Original Research Article

International Journal of Neurology and Neurosurgery
Volume 11 Number 2, April - June 2019
DOI: http://dx.doi.org/10.21088/ijnns.0975.0223.11219.2

HBOT in Traumatic Brain Injury Patients: Prospective Randomized Clinical Trial

Manoj Gupta

Abstract

Background: The use of hyperbaric oxygen therapy in cases with traumatic brain injury is based on the hypothesis that injured or inactive neurons would greatly benefited from increased blood flow and oxygen delivery, which later could act to metabolically or electrically may reactivate the cells.

Objective: To evaluate the optimal number of hyperbaric oxygen therapy sessions required in patients with head injury and to compare the neurological effects of 10, 20 and 30 sessions of hyperbaric oxygen therapy in patients with traumatic brain injury.

Study Design: Prospective randomized clinical trial.

Place of Study: The study was carried out at the Prana HBO Centre, which is owned by the Investigator and located in the Northern parts of Mumbai, in India.

Methods: Study was conducted over a period of 3 years and patient with Head injury referred to the Hyperbaric Unit at Prana HBO center after the initial evaluation and surgical procedure were included. Patients were randomly assigned to any of the three groups and allotted numbers were concealed to receive HBO therapy. HBO therapy was given with compressed with air at a pressure of 1.8 atmosphere absolute (ata). At this pressure the patient breathed 100% oxygen via facial mask. The HBO therapy protocol included 90 minutes oxygen breathing at 1.8 ata, 6 days a week.

Results and Discussion: A significant improvement in GCS scores in group H10 between the end of 10 HBOT sittings and at the end of 30th day. As well significant improvement in scores of group H20 between the end of 20 sittings and at 30th day was being observed. GOS was seen better after 20 and 30 sessions of hyperbaric oxygen therapy as compared to group I of HBOT group III showed maximum improvement in spasticity in comparisons to group I and II, however there was good improvement in spasticity all the three group. Mood swings was less in group III with only 12% patients showing mood swings, whereas in group II and group I it was around 59% and 93% respectively. Fasano carried out first clinical observation and presented a therapeutic effect of hyperbaric oxygen therapy in traumatic brain injury patients and concluded that the HBO improved the outcome following brain trauma.

Conclusion: Our findings shows the beneficial effects of HBO therapy in traumatic brain injury patients on GCS score, GOS, spasticity and mood swings with increase in number of multiple sessions. Despite these encouraging results further research is needed to more clearly define the mechanism and potential role of HBOT following traumatic brain injury.

Keywords: HBOT; Traumatic brain injury; Clinical Trial.

How to cite this article:

Manoj Gupta. HBOT in Traumatic Brain Injury Patients: Prospective Randomized Clinical Trial. Int J Neurol Neurosurg. 2019;11(2):115-121.

Author's Affiliation: : Director, Prana Hyperbaric Oxygen Therapy Center, Sailee Hospital & Diagnostic Center, Prathamesh Horizon, New MHB Colony, New Link Road, Borivali West, Mumbai, Maharashtra 400091, India.

Corresponding Author: Manoj Gupta, Director, Prana Hyperbaric Oxygen Therapy Center, Sailee Hospital & Diagnostic Center, Prathamesh Horizon ,New MHB Colony, New Link Road, Borivali West, Mumbai, Maharashtra 400091, India.

E-mail: drmanojgupta222@gmail.com

Received on 01.03.2019, **Accepted on** 12.03.2019

Introduction

Major cause of mortality and morbidity in young people, general population and arm force personal is trauma; mostly maximum number of deaths is being attributed to traumatic brain injury. Tremendous burden is caused by the morbidity of traumatic brain injury for both families and the society. Life saving procedures and treatment is being done such as hematoma or contusion focus

removal in traumatic brain injuries but it is observed that the prognosis is hardly being improved [1,2]. To be efficient and focused the general consensus is that the focus should be on secondary brain injury; as well major concern should be on stabilization of blood and intracranial pressure in traumatic brain injury cases. It mostly involves prompt administration of neuro-protective drugs, rehabilitative training even though the neglect of hypoxic state of brain tissue is commonly observed after traumatic brain injury.

Many researches had pointed out that secondary ischemic injury exists in brain tissue seen in very early stages of traumatic brain injury and that is being considered as important contributor to morbidity and mortality. Primary aim in general management of traumatic brain injury as such is maintenance of oxygenation and perfusion [1].

