

# General rule and research progress of constitution of traditional Chinese medicine in treating refractory hypertension

Longwei Ran<sup>1,a</sup>, Tongsheng Su<sup>2,b,\*</sup>

<sup>1</sup>Shaanxi University of Chinese Medicine, Xi'an, 712046, Shaanxi, China

<sup>2</sup>Shaanxi Provincial Hospital of Chinese Medicine, Xi'an, 710003, Shaanxi, China

<sup>a</sup>1165332475@qq.com, <sup>b</sup>Chinasuts@126.com

\*Corresponding author

**Abstract:** At present, the clinical research of TCM treatment of hypertension is relatively common, and the related research of refractory hypertension is relatively few. As a result, relatively few articles have been published. By summarizing relevant literatures in CNKI, Wanfang, VIP and other databases in recent years, different methods of TCM compound, acupoint application, acupoint catgut embedding, combination of acupuncture and medicine, foot bath and other treatments for refractory hypertension were summarized. This paper aims to explore the research progress of refractory hypertension in recent years and summarize the relationship between refractory hypertension and TCM constitution as well as the general law of syndrome distribution.

**Keywords:** TCM; refractory hypertension; Physical; research progress

## 1. Introduction

Up to now, refractory hypertension has been defined as failure to achieve target blood pressure in the office and out of the office (including home blood pressure monitoring or ambulate blood pressure monitoring) in spite of a tolerable dose of 3 or more antihypertensive drugs (including a thiazide diuretic) for 4 weeks in the context of a regular and healthy lifestyle [1]. Hu Hui [2] used the HAD scale to evaluate and define the emotional state of the patients. The results showed that 24.73% of them had anxiety, 25.81% had depression, and 15.05% had anxiety and depression. Therefore, it indicates that patients with refractory hypertension are often accompanied by severe anxiety and depression symptoms, which cause serious burden on patients' economy and quality of life, and the prognosis is relatively poor. At present, there is no unified and standardized syndrome differentiation standard and treatment plan for refractory hypertension in traditional Chinese medicine [3]. Therefore, refractory hypertension is a subject worthy of further study and has certain practical significance.

## 2. Pathogenesis of refractory hypertension

### 2.1. Intestinal flora and the incidence of refractory hypertension

In traditional Chinese medicine, the zang-fu organs are closely related to each other in physiology and pathology. It has been reported that the occurrence and development of refractory hypertension may be related to the imbalance of intestinal flora. The specific manifestations are in two aspects: First, the apparent genetic changes of intestinal epithelial cells are induced by the signals of intestinal microbiome, and the intestinal wall permeability changes, which lead to the changes of endocrine, immune, neural pathways and other signaling pathways, resulting in adverse effects on the cardiovascular system and lead to increased blood pressure; The other is the bidirectional effect between intestinal flora and drug metabolism. "Heart", "brain" and "gut" relate the changes of intestinal flora to the mechanism of action and treatment of refractory hypertension, constituting the theoretical system of "heart-brain-gut axis", providing a new idea for the study of refractory hypertension [4].

## **2.2. Understanding of hypertension in TCM**

The clinical symptoms of hypertension include vertigo, headache, chest tightness, irritability and so on. Traditional Chinese medicine classifies hypertension as "vertigo", "headache" and "liver wind". About this disease, many ancient books recorded, such as: "Lingshu · Wei Qi" records: "on the deficiency of dizziness." Lingshu · Kouwen holds that the occurrence of this disease is mainly caused by deficiency syndrome. "On Three Causes and One Disease Syndromes, Syndrome Treatment of vertigo" holds that the occurrence of vertigo is related to the deficiency of organs caused by seven feelings obstruction, which leads to lower deficiency and upper deficiency is the key to the onset, so it is put forward that dizziness caused by deficiency. "Jingyue Book, Vertigo" points out that the deficiency of vertigo is the first disease, and it is believed that the treatment of deficiency should be the main; It is recorded in "Plain Question · The Greatest Theory of Truth" that "all the wind causes dazzle, which all belong to the liver". It is believed that the occurrence of this disease is related to the liver, that is, the wind causes dazzle. Synopsis of the Golden Chamber: "Phlegm under the heart, full chest and side support, dizziness." "Danxi Heart Method · Head dazzle" mentions that "no phlegm does not cause dazzle", and thinks that phlegm causes dazzle; "Plain Question Xuanji original disease type · Five Yun master disease" mentioned: "The head dazzles the carriage, by the wind wood flourishing, it must be gold decay can not make wood, and wood revive fire, wind and fire belong to Yang, mostly for the simultaneous, Yang master move, two moves, then rotation. It is believed that fire evil is closely related to vertigo, that is, glare is caused by fire. "Medical history" in the "external and internal vomiting of blood and vertigo, there is dead blood fans in the chest to close the heart" that blood stasis is the inducement of vertigo, that is, because of blood stasis dazzle. Therefore, traditional Chinese medicine believes that wind, fire, phlegm, deficiency and stasis are important pathological factors leading to the occurrence of diseases.

