Guideline of prophylactic use of Kampo Medicine for new coronavirus infection (COVID-19)

Kampo Industralization Consortium

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1. INTRODUCTION

Kampo Industralization Consortium has been working on various issues surrounding Kampo, from the utilization of Kampo to the securing of herbal medicines, and one of the major themes is the utilization of Kampo at the undiseased stage.

This is a summary of Prophylactic use of Kampo Medicine for the current epidemic of the new corona infection (COVID-19). In preparing this "Guideline of prophylactic use of Kampo Medicine for new coronavirus infection (COVID-19)" (hereinafter referred to as "guideline"), the opinions of many experts both in Japan and abroad, including the specialist who spearheaded traditional medicine in Wuhan City, have been referred to and summarized with a focus on Kampo medicine available in Japan.

Therefore, this guideline deals only with the period of time until the diagnosis of COVID-19 infection is confirmed by PCR, and once the diagnosis is confirmed, it is absolutely necessary to treat the disease in accordance with the national policy.

2. THE CONCEPT OF KAMPO MEDICINE FOR INFECTIOUS DISEASES

Infectious diseases have been a major threat in human history in both Western and Oriental medicine during the development of medicine. One of the Chinese classics written at the end of the Later Han Dynasty (late 2nd century AD), is "Shang han lun" 『傷寒論』. In the preface, the author Zhang Zhongjing (張仲景)states that among 200 relatives, two-thirds died in 10 years and 70% of them died of the plague, which led the author to research and write this book. The history of mankind has been with fights against plagues, and Chinese herbal remedies have developed to overcome every time. We now have to use the wisdom we have developed over the years against this emerging infectious disease.

Traditional medicine says that body's defense function (inner qi) is against the plague (outer evil). At Diamond Princess (cruise ship), there was a case that a husband and wife were in the same room but only one of them developed the disease. That shows it is possible to prevent the virus from multiplying if one's "qi" or body's defense function is strong. Traditional medicine is to strengthen this body's defense function and eliminate the virus.

3. GUIDELINES OF TRADITIONAL MEDICINE FOR COVID-19 IN OTHER COUNTRIES

During current COVID-19 pandemic, 4,900 Chinese medical practitioners from all over China gathered in Wuhan to provide front-line treatment while 42,000 medical practitioners from all over the country also rushed to provide medical support. As a result, Chinese medicine intervention reduced the severity rate from 11% to 4%. Based on this experience, the country developed guidelines for traditional medical treatment (Central People's Government of the People's Republic of China Guidelines for the Treatment of New Type Corona Pneumonia (Trial 7th Edition), http://www.gov.cn/zhengce/zhengceku/2020-03/04/content-5486705.htm). Guidelines for traditional medical treatment have also been published in Korea and Taiwan. For more information, please refer to "The Role of Traditional Medicine in New Coronavirus Infections (COVID-19)" at https://www.jmedj.co.jp/journal/paper/detail.php?id=14426.

4. HOW TO USE THIS GUIDELINE OF PROPHYLACTIC USE OF KAMPO MEDICINE FOR COVID-19

This guideline is open to inform the general public about how Kampo medicine can be used for COVID-19. Therefore, the Kampo and herbal medicines listed here are just representatives of each case, and you should consult a doctor or pharmacist who is familiar with Kampo when actually taking medicines.

It is against the purpose of this guideline to be used by some mail order sites that engage in commercial opportunistic sales. Along with the disclosure of these guidelines, reliable medical institutions and pharmacies will be public as well, so please be sure to consult with them and use appropriate Kampo medicine and herbal medicine guided by experts.

5. KAMPO MEDICINE "YOJO" REGIMEN

How to spend everyday life is called "Yojo" (養生), self-curing in Kampo, and it has priority over all drug treatments. Basically, you need to take a well-balanced diet, moderate exercise, enough sleep, avoid stress and relax mentally. To avoid coldness, is always emphasized in Kampo, you need to be careful to your proper clothes according to different seasons. Especially, it is important to warm the lower part of the body below the waist. Try to warm your body from inside by eating and drinking. For instance, avoiding cold drinks or take cooked vegetables rather than raw. Also, smokers should quit immediately.

Before starting Kampo medicine, it is important to review your daily life and take good self-control.