Hyperbaric oxygen therapy can be defined as breathing of hundred percent oxygen at a pressure which is higher that atmospheric pressure. In the beginning the hyperbaric oxygen therapy was being used for treatment of decompression sickness seen in divers, however over a period of time its major potential of therapy had been clearly recognized and soon got approval for majority of purposes which include in repair of wounds, anemia, thermal burns cases, delayed radiational injuries, carbon monoxide poisoning, osteomyelitis and actinomycosis etc. [3].

As apart from these general conditions, great deal of interest with hyperbaric oxygen therapy had been shown in cases with traumatic brain injury, stroke, cerebral palsy etc. The use of hyperbaric oxygen therapy in cases with traumatic brain injury is based on the hypothesis that injured or inactive neurons would greatly benefited from increased blood flow and oxygen delivery, which later could act to metabolically or electrically may reactivate the cells [4,5,6,7]. However on the contrary hyperbaric oxygen therapy is been clearly approved for the above enlisted clinical conditions and indications [8] the effects of hyperbaric oxygen therapy in relation with traumatic brain injury is yet not been clearly defined.

Hyperbaric oxygen therapy is a mode of treatment where the patient is entirely enclosed in a pressure chamber and he breathes hundred percent oxygen at a pressure which is greater than one atmosphere absolute (ATA). Hyperbaric oxygen is presently being used in an attempt to improve functional outcome following a multitude of brain injuries such as stroke, anoxic brain injury, and traumatic brain injury [9]. Number of other authors had used various numbers of sessions of hyperbaric oxygen therapy and had shown variable results; however the frequency of hyper baric oxygen therapy sessions in patients with head injury had not been standardized [10,11]. Grossly it appears that the clinical outcome and benefit is dependent upon the dose of hyperbaric oxygen sessions [12].

Hence the in our study the aim was to evaluate the optimal number of hyperbaric oxygen therapy sessions required in patients with head injury. To accomplish the aim we laid down a prospective randomized control clinical trial with the intention to compare the neurological effects of 10, 20 and 30 sessions of hyperbaric oxygen therapy in patients with head injury.

Patients and Methods

Study setting

The study was carried out at the Prana HBO Centre, which is owned by the Investigator and located in the Northern parts of Mumbai, in India. The center has one Sechrist Monoplace hyperbaric chamber and a TCOM machine with 3 electrodes. The oxygen gas supply is from oxygen cylinders of 7000 liters' capacity each. The center has all the requisite certifications and registrations as required by the local authority in Mumbai. Study was conducted over a period of 3 years and patient with Head injury referred to the Hyperbaric Unit at Prana HBO center after the initial evaluation and surgical procedure were included. Written informed consent was obtained from the patient and patient's relative.

96 patients of age ranging from 4 years to 78 years with head injury were included in study. Patients with the history of head injury and Glasgow coma scale Score < 9 were included in the study. All patients were resuscitated and stabilized and they received neurological care according to the hospital protocol.

On receiving the patient to the HBO unit at Prana, patients were randomly assigned to any of the three groups and allotted numbers were concealed to receive HBO therapy.

Group HBOT10 (n 32): received 10 sittings of HBOT

Group HBOT20 (n 32): received 20 sittings of HBOT

Group HBOT30 (n 32) received 30 sittings of HBOT.

HBO therapy was given with compressed with air at a pressure of 1.8 atmosphere absolute (ata). At this pressure the patient breathed 100% oxygen via facial mask. The HBO therapy protocol included 90 minutes oxygen breathing at 1.8 ata, 6 days a week. ECG, non invasive automated blood pressure, respiratory rate and pulse oximeter monitoring was done during the management and therapy. Glasgow coma scale score [13] a primary outcome variable and recorded by the principal investigator after every 10 sittings and at 30 days from beginning of hyperbaric oxygen therapy in all three groups. Readings were recorded on a scale of 0 to 100 at 30 days in all three groups [14,15]. Glasgow outcome scale (GOS) in all three groups were recorded after 30 days. Modified Ashworth Scale was used to measure and grade the muscle spasticity [16].

