Status of Hyperbaric Oxygen Therapy in Neurological Illnesses – Review of International and Indian experience

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Neurosciences Today 2003;7:

Hyperbaric medicine is the fascinating use of barometric pressure for increasing delivery of oxygen dissolved in plasma to body tissues. Hyperbaric oxygen therapy (HOT) or hyperbaric oxygen (HBO) involves intermittent inhalation of 100% Oxygen under a pressure exceeding that of the atmosphere, that is greater than 1 atmosphere absolute (ATA). This therapy is given in special therapeutic chambers, which were earlier used primarily to treat illnesses of deep sea divers. Recently there is a renewed interest in this field all over the world. Acute traumatic wounds, crush injuries, burns, gas gangrene and compartment syndrome are indications where addition of hyperbaric oxygen may be life and limb saving. Patients who have been suffering with non healing ulcers, decubitus ulcers (bed sores) and all late sequelae of radiation therapy are also benefited with HBO therapy. Acute hearing loss and many neurological illnesses are also now known to possibly benefit from hyperbaric oxygen therapy. The hypothesis for treatment of select neurology illnesses with Hyperbaric Oxygen is the presence of an ischaemic penumbra having hibernating neurons that can be revived with delivery of additional oxygen. This article discusses the physiological basis of use of Hyperbaric Oxygen and reviews international and Indian literature and existing trends and applications of this therapy in neurological illnesses.

INTRODUCTION

The term Hyperbaric Oxygen Therapy is self explanatory, *Hyper*: Higher and *Baric*: pressure, i.e. higher than atmospheric pressure Oxygen Therapy. The Committee on Hyperbaric Medicine of the Undersea and Hyperbaric Medical Society (USA) defines Hyperbaric Oxygen Therapy as "A mode of medical treatment in which the patient is entirely enclosed in a pressure chamber and breathes 100% Oxygen at a pressure greater than 1 atmosphere absolute (ATA)". (ATA is the unit of Pressure and 1 ATA is equal to 760 mm of Mercury or pressure at sea level).

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Over the past 40 years Hyperbaric oxygen therapy (HBO) had been recommended and used in a wide variety of medical conditions, often without adequate scientific validation of efficacy or safety. Consequently a high degree of medical scepticism had developed regarding its use.[1] Gabb and Robin in the "Chest" (1987) have highlighted the controversies relating to HBO and have documented 132 past and present indications for HBO therapy.[2]

Over the last two decades, animal studies and clinical trials have produced reasonable scientific evidence or well validated clinical experience. This has led to a renaissance of HBO and produced a set of indications for which HBO is beneficial.[3-5] In these

Table 1: Universally accepted indications for hyperbaric oxygen therapy

Acute conditions (where HBO therapy should be given earliest when combined with conventional treatment)

- Non-healing ulcers, problem wounds, compromised skin grafts and flaps
- Crush injury, compartment syndrome, and acute traumatic ischaemias
- Gas gangrene / clostridial infections
- Necrotizing soft tissue infections (subcutaneous tissue, muscle, fascia)
- Thermal burns
- Exceptional blood loss (anaemia)
- Intracranial abscess
- Burns
- Sudden deafness
- Ocular ischaemic pathology
- Air or gas embolism *
- Decompression sickness*
- Carbon monoxide poisoning and smoke inhalation*

**Curative / Primary Line of Treatment*

Chronic conditions

- Non-healing wounds / problem wounds (diabetic / venous etc.)
- Radiation tissue damage
- Skin grafts and flaps (compromised)
- Chronic osteomyelitis (refractory)

conditions early referral is essential. Hyperbaric facilities now form an important part of many hospitals all over the world. China leads with 2600 Hyperbaric centers, Russia: 2000, Japan: 400, approx 200 in the UK, 400 all over Europe and approx 500 in the US. In Asia: Malaysia 5 centers, Middle East: 10, 1 in Sri Lanka and 1 emerging in Bangladesh. With this continuing growth all over the world Hyperbaric Medicine has found a distinct role in the modern era of evidence based medicine.

Experiences with HBO therapy in India have been published recently in a well-read journal[6] besides other articles in journals with limited circulation, but there has been no inter-disciplinary recognition of hyperbaric medicine at a national level. Thus though sufficient evidence supports use of HBO in certain defined conditions, many patients go untreated because of the physicians' unfamiliarity with recent research of HBO as therapy.[6]

Recovery from neurological illnesses is cause for great morbidity and available treatment methods are not adequate. Hyperbaric Oxygen Therapy has been proved to have a well-defined role in certain medical/surgical indications like non-healing wounds etc (Table 1) and is also being used as an adjunctive therapy in neurological conditions in many centers worldwide but there is no consensus on its role.

