International Journal of Pharmacological Research
ISSN: 2277-3312
www.ssjournals.com
Journal DOI:10.7439/ijpr

Role of Hyperbaric Oxygen Therapy in Severe Diffuse axonal Head Injury -Our Experience 2011-2013

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Abstract
Background: Diffuse axonal injury (DAI) is often fatal and one of the major cause of morbidity and mortality. The present study was undertaken to evaluate the role and potential benefits of hyperbaric oxygen therapy (HBOT) in the treatment of DAI.
Method: Total 60 patients of severe diffuse axonal head injury [Glasgow Coma Scale (GCS) < 8] with no other associated injury were enrolled in the study. Out of total cases, 30 received HBOT and were included in the study group. After an initial period of resuscitation and conservative management (10–12 days), all were subjected to three sessions of HBOT at 1-week interval. This study group was compared with a control group of similar severity of head injury (GCS < 8).
Results: Both the study and control groups were compared in terms of GCS, duration of hospitalization, disability reduction, and social behavior. Patients who received HBOT were significantly better than the control group on all the parameters with decreased hospital stay, better GCS, and drastic reduction in disability.
Conclusion: The addition of HBOT significantly improved the outcome/survival and quality of life and also reduced the risk of complications in patients with severe diffuse axonal head injury.
Keywords: Diffuse axonal injury, Traumatic brain injury, Hyperbaric oxygen therapy, Glasgow Coma Scale, Disability.

1. Introduction
Diffuse Axonal Injury (DAI) is considered one of the most common and detrimental forms of traumatic brain injury (TBI) that affects patients and their families. Patients with DAI have a range of multiple neurological deficits that affect the physical and mental status of the patient. It is clinically defined by coma lasting 6 h or more after TBI, excluding cases of swelling or ischemic brain lesions[1]. However, DAI is considered the most important factor in determining morbidity and mortality in victims of TBI and is the most common cause of posttraumatic coma, disability, and a persistent neurovegetative state. Most of the patients with DAI are identified to be severe and commonly have a GCS of less than 8. [1,2]

Road traffic accidents (RTAs) are the most frequent cause of DAI, with assault or falls also being common aetiologies [3]. The most common mechanism involves an accelerating and decelerating motion that leads to shearing forces to the white matter tracts of the brain. This leads to microscopic and gross damage to the axons in the brain at the junction of the gray and white matter. Diffuse axonal injury commonly affects white matter tracts involved in the corpus callosum and brainstem [4]. Moreover, aDAI is a primary injury which usually induces irreversible damage to brain tissues [5]. Not all damage to the brain occurs at the moment of injury; a reduction of the blood flow and oxygen supply to the brain can occur after wards and cause further secondary brain damage that is itself an important cause of avoidable death and disability. In the early stages after injury, it is therefore important that efforts are made to minimize secondary brain damage to provide the best chances of recovery [6].

Hyperbaric oxygen therapy has been proposed as a treatment for minimizing secondary brain damage by improving the oxygen supply to the brain. Patients undergoing HBOT are placed inside a specially designed chamber in which 100% oxygen is delivered at a greater than normal atmospheric pressure. It is sometimes used as a treatment to increase the supply of oxygen to the injured brain in an attempt to reduce the area of brain that will die [6, 7]. The present study was undertaken to evaluate the role and potential benefits of hyperbaric oxygen therapy in the treatment of diffuse axonal injury.

2. Materials and Methods

A total of 60 patients with DAI admitted to the Tertiary Care Hospital from January 2011 to February 2013 were enrolled in the study. Patients eligible for the study had Glasgow Coma Scale (GCS) scores of <8 at admission and a computed tomography (CT) scan showing either normal outcome or signs of DAI. DAI was confirmed by signs of injury identified in CT or MRI scans by neurosurgeons experienced with this type of injury. Cases with GCS <8 and without MRI and normal CT were also diagnosed as DAI [8-10].

Out of total 60 cases, 30 received HBOT and were included in the study group. After an initial period of resuscitation and conservative management (10-12days), all weresubjected to three sessions of HBOT at 1-week interval each. HBOT can be administered by two ways, using monoplace chamber or multiplace chamber. Themonoplace chamber, which we used in present study, serves one patient at a time. The initial cost of setupis less but it provides limited opportunity for patient intervention while in the chamber. These chambersare generally constructed of acrylic or with view ports that allow for patient observation. Thesechambers are pressurized with 100% oxygen.The duration of an HBOT session in common practice is about 90–120 minutes, however, the duration,frequency, and cumulative numbers of sessions have not been standardized. The dose received by thepatient may be affected by the type of chamber used. The study group was compared with a matched control group (30 cases) of similar severity of head injury (GCS < 8) selected by randomization.

