Stroke and Hyperbaric Oxygen

Improvement of memory impairments in poststroke patients by hyperbaric oxygen therapy.

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Several recent studies have shown that hyperbaric oxygen (HBO_2) therapy carry cognitive and motor therapeutic effects for patients with acquired brain injuries. The goal of this study was to address the specific effects of HBO_2 on memory impairments after stroke at late chronic stages.

A retrospective analysis was conducted on data of 91 stroke patients 18 years or older (mean age ~60 years) who had either ischemic or hemorrhagic stroke 3-180 months before HBO_2 therapy (M = 30-35 months). The HBO_2 protocol included 40 to 60 daily sessions, 5 days per week, 90 min each, 100% oxygen at 2ATA, and memory tests were administered before and after HBO_2 therapy using NeuroTrax's computerized testing battery. Assessments were based on verbal or nonverbal, immediate or delayed memory measures. The cognitive tests were compared with changes in the brain metabolic state measured by single-photon emission computed tomography.

Results revealed statistically significant improvements ($p < .0005$, effect sizes medium to large) in all memory measures after HBO_2 treatments. The clinical improvements were well correlated with improvement in brain metabolism, mainly in temporal areas.

Although further research is needed, the results illustrate the potential of HBO_2 for improving memory impairments in post stroke patients, even years after the acute event.

"Assessment of the Efficiency of Hyperbaric Oxygenation Therapy in Early Forms of Cerebrovascular Disorders."

Akimov, G.A. et al.

NEUROSCI BEHAV PHYS, l985; 15: 13 - 16.

We present results of the assessment of the efficiency of hyperbaric oxygenation therapy in 104 patients with cerebrovascular diseases. Of these patients, 32 had chronic cerebrovascular insufficiency and 72 showed transient disturbances of the cerebral circulation. A good effect was noted in 74 patients, a satisfactory one in 22, and a doubtful one in 8 patients. It is concluded from clinical, electro-physiological, psychophysiological, biochemical, and ophthalmoscopic examinations that hyperbaric oxygenation therapy is quite efficient when used as part of a combined therapy and as a means of prompt therapy of acute cerebrovascular crises. Observations over three to five years of patients repeatedly receiving the hyperbaric oxygenation therapy at 6 month intervals allows us to recommend it for the prevention of cerebral strokes.

"Hyperbaric oxygen therapy (HBO) after acute focal cerebral ischemia."

Berrouschot, J. et al.

NERVENARZT, 1998, 69(12): 1037-44.

For a large number of patients with stroke, no therapeutic option can be offered, even after approval of thrombolytic therapy for treatment of acute ischemic stroke in the U.S. In cerebral ischemia local anoxia and energy failure lead to further cellular damage and finally to complete stroke. All therapeutic concepts try to salvage structurally intact tissue which is at risk for irreversible damage (so-called penumbra). Hyperbaric oxygen (HBO) treatment has been reported in animal models of cerebral ischemia, and in a few clinical reports. In general, the results of these studies have been promising.

Undersea Hyperb Med. 2011 Sep-Oct;38(5):375-9.

Improvement of clinical outcome and cerebral perfusion in a patient of atherosclerotic cerebral infarction after repetitive hyperbaric oxygen treatment--a case report and literature review.

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This is a case report of hyperbaric oxygen therapy (HBO2T) for ischemic stroke. HBO2T should be the potential or additional treatment (with thrombolytic therapy) for ischemic stroke according to the preclinical and clinical studies. Hereby, we present a 56-year-old Chinese man with vascular risk factors. He had an acute ischemic stroke on the left corona radiata, with right hemiparesis and dysarthria resulting from atherosclerosis. The patient could not get thrombolytic treatment because the time to ER was in excess of five hours. He experienced great improvement after the general course of HBO2T; this was evaluated with standard rating scales for stroke research and cerebral perfusion images, including brain-computed tomography perfusion (CTP) and single-photon emission computed tomography (SPECT). Although few clinical trials showed a negative result, we suggest that further trials on HBO2T are still needed. Meanwhile, we emphasize the importance of HBO2T protocol and the selection of a suitable patient, which may influence the outcome.

"The Treatment of Cerebral Ischemia with Hyperbaric Oxygen (OHP)."

Hart, G.B. et al.

STROKE, l971; 2: 247-250.

