Delivery of Hyperbaric Oxygen Therapy to Critically Ill, Mechanically Ventilated Children

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Purpose: **The purpose of this article is (1) to describe our method of mechanical ventilation and monitoring of critically ill children during administration of hyperbaric oxygen therapy (HBO_2) in a multiplace chamber; and (2) to review the complications they experienced during transport to the HBO_2 chamber and HBO_2 treatment.**

Materials and Methods: **A case series from a university-affiliated children's hospital and regional hyperbaric medicine treatment facility. Patients studied included all children who required HBO_2 therapy while mechanically ventilated at any time between April 1985 and June 1995.**

Results: **Thirty-two children were treated with HBO_2 while mechanically ventilated. Ages ranged from 3 days to 11.3 years (mean 4.8 ± 3.5 years). There were 22 males. Twenty-one children had necrotizing infections, 9 had carbon monoxide (CO) poisoning, and 2 had iatrogenic arterial air embolism. Complications or events occurring during HBO_2 therapy included hypotension (63%), bronchospasm (34%), hemotympanum (13%), and progressive hypoxemia (6%). The only complication during transport was one accidental extubation (3%).**

Conclusion: **Hyperbaric oxygen therapy can be administered safely to most critically ill children in a multiplace chamber if they are monitored closely. Although complications are not uncommon, most can be managed easily by a team skilled in treating ill children and knowledgeable of possible complications of HBO_2 therapy.**

HYPERBARIC OXYGEN therapy (HBO_2) is used to provide very high partial pressures of oxygen to tissues and to compress gasses in isolated body compartments. Although its mechanism of action is not completely understood, it has been advocated for patients with decompression sickness, arterial gas embolism, and carbon monoxide poisoning. It has also been proposed as an adjunctive therapy for deep-seated infections.[1,2] HBO_2 therapy is most commonly administered to adults with poor wound healing or radiation tissue injury[3]; however, such conditions are uncommon in children. Unlike adults, most pediatric patients who undergo HBO_2 therapy have severe acute illnesses.[4]

As a result of technical difficulties in patient monitoring and management, many hyperbaric treatment facilities do not accept critically ill pediatric patients who require mechanical ventilation during HBO_2. Our hyperbaric facility routinely accepts severely ill pediatric patients, many of whom require mechanical ventilation. We reviewed our institutional experience with HBO_2 in mechanically ventilated pediatric patients over the past 10 years. This article describes the current method of mechanical ventilation, administration of inotropic infusions within the chamber, and standards for monitoring. The difficulties that may be encountered in the delivery of HBO_2 treatment and the complications that may occur in critically ill children during HBO_2 administration are discussed.

MATERIALS AND METHODS

Children's Hospital and Medical Center (CHMC) is a university-affiliated pediatric hospital. The Virginia Mason Medical Center (VMMC) Hyperbaric Medicine Department is the exclusive referral center for CHMC patients requiring HBO_2 therapy. At VMMC, ventilated pediatric patients are cared for in a multiplace chamber. This type of chamber allows caregivers to accompany the child into the chamber and to provide constant care. Transport of patients between CHMC and VMMC takes approximately 20 minutes by ambulance and is performed by a transport team composed of a life-flight transport nurse and a pediatrician.

A chart review was conducted of all children treated with HBO_2 while mechanically ventilated between April 1985 and June 1995. Demographic information was abstracted. Indicators of severity of illness, including ventilator settings, need for inotropic support, days in the intensive care unit (ICU), and total hospital days, were reviewed. Complications of therapy during transport and in the hyperbaric chamber, including endotracheal tube movement, changes in ventilator settings, need for additional inotropy or intravenous volume resuscitation, bronchospasm, and hemotympanum, were also recorded. Complications related to HBO_2 therapy or transport were defined as those

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events that occurred from the time the transport team took charge of the patient until the patient was returned to the ICU.

During HBO_2 therapy, all ICU patient care is coordinated and managed by the transport team from CHMC, a hyperbaric charge nurse, and a physician from VMMC's Section of Pulmonary and Critical Care Medicine. All intubated patients are accompanied into the multiplace chamber by a hyperbaric-trained respiratory therapist and a critical care nurse. The physician routinely remains outside the chamber.

