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Treatment for Multiple Sclerosis: Kidney-Du-Brain Axis (KIDUBA) Acupuncture Protocol

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Abstract

Multiple sclerosis (MS) is a complex autoimmune disease mediated by an immune response to central nervous system antigens. Conventional immunomodulatory therapies are limited to relieve many of the symptoms, such as weakness, pain and depression, but probably cause side effects. Acupuncture, the most popular approach of complementary and alternative medicine (CAM) could improve the quality of life (QoL), fatigue, and pain, and alleviate the side-events of immunosuppressants. The essay summarized the publications and experiences from the leading acupuncture masters in China and clinical trials on acupuncture treatment for MS patients. The review concluded that in Chinese Medicine (CM), the Kidney-DU-Brain Axis (KIDUBA) plays a key role in the pathogenesis of MS. Fundamental acupoints including GB39, SP6, DU4, BL23, SI3, Sishencong are recommended according to the principle of supplementing kidney and marrow and opening blockages in Du channel and the brain. Besides, acupuncture treatment for the side effects of immunomodulatory medications are covered in the protocol.

Keywords: Multiple sclerosis; Chinese Medicine; Acupuncture; Herbal medicine

1. Introduction

Multiple sclerosis (MS) is a complex autoimmune disease mediated by an immune response to central nervous system antigens. Modern immunomodulatory therapies, however, do not relieve many of the symptoms, such as weakness, pain and depression, etc. Many patients with multiple sclerosis use complementary and alternative medicine (CAM) to supplement their traditional treatment. A survey on American MS patients revealed that 57.7% of them had used CAM therapies (acupuncture, massage, osteopathic manipulative treatment, psychotherapy [1]. A large range of CAM treatments were used by individuals with MS in all Nordic countries. The most commonly reported rationale for CAM treatment use focused on improving overall health [2]. Many people with MS explore CAM therapies for their symptoms [3]. Acupuncture is probably the most popular alternative therapy practiced in the United States, Europe and many Asian countries. A meta-analysis research reported acupuncture could improve quality of life, fatigue, and pain [4]. In addition to the analgesic effect of acupuncture, an increasing number of studies have demonstrated that acupuncture treatment can control autonomic nerve system functions and immune modulation [5].

MS is not a common diagnosis term in Traditional Chinese Medicine (TCM). According to the clinical manifestation, MS can be regarded as Wei Zheng (Atrophy Syndrome), Feng Fei (Wind Disablement), Ying Fei (Loss of Voice and Disablement), Xuan Yun (Vertigo or Dizziness), or Gu You (Flaccid Joints), etc. Approaches in TCM e.g. acupuncture, herbal medicine, Tuina, can improve quality of life (QoL), relieve symptoms, and reduce the side-events of prednisone and immunosuppressant.

2. Kidney-Du-Brain Axis

According to the class *Wei Lun, Su Wen*¹, MS is usually considered as Wei-atrophy syndrome and Yangming (spleen and stomach) should be prioritized in treatment. Actually, all the five Zang-organs can manifest Wei-atrophy, not only in Yangming.

When there is heat in the liver, the patient feels bitter in the mouth because the bile leaks, and the sinews and fascia are dry, which result in spasm. Thus Jin Wei (Sinew Atrophy) presents.

When there is heat in the spleen, the patients feel thirst because of the dryness in the stomach. The feeling disorders in muscle and flesh. It is called Rou Wei i.e. Flesh Atrophy. When there is heat in the kidneys, the bone becomes withered and the amount of marrow declines, resulting in Gu Wei (Bone Atrophy).

from *Wei Lun, Su Wen*

¹ *Treaties on Atrophy*, Chapter 44 of *Elementary Question*, *Yellow Emperor's Inner Classic*

In reviewing the clinical practice and experience of almost all the masters, the kidney, liver, Du channel, marrow, and brain are mainly concerned. Based on their thoughts, Kidney (Spleen and Liver)-DU-Brain Axis (KIDUBA) may play important role in the pathogenesis of MS than Yangming does (Figure 1).

