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Original research article

ROLE OF VITAMIN C IN REDUCING MORBIDITY IN PATIENTS WITH COVID- 19

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ABSTRACT:

INTRODUCTION: It is not the corona virus that kills people with COVID; it is usually the immune system over-reacting against dead virus particles, which triggers a "cytokine storm, " an inflammatory fire out of control. That's when very high doses of both steroids and vitamin C are needed. Normally, the adrenal glands, which contain a hundred times more vitamin C than other organs, release both the body's most powerful steroid hormone cortisol as well as vitamin C, when in a state of emergency. The steroid helps the vitamin C get inside cells and calm down the fire. Vitamin C is both an anti-inflammatory and anti-oxidant, mopping up the "oxidant" fumes of the cytokine storm. Without vitamin C the steroid hormone cortisol can't work so well. That's why ICU doctors administer both extra vitamin C and steroids to get a patient out of the danger zone.

AIM OF STUDY: To find out the role of high dose oral liposomal vitamin-c in reducing morbidity,(symptomatic relif in physical, neuro cognitive functions improvement , anxity and depression) in patients admitted in a tertiary care covid 19 hospital between 1 st march to 31 may 2021

MATERIALS AND METHODS: All the patients admitted in between march 1 to may 31 2021 are taken for study irrespective of any co- morbidities. Totally 57,769 covid-19 positive persons are screened . Their RTPCR status, ct scan scores, bio chemical markers all studied, and those who were eligible for admission as per ICMR guidelines admitted(n=8634). All the patients during their entire stay in the hospital were given oral liposomal vitamin c with bio availability 90-95% in a palatable juice form apart from standard treatment protocol for covid-19 prescribed by world health organization and ICMR,AIIMS,AND GOVERNMENT OF TAMILNADU

RESULTS: Of the 8634 patients admitted 5422(62%) required non oxygen beds. –2989(34%) required oxygen beds on admission –223patients(2.5%) required beds (with ,98 on c pap,34 ventilators,64 high flow nasal oxygen, 43 non re-breathing mask and 58 non invasive ventilators), all outcomes are compared with same type of patients admitted in similar hospital and similar set of patients, were 49% required non oxygen bed,42% required oxygen beds 7.8 % (9-13%)required ICUadmissions and with out high dose vitamin c same type of protocol and the results compared and found out the morbidity, and is two third less in patients receiving high dose oral liposomal vitamin -C 4 grams per day.

CONCLUSION: with available standard treatment protocols, addition of high dose oral vitamin c reduces morbidity by two third which is very significant in covid pandemic. it's especially important to understand that no supplement, diet, or other

lifestyle modification other than social distancing, wearing mask properly,and proper hygiene practices can prevent you from COVID-19.

KEY WORDS: LIPOSOMAL VIT-C ,COVID 19, MORBIDITY

INTRODUCTION

No supplement will cure or prevent disease. COVID-19 pandemic, it's especially important to understand that no supplement, diet, or other lifestyle modification other than social distancing, wearing mask properly,and proper hygiene practices can prevent you from COVID-19. Primary end points;1. Improvement in signs and symptoms. Secondary end point improvement in neuro cognitive signs, and psychological improvement . Final point. Overall reduction in admission to/ transfer to intensive care unit assessed. With administration of high dose oral liposomal vitamin c

The pathogenesis of Covid-19is due to virus-induced excessive immune reaction in the host. The activated leucocytes in the host produces a high level of pro-inflammatory cytokines(mainly IL-6) and chemokinesin circulation, which is labelled as"cytokine storm syndrome" (or Hypercytokinemia) and it causes extensive tissue damages. Recently, few study states that, there is a catastrophic microvascular injury (endotheliitis) mediated by terminal complement components C5b-9 (membrane attack complex) and associated procoagulant state lead to thrombogenic vasculopathy. Currently, covid-19 management is limited to symptomatic treatment. No therapies have been demonstrated to prevent the progression of covid-19 to severe illness, but several drugs are under trail. One of the promising drug isvitamin Cor Ascorbic acid.

Severe cases of COVID-19 are associated with hypoxemic respiratory failure, acute respiratory distress syndrome (ARDS), septic shock, cardiac dysfunction, elevation in multiple inflammatory cytokines, thromboembolic disease, and/or exacerbation of underlying comorbidities. In addition to pulmonary disease, patients with COVID-19 may also experience cardiac, hepatic, renal, and central nervous system disease. .

