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OBM Integrative and Complementary Medicine

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Review

Traditional, Complementary and Integrative Medicine Approaches to COVID-19: A Narrative Review

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Academic Editor: Soo Liang Ooi and Sok Cheon Pak

Special Issue: Complementary, Traditional, and Integrative Medicine for COVID-19

OBM Integrative and Complementary Medicine
2021, volume 6, issue 3
doi:10.21926/obm.icm.2103021

Received: April 11, 2021
Accepted: June 30, 2021
Published: July 12, 2021

Abstract

Traditional, complementary, and integrative medicine (TCIM) approaches to COVID-19 represent a paradigm shift from Western medicine, in that TCIM emphasizes prevention, encouraging wellness, and supporting health and recovery. A wide range of TCIM approaches exist: whole medical systems (such as traditional Chinese medicine), mind-body approaches, biological therapies, body-based treatments, and energy therapies. TCIM is used to help people resist infection, but people with moderate to severe COVID-19 symptoms often relied on integrative approaches using both traditional and Western medicine. It is estimated that over 90% of the infected population in Hubei China had used some form of traditional medicine to treat COVID. Ayurvedic medicine promotes immune-boosting strategies. Among biologically based therapies, there are vitamin therapies and "immune-nutrition" as well as

traditional botanical treatments. Energy therapies have been promoted by the Chinese government to treat COVID-19 which may cause a loss of qi energy and an imbalance with too much yang energy in relation to yin. In many ways, it is difficult to apply Western approaches of clinical trials to TCIM, where most treatments are preventive, restorative, and highly individualized. However, the role of TCIM in COVID-19 was significant and underscores the value of TCIM approaches not just in this pandemic but for other infectious diseases as well. This is a narrative review rather than a systematic review or meta-analysis.

Keywords
COVID-19; pandemic; traditional Chinese medicine; Ayurvedic medicine; homeopathy; Long COVID; Long-haul COVID; vitamin D; zinc

1. Introduction

Safe, highly effective, and readily available treatments for coronavirus disease 2019 (COVID-19) have eluded us, and even as the vaccine rolls out in many countries, there are still more questions than answers as to the optimal way to treat COVID-19. In poor countries, sometimes traditional or alternative treatments are the only available care. The search for conventional medical treatments for COVID-19 seems to have fueled interest in traditional, complementary, and integrative medicine (TCIM) techniques [1]. TCIM approaches often emphasize prevention, and the immune-supporting effects of certain TCIM therapies has been thought to offer benefit to patients to help them better resist infection [1]. TCIM is a broad field that has been grouped into five main categorizes by the National Center for Complementary and Integrative Health [2]:

- Whole medical systems, alternative medical systems (traditional Chinese medicine, Ayurvedic medicine, homeopathy)
- Mind-body treatments (meditation, yoga dance, art, music)
- Biologically based therapies (botanicals, herbal supplements, vitamins, whole diets, functional foods, etc.)
- Manipulative and body-based methods (osteopathic manipulation, chiropractic, massage, reflexology)
- Energy therapies (acupuncture, Qi gong, healing touch, therapeutic touch, Reiki)

It is best to call these TCIM strategies “approaches,” as the same or similar methods are often applied for prevention, treatment, and recovery [3]. Ancient and more modern TCIM practices can be challenging to study using Western clinical trial paradigms, because there is a wide range of treatments, many traditional products such as botanicals have inherent variability among strains, TCIM treatments are usually individualized to each patient, and traditional medicine is frequently integrated into a regimen that includes Western medical practices. In many parts of the world, TCIM products are available without a prescription and without even access to professional advice [3]. TCIM may be integrated with other medical practices without informing the various prescribers. COVID-19 makes an investigation of TCIM approaches even more difficult, in that studies of an infectious and highly contagious disease in a time of overstrained healthcare resources were not

always reasonable or even possible. Nevertheless, it is worthwhile to provide an overview of what is currently known about TCIM and COVID-19 as well as what remains to be clarified.

