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ORIGINAL ARTICLE

Use of hyperbaric oxygen in traumatic brain injury: Retrospective analysis of data of 20 patients treated at a tertiary care centre

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Abstract

Traumatic Brain Injury (TBI) related impact results in a permanent need for help in performing daily activities. Standard treatment consists of removing the cause, restore perfusion, support metabolic requirement and limit inflammatory and oxidative damage. Hyperbaric oxygen therapy (HBOT) is one such newer promising treatment that enhances neurological recovery to some extent. HBOT is intermittent inhalation of 100% oxygen at greater than normal atmospheric pressure and is internationally accepted for its role in well-defined indications. It is hypothesised that HBO has a role in reviving 'idling neurons', also called the ischemic penumbra defined as area of reduced cerebral blood flow, abolished synaptic activity but preserved structural integrity. We carried out a retrospective analysis of medical records of 20 patients of TBI who had been treated with HBOT in addition to standard management. These were placed in Group A (test group) and received at least 30 sessions of HBO along with standard treatment. The patients were assessed along the Disability Rating Scale (DRS), Glasgow coma scale (GCS) and Rancho Los Amigos Scale (RLAS). Another 20 patients of TBI, matched in age and severity of brain injury, who received standard treatment but not HBOT, were selected as the control group (Group B).

Assessment on the DRS showed maximum improvement in patients with scores of 22–24 (vegetative state).The percentage of patients in the test group fell from 45% to 5% whereas only 20% patients in Group B had similar progress. After the treatment, a significantly higher proportion of HBOT treated subjects showed a good response in cognitive functions, as measured by RLA. In group A, 90% patients had a score of ≤ 3 and in Group B 95% had a similar score, which improved to ≥ 3 in 60% patients versus 30% patients respectively. **In both groups maximum patients are in 1–6 months post-injury category and within the groups this category showed the greatest recovery, with a greater improvement in the test group as compared to control group.**

Keywords: brain; cognitive function; hyperbaric oxygen therapy; neurorehabilitationischemia; traumatic brain injury.

Introduction

Traumatic Brain Injury(TBI) describes a heterogeneous set of injury mechanisms and pathological conditions, but there are common metabolic pathways leading to depressed aerobic metabolism, reduced cellular ATP production and, ultimately, cell death. TBI is a significant public health problem worldwide and is predicted to surpass many illnesses as a major cause of death and disability by the year 2020. In India, the annual incidence of TBI is 1 240 436 cases leading to 30 000 deaths. Road traffic injuries are leading cause of TBI, accounting for up to 60% cases followed by falls (20–25%) and violence (10%).[1] It is reported that 46% of these cases suffer from severe disabilities, 30% from moderate and 24% minor disabilities at the time of discharge from hospital.[1]

Hyperbaric oxygen therapy (HBOT) is intermittent inhalation of 100% oxygen at greater than normal atmospheric pressure and may be beneficial for TBI because it improves cerebral blood flow into tissues exhibiting low blood flows. Hyperoxia improves cerebral metabolic consumption of oxygen. It also leads to improvement of oxygenation, reduction in cerebral oedema, reduction in intra-cranial pressure. The rationale of use of HBO in neurological conditions is based on the observation in SPECT studies that around the central area of neuronal death is a penumbra or periinfarct 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.[2,4,6,8,12]

While HBO has been used for neurorehabilitation of TBI cases since 1965, there is still no consensus that addition of HBOT to overall treatment plan leads to reduced morbidity and mortality. The Hyperbaric Oxygen Unit at this tertiary care hospital has been treating patients referred with TBI since 2005. However, this study analyses the data of patients treated from 2007–2009.

The objective of this study is to determine whether addition of HBOT to standard treatment plan of patients having TBI improves outcomes and which subgroup of patients will

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or will not respond to HBOT. The results of this pilot study may form the basis of further, larger, prospective studies on the role of HBOT in TBI.

Materials and methods

We approached this study by reviewing the medical records of 20 patients of TBI who had been treated with HBOT in addition to standard treatment during the period 2007–2009 and another 20 patients who received standard care but did not receive HBOT.

The incidence of TBI treated at this hospital is shown in Table I. A total of 705 patients were admitted to the hospital from Jan 2007 to Dec 2009, 562 were males and 143 were females with age ranging from 1 to 91 years.

