中华航海医学与高气压医学杂志

• Case Reports •

Effect of Hyperbaric Oxygen Therapy on Hypoxia in Patients with Severe New Coronavirus Pneumonia: First Report

Zhong Xiaoling Tao Xiaolan Tang Yanchao Chen Ruiyong

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References Export: Endnote NoteExpress RefWorks NoteFirst medical literature Wang

Progressive hypoxemia is the focus and difficulty of supporting treatment of severe new coronavirus pneumonia (NCP). It is the "Diagnosis and Treatment Plan for Pneumonitis of New Coronavirus Infection" (hereinafter referred to as the guideline) issued by the National Health and Medical Commission. The main indicator for the classification of severe and critical severity, oxygen therapy is the main means of NCP supportive treatment. The guidelines have listed all atmospheric pressure oxygen therapy methods, including nasal catheters, masks, non-invasive and invasive mechanical ventilation, extracorporeal membrane oxygenation (ECMO) [1]. However, there have been no reports on the use of hyperbaric oxygen therapy (HBOT). HBOT is to inhale 100% oxygen in the environment above atmospheric pressure to achieve the purpose of treating diseases [2], and it is the most powerful oxygen therapy currently known. However, there have been no reports of HBOT for NCP hypoxic correction. A patient with severe NCP in Wuhan Changjiang Shipping General Hospital could not control the continuous decline of blood oxygen saturation with high-pressure oxygen supply at atmospheric pressure. Based on the analysis of the HBOT principle, HBOT was attempted for the first time. It is found that the effect of HBOT in the treatment of progressive severe hypoxemia is very obvious. The case is reported in detail as follows.

Case information

Tang xx, male, 69 years old, was admitted to the hospital for a long time with fever. On the night of January 22, 2020, there was no obvious cause of chills and fever, and his temperature was 37.8. He went to the hospital for a chest CT scan and showed that his lungs were patchy. Previous hypertension, coronary atherosclerotic heart disease in 2016, acute myocardial infarction, and coronary stent implantation. Nucleic acid tests were positive on admission and CT showed typical lung imaging changes. Methylprednisolone 40mg, 2 times / d (5d),

label **Key words**

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Severe Hypoxemia
Into the cabin
Tissues and organs

immunoglobulin 20g / d (5d), ceftriaxone sodium 3g / d, Abidol 0.2g, 3 times / d, continuous nasal catheter low flow Inhale oxygen. The body temperature returned to normal on the third day. He started to breathe after the activity on the fifth day, and a review of the chest CT revealed that the patchy lesions of the lungs progressed more than before, and the lung affected area (+++) was given a high-flow mask for oxygen inhalation. On the 14th day, the patient had fever again and his temperature was 38 ° C. Re-examination of the chest CT showed diffuse large patches of infection in both lungs and the affected area of the lung (++++). The minimum oxygen partial pressure for blood gas detection is 37mmHg, the minimum oxygen saturation of blood (SO_2) is 66%, and 88% after high-flow oxygen inhalation. Admission of drug treatment for another course of treatment, the patient's temperature returned to normal. But breathing is difficult and hypoxemia worsens. Ventilator-based treatment is recommended without patient cooperation. Hyperbaric oxygen therapy was given from the 21st day (February 11th) of the onset of the disease, daily from 09:00 to 10:35. Clinical medication only retains antibiotic treatment and mask oxygen. Collect all clinical records and examination results of patients from admission to February 17. The clinical examination and monitoring are based on the hospital's routine methods, which will not be repeated here.

Oxygen therapy

HBOT program

HBOT was performed in the Department of Hyperbaric Oxygen of Yangtze River Shipping General Hospital, and the high pressure exposure time was 09: 00-10: 35 every morning. In accordance with the requirements for the detection and control of severe infectious diseases, a division of the contaminated area, a patient transfer route were designed, and a series of control measures to prevent transmission such as the disinfection of the pressurized cabin and hygienic management were strengthened. The patient took the special channel to enter the pressurized treatment cabin, took off the mask, put on a breathing mask, and started to increase the pressure after giving a level of oxygen. Press to 2.0ATA at a constant speed for 15min, and stabilize the voltage for 60min. Continuous ventilation is maintained in the pressurized tank during pressure stabilization. Then reduce the pressure to normal pressure with a constant speed of 20min. Open the door, the patient removes the mask to stop the first-stage oxygen inhalation, puts on a mask, and exits the cabin through a special channel. This patient's HBOT has no medical attendant cabin during the high-pressure exposure process, but the auxiliary compartment is reserved. When needed, medical staff can be pressurized at any time and transferred to the treatment cabin for medical treatment. The patient inhaled oxygen during the whole course, the total oxygen inhalation time was 95 minutes, and the oxygen inhalation dose was 216 UPTD.