While developing countries have long embraced various TCIM traditions, developed nations are increasingly integrating them into their medicine [4]. In a telephone survey in India of 495 COVID-19 patients, 25.8% said they had use at least one type of traditional approach or product to treat COVID-19, with more than half of this group taking the Ayurvedic herbal tea Kadha [3]. No severe adverse events were reported by any of these respondents taking Kadha. A retrospective study of online searches during the COVID-19 epidemic found internet users in the United States, United Kingdom, Germany, Italy, and France (n=32) searched for TCIM-related terms such as "black seed," "vitamin C," "zinc," and "quercetin" which had strong positive correlations with searches by these same users for "COVID-19" and "coronavirus" [5]. Thus, there is an avid interest in whether TCIM techniques can be applied to the pandemic. Our aim was to create a short narrative review of the various types of TCIM strategies and how they have been used against COVID-19.

2. Methods

The PubMed database was searched for "COVID+complementary and alternative medicine" and yielded 28 items. The PubMed database was searched for "COVID+vitamins" and retrieved 839 items. "COVID+acupuncture" obtained 102 itemss. "COVID+Ayurveda" and "COVID+homeopathy" yielded 81 and 28 results, respectively. There was some duplication among the findings of the several searches. The Google Scholar database was searched for "COVID Complementary and Alternative Medicine," which produced over 60,000 results of which only peer-reviewed content was considered (many results were newspaper articles or non-authoritative websites). Study protocols and proposals, editorials, commentaries, or analyses of nonscientific topics (such as quantification of various types of press coverage of COVID-19 topics) along with reports about the potential in vitro antiviral properties *in vitro* of specific compounds were excluded. Searches were conducted in February and March of 2021 with the last search done on March 20, 2021. In addition, the authors reviewed the bibliographies of several of the articles. Only peer-reviewed articles were included. Two of the authors reviewed the abstracts of these articles (JVP and JAL) and grouped them by thematic relevance.

There are limited clinical trials of TCIM therapies for COVID-19 treatments and a paucity of large-scale controlled trials. A search on PubMed for the term "COVID traditional complementary integrative medicine" with the delimiters "clinical trial" or "randomized clinical trial" retrieved only one article and it was a study of exercise intervention. Nevertheless, there is some evidence as well as implications that TCIM approaches may be an adjunct to conventional approaches.

3. Results

3.1 Whole Medical Systems

3.1.1 Traditional Chinese Medicine

Traditional Chinese Medicine (TCM) has a long, documented history, which has reported on at least 321 different infectious diseases over the centuries. A Chinese medical text over a thousand years old reports that many diseases can be transmitted from person to person, and different

diseases can be identified by the symptoms they cause. TCM is less concerned with the nature of the pathogen than the specific symptoms it elicits [6]. Over the centuries, TCM has developed a three-step approach to infectious diseases and various plagues: quarantine of infected persons, staged treatment to prevent worsening of the infection, and post-infection treatment to rebuild strength and vitality in those who had the disease. In the COVID-19 era, this third step was renamed, "prevention of relapse after recovery" [6]. Although a variety of patented TCM medicines and herbal compounds have been described in the literature, no large-scale randomized controlled clinical trials have been conducted using TCM in COVID-19 patients [6].

TCM has been frequently used in China to treat COVID-19 patients [7]. And although it sometimes is reported that TCM has reduced COVID-19 morbidity and mortality, there are no large randomized clinical trials published [6]. Recently, databases have been set up to help monitor the benefits and adverse effects associated with the use of TMC in COVID-19 patients [8-10]. This is complex work, because many TCM remedies consist of multiple ingredients in varying proportions with treatments individualized for each patient [10]. TCM is primarily based on herbal treatments, often prepared as decoctions or taken in tablet form [11]. In China and other parts of the world, TCM remedies are sold prepackaged over-the-counter and involve a blend of two or more botanical products or substances. Furthermore, a TCM practitioner or business can also prepare products specifically for the individual patient, on the order of a compounding pharmacy. The foundational concept of TCM is promoting overall strength and wellness so the treatments are focused more sharply on boosting the immune system to help prevent the infection or to strengthen individuals fighting the earliest stages of infection. The role of TCM, particularly as a monotherapy, in treating patients with severe infections is more limited. Since TCM is believed to play a role in COVID-19 prophylaxis or adjuvant more than monotherapy, it is even more challenging to study using traditional Western clinical trial scientific models.

