Inflammation and Cell Signaling 2020; 7: e1169. doi: 10.14800/ics.1169; © 2020 by Li Zhao, *et al*.
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CASE REPORT

A case that high doses of Vitamin C as a potential therapy for COVID-19

Li Zhao[1,2,*], Yiling Zhang[1,2,*], Jianquan Li[1,2], Guohang Yuan[1,2], Bangyan Zhang[1,2] , Xianwei Ye[1,2,#], Xiangyan Zhang[1,2,#]

[1]*Department of Respiratory and Critical Care Medicine, Guizhou Provincial People's Hospital, State Key Laboratory of Diagnosis and Treatment of Lung Immune Diseases, Guiyang, Guizhou 550002, China*
[2]*Intensive Care Unit, Guizhou Provincial People's Hospital, Guizhou 550002, China*

[*] These authors contributed equally to this work.
[#] Correspondence: Xianwei Ye *or* Xiangyan Zhang
E-mail: yxw1205@163.com *or* zxy3572@126.com
Received: April 21, 2020
Published: August 30, 2020

In December 2019, the outbreak of pneumonia caused by the novel coronavirus (SARS-CoV-2) emerged in China, representing a serious threat to public health and thus attracting worldwide attention. Recent studies revealed that the blockage of small airways by mucus plugs is considered to be an important pathophysiological change in COVID-19 patients. To date, no definite and effective treatments have been presented for COVID-19. Vitamin C is widely available and has shown the potential to inhibit airway mucus secretion, but its effect on improving the outcome of COVID-19 patients is unclear.

Keywords: COVID-19; SARS-CoV-2; Vitamin C

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; RT-PCR, real-time polymerase chain reaction; CRP, C-reactive protein; IL-6, Interleukin-6; HRCT, high-resolution computed tomography; GGO, ground glass opacities; OI, oxygenation index; HFNC, high-flow nasal cannula; PaO2, partial pressure of oxygen; FIO2, fraction of inspiration O2; Lymp, lymphocyte.

To cite this article: Li Zhao, *et al*. A case that high doses of Vitamin C as a potential therapy for COVID-19. Inflamm Cell Signal 2020; 7: e1169. doi: 10.14800/ics.1169.

Introduction

In December 2019, the outbreak of pneumonia caused by the novel coronavirus (SARS-CoV-2) emerged in China, and the resulting disease was subsequently named COVID-19[1, 2]. It presented a serious public health threat. On March 10, 2020, more than 5000 deaths caused by COVID-19 were reported around the world in more than 100 countries. The symptoms of COVID-19 may include fever, cough, general breathing difficulties, organ failure or even death, posing a severe threat to society as a whole. At present, no effective antiviral treatment or vaccine is available for COVID-19. Several studies have assessed the efficacy and safety of drugs such as lopinavir/ritonavir and remdesivir in patients with COVID-19[3, 4]. Chloroquine is currently a possible therapeutic option for COVID-19[5].

Recently, the pathological findings of COVID-19, which are partially similar to those of SARS, were found to include bilateral diffuse alveolar damage with cellular fibromyxoid exudates, and small airway obstruction caused by sputum thrombus was also observed in the lungs of COVID-19 patients[6]. Furthermore, SARS-CoV was demonstrated to depend on activation of the oxidative stress machinery. Based on these results, anti-mucus medications and antioxidants may be effective for the treatment of COVID-19. Vitamin C, a natural antioxidant, is widely available and has shown the potential to inhibit mucus secretion, but its effect on improving the outcome of COVID-19 patients is unclear.

