

GUIDELINE

Traditional Chinese Medicine guidelines for coronavirus disease 2019

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Abstract

OBJECTIVE: To summarize the evidence from Traditional Chinese Medicine (TCM) practice in the treatment of coronavirus disease 2019 (COVID-19) and provide timely clinical practice guidance.

METHODS: The guidelines were developed in accordance with the World Health Organization rapid guideline process. The evidence on TCM for COVID-19 from published guidelines, direct and indirect published clinical evidence, first hand clinical data, and expert experience and consensus were collected. The grading of recommendations assessment, development and evaluation (GRADE) method was used to grade the evidence and make the recommendations.

RESULTS: Based on the available evidence, the guidelines recommended 17 Chinese medicines for COVID-19: 2 Chinese herbal granules, 7 Chinese patent medicines, and 8 Chinese herbal injections.

CONCLUSION: As the literature search was conducted on March, any subsequent versions of these guidelines require an up-to-date literature review. We hope that the evidence summary in these guidelines will be helpful in global efforts to address COVID-19.

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Keywords: COVID-19; Medicine, Chinese traditional; Practice guideline

INTRODUCTION

Since its outbreak, coronavirus disease 2019 (COVID-19) has spread rapidly and unexpectedly and has developed into a pandemic. As of 18 October, more than 40 million people have been diagnosed with COVID-19 all over the world, and deaths have exceeded 1.1 million.¹

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Common symptoms are fever, fatigue, and dry cough,^{2,3} accompanied by nasal congestion, runny nose, sore throat, and diarrhea in a small number of patients.⁴⁻⁶ Some patients experience dyspnea and/or hypoxemia 1 week after onset, and may develop severe conditions such as acute respiratory distress syndrome, septic shock, metabolic acidosis, coagulopathy, and multiple organ failure.⁴⁻⁶

In Traditional Chinese Medicine (TCM) terminology, COVID-19 is a plague caused by pandemic pathogens.⁷ TCM has been previously used to treat epidemic diseases such as SARS and H1N1 influenza and TCM practitioners have acquired extensive experience in managing epidemic diseases.⁸ In China, the use of a combination of TCM and conventional medicine has played an important role in treating COVID-19.⁹ A summary of TCM clinical practice experience in the prevention and treatment of COVID-19 is needed using an evidence-based method. Such a summary could be useful in global efforts to manage COVID-19. These guidelines focus on the use of Chinese patent medicines to treat COVID-19. They have been developed in accordance with the World Health Organization rapid recommendation guideline process and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method, and provide clinical practice guidance for the treatment of COVID-19.^{10,11}

METHODS

Scope

The target population of the guidelines is patients with COVID-19. The guidelines mainly focus on the treatment of COVID-19 with TCM prescription granules, Chinese patent medicines, and Chinese herbal injections. The main users are medical practitioners, public health personnel, researchers, and community residents who require guidance on the use of TCM for COVID-19.

The method of guideline development followed the general procedure in the WHO guideline development manual.¹⁰ We prepared a guideline proposal, which was registered in two languages on the International Practice Registry Platform (<http://www.guidelines-registry.org/>); the registration number is IPGRP-2020CN033.

During the planning phase, we first established a steering group comprising clinical experts and methodologists. The steering group was responsible for forming a guideline development group (GDG), managing conflicts of interest, and monitoring the whole process of guideline development and subsequent updates. The steering group and the GDG defined the most important clinical questions based on a literature review and expert opinion, and formulated 17 questions about Chinese formula granules, Chinese patent medicines, and herbal injections for people with COVID-19 using the PICO (patient/population, intervention, comparison, outcome) format.

