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# Discussion on the Mechanism of Traditional Chinese Medicine in Treating Myasthenia Gravis Based on the Theory of "Atrophy Syndrome" and Its Syndrome Differentiation and Treatment

**Qinrui Liu[1], Xiaoyan Wang[2,*], Furong Lv[2]**

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]The Fifth Affiliated Hospital of Shaanxi University of Chinese Medicine, Xi'an 710021, Shaanxi, China
**Correspondence Author*

**Abstract:** ***Myasthenia Gravis (MG) is an autoimmune disease caused by transmission disorders at the neuromuscular junction. Among them, ocular myasthenia (OMG) is the most common type, mainly manifested as ptosis of the upper eyelid, diplopia, and ocular movement disorders. Traditional Chinese Medicine (TCM) treatment for MG has unique advantages. Through overall regulation and syndrome differentiation and treatment, it can improve symptoms and reduce the side effects of Western medicine. This article systematically reviews the understanding and treatment progress of MG in TCM: MG belongs to the category of "flaccidity syndrome", and the causes involve deficiency of the spleen and stomach, insufficiency of liver and kidney, dampness, heat, and blood stasis. The pathogenesis is related to deficiency of yang qi, obstruction of dampness by pathogenic factors, failure of closure of yangming meridian, and deficiency and stasis of collaterals and pathogenic factors. It explains the main TCM syndrome differentiation types and prescriptions and medications for treating MG. It introduces the research on single herb drugs with distinctive features in treatment, aiming to deepen the mechanism exploration by combining modern technologies in the future, carry out high-quality clinical research, optimize the integrated treatment plan of TCM and Western medicine, and provide more effective strategies for the diagnosis and treatment of MG.***

**Keywords:** Myasthenia gravis, Traditional Chinese medicine, Flaccidity syndrome, Syndrome differentiation and treatment, Immune regulation**.**

## 1. The Purpose and Significance of the Topic Selection

Myasthenia gravis (MG) is an acquired autoimmune disease characterized by skeletal muscle contraction weakness caused by neuromuscular transmission disorders. The exact pathogenesis of MG is still unclear. Research [1] believes that it is related to the decrease in the number of acetylcholine receptors (AChR). The acetylcholine receptors on the postsynaptic membrane are destroyed by circulating antibodies, resulting in a decrease in number and morphological changes, leading to conduction disorders at nerve junctions. Among them, ocular myasthenia gravis (OMG) is the most common type of MG. The main characteristics of OMG are unilateral or bilateral ptosis caused by striated muscle fatigue, diplopia, strabismus or eye movement disorder caused by extraocular muscle paralysis, accompanied by light morning and heavy evening. Its muscle weakness is limited to levator palpebrae superior muscle, extraocular muscle and orbicularis oculi muscle [1], and changes with the progress of the disease.

Traditional Chinese medicine (TCM) has a long history and unique advantages in the treatment of MG. It can not only improve the symptoms, but also reduce the dosage and side effects of western medicine and improve the quality of life of patients through overall regulation and syndrome differentiation. In recent years, the research on TCM in the treatment of MG has increased day by day, showing good application prospects. The purpose of this paper is to systematically sort out the research progress of TCM in the treatment of MG and provide reference for clinical practice and further research.

## 2. Understanding of MG in Traditional Chinese Medicine

Myasthenia gravis (or ocular myasthenia gravis) drops within the class of "flaccidity syndrome" in traditional Chinese medicine. Its causes can be attributed to either deficiency or excess. Deficiency conditions are mainly related to the spleen and stomach, liver and kidney, and yin and yang, while excess conditions are often associated with damp-heat and lifeblood stasis. The "Suwen: Chapter on Flaccidity" [2] states that "the treatment of flaccidity should focus on the Yangming meridian," providing the first systematic discussion on the etiology, pathogenesis, and treatment principles of flaccidity syndrome. Over the centuries, medical practitioners have continuously deepened their understanding of flaccidity syndrome, and by the Ming and Qing dynasties, a relatively complete theoretical system had been established.

