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The effect of mild-pressure hyperbaric therapy (Oasis O_2) on fatigue and oxidative stress

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ABSTRACT

Mild-pressure hyperbaric therapy (mHBT) has become increasingly popular among elite athletes and most recently among the general public yet there is very little scientific underpinnings on its therapeutic use. In this study, fifteen healthy volunteers (8 men, 7 women, mean age 29.7 ± 8.1 years) were exposed to 1.3 atmospheres absolute (ATA) for 40 minutes in a mild hyperbaric chamber called "Oasis O_2" to determine the effect of ambient air at 1.3 ATA on oxidative stress, antioxidant potential, fatigue, and blood chemistry. Reactive oxygen metabolites (ROMs), an index of oxidative stress, significantly reduced by 11% ($p = 0.006$), while biological antioxidant potential (BAP), an index of antioxidant capacity, did not show a significant change ($p = 0.749$). WBC count significantly reduced by 10.4% ($p = 0.005$) whereas WBC differential did not show a marked change. The mean visual analog scale (VAS) score for fatigue significantly decreased from 5.0 to 2.1 ($p < 0.001$). Our findings suggest that mild-pressure hyperbaric therapy reduces oxidative stress as indicated by a significant decrease in serum ROM, and also helps improve fatigue as seen by a significant decrease in VAS fatigue scores.

Keywords: Mild-Pressure Hyperbaric Chambe; Oxidative Stress; Free Radicals; Reactive Oxygen Species (ROS)

1. INTRODUCTION

Mild-pressure hyperbaric therapy (mHBT) has become increasingly popular among elite athletes and most recently among the general public as a modality to improve fatigue, enhance overall health and well-being, heal sports-related injuries, and promote anti-aging. The hyperbaric chambers used for these purposes are soft-sided chambers made of elastic fiber such as the "Oasis O_2" used in this study. Many manufacturers distribute similar chambers for widespread use and they are collectively referred to as "mild-pressure hyperbaric chambers". These are frequently mistaken for hospital grade hyperbaric oxygen therapy (HBO) chambers despite the vastly different specifications between HBO and mHBT. The "Oasis O_2" uses 1.3 atmospheres absolute (ATA) ambient air whereas HBO is the intermittent administration of 100% oxygen at therapeutic pressures of 2-3 ATA with more than 60 minutes of depressurization time.

HBO is claimed to "revitalize" hypoxic tissues, supplement oxygen to under-oxygenated tissues, reduce edema, promote fibroblast proliferation for tissue regeneration, mobilize white blood cells (WBCs), and improve resistance and immunity against infection and inflammation [1]. HBO has been traditionally indicated for decompression sickness and acute carbon monoxide poisoning; its clinical applications have since expanded to include the treatment of other conditions such as external injuries and central nervous system disorders because of its tissue regenerative capacity [2]. The value of oxygen therapy has long been known and HBO is a modern form of this treatment that provides enriched oxygen under high pressure to promote tissue regeneration. However, the delivery of high-density, pressurized oxygen has also been found to create problems by generating free radicals. Oxygen toxicity is a side effect of HBO that results from breathing high partial pressures of oxygen accompanied by an uncontrolled increase in reactive oxygen species (ROS) [3]. Normally the living organism has an "antioxidant system" that controls the development of ROS, but when this system's scavenging capacity is overcome by the enhanced formation of ROS,

the resulting state is called "oxidative stress". Excessive free radicals can damage lipids, proteins, and DNA which main structural and functional integrity of the organism, as well as accelerate aging and cause a variety of diseases [4]. For these reasons, mHBT uses lower concentration and pressure than HBO to deliver oxygen to the tissues while checking the development of free radicals.

Although mild-pressure hyperbaric chambers have become widely prevalent, few researches about mHBT have been made so far. Saito reports mHBT has no significant effect for oxidative stress [5]. On the other hand, mHBT shortens a treatment period of acute lower leg muscle strain in professional soccer players [6] and decreases blood levels of lactate acid and physical fatigue [7]. Scientific validation of their efficacy and mechanisms of action are still necessary to be explored. Therefore, our reason for this study was to determine the effects of mild hyperbaria on oxidative stress, antioxidant potential, and fatigue.