Literature review

Owing to the lack of evidence from randomized clinical trials (RCTs) on COVID-19, the GDG agreed that evidence from observational studies could also be considered. The guidelines use the following sources of evidence: published guidelines, direct and indirect clinical evidence, clinical firsthand data, and TCM expert experience and consensus. Indirect evidence refers to evidence obtained from the treatment of diseases similar to COVID-19, such as influenza, SARS, respiratory diseases, pulmonary diseases, and diseases that may occur during severe cases (e.g., shock, unconsciousness). The MEDLINE (*via* PubMed), Wanfang, China National Knowledge Infrastructure (CNKI), China Biology Medicine (CBM), and VIP databases were searched from their inception to March 1, 2020, and the language was limited to Chinese and English. Google Scholar, the National Health Committee of the People's Republic of China (<http://www.nhc.gov.cn/>), and the State Administration of Traditional Chinese Medicine (<http://www.satcm.gov.cn/>) were also searched. The search terms were "COVID-19" and related terms. In addition, a search was made for indirect evidence using terms such as "SARS," "Severe acute respiratory syndrome," "NCI," "novel coronavirus pneumonia," "MERS," "Middle East respiratory syndrome," "H1N1," and "H7N9." We adjusted the search strategy for different databases and different PICO questions. For each PICO question, we also searched for publications mentioning specific drugs.

Formulation of recommendations

The evidence review group used the GRADE approach to grade the quality of evidence. The evidence quality was categorized as "high," "moderate," "low," or "very low."¹¹ The evidence from RCTs is initially rated as high quality and is then downgraded according to five factors: risk of bias, indirectness, inconsistency, imprecision, and publication bias. The evidence from observational studies is initially rated as low quality and is then downgraded according to the above five factors and upgraded according to three factors: large effect magnitude; dose-response effect; and if the effect of all plausible confounding factors would be to reduce the

effect (where the effect is observed) or suggest a spurious effect (when no effect is observed).¹¹

The GDG formulated the recommendations on the basis of the evidence quality grade, and in consideration of several other factors, such as significant effects in clinical use and safety. The strength of recommendations was rated as "strong" or "weak." Only recommendations on which 70% or more of the experts agreed were proposed.

Recommendations

On the basis of the guidelines, published clinical evidence, clinical firsthand data, and expert agreement, we recommended two TCM formula granules, seven Chinese patent medicines, and eight Chinese medicine injections. Table 1 summarizes the recommendations, their evidence quality level, and their strength. The following text and Supplementary Table 1-17 describe the recommendations for each drug.

Lung cleansing and detoxifying granules. The formula of lung cleansing and detoxifying granules is based on five classic prescriptions in the Treatise on Febrile Diseases. The formula is recommended for all patients with COVID-19 in the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) (abbreviated as Guideline Protocol). Based on previous evidence, the formula has received clinical trial approval from the National Medical Products Administration (supplementary Table 1).

Huashi Baidu granules. The Guideline Protocol recommends Huashi Baidu granules for severe COVID-19 cases. This treatment is formulated and adjusted based on the experience of the national TCM team at Jinyintan Hospital and Fangcang Hospital. Based on previous evidence, the formula has received clinical trial approval from the National Medical Products Administration (supplementary Table 2).