Result analysis

1. Clinical manifestations:

As Figure 1 , the supine patient before treatment of high-flow oxygen mask still experience difficulty in breathing, chest pain, accompanied by significant gastrointestinal symptoms. Dyspnea, chest pain, and gastrointestinal symptoms improved immediately after the first HBOT. After the second treatment, the digestive tract symptoms basically disappeared. After the fourth treatment, the nasal cannula was used to give oxygen daily, but the main complaint of dyspnea after the action remained. At the time of writing, patients were continuing HBOT once a day following the regular HBOT treatment.

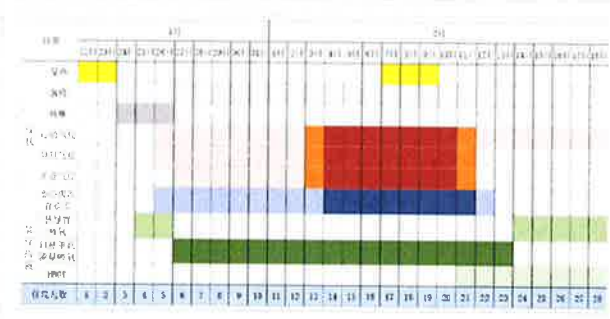

figure 1 Patient Symptom Changes and Oxygen Therapy Schedule

2. Results of finger vein SO_2 monitoring:

The general condition of the patient was acceptable when he was admitted to the hospital. After the active drug treatment, the patient's respiratory symptoms did not improve. As can be seen from Figure 2 , the patient's SO_2 was lowest in the morning and highest in the night. The highest value was 92% on the 13th day of admission (February 4th). On the 19th day (February 9th), under the condition of oxygen inhalation in the mask, the minimum SO_2 was 66% and the highest 86%, and respiratory distress appeared. Mechanical ventilation support has been suggested, which can be diagnosed as critical illness.

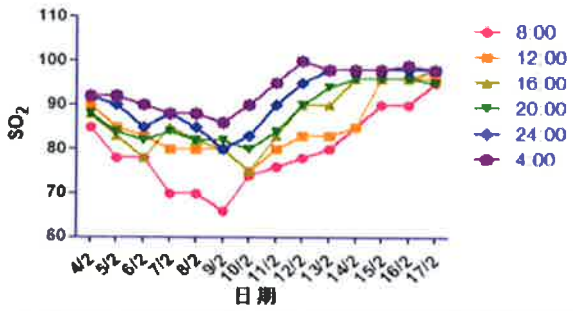

figure 2 High oxygen mask bed SO_2 monitoring results (flow 5 ~ 8min / L)

It can be seen from Figure 3 that the SO_2 before entering the cabin is significantly lower than that under the state of inhaling oxygen in the ward mask (at 08:00). After the first HBOT out of the cabin, SO_2 increased to 90%, suggesting that the treatment process has a significant effect on correcting hypoxemia. However, the results at 08:00, before entering the cabin, and at 12:00 showed that they all gradually increased with the treatment. The SO_2 immediately after leaving the cabin was 90% after the first treatment, and then all were above 93%. After returning to the ward after the first 4 treatments (at 12:00), and in a supine state of oxygen inhalation, SO_2 decreased significantly compared to the exit from the cabin. After the fifth time (February 15th), there has been no drop back at 12:00 compared with the time after departure.

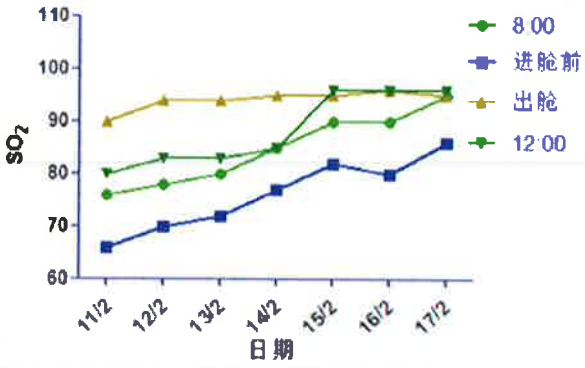

image 3 Changes of SO_2 before and after HBOT treatment

Figure 4 shows that although active drug treatment was given before February 10, the mean SO_2 in patients still decreased day by day (P <0.05). After starting the treatment, the downward trend reversed immediately, and the mean value on February 11 had been significantly higher than that on February 10 (P <0.05), and it increased day by day. After the 5th treatment (February 15), the normal range was basically restored.

