

HYPERBARIC-OXYGEN TREATMENT OF MULTIPLE SCLEROSIS A

Randomized, Placebo-Controlled, Double-Blind Study

BOGUSLAV H. FISCHER, M.D., MORTON MARKS, M.D., AND THEOBALD REICH, M.D.

Abstract Several uncontrolled studies have suggested a beneficial effect of hyperbaric oxygen on multiple sclerosis. We studied 40 patients with advanced chronic multiple sclerosis who were randomly divided into two matching groups. The experimental group received pure oxygen, and the placebo group received a mixture of 10 per cent oxygen and 90 per cent nitrogen; both groups were treated at a pressure of 2 atmospheres absolute for 90 minutes once daily, for a total of 20 exposures. Objective improvement occurred in 12 of 17 patients treated with hyperbaric oxygen and in 1 of 20 patients treated with placebo ($P < 0.0001$). Improvement was transient in seven of the patients treated with oxygen and long-lasting in five. Those with less severe forms of the disease had a more favorable

and lasting response.

At one year of follow-up, deterioration was noticed in 2 patients (12 per cent) in the oxygen group, neither of whom had had an initial response, and in 11 patients (55 per cent) in the placebo group, one of whom had had a positive initial response ($P < 0.0008$). Minor ear problems and reversible myopia were the only side effects observed.

These preliminary results suggest a positive, though transient, effect of hyperbaric oxygen on advanced multiple sclerosis, warranting further study. This therapy cannot be generally recommended without longer follow-up periods and additional confirmatory experience. (N Engl J Med. 1983;308:181-6.)

THE observation that the immunosuppressive action of hyperbaric oxygen may ameliorate experimental allergic encephalomyelitis¹⁻⁵ has created renewed interest in the use of hyperbaric oxygen in patients with multiple sclerosis. In 1958 Layton and Mackay⁶ suggested that breathing a mixture of 5 per cent carbon dioxide and 95 per cent oxygen at ambient pressure could be used as an adjunctive treatment in acute exacerbations of multiple sclerosis, though they did not report the results of this approach. In 1970 Boschetty and Cernoch⁷ reported a small, transient improvement in 16 of 26 patients treated with hyperbaric oxygen at a pressure of 2 atmospheres absolute (ATA). In 1978 Baixe⁸ reported an improvement in 11 patients treated with hyperbaric oxygen, and one year later, Neubauer^{9,10} reported minimal to dramatic improvement in 91 per cent of 250 patients treated with hyperbaric oxygen at a pressure of 2 ATA. Positive results were reported in 1980 in a detailed study by Formai et al.,¹¹ who used hyperbaric oxygen because of certain clinical similarities between decompression sickness and multiple sclerosis. In the same year, Palotta et al.¹² independently obtained substantial improvement with hyperbaric oxygen in six patients with multiple sclerosis.

These reports had several aspects in common: all studies were performed without controls; with only one exception,¹⁰ none of the studies used an established disability scale as a point of reference; there was a remarkable agreement and uniformity in positive observations, although the studies were performed by unrelated and independent researchers in various medical centers; and there were no harmful effects of hyperbaric oxygen in patients with multiple sclerosis.

Because of the lack of effective therapy for multiple sclerosis and in view of these anecdotal reports, we decided to conduct a placebo-controlled, double-blind, randomized study. Our principal objective was

to determine whether hyperbaric oxygen, as compared with placebo, could have any therapeutic effect on multiple sclerosis.

METHODS

Selection of Patients

All patients in this study had definite multiple sclerosis according to the criteria described by Schumacher et al.,¹³ with a duration of the disease of more than five years and a neurologic deficit in at least one functional system for at least two years. Their scores on the disability-status scale (DSS)¹⁴ did not exceed 6. All patients were encouraged to maintain their customary diets as well as habits of more than two years' duration, especially in relation to coffee, cigarette smoking, and moderate alcohol consumption. Patients who had been taking any given drug for more than six months before the trial continued to take the drug if indicated. No new drugs were permitted. Physical therapy was continued if a patient had been receiving it for more than a year. Patients experiencing an exacerbation of multiple sclerosis or in a stage of early recovery after an exacerbation were excluded from this study. The trial was performed on an outpatient basis. None of the patients treated changed their environment or daily activities during the trial. All patients had general medical clearance including chest films and an ear, nose, and throat examination. Before their consent was obtained, all patients were fully informed of the purpose, design, and possible risks of the study. The fact that there are no proved benefits of oxygen treatment in multiple sclerosis was frankly discussed with them.