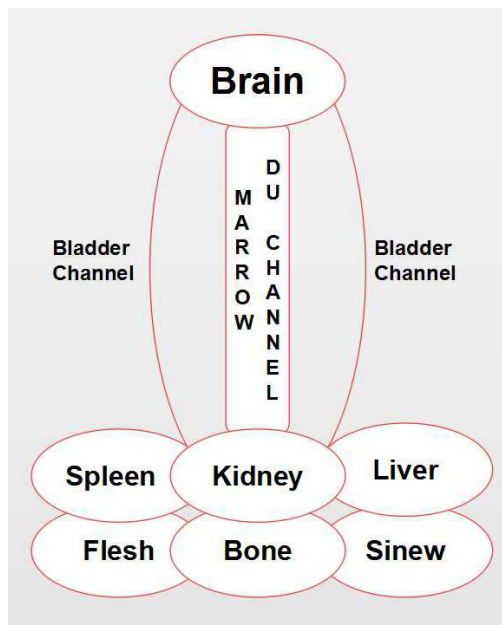


Figure 1. KIDUBA in the pathogenesis of multiple sclerosis in TCM

In TCM, the kidneys govern bones and generate marrow and the brain is the “sea of marrow”. Therefore, brain diseases are closely related to the dysfunction of the kidneys. Besides, the liver and kidneys share the same origins. Strategically, the spleen system including the Yangming stomach is serves to supplement the kidney in clinical practice. If the kidney (yin or essence) fails to supplement the marrow and supply the brain, the limbs are poorly-nourished and become disabled. The liver governs sinews, opens into the eyes and the kidneys also govern the urination and defecation. Once the liver and kidneys are dysfunctional, the symptoms of the eyes and sinews and disorders of the urination and defecation occur. Clinically, it is commonly seen in MS patients manifested as reduced vision, atrophy, weakness and numbness of limbs, unstable gait, and disorders of urination and defecation. DU channel connects the kidneys, marrow and brain. The DU channel is indicated for the symptoms of brain, five orifices (eye, ear, nose, mouth, throat), spine and marrow, and four limbs, e.g. headache, heavy sensation of head, dizziness, tinnitus, blurred vision, mania, back pain, weak limbs with tremor and spasm. The symptoms of brain include dizziness, tinnitus, weakness of leg, fatigue, somnolence, etc.

The mechanism of MS is not only based on the fundamental theory of TCM but also on the biological pathology. Although there is finding suggesting the peripheral nervous abnormalities are involved, the disorders of the brain white matter and marrow demyelination in the central nervous are the primary mechanism. The Liver and Kidney Yin Deficiency Pattern is closely related to the dysfunction of

hippocampus pituitary adrenal axis (HPAA). The secretion of CORT, ACTH and CRH play an important role in the pathogenesis of MS [6]. There are plenty clinical use and research on the herbal medicine which supplement the kidneys that are used to treat MS. Liu and Sun [7] found that BSGS Tablet², a herbal formula supplement the kidneys and marrow, could improve the symptoms and signs of MS patients and reduce the recurrence rate with a total effective rate of 88.37%. High dose BSGS could obviously reduce the incidence of allergic encephalomyelitis (EAE), inhibit inflammatory reaction of brain and spinal cord as well as demyelination, and simultaneously inhibit the activity of serum interleukin-2, interleukin-6, tumor necrosis factor (TNF), and myelin basic protein (MBP). The outcome intervened with the kidney supplementing herbal medicine was like the treatment with prednisone acetate tablets. Fan et al [8] reported that herbs, primarily supplementing the kidneys could reduce the recurrence rate of MS. Du channel is frequently involved in the treatment of MS with both herbal medicine and acupuncture. Du channel points are the most frequently used in clinical practice [9,10]. Electric acupuncture (EA) could improve the expression of NT-3 in the demyelinated marrow region, and the reproduction, differentiation, and remyelination of the endogenous marrow oligodendroglial precursor cells [11]. The combination of Chinese herbal medicine, EA on Du meridian and hyperbaric oxygen could improve the motor score and Barthel score in patients with spinal fracture complicating spinal cord injury [12].

In a word, MS is under the category of the brain and marrow disease with its root in the kidneys and is closely related to the liver and spleen. Therefore, KIDUBA may play the key role in the pathogenesis and treatment of MS.