The treatment of a patient for three and one-half months, following occlusion of the right middle cerebral artery with the associated neurological sequelae, with hyperbaric oxygen combined with methyldopa and hydrochlorthazide is presented. Treatment scheduled was two and one-half atmospheres absolute. The treatment was interrupted after 15 treatments to rule out spontaneous remission for a period of 30 days, and no further improvement occurred until treatments were reinstituted. The dramatic return to a near normal state during treatment appears to indicate that he did benefit from therapy.

"Neurological and EEG Analytical Findings in the Treatment of Cerebral Infarction with Repetitive Hyperbaric Oxygenation."

Holbach, K. H. et al.

PROCEEDINGS OF THE SIXTH INTERNATIONAL CONGRESS ON HYPERBARIC MEDICINE, Aug. 31 - Sept. 2, l979, University of Aberdeen, Aberdeen, Scotland, pp. 205-210; George Smith DSC, MD (Ed), Aberdeen University Press, l979.

These findings indicate that unilateral occlusion or stenosis of the internal carotid or middle cerebral artery can lead to distinct focal neurological deficits and EEG alterations as well as to bilateral reduction of cerebral function and EGA (electrical brain activity). It also appears that such ischemic alterations of the brain can be improved by HBO therapy not only in the acute but also in the chronic post-stroke stage. Accordingly, we feel that this mode of treatment may be considered as an additional measure in the management of stroke."

"Advantage of Using Hyperbaric Oxygenation (HO) in Combination with Extra-Intracranial Arterial Bypass (EIAB) in the Treatment of Completed Stroke."

Holbach, K. H. et al.

ACTA NEUROCHIRUGICA, Suppl 28: 309; l979.

"...The evaluation of the effect of HO treatment on post-stroke alterations of the brain can be helpful in differentiating between reversible and irreversible changes, and thus response to HBO treatment may be used as a criterion for the prognosis of the cerebrovascular lesion and also for selection of patients for EIAB surgery."

"Differentiation between Reversible and Irreversible Post-Stroke Changes in Brain Tissue: Its Relevance for Cerebrovascular Surgery."

Holbach, K.H. et al.

SURG. NEUROL., l977; 7: 325-331.

Thirty-five selected patients with chronic stroke were studied. They had internal carotid occlusion with considerable neurological deficit persisting for an average of ten weeks. First, hyperbaric oxygen treatment was administered to each patient. Subsequently extra-intracranial anastomosis operations were performed on 20 of these patients. These patients were divided into three groups. Group 1 - 15 of the 35 patients - showed a significant improvement of cerebral function at the conclusion of the hyperbaric oxygen treatment. Subsequently an extra-intracranial anastomosis operation was carried out on each patient resulting in considerable further recovery of cerebral functions. Group II consisted of 15 patients who showed only little change in neurological deficit at the conclusion of hyperbaric oxygen therapy. Extra-intracranial anastomosis operations were not carried out in Group II. Group III consisted of five patients with little or no change at the conclusion of hyperbaric oxygen treatment. Subsequent extra-intracranial anastomosis operations were, however, performed in these five patients. Although post-operative angiography revealed considerable filling of the affected middle cerebral territory by the new collateral channel, there was little change in their status. These findings suggest that in the chronic post-stroke stage a) hyperbaric oxygen therapy can improve ischemic alterations of the brain, b) it may be helpful in differentiating between reversible and irreversible alterations of brain tissue, c) extra-intracranial anastomosis may result in additional recovery of impaired neurological functions in those patients who have shown significant improvement from hyperbaric oxygen therapy and d) response to hyperbaric oxygenation may be used as a criteria for selection of patients for cerebral revascularization procedures.

"Reversibility of the Chronic Post-Stroke State."

Holbach, K.H. et al.

STROKE, l976; 7(3): 296-300.

Forty patients with cerebral infarction associated with occlusion of the internal carotid artery (ICA) or the middle cerebral artery (MCA) were treated with hyperbaric oxygenation (HO). EEG analysis were performed regularly in order to assess the course of the cerebral lesion. Patients in an early post-stroke stage (IIIB) and

patients in a chronic post-stroke stage (IV) had the changes in EEG analysis and neurological findings distributed evenly between these two groups.

