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Am J Sports Med 1999 27: 600

0363-5465/99/2727-0600$02.00/0
THE AMERICAN JOURNAL OF SPORTS MEDICINE, Vol. 27, No. 5

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ABSTRACT

To determine whether intermittent exposures to hyperbaric oxygen enhance recovery from delayed-onset muscle soreness of the quadriceps, we conducted a randomized, controlled, double-blinded, prospective study using 66 untrained men between the ages of 18 and 35 years. After the induction of muscle soreness, these subjects were treated in a hyperbaric chamber over a 5-day period in two phases, with four groups (control, hyperbaric oxygen treatment, delayed treatment, and sham treatment) in the first phase; and three groups (3 days of treatment, 5 days of treatment, and sham treatment) in the second phase. The hyperbaric exposures involved 100% oxygen for 1 hour per day at 2.0 atm. The sham treatments involved 21% oxygen for 1 hour per day at 1.2 atm. We monitored recovery using a leg dynamometer to test eccentric torque of the nondominant quadriceps muscle before and immediately after exercise and at 48 and 96 hours after exercise. Pain was tested daily using visual analog pain scales. In phase 1 a significant difference in recovery of eccentric torque was noted in the treatment group compared with the other groups. In phase 2, the recovery of eccentric torque for the 5-day treatment group was significantly greater than for the sham group from immediately after exercise to 96 hours after exercise. The pain data did not differ significantly in any comparison in either phase. The results suggest that treatment with hyperbaric oxygen may enhance recovery of eccentric torque of the quadriceps muscle from delayed-onset muscle soreness.

Evidence increasingly supports the adjuvant use of hyperbaric oxygen (HBO) in healing soft tissue injuries if the trauma is adequately severe.[15,18] Hyperbaric oxygen therapy refers to the medical procedure in which patients inspire 100% oxygen while their entire bodies are subjected to pressure greater than ambient barometric pressure at sea level,[13,18] that is, greater than one atmosphere absolute (atm), or 760 mmHg. Recent experimental evidence implies that pain may be decreased with intermittent to long-term exposure to HBO.[23] The principal benefit provided by HBO therapy is that sufficient oxygen becomes physically dissolved in plasma to keep tissues viable despite the inability of hemoglobin-bound oxygen to reach the injured area.[1,3] In addition, the results of an ischemic rat model suggest increased recovery of muscle strength after a period of insufficient blood flow (ischemia) and subsequent exposure to HBO.[25] The purpose of this study was to determine if the HBO decreased pain perception and hastened the return of eccentric torque to the nondominant quadriceps muscle in delayed-onset muscle soreness. It should be noted that pain and the degree of strength loss have never been shown to be proportional.[22]

In controlled human studies, adjunctive HBO therapy has had definite clinical benefits in wound healing and fractures. In literature on HBO as it pertains to soft tissue, the work of Zamboni et al.[26,27] has provided some evidence for enhanced strength in skeletal muscle after prolonged ischemia followed by HBO treatments. Haapaniemi et al.[11] have demonstrated decreased ischemia-induced skeletal muscle injury in an animal model, with reduced levels of adenosine triphosphate, phosphocreatine, and lactate in the treated groups compared with the untreated groups. It should be noted that the treatment protocol (seven times in 48 hours) was much more aggressive than would be used in any human study. Until now, however, there has been a scarcity of research on HBO treatment in sports medicine.[14] The initial research involved professional soccer players in Scotland, where

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Funding for this work was received from commercial parties named in this study. See "Acknowledgments" for funding information.

researchers claimed up to a 70% reduction in days lost to injury after injured players were treated with HBO.[15] The results compared a clinician's estimate of the time course for the injury and the actual number of days missed when treatment comprised routine therapy and daily (1-hour) sessions of HBO at 2.0 atm.[15] We believe that this study should have included a control group, input from an objective third party (physician), and greater homogeneity of injuries to justify its claims. The anecdotal data must be accompanied by randomized, controlled, and double-blinded studies in which patients have sustained quantifiable injuries. The first attempt at this, a study of ankle sprains, suggested that subjects treated with HBO returned to activity approximately 30% faster than the control group.[19] However, given the large amount of variability in the study, the result was not significant. The authors of the study noted the difficulty experienced in quantifying the severity of ankle sprains, which created much of the observed variability. We designed this study to address the absence of randomized control groups and double-blinding in previous studies.

