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New Coronavirus (2019-nCoV/COVID-19) and Vitamin C

Yeni Koronavirüs (2019-nCoV/COVID-19) ve Vitamin C

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ABSTRACT For the first time in December 2019, a case of pneumonia of unknown etiology was reported in Wuhan, China. Then, in addition to China and on the basis of increasing incidence and mortality rates in other international countries, the global emergency health status was declared by the World Health Organization Emergency Committee, and a new coronavirus was reported.Due to the very high contagion rate of the new Coronavirus (COVID-19), it has affected and continues to affect quite a lot of people from all age groups in the world. General clinical signs of COVID-19 are high fever, cough, nasal congestion, dyspnea, myalgia, fatigue, upper and lower respiratory tract infection and diarrhea. The most important and fatal clinical sign of the virus has been described as pneumonia. Unfortunately, no vaccine or special antiviral drug has been developed against COVID-19 yet. Therefore, the purpose of this review is to examine whether intravenous vitamin C administration is a promising method for the COVID-19 pandemic in accordance with the most recent evidence. Using vitamin C to prevent or treat diseases is often classified in complementary and alternative medicine. For this reason, it should never prevent the actual treatment. Studies have found that high doses of vitamin C reduce lung damage in COVID-19 and other flu infections. Therefore, intravenous vitamin C administration may be useful in addition to COVID-19 treatment.There is a need for high-level clinical studies on the effect of Vitamin C administration on COVID-19.

Keywords: COVID-19; 2019-nCoV; the pandemic; vitamin C; pneumonia; acut respiratory distress syndrome

ÖZET İlk kez, 2019 yılı aralık ayında, Çin'in Wuhan şehrinde, etiyolojisi bilinmeyen bir pnömoni vakası bildirilmiştir. Daha sonra Çin'e ek olarak ve diğer uluslararası ülkelerde artan vaka ve ölüm oranlarına dayanarak, Dünya Sağlık Örgütü Acil Durum Komitesi tarafından, küresel acil sağlık durumu ilan edilmiş ve bu duruma yeni bir koronavirüsün neden olduğu bildirilmiştir. Yeni Koronavirüsün (COVID-19) bulaşıcılık hızının çok yüksek olması nedeni ile dünya üzerinde her yaş grubundan oldukça fazla insanı etkilemiş ve etkilemeye devam etmektedir. COVID-19'un genel klinik belirtileri yüksek ateş, öksürük, burun tıkanıklığı, dispne, miyalji, yorgunluk, üst-alt solunum yolu infeksiyonu ve diyaredir. Virüsün en önemli ve ölümcül seyreden klinik belirtisi ise, pnömoni olarak tanımlanmıştır. Ne yazık ki COVID-19'a karşı henüz herhangi bir aşı veya özel antiviral bir ilaç geliştirilmemiştir. Bu nedenle bu derlemenin amacı en güncel kanıtlar doğrultusunda intravenöz vitamin C uygulamasının COVID-19 pandemisi için umut verici bir yöntem olup olmadığının irdelenmesidir. Hastalıkları önlemek veya tedavi etmek için vitamin C kullanımı genellikle tamamlayıcı ve alternatif tıp olarak sınıflandırılmaktadır. Bu nedenle asla asıl tedavinin önüne geçmemelidir. Yapılan çalışmalarda COVID-19 ve diğer gribal enfeksiyonlarda yüksek doz vitamin C akciğer hasarını azalttığı bulunmuştur. Bu nedenle COVID-19 tedavisine ek olarak intravenöz vitamin C uygulaması yararlı olabilir.Vitamin C uygulamasının COVID-19 üzerindeki etkisine yönelik kanıt düzeyi yüksek klinik çalışmalara gereksinim vardır.

Anahtar Kelimeler: COVID-19; 2019-nCoV; pandemik; vitamin C; pnömoni; akut respiratuar distres sendromu

For the first time, a case of pneumonia of unknown etiology was reported in Wuhan, China in Hubei Province in December 2019. Later on 30 January 2020, the World Health Organization Emergency Committee, based on the increasing rates of cases and deaths in China and other international countries, was declared a global emergency health situation and it was reported that a coronavirus was caused. The situation after the increase in the rates of deaths and deaths in many countries after January has been accepted and announced as a pandemic of the "New Coronavirus (2019-nCoV/COVID-19)".[1,2] In Turkey, the first cases associated with pandemic COVID-19 is described by the Ministry of Health on March 10, 2020.