With a table of random numbers, 40 patients were assigned to the treatment and control groups. Both groups were closely matched with respect to age, sex, age at onset of the disease, duration and type of disease, and DSS score (Table 1).

The randomization code was known only to the chief chamber operator. A separate, sealed copy of the code was deposited with one of us (F.R.) for emergency use only. Blinding was maintained throughout the study, which lasted for 14 months and was extended for an additional six months before the randomization code was broken.

Treatment

A walk-in hyperbaric chamber in which temperature and humidity were controlled was used. Four patients were simultaneously treated during each treatment course. The oxygen group received 100 per cent oxygen by means of a full face mask (Acme Scottoramic No. 707). The placebo group received a mixture of 10 per cent oxygen and 90 per cent nitrogen through an identical type of face mask. In each treatment course the gas was administered for 90 minutes at a pressure of 2 ATA, once daily for five days per week, totaling 20 exposures. Normal air was used to compress the chamber. The rate of compression did not exceed 50 cm per minute.

From the Departments of Neurology and Rehabilitation Medicine, New York University Medical Center. Address reprint requests to Dr. Fischer at New York University Medical Center, 400 E. 34th St., New York, NY 10016.

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Table 1. General and Clinical Characteristics of the Study Groups.

CHARACTERISTIC	OXYGEN N	PLACEBO O
No. of patients (male/female)	20(9/11)	20(10/10)
Mean age (range)	43.3 (25-62)	44.1 (26-63)
Mean age at onset of multiple sclerosis (range)	32.4 (18-47)	30.9 (18-48)
Mean duration of disease (range)	11.8 (6-27)	12.8 (6-20)
Mean disability score (range)	5.1 (3-6)	4.8 (2-6)
Clinical type (no. of patients)		
Chronic progressive	15	14.6
Chronic stable	5	

Blood gas analysis was performed during the third week of a treatment course. A separate team performed the measurements inside the chamber with use of a modified, pressure-adjusted blood gas analyzer (Radiometer No. 27). The results were recorded and immediately sealed after measurements to ensure effective blinding. No other laboratory tests were performed.

The construction of the chamber made it visually impossible to trace the piping leading from the oxygen and air-storage compartment to the actual oxygen and air outlets inside the chamber. Air and oxygen are indistinguishable to the breather.

Evaluation of Patients

Neurologic examinations were performed by two neurologists, independently, approximately two months before the study and again on the first day of each treatment course. Patients were closely observed on a daily basis during the treatment periods. At the end of the 20th exposure neurologic examinations were repeated by the same observers, who were unaware of the type of treatment. All patients were followed for a year after completion of a treatment course. Observations made during each neurologic examination were scored on the DSS, on a functional-systems scale, and on a fatigability scale,^{14,15} providing the basis for assessment of positive or negative responses. Clinical improvement was reported only if it was objectively demonstrated. Reports of improvement by patients were ignored if not substantiated by objective neurologic evaluation. Improvement was arbitrarily described as mild if reflected only in the functional-systems scale and as marked if reflected by a change of two or more points on the DSS.

The DSS ranges from zero (normal) to 10 (dead); grades 1 to 3 represent mild to moderate disability; a grade of 6 indicates that assistance is required with walking; and a grade of 7 indicates restriction to a wheelchair. The functional-systems scale permits numerical grading of dysfunction in each of the functional systems: pyramidal, cerebellar, brain-stem, sensory, bowel-bladder, visual, and mental. Fatigability was assessed with a scale ranging from 0 (normal) to 4 (fatigability preventing sustained physical function).¹⁵

Table 2. Summary of Responses in the Study Groups at the End of Each Treatment Course.*

RESPONSE	OXYGEN GROUP (N = 17)	PLACEBO GROUP (N = 20)
	no. of patients	
Improvement	12/17 (70%)	1/20 (5%) §
No change	5/17	19/20
Deterioration	0/17	0/20

* Each treatment course consisted of 20 exposures.

§ P < 0.0001.

RESULTS

Three patients, all in the oxygen group, were excluded because of noncompliance (two patients) or logistic difficulties (one). Each of these patients had received five treatments. They were followed for one year. All the patients in the placebo group completed the entire treatment course.

Blood pressure and cardiac rate were monitored at weekly intervals throughout the study. There were no differences between values obtained at entry and at the end of each treatment course.

