The Role of Traditional Chinese Medicine in the Treatment of COVID-19 Patients

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Abstract. COVID-19 pandemic, caused by SARS-CoV-2, was the most serious pandemic which strongly impacted people’s daily life. During the three years that it has swept the world, it has caused severe and huge losses to the economies of various countries, resulting in tens of thousands of deaths. At present, the virus is still raging, threatening global human health. Patients showed symptoms similar to people with colds or fevers. As it becomes more and more serious, many scientists found that Traditional Chinese Medicine (TCM) has effects to cure the disease, particularly in the management of fevers and colds. This implies that TCM might be useful in the management of COVID-19 disease. Scientists did experiments on TCM which concluded the fact that TCM indeed is a way to treat COVID-19. TCM can alleviate COVID-19 symptoms by increasing CD4+/CD8+ ratio and recovering damaged body tissues. COVID-19 infected patients who are getting better after they received TCM treatments. The aim of this paper is to introduce the ways of why TCM plays an important role in treating SARS-CoV-2 virus.

Keywords: SARS-CoV-2, viral pneumonia, TLR-NF-kB signalling pathway

1. Introduction
The complex group of viruses known as coronaviruses can infect people and cause respiratory diseases. They were a major cause in three severe pandemics. Three pandemics, their origin and affected regions: In 2002, the first pandemic of the 21th century emerged in Foshan, China. It was caused by SARS-CoV-1 and the disease was later named as SARS. In 2012, another coronavirus, MERS was discovered. Later in 2019, the coronavirus SARS-CoV-2 that caused COVID-19 was discovered. Its outperformed SARS and MERS in terms of the quantity of infected people and the geographic scope of its effects thanks to its incredible potency. According to statistics, there were 572,239,451 confirmed new COVID-19 patients worldwide as of July 29, 2022, 11:33 a.m. EST, and there were 6,390,401 confirmed deaths.

There are many developed treatments around the world, 69% of the global population had, at least, received one dose of vaccines. Chinese scientists found that there are several Chinese medicines that can relieve COVID-19 infected patients’ symptoms and can improve their immune systems and their damaged body tissues.

This paper mainly discussed how TCM can alleviate COVID-19 infected patients’ symptoms and the ways TCM can treat COVID-19.
2. The overview of SARS-CoV-2 virus

According to a phylogenetic study, the SARS-CoV-2 contains 79.5% of the genome that is the same as SARS-CoV virus. Scientists have worked on examining it with a coronavirus strain from bat BatCov RaTG13. The result showed 96% similarity which suggests that the virus might be coming from bats and eventually affected humans [1]. ACE2 receptors are found on the host cells, and the S protein makes it easier for the viral envelope to link to these receptors. The S protein consists of subunits that are involved in cell membrane fusion and receptor binding, respectively. In addition to numerous other body tissues, the ACE2 protein is widely distributed in different tissues. In order to regulate the path taken by the renin-angiotensin-aldosterone pathway, ACE2 receptors are of utmost importance.

There are several steps for the virus to enter the cells. It enters the respiratory tract by recognizing ACE2 as its receptor cell that is similar to the process of how SARS-CoV enters the human body. They both use spike (S) protein as transmission factor, which can be divided into S1 and S2 domains, and are in charge of binding receptors and fusing cell membranes. Transmembrane serine protease 2 creates a cleavage on S2 site and causes cell membrane fusions and viruses being infected. Uncoated genomic RNA from the virus is translated into polyproteins once it has entered the human body, and then it is combined with viral-induced double-membrane vesicles to create replication/transcription complexes. This complex then uses genome transcription to replicate and produce a nested collection of subgenomic RNA that encodes structural proteins and a few auxiliary proteins. The other organelle serves as mediators in the assembly of freshly generated viral particles. Virus particles are finally discharged into the extracellular milieu compartment after budding. At the end of this long process, the viral replication cycle and viral development will finally be activated [2].

ACE2 can be considered as the most important key for virus entrance. ACE2 has a protection role against acute lung failure. This might be the reason why when SARS-CoV-2 is attached to ACE2, patients will express coughing symptoms. This means their respiratory system has been invaded and especially their lung tissues are damaged. ACE2 is also known for its power on control of severity of lung diseases [2].

