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A Controlled Study of Hyperbaric Oxygen Treatment in Multiple Sclerosis

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Hart GB, Rowe MJ III, Myers LW, Afifi AA. A controlled study of hyperbaric oxygen treatment in multiple sclerosis. J Hyperbaric Med 1987; 2(1):1–5.—A randomized, double-blind, crossover study to test the response of multiple sclerosis to hyperbaric oxygen (HBO) was performed. The 2-treatment series (6 mo. apart) consisted of a placebo (sham pressurization) and oxygen at 1.5 ATA. Each series consisted of 20 consecutive, 90-min exposures. Detailed clinical and laboratory testing was performed before and after each session of treatments. Eleven subjects, 3 males and 8 females, age 27 to 57 yr were studied. The pretreatment Kurtzke ranking mean was 6.09 ± 1.76 and the ranking 6 mo. after the last session was a mean of 6.55 ± 1.57. No statistically significant differences at the $P < 0.05$ level were noted on any of the clinical or laboratory parameters tested between placebo and treatment sessions.

hyperbaric oxygen, multiple sclerosis, EMG, EEG, Kurtzke disability scale

Introduction

Recurring reports in the 1970s (1–4) using hyperbaric oxygen (HBO) in treating multiple sclerosis have given rise to several controlled studies (5–8). Excepting the first controlled study by Fischer et al. (5), subsequent reports have not supported the claims of significant neurologic improvement.

A preliminary study at this institution was undertaken in 1978 to treat a small number of multiple sclerosis patients. Eight patients with chronic, progressive multiple sclerosis, of at least 2-yr duration and significant neurologic deficit were treated. The protocol for this group required 2-h daily treatments for 3 wk with HBO at 2 ATA. Neurologic exams before and after revealed no objective measurable improvement in their deficit.

The following study was performed in cooperation with the UCLA Multiple Sclerosis Research Center and represents a double-blind, crossover study extending from January 1984 to July 1985. This effort was stimulated by the possibility that HBO at less pressure might be effective as reflected by Fischer et al. (5), where the volunteers' arterial partial pressures of oxygen would indicate an oxygen delivery equivalent to approximately 1.5 ATA O_2.

Method

Volunteer Selection

Volunteers were accepted with the established diagnosis of chronic progressive multiple sclerosis of at least 2-yr duration and who:

1. Were 20 to 60 yr of age.
2. Would abstain from the use of nicotine products during the course of the study.
3. Were free of contraindications to HBO treatment such as:
   - Claustrophobia
   - Epilepsy
   - Angina pectoris
   - Chronic pulmonary emphysema or asthma
   - Congenital spherocytosis
   - Acute viral infections at time of exposures
   - Females in the child-bearing age, not pregnant at the time of exposures
   - Not requiring aspirin or salicylates in case of other concurrent diseases
   - Not on corticosteroids
   - Not experienced aviators or divers.

Randomization and Control

Randomization was achieved using two groups of sealed envelopes, then randomly numbered before acceptance of patients. One group of envelopes was sorted by "card shuffle" technique and the other by a random number generator. Each group was then placed into separate, identical envelopes. The group in the envelope decided by coin toss was used in this study.

This was a double-blind study; neither the clinicians evaluating the neurologic response nor the patients were aware of the treatment received.

The crossover of the treatment, air vs. oxygen, was performed at 6 mo. when the volunteer received the alternate exposure from the previous 6 mo.

Treatment Schedule

All treatments were performed in a monoplace chamber. The HBO schedule was 1.5 ATA, 90 min daily for 20 consecutive d. The air schedule was 1.0 ATA, 90 min daily for 20 consecutive d with a pressure sham. The sham was created by rapid pressurization × 2 min (not to exceed 1.25 ATA air) and allowed to drift back to 1 ATA air. This was repeated at the end of each exposure.

