

Clinical practice guidelines and experts' consensuses of traditional Chinese herbal medicine for novel coronavirus (COVID-19): protocol of a systematic review

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Protocol

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Abstract

Background: The World Health Organization declared on 11 March 2020 that the spread of the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) has escalated from epidemic into pandemic. As the initial outbreak area, China has taken multiple active measures to deal with the epidemic. Updated versions of diagnosis and treatment guideline for novel coronavirus (COVID-19) patients have been issued, and traditional Chinese herbal medicine has been recommended as a treatment. The objective of this study will be to summarize the recommendations in current clinical practice guidelines about the use of traditional Chinese herbal medicine for COVID-19 patients. We will also evaluate and report on the methodological and reporting quality of these guidelines.

Methods: In this systematic review, we will search for guidelines, expert consensuses and policy documents published since December 2019 in electronic databases (e.g. PubMed, EMBASE, and Chinese databases) and on websites of governments or organizations (e.g. The National Guideline Clearinghouse [NGC], Guidelines International Network [GIN], National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network [SIGN] and WHO). Eligible documents will be independently selected, and relevant data will be independently extracted by two reviewers. We will also independently evaluate the methodological quality and reporting quality of the included guidelines, using the Appraisal of Guidelines for REsearch & Evaluation (AGREE) II tool and Reporting Items for Practice Guidelines in healthcare (RIGHT) statement, respectively. Any discrepancies will be discussed and resolved through discussion among the reviewers. We will use the extracted information to summarize their recommendations for traditional Chinese herbal formulae and Chinese patent medicine for COVID-19 patients, and to summarize the strength and quality of these recommendations with reference to the results of AGREE II and RIGHT tools.

Discussion: This review will summarize the recommendations in current clinical practice guidelines and provide insight into the implementation strategies for traditional Chinese herbal medicine in COVID-19 patients.

Systematic review registration: PROSPERO registration number: CRD42020179205

Introduction

Novel coronavirus (COVID-19) pneumonia, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in Wuhan, China in late December 2019[1]. COVID-19 patients mainly present with flu-like symptoms (such as fever, cough and dyspnoea) and some other systemic symptoms (such as malaise, fatigue, and diarrhea)[2, 3]. With a range of 1 to 14 days for the estimated incubation period and various severity of clinical symptoms[4, 5], human-to-human transmission of infectious disease has rapidly spread across the globe. The World Health Organization (WHO) declared a pandemic

on 11 March 2020[6]. As of 30 April 2020, COVID-19 patients have been diagnosed in more than 200 countries, areas or territories with more than 2 million confirmed cases[7].

As the initial outbreak area, China has taken multiple active measures to deal with COVID-19. The National Health Commission of China established the first version of the Diagnosis and Treatment Guideline of Pneumonia Caused by Novel Coronavirus on 16 January 2020. This contained the etiology of COVID-19, clinical characteristics of patients, diagnosis and treatments of this disease. As more information became available, updated versions of this diagnosis and treatment guideline were issued. Since the third version of National COVID-19 Diagnosis and Treatment Guideline, traditional Chinese herbal medicine has been recommended as a treatment for COVID-19, based on different stages and syndrome differentiations of disease[8].

Traditional Chinese herbal medicine has played an important role in thousand-of-years' combat between Chinese doctors and pandemic and endemic diseases. During the outbreak of severe acute respiratory syndrome (SARS) coronavirus in the late 2002 in Guangdong, China, traditional Chinese herbal medicine showed beneficial effects such as relief of symptoms, decrease of mortality, and control of infection in patients with SARS[9-12]. With accumulated experiences of its anti-viral properties for the treatment of SARS and strong encouragement from the Chinese government[13, 14], traditional Chinese herbal medicine has also been applied in treating COVID-19. The State Council Information Office of China reported on 23 March 2020 that 74,187 COVID-19 patients (91.5% of total confirmed COVID-19 cases in China) had been treated with traditional Chinese herbal medicine with promising outcomes[15].

Along with the guideline issued by the National Health Commission of China, provinces, cities, and autonomous regions have also released clinical practice guidelines recommending traditional Chinese herbal medicine. The syndrome differentiations, treating principles and recommended formulae may differ across these guidelines, because of the different characteristics of their respective regions and population. The objective of this systematic review is to summarize the recommendations in current clinical practice guidelines about the use of traditional Chinese herbal medicine for COVID-19 patients. We will also evaluate and report on the methodological and reporting quality of these guidelines.

Method

Study registration

This systematic review is registered in the Prospective Register of Systematic Review (PROSPERO) database (CRD42020179205). We formulated this protocol in accordance with the Preferred Reporting Item for Systematic Review and Meta-analysis - Protocol (PRISMA-P) statement[16] (Additional file 1).

Eligibility criteria

Inclusion criteria

Study design

We will include clinical practice guidelines, consensus statements and guidance documents published by any advising body or healthcare organization since December 2019, which provide information on the use of traditional Chinese herbal medicine therapy for COVID-19 patients.