Improvement in muscle spasticity ranging from grade 1 or more was considered to be improvement and was recorded. Tracheostomy and its removal requirement were also noted; as well the removal of Ryle's tube was also recorded. During the period of three years of trial all the patients in three groups received intensive standard of care required in traumatic brain injury and was consistent with the protocol. Whenever required surgical interventions were made.

Exclusion criterion

Patients were excluded from the trail if the patient was enrolled in another trail, pregnant, Upper respiratory tract infection, neurologic or pulmonary or otorhinolaryngologic diseases contraindicating HBO therapy.

Baseline computerized tomography (CT) scan was recorded in each case and was categorized in Cat I to Cat IV.

Ethics review

This study was performed within the scope of international ethical guidelines and legislation. Ethics review and approval was provided by Stellenbosch University (number: U16/06/015) and the ethics committee of the Hyperbaric Society in India.

Statistical Analysis

The improvement in patients by GCS score, between all the groups is clinically significant on the basis of this assumption we set a 95% power and taking α = 5% (Level of Significance). In this study we examine total 96 patients which we divide equally in three groups randomly. We use MS Excel to analyses the statistical data, analysis data is represented by graphically and descriptive statistics calculated for different variables. Test of Significance is done by Kruskal-Wallis test & for the parametric test done through one way ANOVA. Decision of test of significance is based on p-value & it is statistically significant if p-value is less than 5% (p-value < 0.05).

Results

In the study total 96 cases were recruited, patient who fulfilled all the inclusion criteria for the study. Total 96 patients completed the study period and no patient was excluded during the study analysis 32 patients in each groups were randomized. During the period of study neither of the group patient had any episodes of cerebral oxygen toxicity nor there any adverse effects of pressurization observed. As per Table 2 all three groups were comparable with respect to demography, mode of injury and various baseline parameters. As per Table 4 neuro surgical interventions were comparable in three groups along with baseline median GCS scores. On observation the significant findings was that GCS score improved along with initiation of hyperbaric oxygen therapy. A significant improvement in GCS scores in group H10 between the end of 10 HBOT sittings and at the end of 30th day. As well significant improvement in scores of group H20 between the end of 20 sittings and at 30th day was being observed.

Table 1: Baseline CT categorization

Sr. No	Baseline Computerized Tomography categorization	CT Findings
1.	Cat I	No visible pathology seen on CT scan
2.	Cat II	Cisterns are present with shift 05 mm, no high or mixed density lesion >25 mL, may include bone fragments and foreign bodies.
3.	Cat III	cisterns compressed or absent, shift of 05 mm, no high or mixed density lesion >25 mL
4.	Cat IV	shift >5 mm, high or mixed density lesion >25 mL

As per Table 4 difference in the average improvement in global rating scale between group I and group II and between groups I and group III was significant, but it was comparable more significantly between group II and Group III. The GOS was seen better after 20 and 30 sessions of hyperbaric oxygen therapy as compared to group I of HBOT group III showed maximum improvement in spasticity in comparisons to group I and II, however there was good improvement in spasticity all the three group. As per Table 4 Mood swings was less in group III with only 12% patients showing mood swings, whereas in group II and group I it was around 59% and 93% respectively. In group I, II and III seven, five and eight patients were tracheostomized respectively. At the end of 30 days of hyperbaric oxygen therapy 29% patients were decannulated in Group I as compared to 60% in group II and 50% in group III. 71% of patients Ryle's tube was removed in group I, 80% in group II and 87.5% in group III at the end of 30 days of starting of therapy.

Table 2: Demographic analysis of baseline parameters

Parameters		Group - I H10 (n = 32)	Group - II H20 (n = 32)	Group - III H30 (n = 32)
Age	Min. Age	4	9	7
	Average	48	45	51
	Max. Age	69	76	78
Sex Ratio		14:18	20:12	17:15
Delay in HBOT from day of Injury (Mean)		13	15	13
Patients on anticonvulsants (n)		24	25	25

Table 3: Patients distribution of preoperative CT category by group

Groups	Pre Operative CT Category			
	I	II	III	IV
Group - I	8	11	7	6
Group - II	2	10	9	11
Group - III	4	9	10	9