MATERIALS AND METHODS

Subjects

To facilitate the induction of delayed-onset muscle soreness, we studied "untrained" male university students (18 to 35 years old), since daily training for 2 hours, as experienced by varsity athletes, may limit the effect of delayed-onset muscle soreness. The term "untrained" referred to subjects who did not regularly participate in physical activity more than 2 hours a week on average. Forty volunteers participated in phase 1 of the study, and 30 volunteers participated in phase 2. Nine additional subjects started but did not complete the study and were not included in the analysis of results. Excluded from participating in this investigation were athletes who were weight training, running, skiing, or participating in team sports (such as basketball, volleyball, football, and soccer), since these activities had some component of eccentric movement of the quadriceps muscle in training. Subjects who had experienced delayed-onset muscle soreness in the previous 3 months were also excluded.

Preliminary examination by a physician excluded subjects with an incompatibility to hyperbaric exposure[2,7] (such as pneumothorax, idiopathic lung cyst, hyperinflation, any other lung abnormality, unresolved upper respiratory tract infection, or fever at the time of exposure to the therapy). We induced delayed-onset muscle soreness in each subject's nondominant leg. If the subject kicked with the right foot, the nondominant quadriceps muscle was in the left leg. Subjects who had had recent knee ligament injuries, knee surgery, or chronic knee pain in their nondominant leg were excluded. For participating in this study, subjects received an honorarium of $100 (Canadian) for phase 1 and $75 (Canadian) for phase 2.

Procedures

The first phase of the experiment involved four groups (control, HBO, delayed HBO, sham) of nine subjects to determine the efficacy of HBO, delayed treatment, or placebo on quadriceps muscle torque recovery and pain perception after inducing delayed-onset muscle soreness. Four subjects (one from each group) were rejected in phase 1 because they had abnormal responses to eccentric exercise. Their eccentric strength increased rather than decreased. The control group had no treatment after induction of delayed-onset muscle soreness. The HBO group subjects were treated in the chamber at 0, 24, and 48 hours after exercise and then given simulated HBO (sham) treatments at 72 and 96 hours. The delayed-HBO group received sham treatments at 0 and 24 hours, then hyperbaric treatments at 48, 72, and 96 hours after exercise. The sham-treatment group had simulated HBO treatments at 0, 24, 48, 72, and 96 hours after exercise. The HBO treatment consisted of the subjects breathing 100% oxygen at 2.0 atm for 1 hour, while the sham/simulated HBO treatment involved subjects breathing 21% oxygen at 1.2 atm for 1 hour. (For proper function of the breathing apparatus of the mask in the chamber, it was necessary to slightly elevate the pressure in the chamber above normal, ambient pressure).

The second phase involved 3 groups of 10 subjects to determine the efficacy of sham treatment and 3 and 5 days of HBO treatment on quadriceps muscle torque recovery and pain perception after delayed-onset muscle soreness. The control group was dropped because no statistically significant difference was noted between the control and sham-treatment groups, and funding limitations made it necessary to drop at least one group. The 3-day HBO-treated subjects were treated at 0, 24, and 48 hours after exercise with HBO, and sham treated at 72 and 96 hours. The 5-day HBO-treated group received hyperbaric treatments at 0, 24, 48, 72, and 96 hours after exercise. The sham-treatment group had simulated HBO treatments at 0, 24, 48, 72, and 96 hours after exercise.

The study protocol was approved by the University of British Columbia Clinical Screening Committee for Research Involving Human Subjects. All subjects were exercised on a KIN-COM Dynamometer (Chattecx, Chattanooga, Tennessee), either at the School of Rehabilitation Medicine or at the Allan McGavin Sports Medicine Centre. Besides the 66 subjects who completed the protocol, 9 other subjects began but did not finish the protocol because their physical status (either recent upper respiratory infection or confinement anxiety) contraindicated further participation. The average heights, weights, and ages of the subjects who completed the study did not differ significantly in either phase 1 or 2.

After random assignment to groups, subjects were asked to perform four deep knee bends to an approximately 90° knee joint angle and subsequently filled out a visual analog scale, with 0 cm indicating "no pain" and 10 cm indicating "worst pain ever experienced." The subjects were instructed to repeat these steps after the exercise session and to report any feelings of pain (not fatigue) in

the exercised leg. The KIN-COM dynamometer was set for each subject such that the weight of the tested limb was subtracted from the force the limb exerted. To prevent unwanted movement, each subject was secured at the upper third of the quadriceps muscle and around the waist.