Table 1 Chinese herbal medicine recommendations for COVID-19

No.	Recommendation	Strength of recommendations and quality of evidence
01	Lung cleansing & detoxifying granules could help relieve clinical symptoms such as fever, cough and fatigue and improve lung function, and can be considered to be used in all stages of COVID-19.	1C
02	Huashi Baidu granules could help relieve clinical symptoms and strengthen autoimmunity, and can be considered to be used for severe COVID-19.	1C
03	Shufeng Jiedu capsules (granules) can be considered to be combined with conventional medicine to reduce clinical symptoms such as fever and cough, improve lung function.	2C
04	Lianhua Qingwen capsules (granules) can be used to improve clinical symptoms such as fever, cough and shortness of breath.	2C
05	Suhexiang pills combined with conventional medicine can improve lung function.	2D
06	Huoxiang Zhengqi capsules (pills, water, oral solution) can be considered to relieve clinical symptoms such as fever, nasal congestion, runny nose and diarrhea.	2C
07	Fangfeng Tongsheng pills (granules) in combination with other drugs can be used to relieve clinical symptoms such as fever and fatigue.	2C
08	Low-dose Jinhua Qinggan granules can be considered to relieve clinical symptoms such as fever.	2C
09	Qiangli Pipa Lu alone or in combination with other drugs can be used to help improve clinical symptoms.	2D
10	Shengmai injection combined with conventional medicine can be considered to improve lung function, respiratory status and inflammation levels, and can be used when dialysis hypotension or septic shock occurs.	2C
11	Xuebijing injection can be used to relieve respiratory distress, improve lung function, reduce lung inflammation, and treat septic shock.	1C
12	Reduning injection combined with conventional medicine can be used to improve clinical symptoms and signs such as fever, cough and lung rales, and improve the level of lung inflammation.	2C
13	Xingnaojing injection can be considered in combination with other drugs to improve respiratory tract infections, high fever convulsions, respiratory failure and other symptoms, and can also be used for patients with consciousness disturbance and stroke.	2C
14	Xiyanping injection can help improve symptoms such as fever, cough and lung rales.	2C
15	Shenfu injection in combination with conventional medicine can be used to relieve symptoms such as cough, fever and lung rales, and improve the level of inflammatory factors, and shorten the time of mechanical ventilation and hospitalization.	2C
16	Shenmai injection in combination with conventional medicine can relieve symptoms such as fever, cough, wheezing and lung rales, and improve lung function.	2C
17	Tanreqing injection combined with conventional medicine can be used to improve clinical symptoms.	2C
18	Lung cleansing & detoxifying granules can be used to all levels of COVID-19; Huashi Baidu granules is suggested to be used to severe and critical cases of COVID-19; Chinese patent medicines can be used for mild and moderate cases of COVID-19 except Suhexiang pills which should be used for severe and critical cases; all Chinese herbal injections should be used for severe and critical cases, but not for mild and moderate cases.	

Notes: A, B, C, D represent high, moderate, low, very low evidence quality, respectively; 1 and 2 represent strong recommendation and weak recommendation, respectively.

Shufeng Jiedu capsule (granules). The Guideline Protocol recommends Shufeng Jiedu capsule (granules) for people with fatigue and fever during the medical observation period. They are also recommended by the Shanghai diagnosis and treatment program. Two studies have shown that Shufeng Jiedu capsule combined with abidor tablets was better at relieving symptoms, shortening nucleic acid negative conversion time, reducing inflammation, and improving the results of chest radiograph than Abidor alone in patients with COVID-19. Systematic reviews (SRs) and RCTs have also demonstrated the effects of Shufeng Jiedu capsules on diseases such as acute exacerbation of chronic obstructive pulmonary disease and acute upper respiratory tract infection in children, which provides indirect evidence to support its use in treating COVID-19 (supplementary Table 3).

Lianhua Qingwen capsule (granules). The Guideline Protocol recommends Lianhua Qingwen capsule (granules) for patients with fatigue and fever during the medical observation period. They can be used for fever, cough, and fatigue in patients with mild and moderate COVID-19. One SR of four studies showed that Lianhua Qingwen capsule combined with conventional medicine was associated with higher effective rate and shorter relief time for symptoms such as fever, cough, fatigue, loss of appetite, chest tightness, and expectoration in patients with COVID-19, with no serious adverse events. Some SRs and RCTs have also shown that Lianhua Qingwen capsule is effective for diseases such as influenza and pneumonia, which provides indirect evidence to support its use in treating COVID-19 (supplementary Table 4).

Suhexiang pill. The Guideline Protocol recommends Suhexiang pill for critical cases of COVID-19 with a symptom pattern of inner blockage causing collapse (manifested as dyspnea, asthma, or the need for mechanical ventilation; fainting, irritability, cold sweat; and dark purple tongue, thick or dry moss, and large floating pulse without root). It is recommended to use Suhexiang pill or Angong Niu Huang pill together with 15 g Renshen (*Radix Ginseng*), 10 g Fuzi (*Radix Aconiti Lateralis Preparata*) (decocted first), and 15 g Shanzhuyu (*Fructus Corni*). One RCT showed that Suhexiang pill combined with conventional medicine was better than conventional medicine alone in reducing lung rales, improving chest radiograph, and improving arterial oxygen partial pressure/oxygen concentration fraction recovery time (supplementary Table 5).

