High-Dose IV Vitamin C on ARDS by COVID-19: A Possible Low-Cost Ally With a Wide Margin of Safety

Posted by PWeekly | Apr 29, 2020

The following is reprinted, at the request of the author, from an article originally posted in Spanish to the IntraMed website.

Intravenous vitamin C has been the object of numerous studies regarding its function as adjuvant therapy on critical patients' care, included ARDS of diverse etiology. In the context of a coronavirus pandemic, with an elevated morbimortality and pressure over the sanitary system, it is of vital importance to use every available resource to improve patients' outcomes in an accessible and safe way. In this article, I briefly analyze the evidence around the use of vitamin C in the critical patient and its potential benefits on admission time, intubation time and mortality on patients affected by ARDS.

Vitamin C was discovered in the 30s by Albert Szent-Györgyi. The first therapeutic function known was to treat scurvy, first described on ship crews who couldn't access fresh fruits and vegetables during long seasons on the sea. Later on, Nobel Prize winner Linus Pauling performed numerous studies on the physiological and therapeutic effects of vitamin C, concluding that we were just beginning to understand its full potential. Humans are one of the few vertebrates that can't synthesize vitamin C, therefore it is

considered to be an essential nutrient. It's estimated that 7% of the general population is deficient in vitamin C, but this percentage increases to 47% in admitted patients. [1][2]

Vitamin C's enteral absorption is limited and its plasmatic levels are strictly regulated. A standard dietary intake maintains plasmatic levels around 70 µmol/L, but intensive oral supplementation of 3 grams a day only rises this level up to a maximum of 220 µmol/L. Therapeutic effects are achieved with plasmatic levels in the range of 20-49 mmol/L (100 times higher than those achieved by oral intake) only possible with intravenous infusion[3][4][5].

Evidence shows that the therapeutic effects take place with a minimum dose of 50mg/k/day and a maximum of 200mg/k/day, divided into four doses given every 6 hours. The largest randomized study performed so far, CITRIS-ALI [6], found that vitamin C supplementation failed to modify biomarkers such as thrombomodulin, C reactive protein and organ failure scores (SOFA), but successfully reduced mortality by 16.5%, respiratory assistance requirements by 2.5 days, ICU stay by 3.2 days and hospital admission by 6.7 days, compared to placebo. This is more relevant than never in view of the worldwide shortages in beds and equipment. Some authors suggest that the reason why biomarkers weren't modified was that the samples were taken at 96 hours, time when more severely ill patients had died and were excluded from the study (survivorship bias)[7][8]. Two meta-analyses that included 685 and 147 critical patients concluded that intravenous vitamin C showed no adverse reactions, reduced the need for fluids and vasopressor support and reduced intubation time up to 25%[9][10].

A series of case reports on ADRS of diverse etiology (aspirative after seizures, inflammatory during a psoriasis flare-up, and viral) describes a fast improvement following vitamin C administration, even when the treatment was started after ECMO was required. In every case there was a symptomatic and radiologic improvement in 24-48 hours after the initial dose and good evolution at discharge, without signs of fibrotic sequels[11][12][13]. Marik et. al. found a 30% mortality reduction in septic patients treated with vitamin C, hydrocortisone and thiamine, when compared to patients treated under standard procedures. In addition, the treated group required 50% less vasopressor support than the control group[14].

Regarding the evidence around vitamin C's mechanisms of action, certain preclinical findings might explain the effects observed on respiratory distress. Vitamin C down-regulates inflammatory genes and inhibits the cytokine storm responsible for the activation of

pulmonary neutrophils, therefore protecting alveolar capillaries from inflammatory damage. In addition to this, it enhances alveolary fluid clearance by increasing the water transporter channel expression[15][16].

In regards to its safety, most studies report no adverse effects on large doses of vitamin C. On rare occasions, the following have been described: Hypersensitivity, oxalate urolithiasis, iron overload in haemochromatosis and anaemia among others, most of them with a prevalence less than 1%. It has also been described the inaccuracy of bedside glucometry when using vitamin C and it is advised to corroborate findings with laboratory results[5][17][18][19].

We live in times of incalculable need. Worldwide medical supplies are in shortage, costs threat to crush even the wealthiest of health care systems, and above all the wellbeing of millions of humans is at risk. Treatment of severe ARDS from COVID-19 is an ongoing challenge and a specific treatment could be months ahead. The evidence around vitamin C is scarce but promising. There probably never was and never will be a better time than the current to explore and make use of every possible tool that could allow us to improve patients' prognosis and expand the body of evidence for the benefit of all.

