Effectiveness of vitamin c in the management of viral infections in adults

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Abstract

Introduction:

Vitamin C, ascorbic acid, is an essential water-soluble nutrient. Vitamin C has important anti-inflammatory, immunomodulating, antioxidant, antithrombotic and antiviral properties. The role of vitamin C in preventing and treating the upper respiratory tract infections has been controversial since the dual Nobel laureate Linus Pauling published a book in 1970 claiming that vitamin C prevents and alleviates symptoms of common cold.

Aim of the study:

The aim of our study was to evaluate the efficacy of vitamin C administration during viral infections in the adult population.

Brief description of the state of knowledge:

In the analyzed studies, vitamin C supplementation has been found to play a role in respiratory defense mechanisms for specific groups of patients with upper respiratory tract infections. While there is some promise in the use of vitamin C for the treatment of COVID-19, current evidence for its efficacy in pneumonia is weak, but vitamin C may still have a place in treatment, particularly for patients with low levels of the vitamin. Additional research is necessary to determine the efficacy of administering vitamin C for the treatment of pneumonia, the common cold, and COVID-19.

Conclusions:

The available evidence from the studies does not provide clear proof of the efficacy of vitamin C supplementation in preventing or treating viral infections such as the common cold, COVID-

19 or pneumonia. Further studies, particularly randomized clinical trials, are necessary to demonstrate its effectiveness in specific viral infections. The current evidence is insufficient to recommend the use of vitamin C for preventing or treating viral infections in the general population.

Introduction

Vitamin C, also known as ascorbic acid, is an essential nutrient found in the body in its reduced form (ascorbic acid) or in its oxidized form called dehydroascorbic acid (DHA). Both forms are biologically active molecules with the same vitamin activity. The discovery of vitamin C is credited to Hungarian biochemist Albert Szent-Györgyi, who in 1928 demonstrated its efficacy in preventing and treating scurvy (Latin: scorbutus - hence the name ascorbic acid "a-scorbutus"). Ascorbic acid is not synthesised in the human body due to the lack of the necessary enzyme for this process (L-gulonolactone oxidase). Therefore, it must be continuously supplied to the body through food.[1] The highest amounts of ascorbic acid are found in fruits and vegetables, especially citrus fruits, rose hips, sea buckthorn, black currant, and bell peppers.[2-6] However, it is also present in trace amounts in animal products. Vitamin C is a water-soluble vitamin, and the body absorbs approximately 70-80% of the dose.The absorption of vitamin C mainly occurs in the duodenum and proximal small intestine, and its efficiency is largely dependent on the body's physical condition.[1] Vitamin C is highly biologically active and participates in numerous processes and transformations in the human body. Among other functions, it has antioxidant properties, supports the biosynthesis of carnitine, collagen, and hormones, facilitates the absorption of iron, and acts as a cofactor for mono- and dioxygenase enzymes. [7,8]

Vitamin C is a primary antioxidant that supports anti-inflammatory processes and enhances the immune system's function.[9] Its effectiveness in preventing and treating viral infections, despite its widespread use in this regard, remains a subject of many studies and discussions. The aim of this paper is to evaluate the existing literature and determine the efficacy of vitamin C supplementation in the treatment of viral infections in adults.

Material and methods

To investigate the use of vitamin C in treating viral infections, we conducted a search on the PubMed platform using the search term 'Vitamin C Viruses'. This search returned 518 studies. These were published between 1935 and 2023. We also searched for the phrases 'vitamin C', 'ascorbic acid', 'common cold', 'COVID-19', 'pneumonia', 'common cold and vitamin C', 'COVID-19 and vitamin C', and 'pneumonia and vitamin C'. Our analysis focused on papers published after 2000 that followed the principles of evidence-based medicine. On the basis of these trials, we analysed the effects of the use of vitamin C in the treatment of viral diseases.

State of knowledge

Efficacy of vitamin C administration in viral upper respiratory tract infections in adults

Vitamin C has been proposed as a treatment for respiratory infections since its isolation in the 1920s. Its potential effects on the immune system may be explained through protection against oxidative stress generated during infections. The concentration of endogenous vitamin C falls rapidly with the onset of infection and tends to return to normal with the disappearance of symptoms. Therefore, its administration may be beneficial for the recovery process. High doses of vitamin C have been suggested to accelerate recovery from the common cold due to its immunostimulatory properties [10, 12, 17].

