

Research Progress in the Treatment of Post-stroke Depression from the Perspective of Liver

Zhuo Chen¹, Dou Wang², Jianfu Ma¹, Mingdong Fan¹, Yan Li¹, Han Wu¹,
Yongmei Yan²

¹The First School of Clinical Medicine, Shaanxi University of Traditional Chinese Medicine,
Xianyang, 712000, China

²Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine, Xianyang, 712000,
China

Abstract

In this paper, literature on post-stroke depression, we found that the etiology, pathogenesis and treatment of post-stroke depression were closely related to liver. Liver-qi ascending, preferring free activity, aversion to accumulating. Liver governing dispersion, regulating qi and blood can regulate emotions. Provide rich theoretical basis for treating post-stroke depression from liver. Clinically, treatment methods such as traditional Chinese medicine prescriptions, acupuncture and moxibustion, and five-element music for post-stroke depression based on liver theory have achieved significant curative effects. This paper expounds the treatment progress in the past five years, so as to provide sufficient basis for clinicians today.

Keywords

Treatment from the liver| Post-stroke depression; Tcm treatment.

1. Introduction

Poststroke depression (PSD) is a common complication of stroke. According to statistics, at least 30 % of stroke patients can show emotional changes at a certain stage in the subsequent course of disease, manifested as depression, depression, restlessness, and even some patients are desperate for the future, resulting in suicide and light birth [1]. The disease greatly increases the recurrence rate of stroke in patients, which seriously affects the therapeutic effect, and increasing the disability rate and mortality rate. It not only causes great psychological burden to relatives and friends, but also seriously endangers the society.

At present, the modern medical treatment of PSD is mainly selective serotonin reuptake inhibitor (SSRI) drugs, but many PSD patients are resistant to antidepressant drugs and are unwilling to take this drug [2]. In addition, in the treatment process, with the increase of medication time, drug resistance will become more and more obvious, and the therapeutic effect will be greatly reduced [3]. Moreover, such drugs also have great toxic and side effects, which will increase the risk of adverse events such as cerebral hemorrhage and fall [4]. There are still shortcomings in this treatment, which needs further discussion [5].

Traditional Chinese medicine believes that PSD belongs to 'depression', which has many treatment methods, small side effects and high compliance of patients. It can make up for the deficiency of western medicine in the treatment of PSD. Fan et al. [6] conducted syndrome clustering analysis on the nine factors of PSD, and found that liver qi stagnation, phlegm turbidity syndrome and blood stasis syndrome ranked the top three. They believed that liver qi stagnation was the basic pathogenesis of PSD, and Zhong [7] found that the drugs for PSD in the past 10 years were mostly attributed to the liver meridian, which provided a rich theoretical basis for the treatment of PSD from the liver. Therefore, the author collected and sorted out the

treatment methods of traditional Chinese medicine in recent 5 years from the perspective of treating PSD by liver, studied its clinical application value, explored the correlation between liver and post-stroke depression, and enhanced the clinical diagnosis and treatment effect of PSD.

2. Chinese medicine treatment

2.1. Classical prescriptions of traditional Chinese medicine

'Psychiatric Sutra·Pingren Juegu' Yun: 'Blood and benefit, spirit is living. Liver governing dispersion can regulate emotions through soothing Qi. Once the liver is out of order, Qi cannot run smoothly, it will lead to depression. The disease is located in the liver, which can involve the heart, spleen, kidney and other organs. At first, it is mainly liver depression. Qing · Ye Tianshi ' clinical guide case · Yu ' puts forward a variety of treatment methods such as soothing liver and regulating qi, calming liver and extinguishing wind. By adjusting the soothing function of the liver, the qi movement can be unobstructed. There are many classical prescriptions and famous doctors ' experience prescriptions from the liver to treat depression syndrome, which has remarkable curative effect. Through literature review, it is found that traditional Chinese medicine of soothing liver and strengthening spleen is used in the treatment of PSD, among which Chaihu, Yujin and Baishao are the main drugs. In addition, in the pharmacological mechanism of Western medicine, Chinese herbal medicines regulating liver qi have the characteristics of antioxidant, antidepressant and anti-inflammatory [7]. It can improve cerebral artery blood supply, reduce the formation of atherosclerotic plaques and reduce the incidence of stroke [8, 9].

2.1.1. Powder of Bupleuri for Dispersing the Depressed Liver-energy

Chaihu Shugan Powder was first recorded in the ' Medical General Purpose '. Bupleurum is cold and bitter, and enters the liver and gallbladder meridians. Then it is combined with Chuanxiong, Chenpi, Fructus Aurantii and other products to regulate Qi, so that the liver is regulated and the Qi is relieved.