		confirmed		CT imagings				Vitamin C started						
	illness day	1	5	10	11	13	15	16	18	19	20	21	22	23
Symptoms	Cough	√	√	improved	improved	improved	improved	improved	improved	improved	/	/	/	/
	Mucscle pain	√	√	/	/	improved	/	/	/	/	/	/	/	/
	Sputum	/	/	√	√		√	difficult	difficult	improved	improved	improved	improved	/
	Breath shortness	/	/	√	√		√	√	improved	improved	improved	/	/	/
Blood	lymphocyte (cells/ul)	780	520	480	580	710	960	920	1100	/	1158	/	/	1320
	CRP (mg/L)	normal	28mg	229	188	165	154	115	52	/	22	/	/	normal
	IL-6 (pg/ml)	normal	normal	125.6	122.1	98	82	52.94	34.14	/	normal	/	/	normal
oxygen by nasal cannula	Flow rate (L/min)	/	/	3	/	/	/	/	/	/	/	3	2	/
HFNC	Flow rate (L/min)	/	/	/	65	65	65	50	40	30	30	/	/	/
	oxygen concentration (%)	/	/	/	80	80	80	60	50	40	30	/	/	/
Arterial blood gas analysis	PaO2 (mmHg)	88	/	55	98.4	108	96	91.2	77.5	75.2	73.2	92.4	82.94	76.4
	oxygenation index (OI , mmHg)	>300	/	167	123	135	120	152	155	188	244	280	286	>300
	SPO2 (%)	98	97	81	96	95	96	95	96	97	96	96	95	97
Drugs	Interferon alfa-2b	√	√	√	√	√	√	√	√	√	√	√	√	√
	Lopinavir/ritonavir	√	√	/	/	/	/	/	/	/	/	/	/	/
	Chloroquine	/	/	√	√	√	√	√	√	√	√	/	/	/
	Ambroxol Hydrochloride	/	/	√	√	√	√	√	√	√	√	√	√	√
	N-Acetylcysteine	/	/	√	√	√	√	√	√	√	√	√	√	√
	High doses of Vitamin	/	/	/	/	/	/	√	√	√	√	√	√	√
	CT	√	/	√	/	/	√	/	/	/	/	√	/	/
nucleic acid	rRT-PCR	throat(+)	/	throat(+)	/	/	/	/	/	/	/	Sputum(-)	Sputum(-)	/

Figure 1. Laboratory results show lymphopenia (780 cells/μl), serum C-reactive protein (CRP), and Interleukin-6 (IL-6) are normal.

Case Report

A 64-year-old woman living in Guizhou, China, was exposed to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) through close contact with confirmed COVID-19 patients. The initial symptoms, including cough and muscle pain, were observed on February 12. She was admitted and isolated in a negative pressure room on the same day. She was confirmed to have COVID-19 by viral nucleic acid detection from a throat swab using real-time polymerase chain reaction (RT-PCR). Apart from a history of diabetes with irregular medical follow-up, she had no other underlying diseases before the onset of COVID-19.

After admission, the laboratory results showed lymphopenia (780 cells/μl), and the serum C-reactive protein (CRP) and interleukin-6 (IL-6) levels were normal (Figure 1). No evidence of abnormalities of liver function, renal function, myocardial enzymes, electrolytes or serum procalcitonin was found. High-resolution computed tomography (HRCT) was performed at the onset of the disease, and the results revealed that ground glass opacities (GGO) were the main radiological finding (Figure 2A) and were distributed subpleurally in the lower lobes bilaterally. The treatments administered after admission included antiviral therapy with interferon alpha-2β (5 million units twice daily via atomization inhalation) and lopinavir/ritonavir (500 mg twice daily orally). On day 10 of the illness, the muscle pain disappeared, and cough was relieved, but the symptoms of shortness of breath and yellow, sticky phlegm appeared (Figure 3A). The nucleic acid test was still positive, and the lymphopenia worsened (480 cells/μl). Moreover, the levels of serum CRP and IL-6 increased significantly (Figure 1). The supplementation of oxygen with a nasal cannula (3 L/min) could not improve the patient's symptom of breathing difficulty, and arterial blood gas analysis indicated respiratory failure with an arterial oxygen tension (PaO2) of 55 mmHg and an oxygenation index (OI) of 167 mmHg. Following therapy with oxygen via a high-flow nasal cannula (HFNC) (concentration 80%, flow rate 65 L/min), the SPO2 reached 93%. The HRCT examination indicated that the lesions showed a bilateral multilobe distribution with diffuse GGO and a crazy-paving pattern (Figure 2B). Considering the failure to control coinfection of SARS-CoV-2 and bacteria, lopinavir/ritonavir were replaced by chloroquine, and piperacillin/tazobactam, ambroxol hydrochloride and N-acetylcysteine were added to the treatment regimen.

