

Effectiveness of Hyperbaric Oxygen Therapy in the Treatment of Complex Regional Pain Syndrome

MZ KIRALP¹, Ş YILDIZ², D VURAL¹, I KESKIN¹, H AY² AND H DURSUN¹

¹Department of Physical Therapy and Rehabilitation and ²Department of Underwater and Hyperbaric Medicine, Gülhane Military Medical Academy, Haydarpaşa Training Hospital, Istanbul, Turkey

In this double-blind, randomized, placebo-controlled study we aimed to assess the effectiveness of hyperbaric oxygen (HBO) therapy for treating patients with complex regional pain syndrome (CRPS). Of the 71 patients, 37 were allocated to the HBO group and 34 to the control (normal air) group. Both groups received 15 therapy sessions in a hyperbaric chamber. Pain, oedema and range of motion (ROM) of the wrist were evaluated before treatment,

after the 15th treatment session and on day 45. In the HBO group there was a significant decrease in pain and oedema and a significant increase in the ROM of the wrist. When we compared the two groups, the HBO group had significantly better results with the exception of wrist extension. In conclusion, HBO is an effective and well-tolerated method for decreasing pain and oedema and increasing the ROM in patients with CRPS.

KEY WORDS: COMPLEX REGIONAL PAIN SYNDROME; HYPERBARIC OXYGEN THERAPY; REFLEX SYMPATHETIC DYSTROPHY; RANGE OF MOTION; PAIN; OEDEMA

Introduction

Severe local pains in the extremities, skin colour changes, hypo- or hyperhydrosis and localized osteoporosis characterize complex regional pain syndrome (CRPS). Since its original description by Mitchell in 1864, CRPS, previously known as reflex sympathetic dystrophy, has been a poorly understood and frequently overlooked condition¹ and its aetiology remains unclear. Trauma, which is often mild, is the main aetiological factor but not the only one.² Moreover, there is no relationship between the severity of trauma and the severity of the

syndrome.³ The pathogenetic universally accepted mechanism proposed by Leriche is sympathetic-reflex imbalance.⁴ A factor contributing to many chronic pain syndromes is overactivity of the sympathetic nervous system. The patient's pain is usually diffuse and does not correspond to a dermatome or peripheral nerve distribution.⁵

The clinical symptoms of CRPS arise from the sensory, motor and sympathetic nervous systems. Early diagnosis influences the response to treatment and the evolution of the disease. There are three stages in the development of CRPS: acute (stage I), dystrophic (stage II) and atrophic (stage III).

The atrophic stage is irreversible and is characterized by stiffness and flexion contractures of the hand. The patient complains of vasomotor pain and the trophic changes in the skin, muscles and skeleton are permanent and progressively worsen until there is ankylosis and complete loss of function.

There are usually no characteristic biochemical abnormalities. The typical radiographic signs of CRPS appear only after several weeks or months and constitute an important, but non-specific, finding in favour of a positive diagnosis of the disease.⁶ The radiographic examination can not be used to classify the stage of the syndrome.

Treatment of CRPS is more difficult than the diagnosis and classification of the disease. There are a variety of treatments, but the treatment window is too short to obtain positive results and the disease progresses quickly to the next stage. Hyperbaric oxygen (HBO) therapy has been used worldwide to treat many diseases and involves breathing 100% oxygen via an endotracheal tube, mask or hood in a pressure chamber, under pressures higher than 1 atmosphere absolute (ATA). Dissolved oxygen in the blood can increase from 0.3% to 6.8% in proportion to the applied environmental pressure with HBO therapy. Both the increased concentration and the partial pressure of oxygen increase oxygenation of the whole body. The increased tissue oxygen enhances the growth of fibroblasts, formation of collagen, angiogenesis and the phagocytic capabilities of the hypoxic leucocytes.^{7,8}

The aim of the present study was to examine the efficacy of HBO for treating CRPS.

Patients and methods

PATIENTS

Patients who were diagnosed with post-traumatic CRPS at the Gulhane Military Medical Academy Haydarpasa Training

Hospital Department of Physical Medicine and Rehabilitation between 2002 and 2003 participated in the study. All patients had stage I and II of the disease. Patients were allocated alternately to receive HBO therapy (HBO group) or normal air (control group). After randomization, a physician blinded to the group allocation evaluated the patients for contraindication to HBO therapy. Patients with contraindications for HBO therapy were excluded from the study, irrespective of their allocated group. Only the physician administering treatment knew whether the patients were receiving 100% oxygen or air. This was necessary for safety reasons.

The time period between the diagnosis and the occurrence of the trauma was approximately 1.5 months. The patients had not received any treatment for CRPS and were given information pertaining to CRPS and HBO treatment. All patients gave informed consent. GATA Military Medical Faculty Ethical Committee approved the study.

TREATMENT

Both patient groups received 15 90-min therapy sessions with either HBO or normal air at 2.4 ATA on 5 days of the week (1 session per day). In addition, 500 mg paracetamol was given three times daily. No physical therapy was given to ensure standardization among the patients and to detect the efficacy of HBO therapy. Patients were evaluated before treatment, after completion of the 15 sessions, and after 45 days.