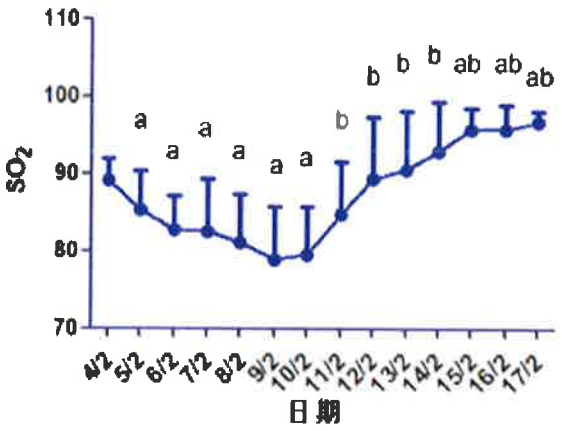

Figure 4 Changes of daily mean value of $SO_{2\ in}$ patients with oxygen inhalation

3 . Arterial blood gas analysis results:

For various reasons, the patient did not review blood gas after the first treatment. As shown in Table 1 , the pre-HBOT partial oxygen pressure (PO_2) decreased progressively, which was consistent with the main complaints and symptoms of patients with dyspnea. Before the first HBOT (day 19 of admission), it was 37 mmHg. The review on the day after treatment had returned to 69mmHg.

表 1 患者动脉血气检查结果

检查项目	检查时间								
	1/27	1/29	1/30	2/1	2/4	2/11 (基础)	2/11 (1T*)	2/20 (基础)	2/20 (10T*)
PH	7.41	7.38	7.43	7.50	7.53	7.39	7.41	7.43	7.39
PCO_2 (mmHg)	41.00	35.00	33.00	31.00	29.00	30.10	32.00	37.30	36.30
PO_2 (mmHg)	82.00	67.00	71.00	76.00	45.00	37.00	69.00	122.00	130.00
Na^+ (mmol/L)	133.00	131.00	139.00	137.00	137.00	134.00	133.00	135.00	135.00
K^+ (mmol/L)	3.10	3.90	3.30	2.90	3.00	3.20	3.10	2.90	3.20
Ca^{++} (mmol/L)	0.79	0.79	0.87	0.83	0.77	0.92	0.71	1.11	0.91
GLU (mmol/L)	10.10	7.30	6.10	5.10	4.90	6.20	6.00	9.50	6.30
Lac (mmol/L)	1.10	1.80	2.00	1.20	1.10	3.03	2.50	1.71	1.05
HCT%	18.00	13.00	12.00	38.00	38.00	29.00	10.00	11.00	30.00
SO2%	92.00	89.00	93.00	96.00	86.00	76.00	91.00	99.00	99.00

注：T 为 HBOT 治疗次数。

Table 1 Patient arterial blood gas test results

4 . Hematology test results:

For various reasons, some hematology has not been reviewed after treatment. Results are provided here before and after. As shown in Table 2 , the lymphocyte count and the percentage of lymphocytes were consistent with the clinical manifestations, and decreased significantly before treatment. The review results after 2 treatments (February 12) showed a marked recovery.

表 2 患者血常规检查结果

项目	检查时间					
	1/24 第 3 天	1/27 第 6 天	1/29 第 8 天	1/31 第 10 天	2/4 第 14 天	2/12 2 次 HBOT
WBC (10^9/L)	3.68	3.50	8.17	5.95	6.38	5.31
NEU%	45.70	54.30	84.80	90.20	85.40	74.90
LYM%	39.90	36.30	10.60	6.90	10.30	18.30
MON%	14.10	9.40	4.00	2.90	3.80	6.60
NEU (10^9/L)	1.68	1.90	6.92	5.37	5.45	3.98
LYM (10^9/L)	1.47	1.27	0.87	0.41	0.66	0.97
MON (10^9/L)	0.52	0.33	0.33	0.17	0.24	0.35
RBC (10^{12}/L)	4.27	3.95	4.10	3.88	3.86	3.61
HGB(g/L)	149.00	136.00	141.00	136.00	136.00	126.00
HCT	41.30	37.70	38.90	36.90	36.70	33.80
PLT (10^9/L)	77.00	47.00	71.00	110.00	146.00	132.00

Table 2 Patient blood test results

The blood coagulation function test results are shown in Table 3 . Fibrinogen (FIB) was detected to be significantly elevated on the 7th day (January 28th) of admission, and the fibrinogen degradation product (FDP) was significantly increased on the 10th day. The blood test results were further found in the morning before the 21st day. D - dimer (DD) was significantly increased. HBOT started on the same day. After 7 treatments, FIB, DD, and FDP significantly decreased, lymphocyte counts, albumin increased, and total bilirubin and direct bilirubin returned to normal ranges.