## **2.3. Correlation between refractory hypertension and TCM constitution**

The theory of TCM constitution was initially formed in the Huangdi Neijing period. The theory of Yin and Yang, the five elements and Qi and spirit influenced the development of TCM constitution. "On the Causes and Syndromes of Various Diseases" records that the etiology, pathology and constitution are related to a certain extent [5]. Based on the theory of human physiology and pathology, health preservation and disease prevention and treatment, physique types and their characteristics are studied through the guidance of TCM theory. According to the research results, the targeted treatment of the susceptible constitution of some diseases reflects the "preventing disease from changing" in the "treating no disease" of traditional Chinese medicine, so as to be more targeted in the prevention and treatment of certain diseases and improve the clinical efficacy. Constitution is a stable trait reflected by the human body in response to external stimuli [6,7]. Tan Maoqing and Lin Jiwei et al took 60 patients with refractory hypertension and 60 patients with normal physical examination during the same period as the research objects, and statistically analyzed the main constitution types of patients with refractory hypertension by questionnaire survey, and compared the blood pressure levels among patients with different constitution types. The results showed that the proportion of Qi deficiency, Yin deficiency and phlegm-dampness in the observation group was higher than that in the control group, while the proportion of peace and quality was lower than that in the control group. Moreover, systolic blood pressure and diastolic blood pressure of Yin deficiency in the observation group were higher than those of qi deficiency, phlegm-dampness, blood stasis and other constitutions, which was consistent with the TCM theory that the disease location of hypertension was in liver and kidney, and the pathogenesis was liver and kidney Yin deficiency and kidney water could not contain liver and kidney, indicating that refractory hypertension was indeed related to the traditional Chinese medicine constitution [8].

## **2.4. Characteristics and general rules of TCM syndrome distribution of refractory hypertension**

Syndrome refers to the generalization of the pathogenesis of a disease at a certain stage; Hou refers to the external manifestation of the pathogenesis or state that can be intuitively felt. Holistic view is a major feature of TCM treatment. Refractory hypertension has complex pathogenesis, multiple pathological factors, long course of disease and difficult clinical treatment. Lack of unified, objective, clear dialectical classification. To study the distribution characteristics and general rules of its syndromes is beneficial to effectively guide the clinical treatment of traditional Chinese medicine. In traditional Chinese medicine, diseases are classified in eight categories. Among them, Yin and Yang are the first of the eight principles of syndrome differentiation, which are the two major principles of disease attribute. The human body is nothing more than Yin and Yang balance, opposition restriction.

So that the body can maintain a dynamic balance. The abnormal rise of blood pressure in patients with refractory hypertension indicates that the stable state of the cardiovascular system is disrupted, the sympathetic nerve is overexcited, and the balance of vasoconstricting peptide and vasoconstricting peptide is broken. Yin and Yang are balanced and blood pressure is stable. If Yin does not control Yang due to various factors, Yang hyperactivity will cause abnormal blood pressure rise, which is called "Yang hyperactivity syndrome" in traditional Chinese medicine.

