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Letter to Editor

Vitamin C Against Ncov-19 Infection: A Hope in the Pandemic COVID-19

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Dear Editor

Vitamin C (also called ascorbic acid, AA), an essential micronutrient for humans [1]. Deficiency of this vitamin results in impaired immunity [2] and higher susceptibility to infections [3]. It is a potent antioxidant and a cofactor for a family of biosynthetic and gene regulatory enzymes [1]. It contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system [2]. It supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity in our body [3]. It accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing [1]. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage [4]. Moreover, it has many important roles in our skin health [5]. It enhances the differentiation and proliferation of B- and T-cells, due to its ability of gene regulating effects [6]. Supplementation with AA appears to be able to both prevent and treat respiratory and systemic infections [3,7]. Prophylactic prevention of infection requires dietary AA intakes that provide at least adequate, if not saturating plasma levels (i.e., 100-200 mg/day), which optimize cell and tissue levels [1].

Vitamin C is evident to manage common cold in experimental animals [8] and can be used to treat infections caused by influenza virus [9]. It is evident to inhibit influenza viral proliferation [10], thus it is thought to be a good option to treat viral infections. AA is evident to inhibit different phases of the cell cycle of various viruses and inhibit the integration of RNA viral genetic material into the host genome [11,12]. In this regard, this vitamin may act against influenza virus, corona virus, or picorna virus.

A stimulates LXR-α gene expression, which downregulates c-myc gene, resulting in cell cycle arrest at G0G1 phase, thus restricts the entrance of cells in S phase and reduces in the number of cells at a G2 M phase of viral genome integration [13,14]. AA also inhibits viral replication of other RNA viruses such as the human immunodeficiency virus and avian tumor virus [15]. AA combined with iron exhibited a sustained anti-viral effect against the influenza virus [16]. It may be due to the pro-oxidant effect of this vitamin [17]. Dehydroascorbate has shown this effect better than the ascorbate form [18]. However, to exhibit a pro-oxidant effect on bronchial epithelium, the availability of iron and oxidants such as hydrogen peroxide should not be a limiting factor for locally available AA because iron and hydrogen peroxide are present in the vicinity of bronchial epithelium [19].

Influenza virus infection produces matrix metalloprotease (e.g., MMP-9) in epithelial cells, which is thought to be a mechanism of spread of the virus [20]. AA has been shown to reduce MMP-9 gene expression in peripheral blood-derived mononuclear cells [13]. It also has been shown to decrease the MMP-9 synthesis induced by hydrogen peroxide in an *in vitro* chorioamniotic membrane model [21]. It is well known that MMPs are important for cancer metastasis and AA has been proved to inhibit the migration of cancer cells independent of its antioxidant activity [22]. Therefore, AA may inhibit possible lethal mediator of inflammation, MMP-9, and reduce the extent of harm due to influenza virus infection in the respiratory epithelium. AA 3 g/d was reported to prevent cold and flu symptoms in human (18 - 30 yr age) [23]. At 300 mg/d, AA was found to treat influenza patients and reduced 25% hospital stay time than the control group [24].

AA has a beneficial effect on common cold, asthma and pneumonia [3]. In a study, *Citrus sinensis* extract (rich in AA) was found to inhibit replication of coronavirus in infected cultured cells [25]. Moreover, in 21 trials with 1766 patients having high blood pressure, infections, bronchoconstriction, atrial fibrillation, and acute kidney injury, AA (oral dose: 1 - 3 g/day) reduced the length of ICU stay on average by 7.8 - 18.2%. AA reinforces the maintenance of the alveolar epithelial barrier and transcriptionally upregulates the protein channels (CFTR, aquaporin-5, ENaC, and Na+/K+ ATPase) regulating the alveolar fluid clearance. To date a number of clinical trials have been done on this hopeful vitamin in order to fight against COVID-19.

Clinical trials

- Hydroxychloroquine,AA,Vit-D,andZinc(600participants)https://clinicaltrials.gov/ct2/show/NCT04335084?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=4
- AA (500 participants; 10 gr of AA intravenously in addition to conventional therapy) https://clinicaltrials.gov/ct2/show/NCT04323514?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=3
- AA Infusion (140 participants; 12g AA will be infused in the experimental group twice a day for 7 days by the infusion pump with a speed of 12ml/h) https://clinicaltrials.gov/ct2/show/NCT04264533?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=5
- Hydroxychloroquine+AAandVit-D+Zinc(80participants)https://clinicaltrials.gov/ct2/show/NCT04326725?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=8
- AA (LOVIT) (800 participants; Intravenous AA administered in bolus doses of 50 mg/kg mixed in a 50-mL solution of either dextrose 5% in water (D5W) or normal saline (0.9% NaCl), during 30 to 60 minutes, every 6 hours for 96 hours (i.e. 200 mg/kg/day and 16 doses in total)) https://clinicaltrials.gov/ct2/show/NCT03680274?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=9
- L-AA 50 mg/kg intravenous infusion (20 participants) https://clinicaltrials.gov/ct2/show/NCT04357782?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=1
- L-AA 100 mg/kg intravenous infusion (200 participants) https://clinicaltrials.gov/ct2/show/NCT04344184?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=2
- Hydroxychloroquine + AA (1212 participants) https://clinicaltrials.gov/ct2/show/NCT04347889?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=6
- AA + Zinc Gluconate (520 participants) https://clinicaltrials.gov/ct2/show/NCT04342728?cond=COVID-19+AND+Vitamin+Canddraw=2andrank=7

In summary, AA is the vastly taken vitamin by human as it is found in various foods and sold as a dietary supplement. Due to its water solubility, dietary excesses not absorbed, and excesses in the blood rapidly excreted in the urine, so it exhibits remarkably low acute toxicity. Sodium or calcium ascorbate may minimize indigestion problem, especially when taken on an empty stomach. Large doses of AA may cause nausea, abdominal cramps and diarrhea. AA increases the absorption of iron, by which hereditary hemochromatosis might be adversely affected. Adequate precautions should be taken during taken this hopeful vitamin in COVID-19. More researches are necessary to understand Vit-C's ability to manage COVID-19.