2. MATERIALS AND METHODS

2.1. Study Design and Subjects

Fifteen healthy volunteers (8 men, 7 women, mean age 29.7 ± 8.1 years) provided oral consent and were instructed to refrain from intense physical exercise before participating in the study. All participants were exposed to 1.3 ATA for 40 minutes in "Oasis O_2", a mild-pressure hyperbaric chamber. Changes in subjective sensation of fatigue and blood chemistry were evaluated before and after hyperbaric exposure to determine the effects of mHBT on those parameters.

Blood chemistry analysis included assessing the derivatives of reactive oxygen metabolites (d-ROMs) as a convenient test to measure the level of oxidative stress in clinical practice, biological antioxidant potential (BAP) as an index of antioxidant capacity, and differential leukocyte count. Blood samples were obtained from participants immediately before and after hyperbaric chamber exposure.

For the d-ROM and BAP tests, the free radical analysis system (FRAS4) (Diacron International, Italy) consisting of a dedicated photometer with an incorporated centrifuge was used. ROM values were reported in Carratelli Unit (CARR.U.) with one CARR.U. equaling 0.08 mg/100 mL of hydrogen peroxide. BAP was expressed as µmol/L.

To evaluate the participants' subjective sensation of physical fatigue, a visual analog scale (VAS) for fatigue (Japanese Society of Fatigue Science) [8] was administered immediately before and after the exposure. The fatigue VAS consisted of a 100 mm horizontal line and participants were asked to mark the point on the line with an "x" that represented the perception of their fatigue level. The possible score ranged from 0 to 100, with "0" on the far left indicating "no fatigue/full of energy" to "100" on the far right indicating "worst possible fatigue/listlessness". The score was obtained by measuring the length of line from "0" to the point indicated by the participant that represented their current state. This was divided by 10 to yield a fatigue rating on a 0 to 10 scale.

2.2. Statistical Anlysis

Student's t-test was used to compare the means of serum ROM, serum BAP and differential leukocyte count obtained from participants immediately before and after mHBT. The significance level for all cases was set at 5%. The SPSS Ver.11.5 software was used for analysis.

3. RESULTS

The mean serum ROM before exposure to mild hyperbaria was 269.4 ± 49.7 CARR.U., which significantly reduced by 11% to 239.7 ± 30.4 CARR.U. after the exposure ($p = 0.006$) (**Figure 1**). In contrast, mean serum BAP values before and after hyperbaric exposure were 2288.3 ± 350.4 µmol/L and 2265.4 ± 284.7 µmol/L, respectively. There was no significance between the two BAP values ($p = 0.749$) (**Figure 2**).

The mean WBC count before hyperbaric exposure was 6233.3 ± 1173.3/uL, which significantly decreased by 10% to 5580.0 ± 984.3/uL after the exposure ($p = 0.005$) (**Figure 3**). There was no significant difference in WBC differential before and after the exposure (**Figure 4**).

The mean VAS fatigue score was 5.0 ± 1.8 before exposure to hyperbaric chambers, which significantly reduced to 2.1 ± 1.6 after the exposure ($p < 0.001$) (**Figure 5**).

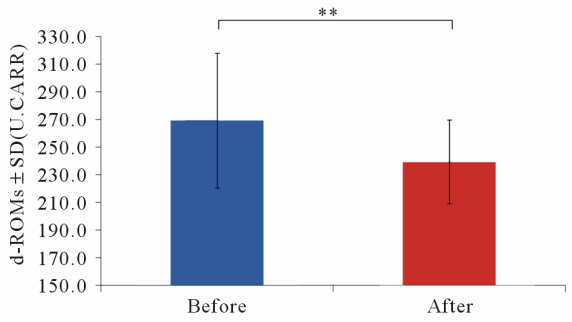

Figure 1. Change in serum ROM after mild HBT. A significant decrease of 11% in mean serum ROM was observed before (Pre) and after (Post) hyperbaric exposure (Pre: 269.4 ± 48.7 CARR.U.; Post: 239.7 ± 30.4 CARR.U; p = 0.006).

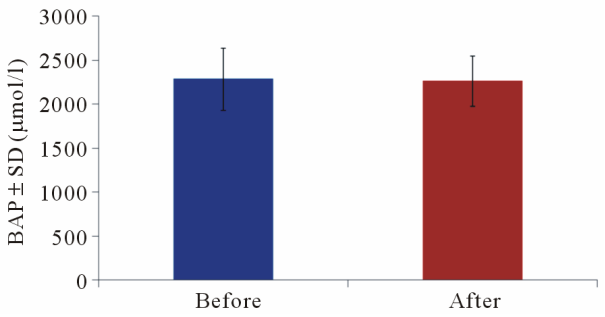

Figure 2. Change in serum BAP after mild HBT. Mean serum BAP decreased from 2288.3 ± 350.4 μmol/L before hyperbaric exposure to 2265.4 ± 284.7 μ after exposure, but the difference was not significant (p = 0.749).