Wu Yu <sup>[9]</sup> et al. included 69 patients with refractory hypertension into the study, and the statistical analysis of the data showed that 56 of them had vertigo symptoms of different degrees, with an incidence of 81.1%. The main syndrome types are divided into two types, including deficiency of Yin and Yang and hyperactivity of liver Yang. Moreover, the syndrome type is affected by its complications, for example, deficiency of Yin and Yang is more common in diabetes patients with dyslipidemia, and most of these patients are caused by kidney water failing to nourish the liver wood and liver qi obstructing the Qingqi. The main influencing factors are Yin deficiency and internal wind. From the perspective of syndrome differentiation of zang-fu organs, the study found that hypertension is related to liver dysfunction, mainly in liver, involving kidney and spleen. Studies have found that the proportion of all pathological elements of refractory hypertension in descending order is: phlegm turbidness (81.9%) Qi deficiency (77.1%) and Yin deficiency (64.8%). Phlegm turbidity was the main factor of solid syndromes, followed by blood stasis. Among the syndromes of deficiency, Qi deficiency is the main factor, followed by Yin deficiency. In addition, the liver accounted for 93.3%, followed by kidney 59%, heart 52.4% and spleen 40%. It was also found that Yin deficiency syndrome was correlated with diabetes and dyslipidemia. Phlegm turbidness syndrome is closely related to alcoholism <sup>[10]</sup>.

### **3. TCM treatment of refractory hypertension**

#### **3.1. TCM compound for treatment of refractory hypertension**

Since ancient times, TCM has played a great role in the treatment of a variety of difficult and complicated diseases, and modern TCM scholars have accumulated rich clinical experience in exploratory research. Chinese medicine master Zhang Xuewen believed that Yang hyperactivity as a basic pathogenesis throughout refractory hypertension; Its important syndroms are phlegm, dampness and blood stasis; This deficiency is its basic disease. According to the theory of traditional Chinese medicine, Yang hyperactivity is mainly related to the liver, so the treatment of refractory hypertension is mostly based on the liver. Gastrodia Guteng Drink is taken as the basis, and it is supplemented by clearing liver heat, tonifying liver and kidney, and culling liver Yang. When the etiology was dampness, the main prescription was Wuling powder combined with Gastrodia Unguteng Yin. When the blood stasis was heavy, the empirical formula Qinggan Tongluo decoction was mainly added or decreased. If phlegm is heavy, vertigo is mainly increased or decreased by the empirical prescription; If deficiency is dominant, Xinjiaqijudihuang decoction should be mainly supplemented or decreased, and qi tonic, blood tonic, Yin tonic or Yang tonic drugs should be added according to the changes of qi and blood Yin and Yang. In combination with the actual symptoms and signs of patients, the pathogenesis can be targeted based on syndrome differentiation. Chief physician Li Qinghai proposed that refractory hypertension is mainly due to liver depression and fire, phlegm turbidness resulting in chronic qi deficiency, and the disease is mixed with deficiency and accumulation. Therefore, for patients with refractory hypertension qi deficiency, the treatment should focus on calming the liver, soothing the liver, eliminating phlegm, turbidity and removing blood stasis. Astragalus membranaceus should be used in prescriptions and tested clinically with good results <sup>[11]</sup>. For patients with Yang-deficiency refractory hypertension, some scholars selected Sini Decoction as the basic prescription, and observed the blood pressure level and blood pressure variability of patients after treatment according to the changes of syndrome types. Results showed that both the blood pressure level and blood pressure variability of patients were improved 24 hours after treatment <sup>[12]</sup>. Wang Chunliang <sup>[13]</sup> found that combined with Rehmannia Yinzi capsule on the basis of conventional Western medicine treatment in the treatment of refractory hypertension with Yin and Yang deficiency syndrome has significant effect, which can effectively regulate the level of neuroendocrine hormones and improve the clinical symptoms of patients. Liu Anping et al. <sup>[14]</sup> included 160 patients with refractory hypertension of Yin deficiency and Yang hyperactivity with prospective self-controlled study method, and 1: One week after treatment, it was found that on the basis of conventional Western medicine treatment, taking Guan Jian Fang could further reduce the blood pressure of patients with Yin deficiency and Yang hyperactivity, improve clinical symptoms, and protect kidney function to a certain extent. Studies have found that Xuefu