3. Diagnosis in KIDUBA Protocol

Once the diagnosis i.e. MS is confirmed, the KIDUBA i.e. kidney-Du-brain axis disorder can also be identified in TCM. Pathogens including wind, phlegm, damp, damp-heat, blood stasis attack channels and organs where there is insufficient Qi and blood. In the acute stage, it's characterized with excess syndrome while in the chronic stage or Relapsing-Remitting Multiple Sclerosis (RRMS), it's featured with the combination of excess and deficiency syndromes.

4. Treatment in KIDUBA Protocol

4.1 Basic Acupoints

Principle: supplement kidney and fill marrow, open the blockage of du and brain

² BSGS, Bu Shen Gu Sui, Supplementing Kidney and Marrow: Yin Yang Huo 15g, Rou Cong Rong 12g, Xian Mao 10g, Sheng Di Huang 15g, He Shou Wu 15g, Yu Jin 10g, Dan Shen 12g etc.

Acupoints: GB39, SP6, DU4, BL23, SI3, Sishencong (EX-HN-1), RN4

GB39, the Hui-meeting point of marrows, supplements marrow and bones, soothes sinew and opens collateral. Clinically, it is used to treat the symptoms of the brain, spine and legs, e.g. headache, stiff neck, hypochondriac pain, lumbago, post-operational pain in orthopedics, sciatica, Wei-syndrome, strephenopodia and strephexopodia, thromboangiitis obliterans.

SP6 the meeting points of the liver, spleen and kidney channels, invigorates three channels/organs to supply the marrow and brain, supplement Yin and nourish joints, sinew and flesh.

DU4, the vital gate, is the point where the kidneys Qi enters Du channel/spine. BL23 is the back-Shu point of the kidneys. The combination invigorates the kidneys to supply the marrow and brain. Moxibustion is possibly applied. RN4, the meeting point of the liver, kidney, spleen, and Ren channel, the front-Mu of the small intestine, supplement the kidney Qi or primary Qi and Qi and blood.

Sishencong are commonly used to replace DU20 which supplements Yang Qi, unblocks Du channels, disinhibits the orifices (eye, nose, mouth, throat, ear) and calm Shen. It's the most frequently selected point for nervous system disorders.

SI3, Shu-stream point of hand Taiyang channel, opens to Du channel. It's frequently used to regulate the Du channel and foot Taiyang channel and brings the heart fire to benefit the kidneys.

Study suggested that moxibustion treatment on GB39 and ST36 improve the learning and memory on the aging rat induced by D-galactose [10]. A case reported showed that electroacupuncture on GB39 and HT5 could activate cerebral lingual function area and improve language function of aphasia patient [13]. Laser acupuncture on SP6 could improve the serum IgG level on patients [14]. Yan [15] reported that acupuncture on RN4, DU4 and ST36 could regulate IL-1, TNF- α , IL-2, IL-18 to alleviate inflammation and improve the release of CRF and ACTH to regulate the the whole HPA. Clinical and laboratory studies have suggested that acupuncture on the region of DU20 and Sishencong can improve the brain micro-circulation, improve sleep, regulate neuro-transmitters and accelerate the recovery from brain damage [16]. Chi et al [17] reported that puncturing on SI3 could activate various brain regions with the examination of applied fMRI.

Manipulation

GB39 and SP6 with supplementing method; SI3 with even method; Sichencong with supplement method, moxibustion recommended; in prone position, DU4 and BL23 with supplementing method, moxibustion recommended; in supine position, RN4 with supplementing method, moxibustion recommended

4.2 Differentiation and Treatment Based on Stages and Patterns

Acupoints needs to be added to the basic points mentioned above in the following conditions

4.2.1 Acute State

Wind and Phlegm Blocking in Collateral

The patient may have suffered cold and wind. Suddenly, the patient shows dizziness, blurred vision and blindness, fever, aversion to cold, headache, numbness and pain of limbs, clumsy finger movement, discomfort throat, difficult walking, epilepsy-like symptoms, urination and defecation disorders, red or light red tongue body, thin (white and yellow) coat, and thin, soggy or floating pulse.

Points: BL62, GB20, DU14 (bleeding and cupping), ST40

Damp Heat

The patient presents fever or afternoon fever, thirst, deep yellow urine, red tongue body, yellow and greasy coat, and fast and slippery pulse.

