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A consensus guideline of herbal medicine for coronavirus disease 2019

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ABSTRACT

Background: The Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2), which originated in Wuhan, Hubei Province, China in late December 2019, is the cause of ongoing pandemic. We analyzed the symptoms of SARS-CoV-2, a classification of the Chinese medicine dialectic and treatment regimen, and promptly enacted the recommendation of Korean medicine preparations in herbal medicine covered under domestic medical insurance benefits depending on the circumstances in our country.
Method: The clinical practice guideline (CPG) for the treatment of SARS-CoV-2 was developed based on consensus from a group of experts.
Results: Two kinds of herbal medicines (HM) were recommended for the prevention of SARS-CoV-2; Youngyopaedoc-san plus Bojungikgitang, and Youngyopaedoc-san plus Saengmaek-san. Two herbal preparations were recommended for people with a history of exposure to SARS-CoV-2; Youngyopaedoc-san plus Bulhwangeumjeonggi-san, and Youngyopaedoc-san plus Bojungikgi-tang. Three herbal preparations were recommended for mildly symptomatic COVID-19 patients; Youngyopaedoc-san plus Galgunhaegui-tang was recommended for those without pneumonia with wind-warmth disease invading the lungs; Sosiho-tang plus Bulhwangeumjeonggi-san was recommended for those with dampness-heat disease in the lungs. For the recovery stage, Samchulkunbi-tang plus Saengmaek-san, or Samchulkunbi-tang plus Chungseuiki-tang was recommended.
Conclusion: The CPG was developed to guide the use of Korean herbal medicine in the treatment of SARS-CoV-2, and it is expected that this will be the basis for providing proper treatment of similar infectious diseases in the future.

1. Introduction

The Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2), which originated in Wuhan, Hubei Province, China in late December 2019, is the cause of ongoing pandemic. As of early March 2020, Korea had the world's second highest number of infections, exceeding 5000 people, and the numbers were sharply increasing.[1]

In a situation where more effective symptomatic treatment is required without special treatment, the Chinese government's novel coronavirus pneumonia guideline (7th edition)[2] recommends combining traditional medicine with modern medicine. For its introduction in Korea, we analyzed the symptoms of SARS-CoV-2 infection, a classification of the Chinese medicine dialectic and treatment regimen, and promptly enacted the recommendation of Korean medicine preparations in herbal medicine covered under domestic medical insurance benefits depending on the circumstances in our country.

2. Methods

The expert committee discussed the key syndromes of traditional medicine in SARS-CoV-2 based on the Chinese government guidelines and Korean medicine clinical practice guideline for

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common cold, and then modified these syndromes and herbal medicines according to the Korean environment.

First, a group of 11 experts from the Society of Korean Medical Pulmonary Diseases met and developed a plan on the development of CPG. The clinical question selected was "Can Traditional Korean Medicine (TKM) alleviate symptoms associated with SARS-CoV-2 infection?'. Clinical questions were developed according to the prevention, initial and recovery periods of infection, and recommendations were developed for herbal medicines that can be covered by medical insurance for respiratory diseases in Korea.

2.1. Constitution and processes of the development committee

The CPG was developed by stakeholders (Table 1). All comments were reviewed by the committee.

In addition, we recommended the usage of Qingfeipaidu-tang,[1] which is the standard herbal decoction recommended by the Chinese government, and its substitute herbal preparations for patients with mild symptoms. As there were no clinical trials on the efficacy of Korean herbal preparations for SARS-CoV-2 infection, we could not assess the quality of evidence of studies, and all recommendations were based on generative process planning (GPP) by experts in traditional medicine used on the pulmonary system. However, we identified local upper respiratory infection guidelines in Korean medicine,[3] such that indirect evidence of herbal preparations on respiratory symptoms of SARS-CoV-2 was included in this guideline.

2.2. Clinical questions

This guideline is applicable to the following groups of patients: 1. those who are waiting for the polymerase chain reaction (PCR) results of their respiratory specimen; 2. those who have mild symptoms with a diagnosis of SARS-CoV-2 without pneumonia in radiologic tests; and 3. those who are in the recovery stage after showing two consecutively negative PCR results, with both tests conducted more than 24 h apart.

2.3. Consensus for recommendations

Generally, the grade of a recommendation is rated from A to C. However, in the guidelines developed here, we used a 4-point grading system called the good practical point (GPP). The recommendations were drafted by a working group that developed the clinical practice guideline (CPG). Agreement over the final recommendations was achieved using the recommendation grades. The Delphi method was used for the consensus processes of selecting recommendations and confirming both evidence levels and recommendation grades. The survey was conducted using online survey program (https://office.naver.com/). The working group members discussed and revised these issues through several meetings and e-mails.

