

A Review of Prevention and Adjuvant Therapy in Acute Respiratory Syndrome Caused by COVID-19 from the Perspective of Persian Medicine

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ABSTRACT

BACKGROUND AND OBJECTIVE: COVID-19 started in December 2019 in Wuhan, China and quickly became a global pandemic. According to studies, traditional medicine interventions along with conventional medicine protocols have been reported to be effective in prevention and treatment. The aim of this study was to summarize the recommendations of Persian medicine based on evidence in the prevention and treatment of symptoms of acute respiratory syndrome.

METHODS: In this review article, keywords related to the symptoms of COVID-19 in Persian medicine sources, review and items related to the prevention and treatment of acute respiratory syndrome were extracted. Individual items with the keywords "Influenza" or "SARS" or "MERS" or "COVID-19" or "Coronavirus" or "Antiviral" or "Anti-inflammatory" or "Immune system" or "Antioxidant" were searched in the databases SID, Pubmed, Scopus, Cochrane, Web of science, Science direct, and Google scholar, and finally those with scientific evidence were presented in the form of auxiliary instructions for prevention and treatment.

FINDINGS: A significant part of the recommendations of Persian medicine to prevent or control the symptoms of acute respiratory syndrome has practical clinical evidence. These include social distance, avoiding heavy meals, and using herbal remedies according to the specific conditions of the patients.

CONCLUSION: According to the results of this study, the use of simple strategies of Persian medicine in preventing and improving the symptoms of acute respiratory syndrome caused by COVID-19 along with common medicine protocols, can help control the epidemic conditions. Also, many of these recommendations can be evaluated as useful research ideas in the prevention and treatment of COVID-19.

KEY WORDS: *Coronavirus, Persian Medicine, Acute Respiratory Syndrome.*

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Introduction

COVID-19 is a beta-coronavirus that has been responsible for many respiratory infections since 1965, such as the common cold, SARS, Severe Acute Respiratory Syndrome (MERS), and Middle East Respiratory Syndrome (MERS) (1, 2). COVID-19 started in Wuhan, China in December 2019 and soon became a global pandemic (3, 4). The disease is in most cases mild and self-limiting, but in a percentage of patients, especially those with the underlying disease can be severe and life-threatening (5, 6).

The main symptoms of the disease include fever, shortness of breath and dry cough, which are often accompanied by weakness, muscle pain, anorexia, nausea and diarrhea, and appear after the incubation period of 3 to 7 days (maximum 14 days). A range of neurological and cardiac complications have been reported with COVID-19 (7, 8). Paraclinical evidence such as changes in lymphocyte count, increase in Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), liver and Ferritin tests, and Ground glass view on CT scan or chest X-ray are helpful for diagnosis. But the final diagnosis is made by performing a Polymerase Chain Reaction (PCR) test on the secretions of the throat or trachea and lungs (9-12).

There is currently no accepted vaccine or treatment for COVID-19. Many studies recommend the use of traditional and complementary medicine in the prevention and treatment of patients (13, 14). A review of recent studies on the effect of traditional Chinese medicine on the prevention and treatment of patients with COVID-19 shows that early initiation of traditional medicine interventions can be effective in prevention as well as reducing the duration and severity of the disease (15). The importance of this issue is such that the interventions of traditional Chinese medicine have been considered as a major part of the clinical guideline articles related to COVID-19 (2).

Considering the linguistic differences of words in Persian medicine, first the common disease in must be explained Persian medicine. The term "cholera" or "plague" refers to the prevalence of infectious diseases or infectious agents. A review of Persian medicine sources shows that Persian medical scientists have repeatedly faced the spread of epidemics over the centuries and have provided useful solutions in this regard. Examining the symptoms of pulmonary involvement caused by COVID-19, it seems that pneumonia is the closest similar word in Persian medicine. In Persian medicine, different types of

pneumonia have been described, which based on the matching of symptoms, the initial pulmonary involvement caused by COVID-19 is most similar to pneumonia with warmth and dryness quality (16-18).