In 27% of the cases, the improvement was considerable, 53% had moderate improvement, and 20% showed no change of condition. The improvement mainly consisted of an increase in alpha-wave and beta-wave activity over the affected brain region. We were able to show this fact clearly by means of the EEG-analysis-system applied. The results show that (a) hyperbaric oxygenation therapy (HOT) has a very favorable influence upon the course of disease, and (b) simultaneous application of HOT and EEG analysis allows for a differentiation between reversible and irreversible post-stroke changes in brain tissue.

"Treatment of Focal Cerebral Ischemia with Hyperbaric Oxygen."

Ingvar, David et al.

ACTA NEUROL. SCANDINAV., l965; 41: 92-95.

Four cases of focal ischemia were treated with inhalation of pure oxygen at a pressure of 2.0 to 2.5 atmospheres ("hyperbaric oxygen") for periods of 1.5 to 2.5 hours. In three of the cases beneficient effects of the treatment were seen which in two of them could be objectively demonstrated in the EEG. In one case with progressive ischemic lesions of the brain stem, treated sub finem, very dramatic effects were seen, which were probably to a great extent due to the effects of the treatment upon the failing systemic circulation.

"Chapter 17: Role of Hyperbaric Oxygen Therapy in the Management of Stroke."

Jain, K. K. pp. 227 - 252; in TEXTBOOK OF HYPERBARIC MEDICINE, Hogrefe & Huber Publishers, Lewiston, NY, l990.

"HBO therapy should be started in the acute phase of a stroke as an adjunct to conventional medical management. Rehabilitation of stroke patients should also be planned during the first few months following stroke. Long-term follow-up studies are required to determine whether such measures would reduce the chronic disability from stroke and reduce the incidence of severe spasticity in stroke patients. The use of HBO may also reduce the need for some surgical procedures…Animal experimental studies and uncontrolled human trials have shown the effectiveness and safety of HBO therapy after strokes. At the Fachklinik Klausenbach (FRG) simultaneous HBO and physical therapies were used in the rehabilitation of stroke patients. Objective evaluation of patients during the HBO session showed a 100% response rate (improvement of spasticity or motor power or both). The improvement was initially transient but could be maintained, following a course of daily treatments (1.5 ATA for 45 min.) for 6 weeks, in most of the cases…with the evidence available, it would unethical to carry out randomized double-blind studies in stroke patients to evaluate the effect of HBO therapy…"

"Hyperbaric Oxygen Therapy in the Rehabilitation of Stroke Patients."

Jain, K.K. et al.

2nd EUROPEAN CONFERENCE ON HYPERBARIC MEDICINE, l990; Organized by the

Foundation for Hyperbaric Medicine in Basel and the Department of Surgery of the University Clinic in Basil.

A 100% response rate was demonstrated in 25 patients in sub-acute and chronic post-stroke stage. In spite of medical management and physical therapy, these patients had shown no day-to-day changes in their neurological status. Increase of motor power of the paralyzed hand was demonstrated by a dynamometer. The improvement was transient initially but was maintained following a course of daily treatments (1.5 ATA for 45

min.) for 6 weeks in most of the cases. There was also a significant reduction of spasticity during HBO treatment and this relief could be extended by instituting physical therapy in the chamber. In conclusion, we feel that HBO is a useful adjunctive treatment in the rehabilitation of stroke patients.

"Effect of Hyperbaric Oxygenation on Spasticity in Stroke Patients."

Jain, K. K.,

J Hyperbaric Med, l989; 4(2): 55-61.

The effect of hyperbaric oxygenation (HBO) at 1.5 ATA on spasticity of stroke was observed in 21 patients undergoing rehabilitation. The patients served as their own controls. HBO reduced spasticity in all the patients, an effect that was more marked than that of physical therapy, hyperbaric air, or 100% normobaric air. Initially the effect was transient and subsided within 24 h after treatment, but by conducting physical therapy simultaneously with daily, 45 min HBO sessions, lasting results were achieved after 5 wks and could be maintained by physical therapy alone during the follow-up, which varied from 6 mo. to 1 yr. The exact mechanism of relief of spasticity is not known but it is probably due to improvement of the function of neurons in the penumbra zone of the cerebral hemisphere affected by stroke. This concept is supported by documented improvement of cerebral metabolism, EEG, rCBF, and motor function in stroke patients after HBO therapy. From the available evidence, HBO is considered to be an invaluable adjunct in the rehabilitation of stroke patients with spastic hemiplegia. Although the effects were documented in the paralyzed limbs, spasticity improved in other groups of muscles as well.