The test group (**Group A**) consisted of patients of TBI referred for HBOT during this period. These patients were in the ages ranging from 17–55 years. They received HBO as an adjunct to standard surgical, medical management and physiotherapy. An equal number of patients matched with respect to baseline characteristics viz. age, severity of injury, lag period and management protocol, but who did not receive HBOT, were identified and labelled **Group B**. (There was no randomization criteria used as it was a retrospective analysis, therefore, the patients referred to the Hyperbaric Oxygen Therapy Unit were considered as subjects of Group A i.e. test group)

The test group received at least 30 sessions of HBOT at 1.5 ATA for 60 minutes O_2 once daily in addition to standard care. HBOT was given in a 'Multiplace Chamber' which was pressurized with compressed air, and 100% O_2 was administered via specialized mask or T-tube if patient was tracheostomized. The control group did not receive HBOT, however, standard treatment was given.

The data in Table II shows the clinical profile of patients included in the study. Most patients were in the age groups of 18–50 years with more males than females and had sustained a TBI within 6 months of having received HBOT. The cause of injury was motor vehicle accident in most cases and had focal or Diffuse Axonal injury.

The clinical characteristics of patients in Group A has been tabulated in Table III. On RLA score, 95%(n = 19) patients had score of ≤ 3 (poor response), and only 5% (n = 1) had > 3 score (good response).On DRS, maximum patients (45%, n = 9) in this group were in vegetative state with DRS of 22–24, and 30% (n = 6) patients in extreme vegetative state with DRS of 25–29. On GCS, 35% (n = 7) patients had score between 3–8 indicating severe injury, and 15% (n = 3) patients were in moderate to mild condition.

The clinical characteristics of patients in Group B is tabulated in Table IV using the same scales as for Group A. On DRS , 90% (n = 18) patients had a low RLA score of ≤ 3

Table I. Incidence of TBI at the Apollo Hospital, New Delhi.

		Sex		Age Group				
Year	Total	M	F	<10	10–20	21–40	41–50	>50
2007	168	127	41	20	19	74	29	26
2008	304	231	73	24	32	146	38	64
2009	233	204	29	16	41	104	38	34

Table II. Clinical Profile of patients included in study.

	Group A* (n = 20)		Group B** (n = 20)	
Variables	n	%	n	%
Age (years)				
<18	03	15	02	10
18–50	16	80	17	85
>50	01	05	01	05
Sex				
Male	13	65	16	80
Female	07	35	04	20
Cause of Injury				
Motor vehicle accident	17	85	18	90
Falls	01	05	01	05
Others	02	10	01	05
Duration since Injury				
<1 Month	05	25	02	10
1–6 Month	12	60	13	65
>6 Months	03	15	05	25
CT Findings				
Focal injury	08	40	09	45
Diffuse injury	07	35	05	25
Others	05	25	06	30

*Group A: Test group.
**Group B: Control group.

and only 10% (n = 2) subjects had higher RLA score. On the basis of DRS, we see that 45% (n = 9) subjects were in vegetative state with DRS of 22–24, and 35% (n = 7) subjects were grouped in extreme vegetative state.

The low score of DRS was present in only 20% (n = 4) subjects. On the basis of severity as shown by GCS, 40% (n = 8) subjects had a score from 3–8 and 25% subjects had moderate to mild severity. (Note: GCS score has been collected on the first day of enrolment of the patients in each group)

Statistical analysis

Sample size relevant for statistical calculation was not performed since data was collected and analysed reterospectivly. All values are expressed as percentage and mean (± S.D.) for comparison of data among groups.

Results

This study investigated the hypothesis that the use of HBOT as an adjunctive treatment to standard care can help improve

Table III. Clinical characteristics of the patients in Test group: Group A (n = 20).

	Pre-HBO		Post-HBO	
Variables	n	%	n	%
Glasgow Coma Score				
3–8(Severe)	07	35	03	15
9–12(Moderate)	03	15	07	35
13–15(Mild)	00	00	01	05
Tracheostimised	10	50	09	45
Ranchos Los Amigos Scale				
≤ 3 (Poor response)	19	95	07	35
> 3 (Good response)	01	05	13	65
Disability Rating Scale				
25–29 (Extreme veg. state)	06	30	05	25
22–24 (Vegetative state)	09	45	01	05
17–21 (Extremely severe)	05	25	04	20
12–16 (Severe)	NIL	-	06	30
7–11 (Moderately severe)	NIL	-	04	20
<7 (Mild to moderate)	NIL	-	-	-

Table IV. Clinical characteristics of the patients in control group: Group B (n = 20).

