient, the minimum heart rate occurred at 04:47 AM and sinus arrests occurred from 3:00 AM to 6:00 AM. Both of them occurred at sleep. It is necessary to screen for sleep apnea syndrome. But the patient denied snoring at sleep and refused to monitor sleep apnea. Sinus arrhythmia with sinus pauses or nocturnal atrioventricular block is common in young male adults.^[8] This patient is a young man with a healthy body. He denied taking drugs, which would influence the heart rate. There is no family history related to bradycardia. Echocardiography showed that there was no clinical evidence of structural heart disease. It is necessary to consider the correlation between bradycardia and symptoms. As he was asymptomatic at night, neither drugs and temporary pacing for acute therapy nor permanent pacing for chronic management of bradycardia is recommended. On the contrary, the patient's AECG report showed a maximum heart rate of 127 bpm, which occurred at midday. At the same time, he was suffering from palpitation and shortness of breath. Does this patient need drugs such as beta-blockers to control the heart rate? A cohort study has found that whether or not taking drugs, the 10-year risk of cardiovascular disease and mortality remained unchanged for asymptomatic bradycardia. However, the

mortality rate increases in patients who take the medicine. While the mortality rate increases in patients who take the medicine.^[9] Therefore, this patient was advised to take CPM for treatment instead of taking antiarrhythmic drugs.

TCM has a long history to treat bradycardia. A meta-analysis was performed to evaluate the effectiveness of TCM formulas in treating bradyarrhythmia. The study concludes that some formulas (Shenxian-shengmai oral liquid, Shensong Yangxin capsule, XinBao pill, Mahuang-Fuzi-Xixin decoction, Zhigancao decoction, and Shengmai injection) might help to relieve bradyarrhythmias.^[10] In clinic, palpitation is more commonly linked with Qi-Yin deficiency and blood stasis. According to the basic theory of TCM, the heart governs the blood circulation and the liver stores blood. The liver governs the time from 1:00 to 3:00 in the evening. According to "Canon of Yellow Emperor", when people lie down, the blood returns to the liver. The patient had stayed up late for a long time, his liver could not get enough rests, which caused insufficient blood supply. Besides, qi is the mother of blood in TCM. Blood deficiency leads to gi losing attachment so gi deficiency syndrome forms. Both deficiencies of qi and blood lasting for a long time can result in the heart failing to promote the blood circulation. On this basis, the heart vessels can be blocked by blood stasis, which will aggravate qi and blood deficiency and lead to insufficiency of heart yang. The blood circulation depends not only on the promotion of the heart qi and blood but also on the warm-up of the heart yang. So, the heart can be dysfunctional. On the contrary, yang qi runs on the surface of the body during the day and enters into the body after sleeping at night. So, staying up late causes yang qi failing to enter into the body, which will bring about yin and yang imbalance.

When determining the treatment methods, we should follow the principle of syndrome differentiation. Syndrome differentiation refers to the analysis of syndrome through the 4 diagnostic methods-observation, hearing, question, and feeling the pulse. According to the patient's initial symptoms, shortness of breath, puffy tongue, and weak pulse are representations of deficient heart qi. Red tongue with cracks is a representation of yin deficiency. Deep pulse is a representation of van deficiency. Insomnia is a representation of imbalance of yin and yang. All of these factors cause blood stasis resulting in palpitation. Therefore, the treatment is based on the principle of benefiting qi and nourishing yin and activating blood circulation, cooperating with the method of warming yan. So, we choose Zhenyuan capsule (approval number: Z22026091), Yixinshu capsule (approval number: Z52020038), and Bingdouling oral liquid (approval number: Z04000389) for treatment. Table 1

