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EDUCATIONAL ARTICLE

Vitamin C and COVID-19: An Orthomolecular Perspective on Physiological Mechanisms

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ABSTRACT

Currently available anti-viral drugs may be somewhat useful in reducing the viral load, but are not providing the necessary physiological effects to combat the SARS-CoV-2 complications efficiently. Treatments that will provide better clinical outcomes are urgently needed. Vitamin C, (Ascorbic Acid, AA), is a nutrient with many biological roles that has been proven to play an important part in immune function, serve as an antioxidant, anti-viral, and exert anti-thrombotic effects among many other physiological benefits. Research has proven that AA at pharmacological doses can be beneficial to patients with Acute Respiratory Distress Syndrome (ARDS), and other respiratory illnesses, including sepsis. In addition, High Dose Intravenous Vitamin C (HDIVC) has proven to be effective in patients with different viral diseases such as influenza, chikungunya, sika and dengue. Moreover, HDIVC has been demonstrated to be very safe. Regarding COVID-19, vitamin C can suppress the cytokine storm, reduce thrombotic complications, and diminish alveolar and vascular damage, among other benefits. Due to these reasons, the use of HDIVC should be seriously considered in complicated COVID-19 patients. In this article, we will focus on vitamin C's role in the most prominent pathophysiological processes presented by the COVID-19 disease.

INTRODUCTION

More than 100 million COVID-19 cases have been reported worldwide. This novel virus has caused a global health crisis. SARS-CoV-2 has three problematic characteristics. First, it appears to be infectious with a relatively small viral load compared to other viruses, which makes it very contagious. Second, SARS-CoV-2 mutates fast, which can make available emergency vaccines less effective against some new emerging strains or variants; and third, this virus causes a dangerous inflammation response that generates numerous free radicals and inflammatory molecules that are highly cytotoxic and damaging (uncontrolled cytokine storm). Meanwhile, hospitals have been treating infected patients with anti-viral drugs such as Remdesivir and Lopinavir. A recent study concluded that these drugs appeared to have little or no effect on hospitalized COVID-19 patients (Pan & Peto, et al., 2021). These and other reasons should ignite our interest to continue searching for treatments that can achieve a better systemic response and better clinical outcomes in complicated COVID-19 patients.

One of the most important aspects in combating the SARS-CoV-2 is to have an optimized immune system, one working properly and efficiently. In order for this complex system to function well, it needs a wide range of specific cofactors. One of these cofactors is Vitamin C (AA). This powerful water soluble antioxidant has been proven to

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be involved in many biological processes of the immune response (Carr & Maggini, 2017). Furthermore, this vitamin has shown potent anti-viral and anti-inflammatory activities in a variety of different viral infections (Sorice et al., 2014) (Luciano et al., 2020) (Gonzalez et al., 2018). It is important to establish that Vitamin C could exert these potential benefits to COVID-19 patients when delivered in high doses especially by intravenous (IV) route. In addition, it has been stated that Vitamin C may reduce the quantity of corticosteroids, antibacterial and antiviral drugs that are given to COVID-19 patients, mitigating the risk of toxicity and immunosuppression (Hoang et al., 2020). Relevant to mention, that Vitamin C even when given in high doses is extremely safe (Miranda-Massari et al., 2020) and it can be easily excreted through the urine.

In this article we will emphasize how Vitamin C can interfere in practically all of the pathophysiological stages presented by the SARS-CoV-2 infection. Also based on this information, we suggest that the administration of the adequate doses of intravenous vitamin C combined with proven conventional supportive medications could provide COVID-19 patients with better clinical outcomes due to the multiple beneficial physiological properties and positive effects AA can exert.