"Neurological Response to Hyperbaric Oxygen - A Criterion for Cerebral Revascularization."

Kapp, John.

SURGICAL NEUROLOGY, l981; 15(1): 43-46.

Twenty-two patients with cerebral infarction secondary to occlusion of a carotid or middle cerebral artery were exposed to hyperbaric oxygen at 1.5 atmospheres absolute pressure. Ten of the patients demonstrated improved motor function during hyperbaric exposure. Seven of these patients had successful surgical revascularization and no recurrence of neurological deficit. In 3 patients who were not successfully revascularized, the neurological deficit recurred. It is concluded that response to hyperbaric oxygen may be of use in the selection of patients with neurological deficit who will benefit from surgical revascularization of the brain.

"Effect of Hyperbaric Oxygenation on the Clinical Course and Complications of the Acute Period of Ischemic Stroke."

Lebedev, V.V., et al.

ZHURNAL VOPR NEIROKHIRNRY, l983; 3: 37-42.

Hyperbaric oxygenation (HBO) was included in the therapeutic complex for 124 patients in the acute stage of ischemic stroke. The effect of HBO on the clinical course was appraised by comparing the dynamics of changes in the clinical symptoms and the frequency of complications in patients exposed to HBO with those in the control group (patients not exposed to HBO). It was established that the depth of unconsciousness and the motor and aphasic disorders decreased during an HBO session, but the effect was usually short-lived. Aggravation of the patients' condition in the first week of the disease, evidently caused by increase of cerebral edema, occurred much less frequently when HBO was included in the complex of therapeutic measures. The number of patients with regression of the neurological symptoms was practically the same with and without the use of HBO, but the regression of the neurological defects was most evident in patients exposed to HBO. HBO prevents the

development of recurrent cerebral circulatory disorders in the acute stage of ischemic stroke and reduces the incidence of some complications in this period (pneumonia, pulmonary edema, thromboembolism of the pulmonary artery, etc).

"Hyperbaric Oxygen Therapy at 1.5 or 2.0 ATA as an Adjunct to the Rehabilitation of Stabilized Stroke Patients. A Controlled Study."

Marroni, A. et al.

PROCEEDINGS OF THE 9th INTERNATIONAL CONGRESS ON HYPERBARIC MEDICINE,

March 1-4, l987; Sydney, Australia, pp. 161-167.

HBO Therapy has been studied by many authors as an adjunctive treatment for stroke patients. Satisfactory results have been reported for the use of HBO as a predictive tool for EC-IC revascularization. The questions of the appropriate treatment pressure has been debated in the literature.

We studied a group of 80 well stabilized cerebral thrombosis patients not any more undergoing any form of treatment or care. Average age was 59.7 yrs., average stroke age 29.2 months. The patients were divided into 8 groups: A: control group not undergoing any care; B: in water rehabilitation, 30 sessions, no HBO; C1: 30 HBO sessions at 2.0 ATA; C2: same at 1.5 ATA; D1: HBO at 2 ATA plus rehabilitation as above; D2: same at 1.5 ATA; E1: HBO and simultaneous rehabilitation in our specially built Hyperbaric pool at 2 ATA; E2: same at 1.5 ATA.

The Rehabilitation protocol was originally developed at our Center as well as a quantitized and repeatable Neuromotor Disability Evaluation Scale. Patients were controlled prior to beginning, every 10 days during treatment, then 1 and 3 months after.

Obtained data show defined and similar HBO effects on the improvement of patients' performance at 1.5 and 2.0 ATA, a clear and significant potentiation of this effect being evident for the Hyperbaric Rehabilitation groups and especially for the group treated at 2.0 ATA. The obtained results were still present at the third month after treatment.

"Hyperbaric Oxygen and Imaging Techniques in Diagnosis and Therapy of Stroke. Does the Ischemic Penumbra Alter the Outcome in Stroke?"

Neubauer, R.A. et al.

INTERNATIONAL SYMPOSIUM: NEUROPSYCHOMOTOR, NEURO-PHARMACOLOGICAL, PSYCHOSOCIAL AND ETHICAL ASPECTS, Oct. 7-11, l992;

Siracusa, Italy. pp. 1-9.