At the end of each treatment course (consisting of 20 exposures), 12 of the 17 patients in the group treated with oxygen had improved (70 per cent), and 5 had no change. One of the 20 patients in the placebo group had improved (5 per cent), and no changes were observed in the other 19. Improvement, if observed, was usually verifiable after an average of 12 treatments (range, 5 to 16). It most frequently consisted of improved mobility, improved equilibratory coordination, and decreased fatigability. No deterioration was observed in either group (Table 2).

Table 3. Improvement in Central-Nervous-System Function after 20 Treatments.

INDEX PLACEBO GROUP	OXYGEN N		
<i>no. with improvement</i>			
Mobility	10/17	1/20	<0.0005
Equilibratory coordination	10/17	1/20	<0.0005
Fatigability	9/17	1/20	<0.0014
Disappearance of intention tremor	3/8	0/15	<0.031
Disappearance of positive Romberg sign	3/5	0/7	<0.045
Disappearance of nystagmus	8/13	0/10	<0.0026
Bladder control	5/13	1/17	<0.039
Pyramidal system	2/17	1/20	NS*
Sensory system	2/11	1/13	NS
Visual system	3/6	0/4	NS

*NS denotes not significant.

Measurements of the partial pressure of arterial oxygen gave a mean value of 998 mm Hg in the oxygen group, with a range from 850 to 1140 mm Hg, and a mean value of 106 mm Hg in the placebo group, with a range from 96 to 145 mm Hg. There was no clear-cut relation between the partial pressure of arterial oxygen and the clinical response.

Since multiple sclerosis produces diffuse lesions it was necessary to analyze the effect of hyperbaric oxygen treatment according to function (Table 3).

Improvement in the Placebo Group

One patient in the placebo group, who had chronic progressive multiple sclerosis and a DSS score of 6, had noticeable improvement after the second treatment. Restoration of urinary continence, increased mobility, improved equilibratory coordination, and decreased fatigability were all noted. These gains lasted only 10 days after the completion of the treatment

course. However, urinary bladder control was maintained for two months. Another patient (with chronic progressive disease and a DSS score of 3) had two episodes of improvement during treatment, lasting for two and three days, respectively, with reversal to pretreatment status during the last five days of the treatment course. The transient improvement consisted of increased mobility and reduction of intention tremor. The remaining 18 patients had no clinical changes during the entire treatment course.

Improvement in the Oxygen Group

Increased mobility, reduced fatigability, and improved equilibratory coordination were the most frequent gains in the oxygen-treated group. Mild improvement was seen after treatment in seven patients, all with a pretreatment DSS score of 6; six of these patients had the progressive form of multiple sclerosis, and one had the stable form. Marked improvement was observed in five patients, four with a pretreatment DSS score of 3, and one with a score of 5. Five patients had no response during the entire treatment period. Three of them had chronic progressive disease (two with a DSS score of 6 and one with a score of 3), and two had chronic stable disease with a DSS score of 6.

The improvement was of short duration in seven patients, averaging only six weeks (range, 4 to 13), after which time regression to the pretreatment level occurred. Five patients had long-lasting improvement, which was mild in two and marked in three patients.

These results, summarized in Table 4, suggest a more pronounced effect of hyperbaric oxygen in relatively mild cases, and a smaller, less consistent, transient response in advanced cases.

Urinary continence was restored during treatment in three patients who had incontinence before therapy. The improvement was maintained at the end of the one-year follow-up period in two. In one patient the improvement lasted only two months. Urinary frequency, urgency, and hesitancy disappeared in two of nine cases. The improvement lasted for four and six months, respectively. One patient with rare incontinence had no change throughout the treatment period.

Nystagmus disappeared in 8 of 13 patients. One year after the trial it was still absent in six. It recurred in two patients, five and nine months, respectively, after the treatment course. No response was seen in one patient with marked oscillopsia interfering with reading.