IMPORTANCE OF HIGH DOSE INTRAVENOUS VITAMIN C (HDIVVC)

There are multiple ways vitamin C is administered. It can be given either orally or intravenously. However, both methods can have different physiological results. In particular, there are studies that established differences between oral and IV vitamin C (Padayatty et al., 2004). This study demonstrated that blood levels of vitamin C on patients were much higher by IV vitamin C than oral dosing. IV vitamin C has the capacity to replenish tissues more easily and rapidly than the oral route. The oral dose has to be absorbed by the small intestine while IV vitamin C bypasses this route and is more readily available. Therefore, it is important to state that in order to have greater physiological effects, IV vitamin C is the most potent method to attain higher blood concentrations. Another important aspect to highlight is that the effect of vitamin C will depend on frequency of application and quantity provided. High doses of IV Vitamin C in a range from 30 to 150 grams showed beneficial effects in cancer patients (Riordan et al., 2005). Recently, there was a study published using high-dose IV vitamin C on COVID-19 patients (Gao et al., 2021), and results showed multiple improvements but most importantly, no adverse effects. Conclusively, high dose IV vitamin C will provide better physiological effects compared to oral intake due to higher bioavailable concentrations while being safe and non-toxic.

ANTI-VIRAL PROPERTIES OF VITAMIN C

As mentioned previously, vitamin C is an essential nutrient for the body that helps in the proper functioning of the immune system. Vitamin C has direct and indirect mechanisms which can exert anti-viral properties. First of all, it has been established that vitamin C can inactivate the DNA and RNA from a wide range of viruses (Jariwalla & Harakeh, 1996). Secondly, it has been proven that vitamin C can have the capacity to damage viral capsids and even inhibit viral replication when provided in large doses (Gonzalez et al., 2020). For example, there was a study proving that pharmacological ascorbate killed influenza virus in cultured human bronchial epithelial cells (Cheng et al., 2012).

On the other hand, an indirect mechanism in which vitamin C exerts powerful anti-viral activity is by increasing the production of anti-viral proteins, such as interferon and anti-viral cytokines (Hunninghake, 2014). These proteins play a role in immune protection and interfere with viral replication by binding to the cell surface. Moreover, a study analyzed the multiple effects of Vitamin C supplementation in the initial stage of Influenza A virus (H3N2) (Kim et al., 2013). They concluded that ascorbic acid can exert anti-viral activity by increasing the production of interferon-α/β. These proteins are considered highly essential as a defense mechanism for different viruses.

There are several studies with good clinical outcomes employing IV Vitamin C on patients infected with different types of viruses. For example, there was a case report of a 54-year-old patient with Chikungunya (CHIKV) fever with multiple symptomatology resolved with HDIVC (Gonzalez et al., 2014). The infected patient was treated with high doses of IV vitamin C for two days. Symptoms resolved promptly without any side effects during or after the infusions. In another case report, a 25-year-old patient tested positive for influenza virus (Gonzalez et al., 2018). Supplementation of IV Vitamin C was given, resulting in fast improvement and a return to normal on day four. These cases highlight the effectiveness of IV Vitamin C against combating viral infections. All of these publications show the anti-viral properties that vitamin C can exert, which should be expected to work as well on SARS-CoV-2 infection, since it has worked with many other types of viruses. Moreover, a case report of a COVID-19 patient with early use of HDIVC showed positive outcomes illustrating the potential benefits of HDIVC in this condition (Gonzalez et

al., 2020). The patient presented with chest X-ray opacities and infiltrations, body pain, dry cough and other COVID-19 symptomatology. As she tested positive for SARS-CoV-2, 25 grams of Vitamin C was administered three times daily for three days in a row. The following day after the first infusion, the patient noted a dramatic improvement. Her body pain and headache were gone. Additionally, the most important aspect to highlight is that the infusions did not cause any adverse effects to the infected patient. These promising findings should incite the community to include HDIVC as part of COVID-19 treatment, since it can rapidly improve and stabilize the patient without causing side effects.

