UHMS Position Statement: Hyperbaric Oxygen (HBO₂) for COVID-19 Patients

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Authorship: John J. Feldmeier, DO, Helen Gelly, MD et al.

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As the worldwide crisis of COVID-19 increased and without any substantial therapeutic or preventative breakthroughs, increased consideration was given to the utilization of hyperbaric oxygen therapy to overcome COVID-19 hypoxemia. This application has its origins in the demonstrated success in treatment of severe anemia and carbon monoxide poisoning, both conditions where hypoxemia is treated by hyperbaric oxygen. In response to requests for guidance the UHMS published the original position statement on April 8, 2020; this position statement was also endorsed by the American College of Hyperbaric Medicine (ACHM).

This position statement supported IRB (Institutional Review Board) approved clinical trials but did not advocate treatment off protocol. In the interim, as knowledge about the SARS-Cov-2 and its mechanisms of injury have evolved, there still have been no major successes in developing definitive pharmacologic interventions. Studies have reported some advantage for patients treated with convalescent plasma, remdesivir and steroids, although none of these provide outright cures and at best mitigate severity and modestly impact length of hospital stays or survival. The initial fervor for hydroxychloroquine with or without azithromycin has mostly faded. Prone patient positioning has empirically been shown to improve patient oxygenation. Some have employed ECMO (extracorporeal membrane oxygenation) as a last-ditch intervention to provide patients with adequate oxygen to support minimum metabolic requirements and sustain life. Significant and rapid progress has been reported in the development of vaccines, and our hopes are that a safe and effective vaccine will be available no later than early next year (2021). Until that time the need for more effective therapies will persist.

It is in this light that we present a brief discussion of the role for hyperbaric oxygen in COVID-19 and state the updated position of the Undersea and Hyperbaric Medical Society in its appropriate application. The United States now leads all nations of the world in both incidence and fatalities due to COVID. Novel therapies have been recommended by some that are brand-new drugs or procedures or novel applications of established therapies[1]. In addition to the original report from China of a series of patients [2] we have a published series from a center in Louisiana [3] and most recently a report of a small case-controlled trial from investigators from NYU [4]. A consistent report from these publications is that the therapy has been safe despite concerns that this group of patients, who are maintained continuously on high FiO₂s (fractions of inspired oxygen), would be especially sensitive to oxygen pulmonary toxicity when a course of HBO₂ was added to their oxygen load. Additionally, investigators report an almost instantaneous relief in fatigued patients laboring to breathe when placed in the hyperbaric chamber under pressure. They are observed to relax and even achieve some much-needed sleep due to the success of HBO₂ in delivering adequate oxygenation [3,5].

"Rationale, study design considerations, and protocol recommendations for treating COVID-19 patients with hyperbaric oxygen" is a report to the UHMS from the Research Committee which presents a strong physiologic and biologic basic science case to support the use of hyperbaric oxygen [6]. In addition to effectively delivering oxygen in patients who may suffer from bilateral pneumonias and exhibit a ventilation perfusion mismatch due to emboli and microemboli preventing perfusion of functional bronchoalveolar units, hyperbaric oxygen has been shown to mitigate inflammatory reactions. Much of the pathogenesis of COVID-19 is due to an overly active immune response generating an inflammation that becomes a major etiology of subsequent consequences of the infection [7]. Hyperbaric oxygen has been shown to offer potent anti-inflammatory stimuli. It also has been reported to "pay back" the oxygen debt incurred in these patients with ongoing undersupply of oxygen to vital organs [8]. In at least one clinical series hyperbaric oxygen has been demonstrated to significantly reduce D-dimers which are a marker for coagulation [9]. If indeed the reduction of coagulation is a consistent effect, pulmonary function and subsequent oxygen delivery to the entire body will be improved.

A much more extensive discussion of mechanisms whereby hyperbaric oxygen is likely to favorably impact the pathologic features of COVID-19 is available in the Research Committee Report posted on the UHMS website [6]. Based on a broad and well-studied and documented description of likely physiologic effects of hyperbaric oxygen and based on the published reports demonstrating consistently positive responses in the trials cited above, the UHMS has updated its position statement to the following:

- 1. The UHMS continues to encourage well-designed IRB-approved clinical trials of hyperbaric oxygen for COVID-19, which will increase our understanding of the virus and promote effective treatment meant to define where hyperbaric oxygen might best fit in a multidisciplinary approach.
- 2. The UHMS recognizes the special value of phase III randomized controlled trials in providing level I evidence.
- 3. The UHMS now supports hyperbaric oxygen treatment on a compassionate basis for COVID-19 and recognizes that not all centers have the ability to initiate clinical trials. Some may not even have access to investigational review boards to permit their participation in IRBapproved research protocols.
- 4. Because the UHMS is seeking to encourage the well-documented scientific observation of the impact and proper application of hyperbaric oxygen, it strongly recommends that all patients treated with hyperbaric oxygen therapy be followed by certain key outcome determinants regardless of whether they are in an IRB-approved trial or treated under compassionate use. A listing of recommended diagnostic studies is provided in the Research Committee Report previously cited. This document also provides guidelines for patient selection and eligibility for treatment as well as a discussion of treatment specifics, including total number of treatments, frequency, total length of each treatment as well as treatment pressure. Valuable additional information is available at this site that we believe will aid those who take on the difficult task of treating these seriously ill patients.
- 5. The UHMS recognizes that the final determination of all aspects of patient care as always should be made at the local level, but because of the novelty of this application, the UHMS provides this guidance as a model for individualized care that reflects the clinical experience

of intellectual leaders in the field to avoid the need to "reinvent the wheel" when considering the use of hyperbaric oxygen in the treatment of these critical patients.

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