Huoxiang Zhengqi capsule (pills, liquid, or oral solution). The Guideline Protocol recommends Huoxiang Zhengqi capsule (pills, liquid, or oral solution) for patients with symptoms of fatigue and gastrointestinal discomfort during medical observation. SRs and RCTs have shown that Huoxiang Zhengqi prescription is effective for influenza, gastrointestinal cold, and acute gastroenteritis, which provides indirect evidence to sup-

port its use to treat COVID-19 (pills, liquid, or oral solution) (supplementary Table 6).

Fangfeng Tongsheng pill (granules). Fangfeng Tongsheng pill (granules) is recommended in the Diagnosis and Treatment Program of Shanxi, Shanghai, Hebei, Ningxia Hui Autonomous Region, Gansu, and Liaoning provinces for patients with fatigue and fever during the medical observation period. RCTs have shown that Fangfeng Tongsheng pill (granules) are effective for hospital-acquired pneumonia in older people, upper respiratory tract infections, and acute suppurative tonsillitis in children, and show that Fangfeng Tongsheng pill (granules) can shorten disease duration and reduce the incidence of adverse reactions. This provides indirect evidence to support its use in treating COVID-19 (supplementary Table 7).

Jinhua Qinggan granules. The Guideline Protocol recommends Jinhua Qinggan granules for people with fatigue and fever during the medical observation period. They can be used for fever, cough, and fatigue in patients with mild and moderate COVID-19. We found no direct research evidence for the use of Jinhua Qinggan granules to treat COVID-19. Some RCTs show that Jinhua Qinggan granules are effective for influenza, which provides indirect evidence to support their use for COVID-19. One of these studies showed that Jinhua Qinggan formula reduced the median fever time in patients with H1N1 influenza (supplementary Table 8).

Qiangli Pipa Lu. Qiangli Pipa Lu is recommended based on TCM expert consensus. We found no direct research evidence on the use of Qiangli Pipa Lu to treat COVID-19. However, RCTs show that Qiangli Pipa Lu is effective for relieving the symptoms of mycoplasma pneumonia and colds (Supplementary Table 9).

Shengmai injection. The Guideline Protocol recommends Shengmai injection for critical cases of COVID-19 with a symptom pattern of inner blockage causing collapse. It is also recommended in the Diagnosis and Treatment Program of Shanghai, Heilongjiang, Jiangxi, Liaoning, Ningxia Hui Autonomous Region, Beijing, and Yunnan provinces. Some SRs on Shengmai injection for the treatment of lung diseases such as chronic obstructive pulmonary disease and small cell lung cancer indicate that it improves lung function and respiratory status, and reduces inflammation. Some SRs also indicate that Shengmai injection is effective for septic shock and dialysis hypotension, which provides indirect evidence to support its treatment of some complications in critical cases of COVID-19 (supplementary Table 10).

Xuebijing injection. The Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) recommends Xuebijing injection for severe cases of COVID-19 with a symptom pattern of flaring heat in qifen and yingfen syndromes (manifested as hot fever, thirst, shortness of breath, blurred vision, spotted rash,

vomiting blood, bleeding, or limb convulsions; little or no moss on the tongue ridges; and either a fine, sinking pulse or a large, floating, rapid pulse), as well as for critical cases of COVID-19 with a symptom pattern of inner blockage causing collapse. It can be used for systemic inflammatory response syndrome or/and multiple organ failure. For severe and critical cases, 250 mL of 0.9% sodium chloride injection and 100 mL of Xuebijing injection are recommended when systemic inflammatory response syndrome and/or multiple organ failure occurs. A non-randomized controlled study showed that Xuebijing injection combined with conventional antiviral therapy can substantially improve the absorption of lung lesions on computerized tomography scan in patients with COVID-19, with no serious adverse events. SRs and RCTs indicate that Xuebijing injection is effective for acute respiratory distress syndrome, lung injury, and pneumonia, which suggest its effectiveness in relieving respiratory distress, improving lung function, and reducing lung inflammation. Some SRs also found an effect of Xuebijing injection on sepsis, which provides indirect evidence to support its treatment of potential complications in patients with COVID-19 (supplementary Table 11).