VITAMIN C REDUCES OXIDATIVE STRESS

Oxidative stress is an imbalance of low antioxidants molecules and high free radical species in the body. This can result in damage of the extracellular matrix, membranes, cells, organelles, genetic material and proteins which can result in complications and the onset of various conditions. These free radicals are also referred to as reactive oxygen species (ROS). Exhibiting an adequate homeostasis of ROS concentration is actually beneficial for the body since they are needed as part of the immune system to fight pathogens, such as viruses. However, in very high concentrations these reactive molecules may be toxic and may exert very damaging physiological effects. It has been observed that when there is a viral infection, viruses can induce, via multiple pathways, severe oxidative stress (Chernyak et al., 2020). Viruses are often associated with oxidative stress that can lead to problems in body homeostasis leading to cell and organ damage. Regarding Coronaviruses and SARS-CoV-2, ROS have shown a tendency to markedly increase levels of oxidative stress in infected patients, causing detrimental effects in the cells and organs (Hoang et al., 2020). In addition, a study proved that oxidative stress is observed in patients showing multiple complications (cytokine storm), and it may be possible that oxidative stress is involved in the chronification of COVID-19 symptoms (Cecchini R & Cecchini AL, 2020).

There was a study on COVID-19 patients evaluating levels of antioxidants and oxidative stress markers which concluded that infected patients had significantly lower levels of antioxidants (Muhammad et al., 2021). Also, they stated that complicated COVID-19 patients are at higher risk of oxidative stress. However, another study highlighted and proved that antioxidants such as Vitamin C can reduce oxidative stress in inflammatory injured lungs (Patel et al., 2020), which is very common in COVID-19 patients. COVID-19 patients present injured lung tissue due to complications like pneumonia. Another important thing to highlight is that COVID-19 patients commonly have lower levels of vitamin C due to the physiological stress of the viral infection (viral load, Holdford et al., 2020). Evaluating this information and observing the properties of vitamin C, it can be deduced that this vitamin could play an important role in managing oxidative stress in COVID-19 patients. This is due to the rationale that ascorbic acid is an anti-oxidant that will react with these ROS molecules neutralizing them into low reactive species, causing suppression of oxidative stress, thus reducing possible tissue damage accompanied by a lower propensity of health complications.

VITAMIN C PREVENTS THE CYTOKINE STORM

The severity of being infected by SARS-CoV-2 is related to the cytokine storm which occurs in the alveoli and can cause a proinflammatory response that leads to pneumonia, ARDS, diffuse alveolar damage (DAD), multiorgan failure and other complications. Studies in Wuhan, China showed that patients with severe COVID-19 symptoms had higher levels of IL-6 and other inflammatory cytokines in their blood samples (Huang et al., 2020). It is normal for the body to increment the secondary (humoral) immune response after a high viral load exposure which subsequently causes the release of these inflammatory cytokines that attack foreign proteins, such as those presented by SARS-CoV-2. However, it is expected that the body itself will gradually lower the immune response. In COVID-19 patients, the immune response does not seem to diminish, causing detrimental and fatal effects to many organs. Due to this, the role of the cytokine storm rampage seen in COVID-19 has generated interest from the medical-scientific community as a potential target for combating the SARS-CoV-2 complications that may lead to death.

Furthermore, the alveolus is a structure that is especially affected by the cytokine storm. A common finding of post-mortem autopsies from COVID-19 patients revealed many with highly damaged alveolar structures. In particular, a study noted that all seven of the COVID-19 lungs specimens being observed had Diffuse Alveolar Damage (DAD) (Ackermann et al., 2020). Another study, observing pathogenesis of two severely infected COVID-19 patients found that the DAD seen in acute respiratory distress syndrome (ARDS) was not unique to Covid19 patients, but occurs in both SARS and MERS infections as well (Wang et al., 2020), which indicates that ARDS may be responsible for the DAD observed in COVID-19 cases. Lastly, a third study stated that the development and progression of ARDS seen in COVID-19 is closely related to the inflammatory cytokine storm (Ye et al., 2020). Outlining this information, suppression of the cytokine storm is of particular interest because it can prevent further complications such as DAD

and ARDS. Also, if a treatment can decrease the possibilities of the generation and/or progression of the cytokine storm, it could greatly decrease the possibilities of mortality in COVID-19 patients since they are highly correlated (Hojyo et al., 2020).

