

Medication Rule and Innovative Application of Oral Administration of Traditional Chinese Medicine Decoction in The Treatment of Amyotrophic Lateral Sclerosis

Zhang Yiwen[†], Zhou Ruqi[†], Zhao Hao, Wang Tianqi*

ABSTRACT

The mechanism of morbidity in amyotrophic lateral sclerosis (ALS) is not yet fully understood. There is also a lack of systematic understanding of the rules of medication in the field of traditional Chinese medicine. In view of this, this article aims to explore the etiology, pathogenesis, and treatment of amyotrophic lateral sclerosis. By integrating the clinical experience of doctors, combining with the clinical signs of amyotrophic lateral sclerosis, and using modern literature retrieval methods, it aims to explore the medication law of traditional Chinese medicine decoction in the treatment of this disease. At the same time, the treatment records of amyotrophic lateral sclerosis in ancient books of traditional Chinese medicine are reviewed to sort out the common clinical syndromes, treatment methods, and Chinese herbal compounds, in order to provide more valuable references for clinical physicians.

INTRODUCTION

Research background

Amyotrophic lateral sclerosis (ALS) is a serious neurological disease. Currently, there is still a lack of effective radical treatment. Although modern medicine has made some progress in the treatment of ALS, it can only alleviate symptoms, but cannot prevent the progress of the disease. Traditional Chinese medicine has a long history and rich experience in the treatment of difficult and complicated diseases. The treatment of ALS by oral administration of traditional Chinese medicine decoction has gradually attracted people's attention.

Many studies have shown that traditional Chinese medicine has a certain potential for the treatment of ALS. For example, Yiqi Qiangji Decoction Su et al. (2006). is composed of Radix Astragali, Radix Codonopsis, Herba epimedii, Poria, Radix Rehmanniae, Radix et Rhizoma Rhei, Rhizoma Cimicifugae, Radix et Rhizoma Glycyrrhizae. By combining cold and dampness, supplementing yin and yang, addressing both symptoms and root causes, and bringing out the best in each other, a certain therapeutic effect can be achieved after being taken by a patient. The traditional Chinese medicine components of the Buzhong Yiqi decoction comprise Ramulus Cinnamomi, Matrimony Vine, Radix Aconiti Lateralis Praeparata, Radix Rehmanniae Preparata, Poria, Rhizoma Cimicifugae, Indian Mulberry, Solomon's seal

and the like. It can invigorate the spleen and tonify the kidney, and persistent use can effectively alleviate symptoms.

Purpose of study

To explore the regularity and innovative application of oral administration of traditional Chinese medicine decoction in the treatment of amyotrophic lateral sclerosis. The purpose is to provide new ideas and methods for the treatment of ALS. Through the analysis of different traditional Chinese medicine decoction compounds, the characteristics and rules of its medication were summarized to provide a scientific basis for clinical treatment. At the same time, combined with the research methods of modern medicine, we explore the innovative application of traditional Chinese medicine decoction in the treatment of ALS to improve the therapeutic effect and the quality of life of patients.

Literature sources

In order to deeply understand the commonly used traditional Chinese medicine and its medication rules in the treatment of amyotrophic lateral sclerosis. In this study, 219 articles on the treatment of amyotrophic frontal cord sclerosis from the perspective of traditional Chinese medicine were retrieved from the CNKI system. And unifies "Prescription and Medication Rules of Professor Gao Ying in Treatment of Amyotrophic

College of Traditional Chinese Medicine, Capital Medical University.

Correspondence to: Wang Tianqi, College of Traditional Chinese Medicine, Capital Medical University. Postal address: No. 10, Xitoutiao, Youan Men Wai, Fengtai District, Beijing 100069, China.

E-mail: wangtianqi2022@ccmu.edu.cn.

Keywords: Amyotrophic lateral sclerosis; traditional Chinese medicine; treatment; medication rule

Lateral Sclerosis Based on Data Mining” li et al. (2022), “Discussion on prescription and medication rules of Chinese medicine treating amyotrophic lateral sclerosis related atrophy disease in ancient books based on data mining” Cao et al. (2020) to implement data statistics. Among them, 25 prescriptions, a total of 86 kinds of traditional Chinese medicine were involved, and the frequency analysis and property analysis of traditional Chinese medicine were carried out. Wang et al. (2016).