Recovery from stroke (a global phenomena) and predictability of outcome may be directly related not only to tissue damage, but also the ischemic penumbra or surrounding zone of idling neurons. The local and global effects of stroke are well known. Actual recovery or evolution in the neuronal tissue may go on for months. All events related to recovery have yet to be elucidated. It is known that recovery of ischemic or hypoxic tissue is more related to the oxygen content than to blood flow. Utilization of Single Photon Emission Computerized Tomography (SPECT) with the radiotracer Iofetamine I123, aids in demonstrating ischemic penumbras (reperfusion amplitudes) in strokes, thus lending support to the work of Symon, Astrup and Holbach. SPECT analysis before and after a single exposure of hyperbaric oxygen at 1.5 ATA for 60 minutes was performed on 15 stroke patients with strokes ranging in time from 6 hours to 15 years. In all of these patients marked changes

in flow and metabolism were seen after hyperbaric intervention, even in cases with neurologic defects present for up to 15 years. This causes speculation as to when stroke is really completed or fully evolved and whether the standard methods of treatment of stroke, and, by extension, all brain injury, encompass the full understanding of the hypoxic or ischemic penumbra. Five cases are presented here: 4 showed varying degrees of improvement associated with a viable halo zone. One patient demonstrated an absent ischemic penumbra. A new protocol combining HBO and surface oxygen will be suggested.

"Enhancing idling neurons."

Neubauer, R. et al.

letter. THE LANCET, March 3, l990; 542.

"After HBO there was a sharp increase in tracer uptake in areas showing hypometabolism on the pre-HBO study...Reduced spasticity, improved ambulation and speech, and cessation of drooling were noted."

"Stroke Treatment."

Neubauer, R. et al.

(letter). THE LANCET, June 29, l991; 1601.

"Hyperbaric oxygen (HBO) efficiently increases the diffusional driving force for oxygen, thereby increasing tissue oxygen availability. This overcomes ischemia/hypoxia and so reduces cerebral edema, restores integrity to the blood/brain barrier and cell membranes, neutralizes toxic amines, promotes phagocytosis, scavenges free radicals, stimulates angiogenesis, and reactivates idling neurons."

"Delayed Metabolism or Reperfusion in Brain Imaging after Exposure to Hyperbaric Oxygenation - A Therapeutic Indicator?"

Neubauer, R. et al.

PROCEEDINGS OF THE XV ANNUAL MEETING OF THE EUROPEAN UNDERSEA

BIOMEDICAL SOCIETY, Sept. 17-21, l989; Eilat, Israel, pp.1-5.

Single Photon Emission Computerized Tomography (SPECT) analysis with Iofetamine I123 was performed in patients with various Central Nervous System (CNS) dysfunctions before and after a single exposure to hyperbaric oxygen (1.5 ATA for 60 minutes) as a guide to potential therapeutic intervention. In CNS disorders current measurements had precluded the identification of idling neurons or the ischemic penumbra, as most techniques involved electrophysiological computerized data. Poorly functioning, yet viable cells, if not electrically active are not identifiable. These cells, however, given the proper oxygen/glucose ratio may return to normal function with dramatic results. Increased Iofetamine I-123 tracer uptake in these ischemic areas (idling neurons) after hyperbaric oxygen therapy probably reflects reactivation of hypometabolic neuronal tissue. Unlike MRI or CT, SPECT reflects regional blood flow as well as grey matter metabolism. The similarity to PET imaging is noteworthy. A variety of patients with central nervous system dysfunction were studied. Reactivation of marginal or idling neurons was seen in many disease entities, the most dramatic being long standing hypoxic encephalopathies. Demonstrative cases will be presented including hypoxic encephalopathy and acute and chronic neurologic deficit of stroke. Reactivation of the idling neuron may be of clinical significance. It is important for the physician to differentiate between viable and non-viable tissue, both from the standpoint of treatment and prognosis.

"Generalized small-vessel stenosis in the brain. A case History of a Patient Treated with Monoplace Hyperbaric Oxygen at 1.5 to 2 ATA."

Neubauer, R.A.

MINERVA MEDICA, l983; 74: 2051-2055.