表 3 患者凝血检查结果

项目	检查时间				
	1/24 第 3 天	1/28 第 7 天	1/31 第 10 天	2/11 第 21 天	2/17 7 次 HBOT
PT（sec）	11.30	11.20	12.10	12.50	12.00
APTT（sec）	28.20	29.60	27.50	22.70	21.30
FIB（g/L）	2.73	3.23	3.30	3.63	1.90
TT（sec）	17.00	16.30	17.00	15.20	15.50
D-D（mg/L）	0.28	0.22	0.38	6.86	0.62
PT-INR	0.98	0.97	1.06	1.09	1.05
FDP (ug/mL)	1.20	1.00	3.90	19.70	1.20
AT-III%	96.20		76.10	80.10	81.20

table 3 Patient coagulation test results

5 . CT examination results:

As in FIG. 5 , the chest CT February 7 patients showed multiple lung spot-like soft tissue density, tube patency, lung vascular texture thickening, lung see multiple sheet-shaped high density. Compared with the imaging on February 3, the degree of bilateral lung infection became worse. On February 18, a chest CT scan was performed after 8 HBOTs, and multiple soft tissue density shadows and sheet-like high-density shadows in both lungs decreased, but it was still obvious.

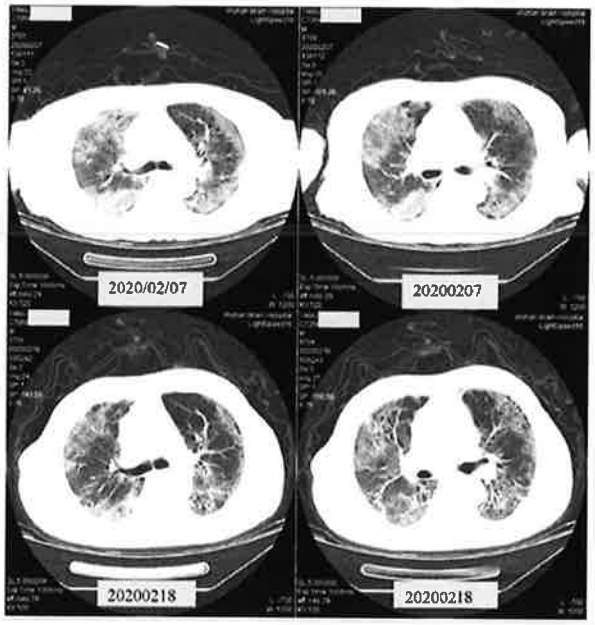

Figure 5 Comparison of CT before treatment (February 7) and after the 8th treatment (February 18)

discuss

The course of this patient's disease is characterized by persistent and progressive hypoxemia and pulmonary pathological changes. The lung is the main target organ of the new coronavirus, and pneumonia is the main disease manifestation of the new coronavirus infectious disease (COVID-19). The consequence is the decline of lung function. Diffuse inflammation of the lung tissue and hypoxemia are the main clinical features of NCP. Among the 41 NCP patients reported by Huang et al., 12 patients with acute respiratory distress syndrome (ARDS) were all critically ill (ICU care), suggesting that progressive hypoxemia is an important pathology for NCP Features. Of the 27 patients who had only nasal catheter ventilation, only 1 (8%) eventually needed access to the ICU. However, 62%

of patients who required high-flow oxygen or non-invasive mechanical ventilation with nasal catheters eventually developed critical illness (ICU) [3]. Chen NS et al.'S case report in 99 cases of abortion is similar [4]. Hypoxemia is also one of the leading causes of death in NCP. The NCP diagnosis and treatment guidelines also take the degree of hypoxemia as the main indicator of the clinical classification of NCP in light, severe and critical. The imaging examination of this patient showed that the lung parenchyma was the main disease and the airway was unobstructed. In the results of arterial blood gas analysis, the pH value is not acidic but alkaline, indicating that the damage to lung function is mainly the gas exchange function. As a general method, nasal cannula was given oxygen upon admission. However, with the development of lung tissue pathology, shortness of breath occurred , and SO_2 continued to decrease. Further switching to a mask to absorb oxygen did not reverse the continued downward trend of SO_2 . The above hints that the existing atmospheric oxygen therapy can not meet the need for the treatment of hypoxemia accompanied by the pathological progress of the lung tissue of the disease.