Analysis of common traditional Chinese medicines and medication rules

Use of common Traditional Chinese medicine

Statistical results are shown in Table 1. The top 11

Chinese herbs used most frequently in the treatment of ALS were Rhizoma Atractylodis, licorice, Poria cocos, prepared Rehmannia, Ginseng, Peony, Astragalus, Radix Angelicae Sinensis, Rhizama Dioscoreae, Radix Achyranthis Bidentatae and Fructus Corni. The cumulative use times of these 11 Chinese herbs were 78 times, accounting for 37.86% of the total cumulative use times. Among them, four herbs in the top 5 are combined into four junzi decoction. They are Radix et Rhizoma Ginseng, Rhizoma Atractylodis Macrocephalae, Poria and Radix et Rhizoma Glycyrrhizae and the addition or subtraction of four junzi decoction is also widely used in the modern treatment of amyotrophy lateral sclerosis. Bao et al. (2016).

Table 1: Use of common Traditional Chinese medicine.

Herbs	Frequency	Prescription occupying frequency (%)	Herbs occupying frequency (%)	Indications
Rhizoma Atractylodis Macrocephalae	10	41.67%	11.63%	Invigorating qi and spleen, eliminating dampness and promoting diuresis, stopping sweating, and preventing miscarriage
Radix et Rhizoma Glycyrrhizae	10	41.67%	11.63%	Invigorating the spleen and replenishing qi, clearing away heat and toxic materials, eliminating phlegm and relieving cough, relieving spasm and pain, and harmonizing various medicines.
Poria	10	41.67%	11.63%	Promoting diuresis and eliminating dampness, invigorating spleen, calming heart and tranquilizing mind
Radix Rehmanniae Preparata	8	33.33%	9.30%	Nourishing blood and yin, replenishing essence and marrow
Radix et Rhizoma Ginseng	7	29.17%	8.14%	Invigorating source qi, restoring pulse and consolidating collapse, tonifying spleen and lung, promoting the production of body fluid and nourishing blood, tranquilizing mind and improving intelligence
Radix Paeoniae	7	29.17%	8.14%	Nourishing blood and regulating menstruation, astringing yin and stopping sweating, softening liver and relieving pain, and suppressing liver-yang
Radix Astragali	6	25%	6.98%	Invigorating qi and lifting Yang, tonifying the defensive and consolidating the exterior, inducing diuresis and detumescence, promoting the production of body fluid and nourishing the blood, removing stagnation and dredging arthralgia, expelling toxin and pus, astringing sores
Radix Angelicae Sinensis	5	20.83%	5.81%	Nourishing blood and activating blood circulation, regulating menstruation and relieving pain, moistening intestines and relaxing the bowels
Rhizama Dioscoreae	5	20.83%	5.81%	Invigorating qi and nourishing yin, tonifying spleen, lung and kidney, and arresting seminal emission and leucorrhea
Radix Achyranthis Bidentatae	5	20.83%	5.81%	Removing blood stasis and dredging meridians, nourishing liver and kidney, strengthening bones and muscles, promoting urination and guiding blood downward
Fructus Corni	5	20.83%	5.81%	Tonifying liver and kidney, astringent and removing prostration

Classification of all 86 Traditional Chinese medicines

The statistical results are shown in Table 2. The frequency of Tonic Medicinals (95 times) is the highest, far exceeding that of other types of traditional Chinese medicine. The frequency of use of Tonic Medicinals accounts for 8 of the 11 herbs most frequently used to treat ALS. The frequencies of other types of traditional Chinese medicine, from high to low except Tonic Medicinals, are as follows: Promoting Urination and Draining Dampness Medicinals (18 times), Exterior-releasing Medicinals (15 times), Heat-clearing Medicinals (12 times), and Blood-regulating Medicinals (12 times). Tonic Medicinals includes

Rhizoma Atractylodis Macrocephalae, Radix et Rhizoma Glycyrrhizae, Radix Rehmanniae Preparata, Radix et Rhizoma Ginseng, Radix Paeoniae, Radix Astragali, Radix Angelicae Sinensis, Rhizoma Dioscoreae. Promoting Urination and Draining Dampness Medicinals includes Poria, Rhizoma Alismatis, Semen Coicis. Exterior-releasing Medicinals includes Rhizoma et Radix Notopterygii, Radix Bupleuri, Radix Saposhnikoviae. Heat-clearing Medicinals includes Cortex Phellodendri Chinensis, Cortex Moutan, Radix Rehmanniae. Blood-regulating Medicinals includes Radix Achyranthis Bidentatae, Rhizoma Chuanxiong.