Complete evaluation of older patients with mental changes always leaves us with a certain percentage whose condition can only be attributed to atherosclerosis. Little is being done for these patients because this generalized stenosis of the brain does not reverse with any known treatment. This writer has treated many such patients with hyperbaric oxygen (HBO), and presents this case history, along with regional cerebral blood flow (rCBF) studies, showing the type of changes which frequently occur. This case initially presented with symptoms of gross mental confusion, memory loss, both recent and remote, irrational speech and occasional violence. Although prior complete evaluations were concluded with no recommended treatment, the initial series of HBO treatment resulted in a well-functioning patient. This was maintained for four years with intermittent HBO. The patient then presented with acute stroke, total disorientation and confusion. He again became functional with HBO. A discussion of the mechanisms of HBO which might account for the changes is given.

"Hyperbaric Oxygenation as an Adjunct Therapy in Strokes Due to Thrombosis."

Neubauer, R.A. et al.

STROKE, l980; 11(3): 297-300.

Results are reported using hyperbaric oxygenation (HBO) in 122 patients with strokes due to thrombosis, both acute and completed. HBO is used as adjunctive treatment and there appears to be justification for a controlled study to delineate the treatment further. The authors believe it is essential to treat patients with stroke at 1.5 to 2 atmospheres absolute (ATA).

"Hyperbaric oxygen in the treatment of acute ischemic stroke: an unsettle issue."

Nighoghossian, N. et al.

JOURNAL OF THE NEUROLOGICAL SCIENCES, 1997; 150(1): 27-31.

Therapy for acute ischemic stroke can be approached in two basic ways: first, by an attempt to restore or improve blood flow in an occluded vascular territory and, second, via therapy directed at the cellular and metabolic targets. As local anoxia and energy failure are the initiating cellular stage in ischemia, the inhalation of oxygen at increased atmospheric pressures might be effective. Treatment of acute focal cerebral ischemia with hyperbaric oxygen (HBO) has been reported in animals and humans. In general, the results of research in animals have suggested a promising role for the use of HBO. More than 400 cases of human ischemic stroke treated with HBO have been reported. In about half of the cases, improvement in status has been claimed on clinical or electroencephalographic grounds. "IT might be speculated that the patients most likely to respond favorably to HBO therapy are those who have infarcts related to large vessel thrombosis and surrounded by ischemic penumbra. In support of this are reports claiming a favorable transient or , less often, permanent response to HBO in cases selected for demonstrated carotid occlusion…A large double-blind study might be required in the future. Based on experimental data, HBO at 1.5 ATA during 1 hour might be proposed, as neurotoxicity is rare with low pressure and short duration. If HBO treatment is safe and effective, it could be added to thrombolytic therapy which has recently shown its efficiency in restoring cerebral blood flow."

"Hyperbaric Oxygen in the Treatment of Acute Ischemic Stroke. A Double-blind Pilot Study"

Nighoghossian, N. et al.

STROKE, l995; 26: 1369-1372.

Background and Purpose: The effects of hyperbaric oxygen (HBO) therapy on humans are uncertain. Our study aims first to outline the practical aspects and the safety of HBO treatment and then to evaluate the effect of HBO on long-term disability.

Methods: Patients who experienced middle cerebral artery occlusion and were seen within 24 hours of onset were randomized to receive either active (HBO) or sham (air) treatment. The HBO patients were exposed daily to 40 minutes at 1.5 atmospheres absolute for a total of 10. We used the Orgogozo scale to establish a pretreatment functional level. Changes in the Orgogozo scale score at 6 months and 1 year after therapy were used to assess the therapeutic efficacy of HBO. In addition, we used the Rankin scale and our own 10-point scale to assess long term-disability at 6 months and 1 year. Two sample t tests and 95% confidence intervals were used to compare the mean differences between the two treatment groups. Student's two-tailed test was used to compare the differences between pre-therapeutic and post-therapeutic scores at 6 months and 1 year in the two treatment groups.

Results: Over the 3 years of study enrollment, 34 patients were randomized, 17 to hyperbaric treatment with air and 17 to hyperbaric treatment with 100% oxygen. There was no significant difference at inclusion between groups regarding age, time from stroke onset to randomization and Orgogozo scale.

