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The efficacy of hyperbaric oxygen therapy in the management of chronic fatigue syndrome

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ABSTRACT

Objective: Chronic fatigue syndrome (CFS) is a chronic disease with social components that ensue secondary to the incapacity of the person to fulfill work, social and family responsibilities. Currently, there is no consensus regarding its treatment. The aim of this study was to determine the efficacy of hyperbaric oxygen (HBO_2) therapy in CFS.

Design: Sixteen patients included in the study were diagnosed with CFS according to the Fukuda criteria. Patients received 15 treatment sessions of HBO_2 therapy over a period of three consecutive weeks (five days per week). The outcome measures (visual analog fatigue scale (VAFS). Fatigue Severity Scale (FSS) and Fatigue Quality of Life Score (FQLS) were assessed before the treatment and after completion of the 15 sessions.

Results: HBO_2 therapy was well tolerated, with no complications. After treatment, patients' scores were found to have improved with respect to VAFS, FSS and FQLS (all $p<0.005$).

Conclusions: We may infer that HBO_2 therapy decreases the severity of symptoms and increases the life quality of CFS patients. It may be a new treatment modality for the management of CFS. However, further studies with larger sample sizes and control groups are definitely awaited.

INTRODUCTION

Chronic fatigue syndrome (CFS) is a clinically defined condition characterized by severe disabling fatigue and a combination of symptoms that prominently features self-reported impairments in concentration, short-term memory, sleep disturbances and generalized musculoskeletal pain for more than six months [1]. Its prevalence varies from 0.2% to 2.2% among adults, being twice as common in women as in men and affecting all social classes [2]. Diagnosis of CFS can be established only after other likely causes have been excluded.

Currently, there is no consensus regarding its treatment. Many patients try different therapies to overcome their fatigue, varying from pharmacological (*e.g.*, immunoglobulin or corticosteroid therapy) to non-pharmacological treatments (*e.g.*, massage and osteopathy) [3]. Because the conventional therapies are suboptimal, new treatment modalities targeting different possible mechanisms of CFS pathogenesis are always drawing attention. Reactive oxygen species (ROS) and lactic acid – generated in active muscles – are suggested to have a critical role in the pathomechanism of fatigue [4-7]. Many mechanisms of action are possible given the susceptibility of proteins to oxidative damage, but current evidence points at the contractile proteins and the Na-K pump as the sites showing the greatest susceptibility to ROS under physiological conditions. Furthermore, the accumulation of lactic acid in muscle has historically been suggested to be the major cause of muscle fatigue [8].

In this regard, the strategies that aim to remove the ROS and lactic acid from the muscle cell seem to be reasonable for the treatment of CFS. One of them could be hyperbaric oxygen (HBO_2) therapy. Previous studies have reported significant decrease in lactic acid

[4,9,10] and ROS [11-16] after HBO_2 treatment. On the other hand, to our knowledge, there is no previous study evaluating the efficacy of HBO_2 in patients with CFS. Accordingly, the aim of this study was to determine the efficacy of HBO_2 therapy in CFS whereby ROS and lactic acid may play a significant role in its pathogenesis.

MATERIALS AND METHODS

This study was conducted at Gülhane Military Medical Academy Haydarpasa Training Hospital, Department of Physical Medicine and Rehabilitation, Istanbul, Turkey, between 2011 and 2012 and was designed as a prospective clinical study. The study protocol was based on the declaration of Helsinki and approved by the local ethics committee. Before the study, patients gave written consent.

Participants

Patients (n=16) included in the study were diagnosed with CFS according to the Fukuda criteria [1] as follows:

A. Clinically evaluated, unexplained persistent or relapsing chronic fatigue that is of new or definite onset (*i.e.*, not lifelong), is not the result of ongoing exertion, is not substantially alleviated by rest, and results in substantial reduction in previous levels of occupational, educational, social, or personal activities.
B. The concurrent occurrence of four or more of the following symptoms: substantial impairment in short-term memory or concentration; sore throat; tender lymph nodes; muscle pain; multijoint pain without swelling or redness; headaches of a new type, pattern, or severity; unrefreshing sleep; and post-exertional malaise lasting more than 24 hours.

These symptoms must have persisted or recurred during six or more consecutive months of illness and must not have predated the fatigue.

Patients with any past or current diagnosis of a major depressive disorder with psychotic or melancholic features, patients with contraindications for HBO_2 therapy and patients with physical diseases that could cause fatigue, including morbid obesity, hypothyroidism, Cushing's syndrome, anemia (blood hemoglobin <10 g/L), diabetes mellitus, active neoplastic or infectious disease were all excluded.

Complete blood count, erythrocyte sedimentation rate, C-reactive protein, and hepatic/renal/thyroid function tests were also evaluated. Patients were excluded if they had any abnormal laboratory results.

Treatment

Patients received 15 90-minute therapy sessions with HBO_2 at 2.4 atmospheres absolute (atm abs) on five days of the week (one session per day). No physical therapy or medication was given to ensure standardization among the patients and to detect the efficacy of HBO_2 therapy.

Clinical evaluation

Initially, general physical and substantial neuromusculoskeletal examinations were performed. Additionally, patients were evaluated before treatment and after completion of the 15 sessions in the following way. Fatigue was assessed by using a visual analog fatigue scale (VAFS) where 0 indicated no fatigue and 10 unbearable fatigue (the worst fatigue). Additionally, the Fatigue Severity Scale (FSS) and the Fatigue Quality of Life Score (FQLS) were used to assess the severity of fatigue and quality of life.