Table 2: Classification of Traditional Chinese medicine

Traditional Chinese medicine	Frequency	Herbs occupying frequency (%)
Tonic Medicinals	95	46.11%
Promoting Urination and Draining Dampness Medicinals	18	8.74%
Exterior-releasing Medicinals	15	7.28%
Heat-clearing Medicinals	12	5.83%
Blood-regulating Medicinals	12	5.83%
Liver-wind Calming Medicinals	10	4.85%
Astringent Medicinals	10	4.85%
Expectorant and Antiasthmatic Medicinals	8	3.88%
Wind-dampness Dispelling Medicinals	7	3.40%
Interior-warming Medicinals	5	2.43%
Dampness-eliminating Medicinals	5	2.43%
Purgatives	2	2.43%
Qi-regulating Medicinals	1	1.16%
Resuscitating Medicinals	1	1.16%
Food Stagnancy-resolving Medicinals	1	1.16%
Mind-tranquilizing Medicinals	1	1.16%

The top five most frequently used are Tonic Medicinals (95 times), Promoting Urination and Draining Dampness Medicinals (18 times), Exterior-releasing Medicinals (15 times), Heat-clearing Medicinals (12 times), and Blood-regulating Medicinals (12 times). Tonic Medicinals is used most frequently, indicating that ALS is dominated by deficiency. Tonic Medicinals has the highest proportion among Qi-invigorating Medicinals (37.9%). ALS belongs to the category of flaccidity syndrome in TCM diagnosis, which is caused by deficiency of qi and blood. Therefore, regardless of the type of patient, there will be symptoms related to deficiency, and Chinese medicine doctors will choose Tonic Medicinals to treat ALS. The frequencies of use of Promoting Urination and Draining Dampness Medicinals, Exterior-releasing Medicinals, Heat-clearing Medicinals, and Blood-regulating Medicinals are relatively high and similar, corresponding to the syndromes caused by the invasion of internal heat and dampness, wind-cold-dampness, and yin deficiency with fire.

Four qi classification of all 86 Traditional Chinese medicines

The statistical results are shown in Table 3. The top three properties are warm (93 times), neutral (55 times), and cold (46 times). Most syndromes of amyotrophic lateral sclerosis have no obvious distinction between cold and heat. The patients are mainly suffering from deficiency of qi and blood. Therefore, the use frequencies of warm herbs and neutral herbs rank the top two. While cold herbs are mainly yin-nourishing

herbs such as Radix Paeoniae and Ophiopogon japonicus. They are used for partial heat syndromes such as yin deficiency with fire hyperactivity. Some cold and cool herbs can also be used to harmonize various herbs and neutralize the nature of warm heat to enhance the effect of this prescription. The frequencies of using cool and hot herbs are the least and there is a big difference from the first three. This suggests that in the treatment of amyotrophic lateral sclerosis, the nature of warmth should not be too strong. In the treatment of partial heat syndromes, strong herbs are needed for treatment.

Table 3: Four qi Classification of Traditional Chinese medicines.

Four qi	Frequency	Herbs occupying frequency (%)
Warm	93	45.15%
Neutral	55	26.70%
Cold	46	22.33%
Cool	7	3.40%
Heat	5	2.43%

Classification of Five Flavors of All 86 Traditional Chinese medicines

The statistical results are shown in Table 4. The top three frequencies of herb flavors are sweet (130 times), bitter (77 times), and acrid (65 times). The sweet flavor has the functions of tonifying, relieving, and harmonizing. The bitter flavor has the functions of discharging and drying. The pungent flavor has the functions of dispersing, promoting qi circulation, and activating blood circulation. Many physicians give important consideration to sweet herbs, mainly taking

advantage of their effects of tonifying and relieving, relieving the middle and tonifying deficiency, and treating diseases. At the same time, herbs with a sweet taste can also harmonize various medicines, making the efficacy of the prescription stronger.

Medicines with a bitter taste are matched to tonify the middle-jiao, relieve heat, and dry dampness.

The compatibility of pungent herbs can promote the circulation of qi and dissipate stagnation, and prevent nourishing, thick, greasy substances from causing stasis in the body.