After reviewing international and national experience it seems that there appears to be evidence of a physiological basis and a possible role of Hyperbaric Oxygen in management of well defined ischaemic and post traumatic neurological illnesses. There is however need for definition of specific indications, patient selection, therapeutic window period, dosage, frequency, and periodicity.

PHYSIOLOGICAL BASIS OF HYPERBARIC OXYGEN IN NEUROLOGICAL CONDITIONS

The usual arterial partial pressure of O_2 is 100mm Hg, Hb is 95% saturated and 100 ml of blood carries 19 ml of O_2 in combination with Hb and 0.32 ml dissolved in plasma. If the inspired O_2 concentration is increased to 100 %, O_2 combined with Hb can increase to a maximum of 20 ml when the Hb is 100% saturated and the amount of O_2 dissolved in plasma may increase to 2.09 ml. During HBO in addition to the Hb which is 100% saturated, the amount of O_2 carried in solution will increase to 4.4 ml % at a pressure of 2 ATA to 6.8 ml % at 3 ATA which is almost sufficient to supply the resting total oxygen requirement of many tissues without a contribution from oxygen bound to haemoglobin (Table 2). It is this increased oxygen in plasma, which is responsible for most of the beneficial effects of hyperbaric oxygen.[1,5]

A neuron is highly sensitive to hypoxia or glucose deprivation and cerebral ischaemia of longer than few minutes causes irreversible neuron damage. However Dai *et al* showed that there was evidence to prove that neurons can survive up to 8 hours after death such that they can recover their functions of energy metabolism and axonal transport.[7]

The rationale of use of hyperbaric oxygen in neurological conditions is based on the observation in SPECT studies that around the central area of neuronal death is a penumbra or peri-infarct zone, which can be revived. SPECT has also shown that areas that appear as gliosis on CT scans may actually be viable tissue for years following the insult and be reactivated with HBO. This is the basis of its use by some centers in acute stroke, post-traumatic brain injuries and Cerebral palsy.

Table 2: Effect of pressure on arterial O_2

Total pressure		Content of oxygen dissolved in plasma (vol %)	
ATA	MmHg	Breathing Air	100% Oxygen
1	760	0.32	2.09
1.5	1140	0.61	3.26
2	1520	0.81	4.44
2.5	1900	1.06	5.62
3	2280	1.31	6.80
4	3040	1.80	O_2 is not
5	3800	2.80	administered
6	4560	2.80	at pressure above 3 ATA

All values assume arterial pO_2 = alveolar O_2 and that Hb oxygen capacity of blood is 20 vol %

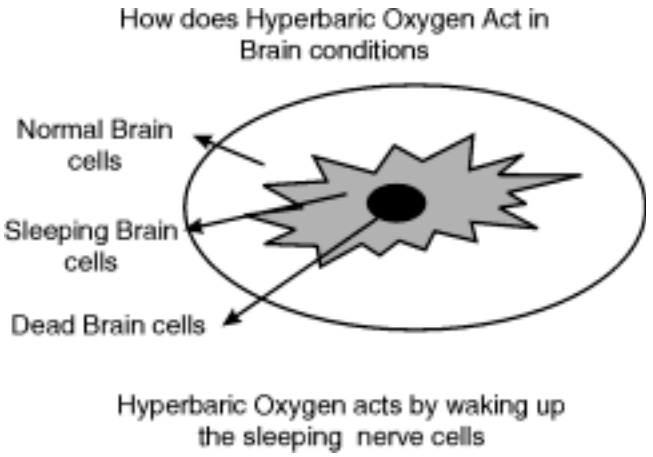

Fig. 1: Physiological basis of hyperbaric oxygen therapy in neurological conditions

HBO leads to improvement of tissue oxygenation by increasing the amount of oxygen dissolved in plasma which can then seep through and deliver oxygen even in total vascular obstruction and nourish tissues even in absence of red cells. The decreasing blood viscosity and increasing red cell deformability due to hyperoxia and increased extravascular diffusion further facilitate supply of oxygen. Secondly, it reduces cerebral oedema and Intra-cranial pressure by inducing vasoconstriction, which leads to reduced extravasation of fluid. This counters the vasodilatation of capillaries in hypoxic tissues.[8] The effect of vasoconstriction and reduction in blood flow is ameliorated by the alignment of red cells in a column instead of moving randomly. According to Koshi reduced ICP is maintained during HBO inhalation by induced hypercapnia.[9] Hyperbaric Oxygen also leads to Improved metabolic function of cerebral tissue by improved glucose metabolism, which prevents glycolysis and intracellular lactic acidosis build-up.[10] HBOT may restore ion pump function in ischaemic cell membranes preventing production of potentially damaging vasoactive mediators and facilitating recovery.[11]

The intermittent periods of hyperoxia with periods of relative hypoxia lead to the development of permanent paths for delivery of oxygen (possible collaterals or neovascular formation), which are responsible for the permanent recovery of these neurons.