MATERIALS AND METHODS:

All the patients admitted in between march 1 to may 31 2021 are taken for study irrespective of any co- morbidities. Totally 57,769 covid-19 positive persons are screened . Their RTPCR status, ct scan scores, bio chemical markers all studied, and those who were eligible for admission as per ICMR guidelines admitted(n=8634). All the patients during their entire stay in the hospital were given oral liposomal vitamin c with bio availability 90-95% in a palatable juice form apart from standard treatment protocol for covid-19 prescribed by world health organization and ICMR,AIIMS,AND GOVERNMENT OF TAMILNADU

As with any patient in the intensive care unit (ICU), successful clinical management of a patient with COVID-19 includes treating both the medical condition that initially resulted in ICU admission and other comorbidities and nosocomial complications. Vitamin C (ascorbic acid) is a water-soluble vitamin that is thought to have beneficial effects in patients with severe and critical illnesses. It is an antioxidant and free radical scavenger that has anti-inflammatory properties, influences cellular immunity and vascular integrity, and serves as a cofactor in the generation of endogenous catecholamines. Humans require more vitamin C in states of oxidative stress**,**During

human evolution, vitamin C lost its synthesizing capacities in humans due to the mutation in L-gulono-γ-lactone oxidase (GLO) gene, which codes for the vitamin C biosynthesis. So, the benefit of vitamin C to the human body is achieved by external sources, which is abundant in Indian gooseberry, limes, oranges, lemon, tomatoes, kiwifruit, potatoes and leafy greens. Since it is a water-soluble vitamin, the oral bioavailability of regular vitamin C is only15-30%. But the advent of nano -technology liposomalized vitamin C has more than 90% absorption. The liposomes are novel delivery system composed of phospholipid of soy or sunflower lecithin, which carries vitamin C into the intestinal cells with higher absorption rate and increases vitamin C in the bloodlevel.The excess amount of vitamin C excretes freely in urine. The recommended daily allowance in male is 90mg and in female is 75mg. The tolerable upper limit of oral vitamin C is 2gm per day with out gastrointestinal disturbances. But there is no scientific evidence of toxicity even in the dosage of 24gm per day. Moreover, vitamin C act as an essential nutrient for collagen formation, wound healing, aid in iron absorption and enzymatic production of certain neurotransmitters. However, the high dose of vitamin C acts as a powerful anti-oxidant, immune modulator and antiviral.

Signs and symptoms

Signs and symptoms	**Percentage**
Fever	42%
Chills	6%
Sore throat	18%
Dry cough	18%
Shortness of breath	8%
Abdominal pain	4%
Diarrhoea	8%
Anosmia	4%
Myalgia	36%

With other standard treatment protocol and adding high dose liposomal vitamin c orally, 89 % of patients **improved symptomatically** on 3-4 days with oral highdose liposomal vit-c The tiredness and myalgia improved in 76 % patients on third day. Anosmia improved in 4 days in 88 % of patients Sore throat and cough improved on 3-4 days in 90 % of patients and diarrhoea improved on 3rd day in 72% of patients

Many reports revealed that cytokine storms, which can be suppressed by VIT-C, are believed to be the main mechanism in the deterioration of patients with COVID-19.as VIT-C, has antimicrobial and immune modulator properties. HIGH DOSE ORAL LIPOSOMAL VIT-C has been proven to be safe and therapeutic in critical care medicine, primarily as an adjunct to the treatment of septic shock and multiple organ failure, where it has been shown to improve outcomes and reduce mortality. .

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Neuro cognitive symptoms

Symptoms	Percentage
Cognitive dysfunction	**82%**
Head ache	**68%**
Numbness or tingling	**52%**
Loss of taste	**58%**
Loss of smell	**64%**
Muscle pain	**88%**
dizziness	**42%**
Blurred vision	**24%**
Tinnitus	**18%**
Non specific pains	**12%**
Fatique	**77%**
Depression or anxity	**64%**
Abdominal discomfort	**45%**

Neuro inflammation is believed to be one of the primary causes of cognitive impairment. Previous studies showed that the antioxidant vitamin C (Vit C) performs many beneficial functions such as immune stimulant and anti-inflammatory actions, but its role in inflammatory cognitive impairment is unclear. In one of the study conducted, it was investigated the effect and possible mechanism of action of Vit C in lipopolysaccharide (LPS)-induced cognitive impairment. Intracerebro-ventricular LPS-induced memory impairment was used as the model for neuro-inflammatory cognitive dysfunction. Vit C was administered by intracerebro-ventricular microinjection 30 min prior to LPS exposure. It was found that Vit C significantly protected animals from LPS-induced memory impairment .Vit C pretreatment inhibited the activation of microglia and the production of pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β). Furthermore, Vit C pre treatment markedly decreased the malondialdehyde (MDA) level, increased superoxide dismutase (SOD) activity, and modulated the Bax/Bcl-2 ratio and p-p38 MAPK activation in the hippocampus of LPS-treated mice. Together, these results suggest that vitamin C pretreatment could protect mice from LPS-induced cognitive impairment, possibly through the modulation of oxidative stress and inflammatory response

