

Discussion on the Treatment of Amyotrophic Lateral Sclerosis Based on the Method of Tonifying Liver and Kidney

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Abstract: Amyotrophic lateral sclerosis (ALS), as a known motor neuron disease, has not been widely studied. Although there has been progress in research on the pathogenesis and clinical treatment of this disease, there is currently no clear guiding treatment plan or standardized treatment standards for curing ALS at home and abroad. Based on the traditional medicine's differentiation and treatment of this disease, as well as related diagnosis and treatment, this article believes that the combination of tonifying the liver and kidney method with modern medicine can provide better clinical efficacy. Regarding the etiology and pathogenesis of this disease, this article elaborates on the role of relevant prescriptions and drugs in improving symptoms from the aspects of basic theory, dialectical treatment, empirical formula, flexible addition and subtraction of drugs, and modern pharmacology research, in order to further promote in-depth research on this disease, Enable traditional Chinese medicine to alleviate pain faster for more ALS patients.

1. Introduction

Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease, commonly known as "ALS disease", the disease is typically characterized by the simultaneous involvement of upper and lower motor neurons, resulting in the gradual loss of motor neuron function in the brain and spinal cord, leading to progressive muscle weakness and eventually death [1]. The course of ALS disease develops rapidly, the disability rate and fatality rate are extremely high, and the average survival time of patients is generally 2-5 years [2]. At present, the mechanism of this disease is still unclear, but it can be confirmed that the pathological mechanism of this disease is complex and diverse, and they interact with each other [3]. There is no specific drug available for clinical treatment, and Western medicine mainly focuses on symptomatic treatment. Clinically, two drugs with reasonable efficacy are generally used: riluzole, a glutamate receptor antagonist, and edaravone, a newly introduced free radical scavenger. The application of these two drugs may only prolong the life cycle of patients for a few months [4], and have no significant blocking effect on disease progression. ALS does not have a specific name in Chinese medicine, but it is generally believed

that ALS should be classified as the category of Wei zheng. The pathogenesis of this disease is complex, and deficiency of liver and kidney is the key pathogenesis of this disease, and the treatment should focus on tonifying liver and kidney [5]. This article will take the deficiency of liver and kidney as the theoretical basis, tonifying liver and kidney, nourishing Yin and reducing fire as the treatment principle, and use Tiger Qian pill as the main prescription to explore and discuss the direction of TCM diagnosis and treatment of ALS.

2. Nature of the disease

2.1. TCM Disease Names

The clinical manifestations of ALS are mostly weakness of limbs and muscle atrophy, which is in line with the understanding and diagnosis of Wei zheng in traditional Chinese medicine. The core symptoms of ALS are shown in the figure 1. Wei zheng is mainly a weakness of hands and feet, gradually losing use, based on clinical symptoms; it is believed that ALS should conform to the category of Wei zheng. Moreover, many TCM doctors have achieved considerable curative effect in the clinical diagnosis and treatment of ALS with the diagnosis and treatment idea of Wei zheng [6].