Despite the pandemic, the use of TCM in China actually dropped sharply in spring of 2020; a total of 1,935,827 visits to TCM practitioners were evaluated from January 2017 to May 2020 and the number of patients dropped by 33% and 40%, respectively, for March and April 2020 [12]. This was attributed to lockdowns, limited availability of medical services, a beleaguered healthcare system, and citizens' concerns about going to clinics where they might encounter infected people. Nevertheless, in China, TCM was considered an important medical option in managing COVID-19. In March 2020 in China, it was estimated that 91.5% of the infected population in Hubei, China had used TCM to treat COVID and over 4,900 TCM practitioners offered their services to pandemic victims [6].

During the previous SARS epidemic, TCM was combined with Western medicine to treat patients and was evaluated in a systematic review of six studies (n=366) which reported modest benefit in terms of lung infiltrate absorption but otherwise offered only modest or equivocal benefits [13]. In a meta-analysis of seven studies of COVID-19 patients (n=732), combining Chinese herbal medicine with the standard care (Western medicine) relieved symptoms, reduced inflammation, and improved lung imaging outcomes with no significant adverse events [14]. In a retrospective matched case-controlled study of 22 COVID patients from January 17 to 28, 2020 in China, all patients received standard supportive care and 11 patients also received natural herbal medicines [15]. The intervention group (natural herbal medicines plus standard care) had significantly shorter duration of fever (3.4±2.4 days vs. 5.6±2.2 days, p=0.03), significantly fewer cases of diarrhea (p=0.03), and a significantly shorter time to improvement of chest computed tomography (CT) scan (5.6±2.3 days

vs. 7.5±1.6 days, p=0.04) [15]. In a study of 50 hospitalized patients with mild COVID treated with TCM (Toujie Quwen granules), patients all returned to a normal temperature within one week with significant symptomatic improvement and no side effects [16].

In a meta-analysis of 42 studies (n=3,793) of patients being treated for pneumonia, including but not exclusively COVID-19-related pneumonia, the use of Lianhua Qingwen, a TCM product, supplementing conventional Western medicine was associated with significant improvement in flu-like symptoms, fever, cough, fatigue, myalgia, and dyspnea compared to patients who used only conventional Western medicine; the two treatment arms had similar adverse events. Lianhua Qingwen is a herbal decoction with antiviral properties consisting of 13 different Chinese herbs and was approved by the Chinese Food and Drug Administration in 2004 as a SARS treatment and which has been used to treat patients with COVID-19 [17]. In a systematic review and meta-analysis of 42 studies (n=3,793) of COVID-19-pneumonia patients, the use of Lianhua Qingwen significantly shortened the duration of flu-like symptoms, decreased catarrh and pulmonary rale, reduced fever, and exerted what was described as a "curative effect" [17]. Symptomatic improvement was also reported with Lianhua Qingwen in 154 COVID-19 patients and shortened the duration of fever [18]. Lianhua Qingwen, along with several other widely used TCM products (Jinhua Qinggan, Xuebijin injection, Qingei Paidu decoction, HuaShiBaiDu formula, and XuanFeiBaiDu granules) has been shown to be effective in downregulating ACE2 receptors, the support of entry for the SARS-CoV-2; analyses of the active components of these products found the compounds effective against the SARS-CoV-2 were quercetin, glabridin, and gallic acid [19]. In a study of 116 active ingredients found in TCM, it was found that Shen Zhu San was one of the most frequently used ingredients in TCM products for COVID-19, and its effects involved suppressing cytokine storm, protecting the alveolar-capillary barrier in the lungs, immunomodulation, and mediation of apoptosis and cell survival [20].

While TCM has not been studied in the same was as Western medical products, TCM advocates maintain that when TCM is used correctly, there are no serious risks [16]. When using TCM, either as monotherapy or adjunctive to Western medicine, early intervention is associated with shortening the course of the infection [8]. The role of TCM in terms of preventing COVID-19 is less clear-cut.

