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Retrospective Review of Traditional Chinese Medicine Treatment of COVID-19 in China: Clinical Practice and Researches

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Abstract

In the fight against COVID-19 in China, traditional Chinese medicine (TCM) has played an important role in relieving symptoms, preventing deterioration, improving cure rate, reducing death rate, and promoting recovery. Since the third edition of the *Diagnosis and Treatment Protocol for COVID-19* (simply referred to as the *National Protocol*), TCM has been included in the national guidance to tackle the epidemic. In order to make the international medical community fully understand the experience of TCM in the prevention and treatment of COVID-19, we comprehensively reviewed the history, etiology and pathogenesis, prevention and treatment, rehabilitation, and clinical and pharmacological research of TCM used in the endemic. The COVID-19 is under the category of plague or pestilence in TCM. Herbal medicine treatment for COVID-19 is mainly performed based on the syndrome differentiation of three stages and four types. The method also applies to acupuncture and moxibustion treatments. Herbal medicine granules and injections are used flexibly, and Western medicine is adopted to rescue patients in critical conditions. In rehabilitation, the integration of Chinese and Western medicine can be used to improve the respiratory and somatic function of patients. The role TCM has been playing in fighting this epidemic is a further proof of the effect of TCM in preventing and treating infectious diseases, and the relevant experience has been summarized and sublimated.

Keywords

COVID-19; TCM; Acupuncture; Integration of Chinese and Western Medicine

1. Introduction to the Treatment of COVID-19 with TCM Methods in China

Covid-19 has spread worldwide, leading the World Health Organization to declare a pandemic [1]. The covid-19 infectious disease presents flu-like symptoms, which can become severe in high-risk individuals. It has spread globally, plaguing 213 countries and territories, with 40 million cases confirmed, and 1.11 million deaths reported globally up to October 20, 2020 [2]. TCM has a long history and reliable curative effect in preventing and treating various pestilences [3]. In this battle against COVID-19, the contribution by TCM cannot be ignored. Among the confirmed cases of COVID-19 in China, 74,187 patients received TCM treatment, accounting for 91.5% of all patients, of which 61,449 are patients from Hubei Province, accounting for 90.6% of patients in this province, and the involvement rate of TCM in some areas was higher than 95% [4]. The cure rate of patients with COVID-19 could be positively correlated with TCM treatment's involvement rate [5]. TCM can effectively relieve symptoms, prevent mild and ordinary cases from developing into severe cases, improve the cure rate, reduce the rate of morbidity and mortality, and facilitate the recovery groups [6]. TCM has been incorporated into the National Protocol since the National Health Council and the State Administration of Traditional Chinese Medicine issued the third edition of the *Diagnosis and Treatment Protocol for COVID-19* (the *National Protocol*). The 25 local programs implemented by various areas are chiefly based on the *National Protocol* with adaptations to

local conditions. Jiangxia Mobile Cabin Hospital operated with full coverage of TCM therapy. During the 26-day operation of the hospital, a total of 564 COVID-19 patients were admitted, and none further developed into critical conditions; thus, good results were obtained with zero cases of deterioration, re-testing positive, reversion, infection (including among medical staff and logistic security personnel) and complaint [7]. The hospital offered custom formulas when patients had fever, cough, no specific symptoms, anxiety, or insomnia, besides giving them standard formulae (Xuan Fei Bai Du Tang and Qing Fei Pai Du Tang). Meanwhile, various approaches, including acupuncture, external treatment, warming moxibustion, ear acupressure, and patting on meridians, were adopted when needed to alleviate pain for different patients. Health-cultivating techniques are also applied to benefit rehabilitation, psychological guidance to adjust the mood. In the end, sound effects have been achieved [7].

