Use of Hyperbaric Oxygen in Rheumatic Diseases: And Critical Analysis

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Hyperbaric Oxygen has been used in patients with Rheumatic Disease for many years with out reports of untoward or unusual complications for a variety of Non Rheumatic indications. Recent evidence that hyperbaric oxygen inhibits the actions of certain cyctokins. Acts as an immune doculator and may help cognitive dysfunction has resulted in a re-examination of its potential role in rheumatic diseases. A case report of a LUPUS/ Scleroderma crossover patient is presented whose cognitive dysfunction improved after hyperbaric oxygen therapy. The history of hyperbaric oxygen and its physiology are related, along with a focused review of its effects on the immune and central nervous systems. Areas, which might warrant further consideration by Rheumatologists, are outlined, as well of areas of concern.

Introduction:

Hyperbaric Oxygen Therapy is defined as the subjecting of patients to pure oxygen breathing at ambient temperatures, which are greater than normal atmospheric pressure.

Although concepts of hyperbaric oxygen therapy were first employed in 1662, its modern use other than for decompression dates from 1956 when hyperbaric oxygen was used to perform cardiac surgery in Holland 1 . Mechanically, the most common applications of hyperbaric oxygen are to dissolve air or gas emboli and treat divers with "bends" or decompression illness.

New insights into the biochemical and immune interactions of hyperbaric oxygen have increased interest in its potential applications over the past decade. The United States Medicare System has approved hyperbaric oxygen for 13 indications ranging from acute Carbon Monoxide intoxications, Gas gangrene, and osteroradionecroisis to acute arteriolar insufficiency. Over the last 20 years, patients with a variety of conditions, especially Multiple Sclerosis, have reported cognitive improvement after undergoing hyperbaric oxygen. One Lupus/ Scleroderma crossover patient, whose case is reported here, underwent hyperbaric oxygen therapy specifically for cognitive impairment. And experienced subjective and objective improvements. Her case is presented and our concepts of hyperbaric oxygen and the immune and central systems are reviewed.

Case Report:

A 53 year old Caucasian Woman flight attendant who was in her usual state of health in 1979 when she underwent Thyroidectomy and inadvertent parathyroidectomy for Graves disease. In February of 1980, her Heyer Schulte saline breast implants (place in 1977 for cosmetic purposes) were replaced with Cox-Uphoff Silicone prostheses. She was well until 1986 when she presented to UCLA Medical Center with subcutaneous arthritis, Raynaud's phenomenon, Sclerodactyly, inflammatory arthritis, and erythermatous rashes. A work-up demonstrated an ANA of 1:40 (speckled), elevated sedimentation rates (averaging in the high 30's) and persistently decreased IgA levels. She was diagnosed as having a Lupus/ Scleroderma crossover. Although the possibility of Eosinophilic fascuiitis was considered. (It was ultimately ascertained that she occasionally took L-troptophan to sleep after long fights.) No disease modifying therapy was given: supportive diuresis and not steroidal anti- inflammatory agents were prescribed. Over the following 7 seven years, Her ANA rose to 1:1280 (homogeneous) a positive IgG anticardiolipin antibody was found and her course was complicated by percarditis and supraventrocular tachyarrhythmias. The latter of the two items were felt to be suggestive of cardiac sclerodrema: anti RNP was negative and her inflammatory arthritis subsided. CD3 levels. B cell and natural killer cell values do not change. Similar findings have been found in mice in two separate studies. 9.10 Interestingly, the administration of Immunoglobulin production by spleen cells 9 Long terms hyperbaric oxygen delayed the development of Proteinuria, facial erythema, and lymphadenopathy in MRI/ 1pr. Mice. Iamoto et al showed that hyperbaric oxygen has immunosuppressive properties modulated by decreasing interluekin 1 and prostaglandin E2 production, but interleukin 6 in production was not altered. 11

How does Hyperbaric Oxygen Affect the Central Nervous System?