6. PROPHYLACTIC USE OF KAMPO MEDICINE FOR COVID-19 IN PEOPLE WITHOUT AN UNDERLYING DISEASE

- 1) 玉屏風散(Gyokuheifusan)
 To whom catch cold and get tired easily, look pale, feel chill when the wind blows.
- 2) 生脈散(Shomyakusan) To whom have less physical strength, weak stomach and intestines, sweats frequently.
- 3) 補中益気湯(Hochuekkito)
 To whom have less physical strength or been exhausted.

The Following are crude drugs used for prevention. They may be added to Kampo medicines mentioned above, or may be used alone.

Herbal medicine with immune-enhancing effects: 薬用人参(Panax Ginseng)・西洋人参(Panax quinquefolius)・冬虫夏草(Cordyceps)・霊芝(Ganoderma lucidum)・紅景天 (Rhodiola rosea)

Herbal medicine with stress-relieving properties: 紅景天(Rhodiola rosea)

Herbal medicine with antiviral effects: 板藍根 (Isatis indigotica Radix)・大青葉(Isatis indigotica Folium)・金銀花(Lonicera japonica)

Herbal medicine to enhance lung function: 十薬 (Houttuynia cordata)

7. PROPHYLACTIC USE OF KAMPO MEDICINE FOR COVID-19 IN PEOPLE WITH UNDERLYING DISEASES

The mortality rate of COVID-19 infection is known to be highly dependent on the presence or absence of the underlying disease. If a person has an underlying disease such as heart disease, lung disease, diabetes, or hypertension, it is necessary to treat those well. Yojo (養生) is similar to general prevention, but it requires more strict management of daily life in order to control each disease well.

The following are typical Kampo herbal medicines, which should be taken under the supervision of a doctor/pharmacist who is familiar with Kampo medicine. Side effects may occur when taking long-term medications, so get proper guidance from your doctor/pharmacist about what signs to call in if you see them.

7-1. Lung Disease

- 1) 人参養栄湯(Ninjinyoeito)
 - Whose lung function weakens progressively, accompanied by general weakness.
- 2) 補中益気湯(Hochuekkito)
 - To whom have strong tiredness and fatigue, don't have much appetite.
- 3) 玉屏風散(Gyokuheihusan)
 - To whom have less physical strength, have cold hands and feet, sweat frequently.
- 4) 蘇子降気湯 (Soshikokito)
 - To whom have cold feet, can't stop coughing and flushed face during a coughin.

7-2 Heart Disease

- 1) 木防已湯(Mokuboito)
 - When cardiac hypofunction, accompanied with difficulty of breathing, stridor or edema recognized.
- 2) 生脈散 (Shomyakusan)
 - To whom have a heart disease, weak stomach and intestines, get tired easily.
- 3) 血府逐瘀湯(Keppuchikuoto)
 - To whom have high blood pressure and have headache, head heaviness, stiff shoulder, hot flash or palpitation.
- 4) 炙甘草湯 (Shakanzoto)
 - To whom have an irregular pulse and get tired easily.
- 5) 冠元顆粒(Kangenkaryu)
 - To whom have a headache, head heaviness, stiff shoulders, dizziness, etc.
- 6) 苓桂朮甘湯(Ryokeijutsukanto)
 - To whom being aware of palpitation, short breath or dizziness, and whose lower limb swells.

7-3 High blood pressure

1) 釣藤散 (Chotosan)

To whom have high blood pressure since their late middle age, progressive arteriosclerosis, and have a headache sometimes when they wake up.

- 2) 八味地黄丸:(Hachimijiogan)
 - To whom have cold hands and feet accompanied with frequent urination in nighttime.
- 3) 杞菊地黄丸:(Kogikujiogan)
 - To whom have hot flashes, dry mouth, dizziness, and poor vision.
- 4) 血府逐瘀湯(Keppuchikuoto)
 - To whom have headache, head dullness, stiff shoulder, hot flash or palpitation
- 5) 冠元顆粒(Kangenkaryu)
 - To whom have a headache, heavy head, stiff shoulders, dizziness, etc.
- 6) 半夏白朮天麻湯(Hangebyakujutsutenmato)
 - To whom have dizziness or headache, and feel a pressure on the chest or solar pleus.
- 7) 真武湯 (Shinbuto)
 - To whom have weak constitution, sensitive to cold, and have dizziness, swelling or palpitation, etc.

