[Todays Wound Clinic]

Ethical Issues in Hyperbaric Medicine

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Define 'Ethics?'

In philosophy, ethical behavior is believed to be good or right. But how can we know what is right? There are fundamental ethical principles that guide clinicians in caring for patients:

1) Nonmaleficence: usually described as, first do no harm. Preventing harm is more important philosophically, morally, and legally than doing good, and in fact, may be the first duty of a healthcare professional.

2) Respect for persons: that is, protecting the autonomy of all people, treating them with courtesy and respect, and allowing informed consent.

3) Beneficence: that is, always acting in the patient's best interest. This is required because patients often cannot act themselves, whether out of ignorance, fear, illness, or vulnerability.

In the past 150 years there has been exponential growth in science and technology. For the most part, this has benefitted patients. However, there are risks to modern medicine. Many therapies remain unproven (hence the drive toward evidence based medicine), marginal technologies still flourish, and patients can have allergic and idiosyncratic reactions to drugs or adverse events from procedures. Patient expectations have never been higher so there is a risk of over-using technology to meet those high expectations. Technology is not a cheap tool—someone must pay for it. Although hyperbaric oxygen therapy (HBOT) is a relatively expensive intervention, it is not difficult to demonstrate its cost benefit in certain conditions when life and limb are at stake. However, as with any technology, analysis of cost benefit can be difficult and involve painful choices. For example, a metaanalysis of HBOT in the treatment of multiple sclerosis estimated that, assuming HBOT provided any benefit at all, 42 patients would need treatment to produce one improvement in disability score. Assuming HBOT were charged at approximately the usual Medicare rate, this would equate to a cost of $856,800 per patient improved. From the 95% confidence interval of the data, the true cost per patient would fall between $216,000 and infinity, without assurance of any benefit. (For further information, see the UHMS Position Paper, https://www.uhms.org/portals/0/pdf/Treatment_of_Multiple_Sclerosis.pdf.) Even if HBOT were demonstrated to provide some incremental benefit in conditions such as chronic stroke, how does an overburdened healthcare system make a decision regarding its cost benefit if the numbers in that condition are similar?

Ethical Issues in Hyperbaric Medicine

HBOT is the primary medical treatment for decompression sickness, arterial gas embolism, and serious carbon monoxide poisoning. It is also an adjunct treatment for chronic refractory osteomyelitis, clostridial myonecrosis (gas gangrene), crush injury, and other acute traumatic ischemias, selected wounds, severe anemia, necrotizing soft tissue infections, radiation tissue damage, compromised skin grafts and flaps, thermal burns, and some types of intracranial abscesses. These conditions comprise the 13 approved indications that the Food and Drug Administration (FDA) recognizes. The FDA calls all other indications off-label. HBOT has been reported for use in more than 130 other clinical conditions and the list increases almost weekly (HOC Hyperbaric Care & Wellness Centers, 2006, available at https://www.hochealth.com/services HBOT.htm). Hyperbaric chambers not only appear in hospitals and freestanding facilities, but also in private homes. Some parents have even installed chambers in homes or garages—reportedly treating their own children and others. Literally thousands of web sites are devoted to the use of HBOT for these indications. However, is it ethical for a physician to use HBOT for any clinical condition in which the benefit is unproven?

Oxygen is not made by a pharmaceutical company. Consequently, funding for large clinical trials is limited and research in all areas of hyperbaric medicine has been slow. Until appropriate studies have been performed, physicians need guidelines on how to respond to patients requesting the use of HBOT for an off-label indication.

The Call for an Ethics Review

In the fall of 1998, the Undersea and Hyperbaric Medical Society (UHMS) invited the major nonprofit professional organizations in hyperbaric medicine to designate representatives to work with professional ethicists (Drs. Evelyn Chan and Baruch Brody) and contribute to a grant fund administered by the Office of Special Projects and Development at the University of Texas Houston Health Science Center. The purpose of the grant fund was to reimburse the authors for their time. A Working Group on Ethics in Hyperbaric Medicine was created which this author chaired. After reviewing the published literature on currently accepted indications for HBOT, the FDA regulations regarding the advertising of hyperbaric chambers, and the extensive information available on the Internet recommendations were created for off-label use of HBOT.