Studies of hyperbaric oxygen on the central nervous system show that at tensions of 1.2- 1.5 atmospheres absolute (ATA), it decreases blood flow by 1-20% (mean of various studies is about 10%), 2 other physiologic changes occur. These include greater permeability of the blood brain barrier to medications and increased oxygen tensions tissues that far outweigh the net effects of mild vasoconstriction. The deformability of erythrocytes is increased resulting in improved transportation in the microvasculature

circulation and lactate removal. 12 Hyperbaric oxygen stimulates the metabolism of nerve cells deprived of oxygen. As early as the 1960's, Meijne reported cognitive improvement in patients to performing mathematical calculations and demonstrated increased typewriter skills after hyperbaric oxygen 13 An area of controversy among Hyperbaricists concerns the possibility that once 1.5 ATA is exceeded, anaerobic metabolism is favored and thus cognitive do not improve as well as they would at lower pressures. Di Sabato et al 14 performed a controlled study (with Sham hyperbaric controls) on patients with cluster headaches. The dramatic improvement was attributed to vasoconstriction, decreased edema, increased serotoin synthesis, and decreased cerebral hypoxia. Additionally, in the central nervous system hyperbaric oxygen decreases adrenaline and monoamine oxidase levels as well as promoting axonal regeneration 15.

Hyperbaric Oxygen for Multiple Sclerosis and other autoimmune diseases:

As hyperbaric oxygen decreases demyelination from per-vascular edema, over 6000 patients with multiple sclerosis have undergone this therapy in the past 10 years. A published trial by The New England Journal of Medicine Suggesting improvement with hyperbaric oxygen in 40 patients in 1983 stimulated considerable interest. 16 However, it was evident that even though hyperbaric oxygen increased helper T lymphocyte levels, patient liked the treatment and reported subjective improvements (especially in the sense of well-being, cognitions and bladder function), Four separated placebo -controlled double -blind trials failed to demonstrate any objective benefits of using the Kutz Disability status Scale or any other parameters 17-20 This was also confirmed in a 22 institution multicenter registry 312 patients followed for 2 years. 21

Occasionally patient with other rheumatic syndromes and associated complications have been held to respond to hyperbaric oxygen. Aseptic necrosis complicating system lupus, for example, appears to be worthy of greater scrutiny. Abstracts and presentations at seminars and meetings of hyperbaric oxygen claim benefits for pneumatosis cystoid intestinal in sclerodrema, livedo reticularis with Vasculitis and Raynaud's phenomenon. Articles have appeared advocating hyperbaric oxygen for Crohn's disease and cyclophophadmide-associated hemorrhagic cystitis

How safe is hyperbaric oxygen?

Hyperbaric Oxygen is generally quite safe, but serious complications can occur.24 Absolute contraindications ***(as of 2010 there remains only one absolute contraindication to HBOT, which is pneumonthorax; others are relative contraindications and some are no longer contratindications)*** to hyperbaric oxygen include pregnancy, underlying malignancy, untreated PNEUMOTHORAX, concomitant therapy with doxorubicin, cis-platinum, or disulfiram. Special considerations need to be taken into account if the patient has upper respiratory tract infections or chronic sinusitis (which make clearing of the ears and sinuses problematic) low seizure thresholds (with high fevers or epilepsy, emphysema with CO 2 retention (which suppresses breathing). And congenital spherocytosis (hempolysis can result) The most common complication of hyperbaric oxygen is barotrauma to the ears and sinuses caused by pressure changes, which has been reported in about 5% of the cases. Occurring in 0.1- 5% of the patients are hypersensitivity reactions confinement anxiety, central nervous system oxygen toxicity, pulmonary oxygen toxicity and temporary changes in eyesight. To minimize risks, patients are advised to have an ear, nose and throat examination by the treating Physician before therapy, not to drink alcohol or take any medication for 4hours prior to treatment, and to wear 100% cotton clothing.

Is there a potential role for hyperbaric oxygen in Rheumatic Diseases?

