

Does Vitamin C therapy play a role in the management of lung pathology in COVID-19? A review of current evidence

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Abstract Ongoing pandemic COVID-19 has posed a huge challenge in the treatment of patients throughout the world. No specific therapy or vaccine has been developed so far. The role of antivirals and antimalarials has been debated; hence, search for an alternative regimen has been going on with Vitamin C showing promising results. Here, we review the role of Vitamin C as an antioxidant, antiviral, anti-inflammatory agent which counteracts the cytokine release that occurs during the development of Acute Respiratory Distress Syndrome in COVID-19 infection.

Keywords: Acute respiratory distress syndrome, coronavirus, COVID 19, cytokines, Vitamin C

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INTRODUCTION

Coronaviruses (CoVs) are large, enveloped RNA viruses that infect the range of vertebrates including both humans and animals. Human respiratory coronavirus causes mild respiratory infections, whereas zoonotic CoV causes high mortality respiratory infections such as severe acute respiratory syndrome (SARS) and Middle-East respiratory syndrome CoV. Behavior of 2019 novel CoV is more like SARS-CoV-2 with clinical progression rapidly to Acute Respiratory Distress Syndrome (ARDS) and septic shock.^[1] It had its first origin in Wuhan city, China. It was declared as a pandemic by the WHO on March 11, 2020.^[1] At the time of writing (June 8, 2020) worldwide, cases were 7 million with COVID-related deaths amounting to 40 lakhs.

ROLE OF VITAMIN C IN THE HUMAN BODY

Ascorbic acid is a known antioxidant with scavenger properties. It protects the body tissues from oxidative damage by destroying reactive oxygen species and boosting immune function. It is needed

during tissue healing and acts as a cofactor in many physiological processes such as collagen, bone, cartilage, muscle, and blood vessel generation. Recommended daily allowance in of Vitamin C is 90 mg for male and 75 mg for female.^[2] During infection, Vitamin C needs to be given, but an optimum dose has not been developed yet.^[3]

Role of ascorbic acid in viral infections, especially poliomyelitis, is known since many decades.^[4] Its beneficial properties have been seen in many other conditions such as Hepatitis, Herpes, measles, infectious mononucleosis, urethritis, arthritis, and cancer. Many studies have concluded the *in vitro* virucidal capacity of Vitamin C in high doses; however, *in vivo* virucidal capacity has not been confirmed.^[5] A research has shown that Vitamin C can decrease the load of Epstein-Barr Virus.^[6] This study concluded that multiple mechanisms are involved in the antiviral therapy of Vitamin C. Generation of cytokine storm is a reality in both bacterial and viral infections.^[7] Antioxidants should be given to combat COVID till a definitive cure or vaccine becomes available.^[8] Vitamin C in large doses have shown successful clinical results in both viral ARDS and Influenza.^[9]

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ROLE OF VITAMIN C IN RESPIRATORY INFECTIONS

CoV and influenza virus are responsible for some of the earlier pandemics with main reasons of high fatality being acute lung injury and ARDS.^[10,11] ARDS results due to severe hypoxemia leading to oxidative injury, severe inflammation, and breach in alveolar-capillary barrier.^[7] Viral infections invoke a cytokine storm and this along with free radical injury is the hallmark of ARDS leading to cellular dysfunction, organ failure, and death.

Nobel laureate Linus Pauling has substantiated the beneficial role of Vitamin C in common cold.^[12] With regular usage, Vitamin C may reduce the duration of cold but the risk of catching cold remains same.^[13] Vitamin C is supposed to augment the function of T-lymphocytes, boost phagocytic activity and immune system, and improve interferon levels.^[14] Although definite evidence to prove that Vitamin C brings about clinical improvement is lacking still its intake has proved to be beneficial in the management of critical patients; hence, its role in the treatment of COVID patients should be researched.^[15] Pneumonia is caused in COVID-19 due to hyperactivation of immune cells. Vitamin C brings about relief by suppressing these immune cells and when used parenterally has an anti-inflammatory properties. It subsides pro-inflammatory expression of chemical mediators, helps in clearance of leaked alveolar fluid, and improves epithelial cells function due to its antioxidant properties.

USE OF INTRAVENOUS VITAMIN C

Intravenous (IV) Vitamin C has been used in China during COVID-19 epidemic especially in the treatment of ARDS and seen encouraging results. Administration of approximately 15 g/day of IV Vitamin C in ARDS decreases morbidity significantly has been shown in a recent Randomized Clinical Trial done in USA.^[7] A study done by Hemila *et al.* showed significant reduction in mortality and intensive care unit stay by high-dose IV infusion (200 mg/kg body weight/day divided into 4 doses).^[16] Similar findings were seen in a study in china.^[10] Oral Vitamin C (6 g/day) administration also showed improvement in symptoms.

CONCLUSION

Use of Vitamin C as antiviral agent in both IV and oral forms (liposomal encapsulated vitamin C) is associated with both benefits and controversy. Some studies have shown promising results while others have not. It is supposed to be especially effective in decreasing cytokine storm due to COVID-19. The WHO has stated that COVID-19 is going to stay for a quite long time with the emergence of secondary waves in future.

Hence, further research studies to exactly pinpoint the mechanism and time of usage of Vitamin C in COVID-19-infected lung injury are warranted. Since the development of vaccine and antiviral drug will take time high dose IV Vitamin C and other oxidants can be used presently to fight COVID-related ARDS, especially as a preventive measure in health-care workers and other at risk individuals. To

conclusively, determine whether Vitamin C therapy is beneficial for the treatment of COVID-19 a double-blind, placebo-controlled study is needed.

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Conflicts of interest

There are no conflicts of interest.

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