7-4 Diabetes

- 1) 八味地黄丸 or 牛車腎気丸:(Hachimijiogan or Goshajinkigan)
 To whom have cold hands and feet, back pain, polyuria, frequent urination in nighttime, ear noise, etc.
- 2) 六味丸 (Rokumigan)
 - To whom have symptoms similar to 八味地黄丸(Hachimijiogan), but the chillness is not as strong.
- 3) 清心連子飲(Seishinrenshiin)
 - To whom have weak stomach and intestines, and frequent urination.
- 4) 生脈散 (Shomyakusan)
 - To whom have weak constitution, week stomach and intestines, get tired easily, don't have much appetite.
- 5) 血府逐瘀湯 or 冠元顆粒(Keppuchikuoto or Kangen Karyu)
 To whom have high blood pressure and whose arteriosclerosis is progressing.

The Following are crude drugs used for patients with underlying diseases. They may be added to Kampo medicines mentioned above, or may be used alone.

Herbal medicine with immune-enhancing effects: 薬用人参(Panax Ginseng)・西洋人参(Panax quinquefolius)・冬虫夏草(Cordyceps)・霊芝(Ganoderma lucidum)・紅景天(Rhodiola rosea)

Herbal medicine with antiviral effects: 板藍根(Isatis indigotica Radix)・大青葉(Isatis indigotica Folium)・金銀花(Lonicera japonica)

Herbal medicine that improves blood flow and is effective for patients with heart disease and hypertension: 鶏血藤(Millettia reticulata Benth)・紅花(Carthami Flos)

8. PROPHYLACTIC USE OF KAMPO MEDICINE FOR OTHER COVID-19 HIGH-RISK INDIVIDUALS

8-1 A close contact

2 weeks observation period is required. During this time, each individual will take immune-boosting herbal medicines (e.g., Hochuekkito and Juzentaihoto), combined with herbal medicines with antiviral effects. Alternatively, take a Kampo medicine that is similar to an infection (e.g., Gingyosan and Kakkoshokisan), combined with a combination of immune-boosting herbal medicines.

- 1) 補中益気湯(Hochuekkito)
 - Immune-boosting Kampo medicine with antiviral effects
- 2) 十全大補湯 (Juzentaihoto)
 - To whom get tired easily and looks pale.
- 3) 銀翹散(Gingyosan)
 - It is a remedy for cold with less chillness, but may be used preventatively.
- 4) 藿香正気散(Kakkoshokisan)
 - To whom have swelling, weak stomach and intestines, coating of tongue.

8-2 Frail and elderly person

The elderly has been reported to be at a higher risk of becoming seriously ill, as have those with underlying diseases. It is also said that refraining from going out can lead to inactivity in life and increase the likelihood of developing frail syndrome for the elderly. In addition to taking Kampo medicine, it is also important to take exercise that can be done at home, eat three proper meals, and take good oral care.

- 1) 玉屏風散(Gyokuheifusan)
 - To whom have weak constitution, sweat easily.
- 2) 補中益気湯(Hochuekkito)
 - To whom get tired easily, have no appetite.
- 3) 十全大補湯(Juzentaihoto)
 - To whom tending to anemia, get tired easily.
- 4) 人参養栄湯(Ninjinyoueito)
 - To whom is rather frail, have weak legs.
- 5) 六君子湯(Rikkunshito)
 - To whom having a small appetite, could not get enough nutrition.
- 6) 生脈散 (Shomyakusan)
 - To whom is rather dehydrate, have less appetite, short breath, and dry cough.

The Following are crude drugs used for high-risked patients. They may be added to Kampo medicines mentioned above or may be used alone.

Herbal medicine with immune-enhancing effects: 薬用人参(Panax Ginseng)・冬虫夏草 (Cordyceps)・霊芝(Ganoderma lucidum)

Herbal medicine with antiviral effects: 板藍根 (Isatis indigotica Radix)・大青葉(Isatis indigotica Folium)・金銀花(Lonicera japonica)

9. HOW TO HANDLE AFTER THE ONSET OF THE FEVER

The speed of viral propagation is determined by the initial viral load that enters and the ability of the organism to defend itself. If Kampo medicine is taken as a preventive measure, various biological defense functions are activated, and the virus growth can be suppressed at an early stage. After the onset of the disease, the main treatment is herbal medicine to eliminate the virus, but it is more effective if it is combined with continued immune-enhancing medicine.