Very little is known about the influence of hyperbaric oxygen on the immune system. Animal models of autoimmune disease and normal mice are conductive to hyperbaric oxygen studies. Hyperbaric oxygen might be useful in combination with other therapeutic modalities. Further study is needed in these areas before proceeding to human trials. Nevertheless, anecdotal testimonials that hyperbaric oxygen helps people think more clearly should be taken seriously and ultimately subjected to a prospective trial.

Systemic lupus erthematosus (SLE) is an autoimmune disorder that affects several hundred thousand Americans. Nearly half manifest in similar cognitive deficits that do not respond to CORTICOSTEROIDS. 26 In the past few years, the development of single photon emission computerized tomography (SPECT) has shown hypoperfusion abnormalities bitemporally and bifrontally in patients with SLE and incidentally, with fibromyalgia/ Chronic Fatigue syndromes. 26-29

Hyperbaric Oxygen is a well -characterized, old technology whose immunodulatory properties and effects on cognition have never been adequately studied. Although relatively expensive**, this reasonably safe procedure might have potential heretofore-unrealized applications to the patients with rheumatic disease.**

Rheumatoid Arthritis and Hyperbaric Oxygen Therapy

Nippon Seikeigeka Gakkai Zasshi, 1985, Jan, 59(1):17-26

"Superoxide dismutase and Hyperbaric Oxygen Therapy for the patient with rheumatoid arthritis." Kamada, T.

Cu, Zn-SOD values were measured by enzyme immunoassay in the synovial fluid, leukocytes in the synovial fluid, synovial membrane, and leukocytes in the blood of patients with rheumatoid arthritis. SOD activity, lipoperoxide value in serum, ESR, and Lansbury's index of the patients with rheumatoid arthritis under Hyperbaric Oxygen Therapy (HBOT) were also investigated. SOD values of synovial fluid and of leukocytes in synovial fluid from the rheumatoid arthritis group were found to be higher than those from the osteoarthritis group. No significant difference was found in the SOD values in leukocytes of blood and synovial membrane between the two groups. In the patients with rheumatoid arthritis under HBOT therapy the SOD activity was increased, whereas lipoperoxide values were decreased. Furthermore, ESR and Lansbury's index showed a remarkable recovery. **These results suggest that HBOT therapy may be an effective treatment for patients with rheumatoid arthritis.**

Wallace, Goldberg et.,al.

Hyperbaric Oxygen Therapy on Auto Immune disorders
Lupus Journal 1996

The Text Book of Hyperbaric Oxygen Therapy, Vol1,2,3
K.K. Jain MD

Mycoplasma Arthritis Antibodies Israel Joints Inflammation Cytokines

Ben-Gurion University of the Negev 27-Mar-01 Common Bacteria May Trigger Onset of Arthritis Library:

MED Keywords: MYCOPLASMA ARTHRITIS ANTIBODIES ISRAEL JOINTS INFLAMMATION CYTOKINES

Description: Evidence implicates common Mycoplasma bacteria in the triggering or exacerbating of rheumatoid arthritis. Journal of Rheumatology 27: 2747 (Dec 2000)

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COMMON BACTERIUM IMPLICATED IN THE TRIGGERING OF RHEUMATOID ARTHRITIS

Beer-Sheva, March 19, 2001 - Researchers at Ben-Gurion University of the Negev have shown that a well-known bacterium of the Mycoplasma family - commonly found in the human throat - may be involved in the triggering or exacerbation of rheumatoid arthritis (RA).

The team found that fluids from the inflamed, arthritic joints of many patients contained the specific DNA characteristic of Mycoplasma fermentans, as well as antibodies against this organism. Their studies also indicate that mycoplasmic membrane proteins capable of triggering inflammation may also be present.

Collaborating in this investigation are Prof. Shulamith Horowitz and research assistant Bela Evinson at BGU's Department of Microbiology and Immunology, and Prof. Jacob Horowitz and Dr. Abraham Borer of the Department of Medicine at the Joyce and Irving Goldman Medical School. Prof. Jacob Horowitz also serves as head of Department of Medicine A at Soroka University Medical Center. A report on their work appears in a recent issue of the Canadian publication Journal of Rheumatology.