Variables	Pre-Treatment n	Pre-Treatment %	Post-Treatment n	Post-Treatment %
Glasgow Coma Score				
3-8 (severe)	08	40	07	35
9-12 (moderate)	04	20	05	25
13-15 (mild)	01	05	01	05
Tracheostimized	07	35	07	35
Ranchos Los Amigos Scale				
≤3 (poor response)	18	90	12	60
>3 (good response)	02	10	08	40
Disability Rating Scale				
25-29 (extreme veg.state)	07	35	06	30
22-24 (vegetative state)	09	45	05	25
17-21 (extremely severe)	04	20	05	25
12-16 (severe)	NIL	-	04	20
7-11 (moderately severe)	NIL	-	-	-
<7 (mild to moderate)	NIL	-	-	-

outcomes. In our study 80% patients were in the productive age group of18–50 years, and TBI was more common in males, traditionally the bread earners of family. Motor vehicle accidents are the leading cause of TBI accounting for more than 50% cases suffering from focal head injuries, and more than one-third population had permanent disability resulting from diffuse brain injuries. **In our retrospective study, 40 patients were included: 20 patients received HBOT with standard care (Group A), and 20 patients received only standard care (Group B).**

During the period 2007–2009, a total of25 patients of severe TBI were referred for HBOT. The patients who completed at least 30 sessions of HBOT were included in the study, while those who had risk factors to hyperbaric treatment or could not complete the treatment cycle were excluded. One patient developed pneumothorax after three HBOT sessions, two patients went against medical advice and two patients did not complete the prescribed HBO sessions due to financial constraints.

Of the patients studied (Group A) 13 were males and 7 were females. Age varied from 17 years to 51 years.Seventeen patients sustained head injury due to road-traffic accidents, one patient was victim of fall and remaining two patient sustained injury due to other causes. Radiological investigations like CT scan/MRI revealed diffuse axonal injury in 7 cases, subdural haematomas in 3 cases, subarachnoid haemorrhages in 5 patients and other contusion injuries in 5 cases. SPECT was not used in any of our patients. The GCS level of the patients at the time of admission ranged from 2–10 T ($E_1V_tM_1$ to $E_4V_TM_6$).

In Group B, 16 were males and 4 were females. Age varied from 19 years to 53 years. Eighteen patients sustained head injury due to road-traffic accidents and one patient was victim of fall and one suffered gunshot injury in the head. Radiological investigations like CT scan/ MRI revealed 5 cases of diffuse axonal injury, subdural haematomas in 5, subarachnoid haemorrhages in 4 and other contusion injuries in 6 cases. The GCS level of the patients at the time of admission ranged from 3–10 T ($E_1V_tM_2$ to $E_4V_TM_6$).

A comparative assessment between the two groups has been tabulated in Table V. The study demonstrated better outcome in the test group compared to the control group.

Assessment using the DRS showed a significant improvement in the test group in the vegetative state. The patients in the vegetative state (DRS Score 22–24) showed maximum improvement, and the percentage dropped from 45% to 5% in test group compared to a reduction from 45% to only 25% in the control group.

Patients in extreme vegetative state (DRS > 24) reduced from 30 to 25% in the test group compared to a reduction from 35 to 30% in the control group. Patients with less severe injuries (scores below 17) increased from 25% to 70% in the test group compared to increase from 20% to 45% after treatment in the control group.

The mean score values of DRS fell from 23.75 to 18.85 in test group compared to reduction from 23.4 to 21.65 in the control group.

In Group A 90% patients had a score of ≤3 on RLA before starting treatment with HBO, and this reduced to 35% after treatment. In Group B 95% had a similar score before treatment, and these reduced to 60% after treatment.

Table VI shows results of recovery of patients on the basis of the onset of injury to initiation of HBOT in both the groups.

Table V. Comparative results of patients in the test and control group.

Variables	Group A Pre-T/t (%)	Group A Post-T/t (%)	Group B Pre-T/t (%)	Group B Post-T/t (%)
Glasgow Coma Score				
3-8 (severe)	35	15	40	35
9-12 (moderate)	15	35	20	25
13-15 (mild)	00	05	05	05
Tracheostimized	50	45	35	35
Ranchos Los Amigos Scale				
≤3 (poor response)	90	35	95	60
>3 (good response)	10	65	05	40
Mean score	1.9 ± 0.85	6 ± 1.26	15 ± 0.98	2.75 ± 1.06
Disability Rating Scale				
25-29 (extreme veg..state)	30	25	35	30
22-24 (vegetative state)	45	05	45	25
17-21 (extremely severe)	25	20	20	25
12-16 (severe)	-	30	-	20
7-11 (moderately severe)	-	20	-	-
<7 (mild to moderate)	-	-	-	-
Mean score	23.75 ± 2.55	18.85 ± 3.2	23.4 ± 0.98	21.65 ± 2.15

%: of number of patients.