The exercise session included a preexercise measurement of the mean maximal torque of the nondominant quadriceps muscle. Subjects performed three submaximal and one maximal contraction, rested, then performed four maximal contractions at 30 deg/sec through a 60° range of motion at a long muscle length (45° of flexion to 105° of flexion). The preexercise mean maximal torque was an average of the last three maximal contractions.

For the remainder of the exercise, subjects were instructed to exert maximum resistance to the downward force of the dynamometer arm through the range of motion for a total of 30 sets of 10 repetitions each, or 300 eccentric contractions. Each set lasted approximately 45 seconds, with a 15-second recovery period for a total of approximately 30 minutes.

On completion of the exercise, there was a brief break, followed by a repeat of mean maximal torque testing. The posttest torque measurement was followed by a repeat analysis of the pain perception using a visual analog scale after four deep knee bends. Subjects were then placed in the monoplace hyperbaric chamber (HYOX, Glasgow, Scotland) at the Allan McGavin Sports Medicine Centre Physiology Laboratory, where they began the first of five HBO treatments. Both the subjects and the researcher involved in torque evaluation were blinded to the assignment of treatment group. Subjects received either an HBO treatment (100% oxygen at 2.0 atm) or a sham treatment (21% oxygen at 1.2 atm). The control group had no exposure to the HBO chamber.

On subsequent visits, subjects were treated approximately 24, 48, 72, and 96 hours after exercise. After each subsequent HBO exposure, the subject performed four deep knee bends and then marked a visual analog scale to indicate the current intensity of pain and discomfort in the quadriceps muscle. In addition, each subject's eccentric quadriceps muscle torque was measured on the 3rd and 5th days of the study (48 and 96 hours after exercise, respectively).

Statistical Analysis

The pain data were analyzed by means of a two-factor mixed design ([4 × 6] and [3 × 6], respectively, group by time [the six time points after exercise at which tests were performed]) analysis of variance (ANOVA) with repeated measures on the time factor. The quadriceps muscle torque data were analyzed by a two-factor ([4 × 4] and [3 × 4], respectively, group by time) ANOVA with repeated measures on the time factor. Comparisons were made according to preplanned contrasts. The threshold for statistical significance level was set at $P < 0.05$.

RESULTS

Phase 1 Data

There were no significant differences between groups in the pain scores over time (Fig. 1).

The total recovery of torque between the HBO group and the other three groups combined (sham, control, and delayed-HBO groups) were compared from the first postexercise value to the 96-hour postexercise value with a one-way ANOVA. The three groups were combined and compared with the HBO group alone to take advantage of the statistical process of linear combination of groups in a post hoc comparison. The group effect suggested a pattern toward increased recovery of eccentric torque ($P = 0.083$) (Fig. 2).

Recovery torque for the HBO group (69.2 N·m increase) was compared with the sham-treatment, delayed-HBO, and control groups (49.6 N·m, 44.9 N·m, and 47.3 N·m increase, respectively). This linear-combination post hoc test was performed to compare the like groups (the ones that did not receive HBO treatments during the first 2 days) with the HBO group. This post hoc test revealed a significant difference between the HBO group and each of the three other groups ($P = 0.021$) for the recovery of eccentric torque from immediately after exercise to 96 hours after exercise (Fig. 3).

Phase 2 Data

There were no significant differences between groups in the pain scores over time. A striking component of the pain data was the variability in the scores indicated on the visual analog scale, which is reflected in the elevated standard deviations relative to the mean (Fig. 4). This may be related to the differences in quadriceps muscle conditioning between the subjects. The eccentric torque data conveyed a different pattern.

Analysis of the phase 2 mean torque data mirrored the pain data, as no significant differences between groups existed except for a significant interaction effect of the group by time effect ($P = 0.025$). Post hoc contrasts were conducted on these data based on the significant interaction to identify which groups were significantly different from one another and at which time periods (to pinpoint exactly what accounted for differences).

When comparing the mean torque for the sham and 5-day HBO groups, a significant difference ($P = 0.023$) was detected at the final test of eccentric quadriceps torque (Fig. 5). The 5-day HBO group had a value of 191.9 N·m, while the sham group had an average of 156.6 N·m. There were no other significant differences noted between individual groups or at any of the other testing periods.

