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The COVID-19 infection and the immune system: The role of complementary and alternative medicines.

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Abstract

Emerging in China in late 2019, the new COVID-19 virus infection epidemic is growing rapidly and new cases are reported around the world. The first cases were linked to a wet market, and subsequently, the virus has spread rapidly in China through human-to-human transmission, and the universal impact of the COVID-19 virus is now spreading worldwide. The disease originated from COVID19 is a type of viral pneumonia that is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Currently, no clinically approved antiviral drugs have been introduced for SARS-CoV-2 infection. Identifying the mechanism of action of the virus and its interaction with the immune system will help prevent and treat the disease. In other words, understanding the disease and its effect on the immune system will improve disease management. The immune system has a fundamental protective function against most infectious diseases such as SARS-CoV-2. This study investigates the effectiveness of Complementary and Alternative Medicines (CAMs) in boosting immune response against infection diseases. The role of vitamins in COVID-19 in its early stages is also investigated and the previous research findings are reported. The result of this study is important especially for the patients with COVID-19 who may found CAMs as effective way in boosting immune response against this virus and useful option for management and treatment of COVID-19 in its early stages. We suggest that further studies through consumers' experience analysis on CAMs are required to come to robust conclusions in the effectiveness of CAMs for management and treatment of COVID-19.

Keywords: Complementary and Alternative Medicines (CAMs), COVID-19, Infection epidemic, Immune system, Vitamins.

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Introduction

Protecting the body against infection, the immune system prevents death by producing protein molecules called antibodies that bind to the antigens of infectious agents [1,2]. Through frequently interacting innate and adaptive mechanisms, the immune system defends against bacterial infection. The immune system assesses the amino acid sequence space of potential antibodies for identifying invader pathogens. According to Deem [1], a hierarchical strategy is evolved by the immune system for recognizing the effective antibodies in the infinite protein sequence space. The two components of the innate immune system and the adaptive immune system form the pervasive immune system [3]. The innate system consists of exterior defenses (e.g. mucous membranes and the skin), serum proteins, and nonspecific phagocytic leukocytes [3,4]. This system is a more primitive one built formerly into cells that are located on the front line of defense against bacterial invasions, including epithelial cells in the lung, gut, skin, and periodontium as well as neutrophils and macrophages [5]. However, the adaptive immune system, which develops in a longer time, responds specifically. In fact, after evolvement, it provides a more specific response against invader organisms. Several investigations have shown that the virus has some effects on immune system operations [6-9]. According to the literature, different parameters of immune function are influenced by viruses including antibody generation, immunoglobulin levels, induction of immunological tolerance, graft-versus-host reaction, graft rejection, delayed-type skin reaction, lymphocyte transformation, and phagocytosis. In Notkins et al. [6], the authors have examined these parameters comprehensively.

Recognizing the disease and its consequences on the immune system will support its better management providing preferred treatment strategies and more effective prevention [10]. The complexity of the disease becomes more apparent when it is revealed that certain segments of the population are more susceptible to severe infection and subsequently to death [10]. The responses of innate and adaptive immune systems make the base of the host anti-microbial defense. In order to quickly control and effectively deal with the viral infection, the innate immune system operates and simultaneously triggers the adaptive immune system. The innate immune system distinguishes influenza viruses through multiple mechanisms [11]. This system, which is programmed genetically for meeting the similar features of attacking microbes, acts rapidly and protects the body against infection early.

Among phagocytic cells, macrophages, neutrophils, and Dendritic Cells (DCs) play a major role in the innate immune response to influenza [10]. Influenza virus targets airway epithelial cells lining the respiratory mucosa. After infecting and lysing these cells, the virus of influenza A can infect alveolar macrophages and DCs residing in the airway [11]. As soon as sensing infection, DCs taking up viral antigens operate the main function in priming effector T cell responses [11,12]. After activation, influenza virus-specified CD4 and CD8 T cells operate together with antibody-generating B cells to elevate viral release in the lung [11, 13]. T cells are principal moderators of the immune response and handle their performances by modulating the functions of other immune cells and modifying the behavior of parenchymal and endothelial cells [14]. In the case of COVID-19, after entering cells, the virus's antigen will be introduced to the antigen presentation cells, which are among the main parts of the body's antiviral immunity [15].

More than 80 percent of the world's population uses Complementary and Alternative Medicines (CAMs). In the US health care system, CAM is becoming an increasing component, with 70 percent of the population using that at least once and costing $34 billion annually [16]. Since the establishment of the National CAM-Center, the number of basic science and treatment-based clinical trials about CAM has increased significantly [16]. It is estimated that the worldwide market for herbal remedies, including herbal products and raw materials, will grow 5 and 15 percent annually. The worldwide herbal drug market is estimated at $62 billion, which is estimated to grow to $5 trillion by 2050. The global pharmaceutical market in 2004 was worth $ 550 billion and in 2008 it was up to $ 900 billion [17]. Herbal sources of immune-boosting materials are consumed in many countries to raise health, to promote the body’s normal resistance against infectious agents and to prohibit as well as to cure various diseases [18].