Zhang Qian et al. [10] divided 80 patients into observation group (escitalopram combined with Chaihu Shugan decoction) and control group (escitalopram). After treatment, the effective rate of the observation group was higher than that of the control group by 15 %. The National Institutes of Health Stroke Scale (NIHSS), modified Barthel Index (MBI) score, Hamilton Depression Scale (HAMD) and TCM syndrome score of the observation group were significantly lower than those of the control group. The serum levels of brain-derived neurotrophic factor (BDNF), norepinephrine (NE) and 5-hydroxytryptamine (5-HT) in the observation group were significantly increased. Zhang Yiwei et al. [11] to the observation group of 30 patients with oral Jiawei Chaihu Shugan San and fluoxetine capsules, control group patients with fluoxetine capsules alone. The results showed that the levels of 5 - HT and NE in the observation group were higher than those in the control group, and the HAMD and NIHSS scores in the observation group were lower than those in the control group. Hamming [12] adopted Chaihu Shugan Powder and paroxetine tablets to treat PSD patients, and the control group was given paroxetine tablets orally. By comparing HAMD scores, the improvement of depressive symptoms in the observation group was significantly better than that in the control group. Li et al.[13] gave 20 PSD patients oral Chaihu Shugan Powder granules and the control group oral sertraline hydrochloride. The results showed that there was no difference in HAMD scores between the two groups ($P < 0.05$). It indicated that Chaihu Shugan Powder was equally effective in treating PSD as sertraline hydrochloride.

2.1.2. Modified Xiaoyao Powder

'The five viscera desire to supplement the cloud; the liver is bitter and anxious... Depression leads to fire and all diseases are ill'. As mentioned in this paper, there are two reasons for liver depression. One is that the deficiency of spleen and soil cannot promote liver wood, and wood qi is all dependent on the nourishment of soil qi. In Xiaoyao Powder, *Atractylodes macrocephala* Koidz and *Poria cocos* are used to promote liver wood to relieve depression. Another is the lack of blood can not nourish the liver, Xiaoyaosan added angelica, peony to honor blood nourishing liver.

Han et al. [14] selected oral Deanxit and Xiaoyao Powder for the treatment of PSD patients. After clinical observation, the total effective rate of treatment, the levels of monoamine neurotransmitter DA, NE and 5 - TH increased more significantly than those in the control group, and the incidence rates of HAMD, nausea and emotional fluctuation were significantly lower than those in the control group. Wang [15] used Xiaoyao Powder to treat PSD patients. Patients in the control group were given conventional treatment, while patients in the observation group were treated with Xiaoyao Powder orally. By comparison, the effective rate of the observation group was 26.47 % higher than that of the control group, and HAMD score and NIHSS score were lower than those of the control group.

2.1.3. Decoction of Bupleuri for Regulating Shaoyang

It is well known that Xiaochaihu Decoction can relieve Shaoyang, soothe liver and gallbladder, but this side can still open depression, qi lifting. Reuse *Bupleurum*, compatibility with *Scutellaria baicalensis*, *Pinellia ternata*, ginger, etc., can have the effect of soothing liver and relieving depression, Tiaochangqi machine.

Ban et al. [16] 30 patients with PSD were treated with Xiaochaihu Decoction (Chaihu, Taizishen, Huangqin 10 g, Qingbanxia 6 g, Dazao 3, Gancao 3 g, Shengjiang 3 tablets). The control group was treated with Baiyoujie. After treatment, the effective rate of the treatment group was higher than that of the control group, and the HAMD score and TESS score were lower than those of the control group. Wang [17] treated 31 patients with PSD by oral administration of doxepin (6-12.5 mg / d). The observation group was treated with modified Xiaochaihu decoction and doxepin. After treatment, the observation group had higher total effective rate as 93.55 % than 80.65 % in the control group, and lower HAMD score than the control group. Xie[18] also used Xiaochaihu decoction combined with doxepin in the treatment of PSD patients. After treatment, the effective rate of the observation group was better than that of the control group, and the HAMD score was significantly lower than that of the control group.

2.1.4. Yueju pill

"Doctor jin jian · Delete fill famous doctor square theory" cloud: "Madam with gas... Incense attached to qi Depression [19] ". Side of the selection of incense with the line of gasification yu, Chuanxiong line qi huoxue, can encourage the force of incense with yu. Therefore, the addition and reduction of Yueju pill can soothe liver and relieve depression, and has unique advantages in the prevention and treatment of PSD.