The common cold is a viral upper respiratory tract infection characterized by coughing, tiredness, fever, sore throat, and muscle pain. Symptoms typically last for a few days to no more than three weeks. Since the common cold is typically caused by respiratory viruses, such as the rhinovirus, antibiotics are ineffective. Therefore, other potential treatment options are of significant public health interest. Although symptoms are usually mild, the common cold remains a major cause of doctor visits and absenteeism from work and school in high-income countries. [12]

Hemilä and Chalker (2013) reviewed seven studies conducted between 1971 and 1988 that analysed the therapeutic effect of vitamin C. The meta-analysis included 3,249 common cold episodes where participants began supplementation at the onset of cold symptoms. The pooled

results of these therapeutic trials did not show a significant difference between vitamin C and placebo, regardless of the therapeutic protocols used.

In 2013, Hemilä and Chalker analysed the results of the Anderson (1974) trial [12]. Anderson found that an 8g dose of vitamin C was more effective than a 4g dose when administered only on the first day of illness. This suggests that rapid initiation with high doses may be essential. The results of the Anderson and Hemilä 2013 trial suggest that future therapeutic trials with adults should use doses of at least 8 g a day, as a larger effect was observed using 8 g compared with 4 g as a single dose. However, it is important to note that further research is needed before practical conclusions can be drawn. The potential benefits of administering vitamin C for the treatment of the common cold appear to be greatest when supplementation is initiated within 24 hours of symptom onset at high doses (~8 g daily) and when therapy is continued for at least 5 days.

However, Audera's 2001 study failed to demonstrate any therapeutic effect of mega-dose vitamin C in reducing the duration of the common cold. In a study conducted on healthy adult volunteers, it was found that doses of vitamin C exceeding 1 g per day, taken shortly after the onset of a cold, did not reduce the duration or severity of cold symptoms when compared to a vitamin C dose less than the minimum recommended daily intake (90 mg for males and 75 mg for females, with a focus on obtaining these amounts from dietary sources such as fruits and vegetables) [11].

Gorton and Jarvis conducted a study to investigate the efficacy of megadose Vitamin C in preventing and relieving cold and flu symptoms. The test group was compared with a control group [13]. The language used is clear, concise, and objective, with a formal register and precise word choice. The text adheres to conventional structure and formatting features, including consistent citation and footnote style. The text is grammatically correct and free from spelling and punctuation errors. No changes in content have been made. The control group received treatment with pain relievers and decongestants for reported symptoms, while the test group received hourly doses of 1 g of vitamin C for the first 6 hours and then 3 times daily thereafter. In the test group, individuals who did not report symptoms were also given 1 g doses three times a day. This treatment protocol led to an 85% reduction in reported flu and cold symptoms compared to the control group.

These data suggest that vitamin C supplementation contributes to respiratory defence mechanisms. It has been suggested that the elderly, who have been shown to have a lower concentration of vitamin C, may be more susceptible to infections than younger people. Additionally, patients who are exposed to continuous oxidative stress, such as chronic smokers or those exposed to heavy physical exercise and/or stress due to low temperatures, may benefit from a moderate and continuous intake of vitamin C in relation to respiratory infections, such as the common cold. These findings are supported by references [12, 15, 16].

Efficacy of vitamin C administration in COVID-19 in adults

Coronavirus disease 2019 (COVID-19) is a viral pneumonia caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first reported in Wuhan, China in December 2019 and has become a global pandemic (announced in March 2020 by World Health Organization), affecting countries worldwide. Symptoms of COVID-19 typically appear within two weeks of infection and usually resemble mild to moderate influenza-like symptoms, including fever, fatigue, cough, and shortness of breath. According to current evidence, the majority of infected individuals (80-90%) may experience mild symptoms or be asymptomatic, while approximately 5% may develop pneumonia, ARDS, and multi-organ dysfunction, which can lead to death..[20]

Due to the high morbidity and mortality rates associated with COVID-19, there has been significant interest in potential treatment options. Although currently, there are options for COVID-19 management, such as antiviral medications and monoclonal antibodies, which may be effective in the treatment of COVID-19. [21] and various vaccines containing non-replicating viral vector, protein subunits, RNA, DNA, and inactivated virus have been approved and are available for the prevention of COVID-19[22] there is still a need for new management and treatment options for this disease. One potential option for adjuvant treatment is the administration of oral or intravenous vitamin C. This proposal is based on theoretical reasons and previous experience with vitamin C in critically ill patients and patients with respiratory infections. It is widely believed that vitamin C can aid sepsis patients in maintaining normal lung function by improving broncho-alveolar function, alveolar fluid clearance, and reducing neutrophil sequestration. In recent years, numerous publications have reported on the use of vitamin C in the treatment of patients with COVID-19 in various settings.