METHOD OF ADMINISTRATION

HBO therapy can be given in a "Monoplace chamber" in which a single patient is placed in a chamber which is then pressurised with 100% oxygen. Monoplace chambers are used to treat stable patients with chronic medical conditions. It can also be given in a "Multiplace chamber" where many patients can be treated at the same time. These chambers are used for acute problems and also for critically ill patients who require a medical attendant within the chamber. These chambers are pressurised with compressed air and the patient breathes 100% oxygen at that pressure through special masks or oxygen hoods. The treatment control panel controls the therapy and monitors the patient during the treatment. Most therapy is given at 2 or 3 ATA and the average duration of therapy is 60 to 90 minutes. Number of therapies may vary from 3-5 for acute conditions to 50-60 for radiation illnesses.[1,3,5]

TOXIC EFFECTS / COMPLICATIONS

When used in standard protocols of pressures that do not exceed 3 ATA (300 kPa) and the length of treatment is less than 120 minutes, hyperbaric oxygen therapy is safe. Commonest side effect is pain in the ears (aural barotrauma) as a result of inability to equalize pressure on both sides of the tympanic membrane due to a blocked eustachian tube. Pneumo-thorax and air embolism are more dangerous complications due to tear in pulmonary vasculature due to pressure changes but are rare. Other rare side effects are pulmonary and neurological oxygen toxicity (Paul Bert effect), retrolental fibroplasia and cataracts.[12] Transient reversible myopia can also rarely occur after prolonged HBO therapy. Fire is a realistic hazard but preventable by strict safety procedures. An occasional patient may be claustrophobic.[1] Rare instances of hypersensitivity to O_2 are also documented.[13] Oxygen toxicity can be prevented in most tissues by using 5 minutes air in the chamber for every 30 minutes of Oxygen. This allows antioxidants to deal with free oxygen radicals formed during the hyperoxic period.[1,5] A suggested carcinogenic effect of hyperbaric oxygen has not been substantiated in extensive studies.[14]

THEORETICAL NEGATIVE EFFECTS OF HBOT ON NERVOUS TISSUE

In hyperbaric setting, tissue levels of Oxygen may approach 1200 mmHg and it is reported that HBOT can worsen reoxygenation injury in brain by promoting free oxygen radicals and lipid perioxidation.[8] Free radicals of oxygen or reactive oxygen species and xanthine oxidase occur during reperfusion following ischaemia. Mitochondrial respiration is impaired after ischaemia and an increase in molecular oxygen can result in an increase in reactive oxygen species, which could further result in tissue injury.[15-18]

Rockswold *et al*[19] in their study found that though the mortality rates of patients decreased in severely head injured patients, functional recovery was not satisfactory which could be due to increased free radical production and peroxidation. However, Yasu in his experimental study could demonstrate this in normal rat brains only, and not in ischaemic rat brains.[18] Also, in separate studies conducted by Mink & Dutka and Sunami and Takeda it was indicated that hyperbaric oxygen does not promote lipid peroxidation in ischaemic rabbit brains.[20, 21]

It is now accepted that in problem wounds there is adaptation by producing increased levels of superoxide dismutase, which take care of the free radicals. Additionally most centers advise use of free radical scavengers (Vit A, E, C etc) during treatment with Hyperbaric Oxygen.

Another argument against HBOT is that it induces vasoconstriction, which may compromise cerebral blood flow. However red cells are aligned in a column instead of moving randomly (Fahraeus Lindquist Effect) and the improved rheology counters the effects of vasoconstriction.[8] Vasoconstriction does not reduce the recovery potential or cerebral metabolism on SPECT imaging.[22] Further the 'Inverse Steal Phenomenon' described by Lassen and Palvogyi, which suggests that constriction of vessels in normal brain may increase blood flow in unresponsive areas, may be responsible.[23]

REVIEW OF LITERATURE

Though ischaemic cerebral injury is a theoretically attractive disease to treat with HBOT, it is not one of the indications under the Undersea and Hyperbaric Society Guidelines (1999). Nonetheless, the growing body of experimental and clinical experience appears to be favourable.[8]

