

Letter to the Editor

Current status of hyperbaric oxygen therapy for COVID-19

Dear Editor,

Since its outbreak in late December 2019, corona virus disease (COVID-19) has become a worldwide pandemic, hitting over 200 countries and regions around the world. In Japan, to prevent COVID-19 infection, the Japanese government recommends that people wear a mask, disinfect their hands with alcohol frequently, stay 2 m from others, avoid going out unnecessarily, and avoid the three Cs of “closed spaces with poor ventilation”, “crowded spaces with many people”, and “close contact”.¹

Standard treatments for confirmed moderate and severe cases of COVID-19 infection in Japan are steroid, remdesivir, baricitinib and/or heparin, in addition to oxygenation supportive therapy, based on the Guideline of Medical Care for COVID-19, version 4.2, from the Japanese Ministry of Health, Labour and Welfare (<https://www.mhlw.go.jp/content/000712473.pdf>).

The Japanese Society of Hyperbaric and Undersea Medicine released a position statement concerning COVID-19 infection on March 20, 2020, as hyperbaric oxygen therapy (HBO₂) requires the three Cs, especially treatments in a multiplace chamber (https://www.jshm.net/file/covid19_1.pdf). Patients with a fever over 37.5°C, cough or sputum, and those with potential COVID-19 infection are not indicated for entrance into the HBO₂ room. If a patient has confirmed COVID-19 infection, HBO₂ is not recommended, excluding cases in which the benefit of HBO₂ is superior to that without HBO₂. The Japanese Society of Hyperbaric and Undersea Medicine has also declared that HBO₂ is not recommended for the treatment of COVID-19-associated hypoxia. Instead, recommended treatment options include ventilator support or extracorporeal membrane oxygenation (https://www.uhms.org/images/MiscDocs/UHMS_Guidelines_-_COVID-19_V4.pdf).

Table 1. Previous reports concerning patients with COVID-19 treated by hyperbaric oxygen therapy (HBO₂)

First author	No. of patients	Age (years)	Sex; F, M	Condition	Day/s	HBO ₂ treatment	Outcome
Thibodeaux K	5	39–63	4, 1	Increasing oxygen requirements, each facing impending intubation	ND	2.0 ATA x 90 min of HBO ₂ x 5 days	None of the patients treated with symptomatic COVID-19 disease needed a ventilator. In addition, all patients had rapid resolution of their tachypnoea and improved oxygen saturation
Gorenstein SA	20	30-79	2, 18	Oxygen requirement ranging from 2 to 15 L	0–14	2.0 ATA x 90 min x 5 days	Hazard ratios were 0.37 for inpatient mortality ($P = 0.14$) and 0.26 for mechanical ventilation ($P = 0.046$)
Guo D	2	57, 64	0, 2	P/F < 300	ND	1.5 ATA x 60 min x 7 days	Dyspnea and shortness of breath were immediately alleviated after first HBO ₂ and remarkably relieved after 7 days of HBO ₂
Zhong X	1	69	0, 1	PaO ₂ 32 mmHg	21	2 ATA x 60 min x 7 days	Hypoxia was improved
Naval Specialty Medical Center Program Team	5	ND	ND	PaO ₂ 37–78 mmHg under 5–8 L/min O ₂	ND	ND	Hypoxia and symptoms were improved

ATA, atmospheres; F, female; M, male; ND, no data; P/F, ratio of arterial to inspired oxygen.

However, there have been five recent reports of patients with COVID-19-associated hypoxia using HBO₂ to ameliorate their hypoxia (Table 1) as the increased amount of oxygen in the plasma due to HBO₂ may mobilize stem cells, block the inflammatory cascade, interfere with interstitial fibrosis development in the lungs, delay the onset of severe interstitial pneumonia, and reduce the risk of multiple organ failure due to an overall abated COVID-19 viral load.²⁻⁵ These five reports included four case reports or case series and one analysis of 20 cases treated with HBO₂ using a propensity-matched controls analysis. The report by Gorenstein *et al.*⁴ described the usefulness of HBO₂ for patients with COVID-19 infection compared with controls without HBO₂ (adjusted subdistribution hazard ratios were 0.37 for inpatient mortality [$P = 0.14$] and 0.26 for mechanical ventilation [$P = 0.046$]). Based on these preliminary reports, a randomized control study to verify the safety and utility of HBO₂ for patients with COVID-19, even severe cases, is now ongoing (https://www.uhms.org/images/Position-Statements/HBO2_and_COVID_8-10-2020_clinicaltrials_8-12-2020.pdf).

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