2.4. Internal and external scrutiny and approval

First, the feedback received from the Report Approval Panel was addressed by the authors in the working group. Second, the Society of Korean Medical Pulmonary Disease circulated the draft guidelines (with modified recommendations, as noted in the internal review) to external participants for review and feedback. In addition, the monitoring committee reviewed and approved the recommendations.

3. Results

3.1. Herbal medicine for SARS-CoV-2

Recommendations on treatment strategies were developed for people in need of prevention, people with a history of exposure to the virus, patients with mild symptoms, and patients in the recovery stage (Table 2). Two kinds of herbal medicines (HM) were recommended for the prevention of SARS-CoV-2; Youngyopaedoc-san plus Bojungikgitang, and Youngyopaedoc-san plus Saengmaek-san. Further, two herbal preparations were recommended for people with a history of exposure to SARS-CoV-2; Youngyopaedoc-san plus Bulhwangeumjeonggi-san, and Youngyopaedoc-san plus Bojungikgi-tang. Three herbal preparations were recommended for mildly symptomatic COVID-19

Table 1
List of clinical practice guidelines developers of SARS-CoV-2.

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13	Youngho Moon	Division of Pulmonary System, Department of Korean Medicine, Dongshin University, Naju, Republic of Korea

Table 2
Recommendations of herbal prescription for prevention and treatment for COVID-19 patients by consensus.

Recommendations of herbal prescription for COVID-19 patients[a]	Herbal preparation
Prevention	
Respiratory health of adults in the COVID-19 epidemic. – Clinical consideration: For high-risk adults with the possibility of close contact with a patient, Youngyopaedoc-san + Bojungikgitang is suitable for qi deficiency and Youngyopaedoc-san + Saengmaek-san for fluid–humor deficiency as preventive interventions.	Youngyopaedoc-san + Bojungikgitang (Lianqiao baidu san + Buzhong Yiqi Tang) or Youngyopaedoc-san + Saengmaek-san (Lianqiao baidu san + Shengmai Yin)
Treatment Herbal preparations for people who contacted patient(s) with COVID-19	
Asymptomatic adults who came in close contact with patient(s) with COVID-19 – Clinical consideration: Consider Youngyopaedoc-san + Bulhwangeumjeonggi-san (Lianqiao baidu san + Buhuan Zhengqi San) for asymptomatic, self-isolated adults who came in close contact with patients with COVID-19 and alternatively Youngyopaedoc-san + Bojungikgi-tang (Lianqiao baidu san + Buzhong Yiqi Tang) for the high-risk group (the old and infirm).	Youngyopaedoc-san + Bulhwangeumjeonggi-san (Lianqiao baidu san + Buhuanjin Zhengqi San) or Youngyopaedoc-san + Bojungikgi-tang (Lianqiao baidu san + Buzhong Yiqi Tang)
Mild symptomatic patients with COVID-19 and wind-warmth disease invading the lungs. – Clinical consideration: Only if there are symptoms of external contraction and respiratory dysfunction due to wind-warmth disease, such as chills with fever, mild chills, weakness, heaviness of head and body, muscle pain, dry cough with thick sputum, sore throat, dry mouth with anorexia, excess thirst, anhidrosis or hypohidrosis.	Youngyopaedoc-san + Galgunhaegui-tang (Lianqiao baidu san + Gegen Jieji Tang)
Mild symptomatic patients with COVID-19 and cold-dampness disease depressing the lungs. – Clinical consideration: Only if there are symptoms of external contraction due to cold and dampness, respiratory symptoms, including fever, weakness, body aches, cough, sputum, chest tightness, and choke, digestive symptoms, including anorexia, nausea, vomiting and sticky stool with discomfort.	Galgunhaegui-tang + Bulhwangeumjeonggi-san (Gegen Jieji Tang + Buhuanjin Zhengqi San)
Mild symptomatic patients with COVID-19 and dampness-heat disease in the lungs. – Clinical consideration: Only if there are symptoms of external contraction due to heat and dampness, respiratory symptoms, including mild or no fever, mild chills, weakness, heaviness of head and body, muscle ache, dry cough with thick sputum, sore throat, dry mouth with anorexia, excess thirst, anhidrosis or hypohidrosis, digestive symptoms, including oppression in the chest and gastric stuffiness or nausea with anorexia and loose stool or sticky stool with discomfort.	Sosiho-tang + Bulhwangeumjeonggi-san (Xiao Chaihu Tang + Buhuanjin Zhengqi San)
Recovery stage	
Patients with COVID-19 in the recovery stage. – Clinical consideration: Recovery means two consecutive sets of negative test results, performed more than 24 h apart.	Samchulkunbi-tang + Saengmaek-san (Shen Zhu Jianpi Tang + Shengmai Yin) or Samchulkunbi-tang + Chungseuiki-tang (Shen Zhu Jianpi Tang + Qingshu Yiqi Tang)
Chungpaebaedoc-tang (Qingfeipaidu-Tang) and its replacement medicines: Consider the use of for symptom improvement in adults with COVID-19. – Clinical consideration: Consider the severity of symptoms of external contraction and respiratory dysfunctions induced by heat as well as digestive symptoms due to dampness: Symptom comparison between Korean patients and Chinese patients is required. ◦ If there are no digestive symptoms due to dampness, caution for adverse reactions due to dryness is required. ◦ If heat sense becomes severe, focus on the herbal composition of Mahaenggamseok-tang (Ma Xing Gan Shi Tang) and Sosiho-tang (Xiao Chaihu Tang); To resolve cough, focus on the herbal composition of Saganmahwang-tang (Shegan ma huangtang); If digestive symptoms are present, including stool problems, focus on the herbal composition of Oryeong-san (Wu lin San) and Gwakhyangjeonggi-san (Huoxiang Zhengqi San).	Chungpaebaedoc-tang (Qingfeipaidu-Tang)
Adults with COVID-19 (replacement medicine of Chungpaebaedoc-tang (Qingfeipaidu-tang))	Galgunhaegui-tang (Gegen Jieji Tang), Sosiho-tang (Xiao Chaihu Tang), and Bulhwangeumjeonggi-san (Buhuanjin Zhengqi San)