3. Symptoms of the SARS-CoV-2 virus infected patients

These symptoms might last for 7 to 14 days depending on different people. The most common symptoms are cold and fever. It has been suspected that TCM which treats cold and fever can actually treat COVID-19. Since patients’ respiratory systems were damaged, they might confront serious coughing, difficulty in breathing, and running nose. By examining patients’ lung autopsy, it suggests that there will be persistent pain and pressure in their chests. Patients might also experience allergy on their skins which are shown in the form of rashes. Loss of taste or smell is also another common symptom for SARS-CoV-2 infected patients. This will probably last about 4 or 5 days after other symptoms appear.

4. The effect of change in the number of lymphocytes in the sars-cov-2 infected patients

Lymphocytes are one of the subgroups in white blood cells (leukocytes). They are directly related to the human immune system. Studies have shown that the reduction of the number of lymphocytes have occurred in patients which causes their body to lose the ability to protect patients from virus invasions.

There are three potential mechanisms which lead to lymphocyte deficiency and cause immune system dysfunction. (1) Disordered inflammatory cytokines are one of the most essential keys which lead to lymphopenia. Scientists have noticed that cytokines like interleukin 6 (IL-6), have been observed at a high level among SARS-CoV-2 infected patients compared to normal people. This suggests that it might be one of the factors which induce lymphopenia deficiency. (2) SARS-CoV-2 infected patients showed reduction of number of lymphocytes [3]. This means that the virus might directly attack lymphocyte cells which leads to lymphopenia. (3) Autopsy of lymphatic organs collected from SARS-CoV-2 infected patients showed massive lymphocytes die. The virus might directly affect lymphatic organs which cause lymphocytic dysfunction.
In conclusion, reduction in the number of lymphocytes is strongly correlated with whether people have COVID-19 or not. Lymphenia is a reliable indicator for COVID-19 patients.

The Respiratory System was damaged mainly in the SARS-CoV-2 patients. C. Huang et al took CT images of the infected patients’ chests. The images showed that patients with severe SARS-CoV-2 had large bilateral areas of consolidation. In contrast, patients with mild symptoms only had small and segmented areas of consolidation.

According to Z. Xu et al, chest x-ray of lung biopsy samples from an infected patient suggested extensive exudation and damage to bilateral lung tissue. His left and right lung tissues suggested that this patient had interstitial mononuclear inflammatory infiltrates (as shown in Figure 1) [3]. SARS-CoV-2 not only affected lungs but also damaged trachea. Chest CT of patients were diagnosed with tracheal membrane rupture (Figure 2) [4].

![Figure 1. Images from SARS-CoV-2 infected patients [3]. (A-B) lung tissue, (c) liver tissue.](image1)

![Figure 2. The changes in chest.](image2)

The data above show that after people are infected, the lung becomes the first tissue being damaged. Alveoli might be the part where there is most damage in the human lung. However, damage to other parts of the lung can also occur, and the mechanisms involved have been described in previous paragraphs. As a result, most patients have relatively similar respiratory failure, the use of noninvasive positive pressure ventilation and high nasal flow treatments were introduced. The analysis showed that high nasal flow has significantly lower rate of intubation compared with conventional oxygen therapy. Because of this, the European Society of Intensive Care Medicine recommends high nasal flow as a therapy for the patients. However, it is strongly suggested that be careful when applying these treatments to COVID-19 infected patients.

5. Reductions in the ratio of CD4+ to CD8+ and lymphocyte populations
According to Saleh M. et al, the number of lymphocytes, CD3+ and CD4+ cells, were significantly decreased and CD4+ to CD8+ cell ratio was also decreased compared to normal people [4].

According to new research, the counts of leukocytes and the percentage of lymphocytes were significantly increased in the severe group [5]. This cannot tell there is a significant difference in the
moderate group. Then, by examining the reduced T lymphocyte counts in different age groups. But there is an obvious decline in T lymphocytes based on age groups which means that patients with younger ages are more likely to have a significant reduction. Also, the results found that the males are easier to develop severe conditions compared to female patients. By measuring each day, the number of T lymphocytes (day 1 to day 14), the number of lymphocytes dropped significantly on the first seven days and there were increases followed by that. It might need to take more than 7 days to return to normal number of T lymphocytes.

6. Damage of liver tissue
The liver biopsy from Zhe Xu et al, showed COVID-19 infected patients had moderate lobular activity with microvesicular steatosis. It suggests that the harm could have been brought on by a SARS-CoV-2 infection or liver damage brought on by drugs [4]. Since blood examination showed the reductions of CD4 and CD8 cells, which may also contribute to hepatocellular dysfunction. Because of high levels of Interleukin-6 in the patients which implicated inflammatory and repair responses in patients’ liver.