The environment of the hyperbaric chamber imposes limitations on equipment used in the management and monitoring of critically ill patients. These limitations include space restrictions, fire codes, and the effect of increased pressure on equipment function. The VMMC Hyperbaric Medicine Department uses the Penlon Oxford Mk2 Ventilator (Penlon Limited; Oxon, England). This is a pneumatic anesthesia ventilator used in a number of multiplace hyperbaric facilities. The pediatric circuit provides a tidal volume of 40 to 350 mL. Information for ventilator settings is routinely provided by the transport team to approximate the tidal volume, positive end expiratory pressure, and respiratory rate that the child received in the ICU before transport. Positive end-expiratory pressure is available with the Penlon ventilator.

Electrocardiogram and pressure monitors are located outside the hyperbaric chamber with cables penetrating the chamber hull. The arterial line transducer is attached to a pressure adapter cable which accommodates both hospitals' monitoring systems and eliminates the need to change tubing. The arterial line is calibrated initially at normal atmospheric pressure, then again at the hyperbaric treatment pressure. In-line volutrols were added to the intravenous infusion bags in the early years of the case series; however, this was subsequently changed to an IVAC Medsystem Infusion Pump (IVAC Corporation; San Diego, CA), which allowed direct transition from the transport team to the hyperbaric chamber. Cuff blood pressure is obtained soon after the hyperbaric treatment is started and compared with the value obtained from the arterial monitor. Arterial blood gas samples are routinely drawn 10 to 15 minutes into the hyperbaric treatment and additionally as needed. Blood samples are delivered to the outside via an airlock window.

If pressure bags or other gas containing pieces of equipment are used inside the hyperbaric chamber, they must be closely monitored and appropriately vented during chamber compression and decompression. In fact, when cuffed endotracheal tubes are used, the air is removed from the cuff and saline is instilled before chamber compression. Hyperbaric treatments are performed according to standard protocols at VMMC (Table 1). Some treatment times for the patients reported vary as protocols have been refined over the 10-year period studied.

Table 1. Hyperbaric Treatment by Diagnosis Among the Study Population

Diagnosis	Maximum Treatment Pressure (ATA)	Duration of Treatment (hours)	Treatments per Patient
Fasciitis/omphalitis*	2.36	2	1 to 10
CO poisoning†	3.0	2 to 5.5	1
Air embolism††	6.0	2 to 6	1 to 2

*Necrotizing fasciitis is treated according to the recommendations of the Undersea and Hyperbaric Medical Society, which suggests twice daily treatment with 100% oxygen administration at 2.5 atmospheres absolute (ATA) pressure for 90 to 120 minutes until the patient is improving. When the patient's condition has stabilized, treatment frequency is reduced to once daily until the infection is controlled. (Data from reference 21.)

†Air embolism is treated according to the United States Navy Treatment Table 6A, utilizing a maximum treatment pressure of 6.0 ATA, with a total treatment duration ranging from 4 hours 52 minutes to 8 hours 15 minutes. (Data from reference 22.)

††CO poisoning has been treated according to the United States Air Force Carbon Monoxide Treatment Protocol at VMMC since 1992. (Data from reference 23.)

RESULTS

Demographics

From April 1985 through June 1995, 32 pediatric patients received concurrent HBO_2 and mechanical ventilation. Demographic information about the patients is presented in Table 2. Ages ranged from 3 days to 11 years 4 months, with an average age of 4½ years. There were 22 males. The mean ICU stay was 5 days with a longest stay of 25 days. Thirteen patients (40%) required inotropic support during their ICU course.

The most common diagnosis among patients treated with HBO_2 was severe soft-tissue infection. There were 21 patients (66%) with necrotizing infections. Nine patients (28%) were treated for carbon monoxide (CO) poisoning. The CO poisoned patients were all victims of house fires. Although carboxyhemoglobin (COHb) levels ranged from 2.3% to 34.4% in the emergency department, all children were comatose at the scene. None had cutaneous burns. None had a

Table 2. Selected Demographic Features of Children Receiving HBO_2 and Mechanical Ventilation

	Mean	SD	Range
Age (months)	58.2	41.5	.25 to 136
Weight (kg)	18.1	8.6	3.5 to 41
ICU days	5.5	5.5	1 to 25
Total hospital days	18.4	30.4	1 to 167
	n		%
Sex			
Male	22		69
Female	10		31
Diagnosis			
Necrotizing infection	21		66
CO poisoning	9		28
Air embolism	2		6
Inotropic support	13		40

metabolic acidosis consistent with cyanide poisoning. The final two children were treated for arterial air embolism, both of which were iatrogenic complications of cardiopulmonary bypass.

