

Neurosurgical forum

Letters to the editor

Hyperbaric Oxygen for Brain Injury

To THE EDITOR: We were pleased to see the article by Rockswold, *et al.* (Rockswold GL, Ford SE, Anderson DC, et al: Results of a prospective randomized trial for treatment of severely brain-injured patients with hyperbaric oxygen. *J Neurosurg* 76:929-934, June, 1992), in which they used hyperbaric oxygen (HBO) for acute treatment of severely brain-injured individuals. This is an important study which adds in a positive way to the significant body of literature amassing that confirms the usefulness of HBO in treating closed head injury, including patients in a vegetative state.²⁻⁴ The authors found that survival was markedly improved by HBO treatment; however, the therapy "did not increase the number of patients in the favorable outcome categories." Although similar to the survival results of Holbach, *et al.*,¹ the outcome in Rockswold, *et al.*'s study did not reach the same extent of favorable results. We would have hoped that the authors might have recalculated their data omitting from the hyperbaric group those individuals who were moribund or who died, since they either never received HBO or did not receive a fair trial of HBO therapy. We suspect that, had they not included these individuals, their survival percentage would have been markedly increased and would probably more closely approximate those obtained by Holbach, *et al.*

Rockswold, *et al.*, used a protocol that included the appropriate pressure, duration of each exposure, and frequency of exposure; however, they unfortunately used only an average of 21 treatments per patient. That number of treatments may be insufficient to favorably affect the outcome of such severely ill patients. In treating major brain injury, including coma, anywhere from 80 to 200 treatments may be required to effect favorable outcomes.⁴⁻⁶ This conclusion is based on our work in which we used a more intensive strategy than that employed by Rockswold, *et al.*

We would like to suggest an extended approach to treating acute and long-standing brain injury with HBO that could enhance the strategies used by Rockswold, *et al.*, and which should improve the number of favorable outcomes. This technique has been shown to be successful in treating traumatic brain injury as well as in treating stroke and toxic and anoxic encephalopathies by recovering the viable, metabolically lethargic, electrically nonfunctioning idling neurons in the ischemic penumbra.⁷ Furthermore, this technique not only helps to determine the extent of brain injury, it also helps to ascertain the presence and extent of potentially recoverable cerebral neurons, as well as to decide

the endpoint of treatment. The degree of success in outcome is dependent not only upon duration, location, and extent of irreversible injury, but also upon the volume of the surrounding zones of potentially recoverable neurons. (We consider the combined intensive use of hyperbaric and physical/vocational rehabilitation therapy to be mandatory for effectiveness.)

This intensive approach^{5,6} originally involved single-photon emission computerized tomography (SPECT) interventional brain imaging using

IMP as the tracer. The initial scan was followed by delayed imaging immediately after a 1-hour, 1.5-atmospheres absolute (atm abs) HBO intervention. Both scans were made within 4 hours of the single injection of the tracer. Unfortunately, as of April, 1991, IMP is no longer commercially available: it has been replaced with radioactive ^{99m}Tc in a hexamethylpropyleneamine oxime (HMPAO) complex. With HMPAO, the delayed scan is performed in one of two ways. The first involved using a half-dose and imaging the brain, exposing the patient for 60 to 90 minutes to 1.5 atm abs of oxygen, after which the patient is reinjected with the other half-dose and the brain is immediately re-imaged. Alternatively, the second scan (using full-dose HMPAO) may be done at a later time, 24 to 48 hours after the initial scan (using full-dose HMPAO) and immediately following a single HBO exposure. Irrespective of which method one selects for the delayed post-HBO imaging, it is the difference between the two scans that helps to determine whether there is potential recoverable brain tissue present. The presence of greater tracer uptake following HBO treatment indicating perfusion/metabolism enhancement is suggestive of oxygen-induced reactivation of idling neuron metabolism and thus suggests potentially recoverable brain tissue. Further, the difference between SPECT imaging and magnetic resonance imaging also helps to determine the volume of injury, with the SPECT demonstrating the larger volume of injury. Thus, the difference of volume in the injury may reflect the ischemic penumbra.

When possible, our procedures include detailed neurological and psychometric tests obtained as baseline data prior to institution of therapy. Continuous HBO therapy (1.5 atm abs oxygen, 60 to 90 minutes once or twice daily for at least 5 days/wk) is then instituted, along with appropriate physical or vocational rehabilitation therapy. After 40 treatments, the patients should be rescanned and retested to determine the extent of progress, if any. Therapy is reinstated until either there is no further improvement or the scans are stabilized or normalized. If a plateau in improvement is reached

and the scans have not normalized, then the pressure may be increased slightly to 1.75 atm abs. This cycle of 40 treatments (raising the pressure if necessary) and testing should be continued until no further improvements are obtained on scans and performance. Many patients will require up to 200 HBO exposures.

The authors' fear of oxygen toxicity is unwarranted since the oxygen pressure-duration relationships used clinically are below the threshold for central nervous system toxicity even in the injured brain. Also, oxygen at these pressures may be acting as a scavenger of free radicals. Oxygen is, perhaps, the safest drug available when established guidelines (time and pressure) are followed. The nationwide incidence of convulsions is about one in every 5000 exposures. Convulsions are controlled by changing the gas from oxygen to air and by administering supplemental vitamins E and C to compliant patients. In managing dozens of brain-injured patients, we have never seen exacerbation of the pathological processes resulting from HBO treatment.

Based on our experience, we believe that the above intensive approach, when instituted in treating acute or long-standing brain injury, will markedly improve the number of favorable outcomes.

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RESPONSE: We appreciate the comments of Drs. Neubauer and Gottlieb regarding our clinical trial using hyperbaric oxygen (HBO) for treating acute severely brain-injured patients. In conducting a prospective clinical trial, one must carefully define the patient population to be treated as well as the treatment protocol to be administered. In our population of patients, in whom there is an expected mortality rate of 30% to 40%, it would be inappropriate to remove retrospectively the patients who died or those who were partic-

ularly severely injured in an attempt to make the results look improved. We agree that this study probably did not use the optimum dosing schedule for HBO treatment in severe head injury. We would disagree that more oxygen treatment is necessarily better for this group of patients. A careful review of the 99 patients treated by Holbach, *et al.*,¹ reveals that these patients received *one to seven* treatments of HBO.

At present, we are using a rat model of head injury to establish the optimum dosing schedule of HBO treatments. Our preliminary findings indicate that pre-oxidation (measured biochemically) is consistently higher in injured brains treated by HBO. We believe that oxygen toxicity in the acutely injured brain is a significant concern.

We have no experience in treating the chronically injured brain with HBO. The use of single-photon emission computerized tomography brain imaging with a tracer and HBO to define areas of reversible injury is intriguing. However, we would point out that brain-injured patients tend to improve over time, and it is essential to have controls to establish the efficacy of any treatment modality used. Since HBO therapy is labor-intensive and expensive, the approach discussed by Drs. Neubauer and Gottlieb should be more thoroughly investigated before it is accepted as standard treatment.

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