Table 1

Chinese name	Ingredient	Actions	Indications	Dosage
Yixinshu capsule	Ren-Shen (Radix Ginseng), Mai-Dong (Radix Ophiopogonis), Wu-Wei-Zi (Fructus Schisandrae Chinensis, Huang-Qi (Radix Astragali seu Hedysari), Dan-Shen (Radix Salviae Miltiorrhizae), Chuan-Xiong (Rhizoma Ligustici Chuanxiong), Shan-Zhai (Fructus Crataegi)	Supplementing qi and recovering pulse, promoting blood circulation and resolving stasis, nourishing yin, and generating body fluid	Blood stasis obstructing vessels due to qi and yin deficiency. Symptoms: chest pain, chest distress, palpitation, shortness of breath, irregularly or regularly intermittent pulse, coronary heart disease, angina pectoris	1.2g, 3 times/d
Zhenyuan Capsule	Saponins of ginseng fruits	Supplementing qi for promoting blood circulation, tonifying the heart and tranquilizing the mind, producing body fluid to quench thirst	It is used for treating coronary heart disease, angina pectoris, arrhythmia, neurosis, and type-2 diabetes, which are linked with chest pain or oppressed feeling in the chest. Other symptoms such as palpitation, dysphoria, insomnia, forgetfulness, thirst and drinking excessively, shortness of breath, lassitude, and listlessness	0.5g, 3 times/d
Bingdouling Oral liquid	Huang-Qi (Radix Astragali seu Hedysari), Zhi-Fu-Zi (Radix Aconiti Lateralis Preparata), Shu-Di-Huang (Radix Rehmannie Preparata), Dan-Shen (Radix Salviae Miltiorrhizae), Yin-Yang-Huo (Herba Epimedii), Gan-Cao (Radix Glycyrrhizae), Hong-Shen (Radix Ginseng Rubra).	Supplementing qi and warming yang, nourishing blood and invigorating pulse.	Sick sinus syndrome	10 mL, 3 times/d
ZhiboDihuang pill	Zhi-Mu (<i>Rhizoma Anemarhenae</i>), Shu-Di- Huang (<i>Radix Rehmanniae Recens</i>), Huang-Bai (<i>Cortex Phellodendri</i>), Shan-Zhu-Yu (<i>Fructus Corni</i>), Shan- Yao (<i>Rhizoma Dioscoreae</i>), Dan-Pi (<i>Cortex Moutan Radicis</i>), Fu-Ling (<i>Poria</i>), Ze-Xie (<i>Rhizoma Alismatis</i>).	Nourishing yin and clearing heat	Hyperactivity of fire due to yin deficiency. Symptoms: tidal fever, night sweating, thirst, pharyngalgia, tinnitus, spermatorrhea, and scanty dark urine	8 pills, 3 times/d

Supplementing qi: Using qi invigorating drugs to boost spirit and replenish energy; Nourishing Yin: Using yin tonics to generate body fluid and tonify internal organs; Warming yang: Using warm natured drugs to invigorate yang qi and dispel cold; Promoting blood circulation: Using blood-activating drugs to remove blood stasis for promoting tissue regeneration.



summarizes the ingredient, actions, and indications of these CPM. As summarized in Table 1, gi deficiency refers to deficient vigor leading to hypofunction of internal organs. Yin deficiency refers to insufficient body fluid leading to internal organs losing moistness and nourishment. Blood stasis means that blood clots lodge in a certain place, which can affect the blood circulation. Yang deficiency refers to a lack of vital energy leading to body metabolic disorders. Among these medicines, Zhenyuan capsule that has high safety can improve the heart function of patients with chronic heart failure.^[11] Yixinshu capsule can protect against myocardial ischemia reperfusion injury.^[12] Schisandrin A and schisandrin B of Yixinshu capsule are demonstrated to be the active components, which have the effect of anti-myocardial dysfunction.^[13] In this case, the patient's clinical manifestations are not immutable. During the process of taking medicine of benefiting qi and warming yang, all the symptoms had alleviated. But too much yang gi transformed into intense heat, which consumed body fluid. So, the patient got constipation and we had to add Zhibai dihuang pill (approval number: Z41021904) to nourish yin and clear heat. In addition, diet and life habits can also affect the balance of gi and blood or yin and yang. In modern society, young people often like to stay up late for various reasons. A scientific statement from the American Heart Association had shown evidence that short sleep and sleep disorders are related to cardiometabolic risks such as obesity, hypertension, diabetes, and cardiovascular disease.^[14] Besides, "Canon of Yellow Emperor" records: pungent flavor enters into gi level so patients with gi diseases cannot eat too much spicy

food. Eating spicy food too much can lead to an imbalance of visceral qi, which is harmful to the body.^[15] Therefore, the patient was advised to fall asleep before 10:00 PM to gain a balance of yin and yang and abandon spicy food to avoid heat-consuming qi or injuring yin. After treatment for nearly 5 months, the minimum heart rate of the patient increased from 33 to 42 bpm (Fig. 1) and the maximum RR interval decreased from 2216 to 1650 ms (Fig. 2). The remarkable sinus arrhythmia had improved obviously and sinus arrests did not occur anymore. The average nocturnal heart rate had increased and became more stable, while the daily maximum heart rate in the whole day has no change as well. So, we can consider that CPM will not increase the average heart rate and the maximum heart rate, while it can increase the minimum heart rate of patients with bradycardia.

4. Conclusion

In clinic, western medicine treatment appears to be the first choice of therapy for arrhythmias. However, in this young patient, both antiarrhythmic drugs and cardiac pacemaker are not suitable for him. This case report shows that TCM can be an effective alternative therapy for sinus bradycardia and cardiac sinus arrests. CPM may have been a successful intervention in bradycardia. It is interesting to note that CPM does not increase the average heart rate and the maximum heart rate while it increases the minimum heart rate of the patient. However, there are different kinds of drugs in CPM and their components are





Figure 3. The hourly heart rate showed by a 24-h ambulatory electrocardiogram before and after Chinese patent medicine treatment.

complex. These Chinese medicines act on human body through multichannel and multitarget so it is hard for us to explain their individual mechanism. Therefore, we need more clinical trials to confirm the efficacy and mechanism of TCM.

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