Participants

Recommendations for patients diagnosed with COVID-19 pneumonia with recognized diagnostic criteria will be included (such as positive real-time fluorescent Reverse Transcription-Polymerase Chain Reaction of respiratory or blood samples for new coronavirus nucleic acid, highly homologous of the respiratory specimen or blood specimen sequenced to novel coronavirus). There will be no restrictions with respect to age, gender or ethnicity.

Intervention

We will include recommendations for Chinese herbal medicine involving extracts from herbs, single or mixture herbal formulas, and Chinese patent medicine, regardless of their forms (e.g. pill, powder, oral liquid etc.).

Exclusion criteria

We will exclude old versions of guidelines or consensus statements published by a single advising body or healthcare organization.

Databases and search strategy

We will search for guidelines, expert consensus and policy documents published since December 2019 in the following electronic databases: PubMed, Embase, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chinese Science and Technology Periodical Database (VIP), and Wanfang database (Wanfang Data). We will also search other sources of guidelines including: The National Guideline Clearinghouse (NGC), Guidelines International Network (GIN), National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) and WHO. We will use search strategies that combine terms relating to novel coronavirus, traditional Chinese medicine and guideline. The search strategy for PubMed is described in Additional file 2, and suitably modified search strategies will be applied to the other electronic databases. We will also search grey literature via websites of governments or organizations. No language restrictions will be applied.

Study selection

We will upload search results into EndNote X9 reference management software. We will filter and remove duplicate references. Two independent reviewers (YXL and DLZ) will screen titles and abstracts to identify potentially eligible documents, which will be retrieved in full text for final review. Any disagreements will be discussed and arbitrated by a third reviewer (YGZ).

Data extraction

We will design a data extraction form based on characteristics of included guidelines and consensus. In order to achieve consistency (at least 80%) in extracted items, we will pilot test the data extraction form with data extractors using a sample of eligible documents. Results of this pilot extraction will be discussed among review authors and extractors before finalizing it. Data extraction will be conducted independently by two reviewers (JL and YZ), and will include the following data: (1) characteristics of guidelines: name, type, source and date; (2) stage of disease; (3) syndrome differentiation; (4) treatment principle; (5) recommended formula; and (6) recommended Chinese patent medicine etc. Disagreements will be resolved by discussion among the review team.

Quality assessment

We will evaluate the methodological quality and reporting quality of the included guidelines using the Appraisal of Guidelines for REsearch & Evaluation (AGREE) II tool and Reporting Items for Practice Guidelines in healthcare (RIGHT) statement, respectively. In order to achieve consistency of at least 80% in the quality assessments, the assessors will pre-assess a sample of eligible documents and discuss their assessment among review authors and assessors. After that, two independent reviewers (YXL and JL) will appraise the quality of included guidelines. Discrepancies will be discussed and resolved among the reviewers.

Data synthesis

With the information extracted from the included guidelines, we will summarize the recommendations made for traditional Chinese herbal formulae and Chinese patent medicine for COVID-19 patients. The recommendations of prescriptions for different stages and syndrome differentiations of COVID-19 will also be summarized. These findings will be discussed in light of the strength and quality of these recommendations with reference to the results of AGREE II and RIGHT tools.

Discussion

This will be the first systematic review that we are aware of which will comprehensively gather information from, and appraise the quality of guideline recommendations for traditional Chinese herbal medicine for COVID-19 patients. Other reviews have either examined the application of traditional Chinese

herbal medicine for COVID-19 patients [17-20] or investigated current management for COVID-19 patients [21]. Examples of other studies, include Ho and colleagues' work on the case definition, clinical classifications, and relevant treatments of COVID-19 patients, in accordance to recommendations of the 7th edition of the National COVID-19 Diagnostic and Treatment Guideline of China[19]. While, Du and colleagues have summarized the theoretical foundation, potential effect of Chinese herbs on COVID-19 patients [17], and Yang and colleagues outlined clinical data for SARS-CoV and compared the evidence of current applications of traditional Chinese herbs in the treatment of COVID-19 patients[18].

In conclusion, given the many guidelines and consensus statements that are now being regularly updated to advise clinical practices on the use of traditional Chinese herbal medicine for COVID-19 patients, this review will provide an important overall summary of their recommendations and provide insight into relevant implementation strategies. This will have relevance outside China because, although traditional Chinese herbal medicine is mainly used in China, our preliminary search has found guidelines containing recommendations of Chinese herbs for COVID-19 patients from elsewhere.

Abbreviations:

COVID-19: the novel coronavirus; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SARS: severe acute respiratory syndrome; WHO: World Health Organization; PROSPERO: Prospective Register of Systematic Reviews; PRISMA-P: Preferred Reporting Item for Systematic Review and Meta-analysis-Protocol; CBM: Chinese Biomedical Literature Database; CNKI: China National Knowledge Infrastructure; VIP: Chinese Science and Technology Periodical Database; NGC: the National Guideline Clearinghouse; GIN: Guidelines International Network; NICE: National Institute for Health and Clinical Excellence; SIGN: Scottish Intercollegiate Guidelines Network; AGREE: the Appraisal of Guidelines for REsearch & Evaluation; RIGHT: Reporting Items for Practice Guidelines in healthcare.

