HYPERBARIC OXYGEN TREATMENT ON A PARKINSON'S DISEASE PATIENT: A CASE STUDY

Hoggard ML, Johnson KE and Shirachi DY.
Chico Hyperbaric Center, Chico, CA 95926 and Department of Physiology and Pharmacology, T. J. Long School of Pharmacy, University of the Pacific, Stockton, CA 95207, USA.

INTRODUCTION

Parkinson's Disease (PD) is a chronic neurodegenerative disorder, which is characterized by the loss of dopaminergic neurons whose cell bodies are located in the substantia nigra pars compacta (SNpc) and project to the striatum. The initiation of this neuronal degeneration is not known, however the process of neuronal loss is suggested to occur via apoptosis rather than by necrosis (1). With the onset of the neurodegeneration of these neurons is the associated loss of the neurotransmitter, dopamine (DA), from its nerve endings and its subsequent release in the striatum. The major symptoms which are observed due to the progressive loss in function of the nigro-striatal dopaminergic neurons may be one or more of the following: resting tremor, rigidity, bradykinesia and/or postural instability. The actual clinical manifestation of the disease in any one patient is highly dependent upon the degree of severity of the neuronal loss, age of the patient and the length of time passed between the onset of the symptoms and the time of diagnosis. Early detection is important in order to institute a therapeutic strategy to relieve the symptoms and/or delay the progression of the disease state.

The major treatment strategy currently used is to affect the function of DA. Because systemically administered DA does not cross the blood-brain barrier; Levodopa (pro drug) is administered, which is taken up into the brain. Since Levodopa is metabolized both peripherally and centrally to DA by a DOPA decarboxylase, carbidopa an inhibitor of this enzyme is administered in combination with Levodopa to decrease its metabolism peripherally increasing its uptake into the brain. DA agonists and monamine oxidase-B (MAO-B) inhibitors are also administered as a monotherapy or as an adjunct to Levodopa-carbidopa (Sinemet) therapy, depending upon the clinical condition.

Taking a very different approach in the treatment of PD, Borromei et al. in 1996 showed that hyperbaric oxygen (HBO) therapy appeared to be effective in ameliorating many of the behavioral and motor deficits observed in PD patients (2). The objective of this study was to determine whether HBO therapy might enhance the effects of an antiparkinson treatment in a PD patient as an adjunct therapeutic modality.

METHODS

Brief patient history: A 72 year old male was diagnosed with idiopathic PD and placed on Sinemet (10/100) three doses 3 times daily. One year after diagnosis for PD the patient was diagnosed with total occlusion of the right coronary artery. A successful total occlusion angioplasty was performed and he was placed on Lopressor and Lipitor 10 mg daily. There were no complications from this surgical procedure. Eighteen months after being diagnosed as a PD patient he was treated with hyperbaric oxygen (HBO) at 1.9 ATA for 90 min. The patient was treated daily 5 times each week for 5 weeks (25 treatments). During the treatment the patient gradually reduced his dose of Sinemet until he was completely off of this medication between the 3rd and 4th week of HBO treatment. At this point his physician placed him on selegiline 10mg twice daily.

Clinical testing: The patient's voice and speech were evaluated by a speech-language pathologist, and the Jebsen-Taylor hand function test was performed by an occupational therapist prior to and after the end of the HBO therapy. The patient was informed of all aspects of hyperbaric oxygen therapy, including all risks of adverse effects according to the Declaration of

Helsinki. The patient also signed an informed consent form detailing the treatment and the rights of the patient.

RESULTS

Voice and speech. There was little change in the overall evaluation of voice and speech after HBO therapy. Communication status changed very little. He appeared to be talking more and his rate was somewhat improved. He still had difficulty projecting his voice.

Jebsen-Taylor Hand Function Test. The results of this test are shown in Table 1. In testing the dominant hand there were small increments of improvement after HBO. The total improvement was more than 10%, while the improvement in the non-dominant hand was nearly 32%.

During the treatment period, the patient voluntarily reduced his Sinemet doses until he was completely off the drug after 3-4 weeks of HBO therapy, which was an unexpected result. He has continued to remain off of Sinemet therapy. No complications or adverse side effects such as myopia were observed. The long-term exposure of HBO was tolerated well by the patient.