The growing tendency of people to use the services of traditional medicine and herbal medicines on the one hand and the reports of side effects and their drug interactions on the other hand as well as unrealistic advertisements about the effectiveness of herbal products and other traditional medicine interventions in COVID-19 show the importance of examining the effectiveness and safety of these services (19). Due to the wide range of symptoms and complications of COVID-19, it is not possible to explain each symptom in this article and the purpose of this study is to provide simple, effective and safe solutions of Persian medicine to help prevent and control the symptoms of COVID-19 based on scientific evidence.

Methods

This review article in the field of Persian medicine was conducted after approval by the ethics committee of Babol University of Medical Sciences with the code IR.MUBABOL.REC.1399.314.

In the first step, to explain the keywords, the guidelines of the World Health Organization in the field of integrative medicine were used. Considering the differences in keywords of common medicine and Persian medicine, keywords related to all conditions of infectious diseases and the closest terms to pulmonary involvement caused by COVID-19 were extracted based on a review of the main references of Persian medicine including al-Qanun fit-Tibb, Tib e Akbari, Al-Hawi, Exir-e-Azam, Kholase Al-Hekmat, Mofarrah al-Qolob and Zakhire Kharazmshahi.

In the second stage, the keywords: cholera air, cholera water, cholera catarrh (Nazleh), infectious fever, cholera fever, cholera cough and catarrh (Nazleh) and pneumonia were searched in more than 500 Persian and Arabic books available on Persian medicine and recommendations related to prevention, treatment and control of its symptoms were extracted.

In the third stage, the instructions related to the recommended lifestyle during the epidemic and more than 200 plants mentioned in the prevention of epidemics or treatment of symptoms of acute respiratory syndrome (pneumonia caused by a warm and dry agent) were extracted and common items mentioned in the sources were selected. It should be

noted that the results of each stage of searching in Persian medicine resources were reviewed by a team consisting of five Persian medicine specialists. Continuation of each search step was done with the unanimity of the expert team.

In the fourth stage, the keywords "Influenza" or "SARS" or "MERS" or "COVID-19" or "Coronavirus" or "Antiviral" or "Anti-inflammatory" or "Immune system" or "Antioxidant" were searched in titles, abstracts, and keywords in databases such as SID, Pubmed, Scopus, Cochrane, Web of science, Science direct as well as Google scholar. Finally, cases with direct scientific evidence (such as a proven association with COVID-19 or similar cases such as SARS, MERS, coronaviruses, or influenza) or indirect evidence (including effects on disease-related mechanisms such as anti-inflammatory effects, immune-response modifiers, and antioxidant or antiviral effects) in their titles, abstracts, and keywords were mentioned.

Results

A search of the databases showed 24,600 articles, most of which were deleted for reasons such as duplication, irrelevance, or review articles, and finally 74 related articles were included in the study. The results of these articles were divided into two sections of prevention and treatment with the aim of providing an auxiliary solution to prevent or control the complications of the disease.

Prevention:

Preventive recommendations in Persian medicine: In Persian medicine, the keyword "cholera air" is used for the spread of infectious diseases in general and "cholera catarrh (Nazleh)" is used for the spread of respiratory infections and refers to the prevalence of epidemics in the respiratory system. The word "cholera" in Persian medicine refers to epidemic diseases and is not limited to diarrhea caused by *Vibrio cholerae*. These two titles seem to be the closest keywords to finding instructions related to disease prevention. From the perspective of Persian medicine, people who have accumulated waste in the body are more prone to pandemics than others, and therefore cleansing the body at this time is very important. On the other hand, this cleansing should not irritate one's nature. The use of laxatives to cleanse the body of waste products is prohibited at this time. Using plain foods and natural laxatives and avoiding overeating is one of the safe ways to cleanse body in these conditions (20-25). According to the basic

theories of Persian medicine, during the epidemic of infectious diseases, people with dominance of coldness and wetness (dominance of phlegm) are more prone to infection than others, and therefore providing preventive recommendations with a warm temperament (Mizaj) is recommended to cause moderation (Etedal). A study to investigate the difference in the prevalence of COVID-19 in different parts of China found that the cold and wet environment were associated with a higher prevalence of infection. Also, paying attention to climate differences in different provinces and Mizaj in different people is very important in providing preventive instructions (15).

