

Vitamin C

Vitamin C in the Prevention & Treatment of Covid-19



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Conflict of interest

Conflict of Interest Disclosure

I have nothing to disclose.

Disclaimers:

The opinions expressed in this talk purely represent that of mine and of the International Society for Orthomolecular Medicine (ISOM) and do not represent that of the NIH.

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Key pathologies

Key Pathologies of Covid-19

Covid-19 primarily affects the respiratory system, causing pneumonia, some of whom may develop acute lung injury (ALI)/acute respiratory distress syndrome (ARDS), sepsis, septic shock & multi-organ failure.¹⁻²

- Acute Lung Injury (ALI)/Acute Respiratory Distress Syndrome (ARDS) (17%);³
- Requiring mechanical ventilation (4%) ;³
- And septic shock (~4%).³

Oxidative stress/cytokine storm

Increased Oxidative Stress/ Cytokine Storm Underlying ALI/ARDS

ALI, ARDS, and sepsis are nonspecific pathologies shared by many viral infections including Covid-19 infection and other pathogens. Cytokine storm or increased oxidative stress is the key underlying common mechanism. Therapeutic agents, primarily antioxidants, including prototypical vitamin C, targeting increased oxidative stress/cytokine storm holds promises.

Vitamin C deficiency

VC Deficiency, a Key Finding of ICU Patients

Vitamin C deficiency is common among patients with acute and chronic diseases.¹⁻⁵

- 40% ICU patients with septic shock have blood VC levels approaching zero, diagnostic of scurvy ($<11.3 \text{ } \mu\text{mol/L}$),¹
 - with the remainder of ICU sepsis patients have hypovitaminosis C ($<23 \text{ } \mu\text{mol/L}$).¹
- ~50% non-septic ICU patients also have hypovitaminosis C.¹
- Low plasma VC levels are associated with more severe organ failure and increased mortality.⁶

High dose IVC and pneumonia

High-Dose IVC Prevents and Improves Pneumonia

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- 148 animal studies show VC can alleviate or prevent bacterial, viral and protozoan infections.
- VC cuts the risks of colds by 50% in physically active adults, although this is not always observed in the general population.
- 2 RCTs show a dose-dependent response in the therapeutic effects of VC in common colds.
- 3 RCTs found VC can prevent pneumonia.
- 2 RCTs found VC improve pneumonia treatment.
- 1 RCT found VC beneficial in the treatment of tetanus.

Mechanical ventilation

High-Dose IVC Shortens Mechanical Ventilation

High-dose IV Vit C (HDIVC) has been used in the treatment of pneumonia, sepsis and ARDS successfully. A recent meta-analysis pooled the data from 9 qualified trials and the analysis found strong evidence that HDIVC improves patient outcome:

- HDIVC shortens patients time on mechanical ventilation by 14% to 25% (when VC dose is 1,000 mg – 6,000 mg).

Multi-organ failure

2 **High-Dose IVC Prevents Multi-Organ Failure**

A 2014 study found very low plasma VC levels, approaching scurvy levels. HDIVC at 200 mg/kg body weight showed a dose-dependent effect of preventing multi-organ failure.

HDIVC group showed plasma VC levels of 3 mM/L on day 4, more than 40 times the average plasma VC level (~70 uM/L for people on balanced diet. For scurvy, VC < 11.3 uM/L).

ARDS mortality

HDIVC Reduces ARDS Mortality

The first HDIVC on ARDS trial was reported in 1989 where 32 patients were divided into 2 groups, 16 each. HDIVC group received VC 1,000 mg + NAC + Selenium + Vit E, every 6 hours.

HDIVC group showed a 47% reduction in mortality. The mortality in the HDIVC group was 37%, compared to 71% in the control group.¹

A 2016 study of 96 septic patients showed HDIVC (6,000 mg VC + hydrocortisone + thiamine cut the mortality by 31.9%.²

Trial on sepsis and ARDS

CITRIS-ALI, the Largest Trial on Sepsis and ARDS

CITRIS-ALI trial is a multi-center RCT, enrolled a total of 167 patients of sepsis and ARDS. HDIVC group was receiving VC 50 mg/kg body weight, every 6 hours for 4 days (3,500 mg IVC for a 70 kg person over 6 hours for 4 days).

- On day 28, HDIVC group showed a reduction of mortality by 35% (HDIVC 29.8% vs. control group 46.3%).
- HDIVC group also had a shortened duration on mechanical ventilation, as well as
- Average of 3-day reduction in ICU stay.

Covid-19

HDIVC on Covid-19

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HDIVC has been used in different settings in China during this pandemic.

- ~50 cases of moderate to severe Covid-19 pneumonia were treated with HDIVC (10,000 mg - 20,000mg/day) out of a total of 358 confirmed cases at the Shanghai Public Health Center.
- HDIVC group had a shorter hospital stay of ~5 days, compared to the 30-day average hospital stay. HDIVC patients also improved faster with no fatality. There were 3 fatalities of 358.
- One of the patient had rapidly deteriorating oxygenation index. This patient received an additional bolus of 50,000 mg VC over 4 hours. Real time improvement of the oxygenation index was observed.

HDVIC on Covid-19

HDVIC on Covid-19

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HDVIC has been used in different settings in China during this pandemic.