Three of six patients had improvements in visual systems. One had a mild reduction in a defect of the lower temporal-quadrant field in the right eye, and another had disappearance of left-upper-quadrant hemianopia. One patient regained the ability to read large printed matter; no quantitative values were ob-

Table 4. Response of 17 Patients to 20 Hyperbaric-Oxygen Treatments, in Relation to Pretreatment Clinical Status and DSS Score.*

TYPE OF RESPONSE	No. RESPONDING	NO. WITH CHRONIC PROGRESSIVE DISEASE RESPONDING	NO. WITH CHRONIC STABLE DISEASE RESPONDING	DSS SCORE (No. OF RESPONDERS)
Mild, short-lasting	5/17	5/5	—	6 (5/5)
Mild, long-lasting	2/17	—	2/2	6 (2/2)
Marked, short-lasting	2/17	1/2	1/2	3 (1/2) 5 (1/2)
Marked, long-lasting	3/17	3/3	—	3 (3/3)

*Five patients had no response (two with chronic progressive disease and a DSS score of 6, one with chronic progressive disease and a DSS score of 3, and two with chronic stable disease and a DSS score of 6).

tained because the patient refused to undergo visual-acuity testing.

Mild spasticity, present in all patients in both groups, improved in two patients in the oxygen group. This mild improvement lasted for four months in one patient and for 12 months in the other.

Follow-up in the Placebo Group

One patient (with chronic stable disease and a DSS score of 3) of the 20 in the placebo group had a spontaneous improvement three days after completion of the treatment course. It consisted of improved equilibrium and almost normal gait endurance, still present one year later. Eleven patients, including the one who improved during the treatment had various degrees of deterioration during the one year of follow-up. Among them, seven patients had mild deterioration, and four became wheelchair-bound, with two totally dependent on human assistance. All had chronic progressive disease with a DSS score of 6. The deterioration, which occurred between six and nine months after the treatment course, consisted chiefly of aggravation of pre-existing deficits, with no new signs discernible.

Follow-up in the Oxygen Group

Two of the five patients who did not respond during the treatment period had deterioration within one year. One of them (who had chronic progressive disease and a DSS score of 6) had increased spasticity and deterioration of gait six months after completion of the treatment. The other (who had chronic progressive disease and a DSS score of 3) was forced to use a cane because of deteriorated equilibrium five months after the treatment. The other three patients who did not respond were clinically unchanged during the entire year of follow-up (two had chronic stable disease and a DSS score of 6, and one had chronic progressive disease and a DSS score of 6). Of the 12 patients who improved during the treatment, seven regressed to pretreatment levels without further deterioration (five had chronic progressive disease and a DSS score of 6, one had chronic stable disease and a DSS score of 5, and one had chronic stable disease and a DSS score of 3). In five patients the improvement lasted throughout the year of follow-up (two with chronic stable disease and a DSS score of 6 and three with chronic progressive disease and a DSS score of 3). To summarize the

above observations, deterioration at one year of follow-up was noticed in two (12 per cent) of the patients in the oxygen group, neither of whom had an initial response during the treatment, and in eleven (55 per cent) of the patients in the placebo group, one of whom had a positive initial response during the treatment ($P < 0.0008$).

None of the patients who were dropped from the study, all in the oxygen group, had any response after five treatments. All five had chronic progressive disease, with DSS scores of 6 (2 patients) or 3 (one patient). At one year of follow-up two patients (both with a DSS score of 6) were unchanged; one patient (DSS score of 3) had deterioration six months after the incomplete trial.

Table 5 shows changes from the initial DSS score that were observed at the end of treatment and over 12 months of follow-up. The differences between the oxygen and placebo groups, though most pronounced at the end of treatment, were still significant one year later.

Side Effects

Minor and transient ear discomfort was encountered in seven patients (four given oxygen and three placebo). It occurred during the compression cycle and was easily managed or prevented by using a very slow compression rate — 50 cm per minute or less if necessary. None of the patients had direct damage to the tympanic membrane.

Transient reversal of the refractive error from hyperopia (present in seven patients in each group) to myopia was observed in six oxygen-treated patients and no placebo-treated patients. This phenomenon preceded clinical improvement by one to two days in five patients. The reversal occurred on average on the 12th day of treatment (range, 8 to 16). It was transient in all cases, with reversion to the pretreatment state in an average of 8 weeks (range, 3 to 16); in three patients, the reversal preceded clinical regression by a few days. Myopic and emmetropic patients in both groups had no changes in refractive status. No changes were observed in the retina and optic disks during the treatment period.

A major impact on periodontal disease was noticed in one patient in the oxygen group. After four treatments the gingival tissue became firm and pink, with total cessation of bleeding. The improvement lasted for two months before there was a reversion to pretreatment status.

No other side effects or adverse reactions were observed during the treatment and follow-up periods.