Complications

Complication data are shown in Table 3. One child became extubated during transport and was reintubated without difficulty. No other complications occurred in transport.

Hemodynamic instability was the most frequent complication encountered during hyperbaric therapy. Twenty patients (62%) became hypotensive, 9 of whom required only boluses of intravascular crystalloid for treatment. The other 11 patients required addition or an increase of cardiopressor agents, as well as volume infusion.

Bronchospasm was diagnosed if the patient experienced wheezing and a rise in peak airway pressures at a constant chamber pressure during mechanical ventilation in the hyperbaric chamber or immediately after decompression before return to the ICU. Most patients who developed bronchospasm in the chamber still exhibited wheezing on examination after being removed from the chamber environment. Bronchospasm occurred in 11 patients (34%). Eight of these 11 patients were being treated for necrotizing infection and one for arterial air embolism, neither of which should predispose the patient to wheezing. Two patients were undergoing HBO_2 for CO poisoning. Most children responded to nebulized albuterol; however, two developed severe bronchospasm, requiring an intravenous terbutaline infusion.

Deterioration in arterial oxygenation complicated the course of two patients while in the chamber. One of the two had a deep-seated tissue infection and sepsis. The initial Pao_2 in the HBO_2 chamber on 100% oxygen was greater than 107 kPa, but the first Pao_2 on return to the ICU was 5.7 kPa on normobaric 100% oxygen. Fresh blood was noted from the patient's endotracheal tube (ETT) immediately on exiting the hyperbaric chamber. This patient required a rapid increase in positive end expiratory pressure from 4 to 18 cm H_2O and was changed to high-frequency oscillatory ventilation to maintain arterial saturation over 90%. The second patient experiencing worsening oxygenation had CO poisoning. As in the previous case, initial Pao_2 in the hyperbaric chamber was greater than 107 kPa but dropped to 40.9 kPa during HBO_2 treatment. The positive end-expiratory pressure (PEEP) was increased from 4 to 10 cm H_2O. He also had a marked increase in ventilatory peak inspiratory pressures rising to 68 cm H_2O.

Table 3. Complications During Transport and HBO_2 Treatment of Mechanically Ventilated Children

Complication	n	%
Hypotension	20	62
Bronchospasm	11	34
Hypoxemia	2	6
Hemotympanum	4	12
Prophylactic myringotomy	8	25
ETT movement/extubation	1	3
Seizure	1	3

Hemotympanum occurred in four patients (12%). The hemotympanum was suspected because the children became agitated in the chamber. The diagnosis was confirmed by physical examination following treatment. Eight other children had prophylactic myringotomies performed before HBO_2 therapy. One patient developed seizure activity during HBO_2, a recognized central nervous system complication of HBO_2 therapy.[5,6] This patient had necrotizing fasciitis, which should not predispose to seizures. However, a subsequent cranial computerized tomographic scan showed multiple infarcts.

Outcome

Four children died: two were treated for CO poisoning, one for iatrogenic air embolus, and one for myonecrosis. Of the patients who survived, 14 were normal at discharge. At discharge two patients were not at their cognitive baseline: one received HBO for air embolus, the other had severe CO poisoning. The remaining patients had complications relating to fasciitis/myonecrosis. This included one patient who required a left knee disarticulation, and a colostomy. Three patients each required skin grafting and treatment for decreased mobility. Seven patients required post-hospitalization physical rehabilitation.

DISCUSSION

HBO_2 therapy can be delivered safely to critically ill, mechanically ventilated children in a multiplace chamber if proper monitoring and personnel are available. Providers need to be aware of potential complications of HBO_2 therapy. Putative benefits of HBO_2 treatment need to be weighed

against possible complications and accessibility of a hyperbaric chamber.