2. COVID-19 in TCM

2.1 Etiology and Pathogenesis

COVID-19 belongs to pestilence diseases and is one kind of warm diseases caused by infection of pestilential Qi. The warm diseases mainly refer to febrile diseases. COVID-19 is the invasion of pestilential Qi into the body from the mouth and nose, from the exterior to the interior, and it stagnates lung Qi and blocks the middle energizer, affecting the spleen and stomach, large intestine, and even the whole body. It transmits rapidly, leading to signs of critical conditions [8]. The pathological features

of COVID-19 can be summarized into six characters: dampness, heat, toxin, stasis, turbid, and deficiency^[9]. Initially, the patient suffers only fever, dry cough, fatigue, and other mild symptoms in the defense aspect. However, as a pestilential disease, COVID-19 quickly invades Qi level, nutrient aspect, and enters viscera. With the characteristic of heaviness and turbidity, the dampness pathogen often results in prolonged disease and consumption of vital Qi. From the perspective of integration of Chinese and Western medicine, when dampness and pestilential Qi are trapped inside the viscera, they transform into heat and blood stasis, scorch nutrient blood and diffuse triple energizer, causing inflammation, acute respiratory distress syndrome (ARDS), sepsis and other clinical critical diseases leading to death^[10].

2.2 Herbal Medicine Treatment based on Three Stages and Four Types

TCM has played a prominent role in preventing and treating epidemic encephalitis B, epidemic hemorrhagic fever, viral hepatitis, SARS, and other infectious diseases in recent years^[11,12]. It is believed that TCM could protect COVID-19 patients from tissue injuries partially attributed to the anti-inflammatory, antioxidant and anti-apoptotic effects. This review provides evidence and support for clinical treatment and novel drug research using TCM^[13]. The state, provincial, and municipal programs generally reach a consensus on the syndrome differentiation and classification of stages and types of COVID-19. The four stages i.e. early, middle, advanced, and recovery stages in medical observation and clinical treatment in the TCM treatment guidelines in the national and local protocols, are similar to the mild, common, severe, and critical

phases of Western medicine. The unique recovery period in the TCM guidelines shows its great strength in restoring patients' health quickly, especially in treating sequelae of COVID-19^[14]. Huang et al^[15] reported that more than 80% of the patients (n=35) were found to have changes in pulmonary CT image, and the syndrome types are mainly dampness pathogen stagnating the lungs (45.71%), followed by heat pathogen obstructing the lungs (37.14%). Zhou et al^[16] found that the pathogenesis of COVID-19 was closely related to the lung and spleen. Pan and Hu^[17] found through clinical observation that the common type of COVID-19 was mainly the dampness and heat syndrome, which involves pathological factors including cold, heat, dampness, and deficiency.

In treatment, emphasis must be laid on the dampness, especially in the mild and common stages. Accordingly, patients should be treated by clearing away heat and dispersing lung, detoxifying and removing turbidity, invigorating spleen to eliminate dampness, and soothing wind and dredging collaterals to avoid further transmission of dampness toxin or pestilential Qi^[6,9,13]. Patients whose conditions have become severe and critical should be first treated by cooling nutrient aspect and opening orifices, detoxifying and eliminating damp turbidity, and restoring yang to stop collapse till their symptoms are relieved. When necessary, cytokine levels in the blood should be reduced by using glucocorticoid inhibition of excessive intensification of the immune system or plasma exchange therapy. TCM drugs are also given at the same time^[10]. The clinical manifestations of children are not entirely consistent with those of adult patients. Most of the children had fever, dry cough, or/and nasal congestion, runny nose, and sore throat as the main symptoms. Therefore, treatment focus is given to

disperse the pathogen in the lungs' defense aspect [18].

In addition to using the classification and treatment of TCM, stage differentiation has also been applied. Chen et al [8] analyzed 25 national and local treatment regimens and found that although the drugs used in the medical observation period and clinical treatment period (four stages in total) had their own rules, they were significantly different. The efficacy of the primary drugs used in each stage was basically the same as that of the above treatment, which corresponded to that of syndrome differentiation.

2.3 Acupuncture Treatment

In this fight against COVID-19, the extensive use of Chinese herbal medicine has played a dominant role. Since ancient times, acupuncture and moxibustion are also widely used in the prevention and treatment of pestilences. For modern acute infectious diseases, like epidemic hemorrhagic fever, influenza, acute bacillary dysentery, epidemic meningitis, viral hepatitis, hand-foot-mouth disease, severe acute respiratory syndrome (SARS), acupuncture can be an intervention with precise and reliable effects achieved [19]. Acupuncture and moxibustion could be used to treat the breathlessness, anxiety, side-effects of COVID-19 western medicine treatments [20-22]. Based on the *National Protocol*, the Chinese Association of Acupuncture and Moxibustion has formulated the *Guidance on Acupuncture and Moxibustion Intervention in COVID-19 (2nd Edition)* [23]. When performing acupuncture, one should strictly abide by quarantine and disinfection requirements and make sure one performs under the condition of ensured safety. Huang et al [24] reported that heat-sensitive moxibustion on Shenque-RN8 and Tianshu-ST25 could effectively alleviate patients' negative emotions with

COVID-19, relieve chest tightness and anorexia, and this treatment is well received among patients.