Cerebrovascular accidents

Sunami and Takeda concluded in their prospective experimental study in rats that HBO at 3 ATA reduced infarct volume by increasing oxygen supply to the ischaemic periphery without aggravating lipid perioxidation, suggesting that HBO can be useful in treating stroke victims.[21] In another study conducted by Anderson, either HBO or air was given to 39 patients with ischaemic cerebral infarction in a double blind prospective protocol. The study was interrupted when they noticed a trend favouring the air treated patients whose neurological deficits were less severe and infarcts smaller.[24] Nighoghossian *et al* in their double blind study of 34 patients detected an outcome trend favouring HBO therapy.[25]

Cerebral injuries

Contreras *et al* in their animal study demonstrated that changes in lesion in rats exposed to HBO are not restricted to the period of time that the animals are in the hyperbaric chamber but are persistent.[10] In another study by Nida to determine the effects of hyperbaric oxygen (HBO) on injured cortical tissue, additional animal groups were exposed to HBO (1.5 ATM, for 60 minutes) beginning 4 hours after head trauma. HBO reduced the water content of the trauma site in animals that had received fluid percussion but not in animals receiving cortical impact injury. The authors conclude that HBO appears to reduce oedema produced by fluid percussion but the number of treatments and the pressure used were not enough to reduce the effects from cortical injury.[26]

Rockswold *et al* conducted a clinical trial with 168 patients with closed head injury to evaluate the effect of HBO in the treatment of brain injury. They found that HBOT dramatically reduced the mortality rate among the severely head-injured patients (GCS < 9), however their functional recovery was not satisfactory.[19] Neubauer in a case report highlighted that the patient responded extremely well to HBOT and he proposed that HBO therapy should be used routinely as an early diagnostic tool and as an aid to physical rehabilitation for patients with brain injuries.[27] Rockswold *et al* in a further study found that HBOT may improve aerobic metabolism in severely brain-injured patients. On the basis of their data the authors suggest that shorter, more frequent exposure to HBOT may be better.[28] Camporessi, Enrico *et al* state "hyperbaric medicine plays an integral role in comprehensive trauma care, from resuscitation to definitive therapy and subsequent recovery".[29] Ren, Wang and Ge in their study of 55 patients found that in the HBO treatment group there was an obvious improvement in GCS, BEAM and GOS compared with the control group and concluded that HBOT is an effective method to treat severe brain injury.[30]

Several experimental studies have been carried out to understand the relationship between HBO and cerebral blood flow (CBF). Omae *et al* in their experimental study in human subjects concluded that hyperoxaemia caused by HBO reduces the cerebral blood flow (CBF) but the high atmospheric pressure *per se* does not influence the CBF in humans.[31] Sukoff in his more elaborate study with brain injured patients found that in patients with reduced CBF before HBO therapy, CBF and cerebral metabolic rate of oxygen ($CMRO_2$) were raised 1 hour and 6 hours after HBO; in patients with normal CBF before HBO, CBF and $CMRO_2$ levels were increased at 1 hour but were decreased by 6 hours after HBO; while in patients with raised CBF before an HBO session, CBF was reduced 1 hour and 6 hour after HBO but $CMRO_2$ was unchanged. Also ventricular cerebrospinal fluid lactate levels were consistently decreased regardless of the patient's CBF category before HBO giving the conclusion that HBO may improve aerobic metabolism in severely brain injured patients.[32] In another experiment, Prass demonstrated that HBO induces tolerance to focal cerebral ischaemia in mice though this effect occurred in one strain of mice only out of the two strains studied. They speculate that the most straightforward explanation for Ischaemic Tolerance after HBO is the induction of oxygen free radicals (OFR) scavenging systems, which protect the brain against OFR produced ischaemia or reperfusion.[33] The induction of HBO triggered tolerance against cerebral ischaemia both global as well as focal (stroke) is a promising concept though there is need of further research to explain the process by which it is executed.

Cervical spinal cord injury

Asomoto and Sugiyama in a retrospective study divided 34 cases of hyperextension spinal cord injury in two groups – those who received HBOT and those who did not. They evaluated the neurological findings at admission and their outcomes by Neurological Cervical Spine Scale and compared the average improvement rates of both groups. They report better improvement rates in patients given HBOT than those who were not given HBOT.[34] In an experimental study, Murakami concluded that HBO applied early within 30 minutes after ischaemic insult

had protective effect against ischaemic spinal cell damage but if administered at 6 hrs after ischaemic insult, it had almost no effect on spinal cell damage.[35]