General lifestyle tips: Personal lifestyle tips include avoiding overeating as well as eating little food, avoiding rich and slow-digesting foods, reducing meat consumption, and increasing the consumption of vegetables such as carrots, turmeric, celery, and coriander, basil, mint, parsley, spinach, turnips and squash and fruits such as apples, sweet citrus, lemons and oranges, having a balanced sleep, and avoiding inactivity, strenuous exercise and overwork, as well as having peace of mind (26-36, 2).

The most important preventive advice in relation to social lifestyle is to stay away from the polluted environment. Seyed Esmail Jorjani states in his book *Zakhireh Kharazmshahi*: "The cure for cholera is not going from the house to the desert in the days of cholera and to take care of the air in the house so that it does not get bad" (37). Also, Hakim Azam Khan, in his book *Exir-e-Azam*, advises in this regard: If there is no need to go out, they should not leave the place, otherwise they should take some vinegar with the garlic and onion with them and keep it close to the nose and mouth, and return to their place soon" (38).

Preventive medicinal plants: This part of the recommendations cannot be used equally by all people and a person must use one or more of them depending on the specific conditions of the person, the underlying disease, history of allergy to herbal medicines and considering the possibility of interference with chemical or herbal medicines and must be prescribed with a preventive dose. Preventive edible plants include borage (*Echium amoenum*) (39), chamomile (*Matricaria chamomilla*) (40), mint (*Mentha piperita*) (41), thyme (*Zataria multiflora*) (42), mountain tea (*Stachys lavandulifolia*) (43), cinnamon (*Cinnamomum verum*) (44), ginger (*Zingiber officinale*) (45), saffron (*Crocus sativus*) (46), black seed (*Nigella sativa*) (47) and licorice (*Glycyrrhiza glabra*) (48). Simultaneous

consumption of multiple herbs and excessive consumption of spices with warm temperament (Mizaj) can be harmful. A review of articles published in recent years shows that all of the above plants have strong antimicrobial and antioxidant effects. Also, antiviral effects, strengthening lung and heart function, modulating the immune system and having the ability to prevent infectious diseases are among the most important mechanisms of action of these plants. Most of these herbs have also been reported in traditional Chinese medicine articles to be effective in preventing COVID-19 (2).

Other plants: Smelling fragrant fruits and herbs such as orange, orange leaf (*Citrus aurantium*), rose (*Rosa damascena*), quince (*Cydonia oblonga*), apple (*Malus domestica*), mint (*Mentha piperita*), cardamom (*Elettaria cardamomum*), cinnamon (*Cinnamomum verum*), clove (*Dianthus barbatus*) and basil (*Ocimum basilicum*) can be effective in preventing epidemics. These plants can also be used as incense in boiling water.

The general recommendation of Persian medicine is the balanced use of incense at a suitable distance so as not to cause dryness and irritation of the respiratory mucosa. The exact amount of incense used in Persian medicine sources is not generally mentioned for everyone. In some studies, for prevention, the use of decoction of these plants for 30 minutes a day and a maximum of once a day is recommended (2, 49).

Smoking plants in the environment has long been used to disinfect the environment and is rooted in popular culture. In some studies of traditional Chinese medicine in the prevention of COVID-19, the smoke of some plants such as frankincense (*Boswellia sacra*), wild rue (*Peganum harmala*), myrtle (*Myrtus communis*), clove (*Dianthus barbatus*), marjoram (*Origanum majorana*) or Agar Wood (*Aquilaria sinensis*) is recommended (50-53). According to the available documents, smoking a maximum of 1 to 2 grams of the plant per cubic meter of room space for a maximum of 15 to 30 minutes, once a day is recommended. Overuse is prohibited in people with a history of allergies or coughing and shortness of breath (2).

