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Role of vitamin C in critically ill patients with COVID-19: is it effective?

Siddique Mohyud Din Chaudhary[1], Robert Matthew Wright[1], Gabriel Patarroyo-Aponte[1,2]

[1]Department of Pulmonary Critical Care Medicine, Einstein Medical Center Philadelphia, Philadelphia, PA; [2]Department of Medicine, Sidney Kimmel College of Thomas Jefferson University, Philadelphia, PA, USA

High-dose vitamin C has been studied for its role in septic shock, with a few randomized controlled trials going on to further evaluate its efficacy in this high oxidative stress state [1,2]. Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, there have been many therapies proposed for treatment. One of them is the possible use of vitamin C due to its antioxidant properties.

Humans have limited ability to synthesize vitamin C and it has to be taken through food or supplements. The regular oral intake of vitamin C can only increase the vitamin C to a certain level due to limited absorption i.e., about 70–85 μmol/L for a daily intake of 300 mg. Padayatty et al. [3] demonstrated that for comparative doses of oral and intravenous (IV) vitamin C the IV doses achieve a significantly higher level of peak plasma concentration, about a 70-fold increase.

A study involving early high-dose vitamin C for the treatment of sepsis showed potential benefits. A small randomized control trial in the surgical sepsis patient population showed promising results with shock reversal, shorter intensive care unit (ICU) length of stay, and improved survival [4,5]. In a meta-analysis on the role of vitamin C in the ICU patients, it was shown that vitamin C reduces the length of ICU stay by 7.8%–8.6% and shortened the duration of mechanical ventilation by 18.2%, all results were statistically significant [6].

Studies on COVID-19 have shown a high inflammatory response state with disease severity correlated with a high level of inflammatory markers including interleukin-6, ferritin, C-reactive protein (CRP), and D-dimers [7]. Most patients with severe disease end up on mechanical ventilation for a long period and therapies that might potentially decrease the number of days on a ventilator will be helpful for this highly inflammatory viral condition.

We had a few patients in our medical ICU that had a rapid turnover once they were started on vitamin C as rescue therapy for the refractory shock. Some of these patients showed marked improvement in terms of weaning from vasopressors. Keeping this information in mind and the role of vitamin C in a high oxidative stress state, we utilized vitamin C on a few patients in our medical ICU who were in a state of refractory shock due to COVID-19.

This was a retrospective study of ICU patients at a large, 700 beds, an academic medical center with a 28 bed medical ICU, and with a surge capacity of 60 ICU beds during the COVID-19 pandemic. Institutional Review Board approval was obtained. We included all adult patients with laboratory-confirmed COVID-19 discharged from our ICU. COVID-19 was diagnosed via reverse transcriptase-polymerase chain reaction assays performed on nasopharyngeal swab specimens. A total of 128 patients were treated in our ICU and tested positive via PCR for COVID-19 from the period of March 15 to May 30, 2020. Out of these 128 patients,

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Corresponding author
Siddique Mohyud Din Chaudhary
Department of Pulmonary Critical Care Medicine, Einstein Medical Center Philadelphia, 5501 Old York rd, Philadelphia, PA 19141, USA
Tel: +1-8103391994
Fax: +1-2154568523
E-mail: chaudhsi@einstein.edu

15 were treated with high-dose vitamin C. The median age was 72 years (interquartile range [IQR], 63.5–78). The median body mass index was 27 kg/m^2 (IQR, 25.5–30). Males were 8 of 15 (53.3%). Our patient population was predominantly African American, 80% of patients. Hypertension was the most common comorbid condition in 93.3% of patients. Two or more comorbid conditions were present in 60% of patients. Only one patient was immunocompromised with a history of a kidney transplant on chronic prednisone therapy. Almost all patients were intubated 13 of 15 (86.7%). The baseline labs (median with IQR) were as follows white blood cell: 8.93 × 10^3/μl (5.96–11.98), platelets: 161 × 10^3/μl (144–229), CRP: 178.4 mg/L (132.8–266.8), D-dimer: 3,105 ng/ml (1,660–4,772), ferritin: 696 ng/ml (503–921). The dose of vitamin C used was 3 g/day given in three divided doses for a total of 3–5 days. These patients were treated before the availability of Remdesivir or convalescent plasma, hence were given hydroxychloroquine (15/15) and tocilizumab (6/15) when indicated. Patients were treated with a standardized dose of 1 mg/kg of IV methylprednisone for 7 days and 80% of the patient got steroids. A decrease in vasopressor requirement was noticed in two patients after starting on vitamin C. Prone positioning was utilized in 6 of 15 (40%) of the patients and 2 of 6 of these patients survived. There was no change in Sequential Organ Failure Assessment (SOFA) score post vitamin C treatment and inflammatory markers trended down in 5 of 15 patients, Ferritin 696 ng/ml (503–921) to 679 ng/ml (398–1,059) and D-dimer 3,105 ng/ml (1,660-4,772) to 2,775 ng/ml (2,450-4,105). For the 128 patients with COVID-19 treated in our ICU, the mortality was 29% and for those requiring mechanical ventilation was 39.3%. In the subset of patients who got vitamin C, the mortality was 80% and withdrawal of care was done in 7 of 15 (46.7%) of the patients.

In our small case series of patients, the mortality was still high despite treatment with vitamin C. This could very likely be due to the severity of illness and refractory shock and the outcome unrelated to whether they got vitamin C. The definitive role of vitamin C in COVID-19 will have to be further studied by larger randomized controlled trials currently enrolling or in process of recruiting patients [8-10]. Till then treatment with vitamin C needs to be made on a case by case basis and will probably have more benefit if utilized early in the disease state.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Siddique Mohyud Din Chaudhary
https://orcid.org/0000-0001-9079-215X
Robert Matthew Wright
https://orcid.org/0000-0001-9307-5498
Gabriel Patarroyo-Aponte
https://orcid.org/0000-0002-2676-6747

AUTHOR CONTRIBUTIONS

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