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Research Progress on Prevention and Treatment of Arrhythmia by Classic Prescriptions in Treatise on Febrile Diseases

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Abstract: ***With the national emphasis on the motherland medicine advocated, more and more research on treating arrhythmia is being done using traditional Chinese medicine. A large number of studies have found that some classical prescriptions of Treatise on Febrile Diseases have a good preventive and therapeutic effect on arrhythmia and are worthy of in-depth mining. This article reviews the clinical application of classical prescriptions in the treatment of arrhythmia in recent years, including Zhigancao Decoction, Guizhi Gancao Decoction, Guizhi Gancao Longgu Oyster Decoction, Chaihu plus Longgu Oyster Decoction, Lingguizhugan Decoction and Mahuang Fuzi Asarum Decoction.***

Keywords: Arrhythmia, Classic Prescription of Treatise on Febrile Diseases, Traditional Chinese Medicine, Research Progress**.**

1. Introduction

Modern medicine believes arrhythmia is a group of diseases with abnormal frequency, rhythm and activation sequence of cardiac pulsation due to disturbance of cardiac activation and conduction system. It can emerge either as a separate disease or further develop from other cardiovascular diseases such as coronary heart disease and dilated cardiomyopathy, which lead to life-threatening risks such as fainting and sudden death. At present, the aetiology of arrhythmia is not clear, so it cannot be generalized. However, it has been shown that risk factors such as mental stress, agitation, overexertion, smoking, and alcohol consumption, hemodynamic disturbances in cardiometabolic function, and various structural heart diseases may trigger arrhythmias. The clinical manifestations of arrhythmia are similar to those of “palpitation” in motherland medicine, so arrhythmia is attributed to the category of “palpitation” in traditional Chinese medicine. As early as the Han Dynasty, Zhang Zhongjing in China put forward the name “palpitation”, and dozens of articles on palpitation syndrome were recorded in his Treatise on Febrile Diseases. Zhang Zhongjing treats palpitation from the aspects of aetiology and pathogenesis, syndrome differentiation, decoction medication and mistreatment prevention and treatment, and has a relatively perfect understanding of palpitation, which has a profound impact on later generations of physicians. [1] Most modern medicine treats arrhythmia with antiarrhythmic drugs or surgery, and these treatments mostly have problems such as more adverse reactions, high recurrence rates, and unsatisfactory long-term outcomes. Nowadays, many physicians have used classical prescriptions to treat arrhythmia and achieved good efficacy. In this paper, the data will be collected through a literature search, and the clinical application and progress of classical prescriptions for the prevention and treatment of arrhythmia in Treatise on Febrile Diseases will be roughly summarized to provide a reference for clinical treatment.

2. Zhigancao Decoction

2.1 Atrial Fibrillation

Chai Yuyan [2], based on the theory of collateral disease in TCM, combined with the pathophysiological characteristics and pathogenesis of atrial fibrillation, interpreted the mechanism of Zhigancao Decoction in the treatment of atrial fibrillation from the perspective of collateral disease theory, enriched the theoretical basis of Zhigancao Decoction in the treatment of atrial fibrillation, and further clarified the clinical efficacy of Zhigancao Decoction in the treatment of atrial fibrillation. Song Pengxi [3] selected 52 patients with paroxysmal atrial fibrillation as the study subjects and randomly divided them into the control group and the observation group, with 26 cases in each group. The control group was treated with conventional Western medicine amiodarone. The observation group was treated with Zhigancao Decoction based on the control group. Both groups were treated for 8 weeks. The efficacy, cardiac troponin I (cTnI), N-terminal prohormone of brain natriuretic peptide (NT-proBNP), left ventricular ejection fraction (LVEF) and 24h dynamic electrocardiogram were compared between the two groups before and after treatment. Conclusion The observation group can effectively improve the clinical efficacy of patients, effectively improve cTnI, NT-proBNP, and LVEF, and promote the good prognosis of patients. Li Zheshan [4] selected 60 patients with persistent atrial fibrillation and randomly divided them into a control group treated with Metoprolol Succinate Sustained-release Tablets and an observation group treated with Metoprolol Succinate Sustained-release Tablets combined with Zhigancao Decoction. After 8 weeks of treatment, the clinical efficacy, TCM syndrome score, cardiac function [left ventricular ejection fraction (LVEF), cardiac output (CO), ejection index (CL), rapid mitral filling blood flow velocity/atrial systolic blood flow velocity (E/A)] and serum hs-CRP, NT-proBNP