Neurological deterioration occurred during the first week in 4 patients in the sham group, 3 of whom died; this worsening was clearly related to the ischemic damage. Treatment was also discontinued for 3 patients in the HBO group who experienced myocardial infarction, a worsening related to the ischemic process, and claustrophobia. Therefore, 27 patients (13 in the sham group and 14 in the HBO group) completed a full course of therapy.

The mean score of the HBO group was significantly better on the Orogozo scale at 1 year. However, the difference at 1 year between pre-therapeutic and post-therapeutic scores was not significantly different in the two groups. Moreover, no statistically significant improvement was observed in the HBO group at 6 months and 1 year according to Rankin score and our own 10-point scale.

Conclusions: Although the small number of patients in each group precludes any conclusion regarding the potential deleterious effect of HBO, we did not observe the major side effects usually related to HBO. Accordingly, it can be assumed that hyperbaric oxygen might be safe. We hypothesize that HBO might improve outcome after stroke, as we detected an outcome trend favoring HBO therapy. A large randomized trial might be required to address the efficacy of this therapy.

Hyperbaric oxygen therapy (HBO) after acute focal cerebral ischemia

Berrouschot J, Schwab S, Schneider D, Hacke W.

Klinik und Poliklinik fur Neurologie der Universitat, Leipzig.

For a large number of patients with stroke no therapeutic option can be offered, even after approval of thrombolytic therapy for treatment of acute ischemic stroke in the US. In cerebral ischemia local anoxia and energy failure lead to further cellular damage and finally to complete stroke. All therapeutic concepts try to salvage structurally intact tissue which is at risk for irreversible damage (so-called penumbra). Hyperbaric oxygen (HBO) treatment has been reported in animal models of cerebral ischemia, and in a few clinical reports. In general, the results of these studies have been promising. This review focuses on the clinical perspective of

HBO therapy and summarizes both the clinical and experimental data available on HBO therapy following ischemic stroke.

Therapeutic use of hyperbaric oxygenation in ischemic strokes.

Elinskii MP, Rafikov AM, Ivanova NE, Kesaev SA.

Hyperbaric oxygenation is a valuable adjunct to the complex of measures devised to treat patients with ischemic cerebral strokes, including those who have undergone surgical operations on the extracranial portion of the cerebral major vessels. Although the best therapeutic effect of hyperbaric oxygenation is observed in the acute period of a stroke, its employment may be useful in many patients in the residual period of the stroke as well. The therapeutic action of hyperbaric oxygenation may be due to not only a certain recovery of the function of the damaged neural centres but also to the mobilization of various mechanisms of the CNS compensatory recovery.

PMID: 6506977 [PubMed - indexed for MEDLINE]

Hyperbaric oxygenation as an adjunct therapy in strokes due to thrombosis. A review of 122 patients.

Neubauer RA, End E.

Results are reported using hyperbaric oxygenation (HBO) in 122 patients with strokes due to thrombosis, both acute and completed. HBO is used as adjunctive treatment and there appears to be justification for a controlled study to delineate the treatment further. The authors believe it is essential to treat patients with stroke at 1.5 to 2 atmospheres absolute (ATA).

Neuroprotection by hyperbaric oxygenation after experimental focal cerebral ischemia monitored by MRI.

Schabitz WR, Schade H, Heiland S, Kollmar R, Bardutzky J, Henninger N, Muller H, Carl U, Toyokuni S, Sommer C, Schwab S.

Stroke. 2004 May;35(5):1175-9. Epub 2004 Apr 01.

Department of Neurology , University of Heidelberg, Germany.