When total eccentric torque recovery was analyzed in a one-way ANOVA, significant differences existed between the groups ($P = 0.014$; 54.9 N·m [5-day], 16.0 N·m [3-day], and 4.3 N·m [sham] change). The 5-day HBO group had significantly improved eccentric torque compared with the sham group ($P = 0.005$). We were surprised to find that

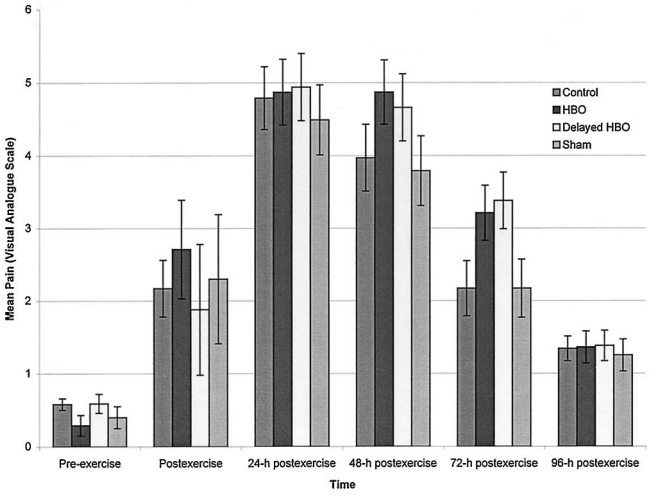

Figure 1. Mean (±SEM) pain values by experimental group and time in phase 1.

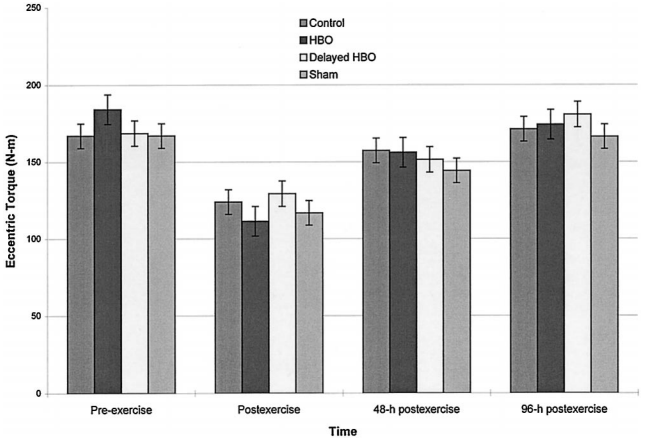

Figure 2. Mean (±SEM) eccentric torque by experimental group and time in phase 1.

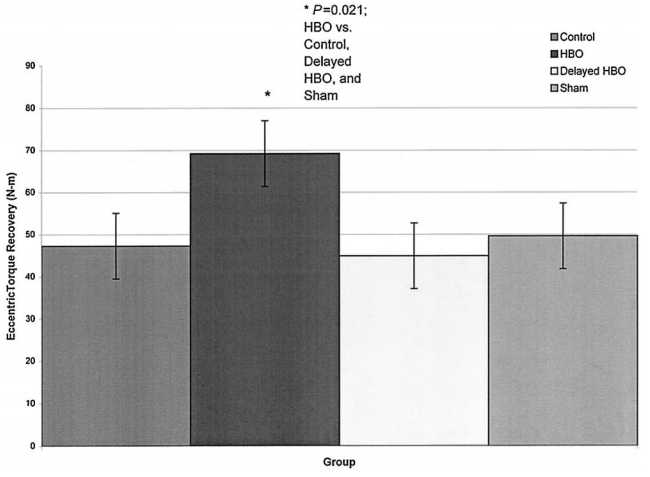

Figure 3. Mean (±SEM) eccentric torque recovery by experimental group and time in phase 1. Torque recovery equals 96-hour postexercise torque minus immediately postexercise torque.

the 5-day HBO group was also significantly different from the 3-day HBO group (Fig. 6).

DISCUSSION

Pain

We hypothesized that pain could be reduced by HBO exposure. The results of this study suggest otherwise. Pain was not significantly affected by exposure to HBO, delayed exposure to HBO, or simply by being in the HBO chamber (placebo effect). Investigators who have observed the effect of HBO on plasma levels of adrenocorticotrophic hormone (ACTH) and β-endorphins have reported significant early increases (after one treatment) and after 5 days of intermittent treatment.[4,23] These studies, however, used a higher pressure (2.8 atm) for their treatments than was used in this experiment. The lack of relief of delayed-onset muscle soreness has been noted in other studies using different modalities (ultrasound, antiinflammatory medications, massage).[13,16,20]

A possible explanation for the lack of significant differences in pain data was that the stimulus in this study did not cause significant damage. Muscle biopsies could have been used to morphologically compare groups. However, since the damage to the muscle tends to be concentrated closer to the musculotendinous junction, and biopsies are normally taken from the muscle belly, the chances of finding damaged muscle tissue in the muscle belly have been compared with "finding a needle in a haystack."[8]

To answer succinctly whether HBO provides effective pain relief, another study should be attempted with pain and pain relief as the only variables. Perhaps objective variables like the levels of stress or pain-related markers would be more sensitive to detect changes attributable to treatment.