Rheumatoid arthritis, notes husband-wife team Jacob and Shulamith Horowitz, is an autoimmune disease, in which the body's immune system is triggered to attack normal body tissues. Determining the ultimate cause of RA therefore requires the identification of an agent in arthritic joints that interacts with the immune system.

Because Mycoplasmas definitely cause arthritis in animals, doctors have suspected since the early '50s that a Mycoplasma found in humans might be involved in the disease in man. While a number of researchers over the decades have claimed to isolate live Mycoplasma bacteria from the joint fluid of RA patients, others who attempted to repeat their findings failed to do so.

However with the development of advanced DNA analysis techniques.

Identification of traces of bacterial genomes has become easier to ascertain. Thus, British and French scientists have recently shown that M. fermentans DNA is present in the joint (synovial) fluid of many RA patients, findings confirmed by the studies at BGU. In their initial test group of three-dozen RA patients, the BGU scientists found that M.fermentans DNA was present in some 20 percent of the arthritic joints examined. None of 57 patients with other forms of arthritis had this DNA in their joints.

Of critical significance was the additional discovery that half of the RA patients studied, even those with no detectable DNA, had abnormally large quantities of antibodies against M. fermentans in their arthritic joints. Because these patients had the same low quantities of anti-M. fermentans antibodies in their blood serum as do healthy individuals; the BGU team believes that the antibodies they found in the synovial fluid were produced there in response to Mycoplasma that had entered the joint. In 57 patients with other varieties of arthritis, the anti-M. fermentans antibody level in their joints was negligible, even lower than that in their serum.

The BGU scientists also identified the mycoplasmic proteins recognized by the antibodies. These are specific membrane components known to activate the production of immune system factors, such as TNF-alpha, which are inducers of inflammation. This finding indicates a further mechanism that may contribute to the appearance of RA because of M. fermentans entering the joint.

"Our studies suggest," says Jacob Horowitz, a Rheumatology specialist "That Mycoplasmas in the joint may stimulate the immune system to produce antibodies and protein factors known as cytokines, several of which produce local inflammation and tissue damage. There are clearly different agents leading to RA. Among them, M. fermentans may play an important role. This finding adds to the growing list of organisms that have long been considered benign residents of the human body but that modern research indicates may be involved in disease."

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Radiation-Modifying Effect of Hyperbaric Oxygen Therapy in Complex Treatment of Patients with Rheumatoid Arthritis and Osteoarthrosis

Ter Arkh 2002;74(12):83-6 (ISSN: 0040-3660)
Varga OIu; Ignat'ev VK; Vezikova NN; Kheifetz IV

AIM:

To evaluate the efficiency of radiotherapy (RT) in combination with HBOT versus PT used in the complex therapy for rheumatoid arthritis (RA) and osteoarthrosis (OA).

MATERIALS AND METHODS:

46 patients with RA and 18 patients with OA were examined, of them 24 patients with RA and 10 with OA received complex therapy involving a course of HBOT. The groups of patients had no statistically significant differences in the characteristics of their disease and in the nature of the therapy performed. All the patients received RT as radiation therapy.

The patients were followed up for 2 years by assessing basic clinical (the Richi articular index, total pain index, local articular index, pain index for knee and hand joints, circumference of knee and wrist joints) and ultrasound (the magnitude of exudate, an erosive process, osteophytes, articular fissure stenosis, the thickness of the synovial membrane and cartilage) indices.

RESULTS:

Use of HBOT in patients with RA and OA just before articular radiation therapy brought about a more pronounced positive effect of complex therapy. In addition to significant positive changes in clinical parameters, there was a slow progression of a pathological process, as evidenced by ultrasound study.

CONCLUSION:

By reducing needs for drug therapy, for nonsteroidal antiflammatory drugs in particular, **HBOT produces a pharmacoeconomic effect.**

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