### 2.1 The Influence of Yang Qi on Atrophy Syndrome

The "Suwen: On the Connection between Vitality and Heaven" [2] of the Yellow Emperor's Inner Classic states: "Yang Qi is like the sun in the sky. If it loses its place, it will shorten one's lifespan and leave no shadow. Yang Qi, when refined, nourishes the spirit; when gentle, it nourishes the tendons." This passage describes the significance of Yang Qi in atrophy syndromes. Yang Qi not only warms and enriches the human spirit but also nourishes the tendons and vessels. The kidney stores essence and houses the original yin and yang; it governs the bones. The liver and kidney share the same origin, and the

liver rule the tendons. The spleen's function of transforming and transporting nutrients requires the warming effect of kidney yang. The spleen governs the flesh. Therefore, kidney yang is closely related to the tendons, bones, and flesh. When kidney yang is plentiful, the tendons and bones are strong and the muscles are full. Thus, when Yang Qi is weak, the muscles become thin and the tendons and bones lose strength.

### 2.2 The Influence of Dampness on Atrophy Syndrome

The "Suwen: On the Connection between Vitality and Heaven" [2] of the Yellow Emperor's Inner Classic states: "When dampness prevails, the head feels as if wrapped up. If dampness and heat are not dispelled, the large tendons become soft and short, and the small tendons become slack and long. Softness and shortness lead to stiffness, while slackness and lengthiness result in atrophy." Dampness is an important pathogenic factor for this disease. Dampness easily obstructs the spleen, causing the qi circulation to be blocked and the spleen's function of transportation and transformation to be impaired, leading to the internal generation of water and dampness, which accumulates in the internal organs and meridians, resulting in atrophy syndrome. Dampness can impair the spleen, and spleen deficiency can further assist dampness, creating a vicious cycle that makes myasthenia gravis difficult to cure and prone to recurrence.

### 2.3 The Influence of Yangming on Atrophy Syndrome

The phrase "Treating atrophy by focusing on Yangming" originated from the statement "Why is it said that treating atrophy involves focusing solely on Yangming?" in the "Discussion on Atrophy" chapter of the "Plain Questions" [2], highlighting the significant role of Yangming in the treatment of atrophy syndrome and establishing it as one of the key principles for treating atrophy. The "Commentary on the Plain Questions by Wu" [4] explains that "Yangming is located internally, receiving and absorbing Yang Qi, and is thus called 'closing'." The "Classified Canon" states, "When Yangming is deficient, blood and Qi are scarce, unable to nourish the main tendons... thus the feet become weak and unable to function" [5]. Strengthening the spleen and elevating Yang Qi ensures the generation of Qi, blood, and body fluids, providing nourishment for the muscles and bones. Yangming receives and integrates the Qi of Taiyang and Shaoyang and stores it internally. When Yangming is closed and the water of the Kidney is abundant, it can descend and distribute the Qi and blood generated by the transformation of food and drink in the stomach and intestines, ensuring the abundance of Kidney essence, which further nourishes the muscles, bones, and internal organs. When Yangming fails to close, the nourishment of the muscles, bones, and internal organs is lost, leading to weakness and lack of strength in the body.

### 2.4 The Influence of "Five Elements and Six Qi" on Atrophy Syndrome

The "Great Treatise on the Changes of Qi" in the "Yellow Emperor's Inner Classic" [2] states, "When water is insufficient in a year, dampness prevails." In such a year, the governing qi is Taiyin Damp Earth, and the seasonal qi is Taiyang Cold Water. When water is insufficient, damp earth prevails, and with Taiyin Damp Earth governing the year, the damp earth qi accumulates, making dampness even more severe. In the first half of the year of Xin Chou, the qi overcomes the climate, with the qi being Taiyin Damp Earth, while in the second half, the insufficient water climate is assisted by the Taiyang Cold Water in the wells, making the climate changes relatively mild, but the cold yin qi is still abundant. MG patients inherently have insufficient primordial yang. When affected by the influence of a year with more abundant cold yin qi, their condition recurs. On top of the original symptoms of MG, they are prone to abdominal distension and fullness, body heaviness and fatigue, loose stools, depression and irritability, cold feet, and even edema of the ankles [6].

### 2.5 The Impact of "Empty, Outer Pathogens, Stasis and Blood Stasis" on Atrophy Syndrome

The qi channels and the neuro-endocrine-immune system share commonalities. The three systems act on the human body through substances such as neurotransmitters, hormones, and cytokines they produce, which are highly consistent with the physiological function of the collateral channels permeating the entire body [7]. When the collateral channels are full and flowing freely, the human body is in a state of harmony and balance. However, when the collateral channels are empty and stagnant, qi is blocked within the channels, causing the qi and blood, and essence and micro-substances that should be distributed to the twelve regular meridians to stagnate within the channels. This leads to abnormal supply of qi and blood and distribution of micro-substances, resulting in malnutrition of the internal organs and limbs. At the same time, the waste and toxins produced within the body cannot be metabolized in a timely manner. The qi and blood, and essence and micro-substances that have stagnated within the channels become stasis and pathogenic factors, and when combined with the waste and toxins accumulated throughout the body, they form "internal pathogenic factors" that cause disease in the body.