Their RTPCR status, CT scan scores, bio chemical markers all studied, and spo2 less than 90 , with ct score more than 32(more than 8/25)percent , and increased D -DIMER, CRP, ,IL6,FERRITIN are all those who were eligible for admission as per ICMR guidelines admitted(n=8634). All the patients during their entire stay in the hospital were given oral liposomal vitamin c with bio availability 90-95% in a palatable juice form apart from standard treatment protocol for covid-19 prescribed by world health organization and ICMR,AIIMS,AND GOVERNMENT OF TAMILNADU

	Non oxygen	Oxygen bed	Icu admission	Symp. improvement
High dose VC	**5422(62%)**	**2989(34%)**	**223(2.5%)**	**5 days- 76% 10 days 97%**
Non hvc	**4408(49%)**	**3888(42%)**	**701(7.8%)**	**5 days 68% 10days 88%**

Results

Of the 8634 patients admitted 5422(62%) required non oxygen beds. –2989(34%) required oxygen beds on admission –223patients(2.5%) required beds (with ,98 on c pap,34 ventilators,64 high flow nasal oxygen, 43 non re-breathing mask and 58 non invasive ventilators), all outcomes are compared with same type of patients admitted in similar hospital and similar set of patients, were 49% (n=4408)required non oxygen bed,42%(n=3888) required oxygen beds 7 .8 % (n=701)required icu admissions and with out high dose vitamin c same type of protocol and the results compared and found out the morbidity, and is two third less in patients receiving high dose oral liposomal vitamin -C 4 grams per day**.**

Discussion

In our study the common clinical manifestations are attention deficit and immediate recall memory**.**All the patients were subjected to mini mental score was done on 5th and 10th day of admission. test results were confirmed in 74% of patients the improvement on 5th day and rest of the patients before 10 th day.The patients treated with high-dose oral liposomal vitamin C had increased rate of recovery from cognitive dysfunction. anxity depresion and mood disorders in covid 1966 percent improved with in 15 days and nearly 95 % improved with in 30 daysimprovement with vitamin c

disorder	<15 DAYS	>30DAYS
Depression	22	10
Fatigue	18	5
Tension	12	3
ANGER	13	10
CONFUSION	7	7
VIGOUR	23	10
	95	45

Cytokine Storm –signs and symptoms

Fevers and chills,Fatigue, Swelling of extremities, Nausea and vomiting, Muscle and joint aches, Headache, Rash, Cough, Shortness of breath Rapid breathing Seizures, Tremor, Difficulty in coordinating movements, Confusion and hallucinations ,Lethargy and poor responsiveness,Very low blood pressure and increased blood clotting can also be hallmarks of severe cytokine storm syndrome. The heart may not pump as well as it normally would. As a result,

cytokine storm can affect multiple organ systems, potentially leading to organ failure and death.. cytokine storm is a cascade of exaggerated immune responses that can cause serious problems. The immune system contains many different components that help you battle infections. It includes many different types of cells that communicate with each other via signaling molecules, known as cytokines. There are many different cytokines that perform many kinds of functions. Some help recruit other immune cells, and some help with antibody production or pain signaling. Some make the blood clot more easily. Some help produce inflammation, which can make blood vessels more leaky than normal. Another group of cytokines helps tamp down the body's inflammatory response. That's an important balance, since too much inflammation causes its own problems. Under normal circumstances, these cytokines help coordinate the response of your immune system to take care of infectious substances, like viruses or bacteria. The problem is that sometimes the body's inflammatory response can get out of control, causing more harm than good.