Vitamin C can inhibit the cytokine storm in COVID-19 patients, based on its antioxidant properties. The main concern of the cytokine storm is the inflammatory response it produces, and one of the principal functions of this vitamin, in addition to its great antioxidant capacity, is that it exerts anti-inflammatory properties. It has already been observed in human and animal models that high doses of Vitamin C may decrease several inflammatory parameters such as inflammatory cytokine release and activity. For example, it was discovered that when high doses of IV vitamin C were given to critically ill COVID-19 patients, their levels of interleukin-6 (IL-6) were lower than the placebo group (Jing et al., 2020). On the other hand, some reviews postulate that Vitamin C can help in removing alveolar fluid caused by distress of the inflammatory response (Hernandez et al., 2020). Another important issue to highlight is that Vitamin C has been shown to favor downregulation of proinflammatory genes on septic lung-injured animals (Bharara et al., 2016). Therefore, this molecule can result promising for treating the cytokine storm itself.

VITAMIN C AMELIORATES ALVEOLAR DAMAGE IN THE LUNGS

One area that SARS-CoV-2 is likely to invade is the lung tissue, and a correlation between the virus and alveolar damage has been observed. It is very common for infected patients to develop ARDS, which is associated with large amounts of inflammation and damage on the alveolar-capillary barrier. Also, infected COVID-19 patients suffer further complications resulting in permanent alveolar damage. When an infected patient has developed complications such as ARDS and DAD, there is higher chance of mortality and the prognosis may seem to worsen. For instance, it has been established that ARDS is one of the principal causes of high mortality in patients with COVID-19 (Hasan et al., 2020). Due to this, better treatments need to be sought that can directly manage these complications and provide the patient with better clinical outcomes that may reduce mortality rates.

One research highlighted that vitamin C levels were undetectable in more than 90% of COVID-19 patients suffering with ARDS (Chiscano-Camon et al., 2020). Conceivably, patients with these complications may need larger amounts of vitamin C due to excessive utilization of this molecule by their immune system due to increased physiological stress. Therefore, the supplementation of IV vitamin C can be beneficial to help maintain optimal levels in these patients and consequently maintain cellular homeostasis. That said, there was a trial with patients suffering from sepsis and ARDS (Fowler et al., 2020) in which Vitamin C infusions were administered. Interestingly, results showed that vitamin C decreased mortality and length of stay of infected patients. Lastly, there was a case report of a woman suffering with ARDS and other complications in which the patient was intubated, presented hypoxemia and chest imaging revealed opacities. Despite various approaches, the patient remained critical. Once IV Vitamin C was initiated, the patient's chest imaging and oxygenation began to improve. Rapidly, the woman became stable (Bharara 2016).

More research needs to be done in order to fully validate the potential effects IV Vitamin C has on ARDS. However, with the current information, IV Vitamin C seems very promising and appears to exert many beneficial properties on patients with ARDS. For example, this vitamin has demonstrated that it can inhibit manifestations of viral ARDS. A case report showed how high doses of IV vitamin C can help stabilize a patient and helps with decreasing the recovery time (Fowler et al., 2017). Also, it was highlighted that ascorbate helps attenuating lung injury produced by the viral infection. It has been seen that even though a COVID-19 patient has already presented with complications and developed critical conditions such as acute respiratory syndrome ARDS or DAD, high doses of Vitamin C can help in the stabilization, condition improvement and even have the capacity to shorten the length of the disease caused by the SARS-CoV-2 virus. For example, it was reported an unusual early recovery case of a critical COVID-19 patient given vitamin C (Waqas et al., 2020). A 74-year-old woman suffering from COVID-19 related ARDS was on mechanical ventilation and in critical condition. Once doctors began administering high doses of IV Vitamin C, the women began to improve significantly causing stabilization and discharge on day 16th. Based on this information, we can deduce that IV Vitamin C can help many COVID-19 patients, since they commonly suffer from ARDS and lung damage.