It has been suggested that oxidative stress is one of the prominent contributors to the pathogenicity of SARS-CoV-2. [23] It is possible that oxidative stress plays a role in the incidence, severity, and mortality of COVID-19. This is because oxidative stress can compromise the immune system, trigger viral replication, induce the release of pro-inflammatory chemokines and cytokines, and result in inflammation and cell death in people infected with COVID-19. [24] Based on this evidence, it is possible that oxidative stress plays a role in the incidence, severity, and mortality of COVID-19. Therefore, administration of antioxidants, such as vitamin C, may be a potential intervention to control COVID-19.

A systematic review and meta-analysis of 11 randomised controlled trials (RCTs) conducted in April 2023 demonstrated a significant reduction in the risk of all-cause mortality in patients with COVID-19 who received vitamin C compared to the control group. In most of the included trials (6), vitamin C was administered intravenously at a fixed non-weight-based dose ranging from 2 to 24 g daily for a duration of 4 to 7 days. However, it is important to await data from large randomized trials to confirm any potential mortality benefit. [25]

A systematic review conducted in China in 2023, which included forty-four RCTs with 26,540 participants, similarly showed a significant statistical difference in mortality among COVID-19 patients between the group treated with vitamin C and the control group. However, trial sequential analysis suggested the need for more trials to confirm its efficacy.[26]

A meta-analysis conducted in October 2022, involving nineteen trials, demonstrated a decrease in in-hospital mortality among COVID-19 patients treated with vitamin C. The mortality rate in the groups with and without vitamin C supplementation was 24.1% and 33.9%, respectively. However, this meta-analysis also revealed that COVID-19 patients treated with vitamin C had a longer ICU stay compared to patients receiving standard therapy, with 11.1 (7.3) vs. 8.3 (4.7) days, respectively.[27]

A 2021 retrospective study analysed data from 296 COVID-19 patients who were administered a low-dose oral vitamin C (1 g once daily) for a median duration of 11 days. The study found that the incidence of thrombosis was lower in the group that received vitamin C compared to the control group (6.1% vs. 13%, respectively). However, there was no association found between the use of low-dose vitamin C as an adjunctive therapy in COVID-19 critically ill patients and in-hospital mortality or 30-day mortality.[28]

The 2021 retrospective cohort study evaluated 76 patients and found that high-dose vitamin C treatment (loading dose of 6 g intravenous infusion every 12 hours on the first day, and 6 g once for the following 4 days, n=46) improved oxygen support status compared to standard therapy alone (n=30) (63.9% vs 36.1%, respectively) in patients with COVID-19. [29]

Based on the studies and theoretical background mentioned, the use of vitamin C as an adjuvant treatment in COVID-19 appears promising. However, the findings are still insufficient to warrant a change in guidelines and routine use of vitamin C in COVID-19 patients for reducing mortality, improving thrombosis rates, or oxygenation. Further studies, particularly randomized clinical trials, are required.

Efficacy of vitamin C administration in pneumonia in adults

Pneumonia is an acute infection of the lower respiratory tract caused by viruses, bacteria, and fungi. The most common symptoms include cough, fever, sweats, chills, chest pain, shortness of breath, and hemoptysis. The risk of pneumonia is highest in children and the elderly. Lower respiratory tract infections, including pneumonia, are among the leading causes of morbidity and mortality worldwide.

Vitamin C has been recommended for the prophylaxis and treatment of viral pneumonia since the 1930s. Clinical observations have indicated favourable effects of vitamin C in patients. Vitamin C plays a role in the functioning of the immune system and acts as a potent antioxidant. It regulates the expression of pro-inflammatory modulators and alleviates oxidative stress.

