

Electroacupuncture with combined Chinese herbal, Qidong Huoluo granule for Amyotrophic Lateral Sclerosis: A 9-month Case Report

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ABSTRACT

Background: Amyotrophic lateral sclerosis (ALS) is an adult-onset neurodegenerative disorder that has no curative treatment and is usually fatal. Modern medicine treatment is mostly supportive. Acupuncture has much more to offer by way of symptomatic relief and improving quality of life (QoL). Useful points for the treatment of bulbar paralysis, paralysis of upper and lower extremities.

Case: A 68-year-old woman had weakness in her right arm and both legs for 26 months. She also had muscle cramps and clumsiness in affected limbs, which rapidly progressed in the 6 months prior to presentation. She was diagnosed with ALS, given 50 mg of oral riluzole and Qidong Huoluo granule, Chinese herbal compound twice a day. She sought acupuncture and was treated for more than 8 months of twice each week.

Results: After acupuncture, this patient's symptomatic relief was improved greatly that she became free from disabling symptoms. This treatment combined Chinese herbal medicine, Qidong Huoluo granule, produced persistent of robust clinical improvement after treatment in terms of speaking, sensation, ambulation, and breathing.

Conclusions: The study on the treatment of amyotrophic lateral sclerosis by electroacupuncture combined with Qidonghuoluo granules showed that this method has a certain delay effect on the development of the disease. Electroacupuncture may protect the bulbar paralysis by improving the blood supply of medulla oblongata. Qidong Huoluo granules regulate and replenish the whole body by invigorating qi and nourishing Yin and activating blood, thus protecting the nerve function of the whole body. This case is an individual case, and it is necessary to further increase the number of cases and randomized control group to determine the efficacy.

INTRODUCTION

Amyotrophic lateral sclerosis, commonly known as "ALS," is one of the World Health Organization's "five most difficult diseases," along with cancer, AIDS, leukemia, and rheumatoid disease. It is a heterogeneous neurodegenerative disease characterized by the degeneration of upper and lower motor neurons, leading to motor and non-motor symptoms and often death from respiratory failure Feldman et al. (2022). The annual incidence of ALS is about 1-2.6 cases / 100,000 people, and the prevalence rate is about 6 cases / 100,000 people Goutman et al. (2022). 90% of ALS patients are sporadic, and a small number are familial. The average age of onset is 58-60 years old, and the average survival time after diagnosis is about 3-4 years Meyer et al. (2021). The core pathological manifestation of ALS is the progressive death of motor neurons,

and its pathological mechanism is complicated, and the treatment of ALS is very limited at present. Riluzole is the current standard drug for ALS treatment, which can only extend the life of patients by 2-3 months, and has adverse reactions such as nausea and fatigue Beswick et al. (2022). At present, there is no effective means for radical treatment of ALS from the source of neuronal damage.

Acupuncture, as a non-drug intervention, plays a particularly prominent advantage in the treatment of neuronal degenerative diseases. Both domestic and foreign scholars have paid attention to the treatment of ALS by acupuncture, believing that it has a good research prospect Yang et al. (2023). Especially since 2016, clinical research on acupuncture as a typical TCM treatment has developed rapidly: the vast majority

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of clinical trials are case reports, accounting for 59% of the total; Cohort studies accounted for the second largest share at 28%. Clinical randomized controlled trials on acupuncture treatment of ALS were only available from 2016, and only 4 have been published so far, accounting for at least 13%. Wang et al. (2023).

CASE

The patient is a 68-year-old woman from Dongcheng district, Beijing area. She was diagnosed with amyotrophic lateral sclerosis in Beijing Hospital in November 15th, 2021. Since September 2021, the patient began to suffer from muscle pain and weakness in the right upper limb after holding and pulling heavy objects, and then suffered from shoulder joint pain and limited movement, manifested as inability to lift, unclear speech, and slow swallowing. After being admitted to a second-class hospital in Beijing, she was diagnosed with "peri-arthritis of shoulder". After she was treated with anti-inflammatory and analgesic drugs, she felt that his shoulder pain was improved, but the weakness of his right upper limb was worse than before, accompanied by a feeling of heaviness, manifested as obvious weakness of the distal knuckle, decreased grip strength, and inability to hold chopsticks while eating. When seeking treatment in Puren hospital, a second-class hospital in Beijing near her living place, the electromyography showed that the right median nerve motor conduction velocity was normal and the amplitude was low. The patient was given aspirin, Pivastatin calcium tablets and other drugs, the symptoms of the patient did not improve significantly after half a month of oral administration, and then stopped taking the drug. In early November 2021, she developed a lack of speech fluency. She was admitted to Puren Hospital for head CT/MRI examination and found lacunar cerebral infarction in the right basal ganglia. She was hospitalized in the neurology ward of a Grade III hospital in Beijing. Physical examination: stable vital signs, clear mind, dysarthria, memory, orientation, calculation and other basic normal. Bilateral pupils are large and round, with a diameter of about 3mm. Shrug her shoulders and roll her neck vigorously. The distal muscle strength of the right upper limb was grade IV, the remaining muscle strength was normal, the muscle tone of the right upper limb was weakened, and the muscle atrophy was observed. Both joint position and vibration are normal. Bilateral rotation test was normal, finger nose test and heel knee tibial test were stable. Hoffmann sign (+), bilateral Babinski sign (-), Chaddock sign (-). Soft neck without resistance, meningeal irritation (-). Auxiliary examination: Head MRI: 1. Possible lacunar cerebral infarction in the right basal ganglia. 2. Mild white matter ischemic changes. 3. Bilateral partial ethmoidal sinus mucosa thickened; Head CT: To consider the formation of bilateral lacunar infarction in the paraventricular, thalamic and basal segments.