COVID-19, coronavirus disease 2019.
[a] Recommendation level is good practice point.

patients; Youngyopaedoc-san plus Galgunhaegui-tang was recommended for those without pneumonia with wind-warmth disease invading the lungs; Sosiho-tang plus Bulhwangeumjeonggi-san was recommended for those with dampness-heat disease in the lungs. For the recovery stage, Samchulkunbi-tang plus Saengmaek-san, or Samchulkunbi-tang plus Chungseuiki-tang was recommended. All levels of recommendations were GPP. The details of the formula compositions of each herbal medicine were listed in supplement 1.

3.2. Consensus for recommendations

A total of 11 experts participated in the rapid Delphi process. All experts were affiliated with the Society of Korean Medical Pulmonary Disease working at Korean medicine hospitals (supplement 2). Delphi consensus was made by single round survey as follows (supplement 3).

4. Discussion

SARS-CoV-2 is easily transmissible, and has resulted in large numbers of infected people worldwide, with many mortalities.[4] Currently, there is no cure for, or vaccine against SARS-CoV-2.[5,6] Therefore, the impact of COVID-19 is expected to be long lasting. HM has been practiced since ancient times for the treatment of respiratory diseases and infectious diseases, and its effectiveness has been proven by various studies.[7] The researchers have recommended symptom-based HM for effective treatment of the coronavirus related diseases. However, until now, there have been no firm evidence on the use of HM for the treatment of COVID-19 infections. Considering the urgency of the COVID-19 pandemic, these treatment guidelines have been developed based on existing clinical practice guidelines. As the guideline is for patients from Republic of Korea, and COVID-19 pandemic should be in the realm of the system of public health, all recommended HMs, except Chungpaebaedoc-tang (Qingfeipaidu-Tang), are covered by the national insurance system of the Republic of Korea. Chungpaebaedoc-tang (Qingfeipaidu-Tang) has been recommended as the main HM by the National Health Commission of People's Republic of China.[2] Although this HM is not covered by the national insurance system of the Republic of Korea, the guideline committee decided to provide its clinical experiences to COVID-19 treatment[8] as well as the plausible pharmacological mechanism[9] and therefore rec-

ommended its use in the clinical practice in the Republic of Korea.

The limitations of these CPGs are as follows. First, the amount of clinical evidence supporting the use of traditional HM for COVID-19 is limited. Second, since this protocol was developed based partially on the guideline for the common cold, it was not possible to suggest a treatment strategy for severe COVID-19.

This is the first Korean Medicine expert consensus guideline on infectious respiratory disease in the Republic of Korea. However, more basic and clinical research is required to produce evidence on the use of traditional medicine for the treatment of viral respiratory diseases, which should then be incorporated in the revised CPG.

Authors contributions

Beom-Joon Lee: Conceptualization, Methodology, Writing - original draft. Ju Ah Lee: Conceptualization, Methodology, Writing - original draft. Kwan-Il Kim: Conceptualization. Jun-Yong Choi: Conceptualization, Project administration, Supervision, Writing - review & editing. Hee-Jae Jung: Conceptualization, Project administration, Supervision, Writing - review & editing.

Conflicts of interest

The authors have no conflict of interest.

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Ethical statement

This article does not contain any research on human or animal subjects performed by any of the authors.

Data availability

The data related to this study are available within this article as Table 1, Table 2, Supplement 1, Supplement 2 and Supplement 3 Other data are not openly available.

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Appendix A. Supplementary material

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.imr.2020.100470.

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