Table 4: Five Flavor Classification of Traditional Chinese medicines.

Five flavors	Frequency	Herbs occupying frequency (%)
Sweet	130	63.10%
Bitter	77	37.38%
Acrid	65	31.55%
Sour	22	10.70%
Bland	16	7.77%
Salty	15	7.28%
Astringent	6	2.91%

Classification of all 86 Traditional Chinese medicines by meridian tropism

The statistical results are shown in Table 5. The top three meridians are the spleen meridian (104 times), kidney meridian (101 times), and liver meridian (94 times). In The Yellow Emperor's Inner Classic, it is written: "Yangming alone is taken for the treatment of flaccidity syndrome." Amyotrophic lateral sclerosis belongs to the category of flaccidity syndrome in traditional Chinese medicine, which has been proven by many clinical trials and verifications from ancient times

to the present. Acupuncture at the Spleen Meridian of Foot-Taiyin has a good curative effect. Most of the herbs entering the spleen meridian have the effect of tonifying deficiency and the efficacy is mild Wang et al. (2023).

Therefore, the majority of physicians will choose herbs that belong to the spleen meridian. In addition to weakness of the spleen and stomach, many patients also have deficiency of the liver and kidney. The use of herbs belonging to these two meridians can also supplement the deficiency of the liver and kidney.

Table 5: Classification of Herbs by Meridian.

Meridian tropism	Frequency	Herbs occupying frequency (%)
Spleen	104	50.48%
Kidney	101	49.03%
Liver	94	45.63%
Lung	88	42.72%
Heart	62	30.10%
Stomach	53	25.73%
Bladder	17	8.25%
Gall bladder	13	6.31%
Large intestine	13	6.31%
Pericardium	6	2.91%
Small intestine	2	0.97%

DISCUSSION

Although ALS is a rare disease, given China's large population base, there are still a significant number of patients. There are more than 20000 new cases in the mainland every year, so the number of patients with rare diseases is not insignificant. It is of great significance to study the treatment of amyotrophic lateral sclerosis from the perspective of TCM. In the diagnosis of traditional Chinese medicine, it belongs to the category of "flaccidity syndrome" Wang et al. (2009), which was mentioned in The Yellow Emperor's Inner Classic.

The etiology of flaccidity syndrome mainly consists of factors such as the five viscera, meridians, exogenous pathogens, constitution, acquired habits, and others. Its pathogenesis can be divided into about eleven kinds. Weakness of the spleen and stomach, deficiency of the liver and kidney, heat in the lung, deficiency and excess, excessive heat in the stomach, deficiency of essence and blood, accumulation of damp-heat, deficiency of primordial qi, Deficiency of meridians, invasion of wind-cold-dampness, hyperactivity of fire due to yin deficiency wang et al. (2012). The survival time of patients with amyotrophic lateral sclerosis is short, only 3-5 years. Muscle atrophy eventually leads to respiratory

muscle atrophy which usually leads to the death of the patient by asphyxia. The social attention of amyotrophic lateral sclerosis has been increasing in the past 10 years, and the progress of modern medicine is difficult. Acupuncture Jin et al. (2013), traditional Chinese medicine compound and other traditional Chinese medicine treatment methods are highly expected, and the effect is good. At present, the prescription with better clinical effect is Qiangjiling from Professor Deng Tietao lu et al. (2002), which is composed of Radix Astragali, Pentaconyx, Radix pseudostellariae, Rhizoma Atractylodis Macrocephalae, Herba Cistanches, Placenta Hominis, Cortex Eucommiae, Fructus Corni, Radix Angelicae Sinensis, Polygonum multiflorum, Ground Beettle, Scorpio, Radix et Rhizoma Glycyrrhizae. The compatibility of the 13 medicines is proper, and the medicines are mainly used for strengthening the spleen, tonifying the kidney and nourishing the liver, and have the effects of strengthening the muscle and strengthening the strength, so the medicines are named as Qiangjiling. Among them, Radix Astragali, as the main herb in Qiangjiling has efficacy for invigorating qi and raising Yang, needs to be used in large quantities, ranging from 45g to 120g. There are also Simiao powder, Fangji Huangqi decoction plus minus formula from Professor Zhou Zhongying, which are also effective

prescriptions. Among them, the amount of Astragalus is also large. In the prescriptions of the two professors, a large number of tonifying herbs were used, and at the same time, the herbs for calming the liver and calming the wind were used a lot too.