Table 4: GCS (E, V, M) Scores of various stages of HBOT

Sittings	Group - I H10 (n = 32)			Group - II H20 (n = 32)			Group - III H30 (n = 32)		
	E	V	M	E	V	M	E	V	M
Baseline	3	3	5	2	4	5	3	5	3
At 10 days/sittings	5	5	6	4	7	6	5	7	5
At 20 days/sittings	5	5	6	4	7	7	5	7	6
At 30 days/sittings	6	5	6	5	7	7	6	7	6

Table 5: Improvement in patients & different parameters after 30 day of starting HBOT

Parameters		Group - I	Group - II	Group - III
Patients Improvement	Moderate	65% (0.0001)	78% (0.0001)	83% (0.0001)
	High	73% (0.0001)	85% (0.0002)	97% (0.0002)
GOS	I	16	27	24
	II	0	1	2
	III	2	0	2
	IV	9	3	4
	V	5	1	0
Patients with mood swings		93% (0.001)	59% (0.001)	12% (0.001)

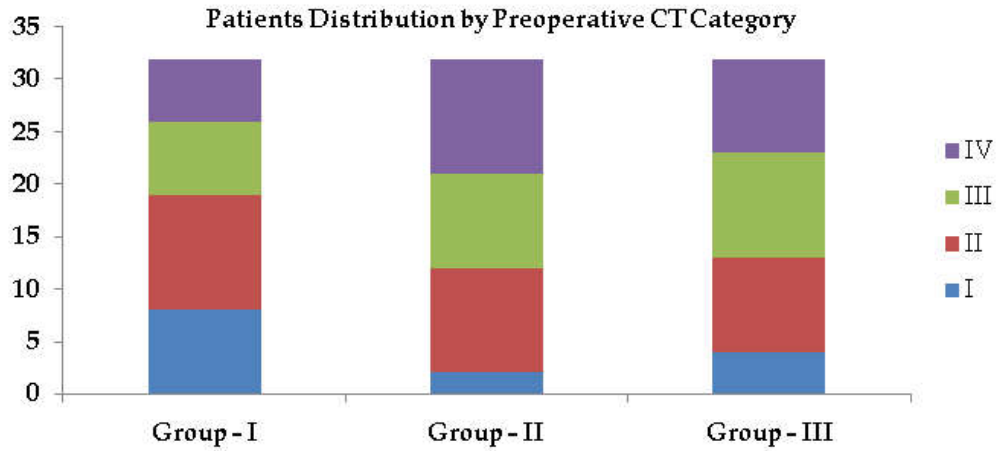

Fig. 1: Patients Distribution by Preoperative CT Category

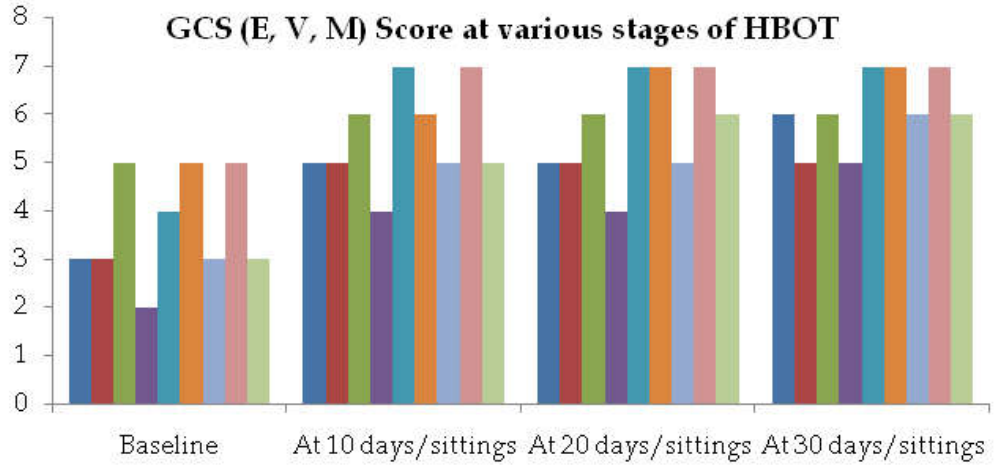

Fig. 2: GCS (E, V, M) Score at various stages of HBOT

Discussion

Various researchers on hyperbaric oxygen therapy in experimental traumatic brain injury have prominently clarified diverse mechanism which leads to neuro-protection in brain; mechanism includes increasing tissue oxygenation, reducing inflammation, decreasing apoptosis, reducing intra cranial pressure and promoting neurogenesis and angiogenesis. Gradually intense clinical research and trail were conducted with the aim of evaluating the efficacy and safety of hyperbaric oxygen therapy in relation with traumatic brain injuries and other neurological disorders. In clinical settings, hyperbaric oxygen therapy is usually implemented in form of repetitive sessions over extensive time periods with the aim of improving neurological outcomes after traumatic brain injury. Usually treatment involved pressurization in a range of 1.5 to 3.0 ATA for period in between 60 to 120 minutes once or more daily with a range of less than one week to several months duration, however average being two to four weeks, mostly dependent upon the response of the patient and severity of the existing problems.

Hyperbaric oxygen therapy is an adjunctive therapy, proposed to improve an outcome in traumatic brain injury patients [17]. The mechanism by which hyperbaric oxygen therapy improves the squeal following traumatic brain injury is just a speculative. The theory is based on that damaged cells are Idling neurons in the ischemic pneumbra which have the very potential to recover [17]. However the clinical efficiency of Hyper baric oxygen Therapy in Traumatic brain injury remains controversial. Since the 1960s, many reports have

demonstrated an HBOT-associated reduction in mortalities and/or improvement of neurological functions after TBI [18]. Most are based on case studies or retrospective analyses. Standardized clinical studies reporting HBOT-associated protective effects on TBI mediated brain damage are scarce, and an explicit benefit of HBOT for TBI patients has yet to be established.

In our study we observed that the administration of hyperbaric oxygen therapy in patients with traumatic brain injury had improved the GCS score along with improvement in global rating, GOS and spasticity. This positive findings improvement gradually increased with the number of increased sittings. Mood swings were also improved with increased sessions as well de-cannulated and ryle's tube removal occurred early with increasing oxygen therapy sittings in patients with traumatic brain injury.