Declarations

Ethics approval and consent to participate

No ethics approval is required for this systematic review because we will be using information from published documents. Our findings will be published in a peer-reviewed journal according to the PRISMA guidelines.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Mike Clarke, Rongjiang Jin and Yan Guo designed the study. Yuxi Li, Juan Li, Yonggang Zhang, Dongling Zhong and Yue Zhang drafted the manuscript.

All authors approved the manuscript

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References

1. Munster VJ, Koopmans M, van Doremalen N, van Riel D, de Wit E. A Novel Coronavirus Emerging in China - Key Questions for Impact Assessment. *N Engl J Med.* 2020;382(8):692-4.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506.
3. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *Jama.* 2020.
4. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Chinese Journal of Epidemiology.* 2020;41(2):145-51.
5. WHO TEAM Health Emergencies Preparedness and Response. Q&A on coronaviruses (COVID-19) 2020 [updated 17 April 2020. Available from: <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>.

6. WHO Director-General's opening remarks at the media briefing on COVID-19 - 1 April 2020 Geneva: World Health Organization2020 [Available from: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—1-april-2020>].
7. Coronavirus disease (COVID-19) outbreak situation 2020 [updated 22 April 2020. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>].
8. National Health Committee of China. Notice on the issuance of a new coronavirus infection pneumonia diagnosis and treatment plan (trial version 3) 2020 [Available from: <http://www.nhc.gov.cn/yzygj/s7653p/202001/f492c9153ea9437bb587ce2ffcbee1fa.shtml>].
9. Liu DH, Liang BZ, Huang LY. Clinical observation on the preventive effect of kangdubufei decoction on acute severe respiratory syndrome. *Chinese Journal of Integrated Traditional and Western Medicine*. 2004;24(8):685-8.
10. Tong X, Li A, Zhang Z, Duan J, Chen X, Hua C, et al. TCM treatment of infectious atypical pneumonia—a report of 16 cases. *J Tradit Chin Med*. 2004;24(4):266-9.
11. Liu B HL, Liang Z, Tong X, Hu J, Ni Q, Liu X, Jiao Q, Xie Y, Li P. Effect of Chinese herbal medicine on adrenal glucocorticoids in SARS. *China Journal of Chinese Materia Medica*. 2005;30(23):1874–7.
12. He S, Li WS, Luo YJ, Ye CL, Zhang ZY. Qingkailing Injection () for Treatment of Children Pneumonia Induced by Respiratory Syncytial Virus: A Meta-Analysis of Randomized Controlled Trials. *Chin J Integr Med*. 2018;24(4):288-95.
13. National Administration of Traditional Chinese Medicine. The Party Group of the National Administration of Traditional Chinese Medicine conveyed the spirit of the key instructions of general secretary Xi Jinping and the request of Premier Li Keqiang to study the prevention and control of novel coronavirus pneumonia (Chinese). 2020 [Available from: <http://bgs.satcm.gov.cn/gongzuodongtai/2020-01-21/12465.html>].
14. Su QJ, Song C, Lu ZZ, Liu ZW, Xiao J, Wu FS. Impact of Herbal Preparations on Outcomes of Highly Active Antiretroviral Therapy: A One-Year Prospective Cohort Study. *Chin J Integr Med*. 2019.
15. The State Council Office held a conference on the important role of Chinese medicine in the prevention and treatment of novel coronavirus pneumonia and effective drugs 2020 [Available from: <http://www.scio.gov.cn/xwfbh/xwfbh/wqfbh/42311/42768/index.htm>].
16. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*. 2015;350:g7647.
17. Du HZ, Hou XY, Miao YH, Huang BS, Liu DH. Traditional Chinese Medicine: an effective treatment for 2019 novel coronavirus pneumonia (NCP). *Chin J Nat Med*. 2020;18(3):206-10.
18. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese Medicine in the Treatment of Patients Infected with 2019-New Coronavirus (SARS-CoV-2): A Review and Perspective. *Int J Biol Sci*. 2020;16(10):1708-17.
19. Ho LTF, Chan KKH, Chung VCH, Leung TH. Highlights of traditional Chinese medicine frontline expert advice in the China national guideline for COVID-19. *Eur J Integr Med*. 2020:101116.

20. Luo H, Tang QL, Shang YX, Liang SB, Yang M, Robinson N, et al. Can Chinese Medicine Be Used for Prevention of Corona Virus Disease 2019 (COVID-19)? A Review of Historical Classics, Research Evidence and Current Prevention Programs. *Chin J Integr Med.* 2020;26(4):243-50.
21. Nicola M, O'Neill N, Sohrabi C, Khan M, Agha M, Agha R. Evidence Based Management Guideline for the COVID-19 Pandemic - Review article. *Int J Surg.* 2020:1743-9191.

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