Among reports of Indian authors and the use of Hyperbaric Oxygen in neurological illnesses, Malik and Gomez of the Air force treated 77 cases at their center. Their experience with CVA patients was mixed and defied any set patterns but they concluded that fresh cases responded better to HBOT, concurrent physiotherapy had a synergistic effect and larger muscles showed better improvement than fine muscles. There was complete recovery of a case of facial muscle weakness post Bell's Palsy but cases of traumatic paraplegia and hemiplegia did not show any improvement.[36] In another report of hyperbaric oxygen therapy in stroke cases, Soodan *et al* found that cases treated with HBOT showed significant improvement in the spasticity and motor functions, speech and facial nerve palsy as compared to cases who were treated with physiotherapy alone.[37] Sahni and Nangpal report use of HBOT as adjuvant therapy in two cases of cerebral oedema at the Naval Hospital Mumbai who were not showing significant improvement with conventional treatment. Both patients recovered completely with no residual neurological deficit. Based on their findings, they recommend that in addition to conventional therapy, HBO should be titrated to lower oxygen levels to prevent rebound and patient should be referred for HBOT in time.[38]

A recent study deals with the role of HBO in *neurosurgical infections* and concludes that HBO is an alternative to standard surgical removal of infected bone flaps in skull infections secondary to trauma. It is particularly useful in complex situations reducing need of operations and the mandatory removal of foreign materials. It is a safe, cost-effective treatment for such post-op cranial and spinal wound infections and should be included in neurosurgical armamentarium. [39]

Multiple sclerosis

Fischer *et al* in their study found a positive though transient effect of HBO on advanced multiple sclerosis and recommended further study. Though later MS was discarded as an indication, a large number of centers opened in the UK continue to treat them.[40]

Bells palsy

It is postulated that the recovery from this self-limiting ailment is hastened with Hyperbaric Oxygen Therapy leading to early return to daily activity.[41]

Cerebral palsy

Although there is yet inadequate scientific evidence to support the use of hyperbaric oxygen in cerebral palsy (CP), private hyperbaric centers in the United States, Canada, Germany, China, Russia, South Africa, England and Brazil have been treating these children since many years. A personal communication from China reveals that HBOT has been used for treating CP children below 3 years since 1985 in China with good results.

Possibly the first scientifically designed study on children with Cerebral Palsy was conducted by Montgomery *et al.*[42] Results showed improved gross motor function and fine motor control, reduced spasticity. In addition the parents noted improvement in alertness, concentration and communication and improvement in sleep. No complications were observed. However, this study has a number of limitations, many of which are acknowledged by the authors. A similar study also showed positive results but had it's own limitations.[43] Though no side effects were reported in either of these studies two complications of aspiration pneumonia, air embolism and barotrauma have been reported during treatment.[44]

In a recent interesting study conducted by Collett *et al*[45] 111 children with cerebral palsy aged 3-12 years were randomly assigned hyperbaric oxygen (n=57) or slightly pressurized room air (n=54). All children received 40 treatments over 2 months. Hyperbaric oxygen treatment was given 1 h in 100% oxygen at 1.75 atmospheres absolute (ATA); children on slightly pressurised air received air at 1.3 ATA (the lowest pressure at which pressure can be felt, thereby ensuring the maintenance of masking). The main outcome measure was gross motor function. Secondary outcomes included performance in activities of daily living, attention, working memory, and speech. Though both groups showed improvement in global gross motor function, speech attention and daily living activities, the difference in those receiving slightly pressurized air compared with HBO was not significant. This raises an important question of whether the improvements seen were due to the classic Hawthorne effect (i.e. any change in any direction leads to improvement irrespective of the nature and the direction of the change). Neubauer advocates the use of SPECT to provide the objective evidence of benefit.

Carbon monoxide (CO) poisoning

Hyperbaric oxygen therapy is used for altered neurological function due to CO poisoning. In a case report given by Dean, aggressive repetitive HBO therapy resulted in significant resolution of coma and cerebral dysfunction after severe acute CO poisoning. The author recommends that patients who manifest signs of serious CO intoxication like unconsciousness, neuro-psychiatric symptoms, cardiac or haemodyanamic instability should be given immediate HBO therapy.[46]

DISCUSSION

The human brain has millions of neurons of which less than 10% are used in one lifetime. The wide variation in clinical pictures of recovery from neurological insults are unexplained by the structural model of neurology alone and it is becoming increasingly accepted that there is more to the plasticity of the brain then was earlier believed. Following an ischaemic or anoxic neurological event (with the availability of newer diagnostics such as MRI and SPECT) it is possible to now identify permanently damaged neurons from those in the ischaemic penumbra, which may be revived. Some of these neurons remain as idling/

hibernating neurons many years after the event. There seems a scientific logic behind the role of Hyperbaric Oxygen and possibly other treatment modalities that may target these ischaemic or hibernating neurons and promote neuronal recovery.