The autopsy of SARS-CoV-2 infected patient’s liver showed lobular activity and fatty degeneration, which suggests that the virus can affect the liver (Fig 1). There is a significant increase in the interleukin-6. This suggests that there are robust inflammatory responses in the human liver.

6.1. Examples of developed related TCM
Traditional Chinese Medicines can regulate damaged human respiratory systems and damaged human livers which suggests that they have roles in treating COVID-19 diseases. TCM such as Lianhuaqingwen (LHQW) and Reduqing (RDQ) has prevention and treatment of common colds. Y. Ma et al showed that both LHQW and RDQ can relieve fever approximately 30 to 60 hours. Both RDQ and LHQW showed significantly greater time in treating patients with above 38 degrees celsius than in treating patients with temperature below 38-degree celsius. Xuebijing (XBJ) is another TCM which has significant effects in treating pneumonia. Y. Song et al experimented-on patients with pneumonia and injected XBJ to observe its effect on treating pneumonia. The patients injected with XBJ showed significantly lower mortality rate compared to patients with no XBJ injections. It was also shown that XBJ injected patients spent much shorter time in the ICU [6]. These examples suggest that TCM can indeed effectively treat patients who have symptoms similar to COVID-19.

Xuebijing injection, and Jinhua Qinggan granules, Lianhua Qingwen capsule (LQC), Qingfei Paidu decoction, Huashi Baidu formula, and Xuanfei Baidu formula, have all been developed as the COVID-19 pandemic affects more and more people. H1N1 influenza, which can cause a cold/fever, runny nose, headache, or bodyache, expanded widely in 2009 and caused catastrophic damage. LQC made a huge difference in China’s response to the H1N1 epidemic. These medications play specific roles in the treatment of the virus. In addition, it can effectively aid in the recovery of SARS-CoV-2 infected individuals [7].

6.2. The role of TCM in the treatment of inflammations in lungs
The TLR-NF-kB pathway is one of the most significant routes that regulates the inflammatory factors. Three TLR subtypes are associated with viruses. The findings demonstrate that nuclear transcription factor NF-kB is activated during SARS-CoV-2 invasion by TLR mediated signaling, which results in the production of proinflammatory proteins. Researchers discovered that the TLR7/MyD88 pathway can be inhibited by gardenin and baicalin to lessen NF-kB activation. Chinese medical formulas such as Pueraria Decoction (Gegen Tang) can also inhibit expression of TLR.

According to C. Zeng et al, a combined TCM was introduced—Maxingshigan-Weijing decoction [8]. MWD is composed of 14 different traditional Chinese drugs. Maxing Shigan decoction is composed of Ephedra sinica (Ma Huang), one of the most important components of MWD and treat asthma, Semen armeniacae amarum (Ku Xing Ren), directs qi down and supports smooth breathing, Gypsum Fibrosum (Shigao), can reduce the synthesis of inflammatory factors, and Glycyrrhiza uralensis (Gancao), relieve cough symptoms. Weijing decoction is composed of Couly phragmitis (Weijing), it
clears away heat and resolving phlegm, removing dampness and purging, Semen persicae (Tao Ren), moistens the intestines and help maintain blood stasis. Semen coicis (Yi Yi Ren), can effectively relieve fever symptoms, and Semen benincasae (Dong Gua Ren helps to moistens the lungs and reduce body heat [9]. All of the Chinese drugs have their own way to manage specific symptoms. By combining them, the efficacy of the TCM will be the highest and most effective in treating the inflammatory and fever symptoms caused by the virus.

By examining results, the percentage of symptoms (fever, fatigue, cough, and difficulty breathing) between SARS-CoV-2 infected people and people after being treated with Maxingshigan has significantly reduced. The boxplot of symptoms recovery time in 0 to 15 days showed that there is significantly decreased in the percentage of all four symptoms among patients after being treated with Maxingshigan. These two results suggest that Weijiang decoction can effectively reduce the patients’ inflammatory symptoms and most importantly, to help patients ‘severe inflammations in lungs (pneumonia) [10]. Maxingshigan focused on relieving patients’ cough and fever symptoms. The combination of these two TCM not only improve patients’ symptoms but also recover damaged lungs.

6.3. The role of TCM in the regulation of cell ratio
According to a study, Shengjiang San can increase CD8 cells and control the balance between CD4 and CD8 cells, both of which will enhance the body's immune system. When mice were used in an experiment with Haoqingingdan decoction, the CD4+/CD8+ ratio fell in comparison to the control group [11].

