Lou Gehrig's Disease, ALS

Hyperbaric oxygen therapy protects against mitochondrial dysfunction and delays onset of motor neuron disease in Wobbler mice.

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The Wobbler mouse is a model of human motor neuron disease. Recently we reported the impairment of mitochondrial complex IV in Wobbler mouse CNS, including motor cortex and spinal cord. The present study was designed to test the effect of hyperbaric oxygen therapy (HBOT) on (1) mitochondrial functions in young Wobbler mice, and (2) the onset and progression of the disease with aging. HBOT was carried out at 2 atmospheres absolute (2 ATA) oxygen for 1 h/day for 30 days. Control groups consisted of both untreated Wobbler mice and non-diseased Wobbler mice. The rate of respiration for complex IV in mitochondria isolated from motor cortex was improved by 40% ($P<0.05$) after HBOT. The onset and progression of the disease in the Wobbler mice was studied using litters of pups from proven heterozygous breeding pairs, which were treated from birth with 2 ATA HBOT for 1 h/day 6 days a week for the animals' lifetime. A "blinded" observer examined the onset and progression of the Wobbler phenotype, including walking capabilities ranging from normal walking to jaw walking (unable to use forepaws), and the paw condition (from normal to curled wrists and forelimb fixed to the chest). These data indicate that the onset of disease in untreated Wobbler mice averaged 36+/-4.3 days in terms of walking and 40+/-5.7 days in terms of paw condition. HBOT significantly delayed ($P<0.001$ for both paw condition and walking) the onset of disease to 59+/-8.2 days (in terms of walking) and 63+/-7.6 days (in terms of paw condition). Our data suggest that HBOT significantly ameliorates mitochondrial dysfunction in the motor cortex and spinal cord and greatly delays the onset of the disease in an animal model of motor neuron disease.

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A Phase I safety study of hyperbaric oxygen therapy for amyotrophic lateral sclerosis.

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BACKGROUND: Vascular endothelial growth factor and mitochondrial abnormalities have been described in ALS and its animal models. We have reported that hyperbaric oxygen (HBO) treatment delayed the onset of weakness in the wobbler mouse. OBJECTIVE: To perform a Phase I safety study of HBO in patients with ALS. METHODS: Five patients with ALS were treated for 60min with 100% oxygen at 2 atmospheres pressure daily for five days a week for four weeks. The patients reported any deterioration in their condition after each treatment, and their neurological condition was measured serially during the four weeks of the treatment, and for four further weeks. RESULTS: Four patients reported decreased fatigue, while one patient dropped out at three weeks because of increased fatigue. Maximum isometric voluntary contraction (MVIC) of all muscle groups except right hand grip improved significantly by up to 97%. Most improvement occurred during the four weeks after treatment. It is possible that the improvement in muscle strength was a placebo or a learning effect, though no such effects have been detected in prior therapeutic trials in ALS using MVIC. No change was detected in other measures of neuromuscular function.