Points:GB34, GB40, GB43, ST44, LI11; Moving cupping from BL13 to BL25

Wind and Phlegm Blocking in Organs

The patient is suddenly attacked by wind and shows Shen disorder e.g. depression, coma or unclear conscious, red tongue body, turbid and greasy coat, and wiry pulse.

Points: LU11, PC9, HT9, LI1, SJ1, SI1 with bleeding; Shixuan (EX-UE 11) or Baxie (EX-UE9) with bleeding

4.1.2 Chronic Stage

Liver and Kidney Yin Deficiency

The patient presents with atrophic and weak limbs or disabled limbs, lower back pain and weak knees, dizziness, dry mouth and throat, blurred vision, double vision, red tongue body, thin or lack of coat, and thin and fast pulse.

Points:KI6, LU7, KI3

Spleen and Kidney Yang Deficiency

The patient presents with afraid of cold, ptosis of eye lids, reduced hearing, incoherent speech, difficult swallowing, dizziness, short of breath, poor appetite, diarrhea, frequent urination, pale tongue body with white coat, and slow and deep pulse.

Points: BL20, DU14 with moxibustion or GB25, LR13, ST36 moxibustion

Heart and Liver Blood Deficiency

Limb tremor, tinnitus and reduced hearing, lots of dreams, susceptible to be terrified, dry stool, reduced vision, insomnia, pale face, lips and nails, pale tongue body with thin coat, and thin and choppy pulse.

Points: BL17, BL15, BL18; or ST36, SP10, RN12

General Qi Deficiency

Fatigue, weakness of limbs

Points: RN4, RN6, ST36 moxibustion; or BL43, DU20 moxibustion

4.1.3 Symptomatic Modification

- (1) Ptosis of Eye Lids: GB20, BL2, GB14
- (2) Vision Disorders: BL1/BL2, ST2, KI7, Eye Regions of Scalp Acupuncture
- (3) Sleep Disorders: Anmian (Ex-HN-20), HT7 or PC7,
- (4) Speech Disorders: Pricking on Jinjin (Golden Fluids) and Yuye (Jade Fluids); Pricking on Shanglianquan (EX-HN21), Panglianquan³, tongue; the Speech Regions of Scalp Acupuncture
- (5) Swallowing Disorders: SJ17, BL10, GB12, deep inserting with long needle; pricking on the tongue surface and internal wall of pharynx.
- (6) Leg's Muscle Atrophy: points along Yangming and Shaoyang channels on the morbid leg in line array
- (7) Yangming: ST36, ST37, ST38, ST39, ST40, ST41
- (8) Shaoyang: GB34, GB35, GB36, GB36, GB37, GB38, GB39, GB40
- (9) Indigestion: RN12, ST25, BL20, and BL21
- (10) Difficult Urination: RN3, ST29 BL28, BL32, BL54, or BL54 penetrating to ST28, or Baliao Points (BL31, BL32, BL33, BL34)
- (11) Constipation: ST25, RN12; or ST37, SJ6; massage on the abdomen
- (12) Sensation Disorders: Plum-blossom needling on the morbid region

³ 1 Cun lateral to RN23

5. KIDUBA Protocol for Reducing Side-events of Medications

TCM has rich experience of treating the side effects from long-term use of prednisone [18]. The commonly used medicine includes glucocorticoids, interferon, and other immunosuppressant e.g. Mitoxantrone, Natalizumab, Azathioprine, Cyclosporine A, etc.

5.1 Glucocorticoids

According to the pharmacological function and manifestation of glucocorticoids such as prednisone, it can be regarded as a Yang medicine like Fu Zi (*Aconitum Carmichaelii*), Gan Jiang (*Rhizoma Zingiberis*), Rou Gui (*Cinnamomum Cassia*) etc. [19]. When it has been used for a long time, Kidney Yin Deficiency symptoms can be seen, e.g. aggression, agitation, blurred vision, dizziness, numbness, headache etc. During the withdrawing, Kidney Yang Deficiency symptoms can be seen because of the reduction of Yang medicine, e.g. lower back pain, fatigue, cold limbs etc. Acupuncture treatment can be performed according to the stage of using prednisone.