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Coronaviruses were first described by Tyrell and Bynoe in 1966 on patients suffering from a cold.[3] In the following process, many new types of coronaviruses were discovered, including SARS in 2003, MERS-CoV in 2012 and CoVID-19 of Wuhan origin. COVID-19 from the coronovirus family is an enveloped RNA virus. There are protrusions on the outer surface of the virus and it is named as coronavirus under the microscope because it resembles the crown sphere of the sun (Latin: corona=crown).[1,4]

COVID-19 has affected and continues to affect quite a lot of people from all age groups in the world due to its high contagion rate compared to other coronaviruses. Clinical symptoms of the disease are generally determined as fever, cough, nasal congestion, dyspnea, myalgia, fatigue and upper-lower respiratory tract infection and diarrhea.[2,4]

The most important and fatal clinical symptom of COVID-19 disease was defined as pneumonia. Pneumonia; decreased oxygen saturation, change in blood pH, prominent frosted glass appearance in the radiological examination, alveolar exudate and interlobular involvement, and respiratory failure. In addition, lymphopenia is frequently seen in these patients and C-reactive protein and proinflammatory cytokines increase.[2] In a study; 98% of the patients had involvement on both sides of the lung and a clear frosted glass was recorded in the radiological examination. Moreover, Acute Respiratory Distress Syndrome (ARDS) (29%) and secondary infection (10%) were identified as COVID-19 complications.[5]

VITAMIN C

Vitamin C, also known as ascorbic acid is a powerful antioxidant. Antioxidants neutralize unstable compounds called free radicals in living things, and antioxidants prevent cellular damage caused by these unstable compounds or allow the cell to regenerate itself.[6] As it is known, oxygen, which is necessary for living creatures to survive, is an essential molecule. If the oxygen molecule is reduced incompletely, reactive oxygen species (ROS) that damage the cells occur. If ROS and free radicals are excessively formed in cells, this phenomenon is defined as "oxidative stress".[7] Oxidative stress may affect the function of the mitochondria of the cell and cause structural changes in the mitochondrial membrane.[8] It has been determined that the change in the mitochondrial membrane prevents antiviral signal transduction and thus reduces the intensity of the antiviral immune response.[9]

There is a balance between free radicals formed under physiological conditions in the organism and their antioxidant defense system, which is their scavenger (reducing). In the disease process, this balance shifts in favor of free radicals, causing a serious increase in oxidative stress. COVID-19 infection is also a serious source of oxidative stress for the organism. Therefore, antioxidant substances such as vitamin C, which have been shown to be effective in correcting the integrity of mitochondria, are needed to reduce oxidative stress, which damages the cells.[8,10]

THE EFFECT OF VITAMIN C ON IMMUNE SYSTEM

Vitamin C affects the immune system in several ways. Antioxidant activity may decrease inflammation by providing improvement in immune function.[11] Vitamin C also enhances the phagocytosis ability of immune system cells and contributes to the destruction of harmful bacteria and other particles.[6] Each disease is stress for the body and psychological and physiological stress causes the response to appear. Although the stress response is necessary to cope with the existing infection in the body, the increased stress response damages the body. COVID-19 also causes an increase in stress response in the body, causing severe symptoms and fatal consequences. Excessive glucocorticoid release due to stress response may induce ROS production and result in systemic suppression of the innate antiviral immune response. In a study, it has been reported that vitamin C may play an important role in stress and stress-related glucocorticoid release. This significantly changed the balance of T cells and reduced natural killer (NK) cell activity.[8]

VITAMIN C, COVID-19 AND PNEUMONIA

No vaccine or a special antiviral drug has been developed against coronavirus diseases, including COVID-19 yet. Symptomatic therapy, isolation and various experimental applications are included in controlling the disease. Hand washing, using a mask, maintaining

social distance and not touching the face without washing hands are recommended measures to prevent the spread of COVID-19, which includes contact and respiratory isolation. In addition to these measures, can intravenous vitamin C administration be a promising method for the disease in addition to the current pneumonia treatment? Vitamin C was first used in the treatment of scurvy disease in 1930.[12] In recent studies, Vitamin C has improved endothelial function, lowered blood pressure, reduced glucose level in patients with type 2 diabetes, decreased bronchoconstriction, shortened the duration of colds and prevented pain has been determined.[12-16] In this context, whether vitamin C is a possible treatment option for flu infections has been the subject of research for many years. In a study conducted by Ritzel in 1961, it was found that vitamin C (1 g/day) treatment applied to children in the ski school reduced the duration and incidence of influenza infection.[17] In one study, 35% of elderly Scottish patients with acute respiratory infections were reported to have very low vitamin C plasma levels.[18]