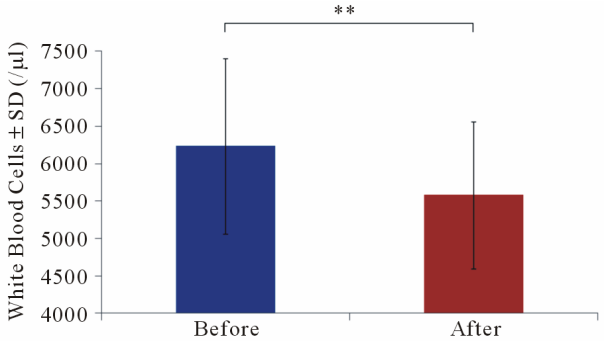

Figure 3. Change in WBC after mild HBT. A significant decrease of 10.4% in mean WBC count was observed before (Pre) and after (Post) hyperbaric exposure (Pre: 6233.3 ± 1173.3/uL; Post: 5580.0 ± 984.3/uL; p = 0.005).

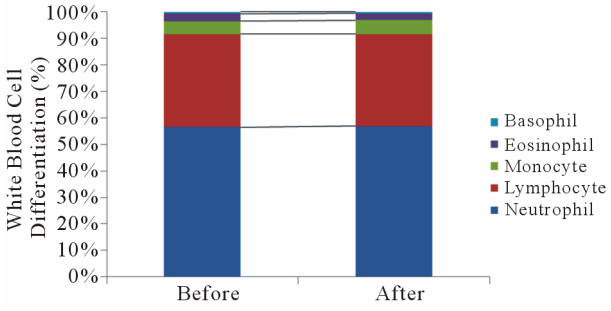

Figure 4. Change in WBC Differentiation after mild HBT. No significant changes were observed in the differential WBC count before and after hyperbaric exposure.

4. DISCUSSION

Our findings revealed that mHBT was effective in lowering oxidative stress. A significant reduction in serum ROM was noted after the therapy whereas there was no change in BAP or antioxidative capacity.

These findings contrast with those obtained by Kongoji *et al.* and Yamami *et al.* which showed elevated ROM and BAP values immediately after exposure to HBO

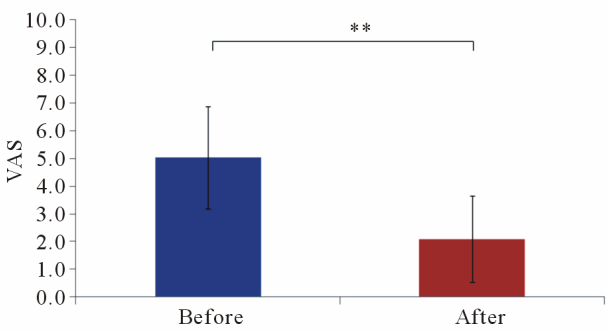

Figure 5. Change in VAS after mild HBT. Mean VAS fatigue scores dropped significantly before (Pre) and after (Post) hyperbaric exposure (Pre: 5.0 ± 1.8; Post: 2.1 ± 1.6; p < 0.001).

[9,10]. Despite conflicting results, our data are highly meaningful because of the paucity of reports on mHBT. The differences in the results may be attributed to the relatively faster exhaustion of antioxidant enzymes and substances due to their increased activity after HBO to counteract oxidative damage. In general, as the level of oxidative stress rises, antioxidative enzymes and substances are mobilized by the body as a defense mechanism to clear ROS and to restore the balance between oxidative stress and antioxidant activity [4]. We surmised that in our study mHBT-induced ROS were effectively eliminated in a relatively short period because our participants were young, were free from underlying diseases, and had strong antioxidative capacity.

In addition, it is empirically known that 100% oxygen administered at pressures greater than 3 ATA induces oxygen toxicity, while pure oxygen at pressures greater than 1.75 ATA demonstrably causes a higher incidence of oxygen toxicity than 1.5 ATA [11]. Accordingly, we used compressed air at a very low pressure of 1.3 ATA in this study to eliminate the need for providing additional oxygen and minimize oxygen poisoning - a worrisome side effect of HBO.