After receiving medication, the serum CRP and IL-6 levels were decreased, and the lymphocyte count (960 cells/μl) returned to normal levels. The HRCT imaging indicated that the GGO were obviously absorbed without any crazy-paving pattern (Figure 2C). However, the patient still had the symptoms of shortness of breath and yellow sticky sputum (Figure 3B). Moreover, the OI was significantly decreased even though the flow rate and oxygen concentration of the

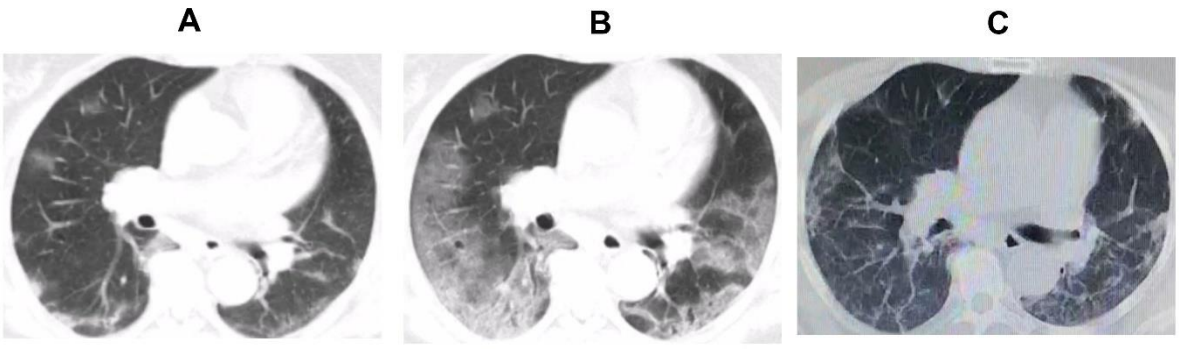

Figure 2. A high-resolution computed tomography (HRCT) revealed that ground glass opacities (GGO) was the main radiological demonstration distributed subpleurally in the lower lobes bilaterally.

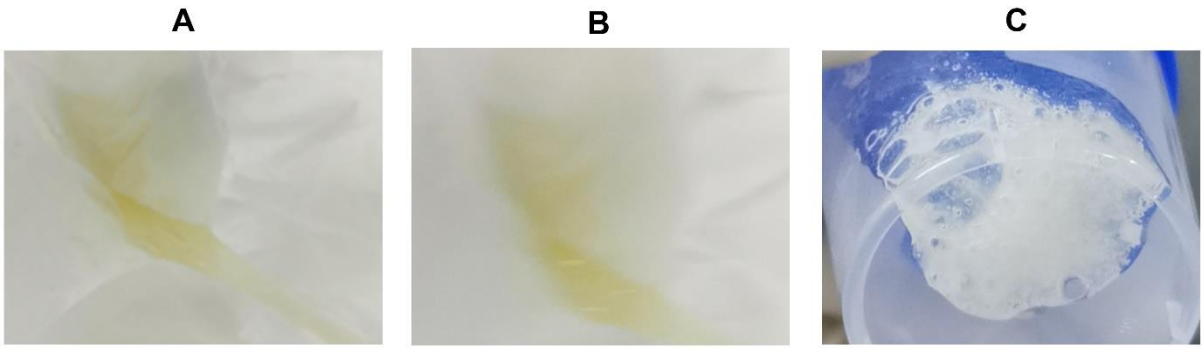

Figure 3. Yellow sticky phlegm.

HFNC-administered oxygen were slightly reduced. Subsequently, high doses of vitamin C were strategically used (3 g was given intravenously tid) for 8 days. Subsequently, the symptoms and signs of the patient, including breathing difficulties and yellow sputum, gradually improved. The OI increased from 152 mmHg to 244 mmHg as the flow rate of the HFNC oxygen therapy was gradually reduced from 65 L/min to 30 L/min, and the oxygen concentration was reduced from 80% to 30%. Fortunately, on day 21 of the illness, the oxygen supplementation via HFNC was switched to nasal administration (FIO2 33%). Finally, the arterial blood gas analysis on exposure to the open air was as follows: PO2 76.4 mmHg and OI $>$ 300 mmHg. Moreover, the result of the detection of SARS-CoV-2 by the RT-PCR assay was negative, and the CT examination indicated that the lesion was gradually being absorbed, and pulmonary fibrosis and the crazy-paving pattern had disappeared. On day 23 of the illness, the patient was discharged, and it was suggested that she quarantine at home for at least 14 days.

