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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 Bojungikigitang, 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 Bojungikigi-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; Sosihoeum-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.

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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) 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
common cold, and then modified these symptoms 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,2 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 Bojungkigitang, 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 Bulhwangumjeonggii-san, and Youngyopaedoc-san plus Bojungkigii-tang. Three herbal preparations were recommended for mildly symptomatic COVID-19

### Table 1

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

| Recommendations of herbal prescription for COVID-19 patients* | Herbal preparation |
|---------------------------------------------------------------|-------------------|
| Prevention<br>Respiratory health of adults in the COVID-19 epidemic.<br>- Youngyopaedoc-san + Bojungikgitang is suitable for qi deficiency patients; and<br>Youngyopaedoc-san + Saengmaek-san for fluid–humor deficiency as preventive interventions. | Youngyopaedoc-san + Bojungikgitang (Lianqiao baidu san + Buzhong Yiqi Tang) or<br>Youngyopaedoc-san + Saengmaek-san (Lianqiao baidu san + Shengmai Yin) |
| Treatment<br>Herbal preparations for people who contacted patient(s) with COVID-19<br>Asymptomatic adults who came in close contact with patient(s) with COVID-19<br>- Clinical consideration: Consider Youngyopaedoc-san + Bulhwangumjeonngi-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).<br>Mild symptomatic patients with COVID-19 and wind–warmth disease invading the lungs.<br>- 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 + Bulhwangemumjeonngi-san (Lianqiao baidu san + Buhuan Zhensing San) or<br>Youngyopaedoc-san + Bojungikgi-tang (Lianqiao baidu san + Buzhong Yiqi Tang) |
| Mild symptomatic patients with COVID-19 and cold–dampness disease depressing the lungs.<br>- 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 chokes, digestive symptoms, including anorexia, nausea, vomiting and sticky stool with discomfort. | Youngyopaedoc-san + Calgunhaegui-tang (Lianqiao baidu san + Gegen Jieyi Tang) |
| Recovery stage<br>Patients with COVID-19 in the recovery stage.<br>- Clinical consideration: Recovery means two consecutive sets of negative test results, performed more than 24 h apart.<br>Chungpaebaedoc-tang (Qingfeipaidu-Tang) and its replacement medicines: | Samchulkunbi-tang + Saengmaek-san (Shen Zhi Jianpi Tang + Shengmai Yin) or<br>Samchulkunbi-tang + Chungsuekui-tang (Shen Zhi Jianpi Tang + Qingshu Yi Tang) |
| Clinical consideration: Consider the use of for symptom improvement in adults with COVID-19.<br>- 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.<br>Adults with COVID-19 (replacement medicine of Chungpaebaedoc-tang (Qingfeipaidu-tang)) | Chungpaebaedoc-tang (Qingfeipaidu-Tang) |
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:10.1016/j.imr.2020.100470.

References

1. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation report - 44. March 04, 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports (Accessed on March 06, 2020).

2. National Health Commission of People's Republic of China. Diagnosis and treatment of pneumonia caused by novel coronavirus (trial version 7). http://www.nhc.gov.cn/yzygj/s7653p/202003/46e929a47df4ecf88dc7f5912eb1989/files/co3f945832a438eeaae415350a8ce964.pdf (Accessed on March 06, 2020).

3. Guideline Center for Korean Medicine and The Society of Internal Korean Medicine. Korean medicine clinical practice guideline for Common cold (pre-certified version). 2017. http://www.nckm.or.kr/main/module/practiceGuide/view.do?guide_idx=19&progress=&mds_code=&guideline_code=&&gubun=INT&code_gubun=mds&agency=EB88C5805ED93553C1ED9553CEEB805A9XE%22%4E%EB88C58ED93553CE%EB805A9XE%22%4E%EB88C58ED93553CE%EB805A9XE%22&continent=&search_type=all&search_text=&sortField=add_Date&sortType=DESC&menu_idx=14 (Accessed on March 06, 2020).

4. World Health Organization. Coronavirus disease (COVID-19) Pandemic. https://covid19.who.int/ (Accessed on April 17, 2020). [Available from: https://covid19.who.int/]

5. Ford N, Vitoria M, Rangaraj A, Norris SL, Calmy A, Doherty M. Systematic review of the efficacy and safety of antiretroviral drugs against SARS, MERS or COVID-19: initial assessment. J Int AIDS Soc 2020;23:e25489.

6. Tu YF, Chien CS, Yarmishyn AA, Lin YY, Luo YH, Lin YT, et al. A review of SARS-CoV-2 and the ongoing clinical trials. Int J Mol Sci 2020;21:2657, http://dx.doi.org/10.3390/ijms21072657.

7. 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;16:1708–17.

8. Wang R, Yang S, Xie C, Shen Q, Li M, Le X, et al. Clinical observation of qingfeipaidu decoction in the treatment of COVID-19. Pharmocol Clinics Chin Materia Medica 2020;36:13–8.

9. Xu D, Xu Y, Wang Z, Lu Y, Zhu H, Song T. Mechanism of qingfeipaidu decoction on COVID-19 based on network pharmacology. Clin Chin Materia Medica 2020;36:26–32.