The Immune System and CAMs against Viruses

It is found that CAMs are effective in boosting immune response vs. diseases. Several cases of CAMs proposed for prohibiting and curing diseases are discussed in this section. It has been suggested that as a CAM, curcumin which is the orange component of turmeric, can enhance the antibody response even if it takes at low doses [19]. In fact, the beneficial effects of curcumin in improving arthritis, atherosclerosis, allergy, asthma, Alzheimer's disease, diabetes, heart disease, and cancer are attributed partly to its ability to modulate the immune system. Furthermore, several surveys demonstrate that curcumin is able to modulate both the activation and the proliferation of T cells [20,21]. It has also been shown that curcumin has the potential of regulating the growth and response of different immune cells. It affects NK cells, T cells, B cells, DCs, neutrophils, and macrophages [19]. Providing minerals, vitamins, amino acids, or herbs, nutritional supplements are used to enrich the diet. These are mostly accompanied with CAMs, which include a group of various medic and health care orders, actions, and supplies not classified as a part of conventional medicines. Nutritional supplements appear to strengthen the immune system profiting transient immunosuppression those results from intense training [22]. It has been demonstrated that Vitamin C [23], Vitamin D [24] and zinc [25] boost the immune system versus viruses. Two assays executed in South Africa have shown promising results about vitamin C supplementation [22,26]. Vitamin D has also considerable effect on immune system. It has been demonstrated that vitamin D modulates innate and adaptive immune systems [5,27].

Both immune systems are adjusted by vitamin D, which suppresses the adaptive immune system but potents the innate immune response [5]. In Hamzaoui et al. [28], it is stated that vitamin D has reinforcing and inhibitory effects for the innate and adaptive immune systems, respectively. In Shirvani et al. [29], it is also stated that vitamin D, which has anti-inflammatory properties and modulates immunity in different ways, is effective in physiology and autoimmunity, and its deficiency is associated with chronic inflammatory diseases. Epidemiological surveys have confirmed that poor vitamin D consumption adheres to the raised risk of multiple diseases including autoimmune drawbacks. It seems that the immune regulatory effect of vitamin D has a significant role in this adherence. Adaptive immune cells are direct targets of vitamin D metabolites [30]. In fact, as concluded in Gruber-Bzura et al. [31], vitamin D is part of a complex set of factors that influence the immune response. Therefore, it is necessary to evaluate the serum level of vitamin D in children and the elderly and to maintain it at optimum levels and micronutrients should be used for improving health and fighting diseases.

The coronavirus disease 2019 (COVID-19) has been spread in Asia and all over the world [32] and has created a universal health emergency case [33]. This virus has infected more than 85,403 people worldwide, far more than people affected by SARS [33]. The radiological, clinical, laboratory, and epidemiological features as well as the clinical consequences and treatment of patients with laboratory-confirmed COVID-19 pneumonia were discussed in the recent study. This is not the first severe respiratory disease that has been spread by the coronavirus type. During the past two decades, different strains of this virus have created three epidemic diseases

including the Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS), and COVID-19 [15,34].

The behavior of new coronavirus 2019 is similar to SARS-CoV so that it called SARS-CoV-2. Continuing by Acute Respiratory Distress Syndrome (ARDS) and septic shock, it eventually causes multiple organs to fail by the virus-induced cytokine storm in the body [35]. Similar to SARS-CoV and MERS-CoV, no clinically confirmed antiviral drug has been introduced for SARS-CoV-2 infection yet [15]. According to Menachery et al. [36], down-regulation of gene expression related to antigen presentation due to MERS-CoV infection demonstrates that coronavirus can effect on the antigen presentation. Therefore, in order to produce a drug and to treat SARS-CoV-2-linked disease, it is necessary to block its evasion from the immune system.

It is claimed that the coronavirus pandemic can be significantly downed or ceased by urgent popular consumption of high amounts of vitamin C [37-39]. Antiviral activity of vitamin C has been recognized and approved in the past decades, but its impact has not been widely broadcasted and, in particular, insufficient information has been provided on its effect on coronavirus. It seems necessary to activate the body's maximum antioxidant capacity and natural immunity to minimize the symptoms of any virus attack. Vitamin C can be administered concurrently with potential medications to treat the disease in acute conditions. The oral administration of vitamin C up to the daily threshold of bowel tolerance will be effective for most people. For serious cases, intravenous infusion of vitamin C is recommended [38]. Besides, it is claimed that the over activity of immune cells results in lung injury following COVID-19 pneumonia [35]. According to [35], high-dose vitamin C administration can suppress cells that are effective in this level of immunity, and intravenous injection of high-dose vitamin C can be a safe and useful option for treatment COVID-19 in its early stages.

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