Discussion

The outbreak of COVID-19 triggered a global public health emergency, and although the serious symptoms and signs of pulmonary disease have caused clinicians and researchers to be concerned, there are still no effective treatments.

The patient showed typical signs and symptoms of cough, yellow sticky phlegm and breathing difficulty after infection with SARS-CoV-2. Additionally, consistent with the current pathological report, the chest CT examination images revealed multiple patchy ground glass opacities in the bilateral subpleural areas. According to the WHO[7], the management of COVID-19 has mainly focused on case detection, infection prevention, and supportive care. However, no specific antiviral drug is recommended for treatment because of a lack of evidence. After admission to the hospital, the antiviral treatments lopinavir/ritonavir and alpha-2β were given to the patient, but the improvement of the illness in response was limited. The Lymp remained decreased, indicating the activity of SARS-COV-2. Studies have indicated that serious and sustained Lymp decreases are associated with disease severity and mortality[8], and the Lymp results and patient pulmonary symptoms and CT images confirmed the progression of the illness.

Chloroquine is used to prevent and treat malaria and is efficacious as an anti-inflammatory agent for the treatment of rheumatoid arthritis and lupus erythematosus. Recent publications have paid more attention to the potential of chloroquine for the treatment of COVID-19 patients and found that it plays an important role in inhibiting the exacerbation of COVID-19 pneumonia, improving lung imaging findings, and promoting a negative viral conversion [5, 9]. However, the symptoms and signs of pulmonary disease in this case were not improved by the use of chloroquine.

The imbalance between oxidation and antioxidants leads to multisystemic inflammation, and the evidence indicates that oxidative stress plays a pathogenic role in inflammatory diseases [10]. During this process, nonenzymatic antioxidants such as vitamin C protect against oxidative stress. When the levels of inflammatory indicators such as CRP and IL-6 increase and hypoxemia or respiratory failure worsens, empirical use of antibiotics to prevent secondary infection and the use of HFNC oxygen therapy are essential to reduce mortality. Unfortunately, although antibacterial and apophlegmatic drugs were also used, respiratory failure still persisted. Recently, the pathological findings included bilateral diffuse alveolar damage with cellular fibromyxoid exudates in patients with COVID-19[6]. Therefore, worsening of hypoxemia or respiratory failure might be associated with small airway obstruction caused by sputum thrombus. Based on these theories, antimucus medications and antioxidants might be effective in resolving these problems. In this case, conventional expectorants, such as ambroxol hydrochloride and N-acetylcysteine, failed to improve the patient's pulmonary function. Vitamin C is the principal dietary antioxidant that protects erythrocytes from damage caused by reactive oxygen species[11] and was found to be effective in inhibiting mucus secretion. Therefore, high doses of vitamin C were used in this case to improve the symptoms. In line with our expectations, 3 days after the use of vitamin C, the clinical observations, laboratory data and CT results indicated that vitamin C significantly improved the clinical symptoms and successfully enhanced the OI. Although the exact mechanism of the improvement of the illness by vitamin C is unclear, it could be a reasonable guess that high doses of vitamin C can improve small airway mucus obstruction to relieve respiratory failure.

Our clinical findings provide new insights into the treatment of COVID-19 pneumonia, which might help physicians implement a timely therapeutic strategy for similar severe patients and increase the cure rate. Considering its low toxicity and easy availability, vitamin C could be recommended to relatively high-risk groups of patients with COVID-19 pneumonia. However, more evidence is needed to prove the clinical efficacy of high doses of vitamin C and to draw definitive conclusions based on well-controlled clinical trials.

Ethics Approval

Ethical approval was granted from the ethics committee of Guizhou Provincial People's Hospital.

Patient Consent for Publication

A written informed consent was obtained from the patient for publication of the information about them that appears within this case report.

Conflicting Interests

The authors declare that they have no conflict of interests.

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