2.4 Prevention

As early as February 1, 2020, Wuhan Health Commission posted on its official website *Wuhan Recommendation Program of Home Prevention for COVID-19* according to the TCM concept of preventive treatment of illness [25]. *The TCM Prevention Program for the COVID-19* formulated by Tongji Hospital includes two parts: prevention formulas and home care [26]. Herbal medicine including Yu Ping Feng San, Gui Zhi Tang, Zhen Qi Fu Zheng Wan, Shen Qi Pian, and home care includes aromatherapy, wearing, diet, and Qigong are recommended [9]. Moreover, many patients and health care workers developed unfavorable psychological disorders such as depression, anxiety, post-traumatic stress disorder (PTSD) based on experience in the prevention and treatment of infectious diseases such as SARS and middle east respiratory syndrome (MERS) [27]. Therefore, it is essential to prevent COVID-19 psychological disorders during and after the epidemic.

2.5 Rehabilitation

On March 27, 2020, academician Zhang Boli and Hubei Integrated Chinese and Western Medicine Hospital Rehabilitation Medical Center, Affiliated Union Hospital of Huazhong University of Science and Technology, Tongji Hospital, and other 11 work units jointly issued the *Standard for Rehabilitation Diagnosis and Treatment of COVID-19 with Integration of Traditional Chinese and Western Medicine* [28]. The National Health Commission proposed that medical rehabilitation institutions should provide an assessment of lung function damage for patients in severe and critical conditions,

formulate a reasonable respiratory rehabilitation plan and provide rehabilitation treatment. Hubei Integrated Chinese and Western Medicine Hospital was the first to offer the rehabilitation department for COVID-19 patients in China and carried out clinical rehabilitation practice under national policy documents and rehabilitation guidance norms. According to the different clinical types of patients and TCM syndrome differentiation and treatment, integrated Chinese and western medicine has been applied. Posture therapy, respiratory training, exercise therapy, and other rehabilitation treatment techniques have been adopted to improve patients' respiratory and physical functions. Tuina therapy, moxibustion, and herbal plaster, and other TCM treatments have been adopted to regulate Qi movement and repair the viscera's function. Taichi, Eight Brocades Brocade, and other traditional health-cultivation techniques have been practiced to improve patients' physical fitness, improve their physical and mental state, etc. In this way, pronounced therapeutic results have been achieved, and valuable clinical experience obtained.

The patients' basic pathogenesis in the rehabilitation period is the lingering of pathogen and deficiency of Qi. According to warm diseases, the disease locates in the lungs, which belongs to the nutrient aspect or blood aspect. TCM treatment during the whole course, especially the lingering period, is vital, which can avoid or reduce the residual pulmonary fibrosis changes, and has important clinical significance for improving patients' quality of life in the future [29]. Zhang et al [30] hold that the rehabilitation from COVID-19 mainly starts with handling deficiency of lung and kidney and qi deficiency and blood stasis. The former can be treated with Jin Shui Liu Jun Jian and Ren Shen Ge Jie San to tonify lung and kidney and relieve

cough and asthma; or Taixi-KI3, Feishu-BL13, Shenshu-BL23, Gaohuang-BL43, Pingchuan, etc. can be chosen for acupuncture treatment. The latter can be treated with Bao Yuan Decoction and Tao Ren Si Wu Tang; or Geshu-BL17, Kongzui-LU6, Hegu-LI4, Quchi-LI11, Sanyinjiao-SP6, etc. can be chosen for acupuncture treatment.

Traditional Qigong plays an important role in the rehabilitation of lung function [31]. Through the study of chronic obstructive pulmonary disease (COPD), asthma, pulmonary heart disease, and other pulmonary diseases, it is found that Qigong can improve cardiopulmonary function, relieve anxiety, insomnia, and other symptoms, thereby improving the quality of life [32-33]. In clinical practice, various forms of Qigong and Taichi techniques can be adopted.