Persian medicine sources have recommended the smelling of vinegar and also spraying it with rose extract in the environment for disinfection. Recent scientific evidence has reported the effects of topical vinegar disinfectants, although their effect on coronaviruses has not been studied and according to existing studies

cannot replace standard disinfectants (54, 55). Foot bath with warm water or warm water containing herbs such as chamomile or thyme are other preventive recommendations. Numerous articles have reported the effects of foot bath on sedation, and anxiety, depression, and sleep improvement (placing the feet up to the wrist in 42 °C water for 20 minutes and then resting for 5 minutes) (2, 56, 57).

Acute respiratory syndrome from the perspective of Persian medicine

A) Explanation of acute respiratory syndrome caused by COVID-19 in Persian medicine: Due to the linguistic differences and classification of diseases in conventional and traditional medicine, it is not possible to fully match the symptoms and diseases in these two schools and different adaptations may be possible at different stages of the disease. In the articles of traditional Chinese medicine, in different stages of COVID-19, similarities with different syndromes of traditional Chinese medicine have been expressed (2).

The most closely related terms based on the symptoms of the disease are: "pneumonia", "cholera catarrh (Nazleh)", "hot swelling", "infectious swelling" and "cholera cough". Due to the set of symptoms, the acute respiratory syndrome caused by COVID-19 seems to be more similar to the term "pneumonia". Hakim Azam Khan, in his book *Exir-e-Azam*, quoting the majority of physicians, considers pneumonia to be hot swelling of the lungs. Ibn Sina describes the substance of this swelling as essentially hot, like sputum of blood and bile, and like foul-smelling Phlegm and Sauda (black bile) due to infection. From the point of view of Persian medical scholars, cold phlegm or Sauda swellings in which there is no infection and warmth are not called pneumonia. Symptoms of pneumonia in Persian medicine include fever, thirst, cough, shortness of breath, feeling of heaviness and stretch in the chest, and pain between the two shoulders, which in some cases intensifies leading to pleural effusion or death. Razi in his book "*Kitab al-Mansouri fi al-Tibb*" points out the difference between a Zukam (a kind of hot catarrh (Nazleh)) and a type of plague that affects the lungs, and differentiates the pulmonary symptoms caused by epidemic diseases and the symptoms caused by possible lung disorders (20-25).

Some studies of traditional Chinese medicine have also explained the presence of fever, dry cough and shortness of breath in COVID-19 disease as equivalent to increased warmth and dryness (2). The general recommendation for dealing with acute respiratory

syndrome is the use of foods and herbal medicines that reduce heat and provide moisture to the body and lungs (refrigerants, moisturizers and laxatives for the chest and body).

B) Treatment in outpatients:

-Lifestyle recommendations: General recommendations for patients with mild to moderate symptoms in the first days of the disease include adequate rest, avoiding insomnia and strenuous activity, adequate ventilation, and maintaining ambient temperature and humidity. It is also recommended to avoid sour, spicy, salty, rich and slow-digesting foods (2, 26-28). In the first few days, the patient's diet should be limited to simple soups, almond porridge with rice flour or starch, and warm liquids with a little sugar or honey (58).

-Adjuvant therapies of Persian medicine: Persian medicine drugs that affect pneumonia include herbs that are especially effective in improving lung function and reducing cough and fever. Recent studies have reported the antioxidant effects of many of these plants and their effectiveness in strengthening the immune system and controlling the symptoms of respiratory diseases such as influenza, SARS, and COVID-19. One of the simplest adjuvant drugs in Persian medicine is the aqueous extract of barley (*Hordeum vulgare*), which is obtained by boiling barley in water and is called medical malt in Persian medicine. In clinical trials, the effects of medical malt in reducing the symptoms of allergic rhinitis have been reported (59). Studies have also reported the effectiveness of aqueous extract of barley

on influenza virus H1N1, H3N2 and B (60). Boiling jujube (*Ziziphus jujuba*), *Cordia myxa* and licorice (*Glycyrrhiza glabra*) with barley is effective in enhancing the effect of medicinal malt. Recent studies have reported the effects of jujube and *Cordia myxa* on fever and cough. Licorice has been reported to be effective in improving the symptoms of patients with influenza and coronaviruses (61-66).