In 1964 Fasano et al. carried out first clinical observation and presented a therapeutic effect of hyperbaric oxygen therapy in traumatic brain injury patients and concluded that the HBO improved the outcome following brain trauma [19]. Hayakawa et al. showed that HBOT had effect in traumatic brain injury patients with change in intra cranial pressure as well reduction in CSF pressure in patients with acute cerebral damage, improved grey matter metabolic activity on single photon emission computerized tomography scan in closed head injury [18].

According to Golden et al. 2002, in chronic brain injury, ameliorated the neuropsychological disorders and enhanced neuropsychological and electrophysiological improvements [20]. Harch et al. 2009 reported to show that positive effects by improving the quality of life in patients with post concussion syndrome or mild traumatic brain injury at late chronic stage. All these studies highlighted the successful use of intensive hyperbaric oxygen therapy as therapeutic modality in various traumatic brain injury patients [21].

Apart from the positive effects of hyperbaric oxygen therapy there were concern for potential adverse effects which includes damage to ears, sinuses and lungs which are the result of pressure, temporary worsening of short-sightedness, claustrophobia and oxygen poisoning [22]. In our study prior we had an exclusion criterion; hence none of our patients had shown such complications during the course of the study. No neurological complications like seizures even though our few patients were on anticonvulsants therapy, still neurological complications were observed in few of our patients.

It is very clear from our study that the study itself had certain limitations by the fact that long term outcome of hyperbaric oxygen therapy in traumatic brain injury patients were not being evaluated. Regarding followed up regarding neuropsychiatric complications were not made. Broadly we had included all most all types of trauma to head rather than a specific group of head injury to study the multiple and increased sessions of hyperbaric oxygen therapy. There is a strong need to further more meticulous evaluation on increased multiple sessions of hyper baric oxygen therapy and concluding on ceiling effect of the multiple sessions needs to be further evaluated.

Conclusion

In this study to conclude the impact of multiple increased session of hyperbaric oxygen therapy in traumatic brain injury patients from range of 10 to 20 sessions, outcome is favorable to traumatic brain injury patients. Our findings shows the beneficial effects of HBO therapy in traumatic brain injury patients on GCS score, GOS, spasticity and mood swings with increase in number of multiple sessions. Despite these encouraging results further research is needed to more clearly define the mechanism and potential role of HBOT following traumatic brain injury.

Acknowledgement

Author acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript.

Conflict of Interest: The author declares no conflict of interest for this study.