Conflict of Interest

None Declared.

Bibliography

1. Padayatty SJ and Levine M. "Vitamin C physiology: the known and the unknown and Goldilocks". *Oral Diseases* 22.6 (2016): 463-493.

2. Carr AC and Maggini S. "Vitamin C and Immune Function". *Nutrients* 911 (2017): 1211.

3. Hemilä H. "Vitamin C and Infections". *Nutrients* 9.4 (2017): 339.

4. Liugan M and Carr AC. "Vitamin C and Neutrophil Function: Findings from Randomized Controlled Trials". *Nutrients* 11.9 (2019): 2102.

5. Pullar JM., *et al.* "The Roles of Vitamin C in Skin Health". *Nutrients* 9.8 (2017): 866.

6. Manning J., *et al.* "Vitamin C Promotes Maturation of T-Cells". *Antioxidants and Redox Signaling* 19.17 (2013): 2054-2067.

7. Garaiova I., *et al.* "Probiotics and vitamin C for the prevention of respiratory tract infections in children attending preschool: a randomised controlled pilot study". *European Journal of Clinical Nutrition* 69.3 (2015): 373-379.

8. Yakoot M and Salem A. "Efficacy and safety of a multiherbal formula with vitamin C and zinc (Immumax) in the management of the common cold". *International Journal of General Medicine* 4 (2011): 45-51.

9. Hemilä Banerjee D and Kaul D. "Combined inhalational and oral supplementation of ascorbic acid may prevent influenza pandemic emergency: A hypothesis". *Nutrition* 26.1 (2010): 128-132.

10. Kim Y., *et al.* "Vitamin C Is an Essential Factor on the Anti-viral Immune Responses through the Production of Interferon-α/β at the Initial Stage of Influenza A Virus (H3N2) Infection". *Immune Network* 13.2 (2013): 70-74.

11. Bissell MJ., *et al.* "Ascorbic acid inhibits replication and infectivity of avian RNA tumor virus". *Proceedings of the National Academy of Sciences of the United States of America* 77.5 (1980): 2711-2715.

12. Harakeh S., *et al.* "Suppression of human immunodeficiency virus replication by ascorbate in chronically and acutely infected cells". *Proceedings of the National Academy of Sciences of the United States of America* 87 (1990): 7245-7249.

13. Kaul D and Baba MI. "Genomic effect of vitamin 'C' and statins within human mononuclear cells involved in atherogenic process". *European Journal of Clinical Nutrition* 59 (2005): 978-981.

14. Kaul D., *et al.* "Importance of LXR-α transcriptome in the modulation of innate immunity". *Molecular and Cellular Biochemistry* 292 (2006): 53-57.

15. Wang H., *et al.* "c-Myc depletion inhibits proliferation of human tumor cells at various stages of the cell cycle". *Oncogene* 27 (2008): 1905-1915.

16. Furuya A., *et al.* "Antiviral effects of ascorbic and dehydroascorbic acids in vitro". *International Journal of Molecular Medicine* 22 (2008): 541-545.

17. Carr A and Frei B. "Does vitamin C act as a pro-oxidant under physiological conditions?" *The FASEB Journal* 13 (1999): 1007-1024.

18. Uozaki M., *et al.* "Antiviral effects of dehydroascorbic acid". *Experimental and Therapeutic Medicine* 1.6 (2010): 983-986.

19. Jöbsis RQ., *et al.* "Hydrogen peroxide in breath condensate during a common cold". *Mediators of Inflammation* 10 (2001): 351-354.

20. Yeo SJ., *et al.* "Influenza A virus infection modulates the expression of type IV collagenase in epithelial cells". *Archives of Virology* 144 (1999): 1361-1370.

21. Hernández Guerrero CA., *et al.* "Vitamin C decreases MMP-9 synthesis induced by hydrogen peroxide in an in vitro chorioamniotic membrane model". *Ginecologia y Obstetricia de Mexico* 74 (2006): 3-12.

22. Wybieralska E., *et al.* "Ascorbic acid inhibits the migration of walker 256 carcinosarcoma cells". *Cellular and Molecular Biology Letters* 13 (2008): 103-111.

23. Gorton HC and Jarvis K. "The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections". *Journal of Manipulative and Physiological Therapeutics* 22 (1999): 530-533.

24. Kimbarowski JA and Mokrow NJ. "Colored precipitation reaction of the urine according to Kimbarowski (FARK) as an index of the effect of ascorbic acid during treatment of viral influenza". *Dtsch Gesundheitsw* 22 (1967): 2413-2418.

25. Ulasli M., *et al.* "The effects of Nigella sativa (Ns), Anthemis hyalina (Ah) and Citrus sinensis (Cs) extracts on the replication of coronavirus and the expression of TRP genes family". *Molecular Biology Reports* 41.3 (2014): 1703-1711.

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