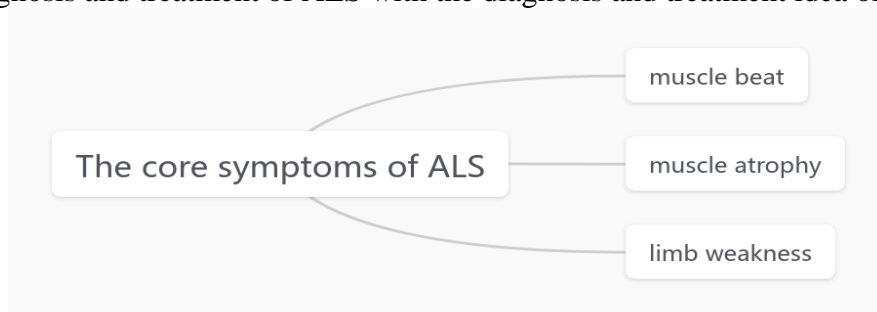


Figure 1: The core symptoms of ALS

2.2. Pathogenesis

The etiology and pathogenesis of ALS are complicated, and different doctors have different opinions in the past. Xie Renming [7] et al believed that the evil of dampness and turbidity is the pathogenic factor of ALS, the invasion of evil poison is the important cause, the deficiency of liver, spleen and kidney is the internal cause of the disease, and the treatment should be detoxification and dampness-fuzheng; Huang Xianghong [8] et al considered that the opening and closing of the Xuanfu and the blocking of the cerebral collaterals were the key to the disease, and the diagnosis and treatment with the deficiency of the spleen and kidney as the basis and the blocking of the brain by the evil toxin of phlegm and blood stasis as the auxiliary; Chen Jinliang [9] et al believed that Eight Extraordinary Meridians are damaged, and the deficiency of the meridians causes the body to lose qi, blood and Yin and Yang, especially the deficiency of the Du pulse. They put forward the view of treating motor neuron disease from Eight Extraordinary Meridians and established a treatment method of Fu Yuan Qi Huan, Yang Rong Sheng ji. Although the etiology and pathogenesis of this disease is complex, most Chinese medicine practitioners conclude that the five viscera deficiencies should be the main damage, and the main responsibility is the liver and kidney two viscera deficiency damage.

3. Academic Thought

3.1. The Theoretical Basis of TCM Based on Deficiency of Liver and Kidney

Dialectical treatment is not only the basic principle of Chinese medicine to understand and treat diseases, but also the advantage and characteristic of Chinese medicine to treat Wei Zheng. Treatment is based on the premise of dialectical accuracy. That is, after a clear understanding of the essence of the disease, we can talk about the rules of treatment, and finally cure the disease.

Huangdi Neijing says: *"The liver governs the tendons, the kidney governs the bones..."*. Liver main tendons, insufficient liver blood, no help to nourish the tendons, then hand and foot flexion and extension; kidney main bone, kidney deficiency, marrow deficiency, bone weakness, difficult to walk. Therefore, liver and kidney deficiency patients are manifested as limp limbs, walking inconvenience, and big meat gradually out of the disease. Lingshu · Meridians said: *"liver foot Jueyin pulse..... Carries the stomach is the liver, gallbladder, the upper diaphragm, cloth, rib, follow the throat on the opponent catfish"* 、 *"kidney foot Shaoyin pulse* From the kidney through the liver diaphragm into the lung, follow the throat, with the tongue ", the meridians of the liver and kidney are followed into the throat, so the patients with liver and kidney deficiency can be seen indistinguishable speech, swallowing disorders, coughing and other diseases [10]. Difficult meridian said: *"five damages to bone, bone flaccidity cannot rise from the bed of death."*、 *"However, foot has little Yin Qi, that is, bone withered. Shaoyin, kidney pulse." Kidney hiding essence, kidney essence is sufficient, the bones are strong and strong; on the contrary, kidney essence is insufficient, then see bone flaccidity, bone withered.* The Danxi Heart Law first mentions the draining the south and supplementing the north law, which not only improves the type of Wei Zheng, but also creates the prescription Tiger Qianwan for treating Wei Zheng. Ye Tianshi's medical case contains: *"flaccidity and antenication, liver and kidney diseases. "*, *"flaccidity and intolerance.... Are the liver and kidney for disease."* its discussion of Wei Zheng is more responsible for the liver and kidney two viscera.

The liver master dredges, that is, the liver qi has the function of dredging and reaching the qi machine. The liver stores blood, which means that the liver has the function of storing blood. The liver in the body and tendons, plays the role of maintaining joints and regulating their movement. The symptoms of limb weakness are the manifestation of weak tendons. The kidney contains essence, which is the most basic substance that constitutes the human body and maintains the human life activity, and is the material basis of the zang-fu body function. Kidney essence deficiency, essence deficiency can not irrigate the end, so that the muscles and muscles are lost, easy to develop this disease. In addition, the kidney Yin and kidney Yang play an extremely important role in promoting and regulating the metabolism and mutual transformation of the body's essence, qi, blood and body fluid. Kidney-yin and kidney-yang are the root of the five viscera and the fundamental of the body's life activities. [11]. Kidney storing essence, liver storing blood, liver and kidney homology, also known as essence and blood homology or ethylene and decane homology. If kidney essence is sufficient, liver blood metaplasia is active; if liver blood is sufficient, kidney essence is filled. If the liver and kidney are properly nourished, the tendons are strong, the gait is steady, and the muscles are full; If the tendons are damaged to the bone, the bone is damaged to the tendons, the muscles are thin, the steps can not be carried out, and the time is lost. Liver and kidney loss at the same time, that is, the muscles and bones are damaged, the kidney essence is insufficient, the liver is displaced and the Yin does not control the Yang, there will be muscle rigidity, tremor and other pathological phenomena.