CLINICAL EVALUATION

Pain was evaluated using a visual analogue scale (VAS) where 0 was no pain and 10 was unbearable pain. Range of motion (ROM) evaluation included goniometric assessment of wrist extension and wrist flexion. Oedema was evaluated by measuring the wrist circumference.

STATISTICAL ANALYSIS

The numerical variables are presented as mean $\pm$ SD. Student's *t*-test was used for comparing the clinical variables before and after treatment. The Mann-Whitney *U*-test was used for between-group comparisons. A *P*-value < 0.05 was considered statistically significant. SPSS software, version 11.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical calculations.

Results

Of the 71 patients who participated in the trial (49 men, 22 women), 37 were in the HBO group (mean age 29.4 ± 10.2 years) and 34 in the control group (mean age 31.4 ± 9.15 years).

The VAS scores, wrist flexion, extension and circumference measurements before and after treatment are given in Table 1. In the VAS evaluation, it was seen that pain started to decrease from the first day and had decreased further after session 15 and day 45. This was statistically significant in the HBO group ($P < 0.001$). A statistically significant increase in wrist flexion was also observed in the HBO group after 15 therapy sessions compared with before treatment, and on day 45 compared with after session 15 ($P < 0.001$). A statistically significant decrease in the wrist circumference (due to decreased oedema) was observed between groups, between the end of treatment (after session 15) and day 45 values ($P < 0.001$).

There was a statistically significant difference between the HBO and control groups for all variables ($P < 0.001$) except wrist extension.

Discussion

Complex regional pain syndrome is a chronic condition characterized by severe burning pain, extreme sensitivity to touch,

swelling, excessive sweating and changes in bone and skin tissues. In previous studies, non-steroidal anti-inflammatory drugs (NSAIDs), narcotic analgesics and vasodilators were used as treatments for CRPS, but complete resolution of the signs and symptoms could not be achieved.

In CRPS, hypoxia and acidosis reduced the pain threshold and tolerance. During HBO treatment hyperoxia causes vasoconstriction, decreases oedema, and increases the partial pressure of oxygen in the tissues. In addition, it stimulates the activity of depressed osteoblasts and decreases the formation of fibrosis tissue. Thus it breaks up the physiopathological mechanism that is the basis of CRPS. These features of HBO therapy led us to evaluate its efficacy for treating CRPS.

Tuter *et al.*⁹ conducted a study on 35 subjects, 20 of whom received HBO treatment and 15 received combined analgesic medication. A significant decrease in the severity of pain was detected in the patients receiving HBO treatment. Moreover, allodynia and oedema decreased, the ROM of extremities affected by CRPS increased and skin colour returned to normal.

In his case report, Peach¹⁰ noted a patient with CRPS who had an allergy to steroids, NSAIDs and narcotic analgesics, and did not respond to vasodilators. His pains disappeared after a session of HBO, however, and his cyanosis decreased significantly.

In our study patients with post-traumatic CRPS of the upper extremity received 15 sessions of HBO therapy or normal air. In the HBO group there was a significant difference between the VAS scores and wrist flexion before and after treatment, and in wrist circumference between the 15th therapy session and day 45. A comparison of the HBO and control group results also revealed significant differences after the 15th therapy

TABLE 1:
The visual analogue scale (VAS) pain scores, range of motion and wrist circumference for patients with complex regional pain syndrome who received hyperbaric oxygen (HBO) therapy (HBO group) or normal air (control group)

	Before treatment		After session 15		Day 45	
	HBO	Control	HBO	Control	HBO	Control
VAS pain (score)	6.81 ± 1.44 ^a	6.44 ± 1.43	4.83 ± 1.4 ^{a,b}	6.14 ± 1.54	3.72 ± 1.42 ^{a,b}	5.61 ± 1.37
Wrist flexion (degrees)	40.54 ± 19.74 ^a	38.23 ± 15.8	50.54 ± 19.03 ^{a,b}	40.29 ± 16.41	59.86 ± 17.38 ^{a,b}	44.55 ± 16.11
Wrist extension (degrees)	36.08 ± 14.19	41.76 ± 12.48	40.54 ± 14.03	43.23 ± 12.42	51.62 ± 12.02	47.50 ± 12.26
Wrist circumference (cm)	18.90 ± 0.84 ^a	18.67 ± 0.66	18.02 ± 0.84 ^{a,b}	18.47 ± 0.79	16.98 ± 0.71 ^{a,b}	18.20 ± 0.72

^aStatistically significant difference between the results after the 15th therapy session and day 45 ($P < 0.001$; within the HBO group).

^bStatistically significant difference between the HBO and control groups ($P < 0.001$).

session and day 45. We consider this significant healing to be a result of the increased oxygenation of the tissues. None of the patients progressed to the third stage of the disease.

In conclusion, HBO is an effective and

well tolerated method of decreasing pain and oedema and increasing the range of motion in CRPS. Our preliminary experience indicates that HBO therapy may be a valuable alternative to other methods for treating CRPS.

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Address for correspondence

Dr MZ Kiralp

GATA Haydarpasa Egitim Hastanesi Fizik Tedavi ve, Rehabilitasyon Servisi, 81010 Kadikoy, Istanbul, Turkey.

E-mail: mkiralp@hotmail.com