Zhuyu Decoction can repair endothelial injury cells, and plasma NO and ET-1 indexes of the study group after treatment were lower than those of the reference group [15]. Pang Yi [16] believed that the disease had a long course and the qi pulse could not be damaged after a long period of illness, resulting in qi deficiency and loss. The treatment should focus on nourishing Yin and replenishing Yang and promoting blood stasis. Therefore, the use of Xuefuzhuyu capsule to promote blood circulation and remove blood stasis, qi analgesia, the treatment of refractory hypertension effect is significant, the ingredient containing ligusticum Chuanxiong can achieve the effect of calming the mind and promoting blood circulation and removing blood stasis; Red peony root, Angelica sinensis and safflower can nourish Yin and Yang, nourish blood and remove blood stasis. The prescription also reduces the adverse effects of Western medicine. Yang Aifeng et al. [17] found that taking rhubarb Zhezhe pills could not only reduce stable blood pressure, but also reduce blood lipid and urinary trace protein, which greatly improved symptoms and the quality of life of patients.

### **3.2. Treatment of refractory hypertension by acupuncture**

Acupuncture and moxibustion is a typical Chinese medicine therapy with the most distinctive characteristics. As a typical non-drug therapy, it is highly valued in the treatment of refractory hypertension. Shen Pengfei and Wang Shu included 135 patients with refractory hypertension. Take Renying, Hegu, Taichong, Quchi, Zusanli point. Shi's twisting and twisting method was applied, that is, small amplitude, high frequency, needle retention 30 min; Hegu and Taichong points were taken, both of which were directly pricked 0.8~1 inch. Shi's twisting and purging method was applied, that is, the doctor used the patient-oriented position, centered on Ren pulse, counterclockwise on the left side of the body and clockwise on the right side of the body. Quchi and Zusanli points were taken and stabbed 1 inch straight. Leave the needle for 20 minutes. Studies have shown that acupuncture can stably reduce patients' 24h blood pressure, effectively improve blood pressure load and protect target organs, and has clinical promotion value [18]. Wang Shuguo [19] included 106 patients with refractory hypertension, classified them by syndrome differentiation and formulated corresponding acupuncture and moxibustion prescriptions: the basic points selected were Zusanli, Yanglingquan, Baihui, Hegu, Quchi and Sanyinjiao. The combination points of phlegm-dampness accumulation type were Xiajuxu, Zhongwan and Xuehai. Liver-fire hyperactivity type matching points for Taichong, Yongquan, Taixi; Yin and Yang two deficiency acupoints for Guanyuan, Qi sea, Taixi, Shenque. And cooperate with the corresponding reinforcing and reducing techniques. The side effects of taking refractory hypertension drugs are obvious. Acupuncture and moxibustion methods are tried to treat the disease. Hand-yangming large intestine meridian, Zouyangming stomach meridian, Zoutaiyin spleen meridian and ZouShaoyang bile Meridian are selected as the basic prescription. Acupuncture and moxibustion can dredge the meridians and coordinate the functions of organs. This kind of treatment has no side effects and has attracted more and more attention from scholars at home and abroad.

### **3.3. Acupoint application for treatment of refractory hypertension**

Acupoint application, which integrates meridians, acupoints and drugs, is a compound treatment method of traditional Chinese medicine. In Treatise on Miscellaneous Diseases of Typhoid Fever, external application of this kind of TCM external treatment method is recorded, and a variety of pasted prescriptions are listed. "Shengji General Record" put forward: "ointment ointment moisten, in order to dispel evil poison, where the skin stored gas, cream can eliminate it, also can rub it", put forward TCM acupoint application can eliminate "skin stored gas" treatment mechanism. From the perspective of traditional Chinese medicine, meridians connect the zang Fu organs, communicate inside and outside, operate qi and blood, and nourish the whole body. Acupoint application stimulates the acupoints to stimulate the Qi of meridians, so that the medicine reaches the Zang fu organs and thus cures diseases [20]. Eighty patients with refractory hypertension admitted to Tang Shanci [21] were randomly divided into the observation group and 40 patients in each control group. Observation group was added with acupoint application on the basis of conventional drug treatment: Yongquan, Sanyinjiao, Quchi, Fengchi point were selected. The application prescriptions were as follows: 10 g Wuzhuyu, 10 g Tribulus white, 15 g achyranthes radix, 15 g Prunella prunus, 10 g ligusticum Chuanxiong, 15 g Honghua, and applied for 6-8 hours. Results The total effective rate of the observation group (97.50%) was higher than that of the control group (82.50%), The difference was statistically significant. The results show that acupoint application can dredge the meridians, regulate the function of zang fu organs, unify the internal and external environment of the human body, the effect is very good, easy to operate. Therefore, on the basis of conventional western medicine treatment, the clinical efficacy of acupoint application in patients with refractory hypertension has been significantly improved, and the treatment