To sum up, all generations of doctors believe that liver and kidney and Wei Zheng connection. This article also believes that the deficiency of liver and kidney is the root of the onset of Wei

zheng, liver and kidney deficit for a long time, the imbalance of Yin and Yang of the body, the imbalance of qi and blood, the loss of zang-fu meridians, and the damage of the body's healthy qi, resulting in the disease later easy to clamp phlegm, clamp dampness, clamp blood stasis, clamp poison and other pathogenic factors, aggravate the deterioration of the condition.

3.2. Take "Tonifying Liver and Kidney, Nourishing Yin and Lowering Fire" as the Core Treatment

According to the characteristics of Wei zheng, this article thinks that the general rule should be tonifying the liver and kidney, nourishing Yin, and reducing fire in the treatment of Wei zheng. The article of Medical prescription Examination Potence Bi gate put forward that Liuwei Dihuang pill plus Huang Bai and Zhi Mu to tonify liver and kidney, nourishing Yin and lowering fire can treat potency syndrome. Liu Wansu, a famous doctor in Jin Yuan period, said: "*King Kong pills (Bi Xie, Du Zhong, Cong Rong, Tu Si Zi) treating kidney damage and bone flaccence cannot rise from the bed, it is appropriate to benefit essence.*" This prescription is to tonify the liver and kidney, nourish the five viscera, strong tendons and bones to treat flaccidity. Zhang Xichun, an outstanding modern doctor, in his book Medical ZhongZhongShenxilu, emphasized in the application of Zhenagnition soup, "For those who are disabled, add antler glue and tiger bone glue for two dollars each. However, there are many two rubber counterfeiters, if afraid of its false, can be intermittent, dodder each three money generation ", honest experience. "Bone flaccidity with deer glue, tiger glue to take its bone also. Bones by the wind, plus tomorrow hemp to take its can search the bones of the wind, but also can supplement the bones. If its impotence is exclusively in the legs, but with the ox knee to lead under the line." Antler glue, tiger bone glue, intermittent, dodder and other kidney filling essence to fill the congenital. In summary, thanks to the unique insights of famous doctors throughout history on the treatment of Wei Zheng, they have always attached great importance to tonifying the liver and kidney, which proves that the treatment of skeletal diseases is closely related to the method of tonifying the liver and kidney, and points out the direction for our future generations to treat Wei zheng disease [12, 13].

Learning from the past and the present, we should apply the method of tonifying liver and kidney to clinical ALS patients as soon as possible. ALS is a chronic progressive disease, urgent treatment of its standard, slow treatment of its root, we should focus on the essence of the disease treatment, distinguish the primary and secondary, must be in the principle of tonifying the liver and kidney for treatment, supplemented by removing dampness, phlegm, blood circulation and stasis, detoxification, the disease is treated, the standard disease natural solution.

4. Feasibility of Tiger Qianwan for ALS treatment

4.1. Origin of the Prescription and Its Application in Ancient Times

Tiger hidden pill was first seen in the Yuan Dynasty Zhu Danxi written Danxi heart Law, the book said: "tiger hidden pill, treatment of potency, and tonifying the kidney pill." It is named Huqian Pill because of the principle of calming the deficiency wind of the liver and kidney. The wind comes from the tiger, and when the tiger hides, the wind also calms down. The prescription is composed of golden cypress (fried with wine), Anemarrhena asphodeloides (fried with wine), prepared rehmannia root, tortoise plastron (cooked with wine), white peony, tiger bone (cooked with wine), cynomorium songaricum, dried ginger, and pericarpium citri reticulataea total of 9 traditional Chinese medicine, ground the above drugs, boiled mutton, pound and into pills, light salt water or warm water to take. The meridian distribution of the nine traditional Chinese medicines mentioned above is shown in the figure 2. Taking the efficacy of nourishing Yin and lowering fire,

strengthening muscles and bones. It is used in the treatment of soreness of the waist and knees, weakness of the muscles and bones, emaciation of the legs and feet, weakness in walking, red tongue with little moss and weak pulse.