DISCUSSION

This study indicates an apparent beneficial effect of hyperbaric-oxygen treatment on multiple sclerosis, supporting the results of uncontrolled studies published elsewhere^{7,12} and making a placebo response unlikely. Although the improvement was mild and transient in most of our patients, it appears that the patients with milder forms of multiple sclerosis and a shorter duration of disease derived a more pronounced and longer-lasting benefit after a course of hyperbaric-oxygen treatment. This difference in response was probably due to the extent of damage to the central nervous system, which in advanced cases had accumulated over time, leaving only a small (if any) reversible component amenable to therapy. The results also suggest a possible slowing of the progression of the disease in patients who initially responded to this type of treatment. Our findings are in general agreement with other reports,⁸⁻¹² especially with reference to fatigability, mobility, equilibratory coordination, and urinary bladder control, as well as short duration of the improvement after completion of a treatment course.

The mechanism of the apparent effect of hyperbaric-oxygen treatment on multiple sclerosis is unclear. All patients treated in this study were in the chronic progressive or stable categories, with neurologic deficits of more than two years' duration, making the probability of spontaneous improvement negligible.¹⁶ This could account for the low number of positive responses in the placebo-treated group. The central role of focal edema in the breakdown of myelin has been postulated by Feigin and Budzilovich¹⁷ and by Bauer.¹⁸ These workers suggest the employment of measures directed toward either prevention or reduction of the extent of focal edema in acute episodes of multiple sclerosis. Prineas and Connell¹⁹ have demonstrated slowly progressing myelin breakdown at the edges of old multiple sclerosis plaques, occurring by a unique mechanism of myelin uptake by microglial cells in the form of pinocytosis vermicularis. The continuing slow demyelination in old plaques, also called "edge activity," was progressing with very few or no lymphocytes in the perivascular area. As noted by Poser,²⁰ this finding suggests a different mechanism of myelin breakdown in chronic lesions, since acute lesions are usually characterized by edematous and inflammatory changes. There are no reports indicating the presence of focal edema in the plaques of chronic multiple sclerosis, making it unlikely that hyperbaric oxygen has an anti-edematous action in chronic cases.

The dominant anatomic feature of multiple sclerosis is the relation of plaques to the venous component of

Table 5. Changes from Initial DSS Scores Observed at the End of Treatment and during 12 Months of Follow-up (Means \pm S.D.)

GROUP	AT END OF TREATMENT	AT 2 MONTHS	AT 6 MONTHS	AT 9 MONTHS	AT 12 MONTHS	
Oxygen (n = 17)	-1.00 \pm 1.00	-1.00 \pm 1.00	-0.76 \pm 1.03	-0.65 \pm 1.00	-0.59 \pm 1.06	-0.59 \pm 1.06
Placebo (n = 20)	0.00 \pm 0.00	+0.05 \pm 0.22	+0.00 \pm 0.32	+0.05 \pm 0.39	+0.25 \pm 0.72	+0.35 \pm 0.81
P value	<0.0001	<0.0003	<0.005	<0.009	<0.006	<0.006

the vascular system. The plaques, at least in the early stages, are almost always perivenular, extending as slender sleeves of demyelination.²¹ There is a pronounced physiologic difference between the partial pressure of oxygen in the arteries and veins: the value is 95 mm Hg in the arterial limb and 34 mm Hg in the venous limb of the capillary loop. Thews²² differentiates primary arterial hypoxia from venous hypoxia. The latter, characterized by a normal partial arterial oxygen pressure but a reduced partial venous oxygen pressure, may be caused by a decreased perfusion rate secondary to stasis in injured tissue. It is known that oligodendrocytes are particularly sensitive to hypoxia. If, indeed, the plaques of multiple sclerosis represent areas of persistent focal hypoxia, it can be hypothesized that the administration of hyperbaric oxygen may temporarily relieve it, leading to improved conductivity of the preserved and still-functioning axons. This could explain the short-lasting positive effect of hyperbaric-oxygen treatment in some patients with advanced multiple sclerosis. The delay in clinical response once treatment was started (average, 12 treatments) also suggests that some kind of "repair" (remyelination?) occurred, which could account for the long-lasting and pronounced improvement in patients with relatively mild neurologic deficits.

