Neurosurgical forum
Letters to the editor

Hypoxia and Traumatic Brain Injury

To The Editor: We read with interest the paper by Toli-
as, et al. (Tolias CM, Rurent M, Seiler R, et al: Normobar-

Abstract

Object. The effect of normobaric hyperoxia (fraction of inspired O2 [FiO2] concentration 100%) in the treatment of patients with traumatic brain injury (TBI) remains controversial. The aim of this study was to investigate the effects of normobaric hyperoxia on five cerebral metabolic indices, which have putative prognostic significance following TBI in humans.

Methods. At two independent neurointensive care units, the authors performed a prospective study of 52 patients with severe TBI who were treated for 24 hours with 100% FiO2, starting within 6 hours of admission. Data for these patients were compared with data for a cohort of 112 patients who were treated in the past; patients in the historical control group matched the patients in our study according to their Glasgow Coma Scale scores after resuscitation and their intracranial pressure within the first 8 hours after admission. Patients were monitored with the aid of intracerebral microdialysis and tissue O2 probes.

Normobaric hyperoxia treatment resulted in a significant improvement in biochemical markers in the brain compared with the baseline measures for patients treated in our study (patients acting as their own controls) and also compared with findings from the historical control group. In the dialysate the glucose levels increased (369.02 ± 20.1 μmol/L in the control group and 466.9 ± 20.39 μmol/L in the 100% O2 group; p = 0.001), whereas the glutamate and lactate levels significantly decreased (p < 0.005). There were also reductions in the lactate/glucose and lactate/pyruvate ratios. Intracranial pressure in the treatment group was reduced significantly both during and after hyperoxia treatment compared with the control groups (15.03 ± 0.8 mm Hg in the control group and 12.13 ± 0.75 mm Hg in the 100% O2 group; p < 0.005) with no changes in cerebral perfusion pressure. Outcomes of the patients in the treatment group improved.

Conclusions. The results of the study support the hypothesis that normobaric hyperoxia in patients with severe TBI improves the indices of brain oxidative metabolism. Based on these data further mechanistic studies and a prospective randomized controlled trial are warranted.

This is a major contribution to the growing body of evidence that supernormal amounts of O2 delivered early to the patient with severe brain injury has the potential for improving metabolic derangement and potentially clinical outcome.

There are, however, a number of issues that need to be raised in response. First, there is no mention in the article of monitoring potential O2 toxicity, particularly to the lungs. This has been a consistent question posed by both editorial boards as well as grant review committees regarding hyperbaric O2 administration to patients with TBI. Such valid concerns raised regarding possible O2 toxicity apply equally to protocols in which FiO2 is used. The concept of the unit pulmonary toxic dose (UPTD) allows a comparison of cumulative pulmonary effects for various exposures to O2.

It is important to keep in mind, as proposed clinical trials go forward, that a 60-minute exposure to 1.5 ATA hyperbaric O2 only produces 106.8 UPTD. We have demonstrated improvement in cerebral metabolism and intracranial pressure lasting at least 6 hours after the completion of hyperbaric O2 treatment for severe TBI. Hyperbaric O2 therapy repeated every 8 hours would generate 320 UPTD per 24 hours. This protocol could be continued indefinitely without excessive O2 exposure. Although cerebral ischemia is most prevalent in the first 24 hours, it is by no means limited to this time frame, especially in areas of contusion and mass lesions. Being able to continue O2 treatment beyond 24 hours may prove to be important.

The authors further state that the feasibility of hyperbaric O2 as a treatment option “remains limited because human chambers are large, expensive, and available only at a few large medical centers.” This is certainly true of multiplace chambers; however, in our first study of hyperbaric O2 and severe brain injury we delivered over 1600 treatments to patients with severe TBI in a monoplace chamber. Monoplace chambers are relatively inexpensive, can be installed in or adjacent to intensive care units, and only the patient experiences exposure to the pressure and O2.

We are currently conducting a National Institutes of Health–supported study in which hyperbaric O2 and enhanced FiO2 are compared in terms of relative effectiveness in improving cerebral metabolism and reducing intracranial pressure while also carefully monitoring relative pulmonary and cerebral toxicity. These two forms of O2 delivery may not prove to be mutually exclusive but synergistic.

Finally, we would like to congratulate the authors on a significant contribution to this important subject.

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References


J. Neurosurg. / Volume 104 / January, 2006
RESPONSE: We are grateful for the opportunity to respond to the letter from our research colleague, Dr. Gaylan Rockswold, and the rest of the hyperbaric O2 team at Hennepin County Medical Center. We thank Dr. Rockswold and colleagues for their laudatory comments regarding our study.

First, a general comment. All of us in the head injury research community are grateful to the Rockswold group for their ground-breaking work, which showed that hyperbaric O2 therapy improved not only outcome,6 but also cerebral metabolism and intracranial pressure in severely brain injured patients.7 We certainly agree that hyperbaric O2 is the “Cadillac” in the field of enhancing brain tissue oxygenation.

The fact remains, however, that unfortunately, in spite of Dr. Rockswold’s excellent publications, there has been little use of the hyperbaric O2 technique in the field of acute head injury research. This is largely because it remains a formidable undertaking to place patients in a hyperbaric chamber, either monoplace or multiplace, and because relatively few Level I trauma centers have this modality available near the neurological intensive care unit. This was a major reason why our group chose to evaluate normobaric hyperoxia as a simpler “poor man’s alternative” to enhancing brain tissue O2 tension.

The major point, which Dr. Rockswold makes in his letter, is that normobaric hyperoxia lasting 24 hours is likely to be more toxic, particularly to the lungs, than a short 60-minute exposure to hyperbaric O2 at 1.5 ATA. The greatest concern for such toxicity regards O2 pulmonary damage.

Although the calculation of the UPTD of O2 raises significant concern for pulmonary damage while administering 100% FiO2, we must realize that the UPTD data are weighted toward hyperbaric O2 administration and uses indices of vital capacity and symptoms. Certainly in normobaric hyperoxia, changes in vital capacity may be caused by resorptive atelectasis,8 are expected to be reversible, and are abated by positive pressure ventilation.9 The issue of pathological damage in this situation remains controversial. In a study of prolonged normobaric hyperoxia involving patients with irreversible brain damage, shunt fraction and PaO2 were adversely affected but no pathological pulmonary damage was noted at autopsy despite a mean of 52 hours on 100% FiO2.10 The authors attributed the decline in pulmonary indices to resorptive atelectasis. Additionally, the full recovery to normal pulmonary function testing in moderate hyperbaric exposure has been shown, with a return to normal indices within 5 hours of exposure to 100% FiO2 at 2.5 ATA.2

Figure 1 shows the different levels of brain O2 tissue tension in the rat following fluid percussion injury. It is seen that the magnitude of increase in tissue O2 tension with hyperbaric O2 is approximately four times higher than that with 100% O2 at normobaria.4

Figure 2 shows pulmonary O2 tolerance curves in healthy men, with different partial pressures of inspired O2 over different durations. Note that the curves show a 4% decrease in pulmonary vital capacity, and that these changes are reversible on cessation of O2 breathing. Note also that the...