Eccentric Quadriceps Muscle Torque

The reason for monitoring eccentric torque was to determine whether subjects would more fully recover with 2 more days of HBO treatment. Unlike the pain data, the statistical analysis of the mean torque data documented some significant results. However, to state that the torque data provide a resounding demonstration of the efficacy of HBO would be misleading.

Several studies observing torque recovery after exercise have found that eccentric torque does not return to normal over the time period being studied, normally the first 48 hours.[6,8–10,17,20] Subjects in this study experienced a gradual return of torque over 5 days. In studies by Friden et al.[10] and MacIntyre et al.,[17] where eccentric torque was measured for longer than 2 days, the torque measurements did not return to baseline (peak) performance for 6 and 7 days, respectively. By not testing on all 5 days, however, significant changes, especially the increase in torque noted in the first 24 hours after exercise, may have been missed.[17] The most notable difference between the data presented in this study and the MacIntyre data was in the recovery phase from 48 hours to the end of the

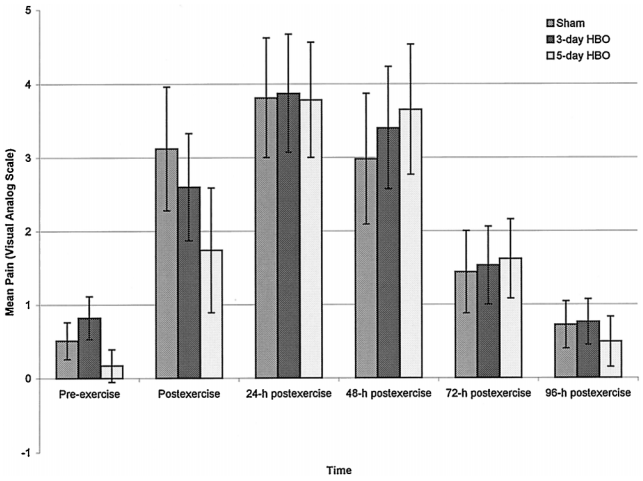

Figure 4. Mean (±SEM) pain values by experimental group and time in phase 2.

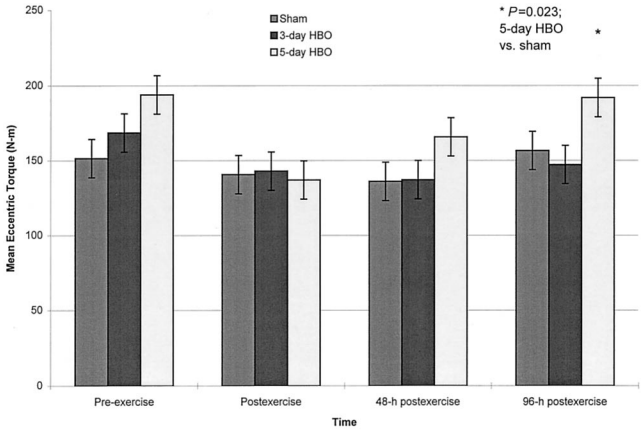

Figure 5. Mean (±SEM) eccentric torque by experimental group and time in phase 2.

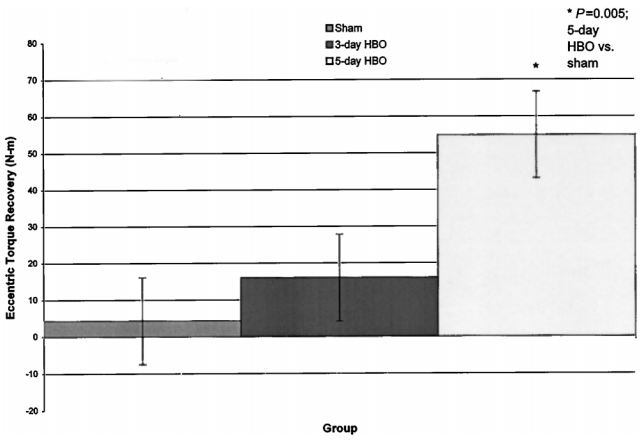

Figure 6. Mean (±SEM) eccentric torque recovery by experimental group in phase 2. Torque recovery equals 96-hour postexercise torque minus immediately postexercise torque.

study. The subjects in the MacIntyre study did not recover their peak eccentric torque in 5, and in some cases, 7 days, whereas in our study the subjects had completely recovered their peak torque in both phases.