The Key Question: Is it ethical to use HBOT for an indication for which its benefit is unproven?

This question is not unique to HBOT; it is common for physicians to use other drugs and therapies on an off-label basis, but there is clearly some dividing line that prohibits physicians from prescribing HBOT for every conceivable unproven indication. Deciding where to draw the line for a particular case will depend on the combination of a physician's individual clinical judgment, an evaluation of the available scientific data, and patient-informed consent.

First, a physician and patient considering an off-label indication must weigh the type and level of scientific data as it is available. This means the physician must understand the physiological rationale of HBOT and whether the mechanism of action might apply to the condition in question. Are there any data (even animal studies) which might be applicable? The Undersea and Hyperbaric Medical Society (UHMS) is an international organization that produces the journal, "Undersea and Hyperbaric Medicine," and produces an evidence-based review of the literature available for sale (The Hyperbaric Oxygen Therapy Committee Report). A highly useful link to a Cochrane review of hyperbaric oxygen data can be found at www.hboevidence.com. The Agency for Healthcare Research and Quality (AHRQ) provides a document entitled, "Hyperbaric Oxygen Therapy for Brain Injury, Cerebral Palsy, and Stroke," free of charge at: www.ahrq.gov/clinic/epcsums/hypoxsum.htm. Then the clinician must help the patient assess the potential benefits in light of the known risks of HBOT for that particular patient. This requires the clinician to be trained and experienced in hyperbaric medicine. The patient and the clinician then may make a determination through the process of informed consent.

For example, in perusing the Internet, this author found the anecdotal report of an elderly man recounting his experience with HBOT which was provided to treat his failing memory. He mentioned that he had advanced emphysema. Did anyone discuss with him the risk of pneumothorax and potentially fatal arterial gas embolism when he decided to undergo HBOT for the unproven (and unsubstantiated) indication of decreased memory? The risk-benefit assessment of using HBOT for failing memory in a man with emphysema is quite different than it would be for an otherwise healthy patient who wishes to undergo HBOT for a complex migraine, an indication for which encouraging (albeit limited) data do exist.

By applying general ethical guidelines to the field of hyperbaric medicine, it is possible to offer HBOT on a case-by-case basis for an unproven indication, assuming the above analysis has been performed and consent has been obtained.

What Are the Components of Informed Consent?

Physicians have a duty to disclose the risks and benefits of HBOT treatment, regardless of whether the indication is approved or off-label, so that patients can make an informed decision about whether to undergo treatment. To be legitimate, informed consent can be obtained in oral or written form, but documentation of the key elements of informed

consent and confirmation that it took place must appear in the medical record. A physician should discuss six main issues with a patient considering off-label HBOT as part of informed consent:

1) Are there alternative medical treatments that are cost-efficient and successful for the proposed indication?

2) What is the level and type of scientific data supporting the potentially therapeutic use of HBOT?

3) Are the risks of HBOT acceptable and relative to the potential benefit? (The physician should also review the ability of the facility to handle complications arising from HBOT or the primary disease, the risks and side effects of HBOT in general, and more specifically in light of a patient's co-morbid condition.)

4) Does the patient understand that they will be responsible for the cost of a therapy, where no benefits are guaranteed?

5) Is there a research protocol or registry available? If a registry exists for an indication the physician could offer the patient the opportunity to participate in it. Separate informed consent for registry participation would be required.

6) Informed consent should include physician disclosure of any financial issues that might affect the physician-patient relationship.