VITAMIN C PREVENTS THROMBOSIS AND VASCULAR SYSTEM DAMAGE

Current research has been stating that SARS-CoV-2 may predispose infected patients to thrombotic diseases causing alteration in the coagulation cascade leading to a worse prognosis (Lopez, 2020). Thrombotic complications could also significantly contribute to mortality. Furthermore, the

COVID-19 disease can have a prothrombic state and it can be seen in multiple organs such as lungs, spleen and gut (Hanff et al., 2020). This dangerous complication is due to the excessive performance of the immune system trying to combat the virus which generates significant amounts of clotting substances in the blood. It can be said that inflammation and coagulation are interrelated when we speak about SARS-CoV-2. Currently, one of the typical ways to treat these thrombotic complications on COVID-19 patients are blood thinners. However, these medications do not always prevent clotting in infected patients and there are minimal studies proving reliability (Willyard, 2020). Furthermore, a study highlighted that regardless of COVID-19 patients receiving anticoagulation medication, they continued to have thrombotic complications (Helms et al., 2020). This coagulopathy described in Covid19 is characterized by an increase in procoagulant factors such as fibrinogen and D dimers that have been associated with higher mortality.

Moreover, another structure that seems damaged by this virus are the endothelium found in the blood vessels. Studies show that particles from SARS-CoV-2 and inflammatory cells were detected in endothelial cells of infected patients (Huertas et al., 2020). This could be directly correlated to the thrombotic complications since blood vessels require healthy endothelial cells in order to inhibit the formation of clots. Also, when a virus is present it can provoke the phagocytosis of important proteins from cells, in this case endothelial cells, causing loss of vascular integrity, cessation of important anti-clotting reactions, leading to severe complications.

One of the many properties of Vitamin C is that it exerts antithrombotic action. It could be beneficial for COVID-19 patients to receive IV Vitamin C to prevent or decrease thrombotic complications. Moreover, a study concluded that providing Vitamin C during an early stage of the disease, prevented coagulopathy and the formation of microthrombi, which are common complications of COVID-19 (Carr & Rowe, 2020). Another important finding involves IV Vitamin C and d-dimer levels. The d-dimer test is a blood test used to detect presence of blood clots. Clinicians order this test since it has been proven to be the best laboratory diagnostic marker for COVID-19 associated hemostatic abnormalities and is directly related with mortality (Soni et al., 2020). Recently, there was a study of 17 COVID-19 patients that were given IV Vitamin C (Hiedra et al., 2020). Results showed that not only Vitamin C decreased the mortality rate but some inflammatory markers such as d-dimer levels were also decreased.

Nearly 40% of the protein content in the body is composed of collagen (Farndale et al., 2004). Collagen is a molecule that plays an important role in the health of the vascular system. This protein strengthens and protects the integrity of blood vessels. Each blood vessel contains a layer of endothelial cells that contain and need collagen to work properly. Also, functional endothelial cells have the capacity of exerting antithrombotic properties and also possess the ability to degrade clots, preventing thrombosis (Yau et al., 2015). Evaluating this information, it can be stated that it is important for COVID-19 patients to have healthy blood vessels that can contribute to preventing thrombotic complications. Furthermore, research has demonstrated that Vitamin C has a role in the endothelial cells, helping in modulation of blood flow and synthesis of collagen (May & Harrison, 2013). Also, it was also shown that it could prevent endothelial dysfunction, which can be the beginning of thrombotic complications we see in COVID-19 patients. It can be suggested that one way of providing and maintaining functionality of blood vessels to COVID-19 patients is by supplementing Vitamin C. HDIVVC could be a viable method to decrease the possibility of thrombotic complications since Vitamin C assists in the synthesis of collagen that endothelial cells require. Also, it exerts other beneficial functions to the blood vessels which helps in maintaining their integrity.

VITAMIN C PROTECTS RED BLOOD CELLS AND AVERTS HEMOGLOBINOPATHY AND IRON METABOLISM DYSREGULATION

SARS-CoV-2 may also affect red blood cells and hemoglobin. Multiple proteins from SARS-CoV-2 can affect the hemoglobin pathway and cause dissociation of iron (Wenzhong & Hualan, 2020). SARS-CoV-2 proteins can interact with hemoglobin and cause denaturation of the molecule. These alterations could inhibit the ability of red blood cells to transport oxygen, leading to hypoxia. Moreover, the hemoglobin pathway can also be altered by the condition of ARDS, which is very common in COVID-19 patients. For example, it has been observed that patients with ARDS can have higher levels of Cell-Free Hemoglobin (CFH) (Shaver et al., 2016). Having high levels of CFH can be detrimental since it can cause inflammation and alveolar injury (Habegger et al., 2019). Also, cell free hemoglobin has the unstable ferric form and therefore it can initiate a cascade of free radical chain reactions, causing more oxidative stress toxicity and tissue damage (Loh, 2020).

