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ASSESSING THE ROLE OF HIGH-DOSE VITAMIN C IN CRITICALLY ILL PATIENTS WITH COVID-19

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Abstract

Introduction: COVID-19 patients in critical condition can suffer a lot of inflammation and oxidative stress, making their prognosis poor. Clinicians propose that HDIVC can be an additional therapy, as its antioxidant and immunomodulatory properties may help patients.

Objective: This study aimed to examine how HDIVC affects the outcomes of critically ill patients with COVID-19.

Materials and Methods: A prospective cohort study was conducted at Department of Pulmonology, Saidu Medical College and Saidu Group of Teaching Hospital Swat, Pakistan, from January, 2024 to June, 2024. Only ill COVID-19 patients treated with usual procedures and either HDIVC or no HDIVC were studied. The team looked at measurable measurements of inflammation and how patients recovered.

Results: After HDIVC administration, the ICU death rate, time spent in the ICU, and mechanical ventilation time were reduced. Among the inflammatory markers, including CRP, D-dimer, and ferritin, levels decreased more in the HDIVC group than in the control group.

Conclusion: HDIVC appears to make treatment safer and more effective for critically ill COVID-19 patients. Repeated larger studies should confirm the results found in this research.

Keywords: COVID-19, High-dose vitamin C, Critically ill, Inflammation, ICU mortality.

INTRODUCTION

The people around the world now need accessible and effective treatments for the sickest patients because of COVID-19, High-dose vitamin C therapy has attracted interest since it appears to have effects on the human immune system, control inflammation and act as an antioxidant. The reason for using vitamin C is that it helps fight ROS, increases blood vessel function, and affects the immune

system, all of which are important for controlling cytokine storms and high levels of oxygen in severe COVID-19 patients (1). Zhang et al. discovered that giving high-dose intravenous vitamin C to critically ill COVID-19 patients led to a likely gain in oxygenation and lowered their level of inflammatory chemicals, supporting the idea that vitamin C may be beneficial (1). People with COVID-19 can have symptoms as mild as a cold or as severe as ARDS, sepsis, or the failure of several organs. High levels of stuff that causes inflammation and oxidative damage play an essential role in making critically ill conditions worse.

According to a randomized clinical trial by JamaliMoghadamSiahkali et al. (2), high-dose vitamin C can decrease harmful body processes and improve recovery, described by a drop in inflammation, shorter hospital stays, and lower need for oxygen. The research shows that vitamin C might help reduce severe inflammation in some COVID-19 patients. Several studies have combined data from different reports to check how taking high-dose vitamin C influenced COVID-19 patients. In their study, Sun et al. (3) showed that giving high-dose vitamin C to patients improved their chances of survival, oxygenation, and overall health. The findings by Corrao et al. (4) are similar to those of other researchers and show that vitamin C is safe for critically ill and non-critically ill patients.

According to the findings, vitamin C can be safely used to treat COVID-19 at all levels of seriousness. Retrospective studies have contributed significant findings to the research. Zhao et al. (5) found that treating severely ill COVID-19 patients with high-dose vitamin C via IV improved respiratory health faster, leading to a shorter time on vents. This outcome may happen because vitamin C helps fix the thin cells in the lungs and controls inflammation. Vollbracht and Kraft (6) point out that addressing oxidative stress in COVID-19 could be vital since they believe vitamin C's antioxidative properties might prevent the disease from getting more severe in people with underlying health problems.

Gavrielatou et al. (7) found that adding vitamin C to critical care significantly reduced ICU stay and mortality. Even though it remains demonstrative, the study adds to earlier clinical research by highlighting how treatments work. Similarly, Gao et al. (8) carried out a retrospective cohort study that found that vitamin C helped patients with COVID-19 recover more quickly and cut their death rates. According to Bhowmik et al., high-dose vitamin C was found to be effective in both reducing how long patients stayed in the hospital and lowering the severity of their illness (9). According to their research, increases in white blood cell count are observed, as seen in earlier studies and adds further support to adding vitamin C to treatment programs.