The immunosuppressive effect of hyperbaric-oxygen treatment is of particular interest. Experimental work in animals has demonstrated suppression of macrophages and reduction of the total number of circulating leukocytes and lymphocytes.^{1,6,5} Hansbrough et al.⁵ found a marginally increased level of endogenous steroids in mice exposed to hyperbaric oxygen. Whether a similar effect occurs in human beings remains to be determined.

The problem of central-nervous-system toxicity was of particular concern. Holbach et al.^{2,3} have studied the oxygen tolerance and oxygenation state of the injured human brain. They found that cerebral glucose metabolism reflecting adequate cerebral oxygenation was optimal at a pressure not exceeding 2 ATA and impaired at a pressure of 2.5 ATA. Increased permeability of cerebral vessels and perivascular edematous zones have been observed in animals exposed to hyperbaric oxygen at a pressure of 2.5 ATA.²⁴ For this reason a working pressure of 2 ATA was selected in our study.

Delivery of oxygen by a face mask does not result in administration of 100 per cent oxygen. Values as low as 60 per cent have been reported.^{25,26} Since normal air is used to compress the chamber, even a minute leak in the sealing area around the face may cause contamination of pure oxygen with ambient air. This explains the scattered values for partial pressure of arterial oxygen in our patients. The problem is limited to walk-in chambers "only, since in monoplace chambers the entire body is bathed by pure oxygen, rendering a face mask unnecessary and eliminating any contamination of administered oxygen.

For this reason caution is indicated whenever one is

comparing results obtained with a monoplace and a multi-place chamber, since the difference in actual partial pressure of arterial oxygen may be substantial at the same pressure when used in both types of chambers. The partial pressure of 1433 mm Hg is the calculated theoretical maximum obtainable at a pressure of 2 ATA when breathing pure oxygen (1520 mm Hg — 47 mm Hg water vapor — 40 mm Hg partial pressure of carbon dioxide). In practice, however, the actual partial pressure of arterial oxygen will always be somewhat lower than the calculated one, because of prevention of complete equilibrium by the alveolar blood barrier; shunting via bronchial, thebesian, and pleural vessels; physiologic shunting in the lungs; and the occurrence of some atelectasis. The partial pressure of arterial oxygen in our oxygen-treated patients ranged from 850 mm Hg (59.3 per cent of the calculated maximum, equivalent to a pressure of 1.11 ATA) to 1140 mm Hg (79.9 per cent of the calculated maximum, equivalent to a pressure of 1.59 ATA), with a mean of 998 mm Hg (69.9 per cent of the calculated maximum, equivalent to a pressure of 1.39 ATA). Monitoring of partial pressure of arterial oxygen should be an integral part of any hyperbaric-oxygen therapy. The method currently used necessitates arterial puncture — a procedure not devoid of risks and complications. The recently introduced noninvasive method of transcutaneous measurement of partial pressure of arterial oxygen in hyperbaric-oxygen chambers is promising, offering ease of application, continuous and accurate monitoring, and freedom from adverse reactions.²⁷

Transient myopia is known to occur during hyperbaric-oxygen treatment. It is conceivable that this sign alone could suggest to a "blinded" observer what type of gas was being administered in a placebo-controlled study. In our study no information was available about whether a similar phenomenon could occur in patients exposed to compressed air. It occurred only in oxygen-treated hyperopic patients and was signaled by blurred distance vision or a sudden ability to read without glasses. Serial funduscopic examinations did not reveal any changes. There are two possible mechanisms involved in transient myopia: increased tone of the ciliary muscle causing spasm of accommodation, or metabolic changes affecting the hydration of the lens or possibly the cornea. The timing was conspicuous, since transient myopia preceded neurologic improvement by a few days and disappeared concurrently with a regression to pretreatment neurologic status. Ultrasonographic measurements of the transverse diameter of the lens performed serially during hyperbaric-oxygen treatment may offer some insight into this phenomenon.

CONCLUSIONS

Because of the small sample and the short follow-up period in our study, the results must be viewed with caution and regarded as preliminary. They also await confirmation by other, independent research centers.

Although our results indicate that further consideration should be given to hyperbaric oxygen as a treatment for multiple sclerosis, this therapeutic regimen cannot yet be generally recommended for these patients. More specific information is needed, especially in regard to hyperbaric-oxygen treatment for acute exacerbations and early active cases of multiple sclerosis and the use of hyperbaric oxygen as an intermittent treatment in patients who have responded to the initial treatment course. A long-term follow-up study is also necessary to determine whether hyperbaric oxygen can moderate the progression of the disease.

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