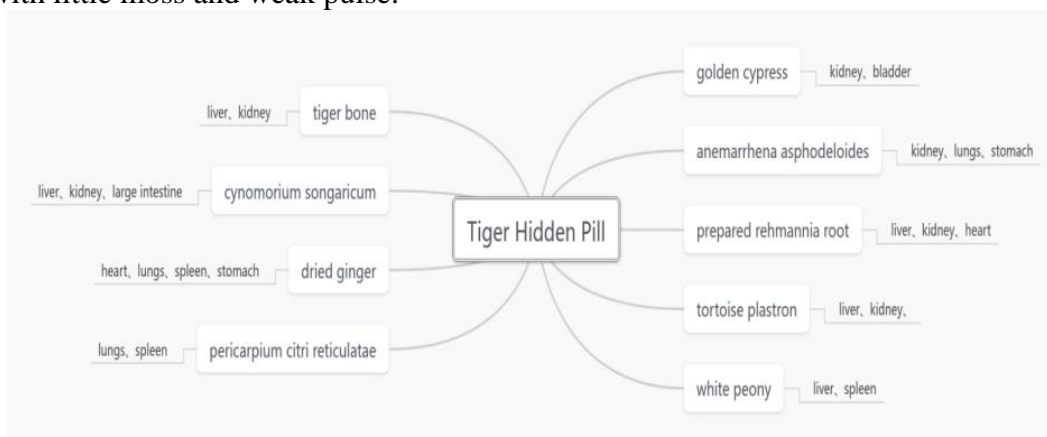


Figure 2: Tiger Hidden Pill

Ye Tianshi's Clinical Guide Medical Record contains as many as 12 clinical medical cases of Tiger Qianwan. Through discussing the related etiology - pathogenesis - dialectical - legislation - rigorous TCM diagnosis ideas, the curative effect of Tiger Qianwan on the treatment of Wei zheng is made clear [14]. This prescription has been used for more than 600 years from the Yuan Ming and Qing Dynasties to the present, among which the widely circulated variant prescriptions are Jianbu Hu Qian Wan written by Zhang Jingyue in Jingyue Shu, Jiawei Hu Qian Wan written by Zhang Lu in Zhang's Medicine Tong in Qing Dynasty, and Jianbu Wan written by Ling Huan in Qing Dynasty, which all take Tiger Qian Wan as the base prescription. On this basis, it is also used for the treatment of muscle and bone diseases, and points out the direction for the treatment of liver and kidney deficiency syndrome, such as Zhu Pingdong [15], a doctor of later generations.

4.2. Analysis and Characteristics of the Formula

4.2.1. Principles of Formulation

Shennong's Classic of the Materia Medica says: "One hundred and twenty kinds of medicine are for the king, the main life-supporting the use of medicines must be combined with the king, ministers and auxiliaries." Jun, Chen, Zuo and Shi is the principle of formula formation in Chinese medicine. It highly summarizes the therapeutic efficacy of this formula and the direction of the action of each flavor of traditional Chinese medicine. This formula also follows the rigorous principle of prescription in Chinese medicine to achieve the expected therapeutic effect.