3.1.2 Ayurveda

Ayurveda may be the most ancient form of traditional medicine and is based on the concept that harmonious living is required for optimal health [21]. As such, Ayurveda may be considered a comprehensive approach to holistic health based on the tripartite nature of human beings as being body, mind, and spirit [22]. Ayurveda has a profound spiritual dimension that sees universal connections among the living and nonliving. Optimal health for an individual is reflected in the degree to which that person is balanced and harmonious. A variety of Ayurvedic herbs have been identified with specific therapeutic activities, prepared in traditional formulations such as arka, asavas, aristas, churna, taila, vati, gutika, bhasma, and others [21]. Ayurveda emphasizes the strengthening of the immune system as a preventive approach to infections. In fact, the Ayurvedic approach to immunity differentiates between natural immunity (Sahaja), age-related immunity (Kalaja), and acquired immiunity (Yuktikrut) [23]. The ancient emphasis on healthful diet and proper digestion supports what today is recognized as a healthy microbiome [24].

Ayurveda views each person has composed of three principle types of constitution that reflect how the person's mind, body, and spirit are connected. These types or doshas are known as vata,

pitta, and kapha, which have to do with movement, digestion and metabolism, and structure, respectively. These three doshas exist in their own balance in an individual. Those with a predominantly Vata nature tend to be creative, restless, and thin. Falling out of harmonious balance, a strongly Vata person might develop anxiety. Those with a predominantly Pitta nature are muscular, physically strong, and tend to be mentally alert but falling out of balance, the Pitta person may experience anger or rage. Finally, a person who is mainly Kapha will be calm, steadfast, and have great endurance and tenacity but can become overweight or greedy if they become disharmonious. (Sharma) Based on these dosha, Ayurvedic care is tailored for the individual.

Ayurveda employs a range of treatments that may incorporate physical exercise, meditation, relaxation, foods, hygiene, and breathing techniques to boost health. General healthy lifestyle practices such as good sleep hygiene, healthful diet, stress management, and avoiding people who are infected are also incorporated under Ayurveda. Some Ayurvedic treatments, such as turmeric, black pepper, garlic, and others, have antiviral properties, but have not been rigorously studied in their application to COVID-19 patients [25]. Curcumin, the main curcumoid in turmeric, is antimicrobial, anti-inflammatory, and is antioxidant, and is widely used in many parts of Asia for symptoms of coughs and colds [26]. In India, the Ministry of Ayurveda, Yoga, and Naturopathy, Unani, Siddha, and Homeopathy has been studying specific COVID treatments and encouraging research into using CAM for COVID-19 therapy [3]. Ayurvedic medicine is mainly promoted in India as an immune-boosting preventive strategy rather than treatment for infection [7, 27].

Typical Ayurvedic practices include the drinking of warm water to reduce fever, calm inflammation, ease rhinitis, and soothe allergies; this warm water may be mixed with certain spices, such as dry ginger or fennel [28]. Special mouthwashes are recommended for oral hygiene, which may help reduce upper respiratory infections [28]. Steam inhalation, sometimes using menthol or other aromatic oils, is recommended to reduce nasal congestion, facilitate breathing, and help with headaches [28]. Like other enveloped viruses, SARS-CoV-2 is heat sensitive and can be destroyed at warm temperatures that humans can tolerate [29]. Fever is the body's initial remedy to fight off the virus, but CAM treatments involving steam inhalation and warmth may indeed be helpful. Heat-based treatments have not been studied in this regard but could be practiced inexpensively by patients at home with little risk of harm, such as taking hot showers, using heating pads, and keeping warm [29].

3.1.3 Homeopathy

Homeopathy, based on the idea that "like cures like," is practiced all over the world including developed and developing nations; it is often used as part of Ayurvedic medicine. The products used in homeopathy are created based on the individual's symptoms rather than the disease pathology. Homeopathic medicines may be derived from botanicals or natural substances and are typically diluted and succussed [30]. The variability of symptomatic presentation in COVID-19 means that there is no standard homeopathic treatment regimen for COVID-19 [31]. In a study of 18 mild COVID-19 patients, homeopathic symptoms were collected and found to belong to one of six different clusters, making up two different sets of homeopathic symptom pictures [32]. However, the study of homeopathy is hampered by the fact that treatments are highly individualized.