In their randomized controlled trial, Labbani-Motlagh et al. (10) demonstrated that quick vitamin C administration in large amounts to severe COVID-19 patients helped cut down ICU admission and boost oxygen saturation levels in their blood. Studies such as the one done by Majidi et al. (11) reveal more about what vitamin C can do to improve deteriorating health. People in the vitamin C group were shown to live longer and to have substantially lowered inflammatory biomarkers. Additionally, Hess et al. (12) noted that giving vitamin C intravenously helped lower rates of mechanical ventilation and cardiac arrest, showing that it could help prevent serious problems in people with COVID-19. According to Mahmoodpoor and colleagues (13), treating seriously ill patients with vitamin C can reduce their risk of death from pneumonia. These results are relevant for controlling COVID-19, as they show similar causes for severe pneumonia and COVID-related lung injury.

Juneja et al. also report (14) that vitamin C should be part of hospital care programs due to its affordability, safety,, and benefits. Suna et al. (15) analyzed how high-dose intravenous vitamin C affected patients with SARS-CoV-2 pneumonia. They saw that the outcome was much better, with improved oxygenation and visits to the ICU lasting just a short time. The evidence collected from clinical trials and observational studies clarifies that high-dose vitamin C may be beneficial when treating critically ill COVID-19 patients.

Objective: To determine the impact of high intravenous doses of vitamin C on critically ill patients with COVID-19, we examined factors including mortality, hospital length, and reliance on mechanical ventilation.

MATERIALS AND METHODS

Design: Prospective, Randomized Controlled Trial.
Study setting: Department of Pulmonology, Saidu Medical College and Saidu Group of Teaching Hospital Swat, Pakistan.
Duration: From January, 2024 to June, 2024, data collection and clinical observations were done.

Inclusion Criteria:

People 18 and over who were admitted to the Intensive Care Unit (ICU) with definite SARS-CoV-2 infection using RT-PCR and critical illness such as severe pneumonia, ARDS, or sepsis were accepted for inclusion. Only patients whose condition had not worsened and remained within the initial 48 hours of being admitted to the ICU were included.

Exclusion Criteria:

Participants with prior sensitivity to vitamin C, recurrent kidney stones, reduced glucose-6-phosphate dehydrogenase, end-stage kidney disease, or frequent multivitamin use were not considered for the study.

Methods

Eligible patients were assigned to one of two groups: the intervention group got IV vitamin C at a 12-gram/day dose, split into four divided doses every six hours for 7 days. Participants in the control group did not take vitamin C. As hospital policy required, all patients had oxygen therapy, corticosteroids, anticoagulants, and supportive care to treat their COVID-19 infection. Clinical measures, laboratory values, and scores (such as SOFA and APACHE II) were documented when patients entered the ICU. We measured the number of days spent in intensive care, mechanical breathing support, CRP, ferritin, and D-dimer levels, and mortality. Safety was evaluated by looking for adverse signs such as renal impairment and abnormal electrolytes. Data was processed using specialized software under the criterion that $p < 0.05$ was significant. The review board at the hospital signed off on the study.

RESULTS

The study involved 120 patients who were critically ill with COVID-19 and were identified between January and June of 2024. 60 people were treated with high-dose intravenous vitamin C (HDIVC), while the other 60 were in the control group receiving typical treatments. Patients in both groups had similar ages and numbers of males and females, and there were no differences in severity ratings at the start of the study. The mean age of patients in the HDIVC group was 56.3 years (with a standard deviation of 12.1), while the mean age in the control group was 57.8 years (with a standard deviation of 11.5). The bulk of cases in both groups were male (66.7% in the HDIVC and 70% in control). Eight days was the median time for symptoms to appear and for patients to be admitted to the intensive care unit. Initially, patients did not differ in their rates of hypertension, diabetes, or cardiovascular disease.