3. Clinical Observation and Studies

Since the outbreak of COVID-19, many clinical observation studies have been carried out in various parts of China. These studies reflect diverse ideas of TCM treatment and accumulate valuable experience and provide clinical data support for the formulation of national protocols and TCM's fight against COVID-19. By analyzing the formulas in the *National Protocol (Seventh Edition)*, we can see that classical formulae have been extensively applied [29]. In the treatment of COVID-19, many TCM clinical experts also accumulated rich experience in using classical formulas. Xu et al [34] summarized and put forward suggestions for treating COVID-19 using classical formulas from the perspective of treatment based on syndrome differentiation.

In this epidemic, local hospitals have formulated hospital preparations regarding the *National Protocol*. The hospitals refer to

specifically developed specific formulae for domestic self-use only upon approval. Professor Mei Guoqiang developed Pneumonia Formula I, also known as Qing Fei Da Yuan Ke Li, based on most patients' clinical syndrome in Wuhan, China. Pneumonia Formula II, relatively bitter and cold, is used to treat exuberance of lung heat. Both hospital-made prescriptions are used for the treatment of COVID-19 common cases and severe cases [35]. Ever since February 21, Sichuan province has successively promoted No. 1 Formula for COVID-19 (Qing Fei Pai Du Tang), No. 2 Formula for COVID-19, No. 3 Formula for COVID-19, which have been used as a hospital preparation in 205 hospitals across the province [36].

Zhang Boli's team found that treating 82 patients with Jin Hua Qing Gan Ke Li after five days could significantly relieve the clinical symptoms of fever, cough, fatigue, and expectoration of sputum and anxiety in mild cases with COVID-19 [37]. Yang et al [38] treated 13 patients with COVID-19 whose patterns were cold and dampness stagnating the lung and found that Qi Gui Ling He Ji could improve fever, cough, fatigue, diarrhea, nausea, and other symptoms. Chen et al [39] used Gan Lu Xiao Du Yin combined with Chinese and Western medicine and cured 131 patients with COVID-19 (95.4% of them were common cases). Xie et al [40] reported the successful clinical experience of treating 8 cases of severe COVID-19 cases by using Po Ge Jiu Xin Tang and Xiao Qing Long Tang.

The National Protocol (7th Edition) points out that Da Huang and Mang Xiao can be used in severe patients with internal block and external collapse syndrome receiving mechanical ventilation. Wu et al [41] found that the purging method could improve patients' fever and

intestinal dysfunction with COVID-19, prevent deterioration, normalize the fecal virus nucleic acid, and benefit rehabilitation. According to the *Expert Consensus on Comprehensive Treatment of COVID-19 in Shanghai*, critical patients who suffered heat pathogen blocking the lung could be treated with Da Cheng Qi Tang enema, reducing high fever and releasing abdominal distention and constipation with dry stool dryness [42].

TCM injection is a unique method of integrated Chinese and Western medicine treatment, which plays a vital role in treating severe and critical cases. Commonly used injections include Xuebijing Injection, Reduning Injection, Tanreqing Injection, Xingnaojing Injection, Shenfu Injection, Shengmai Injection, Shenmai Injection [29]. Xuebijing preparation has the functions of activating blood to remove blood stasis, dredging meridians and collaterals, and dispersing internal toxins, which are targeted at the main symptoms in the course of COVID-19. Xuebijing can delay the lungs' pathological changes while inhibiting respiratory tract virus, protect the liver from injury caused by virus or antiviral drugs, inhibit complicated bacterial infection, enhance body immunity, and reduce cardiovascular damage [43]. The core compounds of Tanreqing Injection can play an antiviral role by binding to 2019-nCoV 3CL hydrolyase and can regulate multiple signaling pathways [44].