- A Zhongnan Hospital, Wuhan University team announced world's 1st HDVIC clinical trial on Covid-19 infection.
- A total of ~40 confirmed Covid-19 patients have been enrolled. HDVIC group received 24,000 mg/day IVC.
- A preliminary analysis shows HDVIC group showed significantly improved inflammatory markers and organ function tests. The final data analysis and report are being prepared.

Covid-19 treatment

HDIVC Included in the Covid-19 Treatment by Shanghai and Guangdong Province

Shanghai Expert Panel Consensus on Covid-19 Treatment
<https://mp.weixin.qq.com/s/bF2YhJKiOfelyimBc4XwOA>

Guangdong Expert Panel Consensus on Covid-19 Treatment
http://wsjkw.gd.gov.cn/zwyw_gzdt/content/mpost_2924849.html

Oral VC and Colds

Oral VC May Prevent Colds

A recent large study of 1,444 South Korean army recruits, average age 21.7 years, were divided into 2 groups, VC group received 6,000 mg VC daily.

At the end of the 30-day training, the VC group showed a 0.8-fold reduction in risks of developing common cold.

Oral VC

Oral VC Reduces Duration and Symptoms of Colds and May Prevent Colds

A 2013 meta-analysis of 29 qualified clinical trials (mostly double blind RCTs) totaling 11,306 subjects, found:

- VC 200 mg daily reduces cold duration in adults by 8%
- VC 200 mg daily reduces cold duration in children by 14%
- VC 1,000 mg - 2,000 mg daily reduces cold duration in children by 18%
- Reduced severity of common cold
- Better results at 8,000 mg daily or higher

High dose oral VC

High-dose Oral VC Reduces Cold symptoms

715 college students, aged 18-32, were divided into 2 groups, test group or control group. Those developed cold symptoms were given: VC in the test group and pain relievers and nasal decongestant in the control group. Those in the test group without symptoms were given VC 1,000 mg 3 times daily. Authors concluded:

- High-dose VC (1,000 mg/hour x 6 hours, then followed by 1,000 mg 3 times daily, reduced the cold symptoms by 85%.
- High-dose VC (1,000 mg 3 times daily) also reduced the risks of catching cold.

HDIVC is safe

HDIVC is Safe without Significant Side Effects

HDIVC (up to 1,500 mg/kg body weight) has been generally well tolerated in clinical trials.¹⁻⁹

Few side effects

Vit C is Safe without Significant Side Effects

- Renal failure after IVC has been reported occasionally in patients with pre-existing renal disorders.¹
- Patients should be screened for G6PD deficiency. HDIVC should be avoided in Patients with G6PD deficiency.²⁻⁴
- HDIVC may increase bioavailability of iron, and high doses of IVC are not recommended for patients with hemochromatosis.⁵

Anti-viral effects

Mechanisms of VC's Anti-Viral and Anti-Inflammatory Effects

- VC's role in prevention and treatment of common cold was proposed as early as 1971 by Dr. Pauling.¹
- Hydrogen peroxide (H_2O_2) production of VC upon its oxidation may have direct virucidal effects.²⁻⁶
- Immunomodulation Effects⁶⁻⁷
 - Increases neutrophil phagocytosis and chemotaxis
 - Increases macrophage migration
 - Affects production of interferon
 - Enhances T&NK cell proliferation and modulates their functions
- Affects replication of viruses⁶⁻⁷
- Powerful antioxidant, can protect cells from oxidative damages during infection from increased oxidative stress.⁸⁻⁹

EFSA endorsement

EFSA Officially Endorses these VC Effects (1)

European Food Safety Authority (EFSA) concluded that

1. A **cause and effect** relationship between the dietary intake of vitamin C and contribution to the normal function of the immune system has been established.

Article 14 of the Regulation (EC) NO 1924/2006

VC effects

EFSA Officially Endorses these VC Effects (2)

European Food Safety Authority (EFSA) concluded that

2. In persons exposed to severe physical stress, it has been established that regular vitamin C intake above 200 mg/d exerts a **cause and effect** relationship with

- the protection of DNA
- proteins and lipids from oxidative damage
- normal collagen formation
- normal function of the nervous system
- normal function of the immune system

Summary

Summary

- A percentage of Covid-19 infection develops into pneumonia, ALI/ARDS, sepsis and death.
- ALI and ARDS are nonspecific pathologies caused by cytokine storm/significantly increased oxidative stress.
- HDIVC has immune boosting effects and probably direct virucidal effects.
- HDIVC seems to prevent pneumonia and reduce pneumonia severity.
- HDIVC seems to improve ARDS and sepsis and reduce ARDS/Sepsis related mortality.
- HDIVC is safe without significant side effects in doses up to 1,500 mg/kg body weight. The doses used for pneumonia, sepsis and ARDS are often lower.
- HDIVC is a promising non-specific anti-viral as well as therapeutic agent for oxidative stress induced ARDS.
- Given VC's safety profile and its nonspecific antiviral effect and its role in oxidative stress induced ARDS, further research is warranted to establish VC as a universal and nonspecific agent in the prevention and treatment of Covid-19 and future epidemics/pandemics.

Summary

Summary

I asked in my article in the journal of Medicine in Drug Discovery (Mar 26, 2020).

Can early and high intravenous dose of vitamin C prevent and treat coronavirus disease 2019 (COVID-19) ?

My answer is **YES. Early and Large Dose VC** is the key to prevention and treatment of Covid-19.

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