Peng [20] selected 60 PSD patients and divided them into experimental group (oral Yueju Pill) and control group (oral estazolam). After treatment, it was found that the daily living ability, depression score, activity recovery and swallowing function of the experimental group were significantly improved. Zhang [21] collected 60 stroke patients as the control group (Daixin) and 60 patients as the observation group (Yueju Pill combined with Guipi Decoction combined with Daixin). After treatment, the depression and anxiety of the observation group were greatly improved, and the levels of IL-6, IL-8, TNF- α and HS-CPR were decreased.

2.2. Experience

2.2.1. Decoction for Soothing liver and Relieving Yu

Li et al. [22] used Shugan Jieyu Decoction (bupelum 6 g×2 bags, xiangfu, Angelica, Yujin, ilong, Astragalus membranaceus, Albizia bark and red peony root 10g, chuanxiong 6 g) to treat PSD patients, and the observation group chose fluoxetine combined with Shugan Jianpi Jieyu Decoction. The control group was given fluoxetine hydrochloride 20mg/ day. After treatment, the effective rate of the observation group was 83.3% higher than that of the control group (60.0%), the scores of HAMD, Montgomery-Asperger depression Scale (MADRS) and NIHSS were lower than those of the control group, and the efficacy evaluation of daily living ability (ADL) and TCM syndrome was higher than that of the control group.

2.2.2. Promoting Blood Circulation and Promoting Liver

Xu [23] used huoxue shugan prescription created by Professor Wang Guichu to treat 50 PSD patients. Drug composition: 30g for wheat, 30g for uncaria, 30g for gegen, 30g for vine, 30g for calcined keel, 15g for sophora flavescens, 15g for cicada exuviae, 15g for gastrodia elata, 15g for ligusticum chuanli, 15g for albizia bark, 15g for bupleurum bupleurum, 15g for radix paeoniae, 15g for yujin, 15g for acorus graminis, 15g for radix paeoniae and 15g for salvia miltiorrhiza. After treatment, HAMD, NIHSS and ADL scores of the observation group were significantly improved compared with the control group.

2.2.3. Liver Soothing Joint Soup

Wu [24] used Gu Ziyue gu Laolao's empirical prescription shugan Joint Decoction (drug composition: bupleurum 20g, Ligusticum chuanxiong 12g, Xiangfu 9g, Lily 30g, Anemu 10g, Paeony root 10g, danshen 10g, jujube seed 20g) to treat 30 PATIENTS with PSD, while the control group took sertraline hydrochloride orally. After treatment, HAMD, NIHSS and ADL scores were significantly improved compared with the control group, the total effective rate of the control group was 83.33%, and the effective rate of the treatment group was 86.67%, proving that Shugan Jiutang decoction and sertraline hydrochloride are equally effective in treating post-stroke depression.

2.2.4. Soothing the Liver and Tranquilizing the Mind

Xiang Qiwan [25] selected 30 PATIENTS with PSD as the treatment group, and the treatment group was treated with oral Shugan Anshen Prescription and duloxetine hydrochloride, and shugan Anshen Prescription was chahu Shugan SAN and Tianwang Buxin Dan as the basic prescription. Compared with the control group treated with duloxetine hydrochloride alone, it was found that Shugan Anshen prescription could significantly improve depression, TCM syndrome, nerve defect recovery and sleep, and the levels of 5-HT and NE in the treatment group increased significantly compared with the control group.

3. Proprietary Chinese Medicine

3.1. Shugan Jieyu Capsule

Liver capsule by st.john's resolve depression of st John's wort and acanthopanax, acanthopanax extracts to protect dopamine neurons play a role, can make the single amine material synthesis of release time of the [26], st.john's st John's wort can promote the neurotransmitter release in the cell, sodium ion concentration increases, the former film has inhibition neurotransmitter reuptake, thus play a role of antidepressant [27].

Liu SHUqing et al. [28] treated 59 patients in the observation group with paroxetine (twice a day) and Shugan Jieyu capsule (2 tablets twice a day), while patients in the control group were only treated with paroxetine hydrochloride. Clinical studies have confirmed that Shugan Jieyu capsule can significantly increase the levels of BDNF, NERVE growth factor (NGF), dopamine

(DA), 5-HT, NE, and decrease the levels of tumor necrosis factor α (TNF- α), interleukin-1 β (IL-1 β), homocysteine (Hcy). The HAMD, SDS and NFDS of the observation group were significantly lower than those of the control group, and ADL was significantly higher than that of the control group. Kang CHUanyu [29] compared 45 patients with PSD who took paroxetine orally with 45 patients in the study group who took paroxetine orally and Shugan Jieyu capsule. After treatment, it was found that Shugan Jieyu Capsule could increase the total effective rate, 5-HT level and NE level, and decrease HAMD score, which was better than the treatment effect of paroxetine alone. Li Y N et al. [30] used Shugan Jieyu Capsule and TRANSCranial magnetic stimulation to treat 60 patients with PSD, while the control group only received TRANSCranial magnetic stimulation. After treatment, it was found that hamD-17 and Pittsburgh Sleep Index (PSQI) scores in the observation group were significantly lower than those in the control group, and MMSE scores were improved.