4. Pharmacological Studies in TCM

Given the pivotal role of TCM in the fight against COVID-19, researchers have carried out a large number of studies on its mechanism of action. Network pharmacology has become a powerful tool for studying multiple components and multiple targets of TCM compounds [6]. Qing Fei Pai Du Tang plays a role in

balancing immunity and eliminating inflammation by regulating several proteins co-expressed with ACE2, as well as a series of signaling pathways closely related to the occurrence and development of diseases. It targets ribosomal proteins essential for viral replication to inhibit viral mRNA translation and protein's interaction with viral proteins to fight against viruses [45]. Lian Hua Qing Wen Ke Li may act on inflammatory cytokines and other targets to regulate AGE-RAGE signaling pathways, Kaposi, IL-17, human cytomegalovirus infection, and Hepatitis B through its active components of mistletoe, luteolin, kanamycin, and sitosterol [46]. The treatment of COVID-19 with Lian Hua Qing Wen Ke Li can inhibit the pneumonia of the novel corona-virus infection and improve patients' clinical symptoms with pneumonia [46]. Active components such as kaempferol, baicalin, and melaleuca papyracea of Jin Hua Qing Gan Ke Li may regulate multiple signaling pathways by combining ACE2 with targets such as PTGS2, BCL2, and CASP3, which may exert therapeutic effects on COVID-19 [47]. Ren Shen Bai Du San may inhibit the anti-COVID-19 effect of cytokine storm formation by regulating chemotactic cytokines, increasing saturation, inhibiting STAT, MAPK, NF κ B, PIK3K, IL-6, and other signaling pathways, suggesting its potential clinical value in the treatment of COVID-19[48]. However, the variability of viruses, the incomplete human understanding of viruses, and the database's limitations leave this study with many questions that need to be further explored and studied. The active ingredients in Xiao Chai Hu Tang play a therapeutic role in the treatment of COVID-19 by inhibiting SARS-CoV-2 activity, blocking SARS-CoV-2 invasion pathway, inhibiting inflammatory storm, and regulating body immunity [49].

5. Limitations and Countermeasures

Because of the sudden outbreak of COVID-19 and the difference in treatment plans used in various regions, it is difficult to carry out high-quality clinical and pharmacological studies. Instead, most studies can only be based on observation and retrospective study. Acupuncture has limited usage since the epidemic is infectious. It is believed that more research will be carried out in the following aspects: comprehensive TCM rehabilitation treatment, new drug research and development, and discipline development of TCM infectious diseases.

At the beginning of the outbreak of COVID-19, TCM still has shortcomings and limitations in dealing with major diseases such as a sudden outbreak of infectious diseases. TCM is basically absent in the disease control system; it is difficult for TCM to participate in the emergency response mechanism of public health; the infrastructure and personnel reserve in TCM hospitals cannot accommodate the prevention and control of infectious diseases; the theoretical and scientific research foundation related to pestilences is weak and so on. The Chinese government and health care personals agreed to establish an emergency management organization for public health events in which TCM participates. The system has been further promoted to prevent and control major infectious diseases with the extensive involvement of TCM [50].

6. Conclusions

The prevention and treatment of COVID-19 can effectively relieve symptoms, reduce mild and common cases from becoming serious ones, improve the cure rate, reduce the morbidity and mortality rate and promote the patients' recovery. COVID-19 is under the category of pestilence or epidemic diseases in TCM. The pestilential Qi enters into the body from the mouth

and nose, from the exterior to the interior, and it stagnates lung Qi and blocks the middle energizer, affecting the spleen and stomach, large intestine, and even the whole body. TCM treatment is divided into "three stages and four types," which mainly uses herbs based on syndrome differentiation and add acupuncture and moxibustion as a supplement. Granules and injections are used flexibly, and Western medicine is adopted to rescue patients with critical conditions.

In the choice of TCM formulas and drugs, formulas related to the school of cold damage and warm diseases are given priority to. Based on the disease's characteristics, specially prepared formulas like Qing Fei Pai Du Tang can be designated. In the rehabilitation, the integration of traditional Chinese medicine and Western medicine should be applied to improve the patient's breathing and body function. Thus a comprehensive rehabilitation can be made, including posture therapy, breathing training, exercise therapy, and TCM methods such as Tuina therapy, moxibustion, and plaster. During the epidemic, the effect of TCM in the treatment of infectious diseases has been verified again. Moreover, the relevant experience has been summarized and sublimated. Because of the sudden onset of COVID-19, it is difficult to carry out high-quality clinical and pharmacological studies. It is believed that, in the near future, the study will be carried out more thoroughly.

7. Conflicts of Interest

The authors declare that they have no conflicts of interests.

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