Physicians have the potential to receive immediate financial benefit to their facilities or themselves when they administer HBOT for an off-label indication. This is particularly true if patients are going to pay in cash and might be desperate, so clinicians are obligated to disclose any financial conflict of interest. The expense of administering the therapy should be reasonable. In the US, it is not unusual for patients to pay for unproven treatments that conform to ethical standards. Patients can even pay to participate in research trials if they are informed of their financial obligations, and accept the fact that they are research subjects.

What Is Research?

As detailed in the Chan & Brody's article, when physicians repeatedly using HBOT on an off-label basis for a particular indication collect information about it in a systematic fashion with the intent to apply the principles of treatment to other patients, they move from practicing medicine to performing research.1 Research requires review by an Institutional Review Board (IRB), and that patients are informed they are research subjects.

Hearing What We Want to Hear

The presence of unsubstantiated information on the Internet produces an extraordinary opportunity to view the interpretation of research through the eyes of the public. A randomized, controlled trial of HBOT in the treatment of cerebral palsy (CP) published by a Canadian group in 2002 showed no difference between the HBOT group and the group treated with air under pressure. Both groups of children improved somewhat during the study period, presumably due to the physical therapy that the interventions offered. From a scientific standpoint, since there was no difference between the groups, the trial failed to support the benefit of HBOT in CP.2 However, the interpretation of these data on the Internet is that oxygen works.

The experimental group breathed 100% oxygen in a hyperbaric chamber at a pressure equivalent to 1.75 times sea level. Meanwhile, the control patients breathed air at a pressure equal to 1.3 times sea level: 1.3 ATA x 760 mmHg = 988mmHg total atmospheric pressure, multiplied by the percentage of oxygen in the air (0.21 = 207 mmHg). If this value is divided by 760 mmHg, the result is 0.27 or ~ 27%. In other words, despite the fact that they were inside a hyperbaric chamber, the partial pressure of oxygen that the control subjects were breathing was identical to what would be achieved if they were breathing 27% oxygen at sea level (a concentration which could be achieved using a nasal cannula). What matters is not how it is provided, but the partial pressure of the gas that is breathed. So, if oxygen works, at such a low concentration for CP, a chamber is not necessary at all. Numerous web sites also advertise inflatable chambers, which provide only nominal

elevation of atmospheric pressure. These were originally designed for the treatment of altitude sickness but are being marketed for a long list of off-label indications. If compressed with AIR rather than oxygen, they achieve lower oxygen partial pressures than breathing 100% oxygen at sea level but at much greater cost. Because patients may not be able to understand the physics involved, they may be persuaded by the space age appearance of the chamber.

Mr. Workman has already addressed in this issue the topic of the FDA and the Federal Food, Drug, and Cosmetic (FDC) Act, which regulates the promotion of hyperbaric chambers. Physicians should know that their medical license could be revoked for producing off-label advertising, and hospital-based facilities could suffer severe penalties.

Another issue is that of expert supervision at hyperbaric facilities. Physicians in the US who operate facilities or supervise patients undergoing hyperbaric treatments must be licensed and are accountable to their state licensing board. State boards are sensitive to physician activities involving unproven therapies and interventions that might be considered experimental. Many freestanding facilities have no physician involvement, thus removing a powerful type of oversight from program operation. At hospital based facilities, physicians who bill traditional indications under Medicare are expected to be physically present for the duration of the hyperbaric treatment. Maintaining compliance with Federal Laws is part of ethical conduct.

In Summary

As hospital profit margins narrow, clinicians will come under increasing pressure to pursue new avenues of revenue. Off-label use of HBOT could be appropriate on a case by case basis, depending on the medical condition in question, the unique patient circumstances, the available scientific data, the medical alternatives, the risk/benefit ratio, and the cost/benefit ratio. Assessing all of these factors can be time consuming and requires the clinician be guided by the principles of nonmaleficence, respect for persons and beneficence. Physicians must remain in compliance with the law, whether with regard to hyperbaric safety, medical billing or promotion and advertising. Beyond that, the obligation of the clinician to the patient is not merely to do what is legal, but what is right from the standpoint of universal justice.

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