This hemoglobin pathway disruption caused by the virus or ARDS can worsen the respiratory condition in COVID-19 patients since the virus already compromises the respira-

tory system. In COVID-19 patients, if there is a decrease in functional hemoglobin, it can result in poor clinical outcomes (Chowdhury & Anwar, 2020). Taking this into account, it should be evaluated how to decrease or inhibit the capacity of the virus to invade this pathway or affect the red blood cells in order to maintain better oxygenation levels and overall stability in patients.

Hemoglobin desaturation accompanied by iron metabolism dysregulation favors the following pathological pathways: hypoxemia and systemic hypoxia, reduction of nitric oxide, coagulation activation, ferroptosis with oxidative stress and lipid peroxidation, mitochondrial degeneration and apoptosis (Cavezzi et al., 2020). This hemoglobin alteration can contribute to the oxygen deprived multifaceted syndrome seen in many COVID-19 patients. Interestingly, the erythrocyte presents other Sars-Cov-2 receptors in addition to the ACE2, such as cyclophyllins, furins, and TMPRSS2 (Radzikowska et al., 2020).

A silent hypoxia is described in Covid19 patients, who show a progressive worsening of hypoxia associated with normal CO2. This condition worsens in later stages when CO2 increases. Finally, hyperferritemia can increasingly affect alveolar/capillary cell membrane integrity/permeability causing inflammation, edema and lung necrosis further complicating the pulmonary condition. Furthermore, hyperferritemia may induce a series of injuries to many organs via autoimmunity, such as coagulopathies, macrophage activation syndrome, hemochromatosis like liver damage and other ferroptosis driven syndromes.

As for vitamin C, it is known that it can maintain hemoglobin iron complex in the ferrous state that allows binding of oxygen and it can also improve heme iron/cell redox balance (Cavezzi et al., 2020). Vitamin C can indirectly decrease furin cleavage and reduce endothelial permability to free heme (Kuck et al., 2018). Also, as mentioned earlier, vitamin C has antioxidant capacities which could help in managing the oxidative radicals produced by the cell free hemoglobin. Lastly, the inflammation linked to high levels of CFH can be possibly managed by vitamin C due to its anti-inflammatory capacity. Vitamin C is required in high amounts in tissues to maintain vascular strength and integrity. The microvasculature when depleted of Vitamin C losses its structural capacity as shown in patients suffering Scurvy. These derangements can further enhance coagulability issues and prone to both venous and arterial blood clots. Vitamin C improves the condition of critically ill and complicated Covid19 patients by its multiple beneficial physiological effects which include attenuation of lipid peroxidation, reduction of vascular permeability, lessening microvascular dysfunction, preserving the endothelial function and microcirculatory flow, improving endogenous vasopressor synthesis, increasing vasopressor sensitivity and hemodynamic stability which ultimately leads to reduced organ injury and dysfunction that may save lives among the critically ill (Wang et al.,2019)

VITAMIN C COUNTERACTS SARS-COV-2 MULTIPLE ORGAN MANIFESTATIONS

It is known that the main place where SARS-CoV-2 invades firstly and most aggressively is in the lung tissue. However, is not uncommon for SARS-CoV-2 to invade other organs. It will all depend on the quantity and origin of receptors that each infected patient possesses. As more research is being published, it is more common for COVID-19 patients to display multi-organ manifestations. For example, there have been reported cases of patients presenting kidney injury, gastrointestinal symptoms, cardiovascular, liver problems and other complications (Gayriatopoulou et al., 2020). In this sense, COVID-19 can be considered as a systemic disease. Additionally, research highlighted and observed via data analyses that multiple organs and tissues were vulnerable to SARS-CoV-2 virus and not only the lungs (Zou et al., 2020).