and Hcy levels were compared between the two groups. The experimental results suggest that Zhigancao decoction can reduce myocardial cell injury play an antioxidant role in the treatment of patients with persistent atrial fibrillation, and can also improve cardiac function and inhibit inflammatory response, with a significant effect.

2.2 Sick Sinus Syndrome

Li Bixia [5] et al treated sick sinus syndrome from the method of harmonizing yin and yang. One case showed that Zhigancao Decoction was effective in eliminating symptoms, preventing recurrence and improving prognosis. Deng Ruiming [6] randomly selected 60 patients with sick sinus syndrome and divided them into a study group and a control group, with 30 cases for each group. The study group was treated with Zhigancao Decoction and Taohong Siwu Decoction based on conventional Western medicine treatment, and the control group was treated with Xinbao Pills and conventional Western medicine. After 6 weeks of continuous observation, the three major routines, liver and kidney function and other safety indicators, TCM syndrome score, total efficacy of TCM syndrome and 24-hour dynamic electrocardiogram indicators (lowest heart rate, average heart rate, long RR interval times, longest RR interval time, atrial premature beats) and other efficacy indicators were compared between the two groups before and after treatment. The results showed that the symptoms of the study group could be significantly relieved, and the average heart rate, the lowest heart rate, reduced the number and time of long RR intervals and atrial premature beats, superior to the control group. He Xiaolian et al7 randomly divided 120 patients with sick sinus syndrome into 2 groups of 60 patients each. The patients in the control group were treated with ShenSongYangXin Capsule and the patients in the observation group were treated with Zhigancao Decoction. The changes in heart rate and TCM syndrome scores before and after treatment were compared between the two groups. The results showed that Zhigancao Decoction could stabilize the heart rate and improve the myocardial function of the patients, which helped improve the clinical symptoms and is worthy of being widely popularized in clinical application.

3. Guizhi Gancao Decoction

3.1 Ventricular Premature Beat

Wang E [8] randomly divided 58 patients with ventricular premature beats syndrome of heart-kidney yang deficiency into an observation group and a control group, with 29 cases for each group. The control group was treated with amiodarone, and the observation group was treated with self-made Guizhi Gancao Decoction based on the control group. 14 days was a course of treatment, after 2 courses of treatment, the clinical efficacy and the standard deviation of all sinus R-R intervals (SDNN), the standard deviation of the mean sinus R-R interval every 5 minutes (SDANN), the standard deviation of sinus R-R interval every 5 minutes (SDNNI), the percentage of normal adjacent R-R interval difference > 50 ms (PNN50)], cardiac function indicators [left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), stroke volume (SV) and B-type natriuretic peptide (BNP)], quality of life scores were compared between the two groups. The results showed that Guizhi Gancao Decoction could significantly reduce heart rate variability, improve cardiac function and improve the quality of life of patients with ventricular premature beats and heart-kidney yang deficiency syndrome. Zhang Xin [9] selected 50 patients with ventricular premature beats of heart-kidney yang deficiency type and randomly divided them into two groups of 25 cases each. The control group was treated with base therapy, and the observation group was treated with Guizhi Gancao Decoction based on the control group. Continuous treatment for 2 weeks. The clinical effects were compared between the two groups. Before and after treatment, the standard deviation of all normal R-R intervals (SDNN), the standard deviation of average R-R intervals every 5 minutes (SDANNI), the mean value of SDNN (SDNNI), the percentage of heartbeats with a difference of > 50 ms between two adjacent normal cardiac cycles to the total heart beats (PNN50), the cardiac function indexes of [stroke volume (SV), left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), serum brain natriuretic peptide (BNP)] levels, and the occurrence of adverse reactions were compared. The results showed that Guizhi Gancao Decoction could significantly reduce the discomfort symptoms, heart rate variability and cardiac function of patients with ventricular premature beats of heart-kidney yang deficiency type, with good safety. It is worthy of being widely popularized.