4.2.2. Tonifying Deficiency Damage and Clearing Deficiency Heat as the Leading

This prescription use much Huangbai to take its efficacy of clearing the real heat and the deficient heat of Lower-Jiao. Zhimu is used for clearing heat and removing fire and tonifying Yin. These two medicines can be matched to remove fire without harming Yin, to nourish Yin but not excessively; cooked dihuang and tortoise board will enter the liver and kidneys meridians, and together they can play a role in nourishing yin and blood, benefiting the kidneys and strengthening the bones; the acidity of white peony can nourish the blood, soften the liver, astringe yin and suppress the liver, in order to prevent the liver and kidneys from being deficient in yin for a long period of time, which will result in the disharmony of Yin and Yang, and the hyperactivity of Yang leading to Wind.

4.2.3. Tonifying Blood and Strengthening Muscles and Bones Aid

The assistant medicines use tiger bones and cynomorium to strengthen the muscles and bones. The original prescription used tiger bones, but later tiger bones were replaced by cow bones or pig bones because our country had listed tiger bones as banned drugs. Tiger bone, a product with blood and flesh, is utilized to calm the liver-wind and strengthen the sinews and bones; cynomorium can tonify the kidney yang, benefit the essence and blood, and strengthen the waist and knees. These two medicines are used together to enter the liver and kidney meridians. They can be matched to play the role of tonifying the essence and blood, strengthening the sinews and bones as well. [16]

4.2.4. Regulating Qi to Protect the Middle and Introducing Drugs Directly

With dried ginger and *Pericarpium citri reticulataea*, the two medicines are combined, one is to take its warm spleen, regulating qi and stomach, and the other is to restrict the bitter cold of golden cypress, and its three Yang seeks Yin; so that the medicine *Achyranthes sinensis* in the *Materia medica Yan Yi* supplement contained: "*can lead the drugs down*", so it is used to lead the drugs down, direct to the disease; Take another mutton to warm up the deficiency, warm kidney to help Yang.

The combined use of various medicines to fill the deficiency as the basis, nourishing but not greasy, filling but not stagnant, draining fire without damaging Yin, supplementing Yin without damaging positive, a total of tonifying the liver and kidney, strong muscles and bones.

5. Modern Research

Modern researchers have analyzed and summarized the experience of ancient people in treating Wei Zheng using the medicinal taste in formulas. The results confirm that the kidney meridian has the highest frequency of traditional Chinese medicine used for treating Wei zheng, followed by the liver meridian, and the commonly used traditional Chinese medicine belongs to the liver and kidney meridians, belonging to the category of tonifying liver and kidney. According to modern pharmacological studies, Huqian Pill has a wide range of pharmacological effects. In addition to anti-inflammatory, analgesic and anti-fatigue effects they can also promote the differentiation of osteocytes, induce the secretion of interleukin-1 receptor and exosome antagonists, and play pharmacological effects by regulating the hypothalamic-pituitary-gonadal axis. The mechanism of improving the body's strength and bone strength may be as follows: promoting the proliferation of bone marrow stromal stem cells, reducing the content of serum alkaline phosphatase and interleukin-6, increasing the content of serum osteoprotectin (OPG) and regulating the secretion of BMP-2.

Huqian pill is used in the treatment of motor neuropathy, specifically related diseases include: Myasthenia gravis, progressive muscular dystrophy, poliomyelitis sequela, rheumatoid arthritis, syringomyelia, rickets, etc., the clinical efficacy is very good, especially in the early and middle stages of the disease, can effectively relieve the symptoms of speech, muscle tremor, muscle atrophy and other symptoms, improve the condition, delay the deterioration of the disease.

6. Conclusions

For most ALS patients, the most painful part is not facing death, but living painfully. Although scientists at home and abroad have explored ALS for many years and have done a large number of clinical experiments, although there is a certain understanding of the etiology and pathogenesis of the disease, but up to now, our understanding of the disease and treatment plans are still very little. However, after many aspects repeated, large number of clinical trials and research have confirmed

that modern medicine combined with traditional Chinese medicine, diagnosis and treatment of this disease, through the multi-target, multi-channel, multi-faceted synergistic effect of traditional Chinese medicine, better improve clinical symptoms, and improve the quality of life of patients and reduce the burden of life of patients. Due to the special nature of the pathogenic groups and the disease, although we lack multicenter and large-sample joint research on this disease, we should still give full play to the characteristics of Chinese medicine, combine the principles, methods and prescriptions of traditional Chinese medicine closely with the dual means of modern medicine, and actively explore and in-depth research on the pathological mechanism and disease progress of ALS without giving up; actively conduct pharmacological research and develop new drugs, and strive to improve the diagnosis and treatment norms of ALS that are more simple, efficient, inexpensive and suitable for promotion. This paper is expected to provide a new argument for the diagnosis and treatment of ALS, so that Chinese medicine can relieve the pain of more ALS patients faster.