The renal system seems to be one of the most frequent target areas for SARS-CoV-2, in addition, autopsies have demonstrated that there is a percentage of COVID-19 patients that suffered from renal tropism (Braun et al., 2020). This includes patients with or without kidney diseases. The study also highlighted that the presence of SARS-CoV-2 RNA in the kidney was associated with increased risk of premature death. Taking this into account, it must be evaluated how to prevent or diminish kidney injury or complications on COVID-19 patients in order to decrease the severity of the disease and provide better clinical outcomes. Vitamin C has demonstrated some potential roles against kidney disease. For example, vitamin C can help in controlling anemia in patients with chronic kidney disease and it can have renoprotective effects since it improves the levels of urea, MDA and catalase (Kalantar-Zadeh & Moore, 2020).

Regarding the nervous system, SARS-CoV-2 can have the capacity to cross the blood-brain barrier and cause multiple symptomatology in infected patients. Recent studies discovered that brain autopsies from COVID-19 patients had cortical neurons with viral load of SARS-CoV-2 (Soni et al., 2020). Also, possible infection and minimal immune cell infiltrates were noted, providing evidence for SARS-CoV-2 neuro invasive capacities. Regarding vitamin C's role in the different manifestations of the nervous system, it has been seen that ascorbate can help in neuronal repair, myelin-

ation and function (May, 2011). Additionally, the review stated that vitamin C is an important anti-oxidant for the CNS since it hunts ROS molecules, causing suppression of oxidative stress in the nervous system. Moreover, Vitamin C is capable of bypassing the blood brain barrier.

On the other hand, it has been deduced that one of the possibilities of neurological manifestations on COVID-19 patients is due to the excessive immune response and the cytokine storm (Gavriatopoulou et al., 2020). So as established previously, it seems that the suppression or inhibition of the cytokine storm could help in preventing neuronal complications in addition to multiple organ manifestations in COVID-19 patients. As mentioned before, this could be done by providing HDIVVC, since various studies have proven the different mechanisms of action this vitamin cofactor exerts on the cytokine storm.

CONCLUSION

Vitamin C should not be seen as a sole cure for SARS-CoV-2 but it does provide the immune system the necessary boost to combat it more efficiently, shorten the length of the disease and prevent fatal complications. This important vitamin cofactor plays many roles in suppressing the pathological processes that SARS-CoV-2 exerts. Vitamin C has immuno-supportive properties, acts as an anti-viral, anti-inflammatory, antioxidant, anti-thrombotic, and many others. By having all these properties, it can be deduced that Vitamin C, especially HDIVVC, can be promising as an important component of the treatment for SARS-CoV-2. What is also important to highlight, is that in practically all of the pathophysiological stages of SARS-CoV-2, vitamin C can have a potential role in diminishing its effects. This is due to the pleiotropic effects that ascorbate exhibits such as inhibiting the cytokine storm, reducing oxidative stress, decreasing inflammation, preventing thrombotic complications and others. Also, vitamin C has the capacity to reduce mortality in COVID-19 patients while providing better clinical outcomes that do not include harsh side effects to the body. Furthermore, by supplementing vitamin C on COVID-19 patients, research states that it can reduce the high doses of medications like corticosteroids that can be toxic. Vitamin C is a safe and low-cost option that should be contemplated as part of the treatment of COVID-19 patients.

Moreover, vitamin C has been used as a treatment for many diseases such as cancer, colds, inflammatory disorders and others. Additionally, ascorbic acid is an important water-soluble molecule that is excreted very easily through the urine. However, it can exert multiple beneficial physiological effects. COVID-19 patients usually possess low levels of Vitamin C due to the stress manifested by SARS-CoV-2 infection. As a result, higher quantities than normal of this vitamin cofactor are needed in order for the immune system to function properly. There is no doubt that the use of HDIVVC will result beneficial to virally infected patients. More research needs to be done to provide better clinical outcomes to COVID-19 patients. It is necessary to search for other available treatments that can optimize the immunity and be less invasive on infected COVID-19 patients. Vitamin C seems to be this additional component of the treatment for Covid19 patients.

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