Discontinuance of Protocol

A volunteer was dropped from the study if he/she:

1. Had uncontrollable confinement anxiety
2. Requested discontinuance
3. Was found to have been using nicotine products, salicylates, or corticosteroids

4. Was found to have a condition normally treated with HBO such as osteomyelitis, carbon monoxide, gas gangrene, etc.

Patient Isolation

Each patient was scheduled for clinical exams, electrodiagnostic exams, and exposures in a way that prevented contact with one another. Each was screened before each series of exposures concerning knowledge of any other participants.

Evaluation

Clinical testing. Each patient was evaluated before each exposure by the same blinded neurologist from the UCLA Multiple Sclerosis Research Clinic. The subjects were rated on the UCLA Multiple Sclerosis Clinic Standard Examination form and on the Kurtzke Functional Systems and Disability Status Scale. The neurologic exam was repeated 1 wk after the last series and 6 mo. preceding the next crossover series. The exam was repeated 1 wk after the last treatment and again at 6 mo. for a total of 5 neurologic exams.

Neurodiagnostic testing. Somatosensory and brain stem auditory evoked responses were performed following the standard protocols of the electrodiagnostic laboratory before and after each series and after 6 mo. Responses were ranked as being normal or abnormal by specific criteria for interpeak latencies, amplitudes, and symmetry values. The follow-up studies were ranked as being the same, worse, or better by specific criteria for change in interpeak latency or amplitude values.

Electroencephalographs recorded before and after each series were analyzed by standard protocols for quantitative EEG testing in the electrodiagnostic laboratory. Quantitative frequency spectral analysis data were studied for specific responses to therapy.

Results

Eleven patients (3 males, 8 females, age 27 to 57 yr, mean 43 ± 9, median 47 yr) were studied. The Kurtzke Disability Scale ranking was 3 to 9 (median 6, mean 6.09 ± 1.76). Actual values were 3,3,6,6,6,6,7,7,7,7,9 before treatment protocols. Three patients did not receive a complete EEG series because initial studies revealed no abnormalities and similarly brain stem evoked responses. Four patients were not candidates for a complete study of somatosensory evoked responses due to pain experienced during same or were not suitable for measurement due to involuntary tremors.

Six patients received the placebo first and 5 received oxygen first (Table 1). The ranking of the subjects at the completion of the study was 3,5,6,6,7,7,7,7,7,8,9 (mean 6.55 ± 1.57).

Two patients had a worsening of the Kurtzke Scale by 1 after oxygen, 2 had improvement after oxygen by 1. One patient had improvement following the placebo by 1 and 2 had a worsening by 1.

Table 1: Kurtzke Disability Scale Ranking

Subject by Entry	Initial Series				Crossover				After 6 mo.
	Placebo		Oxygen		Placebo		Oxygen		
	1	2	1	2	3	4	3	4	5
1			7	8	8	8			7
2	7	7					7	8	8
3			7	7	7	6			7
4	7	7					7	7	7
5			6	6	6	6			6
6	3	3					6	5	5
7	6	7					6	6	7
8	6	6					6	6	6
9			3	2	2	3			3
10	9	9					9	9	9
11			6	6	6	6			7

Statistical Analysis

The following tests were used on this limited amount of data: a) paired t test on difference between treatment effect and placebo effect, and b) McNemar test of equality of effectiveness of treatment and placebo.

No significant differences, at the $P < 0.05$ level, were noted between effect of treatment and placebo in any of the clinical or evoked response parameters. No significant differences at the $P < 0.05$ level were found in the EEG recordings before and after treatment in treatment-vs.-placebo testing. All subjects entering the study completed it.

Discussion

The study was terminated because there was recognition of a gradual worsening of the Kurtzke Scale in this small group. This study does not preclude a treatment response that may be achieved in the acute relapsing form of multiple sclerosis or any synergism that might be achieved with other forms of treatment. It does, however, make unlikely a clinically meaningful response (HBO vs. sham) in the population (chronic progressive multiple sclerosis) studied.

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