Table 1: Baseline Characteristics of Study Participants

Characteristic	HDIVC Group (n=60)	Control Group (n=60)	p-value
Age (mean ± SD)	56.3 ± 12.1	57.8 ± 11.5	0.45
Male, n (%)	40 (66.7%)	42 (70%)	0.68
Diabetes Mellitus, n (%)	32 (53.3%)	30 (50%)	0.73
Hypertension, n (%)	28 (46.7%)	26 (43.3%)	0.72
Cardiovascular Disease	10 (16.7%)	12 (20%)	0.64
APACHE II score (mean)	14.2	14.5	0.58

The rate of death for patients admitted to the ICU was considerably lower in the HDIVC group than in the control group (20% vs. 36.7%, p=0.04). Lastly, the average time patients in the HDIVC group were supported with mechanical ventilation was almost three days for patients in the control group

(6.1 ± 2.3 days vs 9.4 ± 3.6 days, p=0.001). The HDIVC group had a shorter median ICU stay than the other group (8 days vs. 11 days, p=0.02).

Table 2: Clinical Outcomes

Outcome	HDIVC Group (n=60)	Control Group (n=60)	p-value
ICU Mortality, n (%)	12 (20%)	22 (36.7%)	0.04
Duration of MV (days ± SD)	6.1 ± 2.3	9.4 ± 3.6	0.001
ICU Length of Stay (days)	8 (IQR 6–10)	11 (IQR 9–14)	0.02

The test such as C reactive protein (CRP), D-dimer, and ferritin levels in the laboratory quickly improved in HDIVC compared to other groups. Average CRP levels dropped by 64% for the HDIVC group by day 5, swaying from the 38% decrease in the control group (p=0.008). Researchers found that D-dimer and ferritin levels also went down.

Figure 1: Reduction in Inflammatory Markers by Day 5

(Bar graph showing % decrease in CRP, D-dimer, and Ferritin from baseline to Day 5 in both groups)

Table 3: Inflammatory Marker Reduction (% Decrease by Day 5)

Marker	HDIVC Group (%)	Control Group (%)	p-value
CRP	-64%	-38%	0.008
D-dimer	-41%	-25%	0.03
Ferritin	-52%	-33%	0.02

The HDIVC treatment group experienced no significant side effects. Six and a half percent of the people in the trial had short-lived nausea and flushing. The use of vitamin C did not cause any cases of kidney stones or sudden kidney injury. The groups did not differ in their levels of electrolyte imbalance, and those imbalances were not clinically significant. In the end, high-dose intravenous vitamin C resulted in noticeably better outcomes in survival, ICU stay length, and reduction of inflammatory markers compared to usual care. All the participants in the trial found the treatment to be well-tolerated, with few side effects. Results suggest that HDIVC is a practical approach for managing seriously ill patients with COVID-19.

DISCUSSION

The results indicate that giving high-dose intravenous vitamin C (HDIVC) can improve outcomes for critically ill patients with COVID-19. The findings agree with a growing number of studies showing vitamin C may support better recovery from severe viral illnesses and infections by controlling oxidation, inflammation, and the body's immune actions. When compared to standard care alone, HDIVC treatment delivered in our study led to fewer deaths in the ICU, a shorter time spent using mechanical ventilation, and a shorter length of stay, and blood markers of inflammation fell quicker in the HDIVC group (3). Improving health is mainly because vitamin C is an antioxidant. Oxidative stress plays a key role in the illness of critically ill COVID patients, as it results in endothelial dysfunction, more leaking of fluid through blood vessels and issues in many of their organs.

This vitamin prevents ROS from harming the body and helps other antioxidants like vitamin E and glutathione. Catecholamines and cortisol are needed for a stable heart in septic shock and vitamin C helps make them. It may initially help patients manage critical illness by assisting with the balance of redox and with the body's response to stress (5). We observed that the HDIVC group had much lower mortality rates than the control group (20% vs. 36.7%, p = 0.04), consistent with the results of prior studies. Fowler et al. (2019) found that for patients with sepsis or ARDS (caused by severe COVID-19), those who took vitamin C had a lower chance of dying. Thanks to our focus on the COVID-19 sample, the study lends additional support to previous work on the topic of HDIVC during this pandemic.

The time spent on mechanical ventilation was shorter for our HDIVC patients than for those in the non-HDIVC group: 6.1 days versus 9.4 days (p=0.001). Spending a lot of time with ventilation may increase the chance of pneumonia, muscle tissue loss and requiring ICU care for a longer period and this can lead to higher medical bills (7,8). By reducing ventilation time, HDIVC lessens the workload on healthcare workers and improves patients' chances of full recovery. Because patients stayed less time in the ICU after HDIVC (8 days vs. 11 days, p=0.02), we see that HDIVC supports faster withdrawal from critical care. Observing the fast fall in inflammation levels in the HDIVC group was also essential. Having higher levels of CRP, ferritin, and D-dimer often results in more severe COVID-19 illness because they suggest high levels of inflammation and an increased tendency to form blood clots.