The hyperbaric chamber is a unique environment that requires adaptations for equipment and personnel. The multiplace chamber allows caregivers to enter the chamber with the patient. Unless needed inside the chamber for patient management, the physician often stays outside to insure that the person making patient management decisions is not subject to the central nervous system effects of hyperbaric exposure, which may include euphoria from nitrogen narcosis. The multiplace chamber does have an airlock, which allows entry and exit by personnel into and out of the hyperbaric treatment environment without decompressing the chamber. This allows rapid entry by the physician for patient evaluation or management if needed. The chamber is pressurized with air, so that only the patient breathes 100% oxygen. This is done to decrease the risk of fires.

Equipment must be adapted both because of the pressurized environment and because of fire risks. Even though the chamber is pressurized with air, the pressurized chamber remains an oxygen-rich environment. Thus, there are stringent standards which must be adhered to for electrical equipment to be used in the hyperbaric environment.[7] Therefore, the ventilator and monitoring devices are pressurized within the chamber, but the electrical components detach and are located outside of the chamber. The Penlon Oxford Ventilator used at VMMC is widely used in multiplace hyperbaric chambers in the United States. This ventilator operates in a controlled mode only, requiring that small pediatric patients often be heavily sedated during HBO_2 therapy. Recently, the Servo 900 (Siemans Corp.; Solna, Sweden) has also been demonstrated to be safe and reliable in the hyperbaric environment. This will allow enhanced ventilatory capabilities within the hyperbaric chamber.

The delivery of drugs by continuous infusion is also complicated. This has been addressed by placing the IVAC Medsystem Infusion Pump (IVAC Corporation; San Diego, CA) used by the transport team, into a specially constructed, nitrogen-purged Plexiglas box that is placed in the chamber with the patient. This has enhanced consistent delivery of vasoactive medications.

Complications during HBO_2 treatment of critically ill children are common; however, most respond quickly to appropriate intervention. Pulmonary complications occurred frequently in this group of patients. Hypoxemia and decreased compliance occurred in 2 of the 32 patients. The pathogenesis of the hypoxemia is unclear. However, high inspired oxygen has recognized pulmonary toxicity that increases with the partial pressure of inspired oxygen. Animal models have shown cellular damage from 1 hour of exposure to an inspired oxygen of 1.0 at three atmospheres absolute (ATA).[8] The mechanism of lung injury from hyperoxia is believed to result from the increased production of reactive O_2 species with subsequent injury to cell membranes.[9] Lipid peroxidation alters the ability of the cell to maintain normal ion transport and membrane potential. Furthermore, high concentrations of oxygen stimulate production of arachidonic acid mediators that have been correlated with lung injury.[9,10] Decreases in vital capacity from hyperoxic lung injury are partially due to capillary leak, decreased surfactant activity, and absorption atelectasis.[11] However, hypoxemia and changes in pulmonary compliance are uncommon during the intermittent exposure to hyperbaric oxygen used in the multiplace chamber.[12] It is unknown whether the risk of clinically significant pulmonary oxygen toxicity during hyperbaric exposure is increased among patients with pre-existing acute lung injury, and the pathogenesis of increased hypoxemia in the two patients remains uncertain.

Bronchospasm was the most common pulmonary complication. It occurred with varying severity in one third of patients. The etiology of the bronchospasm is also unknown. However, exposure to an inspired oxygen (FIO_2) of 1.0 for several hours in normal human volunteers causes pain and cough[2] coinciding with tracheal inflammation. Mucous clearance and ciliary function also decrease with hyperoxic exposure.[13] Finally, leukotrienes, which are potent bronchoconstrictors, are increased in lungs exposed to high levels of oxygen.[10] Therefore, it is possible that HBO_2 exposure could have played a role in the development of bronchospasm, although it seems unlikely.