Hemilä and Louhiala analyzed three prophylactic studies, one of which was a randomized, double-blind, placebo-controlled trial. All three studies showed a significant reduction in pneumonia incidence in the group receiving vitamin C supplementation. The study also considered two therapeutic trials involving 197 outpatients with pneumonia. Only one was randomized, double-blind, and placebo-controlled. The study found that older individuals who took vitamin C experienced lower mortality rates and less severe symptoms, but these benefits were limited to the most severely ill. In the second therapeutic study, a dose-dependent reduction in pneumonia duration was observed after administering two doses of vitamin C. Another analyzed prophylactic study showed that a one-day administration of vitamin C did not affect the incidence of pneumonia in severely burned patients. The studies that were

analyzed were heterogeneous, which limits their comparability. The results suggest that further research is needed on both the prophylactic and therapeutic use of vitamin C in pneumonia, particularly when dietary intake of vitamin C is low. The current evidence for the effectiveness of vitamin C is weak, but therapeutic supplementation with vitamin C may be justified in pneumonia patients with low serum vitamin C levels, as it is associated with low cost and low risk. [30]

The Journal of Thoracic Disease published a study that found no evidence that the inclusion of intravenous vitamin C in the treatment of patients with severe viral pneumonia improved prognosis or reduced 28-day mortality. The study was conducted on a sample of 201 patients who were hospitalized in the intensive care unit, of which 35 received intravenous vitamin C at a dose of 6g per day. A limited number of patients demonstrated only a tendency to improve survival and resolution of shock symptoms. Although the study did not find evidence of the effectiveness of vitamin C, it emphasized the need for well-controlled, randomized trials to demonstrate its effectiveness against viral pneumonia. Scientists do not exclude the possibility that vitamin C may find a place in the treatment of pneumonia. [31]

In 2021, a review of studies on the impact of vitamin C supplementation on preventing and treating pneumonia in children and adults was published. Five studies involving a total of 2655 participants were considered. Three included children under the age of five, one included school-age children, and one included adult participants. Two studies assessed the impact of vitamin C supplementation on preventing pneumonia, while three studies evaluated the impact of vitamin C supplementation as part of pneumonia treatment. In the studies on pneumonia prevention supplementation at doses of 1 g per day for 14 weeks, 2 g per day for 8 weeks, and 2 g per day for 14 weeks was used. The analyzed trials in pneumonia treatment supplemented vitamin C as adjunctive therapy at doses of 125 mg per day and 200 mg per day until symptoms resolved or the patient was discharged. The conclusions suggest that there is insufficient certainty in existing evidence to reliably assess the impact of vitamin C supplementation on preventing and treating pneumonia. Further high-quality studies are needed to evaluate the role of vitamin C supplementation in the prevention and treatment of pneumonia. [32]

Conclusions

Analyzed studies in general cases do not clearly prove the efficacy of vitamin C supplementation in the prevention and treatment of viral infections such as the common cold, COVID-19 or pneumonia. However, positive results of vitamin C administration in the common cold have been observed in specific cases, mainly among older patients or those exposed to continuous oxidative stress. The use of vitamin C in COVID-19 treatment may lead to positive outcomes. However, it is too early to use vitamin C in patients with COVID-19 treatment to reduce mortality, improve thrombosis rates, or oxygenation. The current evidence for the effectiveness of vitamin C in pneumonia is weak. Nevertheless, therapeutic supplementation with vitamin C may be justified in patients with low serum vitamin C levels. None of the analyzed studies, except for one meta-analysis, found any negative effects resulting from additional vitamin C supplementation. Given the above, and the low cost of such supplementation, it may be justified in some groups of patients to include vitamin C administration in the treatment process. Further studies, especially randomized clinical trials, are required to demonstrate its effectiveness in specific viral infections.

Disclosure

Author's contribution

Conceptualization: Magdalena Kozioł, Kamila Podgórniak, Aleksandra Małgorzata Zajkowska; Methodology: Kinga Klimczak, Marlena Cąkała, Katarzyna Lenczewska; Software: Kinga Klimczak, Julia Piotrowska, Magdalena Kozioł; Check: Karolina Błaszczak, Joanna Skotnicka, Kamila Podgórniak; Formal Analysis: Maria Witkowska, Marlena Cąkała, Julia Piotrowska; Investigation: Aleksandra Małgorzata Zajkowska, Katarzyna Lenczewska, Karolina Błaszczak; Resources: Joanna Skotnicka, Maria Witkowska; Data Curation: Karolina Błaszczak, Joanna Skotnicka; Writing - Rough Preparation: Julia Piotrowska, Kinga Klimczak, Katarzyna Lenczewska, Maria Witkowska; Writing - Review and Editing: Magdalena Kozioł, Kamila Podgórniak, Aleksandra Małgorzata Zajkowska; Visualization: Aleksandra Małgorzata Zajkowska, Marlena Cąkała; Funding Acquisition: Not applicable

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