3.2 Atrial Fibrillation

Liang Li, male [10] selected 90 patients with atrial fibrillation and randomly divided them into a control group and an observation group, 45 cases for each group. The control group was treated with conventional therapy and oral amiodarone, and the observation group was treated with Guizhi Gancao Decoction combined with Wenxin Granules based on the control group. After 4 weeks of treatment, the overall response rate was evaluated. The symptom score, left ventricular ejection fraction (LVEF), stroke volume (SV), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD) and left atrial effective refractory period (LAERP) were compared between the two groups. The duration of atrial fibrillation and the number of attacks per week were also recorded in the two groups. Conclusion Guizhi Gancao Decoction combined with Wenxin Granule has an ideal therapeutic effect, which can promote the alleviation of symptoms, improve cardiac function and left atrial electrophysiological parameters, and reduce the frequency of atrial fibrillation attacks.

3.3 Sinus Bradycardia

Wang Chifeng [11] randomly divided 60 patients with bradycardia of deficiency of both qi and yin and deficiency of yang into a treatment group (n = 30) and control group (n = 30). The treatment group was given Shenmai Powder combined with Guizhi Gancao Decoction orally, and the control group was given Atropine and Cordyceps cephalosporin capsules orally. Fifteen days was a course of treatment, and electrocardiograms were repeated after each course of treatment for a total of 3 – 6 courses of treatment. Observe the changes in heart rate and symptoms. Results In the treatment group, 16 cases were markedly effective, 12

cases were improved and 2 cases were ineffective. The total effective rate was 93.3%. The overall effect was satisfactory. Zhao Wei [12] et al. selected 96 patients with sinus bradycardia and randomly divided them into a treatment group (n = 48) and a control group (n = 48). The treatment group was given Shengjing Decoction and Guizhi Gancao Decoction; the control group was given Xinbao Pills for 90 days. The changes of heart rate, TCM symptoms, tongue, pulse, ECG and 24-hour dynamic electrocardiogram were observed before and after treatment. Results In the treatment group, 20 cases were markedly effective, 10 cases were effective and 6 cases were ineffective, with an overall response rate of 87.50%. In the control group, 22 cases were markedly effective, 21 cases were effective and 17 cases were ineffective, with an overall response rate of 64.58%. Clinical observation Guizhi Gancao Decoction has an obvious effect on increasing heart rate.