References

- [1] Hardiman O, Al Chalabi A, Chio A, Corr E M, Logroscino G, Robberecht W, Shaw P J, Simmons Z, vandenBerg L H. Amyotrophic lateral sclerosis. *Nat Rev Dis Primers*. 2017 Oct 5; 3: 17071
- [2] Guo Jie, Kang Kaiwen, Li Hua et al. Research progress on the pathological mechanism and treatment of amyotrophic lateral sclerosis. *Modern Chinese Medicine*, 2021, 41 (06): 6-10
- [3] Liu Xiaomin, Li Aidong, Hu Jun. Clinical research status of acupuncture in the treatment of amyotrophic lateral sclerosis. *Asian-pacific Traditional Medicine*, 2017, 13(5):73-75.
- [4] Huang Xianghong, He Pengfei, Ma Bin, Yang Qingbo, Wu Huihong. To explore the application of Kaixuan method in the treatment of amyotrophic lateral sclerosis. *Global Chinese Medicine*, 2019, 14(12):2205-2208.
- [5] Chen J L, Ping Yang, Wang Dianhua. Therapeutic effect of Jiweiling series preparations on 240 cases of amyotrophic lateral sclerosis. *New Chinese Medicine*, 2005(09):38-39.
- [6] Wu Huihong, Yang Qingbo, Ma Bin, Huang Xianghong, He Pengfei. Analysis on the theoretical basis of aromatic resuscitation and detoxification in amyotrophic lateral sclerosis. *Global Chinese Medicine*, 2023, 16(02):280-283.
- [7] Liu Yingqi, Wang Zhaoxia. Study on the theory of treating myasthenia gravis from deficiency of liver and kidney. *World Latest Medical Information Digest*, 2019, 19(51):148.
- [8] Cui Y Z, Zhao J Q, Dong X, et al. Origin and current of impotence syndrome. *China Medical Guide*, 2023, 20(8): 141-145.
- [9] Zhang Yuqing, Wang Lei. An analysis on the history of bone flaccwe. *Global Chinese Medicine*, 2019, 12(10): 1610-1614.
- [10] Yao P Y, Zhao J Y. Ye Tianshi's experience in using Tiger Qianwan. *Journal of Chengdu University of Traditional Chinese Medicine*, 2018, 41(4):69-7195.
- [11] Zhu Pingdong, Liu Xiaochun. New clinical use of Tiger Qian pills. *Guangming TCM*, 2014(9):1991-1992.
- [12] Chen Shiqin, Qi Pengkun, Yao Xiaosheng. Discussion on the theory of "equal emphasis on muscles and bones" in the treatment of chronic muscle and bone diseases. *Journal of Practical Chinese Medicine Internal Medicine*, 2022, 36(5):4-6.
- [13] Liu L, Gao L X, Li M, et al. Analysis of drug use rules for flacciness in Medical Records based on data mining. *Journal of Mathematical Medicine & Pharmacology*, 2023, 36(2):88-94.
- [14] Yao Pengcheng, Ma Binxiang, Guan Yonglin et al. Hu Qian pills in the treatment of osteoporosis research progress. *Clinical Journal of Chinese Medicine*, 202, 34(06):1170-1174.
- [15] Zhang L P, Huang X M. Hu Qian Pills for the treatment of four neurological diseases. *Shandong Journal of Traditional Chinese Medicine*, 2012, 31(1):68-69.
- [16] Xu Wenjie, Qin Yong, Wang Qi-Wei et al. Research progress of traditional Chinese medicine in the treatment of amyotrophic lateral sclerosis. *Chin J Pharmacy*, 2015, 26(23): 331-333.