The Hyperbaric Committee of the Undersea and Hyperbaric Medical Society in the US (UHMS) reviews and publishes once in 2-3 years the indications for HBO, which are supported by adequate medical literature. The Committee usually looks for three kinds of evidence: physiological, animal studies and human studies preferably double blinded, and publishes this list of "approved" indications. A similar process is followed by the EUBS (European Undersea and Baromedical Society).

In addition to the use of HBO for the "Approved" indications, growth of Hyperbaric Medicine over the past two decades has also led to its popularity and use for some "unapproved" or the so called "Off Label" indications. Neurological illnesses treated with Hyperbaric Oxygen fall under this category. These indications need further scientific evidence to be placed on the approved list. There has been a recent initiative by the UHMS to provide guidelines for the use of Hyperbaric Oxygen in such yet unapproved indications. They have come forward with recommendations in the form of three sets of proposals.[47]

The First proposal consists of criteria for "potentially therapeutic off label use of Hyperbaric Oxygen". These criteria are: alternative treatments are neither cost effective nor successful, human or animal studies data support its use and thirdly the benefits are greater than the risks considering any co-morbid conditions and the technical capability and safety of the facility. The definition of "successful" treatment is also discussed since for some physicians saving a life is more important whereas for others the quality of life may be the criteria for classifying the treatment successful.

The second proposal recommends the creation of a National Registry for the off label use of HBO. A National Registry would be able to keep record of cases treated in small numbers at many centers and generate data significant enough to allow that indication to be accepted. For inclusion in the national registry, in addition to the above three criteria the following could be added: significant incidence of disease, public pressure or demand, well defined protocols, informed consent forms and funding.

The third proposal is to develop a set of guidelines for physicians responding to requests for the "off Label use of HBO". These require the physician to check if there are any other medical treatments for that indication, which are effective or cost efficient. The physician should also consider risks and benefits on a patient specific basis.

The challenge lies in educating patients and handling their aspirations. Two aspects need to be clearly explained to the patient and his family. The first is the cost benefit ratio of HBO and second is understanding of "meaningful" improvement. Assessment needs to be done of their aspirations and hopes as they may vary greatly. Some may be happy with a small improvement in cognition such as enabling a vegetative patient to respond to the family's touch. Others may only be satisfied if the patient will be able to lead a near normal life style. This softer side of outcome measures may have no scientific relevance but is of extreme importance in clinical setting.

In one of the centers in India who have recently started treating patients with neurological injuries the practice is to triage these patients into two groups : those where addition of Hyperbaric Oxygen may contribute to their ability to perform "activities of daily living (ADL) "or significantly reduce" the burden of care (BOC)" and those in whom this seems unlikely. Treatment is recommended for the former patients. The latter cases are discussed in depth with the family and an undertaking taken to this effect if they choose to continue with HBO treatment. The family reviews the recommendation in accordance with their emotional involvement, financial status and satisfaction levels with small degrees of improvement. Patients from both groups have elected to take the treatment.

Cerebral injury is an "off label" indication for HBO therapy as per the Undersea and Hyperbaric Society guidelines but the concept of improving oxygen delivery in an ischaemic penumbra seems logical.[48] There appears evidence of a physiological basis of Hyperbaric Oxygen in management of some specific neurological illnesses. There is however a need for definition of specific indications, patient selection, therapeutic window period, dosage, frequency, and periodicity.

In the human endeavor to develop therapeutic breakthroughs for ischaemic and traumatic central nervous system injury, HBO needs further study in the laboratory and clinical settings. The role of addition of HBO with neuro-protective pharmacological agents and antioxidants needs to be explored further and the putative risk of oxidative stress in injured central nervous system tissue needs further evaluation. Besides, other strategies to improve oxygen supply/demand in the ischaemic penumbra, such as flow promotion using tissue plasminogen activator; ethanol, adenosine, endothelin-1 antagonists, haemodilution, or other therapies may exacerbate oedema or haemorrhage in injured central nervous system tissue. With advanced radiological techniques, improvement in patients can be documented and correlated with clinical symptomatology.

Clinical data needs to be carefully recorded along internationally acceptable protocols which should be part of a national / international registry. Keeping within the recommendations of the UHMS above should be considered an adequate ethical prescription of Hyperbaric Oxygen. Since there are no available

protocols for unapproved indications we propose in the recommendations below an algorithm, which we can use currently keeping in view our experiences and available international literature and experience.

RECOMMENDATIONS

In the evaluation of patients in whom Hyperbaric Oxygen Therapy is likely to be effective the ischaemic penumbra / hibernating or idling neuronal model may be applicable with existing knowledge. On this assumption degenerative diseases do not benefit from HBO therapy.