Reduning injection. The Guideline Protocol recommends Reduning injection for severe cases with a symptom pattern of flaring heat in qifen and yingfen syndromes, as well as for critical cases with a symptom pattern of inner blockage causing collapse. The suggested dose is 250 mL of Reduning injection plus 250 mL of 0.9% sodium chloride injection for severe and critical cases with viral infection or combined mild bacterial infection. The Diagnosis and Treatment Plan of Shanghai, Heilongjiang, and Liaoning provinces also recommends Reduning injection. SRs have shown that Reduning injection is effective for acute pneumonia, acute upper respiratory tract infection, mycoplasma pneumonia in children, viral pneumonia, and bronchiolitis in children by improving clinical symptoms and signs and reducing lung inflammation. This provides indirect evidence to support its use in treating COVID-19 (supplementary Table 12).

Xingnaojing injection. The Guideline Protocol recommends Xingnaojing injection for severe cases of COVID-19 with a symptom pattern of flaring heat in qifen and yingfen syndromes, as well as for critical cases with a symptom pattern of inner blockage causing collapse. For severe and critical cases with high fever and unconsciousness, 250 mL b.i.d. (i.e., twice daily) of 0.9% sodium chloride injection plus 20 mL of Xingnaojing injection is recommended. SRs and RCTs suggest that Xingnaojing injection has an effect on upper respiratory tract infection with fever, acute upper respiratory tract infection, chronic obstructive pulmonary disease with respiratory failure, unconsciousness, and stroke, which provides indirect evidence to support its use in treating COVID-19 (supplementary Table 13).

Xiyanping injection. The Guideline Protocol recommends Xiyanping injection for severe cases of COVID-19 with a symptom pattern of flaring heat in qifen and yingfen syndromes. For severe and critical cases with viral infection or combined mild bacterial infection, 250 mL of 0.9% sodium chloride injection plus 4 mL (100 mg) bid of Xiyanping injection is recommended. There is no direct research evidence for the use of Xiyanping injection to treat COVID-19. However, there is evidence from SRs and RCTs that Xiyanping injection can treat childhood viral pneumonia, community-acquired pneumonia, and mycoplasma pneumonia by improving the clinical symptoms of fever and cough. This provides indirect evidence to support its use in treating COVID-19 (supplementary Table 14).

Shenfu injection. The Guideline Protocol recommends Shenfu injection for critical cases of COVID-19 with a symptom pattern of inner blockage causing collapse. For severe and critical cases, when shock occurs, 100 mL b.i.d. of Shenfu injection plus 250 mL of 0.9% sodium chloride injection is recommended. There is no direct research evidence for the effectiveness of Shenfu injection on COVID-19. Some SRs and RCTs show that Shenfu injection has an effect on respiratory distress/respiratory failure, chronic obstructive pulmonary disease, severe pneumonia in the older people, mycoplasma pneumonia in children, septic shock/shock, and heart problems by relieving cough and asthma, fever, lung rales, and other related clinical symptoms; reducing inflammation; and shortening the duration of mechanical ventilation use and hospitalization. This provides indirect evidence to support its use in treating COVID-19 (supplementary Table 15).

Shenmai injection. The Guideline Protocol recommends Shenmai injection for critical cases of COVID-19 with a symptom pattern of inner blockage causing collapse. For severe and critical cases, if immunosuppression occurs, 250 mL of glucose injection plus 100 mL of Shenmai injection is recommended. The Shanghai Traditional Chinese Medicine Diagnosis and Treatment Protocol also recommends this Chinese patent medicine.¹⁴ SRs and RCTs have shown that Shenmai injection is effective for chronic obstructive pulmonary disease, severe pneumonia, lower respiratory tract infections, and tuberculous pleurisy by relieving cough, fever, lung rales, and other clinical symptoms. This provides indirect evidence to support its use in treating COVID-19 (supplementary Table 16).