Initial Stage: Kidney Yin Deficiency

Thirst, dry throat, sweating, insomnia, hirsutism, acne, dry and red tongue body, thin coat, thin and fast pulse.

Points: KI2, KI7, KI3, HT5

Herbal Formula: Liu Wei Di Huang Wan including Sheng Di (*Radix Rehmanniae*), Shan Yao (*Rhizoma Dioscoreae*), Fu Ling (*Poria*), Shan Zhu Yu (*Fructus Corni*), Ze Xie (*Rhizoma Alismatis*), Mu Dan Pi (*Cortex Moutan*)

Stage of Reducing Dosage: Kidney Yang Deficiency

Fatigue, short of breath, pale face, vertigo, tinnitus, lower back pain, pale tongue body, deep and weak pulse

Points: KI3, BL23, GB25

Herbal Formula: Jin Kui Shen Qi Wan including Gui Zhi (*Ramulus Cinnamomi*), Fu Ling (*Poria*), Sheng Di (*Radix Rehmanniae*), Shan Yao (*Rhizoma Dioscoreae*), Shan Zhu Yu (*Fructus Corni*), Ze Xie (*Rhizoma Alismatis*), Mu Dan Pi (*Cortex Moutan*)

Stage of Sustaining Dosage: Lung and Kidney Qi Deficiency

Symptoms of reduced immunity, e.g. repeated infections

Points: ST36, LU1, BL13

Herbal Formula: Gu Ben Wan including Huang Qi (*Radix Astragali*), Bai Zhu (*Rhizoma*

Atractylodis Macrocephalae), Fang Feng (*Radix Saposhnikoviae*), Dang Shen (*Radix Codonopsis*), Shu Di (*Rehmannia Glutinosa*), Gou Qi Zi (*Fructus Lycii*), Qian Shi (*Semen Euryales*), Jin Yin Zi (*Fructus Rosae Laevigatae*), Dan Shen (*Radix Salviae Miltiorrhizae*), Suo Yang (*Herba Cynomorii*), Gui Ban (*Carapax et Plastrum Testudinis*), Bian Xu (*Polygonum Aviculare*), Fu Ling (*Poria*)

5.2 Interferon

Interferon medication e.g. INF- α and INF- β may cause alopecia, marrow suppression, disorder of thyroid hormones, showing low fever, muscle and joint pain, fatigue, poor appetite. The side effects of these medication can be regarded as damp heat. Wang and Xin [20] reported that herbal medicine⁴ used to remove damp heat could release the side events of interferon- α in the treatment of chronic Hepatitis B. Li and Zhang [21] reported that the herbal medicine Da Yuan Ying⁵, a representative formula for turbidity (damp-heat) retaining in the diaphragm could reduce the flu-like symptoms of using INF- α -2a and Ribavirin in the treatment of Hepatitis C. Based on above reviewing, we could understand the toxicity of interferon as damp heat toxin. Therefore, acupoints to clear heat and remove damp should be selected. Acupoints: GB34, LI11, RN12, LI4 with draining techniques

5.3 Other Immunosuppressant

Other immunosuppressant e.g. Mitoxantrone, Natalizumab, Azathioprine, Cyclosporine A may cause serious side events such as heart disease, progressive multifocal leukoencephalopathy (PML), myelosuppression etc. Although there aren't sound reports on the application of TCM approaches to reduce the side effects of these medications so far. When there is a chance to treat the patient, who is taking those medications and suffering side effects, it could be helpful to use acupuncture based on the methods of treat the side effects of glucocorticoids and interferon. The fundamental principle in TCM i.e. analyzing patterns can always be used to deal with "new tasks" in practice.

6. Acknowledgement

HZ and HL composed the manuscript and YXL analyzed the references.

7. Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

⁴ Yin Chen Hao 24g, Fu Ling 15g, Huang Qin 20g, Che Qian Cao 15g, Bai Hua She She Cao 12g, Huang Lian 10g, Lian Qiao 15g, Yi Yi Ren 15g, Dan Shen 20g, Bai Zhu 15g.

⁵ Da Yuan Ying: Bing Liang 6g, Hou Po 3g, Cao Guo 1.5g, Zhi Mu 3g, Shao Yao 3g, Huang Qin 3g, Gan Cao 1.5g

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