BACKGROUND: Hyperbaric oxygenation (HBO) after focal cerebral ischemia reduces infarct size and improves outcome when applied early after stroke. Here, we evaluated effects of HBO on permanent focal cerebral ischemia and applied magnetic resonance imaging (MRI) monitoring to study lesion evolution. METHODS: Rats underwent permanent middle cerebral artery occlusion (MCAO). Two hours later, animals were treated with HBO (100% O(2)/2 atm; n=17) for 1 hour or treated with room air (n=17). Animals underwent serial MRI studies (DWI, PI, T2) beginning 90 minutes after MCAO. Neuroscore was assessed (5-point rating scale). Animals were euthanized and brains were 2,3,5-triphenyltetrazolium chloride (TTC)-stained for infarct volume calculation 120 hours after MCAO. Immunohistochemistry was performed with antibodies against c-FOS and 4-hydroxy-2-nonenal-modified proteins (HNE) to check for effects of oxidative stress caused by HBO treatment. RESULTS: HBO reduced infarct volume by 38% ($P<0.001$). As shown by MRI, neuroprotection began 5 hours after ischemia and remained effective for 5 days. The relative regional cerebral blood flow was not different between groups at 3.5 and 5 hours after occlusion. There was less neurological deficit in HBO-treated animals compared with controls ($P<0.05$). Lipid peroxidation of cerebral vessels after HBO treatment as measured by HNE staining and pattern of c-FOS induction were not significantly different between groups at 3.5 and 8 hours after ischemia. CONCLUSIONS: As monitored by MRI HBO treatment

reversed ischemic lesion size between 3 and 5 hours after ischemia and achieved a long-lasting neuroprotective effect without significant oxidative damage.

Hyperbaric oxygen in the treatment of patients with cerebral stroke, brain trauma amd neurologic disease.

Al-Waili NS, Butler GJ, Beale J, Abdullah MS, Hamilton RW, Lee BY, Lucus P, Allen MW, Petrillo RL, Carrey Z, Finkelstein M.

Life Support Technologies, Inc., and NewTechnologies, Inc., The Mount Vernon Hospital, Westchester Medical Center, New York Medical College, New York, USA.

Adv Ther. 2005 Nov-Dec;22(6):659-78.

Hyperbaric oxygen (HBO) therapy has been used to treat patients with numerous disorders, including stroke. This treatment has been shown to decrease cerebral edema, normalize water content in the brain, decrease the severity of brain infarction, and maintain blood-brain barrier integrity. In addition, HBO therapy attenuates motor deficits, decreases the risks of sequelae, and prevents recurrent cerebral circulatory disorders, thereby leading to improved outcomes and survival. Hyperbaric oxygen also accelerates the regression of atherosclerotic lesions, promotes antioxidant defenses, and suppresses the proliferation of macrophages and foam cells in atherosclerotic lesions. Although no medical treatment is available for patients with cerebral palsy, in some studies, HBO therapy has improved the function of damaged cells, attenuated the effects of hypoxia on the neonatal brain, enhanced gross motor function and fine motor control, and alleviated spasticity. In the treatment of patients with migraine, HBO therapy has been shown to reduce intracranial pressure significantly and abort acute attacks of migraine, reduce migraine headache pain, and prevent cluster headache. In studies that investigated the effects of HBO therapy on the damaged brain, the treatment was found to inhibit neuronal death, arrest the progression of radiation-induced neurologic necrosis, improve blood flow in regions affected by chronic neurologic disease as well as aerobic metabolism in brain injury, and accelerate the resolution of clinical symptoms. Hyperbaric oxygen has also been reported to accelerate neurologic recovery after spinal cord injury by ameliorating mitochondrial dysfunction in the motor cortex and spinal cord, arresting the spread of hemorrhage, reversing hypoxia, and reducing edema. HBO has enhanced wound healing in patients with chronic osteomyelitis. The results of HBO therapy in the treatment of patients with stroke, atherosclerosis, cerebral palsy, intracranial pressure, headache, and brain and spinal cord injury are promising and warrant further investigation.

Mechanisms of hyperbaric oxygen and neuroprotection in stroke.

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Cerebral vascular diseases, such as neonatal encephalopathy and focal or global cerebral ischemia, all result in reduction of blood flow to the affected regions, and cause hypoxia-ischemia, disorder of energy metabolism, activation of pathogenic cascades, and eventual cell death. Due to a narrow therapeutic window for neuroprotection, few effective therapies are available, and prognosis for patients with these neurological injuries remains poor. Hyperbaric oxygen (HBO) has been used as a primary or adjunctive therapy over the last 50 years with controversial results, both in experimental and clinical studies. In addition, the mechanisms of HBO on neuroprotection remain elusive. Early applications of HBO within a therapeutic window of 3-6h or delayed but repeated administration of HBO can either salvage injured neuronal tissues or promote neurobehavioral

functional recovery. This review explores the discrepancies between experimental and clinical observations of HBO, focusing on its therapeutic window in brain injuries, and discusses the potential mechanisms of HBO neuroprotection.