3.2. Shugan Granule

Zhang [31] selected 102 patients with brain PSD. The control group adopted psychological intervention, and the experimental group took Shugan granule orally on the basis of it. After comparison, the effective rate of the experimental group (96.1%) was significantly better than the control group (82.6%), and the depression score was significantly lower than the control group. Liu Jie [32] set 120 PSD patients as the control group to take Daixin orally, and the research group as Daixin plus chongshugan granule. After treatment, it was found that the levels of NE, DA and 5-HT in the research group increased more significantly than those in the control group, and SDS and HAMD scores were significantly lower than those in the control group. Jiang et al. [33] processed Danzhi Xiaoyao Powder into Shugan granules, and 148 PSD patients were randomly divided into control group (escitalopram oxalate tablets) and observation group (escitalopram oxalate tablets combined with Shugan granules). The results showed that the total effective rate of observation group (87.84%) was better than that of control group (74.32%). Xiaoyao-san could improve PSD by increasing the mass concentration of 5-HT and NE in hypothalamus and decreasing the mass concentration of TNF- α , IL-1 β and interleukin-6 β (IL-6).

3.3. Chaishao Calming and relieving Depression granules

Li Y T et al. [34] found through animal experimental studies that Chaishao Anshen Jieyu granules can significantly increase the horizontal and vertical movement scores of PSD rats, improve the levels of adrenocorticotropin-releasing hormone (CRH), adrenocorticotrophic hormone (CORT) and adrenocorticotrophic hormone (ACTH), and improve the depressive symptoms after stroke in rats. Li [35] found that Chaishao Anshen granules may inhibit the damage of hippocampal nerve cells secondary to inflammation by down-regulating JAK1/STAT3 pathway and up-regulating cAMP/PKA/CREB pathway, and promote the survival, regeneration and post-injury repair of hippocampal nerve cells of rats after embolization, thus improving depression in PSD rats.

4. Acupuncture

4.1. Acupuncture treatment

As mentioned in "Acupuncture and Moxibustion Dacheng": "Four passes... Taichong and Hegu are also." Taichong point to fall for shun, blood in the gas. Hegu point to sheng shun, regulating the blood in the gas. Acupuncture at Taichong and Hegu, combined with other acupoints, can integrate Yin and Yang, one up and one down, dredge the liver, promote qi and relieve depression. Liu Jia et al. [36] counted and compared the frequency of acupoints in the treatment of depression, and the top ten selected acupoints were Hegu and Taichong, which were selected

to "relieve the liver". It is indicated that acupuncture treatment of PSD with the method of "regulating the liver" has a significant effect.

Ma [37] selected 63 patients and gave fluoxetine capsule combined with the acupuncture method of waking the brain, soothing the mind, soothing the liver and relieving depression. After dialectical selection of acupoints, they carried out twisting, lifting and inserting. Results: The total effective rate in the treatment group was 92.1% higher than that in the control group (fluoxetine group), and NIHSS and HAMD-17 scores were significantly lower than those in the control group. Modified Bal-THEL index (BI) score and serum 5-HT and NE levels were significantly higher than those in the control group. Wang et al. [38] adopted the acupuncture method of refreshing the brain and calming the nerves, soothing the liver and relieving depression for 160 patients (Four Shencong, Baihui, Shenting, Taichong, Hegu and Shimen). According to no needle retention, 30min, 60min and 90min after acupuncture, the patients were divided into four groups, with effective rates of 84.6%, 85%, 97.29% and 97.36%, respectively. HAMD score was improved compared with that before treatment, indicating that this acupuncture method was safe and effective for PSD patients, and the best effect was achieved by leaving the needle for 1h. Li [39] found that yangxue And Rou Gan acupuncture can greatly improve the depressive state of PSD patients and significantly increase the plasma 5-HT content of patients.

4.2. Moxibustion Treatment

Moxa leaf has the power to awaken the body and dredge the liver qi, and it is convenient to operate. Therefore, through moxibustion therapy, combined with the special points on the liver meridian, it can fuzheng quxie, Yiqi back to Yang, liver qi unobpatency, and Baimaitong.