Suitable drinks include Citrus Lemon Syrup (67), *Echium amoenum* (39), *Viola odorata* (68), *Malva sylvestris* (69), *Althea officinalis* (61), *Cydonia oblonga* (62) or *Plantago ovata* (63) soaked in warm water. Most patients complain of gastrointestinal symptoms such as anorexia, nausea, diarrhea, or constipation along with respiratory symptoms. Using syrups of lemon (*Citrus lemon*) (70), apple and barberry (*Malus domestica* and *Berberis vulgaris*) (71), and pomegranate is effective for anorexia and nausea, using mint (*Punica granatum* and *Mentha piperita*), sweet pomegranate (*Punica granatum*) (72), apple (*Malus domestica*) (71), myrtle (*Myrtus communis*) (73) or Gum arabic (*Acacia arabica*) (74) is effective for diarrhea while using plantain (*Plantago ovata*) (75) or golden shower (*Cassia fistulas*) (76) soaked in hot water with almond oil is effective for constipation (Table 1).

Hot foot bath with a temperature of 42 degrees for 20 minutes is effective in improving sleep and reducing the patient's anxiety (56, 57, 77). Also, the rapid effects of foot bath in reducing shortness of breath in patients with asthma (78) have been reported.

Table 1. Commonly used plants with oral consumption to control the symptoms of acute respiratory syndrome in the perspective of Persian medicine (79-90)

Scientific name	Common name	The used part	Evidence of Persian medicine	Evidence of conventional medicine
<i>Plantago ovata</i>	plantain	Seed	Laxative, relieves fever and roughness of chest and throat	Enhancement of humoral and cellular immune activity in animal studies (79)
<i>Prunus dulcis</i>	Almond	Fruit	Tonic for the brain, laxative, useful in coughs, shortness of breath and hoarseness	Inhibition of TNF- α , IL12 and myeloperoxidase proinflammatory cytokines in animal samples with acute pneumonia (80)
<i>Viola odorata</i>	Sweet violet	Flower	Relieves cough, fever and sore throat, effective in pneumonia	Effects comparable with corticosteroids in the prevention and treatment of formalin-induced pneumonia (reduction of inflammation and bleeding in the alveoli and regeneration of bronchial mucosa) in an animal study (81)
<i>Cydonia oblonga</i>	Quince	Seed	Relieves sore throat, useful in dry fever and cough, hoarseness and shortness of breath	Antioxidant and antimicrobial effects in laboratory and animal studies (62, 65)

Scientific name	Common name	The used part	Evidence of Persian medicine	Evidence of conventional medicine
<i>Malva sylvestris</i>	Cheeses	Flowers, leaves, seeds	Relieves fever and dry cough and hoarseness, laxative	The effect of extract on improving the immune response in animal study (69)
<i>Hordeum vulgare</i>	Barley	Seed	Relieves fever, dry cough, inflammation and ulcers of the lungs and chest pain	The effect of malt in comparison with fexofenadine on the symptoms of patients with allergic rhinitis (59), antiviral activity of barley aqueous extract in influenza H1N1, H3N2, B (60)
<i>Althea officinalis</i>	marsh-mallow	Flowers, leaves, seeds	Useful in fever and hot cough and pulmonary hemorrhage, laxative	Animal study of the effect of marshmallow extract on cough caused by mechanical stimulation of mucosa with nylon fiber (61)
<i>Cassia fistula</i>	golden shower	Fruit	relief for the chest and temper, relieves fever and cough, solution for sore throat	Antitussive effect comparable to codeine phosphate in cough induced by inflammation with SO ₂ gas in an animal model (82)
<i>Hyssopus officinalis</i>	Hyssop	Flowers, leaves	Useful in coughs, shortness of breath and pneumonia, useful in catarrh and acute pneumonia	Reduction of inflammatory cytokines IL4, IL6, IL17 and interferon γ in the animal model, Reduction of respiratory tract inflammation (83)
<i>Cordia myxa</i>	Assyrian plum	Fruit	Relief for the chest, useful in fever, dry cough, shortness of breath and hoarseness	Effects of bronchodilators following stimulation of nitric oxide synthesis in animal models (84)
<i>Glycyrrhiza glabra</i>	licorice	Root	Useful in shortness of breath and hoarseness and a variety of coughs	Anti-corona-viruses including SARS (66), anti-influenza effects of H1N1 (85), useful in chronic cough (86)
<i>Acacia arabica</i>	Gum arabic	Tree gum	Relief for the chest, stops pouring substances into the chest, useful in chest pain, sore throat, lung ulcers, cough and hoarseness	Reducing inflammation and increasing airway sensitivity due to cigarette smoke in an animal model (87), antitumor effects on lung cells (88)
<i>Ziziphus jujube</i>	Jujube	Fruit	Relief for the chest, useful in hoarseness, chest wall pain, shortness of breath and cough	Strong antiviral effects of influenza and inhibition of inflammatory cytokines IFN- γ , IL-1 β and TNF- α (64)
<i>Echium amoenum</i>	borage	Flowers, leaves	Tonic for inner heat and heart, laxative, relieves fever and cough, shortness of breath and hoarseness, useful in lung diseases	Significant reduction in clinical symptoms in patients with asthma such as cough, shortness of breath and hypersensitivity of the respiratory tract (89)
<i>Nymphaea alba</i>	White Water-Lily	Flowers	Tonic for the heart and brain, useful in hoarseness, pneumonia and fever	Antioxidants, antitumor, antifungal and antiviral effects in Invitro study (90)

