# The Effectiveness of Intermittent Hyperbaric Oxygen in Relieving Drug-Induced HIV-Associated Neuropathy

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This 3-month study evaluated the effects of hyperbaric oxygen on drug-induced neuropathies in 22 patients with human immunodeficiency virus. All patients included in the study had been taking an antiretroviral medication for at least 12 months and had subjective symptoms of numbness or tingling, lethargy, and a decrease in deep tendon reflex. Patients with an active substance abuse history or Kaposi's sarcoma were excluded. Of the 20 patients who completed the series, 17 had significant improvement, 2 had a demyelinating disorder that may have affected the outcome, and 1 had no change. (*J Natl Med Assoc.* 1998;90:355-358.)

**Key words:** human immunodeficiency virus ◆ substance abuse ◆ hyperbaric oxygen

Hyperbaric oxygen therapy is a treatment in which a patient breathes 100% oxygen continually or intermittently while the pressure of the treatment chamber is increased to a point higher than sea level pressure (ie, >1 atmosphere absolute). It can be viewed as a new application of an old established technology. Treatment can be carried out in either a monoplace or multiplace chamber. The former accommodates a single patient; the entire chamber is pressurized with 100% oxygen, which the patient breathes directly.

At the 1992 International Conference on Acquired Immunodeficiency Syndrome (AIDS), Riello and Myers[1] from the University of Maryland described their success using hyperbaric oxygen in patients with human immunodeficiency virus (HIV). Sixteen patients with CD4 counts of ≤300 were enrolled as a control group and 11 patients were placed in hyperbaric chambers, but these received only surface air (ie, 20% oxygen). All were treated for the same period of time in the chamber, with the control group breathing pressurized surface air versus the hyperbaric patients breathing 100% oxygen. The authors concluded that hyperbaric oxygen therapy may be effective in relieving HIV-related fatigue and improving the quality of life in patients with HIV/AIDS by inhibiting the production of cytokines, such as tumor necrosis factor.

Theoretically, hyperbaric oxygen may act to slow the uncontrolled activation of mononuclear cells that lead to the overproduction of cytokines, such as tumor necrosis factor-alpha, interleukin-2 and interleukin-6, granulocyte colony-stimulating factor, interferon-gamma, and other activation markers.[2] The consequences of overproduction of cytokines could have an adverse effect on the constitutional symptoms of the HIV-infected patient. Tumor necrosis factor, for example, acts on the hypothalamus to induce prostaglandin production and subsequent fever and wasting syndromes (cachexia) associated

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**Table 1. Changes in Patients Receiving Hyperbaric Oxygen Therapy**

| | Initial | 1 Month | 3 Months | 6 Months* |
|---|---|---|---|---|
| Average CD4 count (range) | 119.5 (10-320) | 118 (10-320) | 119.2 (10-290) | 117.7 (10-280) |
| Average Karnofsky score (range) | 58 (40-70) | 78 (40-80) | 82 (60-90) | 82 (60-90) |
| Average self-assessment score† (range) | 4.3 (3-6) | 7.2 (4-8) | 8.1 (5-9) | 8.1 (5-9) |
| No. patients with neuropathy | 22‡ | 3 | 3§ | 3§ |
| Did not complete study | 0 | 1 | 2‡ | 2‡ |

*3 months after study.
†On a scale of 1 to 10.
‡Two patients did not complete the study.
§Two patients had demyelinating disorders; one had no appreciable change.

with AIDS, cancer, and other invasive diseases. A strong negative correlation between tumor necrosis factor, hemoglobin levels, and anemia associated with AIDS also has been reported.[3] Overproduction of tumor necrosis factor also contributes to the hemopoietic failure in hairy cell leukemia and severe aplastic anemia.

Polonis and Anderson[4] noted a 15-fold increase in HIV-1 specific FNA in unstimulated ACH.2 T cells within 24 hours of oxygen deprivation, or anoxia. A 24-hour reoxygenation period resulted in a return to "resting state" levels of HIV-1 RNA, indicating that oxygen tension within the cellular environment modulates HIV-1 expression.

The study described here examined the efficacy of hyperbaric oxygen as a therapy for chronic fatigue and drug-induced neuropathy in patients with HIV.

## METHODS

Twenty-two patients received hyperbaric oxygen 2 hours twice weekly for 3 months. Patients with noticeable neuropathy, numbness, tingling for $\geq$30, and CD4 counts $\leq$300 were included. For the purpose of this study, neuropathy is defined as a loss of sensation in the extremities with concurrent loss in deep tendon reflexes.

All patients had a history of recent treatment with an antinucleoside reverse transcriptase drug, specifically zidovudine, dideoxyinosine, or zidovudine and dideoxycytidine in combination. Patients were divided into three groups: zidovudine monotherapy, dideoxyinosine monotherapy, or zidovudine/dideoxycytidine in combined therapy.

All patients received 2 hours of hyperbaric oxygen at two atmospheres twice weekly. Complete blood cell counts and CD4 counts were obtained three times during the study: prior to starting hyperbaric oxygen therapy, at 1 month, and after the study period ended. Karnofsky scales and patient self-assessments were obtained initially and at monthly intervals thereafter.