Hypoxemia refers to a decrease in blood oxygen levels, while hypoxia refers to a state of oxygen deficiency in tissues or organs or the whole body. Hypoxemia is the cause of hypoxia, but is not the only one. The ultimate method of atmospheric oxygen therapy is ECMO. The application of ECMO theoretically solves the problem of the source of hypoxemia in patients, but the clinical use of NCP in critically ill patients is limited, mainly due to the presence of concurrent multiple organ failure. Targeting NCP with the lung as the main target organ, leading to systemic dysfunction such as multiple organ failure, in addition to the role of virus and immune response, it is not ruled out that it is related to the persistent general hypoxia of systemic tissues and organs. From the air environment to the cells of tissues and organs, the amount of oxygen delivered is affected by the oxygen partial pressure of breathing gas, lung ventilation function, ventilation function (including the effect of gas-blood barrier and ventilation / perfusion ratio on gas exchange), blood carrying capacity, Tissue hemoperfusion and other five links. The difference in effectiveness of the existing oxygen therapy methods is related to their ability to intervene in these five links (Figure 6). The clinical choice of oxygen therapy needs to fully consider the impact of the disease on each link and the specificity of the oxygen therapy measures.

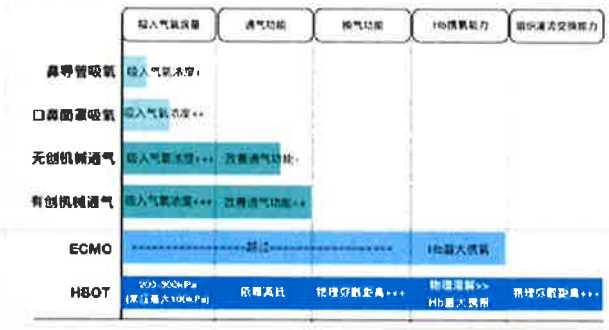

Figure 6 Intervention of different oxygen treatments on the process of oxygen from the external environment to tissues and organs

Oxygen debt (also called exercise excess oxygen consumption) is the difference between the amount of oxygen required (oxygen demand) and the actual amount of oxygen supplied (oxygen supply), which is commonly used in sports medicine [5]. The fever and strong immune response caused by the virus infection will inevitably lead to an increase in the body's metabolic rate and increase in oxygen demand; however, the persistent hypoxemia caused by the lung tissue pathology of NCP also reduces the amount of oxygen supplied by the heart and lungs to systemic organs . Therefore, when the NCP disease develops to a certain degree, there must be a gap between oxygen demand and oxygen supply, which can also be understood as a special "oxygen debt". Studies have found that under a certain intensity of exercise load, pre-pulmonary diseases can lead to hypoxemia [6]. In this case, the SO_2 before HBOT entering the cabin was significantly lower than that under the mask inhalation of oxygen in the ward (at 08:00). The patient was unable to inhale oxygen from the ward to the HBOT department and increased a certain amount of activity. The reduction of $SO_{2\ and\ the}$ decrease of SO_2 caused by the increase of consumption . This phenomenon suggests that the lung pathological changes caused a severe imbalance between the patient's oxygen demand and oxygen supply. The arterial blood gas analysis before the first HBOT entry on February 11 showed that the blood lactic acid content was significantly increased (3.03 mmol / L), suggesting that the patient's body was in a state of severe anaerobic metabolism.

HBOT is based on the physical properties of gas. By substantially increasing the partial pressure of oxygen, HBOT can increase the partial pressure of alveolar oxygen, increase blood oxygen tension, increase the effective diffusion radius of tissue oxygen, and increase the total oxygen transport capacity under the same cardiopulmonary function. To achieve (1) effectively and thoroughly correct tissue hypoxia while improving acidosis and enhancing tissue cell viability; (2) capillary endothelial cells re-oxygenate to restore capillary function and block exudation caused by hypoxia And edema; (3) increase the effective diffusion radius of tissue oxygen, correct tissue hypoxia and increase tissue oxygen reserve [2]. In this case, the blood gas analysis result of PO_2 after the first HBOT exit from the cabin increased from 37.0 mmHg to 69.0 mm Hg before entering the cabin, showing that HBOT has a good effect, but there is still a significant gap from the normal value, and SO_2 has only increased. To 90%. This state before entering the cabin can best reflect the degree of hypoxia in the patient's general tissues and organs. The ultimate goal of clinical oxygen therapy is to solve the hypoxia state of the body. This result suggests that the patient's previous "oxygen debt" accumulation exceeded the ability of one HBOT to correct, further reflecting the degree of imbalance between the oxygen demand and the oxygen supply in the patient's body.