Table VI. Comparative results of recovery of patients on basis of time lag between injury and start of HBOT in Group A and Group B.

	<1 Month		1-6 Months		>6 Months	
	Pre n	Post n	Pre n	Post n	Pre n	Post N
GROUP A						
RLA						
≤3	5	2	11	2	3	2
>3	-	3	1	10	-	1
Mean score	1.6 ± 0.54	3.4 ± 0.89	2.08 ± 0.79	4.00 ± 1.30	2.3 ± 0.57	2.6 ± 0.58
DRS						
22-29	5	3	8	3	2	1
12-21	-	2	4	8	1	2
07-12	-	-	-	1	-	-
<7	-	-	-	-	-	-
Mean score	26.0 ± 2.54	22.4 ± 1.51	23.3 ± 3.22	17.25 ± 5.04	22.6 ± 3.21	19.0 ± 3.0
GROUP B						
RLA						
≤3	1	-	13	10	4	2
>3	1	2	-	3	1	3
Mean score	2.5 ± 2.12	4	1.69 ± 0.48	2.69 ± 1.25	2.79 ± 0.89	3.4 ± 0.89
DRS						
22-29	2	1	11	8	3	2
12-21	-	1	2	5	2	3
07-12	-	-	-	-	-	-
<7	-	-	-	-	-	-
Mean score	25.5 ± 0.70	22 ± 2.82	23.38 ± 2.43	21.92 ± 3.40	22.2 ± 3.83	18.6 ± 4.39

It is observed that within Group A the improvement is maximum when hyperbaric treatment is started within 1-6 months (RLA:2.08-4.00,DRS:23.3-17.25) as compared to the < 1 month (RLA:1.6-3.4,DRS:26.0-22.4) and the > 6 month group (RLA:2.3-2.6, DRS:22.6-19.0).

Maximum improvement in both groups is in patients within 1-6 months injury. Within this category, patients in Group A showed greater recovery than Group B with significant increase in mean score values of RLA in Group A (2.08-4.00) compared to Group B (1.69-2.69) and fall in mean score of DRS from 23.3 to 17.25 as compared to Group B in which it was 23.38-21.92.

The number of tracheostomised patients was 50% in the test group and 35% in the control group. This may have been a possible cause that we did not find the GCS assessment a suitable assessment tool in cases of TBI. Additionally, since GCS only assess three parameters, it is possibly not sensitive enough when compared to other scales.

Discussion

TBI is a significant public health problem worldwide and is predicted to surpass many diseases as a major cause of death and disability by the year 2020.[1] TBI related injury results in a permanent need for help in performing daily activities. While the degree of neurological impairment may vary depending on the location of the injury and resulting damage, the behavioural changes have significant social impact and may not correlate with the injury. India and other developing countries face the major challenges of prevention, hospital care and rehabilitation in their rapidly changing environments to reduce the burden of TBIs.

TBI describes a heterogeneous set of injury mechanisms and pathological conditions, however, it leads to a common pathway leading to depressed aerobic metabolism, reduced cellular ATP production and ultimately cell death. Immediately after a brain injury, brain cells can be inactivated permanently or temporarily by local, injury related sequel such as ischemia and oedema which compromise local perfusion. Patients with TBI have few options for rehabilitation. Drug treatments have been inadequate to provide significant recovery and no proven treatments emerging in the last 30 years have been considered to be effective.

Several studies have focussed on HBO in populations with severe TBI .On a microscopic level, various animal studies have demonstrated that HBO promotes new neuron and blood vessel regrowth, improves cellular metabolism and cell survival, and reduces brain inflammation and swelling. HBO involves exposing the individual to pure oxygen in an environment with greater than normal atmospheric pressure. Some literature suggests that HBO can decrease mortality and improve neuropsychological and functional outcomes after severe TBI but there is still insufficient evidence to recommend its use.[5-8] Current research is focussed on comparing the utility of HBO to that of normobaric hyperoxia, a less expensive and easier to administer alternative, and examining the mechanisms of action of HBO.[8-12,16,18]

Current research is underway to ameliorate the inflammatory biochemical milieu in the acutely head injured patient by employing 21-amino steroids,[11,19,21,23,24] iron chelators, superoxide anion scavengers, inhibitors of excitatory amino acids,[25] opioid peptide antagonists, ACTH hormone analogs ,prostaglandin synthetase inhibitors and hydroxyl radical scavengers (e.g. mannitol).