References

1. Chua KS, Ng YS, Yap SG, Bok CW: A brief review of traumatic brain injury rehabilitation. Ann Acad Med Singapore. 2007;36:31–42.
2. Flanagan SR, Cantor JB, Ashman TA: Traumatic brain injury: future assessment tools and treatment prospects. Neuropsychiatr Dis Treat. 2008;4:877–92.
3. M. McDonagh, S. Carson, J. Ash et al. Hyperbaric oxygen therapy for brain injury, cerebral palsy, and stroke. Evidence report/technology assessment (Summary). 2003;85:1–6.
4. P.G. Harch, E.F. Fogarty, P.K. Staab, and K. Van Meter. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-

concussion syndrome) and post traumatic stress disorder: A case report. Cases J. 2009 Jun 9;2:6538.

5. R. Neubauer, S. Gottlieb, and R. Kagan. Enhancing "idling" neurons. eLancet. 1990;335(8688):542.
6. A. Francis and R. Baynosa. Ischaemia-reperfusion injury and hyperbaric oxygen pathways: A review of cellular mechanisms. Diving and Hyperbaric Medicine. 2017;47(2):110–17.
7. Z. Deng, W. Chen, J. Jin, J. Zhao, and H. Xu. Te neuroprotection effect of oxygen therapy: A systematic review and metaanalysis. Nigerian Journal of Clinical Practice. 2018;21(4):401–16.
8. L. B. Gesell. Hyperbaric oxygen therapy indications, 2008 Committee report. Undersea and Hyperbaric Medical Society, 2008.
9. Lin JW, Tsai JT, Lee LM, Lin CM, Hung CC, Hung KS, et al. Effect of hyperbaric oxygen on patients with traumatic brain injury. Acta Neurochir Suppl 2008;101:1459.
10. Chorr V, Canini F, De Rudnicki S, Dahmani S, Gressens P, Constantin P. Hyperbaric oxygen therapy and inert gases in cerbral ischaemia and traumatic brain injury. Ann Fr Anesth Reanim. 2013;32:863-71.
11. Bennett MH, Trytko B, Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. Cochrane Database Syst Rev 2012;12:CD004609.
12. Rockswold SB, Rockswold GL, Defillo A. Hyperbaric oxygen in traumatic brain injury. Neurol Res. 2007;29:162-72.
13. Teasdale G, Jennett B. Assessment of coma and impaired consciousness A practical scale. Lancet. 1974 Jul 13;2(7872):81-4.
14. Tsevat J, Dawson NV, Matchar DB. Assessing quality of life and preferences in the seriously ill using utility theory. J Clin Epidemiol. 1990;43:737.
15. DeGuise E, leBlanc J, Feyz M, Meyer K, Duplantie J, Thomas H, et al. Longterm outcome after severe traumatic brain injury: The McGill interdisciplinary prospective study. J Head Trauma Rehabil 2008;23:294-303.
16. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth Scale of muscle spasticity. Phys Ther. 1987 Feb;67(2):206-7.
17. McDonaugh M, Helfand M, Carson S, Russman BS. Hyperbaric oxygen therapy for traumatic brain injury: A systematic review of the evidence. Arch Phys Med Rehabil. 2004 Jul;85(7):1198-204.
18. Hayakawa T, Kanai N, Kuroda R, Yamada R, Mogami H. Response of cereborspinal fluid pressure to hyperbaric oxygenation. J Neurol Neurosurg Psychiatry. 1971;34:580-86.
19. Fasano VA, Nunno T, Urciolo R, Lombard G. First observation on the use of oxygen under high pressure for the treatment of traumatic coma. In: Boerema I, Brummelkamp WH, Meijne NG, eds. Clinical application of Hyperbaric Oxygen. Amsterdam: Elsevier. 1964.
20. Golden Z, Golden CJ, Neubauer RA. Improving neuropsychological function after chronic brain injury with hyperbaric oxygen. Disabil Rehabil. 2006;28:1379-86.
21. Harch PG, Fogarty EF, Staab PK, Van Meter K. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (postconcussion syndrome) and post traumatic stress disorder: a case report. Cases J. 2009;2:6538.
22. Plafki C, Peters P, Almeling M, Welslau W, Busch R. Complications and side effects of hyperbaric oxygen therapy. Aviat Space Environ Med. 2000;71:119-24.