DISCUSSION

PD is characterized by the loss of dopaminergic neurons of the nigro-striatal pathway. It is not clear how this neuronal degeneration is initiated, but there appears to be a number of potential ways in which this might occur in any one individual, including genetics, disease, drugs or other chemicals, oxidative stress and/or other environmental factors. However, once it is initiated there seems to be agreement that the degenerative process involves apoptosis and not necrosis.

The results of this study suggest that HBO might be a possible new modality of treatment for PD because it appeared to be able to replace Sinemet as a therapeutic regimen. The mechanism by which the HBO effect might be occurring may be partly due to an anti-apoptotic effect. It has been shown that HBO increased the expression of Bcl-2 protein, a major anti-apoptotic protein, in treating forebrain cerebral ischemia in gerbils (3). The Bcl-2 protein has also been elevated by repeated HBO treatment in normal gerbils (4). So it is possible that HBO in this study inhibited the apoptotic pathway involved in the progressive neuronal degeneration by stimulating the expression of the Bcl-2 proteins.

Other possible HBO effects should not be discounted such as improved oxygen perfusion due to increased extravascular oxygen diffusion and to possible angiogenesis (5). Axonal repair and regeneration and/or synaptogenesis could occur due to increased expression of neurotrophin(s), since HBO has been shown to increase vascular endothelial growth factor (6) and act synergistically with platelet derived growth factor and transforming growth factor-beta (7).

The results of this case study agree with much of the results observed in the clinical study by Borromei and his coworkers. It is not clear from their study whether some of their patients were concurrently being treated with anti-parkinson drugs. In our study, HBO replaced the Sinemet therapy and appeared to improve the clinical condition. Thus, results from this case study suggest that HBO therapy might be a potential therapeutic modality in treating patients suffering from PD without causing untoward side effects such as dyskinesia observed in long-term Sinemet therapy.

In conclusion, we suggest that HBO therapy might be neuroprotective in nature to the nigro-striatal neurons by acting as an antiapoptotic process. This could stabilize neuronal function, thereby potentially decreasing the progression of the neurodegeneration observed in Parkinson’s Disease.

REFERENCES

1. Thatte U and Dahanukar S. Apoptosis: clinical relevance and pharmacological manipulation. Drugs. 1997; 54(4): 511-532.
2. Borromei A. OTI efficiency in decompensated-complicated Parkinson's Disease. In: Proceedings of the International Joint Meeting on Hyperbaric and Underwater Medicine. Marroni A, Oriani G and Wattel F, eds. XII International Congress on Hyperbaric Medicine. Milano, Italy. 1996, pp 599-604.
3. Zhou J-G, Liu J-C and Fang Y-Q. Effect of hyperbaric oxygen on the expression of proteins Bcl-2 and Bax in the gerbil hippocampus CA1 following forebrain ischemia reperfusion. Chin J Appl Physiol. 2000; 16(4): 298-301.
4. Wada K, Miyazawa T, Nomura N, Yano A, Tsuzuki N, Nawashiro H and Shima K. Mn-SOD and Bcl-2 expression after repeated hyperbaric oxygen. Acta Neurochir. 2000 (Suppl) 76: 285-290.
5. Marx RE. Radiation injury to tissue. In: Kindwall EP, (Ed) Hyperbaric Medicine Practice. Best Publishing Co. Flagstaff, AZ. 1995:450-455.
6. Sheikh AY, Gibson JJ, Rollins MD, Hopf HW, Hussain Z and Hunt TK. Effect of hyperoxia on vascular growth factor levels in a wound model. Arch Surg. 2000; 135(11): 1293-97.
7. Zhao LL, Davidson JD, Wee SC, Roth SI and Mustoe TA. Effect of hyperbaric oxygen and growth factors on rabbit ear ischemic ulcers. Arch Surg. 1994; 129(10): 1043-9.

Table 1. Jebsen-Taylor Hand Function Test.

Clinical Testing : Time (in sec)	**Pre-HBO**	**Post-HBO**
Dominant Hand		
Writing	14	12
Card Turning	7	6
Manipulating Small Objects	11	11
Simulated Feeding	11	10
Stacking Small Objects	8	5
Lifting Large Light Objects	11	10
Lifting Large Heavy Objects	8	6
Total	**70**	**60**
Non Dominant Hand		
Writing	41	28
Card Turning	8	4
Manipulating Small Objects	11	7
Simulated Feeding	12	12
Stacking Small Objects	13	8
Lifting Large Light Objects	9	6
Lifting Large Heavy Objects	7	5
Total	**101**	**70**