## RESULTS

Table 1 compares initial findings with results at 1 and 3 months into the study as well as 3 months after the study. Table 2 compares the success of hyperbaric oxygen in patients with monotherapy versus combination therapy drug-induced neuropathy.

Most patients reported subjective feelings of wellness, improved energy, and loss of neuropathy. In fact, 3 months after the study, 17 still felt better and had no neuropathy, even when taking another antiretroviral agent. However, these subjective changes were not confirmed by electromyography. All of the 17 patients who had loss of neuropath, remained symptom-free 3 months after hyperbaric oxygen therapy had ended.

Two patients did not complete the study. One developed a severe rash due to bacterium and required hospitalization. The other was unable to continue due to the distance from the clinic. The chamber was in a hospital 20 miles away for most participants.

One patient had multiple sclerosis. He did not notice an appreciable change during the study. However, 3 weeks later, his gait and ability to walk were noticeably improved, as was his libido. Another patient had amyotrophic lateral sclerosis (Lou Gehrig's disease) and had no appreciable change in symptoms. A third patient reported no change in symptoms.

## DISCUSSION

Hyperbaric oxygen therapy appears to be of some benefit. The question is whether it deserves to be further defined. Arguments for hyperbaric oxygen therapy include:

- the patient may feel better,
- neuropathy decreases or disappears (this is mostly subjective),
- by instituting hyperbaric oxygen therapy at an earlier stage of neuropathy, the patient may be able to continue the antiretroviral,
- it is painless, and
- a controlled study with patients breathing room air at 1 atmosphere absolute in a hyperbaric chamber would be definitive.

However, there are some strong arguments against the use of hyperbaric oxygen therapy:

- it is expensive and not cost effective,
- two chambers operating 24 hours can provide therapy for a maximum of 30 patients each for every 3 months, and
- hyperbaric oxygen therapy may potentiate underlying Kaposi's sarcoma.

Some individuals have purchased chambers on their own. Such ventures should be done with some medical guidance and in association with a clinic or hospital. These patients should not be adminstering their own therapy in an apartment or isolated room.

Patients with early neuropathy benefit the best. If antiretroviral therapy is going to be used earlier in patients with higher CD4 counts, greater benefits may be realized from using hyperbaric oxygen in healthier patients who exhibit signs of neuropathy. Further study is indicated in this area, especially a controlled study in which a control group would breathe only room air in the hyperbaric chamber.

In this study, all patients who were taking zidovudine/dideoxycytidine in combination showed improvement, except for the two patients who had demyelinating disorders. Both of these patients, one with "Lou Gehrig's disease" and the other with multiple sclerosis, were on combination therapy at the time they were enrolled in this study. Both had been taking zidovudine initially and then were started on dideoxycytidine when it became available.

At the time of the study, no patients who had been on both zidovudine/dideoxycytidine as an initial therapy developed symptoms that could be defined as neuropathy. Two of the patients who had been on zidovudine did not show any response due in part to not completing the study. All 4 patients who had been on dideoxyinosine showed dramatic improvement. Again, this was subjective, in that all of these patients insisted they were feeling better. They looked better and were more energetic, but for those who had an electromyelogram, there was no appreciable difference. Because electromyegraphy is expensive, it was decided not to use this as a measure.

**Table 2. Monotherapy Versus Combination Therapy**

| Drug | No. Taking Drug | No. Showing Improvement |
|---|---|---|
| Zidovudine | 8 | 6 |
| Dideoxyinosine | 4 | 4 |
| Zidovudine and dideoxycytidine | 10 | 8 |

Riello and Myers[1] reported that hyperbaric oxygen therapy alleviated fatigue in 1 month when treatments were scheduled thrice weekly. Their experience also showed that three patients who were unable to work at the onset of the study were able to return to work. The use of hyperbaric oxygen in AIDS patients was first suggested in 1987.[5]

While hyperbaric oxygen is useful in relieving HIV drug-induced neuropathy, its cost effectiveness must be considered. Presently, private chambers charge $250 per hour. This cost may be justified when treating osteomyelitis, the bends, radiation necrosis, and severe anemia, but it can pose a hardship on HIV-positive individuals who are expected to pay (ie, this therapy is not a covered service). Community-based programs charge $87.50, but this removes the project.

No effect was noted on CD4/CD8 cells with this short term of hyperbaric oxygen; polymerase chain reaction levels were not obtained. Whether this has advantages on healthier persons remains to be answered.

## CONCLUSION

The advent of protease inhibitors and newer drugs make combination therapies such as zidovudine/3TC, zidovudine/dideoxycytidine, or other combinations of antinucleoside reverse transcriptase inhibitors with protease inhibitors the standard of care in treating HIV-positive patients. With these

new drugs comes the hope for the first time that these patients are remaining healthier for longer and also living longer. This increases the chance for the development of neuropathies. Further study is needed to document the effectiveness of hyperbaric oxygen in treating drug-induced neuropathies in HIV-positive patients.

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