Wei et al. [40] treated 40 PATIENTS with PSD by liver-clearing moxibustion combined with fluoxetine hydrochloride capsule, and used sparrow peck moxibustion method to moxibustion Sanyinjiao, Baihui, Zusanli, Taichong, Ganshu, Neiguan, Sishencong and Shenmen. Patients in the control group received fluoxetine hydrochloride monotherapy. Compared with the control group, the effective rate of observation group was 95.0%, NIHSS, HAMD and SDS scores were significantly lower than the control group. The serum 5-HT level in observation group was better than that in control group, and the serum OFQ level was lower than that in control group.

4.3. Acupoint Application

"Yu Syndrome" : "Although there are many yu syndromes... The law should be in harmony with the first ". Qi can not be unblocked, it will be depression syndrome, treatment should be the first choice for ease of qi. Acupoint application through the contact of drugs and the body, the continuous stimulation of acupoints, so as to activate the cortex to regulate autonomic nervous function, compared with other therapies, the side effects are small, the gastrointestinal stimulation is reduced, and the patient compliance is high. Lu [41] added Acanthopanax acanthopanax, Astragalus membranaceus, mint, turmeric and azalea flowers to the base formula of Chaihu Shugan Powder. The above ointment was applied to the acupoints (selected acupoints: liver, heart, spleen, kidney, neiguan) of PSD patients for 3-4 hours/day, and then combined with sertraline hydrochloride and emotional therapy. Sertraline alone was used as the control group. Results: After treatment, HAMD score decreased and BI index increased, and depressive symptoms of patients in the observation group were significantly improved.

4.4. Point Injection

Guo [42] believed that acupoint injection at Baihui Point could not only balance Yin and Yang, awaken the body, but also stimulate the meridians of The Governor, dredge the liver qi, and regulate the qi mechanism. He randomly divided 78 patients with post-stroke depression into control group (Prozac 20mg) and treatment group (Baihui point injection combined with dialectical medicine of Traditional Chinese medicine). After treatment, the total effective rate

of 89.74%, HAMD score and depression improvement degree in the treatment group were better than those in the control group.

5. Angle Adjustment Therapy of Five Elements of Music

Wuxing music therapy is a type of psychotherapy based on the emotional theory of Traditional Chinese medicine. It can make people feel happy and improve uncomfortable emotions such as anxiety and depression through different melodies and tones. Huangdi neijing first mentioned the corresponding relationship between the five notes and the five Zang organs, which was further connected with anger, joy, thought, sadness and fear. "Lingshu · Evil Guest" mentioned: "the liver is wood, in the horn sound... In the ambition for fear ". It shows that the horn tone corresponds to the ganmu, so the horn tone in the five elements music can soothe the liver and relieve depression, and greatly improve the mood. Lin [43] used the Angle tone of five elements music to treat PSD patients. Methods: Selected isometric tunes such as "Partridge Flying" and "Jiangnan Hao", played at 19:00 to 21:00 before going to bed, volume 40-60dB, lasting 40-60min/ night. The results showed that the effective rate of the intervention group (77.5%) was significantly higher than that of the control group (47.5%), and the SDS and BI scores of the intervention group were significantly higher than those of the control group.

6. Conclusion

PSD is a common complication of stroke with a high incidence. The occurrence of this disease will lead to antipathy to patients' previous work and life, seriously affecting their daily life and physical and mental health, and gradually lose confidence in rehabilitation training, and even feel disappointed about the future. Nowadays, the treatment of PSD is mainly based on western antidepressants, but there are poor patient compliance, some toxic and side effects, and even some clinicians refuse to recommend antidepressants for PSD patients considering that the therapeutic effect is less than the side effects. However, TCM adopts a holistic approach in treatment, treating symptoms and root causes and multi-target therapy. The therapeutic methods include traditional Chinese medicine, acupuncture, moxibustion, five elements music therapy, etc., with significant therapeutic effect, light toxic and side effects and high compliance of patients.

In conclusion, treating PSD from the perspective of liver has achieved extraordinary clinical efficacy. Through this paper, we can understand the clinical application of treating post-stroke depression from the perspective of liver, which provides reference and basis for clinical treatment of PSD. However, the onset of PSD is extremely difficult to detect, so the prevention and early diagnosis of PSD are relatively insufficient. And relatively lack of relevant pharmacological research and experimental basis. In the future, we should pay attention to the above problems, increase the research on experimental pharmacological effects, provide rich experimental theoretical basis for the treatment of PSD in the future, and explore more effective new diagnosis and treatment methods.

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