3.1.4 Mind-Body Treatments

Mind-body practices such as meditation are sometimes promoted in the context of COVID-19 as a means to reduce stress, improve coping skills, and alleviate feelings of loss and loneliness [28]. Meditation has been shown to reduce inflammatory markers [33, 34]. Meditation is practiced by many traditions and is sometimes combined with Pranayama or breathing techniques that have been shown to improve lung function in healthy individuals [28, 35]. Yoga techniques which are thought to boost the immune system and help prevent COVID-19 infection, include meditative postures, mantras, breath regulation, and stress reduction. Specific yoga asanas or poses may be helpful to promote a strong immune system [36]. Yoga also emphasizes the cultivation of specific mental attitudes to help individuals feel balanced and positive rather than fearful or depressed [36]. While there is a paucity of evidence in support of these mind-body practices, they are mainly utilized to help people feel well and to strengthen their immune systems, rather than as a COVID-19 treatment [37].

3.1.5 Biologically Based Therapies

The novel term “immuno-nutrition” has been coined to describe a burgeoning interest in vitamin and mineral supplements, particularly in light of their alleged immune-boosting powers for COVID-19 prophylaxis. Because of the pro-inflammatory response in COVID-19 and cytokine storm, antioxidants are considered to be beneficial [38]. Lower concentrations of vitamin A have been correlated to increased host susceptibility to influenza, which suggests it might benefit against other pathogens [39]. However, it is not known if lower concentrations of vitamin A are related to COVID-19 susceptibility or exacerbated course of the disease. Vitamin C has antioxidant properties and is known to be effective in attenuating upper respiratory tract infections, which suggests a possible role in COVID-19 and vitamin C is often included among many multimodal or vitamin-based CAM treatments [39]. However, vitamin D is by far the most studied in the context of COVID-19, namely because vitamin D deficiencies appear to exist in the same populations at highest risk for COVID-19 morbidity and mortality, namely the elderly, Blacks, and Asians. Further, vitamin D may help to mediate inflammation [39, 40]. Risk factors of vitamin D deficiency mirror the risk factors for COVID-19: older age, obesity, male sex, hypertension, and coagulopathy [40]. The use of vitamin D supplements has been shown to reduce the incidence and severity of viral infections in general [40]. Further study is needed, but when taken at recommended doses (10,000 international units [IU]. a day are safe but likely 1,000 to 2,000 IU suffice for beneficial effects), vitamin D is safe and promotes a healthy immune system [41].

Zinc deficiency has been associated with increased inflammation and remodeling of lung tissue in an animal model [42]. Zinc was shown to inhibit the synthesis, replication, and transcription of coronaviruses [43]. Zinc is sometimes used as an adjunctive agent with both conventional and CAM regimens in the treatment of COVID-19 [44].

While there are intriguing findings about the role of vitamins with respect to COVID-19 and, indeed, with viral infections in general, there is very limited evidence in support of their use [45]. However, the beneficial effects of these vitamins and minerals cannot be disputed when used appropriately; it is their specific role in the prevention or treatment of COVID-19 that warrants further investigation.

From a study of medicinal plants by the World Health Organization and the European Medicines Association, a list was compiled about botanical products for use in adults with mild COVID-19 symptoms and compared to acetaminophen, ibuprofen, and codeine as reference drugs [46]. A total of 39 herbal remedies were identified with positive benefits over reference drugs in 5 cases, promising results in 12 cases, and unknown for the balance. No compelling evidence could be found in support of acetaminophen or codeine for COVID treatment, although ibuprofen was promising [46]. The antiviral properties of certain essential oils has led to speculation that these agents might be beneficial in treating COVID although poor solubility, solvent toxicity, and volatility can limit their use [47]. It has been proposed that combining such agents with carriers based on nanotechnology ("nano-carriers") might expand their potential use to treat viral infections [47].

3.1.6 Manipulative and Body-Based Methods

Chiropractic care has been cautioned about overpromoting the benefits of manipulative treatments in terms of COVID-19 prevention or treatment. Social media claims, in specific on Twitter, suggested that spinal manipulation could boost immunity and help prevent COVID-19, a claim that is unfounded and was called out as such by some in the chiropractic community [48, 49]. The Chinese practice of Qigong is less familiar outside China but involves body movement synchronized to breathing combined with meditation. These are gentle, low-stress postures and exercises which are thought to be helpful to prevent COVID-19 infections and promote recovery [50]. T'ai Chi, a similar movement-based low-stress therapy is being studied now in a clinical trial for its effectiveness in helping COVID-19 patients recovery [51].