Several authors have evaluated patients with marked cerebral injuries and studied metabolism as measured by cerebral glucose consumption under conditions of normobaric air, 100% normobaric oxygen, 1.5 ATA oxygen and 2.0 ATA oxygen. Cerebral metabolism was found to be optimal at a pressure of 1.5 atmospheres absolute of oxygen. The author concluded that 1.5 ATA was the optimum treatment pressure for patients suffering marked cerebral injuries because

cerebral metabolism was optimum at that pressure and was equal to that of normal brain tissue.[7,31-34]

Neubauer et al.[37] proposed a theory of 'idling neurons' in 1990 with a report of a single patient having suffered a right middle cerebral artery infarction 14 years previously. The author concluded that 'idling' neurons exist in an area surrounding dense, gliotic, neuronal scar tissue and that these 'idling' neurons are salvageable with 1.5 atmospheres absolute HBOT and can be identified and followed sequentially for improvement using SPECT brain imaging.[2,15,18,20,21,35]

Despite abundant experimental evidence showing that neurons surrounding an area of trauma or infarct could survive albeit in an electrically silent or vegetative state, a means to visualize this region remained to be found. With the advent of PET and SPECT, a method was found to visualize the functional areas of the brain. In 1991, a study by Gray et al.[15] found that HMPAO-SPECT brain imaging of patients with remote TBI was superior to CT scan or MRI in detecting regional cerebral blood flow deficits.

In 1994, Neubauer et al.[37,40] reported on the case of a 40-year-old male who sustained a traumatic head injury as a result of a single car accident and compounded by the additional insult of an anoxic injury following an improper intubation at the scene that occurred approximately 18 months prior to receiving HBOT. After one single, 1.5 ATA HBOT, a repeat SPECT brain scan showed marked filling-in of the defect, as evidenced by increased tracer uptake. Physiologically, this patient went from an individual with marked spasticity of all extremities and a level 7 RLA scale, requiring total life support and intensive nursing home care to one where he was able to fully ambulate and required only minimal care.

A number of previous studies have studied the role of HBOT in acute severe TBI and chronic brain injuries.[4,6,7,18-20,40] However, the correlation of neurological improvement between onset of injury and start of HBO is not well understood. Lin JW et al. concluded that HBOT can provide some benefits for sub-acute TBI patients with minimal adverse effects.[27] Paul G. Harch et al. demonstrated that with delays longer than 1 month, HBO assumes trophic role stimulating brain repair and manipulating brain blood flow and metabolism.[21] In our study the largest number of patients in whom HBO was started was within 1-6 months, and these patients also showed maximum recovery. The large numbers in this category is possibly due to our centre being within the hospital and correlates with the time taken for acute care to be completed and patients considered stable to undergo HBOT. The patients in this category in both group showed maximum recovery with significant improvement in the hyperbaric group. We hypothesise that the delivery of oxygen to the brain tissues has a maximum effect during this period and leads to an enhanced reduction of oedema , expedites the natural process of recovery of neurons leading to better outcomes in shorter period of time. It is recommended that subsequent studies also assess the best time to start HBOT after TBI.

HBOT is gradually receiving greater recognition as a possible treatment modality which may contribute to reduce the morbidity resulting from TBIs and could emerge as an important part of the comprehensive neurorehabilitation programme in such conditions. HBOT has a synergistic effect with other treatments, strongly suggesting that combining therapies with HBOT could yield better results than either alone. We have, in our tertiary care hospital, a multi occupancy chamber which is designed to accommodate several patients, attendants and medical personnel offering treatment to many patients at one time.

In view of the modest number of patients, methodological shortcomings and poor reporting, the result of study should be interpreted cautiously, and an appropriately powered trial of high methodological rigour is justified to define these patients who can be expected to derive most benefits from HBOT.

Conclusion

A reasonable summary of the research cited above would establish that there exists a penumbra of viable, neuronal tissue that exists around areas of dead gliotic, cerebral tissue. This penumbral area is recoverable with the use of hyperbaric oxygen. Progress is measurable, not only by SPECT brain imaging, but also by conventional neurologic testing and psychometric testing. Patients with traumatic head injuries treated with HBOT can be expected to recover more than previously thought to be possible. The patients in our study have shown significant improvement; but, this is a retrospective study and the small numbers precludes a statistical conclusion. However, this justifies and encourages a larger prospective study at the earliest.

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Disclosure

The authors report no conflicting financial interests.

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