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Effect and application of vitamin C on Immune function during the COVID-19 pandemic

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Abstract. To present a fresh idea for the COVID-19 treatment, the vitamin C influence on the immunity of the novel coronavirus was studied, by browsing through the pertinent literature. Using keywords such as "vitamin C", "COVID-19", "nutrition" and "immunity", Chinese and English searches were conducted in PubMed, Google Scholar, CNKI, Wanfang Medical, and other databases to analyze and summarize the vitamin C immune effect on the epidemic situation of COVID-19. In the treatment of COVID-19 patients, it could be concluded that vitamin C could have a certain positive influence, but the specific mechanism, the best use time, and the correct dose still need to be studied.

Keywords: Vitamin C, COVID-19, immune function.

1. Introduction

The SARS-CoV-2 was found to be responsible for COVID-19, a serious infectious disease. Around 600 million cases of COVID-19 have been confirmed by September 2022 the world over, and death amounting to more than 640, since the first report in China in December 2019 [1]. World operations were severely impacted by the emergence of COVID-19. Leading to the activation of the T cells, macrophages, and neutrophils to be activated through the continuous increase of the Tumor Necrosis Factor α (TNF α), IL-6, along with the cytokines (including Interleukin (IL)-1), the COVID-19 is known to infect only the epithelial cells of the pulmonary region through the Angiotensin Converting Enzyme-2 (ACE-2) receptor, further infecting the macrophages and activating them through the pertinent receptor. This uncontrolled inflammatory congenital response and impaired adaptive immune response can lead to local and systemic tissue damage, which is often the cause of serious consequences of COVID-19 [2]. It has been proved that vitamin C can be used as a strong oxidant to participate in a variety of physiological functions of the human body [3].

2. Literature review

2.1. Status of COVID-19 Infection

The infective status of COVID-19 has been known to be closely associated with a Cytokine storm. Being a major factor in patient deaths under COVID-19, the Cytokine storm happens to be a common risk

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factor for the severe conditions of such patients. Leading to a variety of immune cells (like the lymphocytes, macrophages, and dendritic cells) being activated abnormally, besides releasing a large number of cytokines (IFN-γ, IL-6, IL-10, and TNF-α), the cytokine storm is caused by a viral infection disrupting the relative balance of the anti- and pro-inflammatory factors of the immune system, inducing serious complication along with Acute Respiratory Distress Syndrome (ARDS) [2]. cytokine storms can also cause damage to a series of important organs, such as heart, lung and liver [4].

2.2. Vitamin Intake and Synthesis

Vitamin C exists mainly in humans in the form of reduced ascorbic acid, while compared with most vertebrates, and humanoid primates (including humans), but it cannot be synthesized by itself and can only be ingested through food [5].

The concentration of vitamin C in normal people should be more than 23 μ mol / L, less than this value indicates that they are in a state of hypovitaminosis C, and when the plasma concentration of vitamin C is less than 11 μ mol / L, there will be symptoms of scurvy [6]. At present, there is no consensus on the intake of vitamin C in the world, and there is a big difference between them, and there are also differences in the recommended intake of vitamin C among people at different physiological stages [7].

A crucial role in the absorption and transportation of vitamin C is played by the transporter of vitamin C dependent on sodium, is divided mainly into SVCT1 and SCVT2. The distribution of SVCT2 is expressed in most of the organs, whereas, the SVCT1 has limited distribution, mainly in the absorptive cells. SVCT1 absorbed and transported has a saturation effect, and this limitation can be avoided by intravenous injection [8]. At the same time, the affinity of SCVT2 to vitamin C was higher than that of SVCT1, even though the transport rate of vitamin C was lower than that of SVCT1, which led to the transport can be carried out under the condition of low plasma vitamin C concentration [9]. This suggests that injection may be a better choice than oral administration of vitamin C.

2.3. The Status of Vitamin C In COVID-19 Patients

In patients with COVID-19, vitamin C deficiency is very common. Sinnberg et al. [10] found that the content of plasma vitamin C in COVID-19 patients was significantly lower than that in people without COVID-19 infection, besides, between the severity of COVID-19 and the vitamin C concentration, an inverse relationship was found to exist. Various factors affecting the normal expression of SVCT1 and SVCT2, the conditions of various diseases, inflammatory factors, and oxidative stress, could be the reason for this vitamin C deficiency, thus reducing the efficiency of vitamin C absorption in the human body [11]. Of course, it is also possible that vitamin C is heavily consumed in the process of protecting human cells from reactive oxygen species (ROS) released by phagocytic activation caused by infection [12].