3. Results

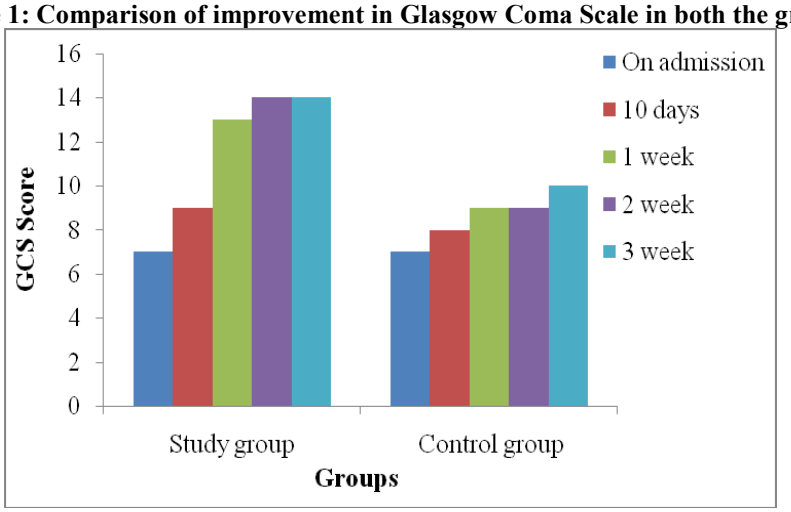
Out of 60 patients, 51(85%) were males and 9(15%) were females. The various clinical, social and functional parameters were compared between study and control groups,where the study groupthat receiving HBOT showed distinct advantage over thecontrol group as shown in Table 1.

Table 1: Comparison of various parameters between two groups

Parameters	Study group (n=30)	Control group (n=30)	P value
GCS	14 (post HBOT)	<10	0.061
Hospital stay	37 days	63 days	0.008
Social behaviour	Acceptable improvement	Slight improvement	-
Disability reduction	Early return to routine activities	Disability persistenceor delayed return ofroutine activities	-

On contrasting the GCS of both the groups; observed at thetime of admission, after 10 days of conservative managementand then at 1-week interval, it was quite evident that patientswho received HBOT showed marked improvement ascompared to the control group as shown in figure 1.

Figure 1: Comparison of improvement in Glasgow Coma Scale in both the groups



4. Discussion

Diffuse axonal injury is a microscopic lesion associated withsignificant mortality and morbidity.The true incidence of DAI is unknown. Each year, approximately 1.5 million Indians sustain traumaticbrain injuries, ranging in severity from mild to fatal [11]. However, it is estimated that roughly 10% of all TBI admitted to the hospital will have some degree of DAI. Of the patients with DAI, it isestimated that roughly 25% will result in death. This statistic may be underestimated as patients with subdural hematomas, epidural hematomas, and other forms of TBI will not carry a true diagnosis of DAI. Postmortem studies have shown that patients with severe TBI have a significant incidence of DAI [12].

No single instrument can measureall of the consequences of TBI. The oldest formal scale,the Glasgow Outcome Scale, categorizes patients into fivebroad categories: good recovery, moderate disability, severedisability, persistent

vegetative state, and death [13]. Thismeasure, although convenient and widely used, is insensitiveto many cognitive and emotional deficits which strongly affectthe quality of life. Since the 1970s, the GCS which ranges from 3 to 15 has been the most widely used measure of the severityof an acute brain injury [14, 15]. A GCS between 3–5 indicatesserious injury with grave outcome, while GCS between 13 and15 represents mild injury with the best prognosis. "Severe"injury is often defined as a GCS score of 8 or less indicatinga mortality rate of 50% and high likelihood of suffering fromsevere long-term disabilities [16, 17].

Moreover, physiological changes after TBI, such as hypoxia and hypotension, can result in secondary brain damage. Preserving theairways after trauma may result in favorable outcomes after severeTBI. Hypoxia and hypotension in severe TBI victims arecommon, and their occurrence in the initial hours is significantlyassociated with increased mortality [18, 19]. Thus,secondary ischemia and oxygen deficiency are thought to beimportant mechanisms of cell death in TBI 20. Aggressivemanagement of trauma significantly reduces the hypoxic andischemic episodes, but does not eliminate it. For this reason,there is renewed interest in finding more effective strategiesfor ensuring adequate oxygenation and redistributing cerebralblood flow (CBF) to injured areas of the brain [21]. The metabolic effects of brain injury are not easily demonstratedand are by no means fully understood. Immediately after abrain injury, brain cells can be inactivated temporarily byischemia and edema which compromise local perfusion. Thisobservation forms part of the rationale for the use of HBOT,which increases blood flow to the damaged areas of the brain,as documented by serial single photon emission computedtomography (SPECT) scans and other techniques [22, 23].