The initial symptoms of COVID-19 infection are the usual symptoms of the common cold, which may begin with fever, headache, and sore throat. Those symptoms may go away, but it also may bring various symptoms such as cough and sputum, diarrhea (sometimes constipation), olfactory disorder, loss of appetite and decreased urine output. Coronaviruses bind to the ACE2 receptor and invade cells, and because the receptor is spread over multiple organs, a variety of symptoms are thought to appear.

It is important to recover at this stage. However, patients may have cytokine storm suddenly and blood clot may form and cause a myocardial or cerebral infarction. Thus, it is important to see a health care provider as soon as possible.

Based on the above, here are some Kampo herbal medicines that you can take until you see the doctor or have a PCR test.

9-1 When patient have a fever

If there are no other symptoms within 1-2 days after the onset of fever, take 葛根湯(Kakkonto)or 麻黄湯(Maoto)combine with 薬用人参(Panax ginseng), 冬虫夏草(Cordyceps)and 霊芝(Ganoderma lucidum)in order to enhance immunity. If more than 3 days have passed since the onset of symptoms, or if the fever does not decline even the patient take 葛根湯 or 麻黄湯 constantly for 3 days, take 柴葛解肌湯(Saikatsugekito). Or combine of 葛根湯(Kakkonto)and 小柴胡湯(Shosaikoto)until the fever declines.

When taking a combination of extracts, the amount of 甘草(Licorice), one of the herbal medicines contained in Kampo medicine, is increased, and side effects such as dullness in the hands and feet, numbness, and weakness may appear. Contact your doctor or pharmacist as soon as you develop symptoms of side effects.

- 1) 葛根湯(Kakkonto)
 - Take it immediately after the onset of the disease, when there is a chill, the back of the neck is stiff and the fever rises.
- 2) 麻黄湯(Maoto)
 - To whom feels chill strongly, have joint pain, back pain, etc.
- 3) 麻黄附子細辛湯(Maobushisaishinto) To the elderly.
- 4) 銀翹散 (Gingyosan)
 - To whom have sudden fever without a strong chill
- 5) 藿香正気散(Kakkoshokisan)

To whom have chilling and fever, headache, chest tightness, vomiting, diarrhea and coating of tongue.

9-2 When patient have a cough and phlegm

If the fever is persistent, it is better to use: 柴葛解肌湯(Saikatsugekito),麻杏甘石湯(Makyokansekito),麻杏甘石湯 + 銀翹散(Makyokansekito + Gingyosan). If the fever is calm: 小柴胡湯加桔梗石膏(Shosaikoto ka Kikyosekko), if the patient complains chest pain: 柴陥湯(Saikanto). In every case, continue to take them until the fever declines.

When taking a combination of extracts, the amount of 甘草(Licorice), one of the herbal medicines contained in Kampo medicine, is increased, and side effects such as dullness in the hands and feet, numbness, and weakness may appear. Contact your doctor or pharmacist as soon as you develop symptoms of side effects.

- 2) 麻杏甘石湯 + 小柴胡湯 (Makyokansekito + Shosaikoto)
 To whom have airway stenosis and feel short of breath. When using the extract, be careful of swelling as 甘草 (Licorice) will be 4g.
- 新杏甘石湯 + 銀翹散(Makyokansekito + Gingyosan)
 The formula used during the 2009 influenza epidemic. It is widely used for fever, cough and phlegm. Be careful of over taking 甘草(Licorice).
- 4) 小柴胡湯加桔梗石膏 (Shosaikoto ka Kikyosekko)
 To whom have a swollen and sore throat.
- 5) 柴陥湯(Saikanto) To whom have a chest pain.
- 6) 蘇子降気湯 (Soshikokito)
 To whom are tangled in phlegm and feel short of breath.

This is the end of the guideline of prophylactic use of Kampo Medicine for new coronavirus infection (COVID-19), which is summarized by Kampo Industralization Consortium. In Wuhan City, China, PCR-positive COVID-19 also played a major role in the prevention of severe disease in patients with mild disease. Please refer to "The Role of Chinese Medicine in New Coronavirus Infection (COVID-19)" https://www.jmedj.co.jp/journal/paper/detail.php?id=14426 for specific treatment options.