method has the value of popularization. Lin Qiue <sup>[22]</sup> et al. ground *Cornus officinalis* into powder, made a paste with vinegar, and applied it to Yongquan Point of Shuangzu. Once a day for 2 courses of treatment. 40 patients with refractory hypertension were included and divided into observation group and control group. The control group was treated with conventional drugs, and the observation group was treated with acupoints on the base. The effective rate was 90% in the observation group and 70% in the control group, and the incidence of adverse drug reactions was 10% in the observation group and 40% in the control group. The results showed that non-invasive acupoint application could stabilize blood pressure, reduce the incidence of adverse reactions, with high price acceptance, little impact on patients' lives, and good patient compliance. Although acupoint application is safe and has no side effects, due to individual differences, some patients may have allergic reactions or mild poisoning to some drugs in clinical application. Therefore, before use, skin reactions of patients should be checked to avoid allergies and poisoning <sup>[23]</sup>.

### **3.4. Acupuncture point embedding**

Acupoint catgut embedding therapy is a kind of compound therapy, which integrates many kinds of therapy and many kinds of effects. It is mainly to insert medical catgut into the corresponding acupoints to continuously stimulate the acupoints, stimulate the meridians, harmonize the Yin and Yang qi and blood, and achieve the purpose of disease treatment <sup>[24]</sup>. Obesity-resistant hypertension mostly belongs to phlegm-dampness obstructing type. Therefore, Wang Xinyi, Zhang Tingting <sup>[25]</sup> et al. treated 48 obese young patients with hypertension. Fengchi, Tianshu, Daheng, Daimai, Zhongwan, Qihai, Zusanli, Fenglong, Yinlingquan and other acupoints were selected on the principle of invigorating spleen and dispelling phlegm. Acupoint catgut embedding method was used to treat refractory hypertension. The results showed that the effective rate of acupoint embedding method was 93.75%. From the perspective of TCM syndrome curative effect, the effective rate reached 91.67%. Compared with before treatment, blood pressure, body weight index and body fat percentage were all reduced. The results show that acupoint catgut embedding method has definite curative effect on refractory hypertension.

### **3.5. Foot bath therapy**

Wu Xiaohe, Dai Yu et al. <sup>[26]</sup> studied the different types of refractory hypertension (hyperactivity of liver fire, deficiency of Yin and Yang, hyperactivity of Yin and Yang, excessive accumulation of phlegm-dampness). Different foot bath formulations were developed respectively. 90 patients with refractory hypertension were included and randomly divided into observation group I, observation group II and control group with 30 cases in each group. Observation group I began to use foot bath formula after routine hypotension to 140/90mmHg; Observation group II received foot bath prescription at the same time of routine hypotension; The course of treatment is 8 weeks. The results showed that the effective rate and total effective rate of observation group I were 63.33 % and 86.66 %, respectively, and that of observation group II were 70 % and 90 %, which were significantly higher than that of control group 36.66 % and 70 %. To sum up, the special foot bath formula enables the ions of the liquid medicine to be absorbed by the mucosa and the skin into the blood circulation of the human body under the warm and mechanical action of water, so as to be transported to the viscera of the whole body of the human body, so as to accelerate the absorption of drugs, improve the spasm of small arteries, dilate blood vessels, reduce peripheral resistance and thus reduce blood pressure <sup>[27]</sup>.

## **4. Conclusion**

The adjuvant treatment of refractory hypertension by traditional Chinese medicine has achieved remarkable results. At present, the clinical focus is mainly on the treatment of hypertension, and there are few studies on the exploration and treatment of refractory hypertension. Refractory hypertension has higher risk, high risk, serious threat, damage to target organs with high disability rate and fatality rate. Modern people's life pressure increases, obesity rate increases, life and work are affected by various uncontrollable factors extremely irregular. There are still few high-quality randomized controlled clinical trials in TCM for refractory hypertension. The research on the occurrence of refractory hypertension and human body constitution is still unclear. More clinical trials are needed.

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