Tanreqing injection. The Guideline Protocol recommends Tanreqing injection for severe cases of COVID-19 with a symptom pattern of flaring heat in qifen and yingfen syndromes, as well as for critical cases with a symptom pattern of inner blockage causing collapse. For severe and critical cases, the recommended dose is 40 mL b.i.d. of Tanreqing injection plus 250 mL of 0.9% sodium chloride injection if viral infection or

combined mild bacterial infection occurs. Some SRs suggested that Tanreqing injection has an effect on community-acquired pneumonia, influenza A, acute respiratory distress syndrome, acute bronchitis, and upper respiratory tract infections in children, which provides indirect evidence to support its use in treating COVID-19 (supplementary Table 17).

DISCUSSION

Although the number of published papers on COVID-19 has increased, many questions remain and available treatment options are limited.¹² Practitioners in China have much experience in using integrative medicine to prevent and treat COVID-19. It is therefore important to draw on this experience and summarize the evidence for the effectiveness of TCM for treating COVID-19 and similar lung and epidemic diseases.

This research followed the WHO rapid guideline process to develop guidelines on TCM for COVID-19. This shortened the guideline development process without reducing the quality of the guidelines. The experience of several authors of the present paper in rapid guideline development ensured the methodological quality of these guidelines.¹³ The present research established a body of evidence comprising published guidelines, clinical firsthand data, and expert experience to support the recommendations of two Chinese prescription granules, seven oral Chinese patent medicines, and eight Chinese herbal injections for COVID-19.

As the literature search was conducted on March 1, 2020, any subsequent versions of these guidelines require an up-to-date literature review. We hope that the evidence summary in these guidelines will be helpful in global efforts to address COVID-19.

Electronic Supplementary Material: supplementary materials (appendixes) are available in the online version of this article at <http://www.journaltcm.com>

REFERENCES

- 1 World Health Organization. COVID-19 Weekly Epidemiological Update, 2020-10-18, cited 2020-10-28. Available from URL: https://www.who.int/docs/default-source/coronavirus/situation-reports/20201020-weekly-epi-update-10.pdf?sfvrsn=58786643_26&download=true.
- 2 National Administration of Traditional Chinese Medicine. Diagnosis and treatment protocol for novel coronavirus pneumonia (Trial Version 6), 2020-02-18, cited 2020-02-22. Available from URL: http://www.satcm.gov.cn/d/file/p/2020/02-19_af5165ab83bc961eb8c20f883c4dd594.pdf#b218cfeb1bc54639af227f922bf6b817.pdf#3.05%20MB.
- 3 Wang DW, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323(11): 1061-1069.
- 4 Huang CL, Wang YM, Li XW, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395(10223): 497-506.
- 5 Liu Kui, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J* 2020; 133(9): 1025-1031.
- 6 Chen NS, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395(10223): 507-513.
- 7 Fan YP, Zhang HM, Wang YP, Lü C, Wang YY. A brief analysis of the classification of Traditional Chinese Medicine disease attributes of new coronavirus pneumonia. *Zhong Yi Za Zhi* 2020; 61(11): 921-927.
- 8 Shu J, Yang HW. Exploration and application of TCM in the public health emergencies. *Xi Bu Zhong Yi Yao* 2013; 26(1): 59-61.
- 9 Gao SM, Ma Y, Yang FW, Zhang JH, Yu CQ, Zhang BL. Zhang BL: Traditional Chinese Medicine plays a role in the prevention and treatment on novel coronavirus pneumonia. *Tianjin Zhong Yi Yao* 2020; 37(2): 121-124.
- 10 World Health Organization. WHO handbook for guideline development. 2nd Ed. Geneva Switzerland: WHO Press, 2014: 133-156.
- 11 Canfield SE, Dahm P. Rating the quality of evidence and the strength of recommendations using GRADE. *World J Urol* 2011; 29(3): 311-317.
- 12 Wolkewitz M, Puljak L. Methodological challenges of analysing COVID-19 data during the pandemic. *BMC Med Res Methodol* 2020; 20: 81.
- 13 Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res* 2020; 7(1): 4.