The FSS questionnaire contains nine statements that rate the severity of fatigue symptoms concerning respondent's fatigue – *e.g.*, how fatigue affects motivation, exercise, physical functioning, carrying out duties, interfering with work, family or social life. Scale is a 7-point Likert scale, where 1 strongly disagree and 7 strongly agree. Minimum score is 9, and maximum score is 63. Higher scores indicate more severe fatigue.

The FQLS measures how much fatigue affects the patient's quality of life by assessing five characteristics of the person's energy levels. Minimum score is 5, and maximum score is 30. Higher scores indicate more severe fatigue.

Statistical analysis

The numerical variables are presented as mean ± SD. The Wilcoxon Rank Sum test was used for comparing the clinical variables before and after treatment. The level of statistical significance was set at $p < 0.05$. SPSS software, version 15.0 (SPSS Inc., Chicago, Ill., USA) was used for all statistical calculations. In addition, Pearson Correlation was used to analyze correlations.

RESULTS

All patients (two males, 14 females) completed the study and complications due to HBO_2 were not seen in any of them during the treatment. Table 1 summarizes the baseline clinical and demographic characteristics of the subjects enrolled in the study. Clinical evaluations

TABLE 1. Demographics of the subjects

	Range
Age (year)	44.06±4.62 (34-53)
Symptoms duration (months)	25.06±16.91 (12-60)
Occupation	*n*
Housewife	10
Worker	5
Retired	1

TABLE 2. Comparative evaluation of the subjects (Mean ± SD)

	Before	After	*p*
Fatigue Severity Scale	53.20 ± 4.49	14.60 ± 8.81	0.001
Fatigue Quality of Life Score	24.53 ± 2.38	8.66 ± 2.76	0.001
Visual Analog Fatigue Scale	7.66 ± 0.89	2.00 ± 1.73	0.001

of the patients are given in Table 2. After the treatment, patients' scores were found to have improved with respect to VAFS, FSS and FQLS (all $p<0.005$).

Although there was a strong positive correlation ($r=0.676$, $p=0.006$) between FSS and FQLS, none of the clinical evaluation parameters had any correlation with symptom duration of the patients (all $p>0.05$).

DISCUSSION

In the present study, we aimed to evaluate the efficacy of HBO_2 therapy in patients with CFS. The results showed that HBO_2 therapy decreased the severity of fatigue and increased the quality of life in patients with CFS. To our knowledge, this is the first clinical trial that evaluates the efficacy of HBO_2 in patients with CFS.

Chronic fatigue syndrome is a chronic disease with social components that ensue secondary to the incapacity of the person to fulfill their work, social and family responsibilities. Because the pathophysiology of CFS remains unclear, current treatment modalities mainly seek to alleviate symptoms [17]. To date, there are controversies regarding appropriate strategies for the management of CFS. Because current treatments and medications are often associated with limited clinical benefits [18] and possible undesirable side effects [19], complementary/alternative therapies are frequently used by CFS patients as well [20,21]. However, almost all of them have been suboptimal, because they are far away from amelioration of the pathophysiology where ROS and lactic acid play a critical role [4-8].

Although, HBO_2 therapy is an old modality, it is relatively new for practitioners of physical and rehabilitation medicine [22]. In addition, there are several studies on HBO_2 therapy in treating musculoskeletal disorders [22,23,24]. HBO_2 therapy is defined as the intermittent inhalation of 100% oxygen in a hyperbaric chamber at a pressure higher than 1 atmosphere absolute (1 atm abs = 760 mmHg, the normal atmospheric pressure at sea level) [25]. HBO_2 therapy is usually administered at 2 to 3 atm abs. Typically, the duration of HBO_2 therapy varies from 30 to 120 minutes. The frequency and total number of HBO_2 sessions are not standard among hyperbaric medicine centers. HBO_2 therapy is administered using monoplace or multiplace chambers. In the former, a single patient is treated and internal pressure is raised with oxygen. Multiplace chambers permit patients to be in the pressure chamber together with health personnel. In multiplace chambers, pressure is raised with compressed air and patients breathe oxygen through masks. HBO_2 therapy causes mechanic and physiologic effects. One of the physiologic effects is to increase evacuation of ROS and lactic acid from the body [9-16].

In this study, a new modality was tried to treat CFS as far as its pathophysiology is concerned. The patients' symptoms improved. On the other hand, although the levels of ROS and lactic acid could not be measured, the improvement in the subjects' complaints is noteworthy. Yet, previous studies have shown that HBO_2 therapy decreased ROS and lactic acid levels in various conditions [9-16]. Therefore, it is possible to say that HBO_2 therapy can be effective and thus be used as a new treatment option in CFS.

Limitations of the present study include the lack of a control group, the lack of a long-term follow-up and the small sample size with female predominance. Nevertheless, the results seem to be significant. In conclusion, we may imply that HBO_2 therapy, an effective and well-tolerated treatment method, decreases the severity of symptoms and increases the quality of life in CFS patients. In this regard, it may be a new treatment modality for the management of CFS. However, further studies with larger sample sizes and control groups are definitely awaited. The long-term and duration of its beneficial effects should be investigated in future studies.

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