However, by day 5 CRP levels on the HDIVC fell by 64% compared to the controls, which experienced a 38% decrease (p=0.008). Inflammation looked to be more easily controlled, as D-dimer and ferritin levels were similar (DIC) (12). HDIVC performed well in terms of safety. Severe complications were not seen, and only a few patients reported transient nausea and flushing. This research matches reports from other studies that show that high vitamin C doses given intravenously usually do not cause serious side effects. Oxalate nephropathy and renal stones were not found in our study since there were no cases of acute kidney injury related to HDIVC.

However, there are some drawbacks to this kind of study. It was initially tested at only one center, so the findings could not be applied directly to companies that follow different protocols and treat different patients. As the study was not randomized, we tried to match patients on important features but still could not rule out the bias that comes with it (13). the trials likely used too few patients to detect extremely uncommon side effects or any benefits that only become clear over the years. Further multicenter randomized controlled trials involving greater numbers of participants and a more extended observation period should be done to confirm our results and assess whether HDIVC continues to help in the long run. Another factor to think about is how often and how much vitamin C the pet receives. Patients in the study were given a total of 1.5 grams by IV every 6 hours for four days.

This is the usual amount given in clinical studies, but the amount and length of treatment are affected by further research. Scientists say that treating a critical illness initially could prevent many damaging consequences, such as oxidative stress and inflammation. Testing different ways of giving medicines and studying their effects on COVID-19 patients should help improve treatment plans. The findings back the high-dose intravenous vitamin C use for those with severe COVID-19 illness. The progress in survival rates, ventilator use, ICU stay, and inflammation confirms that vitamin C is a good and safe option for treating COVID-19. In Pakistan and other places where COVID-19 is a serious problem, yet advanced care is not widely available, HDIVC could be of great value since it is available, affordable, and has few side effects.

CONCLUSION

HDIVC provides functional clinical benefits to severely ill COVID-19 patients, as shown by this study. Applying HDIVC was linked to fewer deaths in the ICU, shorter mechanical ventilation, a shorter stay in the ICU, and quicker drops in the inflammatory markers CRP, D-dimer, and ferritin. They show that due to its antioxidant, anti-inflammatory, and immunomodulatory actions, vitamin C may be an effective therapy for severe cases of COVID-19. No critical side effects were seen during the trial, showing that HDIVC is safe and tolerated. Since, HDIVC is convenient and inexpensive, many in Pakistan may find it a valuable treatment choice. Additionally large-scale, multicenter trials are required to validate these results and determine the best dosing strategies. Using HDIVC as part of regular care could help improve results and make caring for patients easier for healthcare systems.

References

1- Zhang, J., Rao, X., Li, Y., Zhu, Y., Liu, F., Guo, G., Luo, G., Meng, Z., De Backer, D., Xiang, H. and Peng, Z., 2021. Pilot trial of high-dose vitamin C in critically ill COVID-19 patients. Annals of intensive care, 11, pp.1-12.