## 3. TCM Syndrome Differentiation and Treatment of MG

**3.1 Spleen and Stomach Weakness Type:** Commonly seen in ocular myasthenia gravis or mild generalized myasthenia gravis, it is characterized by ptosis, limb weakness, poor appetite, loose stools, pale tongue with white coating, and weak pulse. Treatment should focus on strengthening the spleen and benefiting qi, and the formula to be used is Modified Buzhong Yiqi Decoction.

**3.2 Spleen and Kidney Yang Deficiency Type:** Commonly seen in generalized myasthenia gravis, it is characterized by general frailty, chilly aversion, cold part, soreness and frailty in the waist and knees, difficulty in swallowing, pale and plump language with tooth marks, and big and fine pulse. Treatment should focus on warming and tonifying the spleen and kidney, and the formula to be used is Modified Yougui Pill combined with Modified Buzhong Yiqi Decoction.

**3.3 Liver and Kidney Yin Deficiency Type:** Commonly seen in patients who have been taking hormones for a long time, it is characterized by emaciation, weakness, dizziness, tinnitus, hot flushes in the palms, soles and chest, red tongue

with little coating, and fine and rapid pulse. Treatment should focus on nourishing the liver and kidney, and the formula to be used is Modified Zogui Pill combined with Modified Yiguanjian Decoction.

**3.4 Qi and Blood Deficiency Type:** Commonly seen in patients with a long course of the disease, it is characterized by pale complexion, shortness of breath, laziness in speaking, palpitations, and a pale tongue with a weak pulse. Treatment should focus on benefiting qi and nourishing blood, and the formula to be used is Modified Bazhen Decoction.

**3.5 Damp-Heat Penetration Type:** Commonly seen during acute attacks of myasthenia gravis or when there is a concurrent infection, it is characterized by heavy limbs, chest tightness, fullness in the epigastrium, dry and bitter mouth, red tongue with yellow and greasy coating, and slippery and rapid pulse. Treatment should focus on clearing heat and draining dampness, and the formula to be used is Modified Simiao Pill.

When making clinical diagnoses, it is necessary to pay attention to the dynamic changes and coexistence of syndrome types and apply treatment flexibly. As the condition progresses and treatment is administered, the syndrome type may transform, such as from spleen and stomach weakness to spleen and kidney yang deficiency, or from damp-heat infiltration to qi and blood deficiency.

## 4. Research on Single Herbs for the Treatment of MG

### 4.1 Astragalus Membranaceus

Astragalus membranaceus is a commonly used medicine for the treatment of MG. It has the effects of replenishing qi and elevating yang, replenishing Wei and strengthening the appearance. The main chemical components of Astragalus include APS, flavonoids, saponins, amino acids, etc. [8]. Astragalus polysaccharide regulates T cell subsets, inhibits the production of acetylcholine receptor antibodies, and protects neuromuscular junctions. AChR is present on the surface of muscle cells, concentrated at the synapses between nerve cells and muscle cells, and consists of a protein chain that forms a channel through the cell membrane, allowing positively charged ions to pass through the membrane, creating endplate potentials and causing muscle contraction. In MG patients with anti-AChRAb, the density of AChR at the neuromuscular junction is reduced, leading to a decrease in endplate potential. On muscle biopsies, disease severity is correlated with loss of AChR [9]. APS can reduce the level of AChRAb in serum, reduce AchR damage at neuromuscular junctions, and relieve clinical symptoms of MG.