In people experiencing cytokine storm ,certain cytokines are present in the blood at higher-than-normal amounts. In COVID-19, elevations in several inflammatory cytokines CRP, FERRITN, LFT,RFT,D-DIMER,IL6) seem to be involved in the development of acute respiratory distress syndrome, the leading cause of death in people dealing with COVID-19 illness

Studies suggested a protective role of vitamin C infusion in acute lung injury (ALI) and ARDS . Moreover, the latest meta-analysis from eight vitamin C trials of a total of 685 patients indicated that vitamin C shortened the duration of mechanical ventilation in critically ill patients -. SARS-CoV-2 primarily affect, s the lung and causes pneumonia. Respiratory failure from ARDS is the leading cause of mortality from COVID-19 . Similar to sepsis-induced ALI/ARDS, the rapid increase in cytokines in COVID-19 causes neutrophil sequestration in the lung, which damages the alveolar capillaries . In sepsis modeling of mice, parenterally infused VC demonstrated a protective effect on the lung . The potential mechanisms included limiting cytokine surges, improving alveolar fluid clearance, preventing vascular injury, restoring endothelial and alveolar epithelial integrity, and augmenting lung barrier cell function and initiating HIGH DOSE ORAL LIPOSOMAL VITAMIN C. However, the P/F increased, which was likely the result of pulmonary ventilation function improvement, based on the above mechanisms.

Clinical trials showed that HIGH DOSE ORAL LIPOSOMAL VITAMIN C may reduce the extent of multiple organ failure and may improve the short-term outcomes of sepsis, plasma ascorbic acid levels were inversely correlated with the incidence of multiple organ failure and the risk of mortality . We suspected that patients with worse organ dysfunction may have a more severe vitamin C deficiency, while high-dose intravenous VC effectively improved the deficiency and subsequently improved organ function . Thus, the benefit was more significant in more severe COVID-19 patients

In this study, 4 GRAMS OF ORAL LIPOSOMAL VITAMIN C EQUAL TO 16 GRAMS OF INTRAVENOUS VITAMIN C. is given to all patients . The main reason was based on two aspects: the efficacy and safety. The metabolism of vitamin C (VC) in the blood is very fast, only large dose and long course of VC supplement can maintain an adequate concentration in blood. In a previous study 4 days VC treatment showed a signal of benefit in sepsis or ARDS patients. Similar daily doses were used in the Fowler paper (JAMA), which was associated with an improved outcome .

In addition, high levels of IL-6 were observed in patients with COVID-19 and might serve as a predictive biomarker for disease severity .IL-6 acts as a critical cytokine in the systemic inflammatory response , leading to a myriad of biological effects that contribute to pulmonary infiltration and organ damage . Tocilizumab , a recombinant humanized anti-human IL-6 receptor antibody, improved clinical symptoms by attenuating inflammation in COVID-19. The findings of the decline in IL-6 in our cohort were consistent with basic research showing that vitamin C inhibited the production and release of proinflammatory cytokines from human monocytes (IL-1, IL-2, IL-6, and TNF-α) [42]. Previous animal studies on SARS-CoV also demonstrated that inhibiting NF-κB, together with reduced IL-6 levels, could increase the survival rate in infected animals .

More than 67% of individuals in all age groups were showing improvement in cytokines 54% reduction in crp , 64% reduction in serum ferritin in five days and 82 % in 10 days that shows there will be reduction in the chance of getting life threatening cytokine storm, multi organ failure and death in covid 19

Much like Lind's limes, twice Nobel Prize winner Dr Linus Pauling proved the power of high dose vitamin C in the 1970. It is thanks to him we know about the benefits of high dose vitamin C. The cover of his landmark book "Vitamin C and the Common Cold" has a statement that reads, in relation to a predicted swine flu epidemic at that time "it is especially important that everyone know that he can protect himself to a considerable extent against the disease, and its consequences, with this important nutrient, vitamin C." It's been 50 years since Pauling proved the anti-viral power of vitamin C. Isn't it time we took this seriously?-*(Patrick Holford is author of over 30 books including* Flu Fighters *(https://www.patrickholford.com/flu-fighters) and* The Optimum Nutrition Bible*. He is a member of the Orthomolecular Medicine Hall of Fame.)*

All the patients admitted in between march 1 to may 31 2021 are taken for study irrespective of any co- morbidities. Totally 57,769 covid-19 ,RTPCR PROVED positive persons are screened .

Conclusion

With available standard treatement protocols,addition of high dose oral vitamin c reduces morbidity by two third which is very significant in covid pandemic. Many centres across the globe are now currently using vitamin C as a supportive therapy for hospitalized patients with Covid-19, despite extremely limited clinical data supporting its effectiveness. But our centre has used high-dose oral liposomal vitamin C in a drink form and obtained a remarkable outcome. However, we require large scale multi centric clinical trials on high-dose oral liposomal vitamin C for including it in standard treatment protocol.

Conflict of Interest: None of the authors have conflict of interest.

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