4. Guizhi Gancao Longgu Oyster Decoction

4.1 Ventricular Premature Beat

Liu Qin et al. [13] selected 80 patients with ventricular premature beats as the study subjects and randomly divided them into the Guizhi Gancao Longgu Oyster Modified Decoction group and the conventional method group. The total number of ventricular premature beats, TCM syndrome score, clinical efficacy, adverse reactions and heart rate deceleration in 24h dynamic electrocardiogram were compared between the two groups. Results After treatment, the TCM syndrome score of the observation group was lower than that of the control group, the heart rate deceleration of the observation group was higher than that of the control group, and the total number of ventricular premature beats in the 24h dynamic electrocardiogram was decreased. The ORR of the observation group was 95.00% (38/40), which was higher than that of the control group (70.00%, 28/40). The results showed that Guizhi Gancao Longgu Oyster Modified Decoction could reduce the incidence of adverse reactions, increase heart rate deceleration, improve TCM syndrome score, with high safety, and reduce the total number of ventricular premature beats in 24h dynamic electrocardiogram, which was suitable for clinical promotion. Zhang Ling [14] selected 66 patients with coronary heart disease ventricular premature beats and randomly divided them into two groups. The reference group was treated with propafenone tablets (n = 33); the study group was treated with Guizhi Gancao Longgu oyster-modified decoction (n = 33); the overall response rate, TCM syndrome score and ECG indicators (T wave changes, 24h ventricular premature beats, ST segment depression amplitude and ST segment depression) were compared between the two groups. Results Guizhi Gancao Longgu oyster modified decoction could significantly improve the therapeutic effect of premature ventricular contractions (PVCs) in patients with coronary heart disease (CHD), significantly reduce the TCM syndrome, effectively reduce the number of T wave changes, the number of PVCs in 24 hours, and the number of ST segment depressions, significantly reduce the amplitude of ST segment depressions and promote a good prognosis. Guo Hailing [15] selected 60 patients with ventricular extrasystoles and randomly divided them into the treatment group and control group. The control group was given metoprolol orally, 12.5 mg or 25 mg twice a day. The treatment group was given Tianwang Buxin Dan plus Guizhi Gancao Longgu Oyster Decoction orally, 1 dose/d, based on the control group. One course of treatment was 4 weeks in both groups. The effects of ventricular extrasystoles, Myerburg grade, TCM syndrome, number of ventricular extrasystoles, the standard deviation of all normal RR intervals (SDNN), root mean square of difference of adjacent RR intervals (rMSSD), percentage of adjacent RR interval difference more than 50 ms to total sinus beats (PNN50),] of bigeminy, trigeminy, number of paired ventricular extrasystoles, and TCM syndrome scores were compared between the two groups before and after treatment. It is concluded that Tianwang Buxin Dan combined with Guizhi Gancao Longgu oyster decoction is superior to Western medicine alone in the treatment of ventricular extrasystoles with deficiency of both qi and yin, without increasing adverse reactions.

4.2 Atrial Premature Beats

Bai Yanrong [16] selected 61 patients with atrial premature beats after viral myocarditis and randomly divided them into a control group (n = 31) and a study group (n = 30). The control group was treated with conventional Western medicine + Guizhi Gancao Longgu Oyster Decoction. After 6 weeks of treatment, the frequency of atrial premature beats, cardiac ultrasound, sleep quality index score and TCM symptom score were recorded during and after treatment, and the clinical efficacy of the two groups was compared. Conclusion Guizhi Gancao Longgu oyster decoction can significantly reduce the frequency of atrial premature beats in patients with atrial premature beats caused by viral myocarditis, improve sleep status, reduce symptoms, indirectly inhibit left ventricular myocardial remodelling, and improve clinical efficacy.

4.3 Atrial Fibrillation

Li Junjia et al. [17] believed that atrial fibrillation is based on heart-yang deficiency and blood stasis for a long time. The method of warming yang and activating blood circulation is given in the treatment, often Guizhi Gancao Longgu Oyster Decoction is the main prescription, warming heart yang. Example of test case: Gao, intermittent palpitation and chest tightness for more than 1 year, aggravated with insomnia for 1 week, 24h dynamic electrocardiogram showed paroxysmal atrial fibrillation, TCM dialectical: palpitation yang deficiency and blood stasis syndrome, side selection Guizhi Gancao Longgu oyster decoction combined with Taoren Honghua decoction addition and subtraction, and then revisited twice, adjusted the prescription with the syndrome, a total of 28 doses were taken, the patient's symptoms were significantly improved, reexamination of dynamic electrocardiogram suggested the recovery of sinus rhythm.

5. Chaihu plus Longgu Oyster Decoction

5.1 Atrial Premature Beats

Cheng Yu [18] collected 60 patients with frequent atrial premature beats due to arrhythmia and divided them into the treatment group and control group. The treatment group was added with Chaihu plus Longgu oyster decoction based on

conventional Western medicine treatment. After one course of treatment, the total effective rate of clinical symptoms in the treatment group was 93.3%, superior to 76.7% in the control group. The total effective rate of dynamic electrocardiogram premature beats in the treatment group was 76.7% (23/30), higher than 53.3% in the control group. The results showed that Chaihu plus Longgu oyster decoction was effective in the treatment of frequent atrial premature beats due to arrhythmia, with high safety and clinical application value.