Pontine density is uniform; Mild demyelination of white matter; Senile changes, cerebral arteriosclerosis. Carotid ultrasound: bilateral subclavian endarteriosclerosis with right initial plaque formation; Bilateral carotid intimal lesions; Bilateral carotid arteries were normal. There were no significant abnormalities in myocardial enzymes, blood clotting items, tumor markers, thyroid function and paraneoplastic related tests. Antinuclear antibody granule type was 1:40, thyroid function and other autoimmune-related tests showed no significant abnormalities. Electromyography: Consistent with neurogenic lesions, more extensive, with the exception of anterior horn lesions. The MCV of the right ulnar nerve was slow and the amplitude was low. The NCV of the remaining nerves was generally normal, and no nerve block was found. The content of light chain protein NfL in neural filament is 108.51pg/ml. Routine, biochemical, OB+lgG index of cerebrospinal fluid, anti-ganglioside antibody and other relevant examinations showed no obvious abnormalities.

Study treatment

The patient was admitted to the out-patient Department of Traditional Chinese Medicine of Capital Medical University on April 11, 2023, and was treated by Associate Professor Cui Hai (Deputy chief physician). He had 35 years clinical experience. Andi brand disposable, sterile steel needles (size 0.40×40 mm, manufactured by Suzhou Medical Appliance in Jiangsu, China) were used. Pragmatic placebo needles (size 0.30 × 25 mm) were also used.

Fengchi (GB 20) and Gongxue points on the neck, Lianquan (RN23) and Tunyan points on the pars laryngea were selected by acupuncture. 0.25mm×40mm millimeter needle was used to quickly insert the needle, and the neck and lumbar spine points were directly stabbed for 15~25mm, and the tonifying, reducing or draining techniques combined with twisting and lifting were adopted. The degree of the patient's self-consciousness was local acid swelling. The same set of electrodes of KW808-2 electric anesthesia instrument of Great Wall brand were connected to Fengchi and Gongxue acupoints on both sides of the spine (Figure 1). The electrode connection made the current direction consistent with the direction of the motor nerve conduction bundle. The frequency of electroacupuncture was 2Hz and the intensity was determined by the patient's self-reported muscle jerking and tolerance. The above therapy lasted for on Tuesday and Thursday per week of electroacupuncture treatment. She also took Qidong Huoluo granules (Huangqi80 Maidong15 Tiandong15 Jixueteng20 Beishashen15 Qinghao9 Wuyao12 Zhiheshouwu6 Baishao 15), a compound Chinese medicine designed by our research group, one pack for a day and was taken every day. Take one dose daily by decoction.

Administer 30 minutes after breakfast and dinner. Manual acupuncture by acupuncturist used a small, equal manipulations of twirling, lifting, and thrusting performed on all needles to obtain “Deqi”. The patient felt the “Deqi” sensation, such as soreness, numbness, distention, heaviness, and other sensations. We used the internationally recognized ALS Functional Rating Scale-Revise (ALSFRS-R) as the primary outcome indicator to evaluate the efficacy. This scale consists of 12 items: ① speech; ② Salivation; ③ Ingurgitation; ④ Writing; ⑤ Cut food; ⑥ Clothing and hygiene; ⑦ Turn over and tidy the bedding on the bed; ⑧ Walking; ⑨ Climb stairs; ⑩ Difficulty breathing; ⑪ sitting and breathing; ⑫ Respiratory function. Each item is rated on a scale of 0 to 4 points. The total score ranges from 0 (severely impaired) to 48 (normal).

