



Is vitamin C an effective agent for the prevention of COVID-19 and treatment of severe infection in the ICU?

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Both dietary and high doses of vitamin C have been reported to have various immune modulatory effects, including modulation of complement activation followed by cytokine release [1]. These effects on the immune system set vitamin C apart from other anti-oxidants. Vitamin C deficiency has been shown to be related to increased risk of viral upper respiratory tract infections (URTI), and in several studies published in the 1970s, it was used for the prevention and treatment of viral URTI. A systematic review showed that regular vitamin C treatment plays a preventive role only in certain populations, e.g. in professional athletes, people with a history of frequent viral URTI, and people exposed to extreme cold stress [2]. In that review, high-dose (≥ 0.2 g/day) vitamin C did not affect the duration of URTI except in the common cold. It reduced the duration of common cold in children by 14% and in adults by 8%. Higher doses (1–2 g/day) were more effective in children, reducing duration by 18% with accompanying reduction in severity of symptoms. No specific benefit was shown in influenza infection due to the study designs [3]. In two recent meta-analyses of randomized controlled trials in children, vitamin C did not prevent URTI, but shortened its duration in children under 6 years of age [3, 4]. Moreover, extra doses of vitamin C decreased the severity of symptoms only when used during infection. These scientific evidences suggest that vitamin C may be of benefit in the prevention of URTI in certain age groups, such as in children under 6 years of age and in special high-risk populations. Although vitamin C failed in prevention, it shortened the duration of common cold and reduced the severity of symptoms in a limited population. Furthermore,

vitamin C was well tolerated in these studies without any serious side effects. While it seems there is no strong evidence to recommend universal vitamin C use to prevent and reduce severity of symptoms in COVID-19, physicians should recommend vitamin C against COVID-19 after considering the risk-benefit ratio.

In septic patients, poorer clinical outcomes were reported to correlate with lower vitamin C levels [5]. This fact led to consideration of vitamin C use in serious clinical situations like acute respiratory distress syndrome (ARDS). ARDS is the most severe clinical form of COVID-19 infection, and is the result of overproduced cytokines. It is related with high mortality rates, and there is no definite curative treatment modality to date. Since vitamin C has been shown to exert anti-inflammatory effects in pre-clinical studies, it has been used in some centers to treat COVID-19-related ARDS and severe pneumonia. However, evidence suggesting the favorable effects of high-dose vitamin C infusion in severe sepsis and ARDS is limited. In a recent study, high-dose vitamin C infusion in patients with ARDS showed no benefit on mortality and other parameters of ARDS, such as markers of inflammation, vascular injury, and sepsis [6–8]. No significant side effects were reported, including no oxalate stone formation in the kidney, which is a proposed side effect for vitamin C. Further clinical evidence from randomized controlled studies is mandatory to recommend vitamin C infusion in sepsis and COVID-19-related ARDS. Of note, COVID-19-related ARDS is a severe condition, and vitamin C infusion seems relatively safe in clinical studies. Clinicians should consider its use in critical patients in intensive care units after weighing the risk-benefit ratio.

Artifacts in blood glucose readings may be an issue during vitamin C infusion [9], and high blood sugar readings should be confirmed in laboratory before deciding treatment of hyperglycemia.

In conclusion, the role of regular use of vitamin C in the prevention of COVID-19 and high-dose infusion of vitamin C in severe infection need to be clarified with further scientific evidence. Due to the severity of the outbreak, the safety profile of vitamin C may be a parameter by which to consider its use in these situations.

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