The application of hyperbaric oxygen (HBO) in treatment of TBI started in 1960s. The first study reporting the neuroprotection of HBO in experimental brain injury in rats was published in 1966 [24]. At the same year, Dunn and Lawson demonstrated that HBO significantly improved outcomes and reduced mortality in a dog freeze-lesion model of brain injury that simulated a brain contusion [25]. In the following years, several experimental studies focusing on the effects of HBO on brain edema, intracranial pressure (ICP) and cerebral blood flow (CBF) appeared. In some experimental models of acute cerebral ischemiaand acute carbon monoxide poisoning, HBOT preventscell death. The mechanism is unclear, but effects ofoxygen on the cellular and inflammatory response to injuryare considered important [26]. Recently, in a rat model offocal cerebral ischemia, HBOT reduced brain leukocytemyeloperoxidase (MPO) activity, which is produced bywhite blood cells (polymorphonuclear neutrophils) and is amarker of the degree of inflammation. Rats randomized to HBOT had reduced infarct size and improved neurologicaloutcomes compared with untreated rats, and the degreeof neurologic damage was highly correlated with the levelof MPO activity [27].

With the sound theoretical underpinning and demonstrated efficacy in experimental studies, intense clinical studies are conducted with the aim of evaluating the efficacy and safety of HBOT in relation to brain injuries and neurological disorders. HBOT in a clinical setting is usually implemented in the form of repetitive sessions over extensive time periods in order to improve neurological outcomes following TBI. The clinical efficiencyof HBOT in TBI remains controversial.The first clinical observation that presented a therapeuticeffect of HBOT in TBI patients was carried out by Fasano et al [28], in which HBO improved the outcome followingbrain trauma. HBOT has been shown to change ICP and reduce CSF pressure in patients withacute cerebral damage 29, improved grey matter metabolic activity onSPECT scan inclosed head injury [30], and improvedglucose metabolism after brain injury[31]. In severe TBI, HBOT has decreased mortality andimproved functional outcome[21,32]. In chronic brain injury, HBOT improved CBF, ameliorated theneuropsychological disorders [33], and enhanced neuropsychological and electrophysiological improvements. HBOT has also beenreported to show positive effects by improving the qualityof life in patients with post-concussion syndrome or mild TBI at late chronic stage [34, 35]. These cases and studies showed thesuccessful use of intensive HBO as a therapeutic modalityin various TBI patients.However, it should also be noted that there were conflicting results of HBOT in TBI patients. Various authors [36, 37] concluded that HBOT showed no evidence in improving life quality after TBI, although the evidence did suggest an improvementin survival [6]. Currently, the results of HBOT in clinical TBI trials arecontroversial and the efficiency of HBOT in TBI has notbeen well established.

Many brain-injured patients progress spontaneously fromcoma to consciousness and eventually recover some ofthe cognitive functions. This phenomenon of spontaneousrecovery from brain injury implies that some brain cells thathave lost function can regain it, sometimes after long periodsof time. Several theories of recovery after injury in the centralnervous system invoke the concept of temporary, reversibleinactivity of brain tissue to explain this phenomenon.The use of HBOT for chronic brain injury is based on thetheory that, in any brain injury, there are inactive cells thathave the potential to recover. According to this theory, these"idling neurons" exist in the ischemic penumbra, a transitionarea of dormant neurons between areas of dead tissue andthe unaffected healthy tissue [22,26,38]. The oxygen availabilityto these cells stimulates the cells to function normally,reactivating them metabolically or electrically.

5. Conclusion

The addition of HBOT significantly improved the outcome/survival and quality of life and also reduced the risk of complications in patients withsevere diffuse axonal head injury. HBOT for brain injury is unlikely to gain acceptance in routine clinical use before a clinical procedure is established for evaluating its effectiveness in the individual patient. Specifically, the diagnostic value of SPECT scans and of otherintermediate indicators of the effects of HBOT should beexamined by large and high-quality studies. A longitudinalcohort study in which all patients undergo proper diagnostic evaluation as well as standardized follow-up tests would be amore prudent and ideal approach.

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