Through statistics, this study explores the medication rules of oral administration of traditional Chinese medicine decoction in the treatment of amyotrophic lateral sclerosis, and synthesizes the research results. An important compound prescription is use for treating amyotrophic lateral sclerosis, which is mainly use for relieving middle-jiao and tonifying deficiency, The most commonly used herbs are Rhizoma Atractylodis Macrocephalae, Radix et Rhizoma Glycyrrhizae and Poria. The results of this study are consistent with the theory of traditional Chinese medicine, indicating that the data analysis method adopted in the study Zhao et al. (2013) is scientific and effective. It is of great significance for the innovative application of traditional Chinese medicine decoction in the treatment of ALS, improving the therapeutic effect and improving the quality of life of patients.

DECLARATIONS

Acknowledgements

The authors thank the Beijing Hengyihua Charity Foundation and Beijing Askang Medical Technology Co., LTD for their fund support.

Authors' contributions

Conceptualization, Wang TQ and Zhang YW; Statistics, Zhao H and Zhou RQ; Supervision, Wang TQ. All the authors read and approved the final manuscript for submission.

Funding

1. R&D Program of Beijing Municipal Education Commission 2024: Study on the improvement of clinical symptoms and mechanism of acupuncture in amyotrophic lateral sclerosis (KM202410025018).
2. This study was supported by the China National Natural Science Foundation of youth project in 2024 (No.82405557).
3. Funding Project Name: 2023 Research and Cultivation Fund of Capital Medical University—Study on the correlation between intestinal flora and neurofilament light chain in mice with amyotrophic lateral sclerosis by acupuncture (PYZ23032).

REFERENCES

1. Su G, Zhang J, Hong Y. 2006. Yiqi Qiangji Decoction treating 25 cases of amyotrophic lateral sclerosis. *Journal of Cardio-cerebrovascular diseases of Integrative Chinese and Western Medicine*.5(4):452-53.

2. li M, Song Y, Jia Q, et al. 2022. Prescription and Medication Rules of Professor Gao Ying in Treatment of Amyotrophic Lateral Sclerosis Based on Data Mining. *ACTA Chinese Medicine*.288(37):1114-19.

3. Cao T, Teng Y, Zhuo Y, et al. 2020. Discussion on prescription and medication rules of Chinese medicine treating amyotrophic lateral sclerosis related atrophydisease in ancient books based on data mining. *Global Traditional Chinese Medicine*.13(6):986-92.

4. Wang T, Xu W, Wang A, et al. 2016. Discuss on Medication Rules of Compound Recipe in Traditional Chinese Medicine Decoction on Acute Orchitis. *JETCM*. 25(6):957-60

5. Bao Jie, Fu M, Shen B, et al. 2016. Clinical Study on the Treatment of Amyotrophic Lateral Sclerosis with Jiaweisijunzi. *China Pharmaceutical Bulletin*. 8(35):43-45

6. Wang L, Fan X, Shen W, et al. 2023. Zhang Yunling's experience in treating amyotrophic lateral sclerosis from the perspective of "attaching equal importance to spleen and kidney. *Journal of Traditional Chinese Medicine*. 64(20):2067-70

7. Wang J, Gao J, Guo Y, et al. 2009. Clinical Study of the Effect of Fuyuanhengji Granule on Symptoms of the Patients with Amyotrophic Lateral Sclerosis. *Neurol Neurorehabil*. 6(3):173-75

8. Wang Y. 2012. Summary and analysis of ancient and modern Chinese medicine literature on amyotrophic lateral sclerosis related impotencesyndrome. *Beijing University of Chinese Medicine*. 5:127.

9. Jin P. 2013. Clinical observation on treating amyotrophic lateral sclerosis by Guilu Erxian glues. *Clinical Journal of Chinese Medicine*. 5(24):28-30

10. Luo R, Liu Y, Liu X, et al. 2002. Treatment of Amyotrophic Lateral Sclerosis by TCM: A Clinical Observation of 26 Cases. *New traditional Chinese medicine*. 34(12):17-19

11. Zhao Y. 2013. Academic Study of Xie Shi BTJWF in the Treatment of ALS. Dalian Medical University.