There were no significant differences in mean torque in phase 1. By contrast, there was a significant difference between the sham and 5-day HBO group at 5 days in phase 2. The significant interaction verified a difference between the treated and untreated groups over time. As part of preselected contrasts, the difference between the sham and 5-day groups at the final torque measurement (96 hours after exercise) led us to find that the recovery of eccentric torque for the 5-day treatment group was significantly greater than that for the sham group. This comparison was important because of nonsignificant differences in recovery of eccentric torque between the other groups. We concluded that recovery over 96 hours was enhanced at least in part by exposure to 5 days of HBO therapy. The scope of this finding is limited to the comparison of the sham and 5-day HBO groups.

A problem with the phase 2 mean torque data was the inconsistency of torque recovery. The data for the 3-day HBO subjects more closely resembled the data for the sham group than that of the 5-day HBO group. In theory, given the same number of HBO treatments for the HBO groups over the first 3 days, the subjects in each group should have reacted in a similar manner. This result was inconsistent with the significant difference noted between the sham and 5-day HBO groups. A learning effect may have occurred because subjects with 300 repetitions of practice acquired better coordination and a more refined motor program for the novel task. However, this alone does not explain the 3-day HBO group's results of torque recovery and remains a concern in the validity of the interpretation of the 5-day HBO group.

The strength outcomes in this study may be related to the timely application of HBO. In previous HBO studies in burn therapy,[5] spinal cord injuries,[24] and reperfusion of ischemic skeletal muscle,[26] the most beneficial results occurred when HBO treatments were commenced in the first 8 hours after injury. In this study, since subjects in this protocol began their treatments no later than 20 minutes after exercise, they received HBO well within the time limit for effective treatment.

A review by Smith[22] suggests that similarities in pain, swelling, and loss of function in acute inflammation and delayed-onset muscle soreness are due to a general response of the body to a stressful or traumatic insult. That is, since the body responds to all forms of tissue injury by activating the inflammatory response, it is unlikely that a separate response has evolved to deal with injury incurred by unaccustomed eccentrically biased exercise. Of course, an acute but otherwise normal injury does not accumulate the same degree of damage as does a chronic injury. Moreover, to imply that the neutralizing effect of HBO on oxygen free radicals is the only mechanism at work would be misleading and probably erroneous. A combination of the edema-reducing properties of HBO,[21] reduced neutrophil adhesion to injured muscle cells,[27] and free-radical-quenching ability of HBO[12] may explain the beneficial

effects noted in these studies, but further research needs to be conducted.

Future Directions

To elucidate the underlying mechanism of HBO in humans, further research should examine objective biochemical markers such as malondialdehyde as a measure of lipid peroxidation (oxygen free radical damage) and muscle myeloperoxidase from muscle biopsies to measure the inflammatory response. Researchers should consider using radioactive markers to perform 24-hour serial measurements of white blood cells in the exercised muscle, before and after HBO exposure.[17] Observing the biochemical markers as well as indices for collagen synthesis and polyamines may help ascertain whether the benefits of HBO stem from a reduction in the inflammation caused by the initial injury or an actual enhancement of the healing capacity of the body. If future studies prove fruitful, sports medicine and rehabilitation practitioners will have a powerful new modality with which to heal muscle injury more expeditiously and, in the end, more cost effectively.

CONCLUSION

Pain is not influenced by exposure to HBO at 2 atm for 3 to 5 days after eccentric-exercise-induced delayed-onset muscle soreness. Exposure to 1 hour of HBO treatment initiated within 20 minutes after exercise for 3 to 5 days enhances muscle torque recovery.

ACKNOWLEDGMENTS

The authors thank OxyMed Systems, Inc. (Vancouver, British Columbia, Canada [no longer exists]) for financial assistance in this project and HYOX Systems, Inc., for the use of the monoplace hyperbaric chamber.

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