In a study where vitamin C supplementation was applied to mice with H1N1 infection, it was determined that the activation of immune cells such as NK and T lymphocytes increased in mice after vitamin C administration. After these studies, vitamin C has been reported to have antiviral effects. In addition, it has been found that in mice infected with influenza virus, it suppresses viral replication and lung inflammation, decreases proinflammatory cytokine production and ultimately increases survival rate.[10] In a study conducted by Cai et al., externally induced stress was applied to mice infected with influenza viruses. Oral vitamin C (125 and 250 mg/kg) was administered to the experimental group mice. It was determined that control group mice without vitamin C significantly increased the severity and mortality of influenza-induced pneumonia, but vitamin C administration decreased these rates. As a reason for this decrease, it has been stated that vitamin C is associated with the inhibition of enzyme synthesis called CORT in mice equal to human corticosteroids. Physiological and psychological stress causes excessive release of corticosteroids in the body. This leads to the formation of negative nitrogen balance in the body and weakening of the immune system. Vitamin C, on the other hand, is stated to regulate the steroid hydroxylate enzyme in the adrenal gland and suppress excess corticosteroid synthesis. In addition, vitamin C treatment to mice has been found to inhibit pulmonary morphological changes induced by influenza virus and reduce structural damage to blood vessels and alveoli. After oral vitamin C administration, inflammatory cytokine levels decreased four days after infection. As a result, vitamin C has been found to prevent influenza virus and associated pneumonia in mice.[8] Another study found that vitamin C reduced the incidence of pneumonia by 80% in influenza A patients.[19] In the study conducted by Nathens et al. with 594 patients with critical surgical disease (91% traumatized), the incidence of acute lung injury and multiple organ failure was found to be significantly lower in those who received vitamin C in the early period. In addition, it was reported that the duration of mechanical ventilation and the duration of intensive care stay were shorter in patients randomized to vitamin C supplementation.[20] In a study conducted by Fowler et al., it was found that multiple organ damage was significantly reduced and inflammatory biomarkers decreased in septic patients who received high-dose intravenous vitamin C.[21] In a meta-analysis study, it was stated that oral and intravenous high-dose vitamin C treatment can help by reducing the stay time in intensive care units by 8% and mechanical ventilation time by 18.2%. In addition, intravenous vitamin C administration has been reported to shorten the length of hospital stay compared to oral intake.[12]

Influenza viruses and coronaviruses (H5N1, H1N1 2009, SARS, MERS and COVID-19 coronavirus family) are potentially deadly pathogens known to cause lung damage and ARDS-related deaths. ARDS is a picture of intense cellular infiltration, especially neutrophilic infiltration, resulting in lung damage, hypoxia and pulmonary edema as a result of increased permeability of the alveolar capillary membrane. Viruses such as COVID-19 target the alveolar epithelium, causing the formation and increase of reactive oxygen species in the vascular space. By disabling sodium pump activity in the epithelium, it damages tight connections and induces cell death. Cytokines produced by virally infected alveolar epithelial cells activate other capillary endothelial cells, leading to neutrophil infiltration. Afterwards, neutrophils fur-

ther harm the barrier (protective) function of the lungs through increasing reactive oxygen species production more. This condition converts to a fatal vicious cycle like progressive respiratory failure.[22,23] In a case study, a 20-year-old patient who developed ARDS as a result of viral infection and received extra corporeal membrane oxygenation (ECMO) treatment in intensive care, received, high-dose intravenous vitamin C treatment [(24 h 200 mg/kg) the total daily dose of vitamin C is divided equally into four doses and infused every 6 h] in addition to his current treatment, and its effects were analyzed. In the case, improvements were observed from the first day of intravenous vitamin C administration, and a month later review indicated that the patient recovered rapidly after long-term ARDS without fibroproliferative sequelae. In addition, vitamin C can help eliminate pulmonary edema as it reduces alveolar epithelial cell damage by preventing activation and deposition of neutrophils.[23] In an article published in the Chinese Journal of Infectious Diseases, the Shanghai Medical Association has approved the use of high doses of vitamin C for the treatment of inpatients with COVID-19. It is recommended to administer doses larger than the daily dose intravenously to shorten a patient's mechanical ventilation time and thereby improve lung function.[24]

CONCLUSION

Since the effectiveness of vitamin C on COVID-19 and other viruses is still not tested, it has not yet been included in the standard treatment plan of COVID-19 for each patient. In addition, high doses of vitamin C can cause complications such as diarrhea. Using vitamin C to prevent or treat diseases is often classified in complementary and alternative medicine. For this reason, it should never prevent the actual treatment. However, in line with the stated evidence, it is thought that its use with the current treatment may be effective in the treatment of fatal complications caused by COVID-19 such as pneumonia and ARDS. There is a need for high-level clinical studies on the effect of Vitamin C administration on COVID-19.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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