10. WHAT TO DO IN CASE OF SEQUELAE

As the knowledge from COVID-19 accumulates, there have been many reports of sequelae. Regardless of the severity of the symptoms, malaise, coughing, brain fog, anosmia, ageusia, and hair loss may persist for a long time. This condition, known as "long COVID" in other countries, is considered as an inflammatory scar caused by the virus that invaded various tissues via ACE-2, the receptor for SARS-CoV-2 distributed throughout the body, and causes long-term suffering to patients. Kampo therapy can be used to treat a wide range of these sequelae. Because of the wide variety of sequelae symptoms and each

patient manifest a different Kampo pattern in traditional medicine diagnosis, it is important to have patients choose their prescriptions in person under the guidance of a doctor or pharmacist who is familiar with Kampo.

10-1. Malaise

- 1) 補中益気湯(Hochuekkito)
 - When malaise persists after defervescence.
- 2) 十全大補湯(Juzentaihoto):
 - When malaise persists and physical fitness is exhausted.
- 3) 人参養栄湯(Ninjinyoueito)
 - When dyspnea occurs with malaise after a short time movement.
- - Physical fitness is exhausted and daily activities are extremely impaired.

10-2. Cough

- 1) 麦門冬湯 (Bakumondoto)
 - When interstitial pneumonia remains due to COVID-19 and dry cough is prolonged.
- 2) 桔梗湯 (Kikyoto)
 - It is used for tonsillitis with swollen throat with strong pain, as well as purulent sputum.
- 3) 甘草湯(Kanzoto)
 - For severe coughing, sore throat, mouth ulcer, hoarseness.
- 4) 板藍根 (Banrankon)
 - It is a single crude drug, and used when tonsillitis and sore throat are prolonged.

10-3. Brain fog

A wide range of SARS-CoV-2 receptors are also present in the brain, causing various disorders of brain activity such as loss of concentration, brain freeze, and dizziness.

- - postural hypotension and dizziness is prolonged.
- 2) 釣藤散 (Chotosan)
 - When brain freezes and cause dizziness.
- 3) 桂枝加龍骨牡蛎湯(Keishikaryukotsuboreito)
 - Strong anxiety, irritability or insomnia is prolonged.
- 4) 柴胡加竜骨牡蠣湯(Saikokaryukotsuboreito)
 - Have anxiety or insomnia, have a sensitive nerves such as being surprised by a slight noise.
- 5) 加味逍遥散(Kamishoyosan)
 - When vague anxiety and insomnia persist.

10-4. Hair loss

- 1) 十全大補湯 (Juzentaihoto)
 - Supplement for dual deficiency of gi and blood, effective for hair loss.
- 2) 四物湯(Shimotsuto) Strong blood deficiency, hair loss and deformed nails and dry skin.

Crude drug that can be added to these or used alone are as follows.

- 3) 何首鳥(Kashuu)
 - A single crude drug effective for hair loss and premature gray hair.
- 4) 女貞子 (Jyoteishi)
 - A single crude drug effective in preventing gray hair and improving hair loss.
- 5) 旱蓮草(Kanrenso)
 - A single crude drug improves hair loss as it supplements kidney qi.
- 6) 夜交藤 (Yakoto)
 - Effective in invigorating the circulation of blood and itchy skin.
- 7) 枸杞子 (Kukoshi)
 - Effective in hair loss and premature gray hair as it supplements liver and kidney.

10-5. Anosmia, Ageusia

- 1) 補中益気湯(Hochuekkito)
 - By improving the digestive and absorptive functions of the gastrointestinal tract, it improves anorexia and improves the sense of smell and taste.
- 2) 当帰芍薬散(Tokishakuyakusan)
 - Use for olfactory dysfunction in who is weak and has anemia.
- - It is effective for dysgeusia by improving nausea, loss of appetite, thirst, and dry mouth.
- 4) 加味帰脾湯(Kamikihito)
 - To whom have no appetite and have prolonged anosmia.
- 5) 人参養栄湯(Ninjinyoeito)
 - For smell and taste disorders associated with loss of appetite and decreased physical strength.

11. SUMMARY

To summarize this guideline, we heard directly from Prof. Zhang Boli (張伯礼) of Tianjin Chinese Medical University and Prof. Zhang Zhongde (張忠徳) of Guangzhou Chinese University, both of whom contributed to the suppression of COVID-19 in Wuhan City. It was stressed that this virus is persistent, seemingly stable, but can rapidly deteriorate, so it was important to have a daily reminder (to raise your inner "Qi"). It should be noted that 4,900 traditional medicine doctors who treated COVID-19 infection in Wuhan City took their own herbal medicines and no one was infected.

I would be happy if this guideline could contribute to saving as many precious lives as possible.

12. ACKNOWLEDGEMENT

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