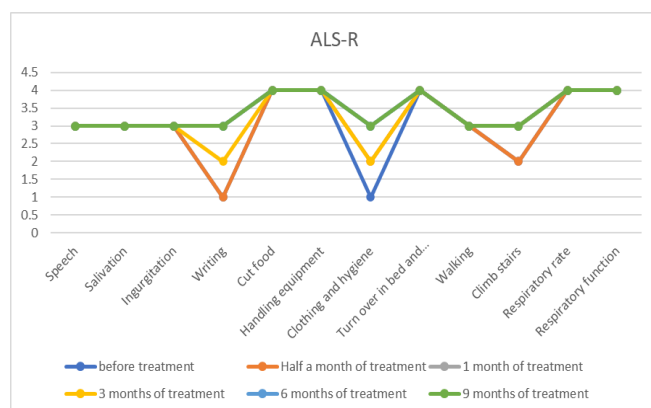
Figure 1: Acupuncture point diagram



RESULT

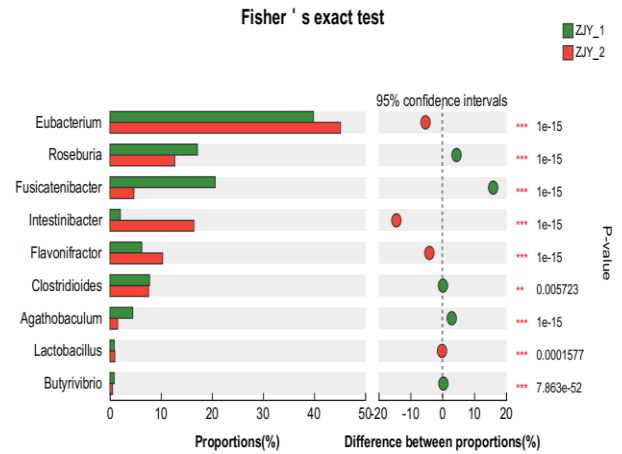
As shown in the figure 2, after 9 months of acupuncture treatment, the patient had varying degrees of improvement in clothing (2 points higher than before treatment), writing (2 points higher than before treatment), and climbing stairs (1 point higher than before treatment). The patient's articulation improved significantly, hearing improved, speaking freely, and qi sufficient by electroacupuncture treatment. However, there was no significant improvement in the treatment of high muscle tone of lower extremity by clipping spine electroacupuncture.

Figure 2: Improvement of ALS functional scale in patients at different time points



Meanwhile, stool samples was taken from the patient prior to initiation of acupuncture treatment and at 1 month of treatment, finding that Eubacterium, Flavonifractor, Lactobacillus were significantly increased after 1 month electroacupuncture combined Chinese herbal medicine treatment.

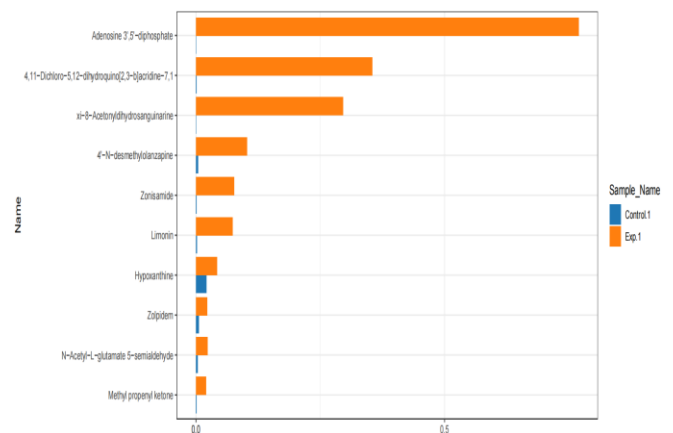
Figure 3: Changes of intestinal flora before and after 1 month of treatment



(-1 before treatment; -2 1 month of treatment)

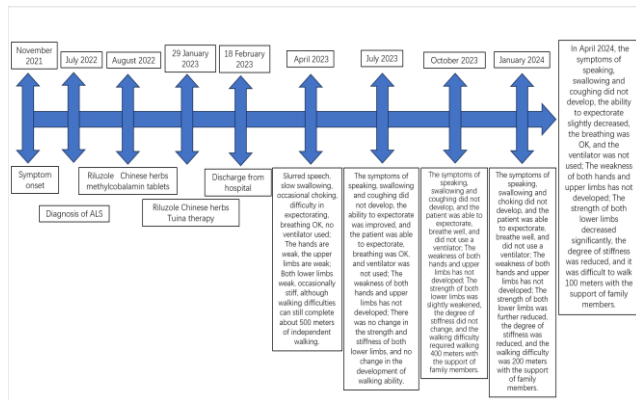
Besides, we also made a metabolite linear correlation analysis in urine sample between ALS patient and her husband (healthy control) using pearson correlation in Figure 4, finding that Adenosine 3',5'-diphosphate had a positive correlation between 4,11-Dichloro-5,12-dihydroquino[2,3-b]acridine-7,14-dione and Cyclobassinin, while had a negative relationship with Hamamelitannin (all $P < 0.05$).