3.1.7 Energy Therapies

One of the premises of TCM is that the body contains a fundamental energy called qi [6]. Vital qi in proper flow and balance brings health, but disruptions in qi or insufficient amounts of vital qi can cause physiologic disease. With adequate vital qi, the body has strong natural immunological defenses against disease. Pathogens, such as viruses, may attack the body, but they end up doing battle with qi. TCM treatments aim at supporting qi in fighting disease and restoring balance and vitality [6]. From the Chinese government, a document entitled the Diagnosis and Treatment Program for Coronavirus Disease 2019 describes the pathogenesis of COVID-19 as an "epidemic pathogen invading the body, followed by entering the internal organs and transforming into heat, resulting in pathogen trapping in the interior, and healthy qi [energy] collapsing and deficiency of qi and yin." Yin and yang refer to complementary forms of energy, with yin referring to cooler expansive energy and yang to warmer contracting energy [52]. Based on this understanding, COVID would be more dangerous to older people or those with diseases that weakened their natural qi, while younger people would have more natural immunity. Improving the flow of qi is a fundamental of TCM and acupuncture as well.

Acupuncture clinical trials and meta-analyses with COVID-19 patients are ongoing [53-55]. Two case studies report on improvement with acupuncture as adjunctive to conventional therapy in COVID-19 patients [56]. A third case study described a COVID-19 patient with pneumonia complicated by hypoxic-ischemic encephalopathy that was improved with conventional treatment plus acupuncture; the patient had spontaneous eye opening and limb movements after the first

acupuncture treatment and he could be weaned off the ventilator following two weeks of acupuncture treatments [57].

In TCM, moxibustion is a technique that involves burning moxa, a cone composed of mugwort leaves, on acupuncture points of the body to help enhance the flow of qi. Acupuncture with and without moxibustion has been used predominantly in China to help relieve COVID symptoms [58]. Acupuncture with moxibustion has also been proposed as a prophylaxis, for example, for patients exposed to the virus but who were not yet symptomatic [59].

4. Discussion

TCIM poses formidable challenges to Western medical way of thinking, in that it approaches care and treatment using a different paradigm. TCIM stresses preserving wellness rather than treating disease. Many of these TCIM approaches to COVID-19 emphasize prophylaxis with specific strategies: boosting the immune system, restoring mind/body balance, and promoting a positive mental energy. Furthermore, TCIM has also introduced specific care paradigms to aid those who have recovered from COVID-19 to regain their old energy and vitality; this runs somewhat contrary to Western medicine, which emphasizes care for the sick and then, upon recovery, dismisses the patients from the system, TCIM was often integrated with Western medicine [60]. The great advantage to TCIM approaches is that most of them are not associated with serious side effects. Patients may often benefit from traditional medicine at home at minimal expense with little to no risk.

TCIM approaches often focuses on prevention and recovery, and these are aspects of the disease trajectory that Western medicine seems to neglect. As the syndrome of Long-haul COVID or Long COVID emerges, TCIM may play an important role.

Our study is limited by several factors. It is a short narrative review of a vast topic. It was impossible in this study to go into depth with specific agents, botanicals, or treatments. The paucity of randomized clinical trials and the weakness of some of the trials that have been conducted makes a meta-analysis or systematic review impossible.

5. Conclusions

TCIM approaches offer a multifaceted approach to wellness, disease prevention, holistic health and well-being, mind/body balance, and strengthening of body and immune system. To this end, TCIM strategies have been used in the prophylaxis of COVID-19, in its treatment, and to help revitalize those who have recovered. When treating an active infection, particularly when the infection is severe, traditional medicine is often integrated into Western medical techniques. TCIM represents a paradigm shift in Western medical thinking and one that makes study and quantification challenging. Nevertheless, there is much value in TCIM practices for treating infectious diseases, including but not limited to COVID-19.

Author Contributions

Concept: JP, GV; Literature Search: JL; Analysis of literature: JP, JL, PM, GV; Structure and outline: PM; Medical writing: JL; Critical review and revisions: JP, PM, GV.

Competing Interests

The authors have declared that no competing interests exist.

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