HCoV-229E is a type of coronavirus which triggers cold symptoms. X. Lu et al showed that another TCM, Shufeng Jiedu (SFJDC) has a significant effect on increasing T cells. They experimented on HCoV-229E infected mice and suggested that the number of T cells were significantly increased after SFJDC was administered [11].

SFJDC not only can promote the amount of T cells, it can also reduce the pneumonia in infected coronavirus animals or humans. Increase of IL-6, TNF-α, and IFN-γ are the main factors that cause inflammations in lung tissues. The percent of those factors in coronavirus infected mice decreased after SFJDC was administered. The number of IL-6 was approximately 145 pg/ml in the model group (mice with virus load in lungs) and after SFJDC was applied, the number of IL-6 decreased to 50 pg/ml [12]. Same results happened after SFJDC was introduced. These findings imply that the use of SFJDC to SARS-CoV-2 infected individuals can successfully reduce lung tissue inflammation.

Unlike MWD, SFJDC is consisted of Huanghai and Lianqiao, have the ability to reduce heat and detoxifying, relieve pain and coughs, eliminating lumps, Isatis indigotica (Ban-lan-gen/Dian Lan), most effective in treating cold and fever, Bupleurum Chinese (Chaihu), Patrinia scabiosifolia (Baijiang Cao), and Phragmites australis (Lu Gen/Lu Wei), detoxifying liver and raising qi/yang, Verbena officinalis (Ma Bian Cao), can promote blood circulation, remove sepsis, cut malaria, detoxify, diuresis and reduce swelling.

6.4. Data of clinical trials
M. Xiao et al used Lianhuaqingwen granules and Huoxiangzhengqi dropping pills to treat patients suspected of carrying the virus [10]. Those people were selected to treat with different medicines and divided into three groups, Lianhuaqingwen granules group, Lianhuaqingwen and Huoxiangzhengqi group, and western medicine group. They found that there was no significant improvement on the symptoms in all three groups but patients’ fever and diarrhea were significantly improved. Also, the combination of Lianhuaqingwen granules and Huoxiangzhengqi dropping pills was more effective on the treatment of some symptoms. Patients in the Huoxiangzhengqi and Lianhuaqingwen group showed the lowest percent of severe symptoms and western medicine group has relatively high percent of patients with severe symptoms, which suggests that the combination of TCM will be a way for COVID-19.

Another TCM, Xuebijing (XBJ), can reduce inflammatory cytokines in liver tissues.
W. Zheng et al experimented on XBJ injection on COVID-19 patients and found that XBJ can act on COVID-19 through forty different pathways to produce immune regulatory response and anti-inflammatory [11]. H. Guo et al have selected 42 patients, eight of them have mild symptoms and the rest (thirtyfour) have severe COVID-19 symptoms. After 7 days of XBJ injections, 60% of the patients showed improvement in their CT images. By examining the blood samples from 16 patients after XBJ injections, there were significant changes in routine blood test. Pro-inflammatory variables were found to increase inflammation, and the results indicated that XBJ can treat COVID-19 condition [12].

Xyianping (XYP) is a popular TCM which you can simply get in any pharmacy. Chinese people used it mainly to cure respiratory infections and other diseases. It can also recover the damaged lung and liver tissues. X. Zhang et al injected XYP to COVID-19 infected patients. The result showed that XYP reduced patients’ coughing period and effectively relieved coughing symptoms. The treatment group, which is the group that patients received XYP, took a much less time to complete SARS-CoV-2 RNA assays [13].

All of the clinical data above strongly suggest that TCM have an essential role in treating COVID-19 disease. Patients are becoming better and healthier under the treatment of these different TCM.

7. Conclusion

COVID-19 pandemic is a very serious issue. It has caused students to have to stay at home and cannot go to school. It has stopped people from traveling to other countries. It has a strong impact rate of world economic growth. Scientists have developed many different medicines to treat this disease. There are profound discoveries showing that Traditional Chinese Medicines have their own ways in treating COVID-19 disease. Gradually, many different TCM were being developed. They effectively help COVID-19 infected patients get better and reduce their symptoms. The scientific experiment also showed that the combination of two different TCMs is a much faster way to treat patients compared to only using one TCM. TCM can help patients’ lymphocytes ratio back to normal, effectively play a role in treating the inflammations in patients’ bodies, and most importantly help to recover infected patients’ damaged body tissues.

References