Figure 4: Differences in metabolites between amyotrophic lateral sclerosis patient and her husband (Exp.1-ALS patient; Control- healthy control)



As is shown on timeline of the follow up in Figure 5, speech, swallowing, and choking symptoms did not develop until now.

Figure 5: Timeline for diagnose, treatment and follow-up



DISCUSSION

At present, most scholars ascribe ALS to the category of "flaccidity syndrome" in Chinese medicine. Its main pathogenesis is deficiency of Qi and blood, deficiency of spleen and stomach, deficiency of liver and kidney Liu et al. (2023). The symptoms and signs of the patient in this case belong to the weakness of the spleen and stomach in the flaccidity syndrome, and the treatment should be based on tonifying the spleen and stomach. Qidong Huoluo Granules, self-designed by the Out-patient Department of Traditional Chinese Medicine of Capital Medical University, was based on the experience of national famous old Chinese medicine in the diagnosis and treatment of muscle weakness and muscle atrophy caused by nervous system diseases and combined with the pharmacological mechanism of modern Chinese medicine on the nervous system. Our clinic collected and analyzed the prescription for the treatment of "flaccidity syndrome" in classical Chinese medicine literature among more than 500 articles from 1980 till now on.

The etiology and pathogenesis of ALS are still unclear in modern medicine, resulting in a lack of effective treatment options. Acupuncture is considered as a secure and powerful tool for improving the power of muscles Sawada et al. (2020). We speculate that the possibility that improvements on combination of acupuncture and medicine may through shaping the structure of gut microbiome, especially through reducing the biomarker flora of sarcopenia Eisenbergiella abundance Li et al. (2023), thereby achieving rapid reduction in signs and symptoms of amyotrophic lateral sclerosis. Moreover, mechanisms on regulating intestinal flora may be explained that stimulation of acupuncture and Chinese herbal could increase the content beneficial bacterium of Ruminococcus, Eubacterium, Bacteroides, Lactobacillus and Agathobacter, which microbiota have been shown to produce different amounts and profiles of short-chain fatty acids (SCFA) from the same carbohydrate

substrates Yan et al. (2023). SCFA-producing bacteria with elevated fecal SCFA concentrations may promote the energy intake from fibers, inhibit opportunistic pathogens and protect the hosts against inflammation and colonic diseases Zhu et al. (2024).

Metabolomics results show that purine metabolism is the most different between patient and healthy subject. Uric acid is the end product of human purine metabolism Tangudu et al. (2023), and abnormal uric acid level in patients may be an important factor that triggers oxidative stress leading to ALS Pinilla-González et al. (2024), Oliveira et al. (2024). Oxidative stress can cause gene mutation of superoxide dismutase 1 (SOD1), which mainly encodes antioxidant defense protein. By reducing niacinamide adenine dinucleotide phosphate (NADPH) oxidase, the production of peroxide increases, the consumption of antioxidants in the body increases, the uric acid decreases, and motor neuron damage leads to the incidence of ALS Ceccarelli et al. (2024). In vivo and in vitro studies have shown that high uric acid levels protect neurons against oxidative stress Wei et al. (2024), Ankul Singh et al. (2023). Therefore, increasing uric acid levels through acupuncture and Chinese herbal can reduce oxidative stress and can slow down the rate of disease progression. This article explores the case of amyotrophic lateral sclerosis treated with electro-nape acupuncture combined with Qidong Huoluo Granule. Through 6 months of treatment, the patient's swallowing and respiratory functions have been basically maintained stable and the disease progression has been delayed, providing a new treatment method for this disease. However, future research needs to increase the number of cases and conduct randomized controlled studies to further clarify the efficacy.

CONCLUSION

The use of electro-nape acupuncture combined with Qidong Huoluo Granules, which have the effects of replenishing qi and nourishing yin, promoting blood circulation, and nourishing blood, to treat amyotrophic lateral sclerosis may delay the development of swallowing, articulation, and choking symptoms and further delay disease progression by improving the blood supply to the medulla oblongata and exerting its protective function.

DECLARATIONS

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Authors' contributions

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Ethics approval and consent to participate

Participation in the study was voluntary and a signed informed consent was obtained from each participant before treatment.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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