Discussion

The increasing desire to use herbal medicines and traditional therapies in communities over the past decade has increased the importance of research in this area. Proper ability to provide a special lifestyle for each person and prevention at different stages such as prevention of disease and in case of disease, prevention of disease progression is a prominent feature of Persian medicine. On the other hand, from the perspective of traditional medicine schools, a set of external and internal factors are effective in the emergence of the

disease and creating a balance between these factors based on basic theories can play an effective role in disease prevention (91-93). A study by Cui et al. on the effect of traditional Chinese medicine on COVID-19 treatment found that heavy rainfall before the outbreak in Wuhan was one of the main causes of the rapid epidemic in the city. According to the theories of Chinese medicine, rainfall causes the environment to become cold and humid and increases the risk of infection. Adjusting the cold and humidity of the

environment by making lifestyle changes and using traditional medicines can be effective in preventing the disease (15).

Clinical experience of COVID-19 treatment showed that early intervention of traditional and complementary medicine along with common therapies leads to shortening of the disease period, delayed disease progression and reduced mortality rate. From the perspective of Persian medicine, improving nutrition, sleep and rest, exercise and mobility in accordance with Mizaj and staying calm, along with recommendations related to cleansing with emphasis on retaining essential substances and excretion of waste is effective in improving the immune system and this effect is significant both in a healthy person to prevent the disease and in a sick person to reduce the complications of the disease and shorten the recovery period (2, 13).

Although the mechanism of action of traditional medicine therapies is not fully understood, it seems that with a unique perspective in the diagnosis of specific syndromes based on theories of several thousand years, we can balance the body and increase resistance to epidemics. According to the available documents, traditional medicine drugs, in addition to inhibiting the virus, help to improve the sickness and reduce complications by modulating the immune response and reducing tissue inflammation. The clinical experience of COVID-19 treatment in China shows an increase in

the recovery rate of patients with early intervention of traditional therapies combined with conventional medicine. Furthermore, shortening of the disease period, delay in disease progression and reduction of mortality rate following the use of traditional and complementary medicine strategies have been reported (13, 14).

Emphasis on avoiding contact with the pathogen during the outbreak of a disease, use of available health facilities such as covering the mouth and nose when leaving the house, use of topical disinfectants such as vinegar in the environment, along with increasing the body's defenses through lifestyle modification and the use of some herbal medicines are considered as important pillars of epidemic control in Persian medicine (16-18).

Although many of the recommendations of Persian medicine in the prevention and treatment of diseases are used as adjunctive solutions alongside conventional medicine treatments, additional studies are needed for more accurate evaluation. The results presented in this article are recommended for preventive, therapeutic and research applications.

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