5.2 Atrial Fibrillation

Li Mianmian et al. [19] treated atrial fibrillation from the liver and fire, and applied Chaihu plus Longgu oyster decoction to treat rapid atrial fibrillation patients with emotional disorders combined with insomnia with satisfactory results, and even for some patients with long-range persistent atrial fibrillation can play a cardioversion effect.

6. Mahuang Fuzi Asarum Decoction

6.1 Sinus Bradycardia

Sun Yanjun et al. [20] concluded that the fundamental pathogenesis of sinus bradycardia is a deficiency of both qi and yang and internal excess of yin and cold, while the pathogenesis of ephedra aconite Asarum decoction syndrome is a deficiency of less yin and yang, re-sensation of external cold, and too little the same disease. Different diseases with the same treatment, side with ephedra aconite Asarum soup, warm yang cold, directly refer to the pathogenesis of the disease, so that Yang Qi get nourished, Yang Qi enough to return to normal, and then instigate the blood vessels, so that the pulse rate returned to normal. Case evidence: A 42-year-old female patient presented with intermittent palpitations for more than 1 year and aggravation with dizziness for 1 month. Electrocardiogram showed a heart rate of 37 beats/min, and sinus bradycardia; the patient was diagnosed with palpitations (deficiency of both qi and yang), and was given Mahuang Fuzi Asarum Decoction, followed by 3 visits, and the prescription was adjusted with the syndrome, a total of 42 doses were taken, and the patient's heart rate could be maintained at about 56 beats/min.

6.2 Sick Sinus Syndrome

Wang Xinyi et al. [21] concluded that the pathogenesis of sick sinus syndrome is related to deficiency of yang qi and stagnation of qi and blood, and warming yang and dispersing cold are the basic rules in the treatment, while Mahuang Fuzi Asarum Decoction is used as a representative prescription for the treatment of Taiyin Shaoyin sensation, and the effect of warming yang and dispersing cold is significant, so Mahuang Fuzi Asarum Decoction can be used to treat sick sinus syndrome of yang deficiency and cold coagulation type. Case evidence: Xuan, female, 43 years old, complained of premature beats and arrest for more than half a month. 24-hour dynamic electrocardiogram showed sinus bradycardia (mean heart rate 46 beats/min, minimum heart rate 26 beats/min, maximum heart rate 103 beats/min), sinus arrest (178 in more than 2 seconds, up to 3.91 seconds), nodal escape beats, and ventricular premature beats. TCM diagnosis: vertigo, syndrome belongs to deficiency of heart-yang, deficiency of spleen and stomach qi, ephedra aconite Asarum decoction was selected, and ephedra aconite Asarum decoction was successively reexamined many times. Two months later, a 24-hour dynamic electrocardiogram was reexamined. The results showed sinus bradycardia (mean heart rate 53 beats/min, minimum heart rate 39 beats/min, maximum heart rate 114 beats/min), ventricular premature beats (113), and atrial premature beats (128).

7. Conclusion

Clinical and experimental studies have shown that traditional Chinese medicine has the advantages of stable efficacy and fewer adverse reactions in the treatment of arrhythmia. However, there are still some shortcomings: the mechanism of traditional Chinese medicine in the treatment of arrhythmia is not yet fully clarified, most conclusions need to be further demonstrated, there is a lack of systematic research and perspective in line with evidence-based medicine, there is a lack of large-scale randomized controlled double-blind clinical studies with large samples, there is a lack of animal models combining disease and syndrome, there is a lack of systematic collation and many other problems, which limits the clinical application of traditional Chinese medicine in the treatment of arrhythmia. In this paper, the results of traditional Chinese medicine in the treatment of arrhythmia were roughly summarized to provide more evidence support for the study of traditional Chinese medicine in the treatment of arrhythmia.

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