Moreover, we found that mHBT had a beneficial effect on fatigue. VAS fatigue scores significantly improved after the therapy in nearly all the participants who felt the physical improvement. These findings are in line with Ishihara's data that showed reduced blood lactate level and improved muscle stiffness and fatigue in college volleyball players after exposure to 35% oxygen at 1.25 ATA [12]. It is possible that a placebo effect from mHBT may have influenced a subjective symptom like fatigue; however, the effect of mild hyperbaria in alleviating fatigue was confirmed by all the participants who reported feeling "refreshed", "warmer", or "lighter" afterwards. For this study, data were obtained from participants who abstained from intense physical activity before undergoing mHBT. To further probe the efficacy

of mHBT on fatigue, future studies would benefit from manipulating fatigue induction and evaluating the effects in participants undergoing similar physical load.

Although WBC count significantly decreased after mHBT, WBC differential did not show a remarkable change. These findings are congruent with Osbourne *et al.*'s data which showed a decrease in WBC count by 32% and 13% in rats exposed to hyperbaric pressures at 4 ATA with 100% oxygen for 90 minutes and at 4 ATA with 21% oxygen for 90 minutes, respectively. Additionally, the investigators hypothesized that stress from HBO induced greater adrenal cortisol secretion, which in turn caused a decrease in WBCs [13]. In this study WBCs decreased in almost all the participants after mHBT; however, WBC differential did not change in response to the therapy. A re-evaluation of the latter 4-6 hours after the exposure is warranted as differential leukocyte activity is known to change over time.

Much controversy currently exists over the efficacy of mHBT. In May 2006, a panel entitled "Round table discussion on mild HBT" was held at the Third Annual Meeting of Japanese Association for Clinical Hyperbaric Oxygen and Diving (JACHOD). At this meeting, a vigorous debate over the efficacy of mHBT ensued between JACHOD, an opponent of mHBT, and Japan International Hyperbaric Association Inc. (JIHA), a proponent of mHBT. Although the main purpose of HBO is to raise the levels of oxygen in body fluids, most oxygen carried in the blood is bound to hemoglobin, rendering absolute hemoglobin concentration as the limiting factor for oxygen uptake. However, the mechanism of HBO rests on Henry's Law that states a gas is dissolved by a liquid in direct proportion to its partial pressure, *i.e.*, HBO utilizes increased atmospheric pressure to enhance oxygen dissolution in the plasma and resultant higher concentration of liquefied oxygen to reverse hypoxia. Further, mHBT was developed and based on the theory that liquefied oxygen is more refined than conjugated oxygen and therefore has a greater capacity to transport oxygen to peripheral tissues. However, several studies have found that mild hyperbaria at 1.3 ATA yields 0.57 mL/dL of liquefied oxygen, which is significantly less than 2.0 mL/dL of liquefied oxygen from compressed air at 1.0 ATA, leading to some investigators to refute the ability of mHBT (pressurized ambient air at 1.3 ATA) to deliver the benefits of oxygen therapy [14-16].

Meanwhile, Ishii *et al.* studied the effects of various hyperbaric pressures and discovered that lactate clearance rate after maximal exercise at 1.3 ATA and 100% oxygen was significantly greater than the rate at normal atmosphere and room air; hence, the authors reported that atmospheric pressure need not be raised to 2.0 ATA because 1.3 ATA, which imposes comparatively less stress than 2.0 ATA on the biological system, was sufficiently effective [7]. Moreover, Ikeda *et al.* found that compressed air at 1.3 ATA using Oasis O_2 for the treatment of acute lower leg muscle strain in professional soccer players significantly reduced the time to return to sport after injury, as observed from the difference in recovery time between the non-treatment group versus the treatment group (2.9 ± 1.4 weeks vs. 1.9 ± 0.5 weeks) [6]. It appears that further research is necessary to clarify the dearth of studies on the controversial effects of 1.3 ATA

5. CONCLUSIONS

Our findings suggest that mHBT is helpful in reducing oxidative stress and improving fatigue while posing minimal risks, yet its effect on antioxidant capacity is less clear. Research will be needed to examine the therapeutic significance of 1.3 ATA in health promotion and disease prevention.

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