The following protocol is recommended for the use of Hyperbaric Oxygen in neurology patients. Patients who are likely to have ischaemic or hibernating neuronal tissue be placed into two groups: In Group A are patients where addition of Hyperbaric Oxygen may contribute to their ability to perform ADL or significantly reduce burden of care and in Group B are those patients where it seems unlikely. We recommend Hyperbaric Oxygen for the first group. For the second group we get special consent forms signed and offer HBO therapy only after they understand the limited outcome and are still desirous of continuing treatment.

Neurological illnesses present with different clinical pictures even in age matched patients with identical neurological insults. There is difficulty in carrying out a double blind controlled study in such patients and we propose that progress on a disability scale be used as a parameter to evaluate efficacy.

The patients' detailed clinical evaluation be recorded in a scientifically designed evaluation proforma, which would include an internationally acceptable disability scale. Evaluation be carried out before starting treatment and then at regular predefined intervals. Patients who do not receive Hyperbaric Oxygen will also be followed up and their progress also recorded on the disability scale, these will be the control group. Comparison between the two groups be carried after a year.

For Cerebral Palsy, the current treatment protocol of 40 sessions of HBO at 1.75 ATA given once daily will be continued. In a recent review by Udaan (presented at an international

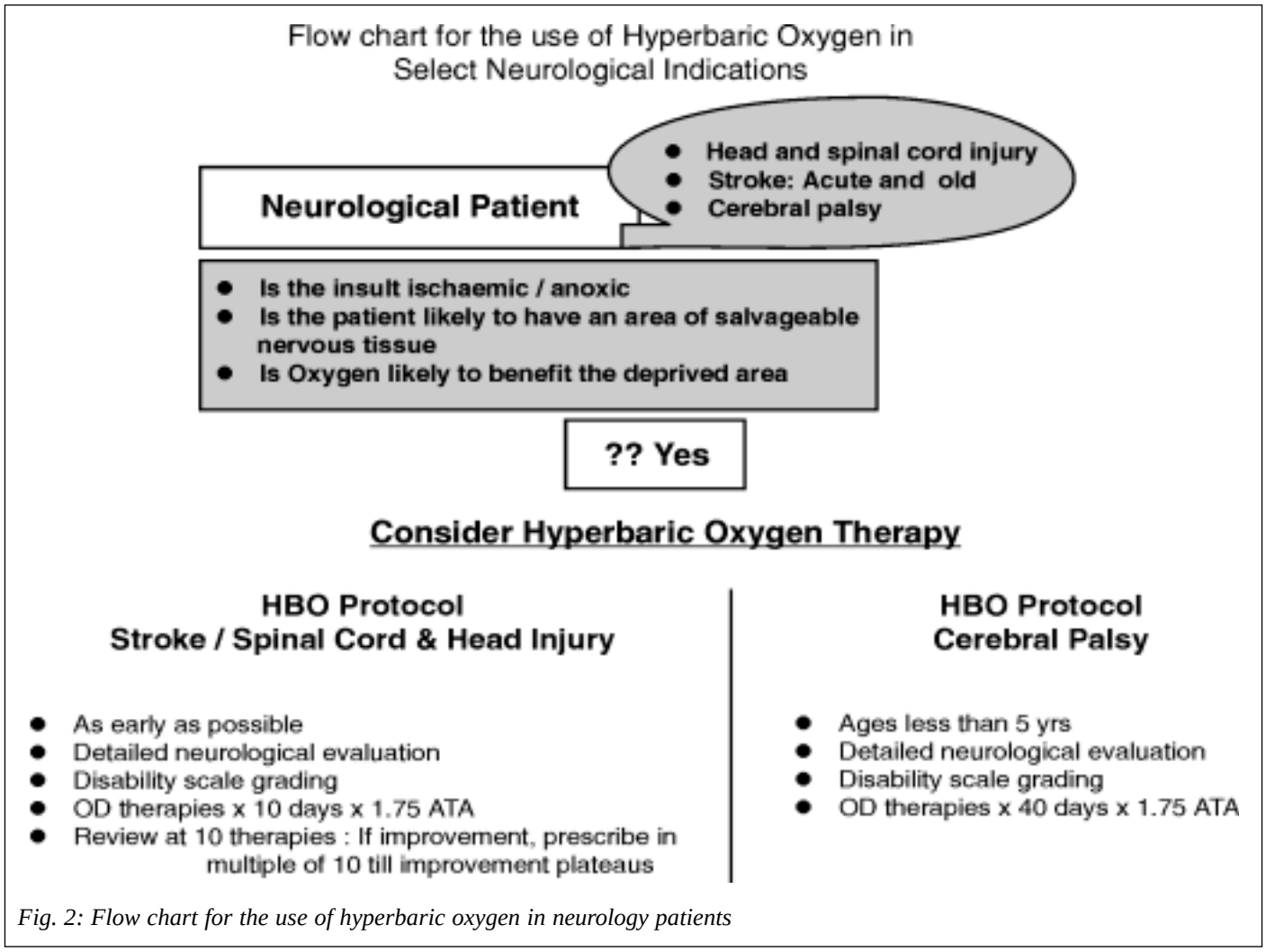

Fig. 2: Flow chart for the use of hyperbaric oxygen in neurology patients

Table 3: Summary of proposed HBO protocols for specific Neurological illnesses

Indication	Inclusion criteria	Diagnostics Recc	No of therapies	Dosage & frequency	Evaluation
Cerebral Palsy	Age < 5 yrs	SPECT before and after HBO therapy	40	Once Daily 1.75 ATA / 1.5 ATA	By Developmental Paediatrician / Udaan
Stroke: Acute	Earliest	Diffusion/perfusion MRI/SPECT	Multiple of 10 therapies.		Independent neurophysician
Stroke: Old	>1 yr post stroke				
Head Injury	Earliest				
Spinal Cord Injury	Earliest				

conference)[49] of 36 CP patients treated with HBO, the results are encouraging. The disability scale model is used in these children.

In other categories (Stroke - acute and old, Head Injury, Spinal Injury and acute anoxic encephalopathy), we propose protocol based treatment of small numbers of patients (10 cases in each category) and with detailed records on the basis of the ischaemic penumbra / hibernating neuron model. Early referral for HBO therapy is recommended to salvage the ischaemic neurons before they become irreversibly damaged.

We can use the Chinese protocol of giving treatment in multiples of 10 therapies. After every 10 therapies the patient is reviewed by a neurologist and if there is improvement then further 10 therapies are recommended and continued till the improvement has plateaued. Since there is no international consensus on the number of therapies the data be reviewed after treatment of 10 cases and make recommendations for future.