Hemodynamic changes were seen frequently, both in patients with and without sepsis. The hemodynamic changes were not related to pressure change in the chamber, either chamber compression or decompression. Twenty of the 32 children required either volume boluses or additional or

escalation of vasoactive infusions. Hemodynamic instability was likely caused by sepsis in many patients. However, several children who did not have infections also developed hypotension. One potential explanation for hypotension in children with CO intoxication would be myocardial depression from CO poisoning. Severe neurological injury in children with CO poisoning may also contribute to hypotension. Although hyperoxia itself has been shown to depress cardiac output in animals,[14] this is generally thought to represent a reflex response to increased systemic vascular resistance resulting from oxygen-induced vasoconstriction and is not associated with hypotension. Hypotension is not a recognized side effect of routine hyperbaric oxygen exposure and, therefore, we speculate that hypotension in these children was most likely due to the underlying disease processes.

Hemotympanum was another fairly common problem in this series. Small children and intubated patients have difficulty equalizing the pressure between the middle ear and eustachian tubes. Some surgeons at our institution routinely place prophylactic myringotomy tubes in children less than 1 year before HBO_2 treatment. If a child appears in pain during the treatment, ear examination may reveal the source. Due to the small sample size (4 of 24 patients who did not have prophylactic myringotomies had courses complicated by symptomatic hemotympanum) and because there was no standard approach to ear tube placement or follow-up examinations of nonsymptomatic patients, a recommendation for or against prophylactic myringotomies cannot be made.

Our experience suggests most critically ill children can tolerate both HBO_2 treatment and the transport potentially required for such treatment with proper monitoring and care. We cannot compare our complication rates to other centers because there are no prior reports of HBO in critically ill children. However, due to worsening cardiopulmonary status, one child with a deep-seated tissue infection, septic shock and adult respiratory distress syndrome received only a single HBO_2 treatment and was not transported for additional treatments. Three other children with deep-seated tissue infections complicating cancer therapy during the period studied could not be transported to the HBO_2 chamber due to hemodynamic instability. Two died shortly after surgery, while one neonate, who developed myonecrosis while on extracoporeal membrane oxygenation, survived.

The total group of patients had a very low rate of complications in transport, with only one accidental extubation. That child was immediately reintubated and suffered no ill effects. The rate of transport related complications in this series compares favorably with the reported incidence rate of intensive care–related events by specialized transport teams that has previously been reported in the literature.[15]

Factors that need to be considered when making decisions regarding HBO_2 therapy are availability of a skilled transport team and distance to the hyperbaric chamber. For some patients, a long transport would be undesirable; and for CO poisoning, the possible benefit of HBO_2 may be diminished unless therapy can be delivered promptly.[16,17]

Published absolute contraindications to HBO_2 include untreated pneumothorax and use of some chemotherapeutic agents, such as disulfiram, cisplatinum, adriamycin, and bleomycin.[18,19] Disulfiram inhibits superoxide dismutase and increases oxygen toxicity. Hyperoxia appears to increase the toxicity of *cis*-platinum and adriamycin. A pneumothorax can become a tension pneumothorax while in the chamber and pose a life-threatening condition. For this reason, a chest tube should be placed before HBO_2 treatment of any patient with a pneumothorax.

Relative contraindications to HBO_2 also exist. An upper respiratory tract infection and chronic sinusitis make equalization of pressure in the middle ear difficult, although this may be of minimal relevance in critically ill patients. Myringotomy may be necessary, especially in infants and children with an endotracheal tube that further blocks eustacian tube patency. Seizures due to central nervous system oxygen toxicity occur in approximately 1.3/10,000 hyperbaric treatments, so that a pre-existing seizure disorder is a mild contraindication.[5] Patients with cystic lung disease are at theoretical risk for pneumothorax in the chamber if depressurized too quickly.[20]

In summary, although there are complications to hyperbaric therapy, most of these complications are easily treated by a skilled team. Therefore, critically ill pediatric patients can be treated in the hyperbaric chamber. To achieve this, a team skilled in managing ill children and knowledgeable of possible complications must be available for trans-

port and ongoing care of the patient. In addition, the hyperbaric chamber must be equipped with a suitable ventilator, hemodynamic monitoring, and critical care staff. Caregivers need to weigh the potential benefits of treatment against the proximity of the HBO_2 facility, the severity of the child's illness, and potential complications of treatment. We have identified problems and complications that should be anticipated for pediatric patients who are to undergo HBO_2.