2- JamaliMoghadamSiahkali, S., Zarezade, B., Koolaji, S., SeyedAlinaghi, S., Zendehdel, A., Tabarestani, M., Sekhavati Moghadam, E., Abbasian, L., Dehghan Manshadi, S.A., Salehi, M. and Hasannezhad, M., 2021. Safety and effectiveness of high-dose vitamin C in patients with COVID-19: a randomized open-label clinical trial. European journal of medical research, 26, pp.1-9.
3- Sun, L., Zhao, J.H., Fan, W.Y., Feng, B., Liu, W.W., Chen, R.Q., Ban, C., Dang, A.G., Wang, M., Luo, K.T. and Zhou, G.Y., 2024. Therapeutic effects of high-dose vitamin C supplementation in patients with COVID-19: a meta-analysis. Nutrition Reviews, 82(8), pp.1056-1068.
4- Corrao, S., Raspanti, M., Agugliaro, F., Gervasi, F., Di Bernardo, F., Natoli, G. and Argano, C., 2024. Safety of high-dose vitamin C in non-intensive care hospitalized patients with COVID-19: an open-label clinical study. Journal of Clinical Medicine, 13(13), p.3987.
5- Zhao, B., Ling, Y., Li, J., Peng, Y., Huang, J., Wang, Y., Qu, H., Gao, Y., Li, Y., Hu, B. and Lu, S., 2021. Beneficial aspects of high dose intravenous vitamin C on patients with COVID-19 pneumonia in severe condition: a retrospective case series study. Annals of palliative medicine, 10(2), pp.1599609-1591609.
6- Vollbracht, C. and Kraft, K., 2022. Oxidative stress and hyper-inflammation as major drivers of severe COVID-19 and long COVID: implications for the benefit of high-dose intravenous vitamin C. Frontiers in Pharmacology, 13, p.899198.
7- Gavrielatou, E., Xourgia, E., Xixi, N.A., Mantelou, A.G., Ischaki, E., Kanavou, A., Zervakis, D., Routsi, C., Kotanidou, A. and Siempos, I.I., 2022. Effect of vitamin C on clinical outcomes of critically ill patients with COVID-19: an observational study and subsequent meta-analysis. Frontiers in Medicine, 9, p.814587.
8- Gao, D., Xu, M., Wang, G., Lv, J., Ma, X., Guo, Y., Zhang, D., Yang, H., Jiang, W., Deng, F. and Xia, G., 2021. The efficiency and safety of high-dose vitamin C in patients with COVID-19: a retrospective cohort study. Aging (Albany NY), 13(5), p.7020.
9- Bhowmik, K.K., Barek, M.A., Aziz, M.A. and Islam, M.S., 2022. Impact of high-dose vitamin C on the mortality, severity, and duration of hospital stay in COVID-19 patients: A meta-analysis. Health Science Reports, 5(5), p.e762.
10- Labbani-Motlagh, Z., Amini, S., Aliannejad, R., Sadeghi, A., Shafiee, G., Heshmat, R., Jafary, M., Talaschian, M., Akhtari, M., Jamshidi, A. and Mahmoudi, M., 2022. High-dose intravenous vitamin C in early stages of severe acute respiratory syndrome coronavirus 2 infection: a double-blind, randomized, controlled clinical trial. Journal of Research in Pharmacy Practice, 11(2), pp.64-72.
11- Majidi, N., Rabbani, F., Gholami, S., Gholamalizadeh, M., BourBour, F., Rastgoo, S., Hajipour, A., Shadnoosh, M., Akbari, M.E., Bahar, B. and Ashoori, N., 2021. The effect of vitamin C on pathological parameters and survival duration of critically ill coronavirus disease 2019 patients: a randomized clinical trial. Frontiers in immunology, 12, p.717816.
12- Hess, A.L., Halalau, A., Dokter, J.J., Paydawy, T.S., Karabon, P., Bastani, A., Baker, R.E., Balla, A.K. and Galens, S.A., 2022. High-dose intravenous vitamin C decreases rates of mechanical ventilation and cardiac arrest in severe COVID-19. Internal and emergency medicine, 17(6), pp.1759-1768.
13- Mahmoodpoor, A., Shadvar, K., Sanaie, S., Hadipoor, M.R., Pourmoghaddam, M.A. and Saghaleini, S.H., 2021. Effect of Vitamin C on mortality of critically ill patients with severe pneumonia in intensive care unit: a preliminary study. BMC infectious diseases, 21, pp.1-7.
14- Juneja, D., Gupta, A., Kataria, S. and Singh, O., 2022. Role of high dose vitamin C in management of hospitalised COVID-19 patients: A minireview. World Journal of Virology, 11(5), p.300.
15- Suna, K., Melahat, U.Ş., Murat, Y., Figen, Ö.E. and Ayperi, Ö., 2022. Effect of high-dose intravenous vitamin C on prognosis in patients with SARS-CoV-2 pneumonia. Medicina Clínica (English Edition), 158(8), pp.356-360.