A diffusion perfusion MRI is probably the ideal tool to record the ischaemic penumbra / hibernating neurons but since that is yet unavailable, a SPECT be carried out before and after treatment with HBO therapy. Physiotherapy and additional therapies would continue and special low packaged costs will be worked out for these patients. Informed consent will be taken and free radical scavengers prescribed in all cases.

The site of improvement in these cases is at ischaemic neuronal level. Restoration of neuronal function may not immediately result in dramatic visible motor improvements but the presence of additional neurons will prove beneficial during the process of neurorehabilitation (including biofeedback) and it is felt that visible results will emerge later therefore these patients be followed up for 1year. In treatment of children with CP the peak improvement was seen after 2-3 months.

Following are the proposed treatment protocols for different subgroups of patients with neurological illnesses. Finer details of Inclusion and exclusion criteria will be finalized prior to starting treatment.

Cerebral palsy

Children less than 5 years of age are best candidates. They undergo a SPECT prior to starting treatment and those with high perfusions be recommended treatment. Those with poor perfusion be taken up for treatment if families understand the limited improvement and undertake the same in writing. 40 days of Hyperbaric Oxygen at 1.75 ATA be administered along with other occupational and physiotherapy. Post therapy SPECT be recommended to document changes.

Stroke / Spinal cord injury / Head injury

Two groups of patients with stroke be taken up for treatment: Acute Stroke (both haemorrhagic and non haemorrhagic) at the earliest and Old stroke (greater than 1 year). Head and spinal injury patients be referred for Hyperbaric Oxygen at the earliest. A minimum of 10 sessions be given and reviewed for improvement. If there is clinical improvement then further 10 treatments be proposed. Once diffusion / perfusion MRI is available, patients could be recommended the same before and after HBO to document changes.

Anoxic encephalopathy / Coma

Experience has not been encouraging and this was removed from the approved list of UHMS a few years ago.

CONCLUSION

The Annual Incidence of Neurological Illnesses is approx 2% to 2.6% of population / year (Continuum Neuro Epidemology 1998) and approximately 0.82 million people become disabled every year in India. It is estimated that around 38-40 million people in India require rehabilitation and half of them are due to neurological disorders.

Evidence based Neurorehabilitation as a science is yet evolving and few centers have opportunity to explore the role of a range of modalities in these patients. Hyperbaric Oxygen seems to have a physiological basis and possibly has a role to play in a select group of patients with neurology illnesses.

Every effort should be made to alleviate the suffering of this often-neglected segment of society and bring about some happiness in their lives and that of their families.

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