Hyperbaric oxygen therapy and neurologic disease: The time has come

In academic medicine today, there is widespread opinion that investigational funding, especially through the National Institutes of Health (NIH), is harder to obtain than ever before in history. This is particularly true in basic and translational research, where a direct cost benefit to a commercial enterprise is tenuous, at best.

At a time when unemployment is in the double digits, housing prices are stagnant and the cost of health insurance is the most contentious national policy issue in memory, it becomes conceptually difficult to justify government expenditure to examine NMDA receptor subtypes in neonatal piglets. In this era, even well-designed and highly scored research proposals simply go unfunded.

Ultimately the question facing fiscal decision-makers is: “What is the best investment of the very limited funds available?” Or, to put it another way: “How do public funds do the greatest potential good for the greatest number of people?”

For an example, consider the challenges of hyperbaric oxygen therapy (HBO₂) and autism. Autism is a complex neurologic developmental disorder, characterized by varying difficulties in social interaction, limitations in speech and communication and impaired ability to function in society. The Centers for Disease Control estimates the incidence of autism at 1 in 166, making it more prevalent than all cancers, combined (1). The cost of this condition, in terms of supportive care, lost productivity and the secondary impact on caregivers and families is staggering. Simply the direct cost of treatment is estimated at $35 billion per year (2). When this is considered in terms of overall societal impact, it becomes not only a health policy issue, but also a national security issue. It should be remembered that these autistic children grow into adults, who require even greater levels of support.

Although American popular media is overly enamored of hyperbole, it is not an understatement to call this a crisis. Unfortunately, research regarding the mechanisms and pathophysiology of autism remains elusive. Being a largely clinical diagnosis of humans, the traditional mainstays of animal models, biomarkers and imaging studies are lacking, and it is difficult to engage in lower-cost, higher-yield investigation. We are then forced to look at demographic and epidemiologic data and make inferences from the limited animal studies available.

Given the spectrum of clinical presentation, it is likely that what we call autism is a group of conditions sharing a common phenotype and having differing etiologies. It is not unreasonable to speculate that some percentage of autism is a result of environmental exposure to as-yet undefined agents. Although the role of mercury in vaccines continues to be debated, one area that has, thus far, escaped close scrutiny is volatile anesthetics.

Sevoflurane is one of the newer volatile anesthetics, also commonly called an anesthetic gas. It is a halogenated hydrocarbon used for the induction and maintenance of general anesthesia. First introduced in 1990, its ease of use and overall safety, compared to other anesthetics available at the time, resulted in its rapidly becoming the most widely used drug in pediatric anesthesia and surgery. Today, sevoflurane enjoys the largest market share of all volatile anesthetics in the United States (3).

There are some troubling issues, however, that have recently come to light. Sevoflurane is associated with seizure activity in both animals and humans, and there is increasing evidence in the literature that exposure of the developing brain to sevoflurane may result in long-term neurobehavioral disorders and learning disabilities (4,5).
Again, much of this is animal data and difficult to apply in humans, but there is widespread concern among clinicians that, while a safe and easily used drug in acute settings, sevoflurane may have long-term unrecognized consequences. There is very limited evidence to suggest that, even brief exposures to sevoflurane, in otherwise healthy adults, may be neurotoxic (6).

Is it a coincidence that the incidence of autism in the United States started to increase in 1992 and has continued to increase without explanation, correlating with the increasing use of sevoflurane in anesthesia? Definitive studies are yet to be done, and they will be complex, costly and time-consuming. It is possible that all this is just correlation and coincidence rather than cause and effect, but it is also possible that sevoflurane may be the thalidomide of the new millennium.

Patients and their caregivers, on the contrary, have little time or inclination to wait for the complex and time-consuming studies. In many instances, parents seek any therapy, regardless of its validation, in an effort to help their children. The very nature of autism makes it difficult to sort treatment effect from placebo, and behavioral milestones become subjective and individualized.

Currently we are trying to establish a database of centers in the U.S. utilizing hyperbaric oxygen as part of a treatment regimen for autism. It is our initial impression that the number of patients undergoing this treatment is very large, even constituting the mainstay of some facilities. The work by Rossignol, et al. (7) is among the first to attempt a proper prospective, randomized and blinded study of hyperbaric oxygen therapy and autism, but a lot more needs to be done.

The widespread "off-label" use of HBO₂ for neurologic indications is, in essence, a public health issue, as a substantial number of patients are undergoing therapies that have not been validated using traditional scientific methods. When this is considered, it is likely that the NIH will fund studies to validate a widely used but unproven treatment. Should these studies demonstrate a beneficial result, as we speculate they will, then the impact of this scientific rigor will likely lead to recognition of these conditions as approved indications for HBO₂ that will, in turn, be covered by Medicare, Medicaid and other third-party payers.

As part of this evidence-building, Undersea and Hyperbaric Medicine is calling for papers addressing HBO₂ and neurologic disease for a special Spring 2011 issue. We are particularly interested in well-designed work of high rigor addressing off-label areas such as autism, cerebral palsy, concussion, post-traumatic stress disorder and stroke, to name but a few. Papers will undergo our usual peer review, and we endeavor to expedite turn-around time as quickly as possible. We feel that there is now a critical mass of HBO₂ being conducted for neurologic indications and that, by critically reviewing and publishing scientific papers addressing its use, we may be moving closer to this becoming a proven and accepted therapy that may quite possibly change the natural history of some of the most devastating and challenging conditions afflicting our patients.

George Mychaskiw II, DO, FAAP, FACOP
Philadelphia, Pennsylvania
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REFERENCES:


