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Letters to the Editor

Title

A preliminary evaluation on the efficacy of ozone therapy in the treatment of COVID-19

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Abstract

Currently, coronavirus disease 2019 (COVID-19) is a global pandemic disease with significant morbidity and mortality. Ozone may exert its antiviral actions and ozone therapy has been demonstrated therapeutically usefulness in influenza and novel viruses. In this letter, two severe cases with COVID-19 received ozone therapy were described. The results showed that ozone therapy may promote recovery of clinical condition and improvement of chest CT images, shorten the duration of viral shedding and length of hospital stay.

Keywords

Coronavirus < Virus classification, SARS coronavirus < Virus classification, Reovirus < Virus classification

To the Editor:

No therapeutics has been proven effective for treatment of COVID-19 [1,2]. China has explored important clinical trials on a host of possible effective treatment options including ozone therapy. We introduced our experience in treating two confirmed cases by ozone therapy -- Major Autohemotherapy (MAH)

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[3]. After the written informed consent was obtained, MAH was given to patients once daily for 7 consecutive days. Each time, 100 ml of venous blood was collected and mixed with O_3 gas at the 1:1 ratio of oxygen-ozone to blood volume, with the final concentration of oxygen-ozone being 20μg/ml. The clinical study was approved by the Clinical Research Ethics Committee of Renmin Hospital of Wuhan University (WDRY2020-K020).

Case 1

A male of 53-year-old was admitted to Renmin Hospital of Wuhan University on 2020/2/20 due to mild fever and dyspnea for 7 days, accompanied by headache, runny nose, fatigue and loss of appetite. On admission, he presented a clear consciousness with a body temperature of 37.5℃. Chest CT imaging on 2020/2/19 revealed multiple small patchy shadows, linear interstitial changes and consolidation in both lungs. He was confirmed COVID-19 on 2020/2/21. Lymphopenia, elevated CRP and IL-6, mild hypoxemia were noted in laboratory tests.

After admission, the patient was given antiviral therapy, antibiotics, immunoglobulin, omeprazole, supplemental oxygen of 3L/min. He was treated with O_3-MAH on 2020/2/25, once daily for 7 consecutive days. With the treatment of MAH, his symptoms disappeared soon. Abnormal laboratory indicators within normal range were recorded (Table 1). Compared to baseline chest imaging, follow-up serial CT scans showed gradually absorbed bilateral lung lesions (Supplementary Figure 1). The patient was discharged on 2020/3/14, after nuclei acid tests negative twice consecutively on nasopharyngeal swabs and meeting other discharge criteria [4]. No MAH-related adverse events were reported.

Case 2

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A male of 66-year-old was referred from a community clinic on 2020/2/5. He suffered from fever on 2020/1/22 accompanied by cough and sore throat, with the highest body temperature of 39.2℃. He had a history of chronic respiratory disease. For chest CT scan on 2020/1/23 showed “viral pneumonia-like changes”, the patient was admitted to a community health center with “suspected COVID-19” and confirmed COVID-19 on 2020/1/25. However, antiviral therapy and antibiotics did not improve his condition, cough, hemoptysis and dyspnea occurred. Repeated chest CT scan revealed lesion progression, with multiple ground-glass opacities and interstitial changes in both lungs.

After referred, he was given antiviral therapy, antibiotics, immunoglobulin, supplemental oxygen of 3L/min of. The patient was treated with O_3-MAH since 2020/2/15, once daily for 7 consecutive days. After MAH treatment, he recovered rapidly with normal range of laboratory indicators. Compared to baseline chest imaging, follow-up CT scan showed obviously absorbed bilateral lung lesions (Figure 2). After meeting the discharge criteria [4], the patient left hospital on 2020/2/22. No MAH-related adverse events occurred.

To show the advantages of this treatment, the two cases were compared with other two subjects without MAH, being age- and illness severity-matched. We found that the patients without MAH had longer duration of viral shedding and length of hospital stay.

Discussion

We present the possibility of ozone therapy as a treatment for COVID-19 in two severe confirmed cases. MAH was carried out to each patient for seven days. After treatment, two patients remitted symptoms and discharged with negative RT-PCR testing for SARS-CoV-2.

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No specific therapeutic agents have been confirmed to be effective to COVID-19, therefore, a number of anti-viral drugs or therapeutic measures have been tested in China. Ozone therapy has been continuously used for a decades-long history of practices, especially in Europe for a variety of infectious, immunological and circulatory conditions [3]. Recently, the potential effect of ozone on viral inactivation in vivo has been found [3]. Studies have also reported the efficacy and safety of ozone administration on patients of HIV, hepatitis C, Ebola, influenza [3,5,6]. As a new immunotherapy and an inexpensive, safe modality, ozone therapy has its rationality in the treatment of COVID-19 patients [7, 8], which was confirmed by our preliminary observational results. However, its use combined with other treatments may be justified and synergic [7]. Since the treatments for four patients with COVID-19 were followed the recommendation outlined in *the Chinese Guidelines* [4], we think ozone therapy may be responsible for the good effects observed in the two cases.

In short, ozone therapy may be a useful modality in controlling COVID-19 infection, however, further clinical studied are needed to determine effectiveness, optimal ozone dosage and appropriate treatment duration.

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Table 1. Demographics, clinical and laboratory results of Cases with or without Ozone therapy

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Parameters (Normal range)	**Ozone therapy**				**Without Ozone therapy**			
	Case 1		Case 2		Case 1		Case 2	
	Baseline	After treatment	Baseline	After treatment	Baseline	After treatment	Baseline	After treatment
Age (years), Sex	53, M		66, M		65, M		48, M	
WBC (3.5-9.5×10^9/L)	4.27	7.73	9.06	7.62	2.37	8.88	7.16	6.58
N (1.8-6.3,×10^9 /L)	2.68	5.70	6.32	4.7	1.49	6.61	4.12	4.2
L (1.1-3.2×10^9 /L)	0.73	1.40	1.77	2.15	0.59	1.6	2.12	1.76
Platelet count (125-350×10^9/L)	271	201	220	156	196	251	142	211
CRP (0-10 mg/L)	51.8	<5.0	108.4	<5.0	181.2	<5.0	77.3	8.0
Alkaline phosphatase (45-125 U/L)	52	59	53	57	43	54	70	89
Bilirubin (0-23 mmol/L)	4.8	7.3	13.9	4.43	5.7	11.7	10.1	7.1
Creatinine (57-111 umol/L)	48	55	47	48	98	66	106	89
Creatine kinase (18-198 U/L)	466	22	48	17	225	31	56	46
LDH (120 ~ 250 U/L)	283	140	263	211	302	210	336	198
Oximetry saturation (≥95%)	94	99	99	--	93	--	100	97
PaO_2 (80-100 mmHg)	68	163	159	--	65	--	173	92

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$PaCO_2$ (35-45 mmHg)	45	48	37	--	38	--	39	42
Ultra-TnI (0-0.04 ng/ml)	<0.006	<0.006	0.077	<0.006	<0.006	0.012	<0.006	<0.006
IL-6 (≤20.0 pg/mL)	28.26	4.58	--	--	--	--	2.09	6.68
IL-10 (≤5.9 pg/mL)	7.47	6.70	--	--	--	--	4.68	5.38
Duration of viral shedding (d)	14		13		26		43	
Length in hospital (d)	23		17		28		41	

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