### 4.2 Ginseng

Ginseng is a powerful tonic for vital energy. Ginsenosides have immunomodulatory activity, can enhance muscle contractility, improve exercise endurance, and alleviate hormone side effects by regulating the hypothalamic-pituitary-adrenal axis. According to their structural characteristics, ginsenosides can be classified into Rb1, Rd, Rg1, Re, and Rg3, etc. [10]. One of the possible mechanisms of action for the effective extract components in traditional Chinese medicine in treating myasthenia gravis may be to improve the imbalance of B lymphocyte immunity. CHEN W et al. [11] studied the effect and mechanism of ginsenoside Rb1 in treating myasthenia gravis in a rat model. The data showed that ginsenoside Rb1 might delay the progression of experimental autoimmune myasthenia gravis (EAMG) and improve the symptoms of EAMG rats by inhibiting B cell function and regulating the balance between Th2/Th17/Treg cells in EAMG. Specifically, ginsenoside Rb1 can reduce the proportion of Th17 cells in MNCs, inhibit IL-17 secretion, and increase the number of Treg cells and Th2 cells in MNCs.

### 4.3 Brucellosis

Zhang Xichun said that strychun “can moisten nerves and make them flexible”, “its power to open meridians and penetrate joints is far better than other drugs.” “Chuanyabu” said that it “can drill muscles and bones, activate the circulation and search for wind.” All pointed out that it has a prominent effect in dredging meridians, and its effect of relaxing meridians and opening and closing knots is also conducive to the dissipation of blood stasis in the vessels and the smooth flow of blood flow. It has realized that this product has unique pharmacological effects on neuromuscular diseases. Modern pharmacological research has shown [12] that strychnine, the main component of strychnine, can selectively improve the stimulation function of the spinal cord. The therapeutic dose can increase the irritability of the spinal cord reflex, shorten the reflex time, make nerve impulses easier to conduct, and increase the tension of the skeletal muscles., thereby improving the state of muscle weakness. The level of acetylcholinesterase (CHE) activity in the blood of patients with myasthenia gravis increased.

Although brucellosis is toxic, its small-dose use after processing can significantly improve the symptoms of myasthenia. Research suggests [13] that processed brucellosis may inhibit the activation of T and B cells by reducing the content of ACh Rab in the serum of EAMG rats and regulating the level of TGF-β1 in the serum to maintain the dynamic balance of immune activation and immune suppression, thereby reducing the damage to Ach R on the postsynaptic membrane. Within a certain dose range, processed brucellosis performs better in improving the body weight of EAMG and regulating immune function. Pharmacological research on strychni has also shown that the ingredients contained in strychni have the effect of improving microcirculation and can resist thrombosis when administered in vivo. Myasthenia gravis is a stubborn disease with a long treatment cycle. The chronic disease has many blood stasis. Removing blood stasis and dredging channels should be a combination method. The effect of nuxvomica to promote blood circulation and eliminate blood stasis can also play a good therapeutic effect on myasthenia gravis.

In short, the above drugs have a unique therapeutic effect on myasthenia gravis, and their therapeutic effect may be the result of their multiple effects, rather than just a single therapeutic effect. Recognizing this, providing unique combinations of traditional Chinese medicines based on patient syndromes and formulating individualized treatment

plans will undoubtedly have positive effects on the clinical treatment of myasthenia gravis and further expand its application in other neuromuscular diseases. Clinical significance.

## 5. Problems and Prospects

Although traditional Chinese medicine has shown good prospects in the treatment of MG, there are still some problems that need to be solved urgently, and the criteria for syndrome differentiation and classification are not yet unified, which affects the evaluation of efficacy and the promotion of plans. In the future, large-scale clinical studies and expert consensus are needed to establish standardized syndrome differentiation criteria. Current research mainly focuses on clinical observations and small-sample trials, with few high-quality randomized controlled trials, and the level of evidence needs to be improved. Multi-center, large-sample, and standardized clinical research should be carried out. The research on the mechanism of action is not deep enough, especially for the multi-component and multi-target mechanism of action of compound traditional Chinese medicines, which requires further clarification through modern technologies such as systems biology and network pharmacology. The evaluation criteria for therapeutic effects are not unified, and there is a lack of an assessment system tailored to the characteristics of traditional Chinese medicine. A comprehensive evaluation standard that integrates objective indicators of Western medicine and changes in TCM syndromes should be established.

Future research directions include: carrying out evidence-based medicine research on traditional Chinese medicine for the treatment of MG; in-depth discussions on the molecular mechanisms of traditional Chinese medicine regulating immunity and protecting neuromuscular junctions; developing new traditional Chinese medicine preparations for different syndrome types; optimizing treatment options with integrated traditional Chinese and Western medicine; exploring standardized treatment options for acupuncture treatment, etc.

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