After 90 minutes out of the cabin (at 12:00), the patient's oxygen saturation decreased significantly, suggesting that the tissue oxygen reserve with increased physical dissolution of HBOT was exhausted in a short time. Overall, however, the daily mean SO_2 of patients after HBOT treatment increased steadily. The residual oxygen cannot be explained by HBOT. On the one hand, the possible mechanism is that HBOT provides the intermittent aerobic metabolism of the body (anaerobic metabolism before treatment-aerobic metabolism during treatment-anaerobic metabolism after treatment), which greatly improves the body's continued resistance. by the ability of the anaerobic metabolism, similar to oxygen toxicity tolerance HBOT oxygen intermittently as the mechanism of [2]. In addition, the significant increase in D 聚 dimer, plasminogen, and TDP in the hematological parameters of this patient suggests that the patient already had a certain degree of disseminated intravascular coagulation (DIC) before HBOT. Secondary to viral infection. There are peripheral hemodynamic changes and perfusion disorders. Changes in the coagulation index of this patient also suggest that HBOT has a significant effect on improving end-stage circulation and tissue oxygen supply. DIC combined with persistent hypoxemia leading to ischemic loss of capillary endothelial cells and tissue edema at the periphery of the circulation, whether it is also a common phenomenon in NCP severe patients requires more clinical research and observation.

In this case, because there was no medical care in the cabin, the patient continued to inhale oxygen for 95 minutes from the beginning of the compression to the end of the decompression. Oxygen poisoning has always been an important issue for many hyperbaric oxygen clinicians in the application of HBOT. The human body adapts to a 20kPa oxygen partial pressure environment under normal pressure air, and when exposed to high partial pressure oxygen of HBOT, it will inevitably have an impact. Because the diving process will inevitably breathe a mixture of high partial pressure oxygen or oxygen, a diving program is designed to limit the high partial pressure oxygen exposure dose to avoid large pulmonary oxygen poisoning damage [2]. Conventional HBOT has a high oxygen exposure dose of about 150 UPTD. The exposure dose for this patient was 216 UPTD, but it was still much less than 615 UPTD. This dose implies a reduction in vital capacity of about 1%, which is the safety limit for conventional high partial pressure oxygen exposure. Therefore, the patient's HBOT need not worry about the risk of pulmonary oxygen poisoning.

In this case, a CT scan of the patient after 8 HBOTs showed that although the patient's lung lesions had improved significantly, the lesions still existed. However, the patient's SO_2 remained within the normal range under nasal cannula oxygenation. This separation of lung pathological changes from SO_2 suggests that although HBOT does not directly have a clear role in the cause (virus), the powerful oxygen therapy provided by it directly cuts off the persistent low that may be caused by lung tissue pathology. Oxygenemia, especially the continuous accumulation of oxygen debt in the hypoxic state of tissues and organs throughout the body, and its subsequent damage to important oxygen-consuming tissues and organs, maintain a relatively good functional state of the body, and provide a good body for the body to fight viral infection Sexual function foundation.

In summary, according to the pathological characteristics of NCP, HBOT has a clear mechanism of action that is different from normal pressure oxygen therapy. Conventional HBOT has been widely used in clinical practice for decades, and has a strong therapeutic capacity. On the premise of solving the problem of sensory control during transport, large-scale treatment of NCP patients can fundamentally solve the problem of supportive treatment of

progressive hypoxia that cannot be curbed by the existing atmospheric oxygen therapy, thereby reducing the critical illness rate and mortality. Expected effect. From the clinical manifestations of the patient changes, view test results, once HBOT oxygen can be atmospheric pressure conditions high flow oronasal mask, SO_2 heavy critically ill patients NCP type is still less than 80% of the daily average play Obvious improvement, 4 times of HBOT can basically correct persistent hypoxemia in critically ill patients. According to the existing stock of severe NCP in Wuhan, in the clinical use of HBOT, we can further explore the measures and methods of combining the use of HBOT and atmospheric oxygen therapy to improve the efficiency of treatment of large numbers of patients.

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