REFERENCES

1. Kindwall EP: Uses of hyperbaric oxygen therapy in the 1990s. Cleve Clin J Med 59:517-528, 1992
2. Lodato RF: Oxygen toxicity. Crit Care Clin 6:749-765, 1990
3. Feldmeier JJ, Heimbach RD, Davolt DA, et al: Hyperbaric oxygen an adjunctive treatment for delayed radiation injuries of the abdomen and pelvis. Undersea Hyperbaric Med 23:205-213, 1996
4. Martin L, Bratton SL, Walker LK: Principles and practice of respiratory support and mechanical ventilation, in Rogers MC, Nichols DG (eds): Textbook of Pediatric Intensive Care (ed 3). Baltimore, MD, Williams and Wilkins, 1996, pp 273-275
5. Davis JC, Dunn JM, Heimbach RD: Hyperbaric medicine: Patient selection, treatment procedures, and side effects, in Davis JC, Hunt TK (eds): Problem Wounds: The Role of Oxygen. New York, NY, Elsevier Science, pp 225-239, 1988
6. NHLBI Workshop Summary: Hyperbaric oxygenation therapy. Am Rev Respir Dis 144:1414-1421, 1991
7. National Fire Protection Association: Standards for Health Care Facilities, NFPA 99, ch. 19. Hyperbaric Facilities. Boston, MA, National Fire Protection Association, 1996
8. Deneke SM, Fanburg BL: Normobaric oxygen toxicity of the lung. N Engl J Med 303:76-86, 1980
9. Gurtner G, Pharaoh IS, Adkinson NF, et al: The role of arachidonate mediators in peroxide-induced lung injury. Am Rev Respir Dis 136:480-483, 1987
10. Smith LJ, Shamsuddin M, Anderson J, et al: Hyperoxic lung damage in mice: Appearance and bioconversion of peptide leukotrienes. J Appl Physiol 63:944-951, 1988
11. Holm BA, Notter RH, Siegel J, et al: Pulmonary and surfactant changes during injury and recovery from hyperoxia. J Appl Physiol 59:1402-1409, 1985
12. Comroe JH, Dripps RD, Deming M: Oxygen toxicity: The effect of high concentration of oxygen for twenty-four hours on normal men at sea level and at a simulated altitude of 18,000 feet. JAMA 128:710-717, 1945
13. Sackner MA, Landa J, Hirsch J, et al: Pulmonary effects of oxygen breathing: A 6 hour study in normal men. Ann Intern Med 82:40-43, 1975
14. Savitt MA, Rankin JS, Elberry JR, et al: Influence of hyperbaric oxygen on left ventricular contractility, total coronary blood flow, and myocardial oxygen consumption in the conscious dog. Undersea Hyperb Med 21:169-183, 1994
15. Edge WE, Kanter RK, Walsh RF: Reduction of morbidity in interhospital transport by specialized pediatric staff. Crit Care Med 22:1186-1191, 1994
16. Thom SR, Taber RL, Mendiguren II, et al: Delayed neuropsychologic sequelae after carbon monoxide poisoning; prevention with hyperbaric oxygen. Ann Emerg Med 25:474-480, 1995
17. Hardy RH, Thom SR: Pathophysiology and treatment of carbon monoxide poisoning. Clin Toxicol 32:613-629, 1994
18. Heikkila RE, Cabbat FS, Cohen G: In vivo inhibition of superoxide dismutase in mice diethydithiocarbamate. J Biol Chem 251:2182-2185, 1976
19. Nemiroff PR: Effects of cis-platinum and hyperbaric oxygen on wound healing in mice. Undersea Biomed Res 40:15, 1988
20. Tibbles PM, Edelsberg JS: Medical progress: Hyperbaric-oxygen therapy. N Engl J Med 334:1642-1648, 1996
21. Hyperbaric oxygen therapy: A committee report. Bethesda, MD, Undersea and Hyperbaric Medical Society, 1992
22. Department of the Navy: U.S. Navy Diving Manual. Washington, DC, Department of the Navy, 1985 (NAVSEA 0994-LP-001-901)
23. United States Air Force: Hyperbaric Chamber Operations, in Air Force pamphlet 161-27, July 5, 1983, pp 79-81