References

Schleicher, Rosemary L., et al. "Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003–2004 National Health and Nutrition Examination Survey (NHANES)." The American journal of clinical nutrition 90.5 (2009): 1252-1263.
2. Fain, Olivier, et al. "Hypovitaminosis C in hospitalized patients." European journal of internal medicine 14.7 (2003): 419-425.
3. Jacob, Robert A., and Gity Sotoudeh. "Vitamin C function and status in chronic disease." Nutrition in clinical care 5.2 (2002): 66-74.
4. Padayatty, Sebastian J., et al. "Vitamin C pharmacokinetics: implications for oral and intravenous use." Annals of internal medicine 140.7 (2004): 533-537.
5. Stephenson, Christopher M., et al. "Phase I clinical trial to evaluate the safety, tolerability, and pharmacokinetics of high-dose intravenous ascorbic acid in patients with advanced cancer." Cancer chemotherapy and pharmacology 72.1 (2013): 139-146.
6. Truwit, Jonathon D., et al. "Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI randomized clinical trial." Jama 322.13 (2019): 1261-1270.

7. Spiegel, Rory. “Myths in Emergency Medicine: Vitamin C Trial Lacks Answers for Sepsis.” Emergency Medicine News 42.1 (2020): 1-32.
8. Hager, David N., Jeremiah S. Hinson, and Richard E. Rothman. “Vitamin C for Sepsis and Acute Respiratory Failure.” Jama 323.8 (2020): 791-792.
9. Zhang, Michael, and David F. Jativa. “Vitamin C supplementation in the critically ill: A systematic review and meta-analysis.” SAGE open medicine 6 (2018): 2050312118807615.
10. Hemilä, Harri, and Elizabeth Chalker. “Vitamin C may reduce the duration of mechanical ventilation in critically ill patients: a metaregression
analysis.” Journal of Intensive Care 8.1 (2020): 15.
11. Marik, Paul E., et al. “Hydrocortisone, vitamin C, and thiamine for the treatment of severe sepsis and septic shock: a retrospective before-after study.” Chest 151.6 (2017): 1229-1238.
12. Marik, Paul Ellis, and Ashleigh Long. “ARDS complicating pustular psoriasis: treatment with low-dose corticosteroids, vitamin C and thiamine.” Case Reports 2018 (2018): bcr-2017.
13. Kim, C., et al. “Vitamin C infusion for gastric acid aspiration-induced acute respiratory distress syndrome (ARDS).” Pulm Res Respir
Med Open J 4.2 (2017): 33-37.
14. Fowler III, Alpha A., et al. “Intravenous vitamin C as adjunctive therapy for enterovirus/rhinovirus induced acute respiratory distress
syndrome.” World journal of critical care medicine 6.1 (2017): 85.
15. Fisher, Bernard J., et al. “Mechanisms of attenuation of abdominal sepsis induced acute lung injury by ascorbic acid.” American
Journal of Physiology-Lung Cellular and Molecular Physiology 303.1 (2012): L20-L32.
16. Fisher, Bernard J., et al. “Ascorbic acid attenuates lipopolysaccharide-induced acute lung injury.” Critical care medicine 39.6 (2011):
1454-1460.
17. Padayatty, Sebastian J., et al. “Vitamin C: intravenous use by complementary and alternative medicine practitioners and adverse effects.” PloS one 5.7 (2010).
18. Canavese, Caterina, et al. “Long-term, low-dose, intravenous vitamin C leads to plasma calcium oxalate supersaturation in hemodialysis patients.” American journal of kidney diseases 45.3 (2005): 540-549.
19. Hager, David N., et al. “Glucometry when using vitamin C in sepsis: a note of caution.” Chest 154.1 (2018): 228-229.

SHARE:

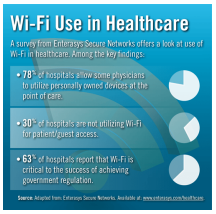
Dutch coronavirus cases rise to 38,802, with 145 new deaths: health authorities

Sweden's confirmed COVID-19 cases rise above 20,000

ABOUT THE AUTHOR

Dr. Florencia Paula Loza

RELATED POSTS



Wifi Use in Healthcare

April 22, 2013

Can Financial Incentives for Patients Induce Weight Loss?

October 18, 2013

Diagnostic Stewardship for Blood Cultures

September 27, 2018

Helpful Guidelines for Heart Health in Diabetes

November 29, 2010

2 Comments

George Francis on April 30, 2020 at 7:39 am

Liposomal vitamin c is just as effective is intravenous vitamin c fine this out on George

REPLY

Joe arsanis on April 29, 2020 at 11:45 pm

Yes after reading whether vitamin C helps fight Covid-19 I still don't know, do you?

REPLY

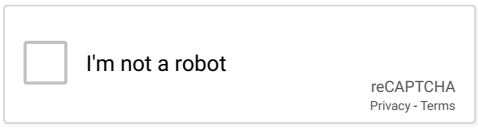
Leave a reply

Your email address will not be published. Required fields are marked *

COMMENT

NAME * EMAIL * WEBSITE

Save my name, email, and website in this browser for the next time I comment.



Sign me up for the newsletter!

POST COMMENT