2.4. The Physiological Role of Vitamin C In the Immune System

(1) Reduced inflammatory Factors. The serious result of COVID-19 is often due to systemic organ and system damage caused by cytokine storms, and vitamin C can reduce the release of related factors to alleviate inflammation. For example, IL-6, as a key factor of inflammation, is often elevated in cytokine storms in patients with COVID-19. Vitamin C can delay the level of inflammation in patients by blocking the release of IL-6 from human endothelial cells induced by endothelin-1 (ET-1) [13]. At the same time, coronavirus upregulates key pro-inflammatory cytokines (TNF-α, IL-1) through the NF-κB pathway, and vitamin C can reduce ROS production and inflammation by inhibiting NF-κB activation induced by TNF-α [14].

(2) Treatment Complications. The study of Wald et al. [15] suggested that the addition of vitamin C had a beneficial effect on the outcome of patients with sepsis, whether it is used alone or combined therapy. The adrenocortical, antioxidant, immunomodulatory, and anti-inflammatory hormonal effects of vitamin C could have been the cause for this.

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(3) Enhance Immune Cells. A highly regulatory role is played in the immune system by vitamin C as an important element of nutrition for the human body. For example, with vitamin C in normal levels also being necessary for the full performance of their functions by the NK cells and having a positive impact on the growth and development of the T cells and B cells, vitamin C is important for the lymphocytes in the immune system [16]. At the same time, vitamin C accumulates in phagocytes including neutrophils and macrophages, thus enhancing their chemotaxis and phagocytosis, increasing the production of ROS and killing microorganisms [17].

3. Progress in clinical research

Due to the participation of vitamin C in human physiological function, vitamin C has certain benefits to COVID-19 patients in theory, and some studies have confirmed this.

For example, vitamin C does have a certain effect on preventing the deterioration of COVID-19 symptoms. Compared to the patients having normal treatment, the patients given glycyrrhizic acid and vitamin C by mouth, the probability of ARDS is significantly reduced, as observed by Tan et al. indicating that the deterioration of COVID-19 due to the reduced complications was aided by vitamin C and glycyrrhizic acid [18].

Thus, in treating patients with acute COVID-19 also vitamin C plays an important role. Besides significantly delaying the average time of death and reducing significantly their mechanical ventilation rate and the rate of sudden cardiac arrest, high levels of intravenous vitamin C were found to be highly beneficial to patients having severe COVID-19, by Hess et al. [19].

At the same time, vitamin C also has a certain effect on reducing the length of stay and improving the prognosis of patients. Studies by Cheng et al. [20] have presented that patients who receive vitamin C (10g/d for ordinary, 20g/d for severe) intravenously spend less time in the hospital than those who receive standard treatment.

The way vitamin C is given may have an effect on the response of COVID-19 patients to vitamin C. Fogleman et al. [21] gave mild to moderate COVID-19 patients an oral placebo, vitamin C (1000mg/day) and melatonin (10mg/day), respectively, while the results showed that only oral melatonin patients showed a faster rate of disappearance of COVID-19 symptoms.

Nonetheless, the vitamin C impact on patients with COVID-19 has not been supported by any study so far. Between those patients receiving vitamin C injections and those not receiving, a retrospective study by Suna et al. [22] found not a significant difference in the mortality rates, the need for advanced oxygen support, intensive care, readmission rate, and stay in the hospital. Likewise, no significant benefit was found for the patients by the mendelian randomization study of vitamin C for treating the patients of COVID-19 by Hui et al. [23]

4. Conclusion

While some countries incorporated vitamin C support in their treatment guidelines for COVID-19 patients, certain studies have indicated the impact of the positive nature of vitamin C on the treatment of such patients in the world. For example, the ‘Shanghai 2019 expert consensus on Comprehensive treatment of Coronavirus Diseases’ in China recommends that patients be given high doses of intravenous vitamin C (100-200mg/kg/d) to prevent cytokine storms. Nevertheless, with certain studies not supporting the benefits to patients with COVID-19 with vitamin C in their treatment process, the specific mechanism of vitamin C on COVID-19 has remained unclear. Hence, for determining the best time for use, the correct dosage, and the mechanism of treatment, further studies need to be conducted about the effect of vitamin C on COVID-19 patients.

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