

Hyperbaric Oxygenation in Treatment of Alcohol Withdrawal

*Geomy George Chakkalakkudy¹, Prashanth Varkey¹, James T Antony¹,
Merin Poulose¹, Angel Abraham²

¹Department of Psychiatry, Jubilee Mission Medical College & Research Institute, Thrissur, Kerala, India

²Department of Biochemistry, Kerala Medical College, Cherpulassery, Palakkad Dt, Kerala, India

Abstract: The duration and severity of alcohol withdrawal is a great concern while treating alcohol dependent patients. Hyperbaric oxygen therapy (HBOT) has been used in few centers world over, for faster recovery of withdrawal symptoms. The present study aimed to undertake a preliminary study exploring this possibility. Thirty alcohol dependent patients were recruited in this study. They were divided into A: HBOT group (received hyperbaric oxygen therapy for 90 minutes) and B: non-HBOT group (received normobaric oxygen therapy for 90 minutes) using simple randomization technique. Withdrawal symptoms were assessed daily, using the Clinical Institute Withdrawal Assessment scale (CIWA-Ar). The data collected from the two groups were compared. Statistical analysis used was Independent two sample t test. When the two groups were compared, it was found that the mean period (in days) required for the control of withdrawal symptoms for the HBOT group was 3.72 and for the non-HBOT group was 9.03 and the difference was statistically significant ($P = 0.0001$). A better outcome among the HBOT group indicates that the effect of HBOT as an adjunct to the current detoxification regime, in the treatment of alcohol dependent patients is definitely worth consideration and stronger evidence can be brought out in a larger multicenter trial.

Keywords: Hyperbaric Oxygenation, Alcohol dependence, Alcohol withdrawal

Date of Submission: 21-12-2017

Date of acceptance: 23-12-2017

I. Introduction

Alcohol is a psychoactive substance and its high consumption has caused risk of developing health problems.^[1] Its increasing availability and use in the last decade has caused a myriad of problems to the individual and the society. According to Organization for Economic Cooperation and Development (OECD) report released in May 2015, alcoholism increased by about 55 percent between 1992 and 2012.^[2] Alcohol related deaths is a major cause for concern in the country. In 2012 alone about 3.3 million deaths in India were attributed to alcohol consumption. This amounts to 5.9 percent of the global deaths that year.^[1]

One of the major difficulties while treating an alcohol dependent patient is the alcohol withdrawal state. Alcohol withdrawal is accompanied by a maladaptive behavior change and cause clinically significant distress or impairment in social, occupational or other important areas of functioning. These include a coarse tremor of the hands, insomnia, anxiety & increased blood pressure, heart rate, body temperature and respiratory rate. The symptoms persist in a more mild form for as many as 3 to 6 months as part of a protracted withdrawal syndrome, which might contribute to relapse.^[3]

The prevalence of alcohol withdrawal (AW) in the general population is low (5% in US adults in 1995), but is higher among those admitted for detoxification and rehabilitation for alcohol abuse (up to 86%).^[4] Majority of the patients are admitted for de-addiction, as they consume alcohol heavily and have severe withdrawal symptoms. An ideal de-addiction center should function under the Psychiatry Department in a multispecialty hospital, since AW is mostly associated with number of medical and surgical complications which might be lethal. However, even at such centers, many a times the severe withdrawal symptoms that the patient suffers during the de-addiction therapy demotivate both the patient and relatives from continuing such a therapy. An urgent need is felt to improve the present detoxification therapy of patients having Alcohol Dependence Syndrome (ADS) that would help in a faster recovery from AW.

AW occurs because the brain has adapted to the presence of a brain depressant and cannot function adequately in the absence of the drug. The pathophysiology of AW is explained by the action of alcohol on the N-methyl-D-aspartate (NMDA) receptors and gamma-amino butyric acid type-A (GABAA) receptors. During prolonged exposure to alcohol, NMDA receptors are up-regulated and GABAA receptors are down-regulated, leading to tolerance.^[5] The roles are reversed during abstinence, with enhanced NMDA receptor function, reduced GABAergic transmission and dysregulation of the dopaminergic system, leading to many of the symptoms and signs of AW.^[6,7] The current management of withdrawal symptoms is based on the mechanisms mentioned above. Few studies suggest severe oxidative stress and weakened antioxidant activity in alcoholic patients, limits

changes in oxidative stress in the early stages of alcohol withdrawal.^[8,9,10] Alcohol-induced oxidative stress is the result of the combined production of reactive oxygen species [ROS; e.g. malondialdehyde (MDA), an index of lipid peroxidation] and impairment of antioxidant defenses [e.g. superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX), which are involved in the elimination of ROS].^[8] Oxidative stress parameters show changes during alcohol withdrawal and during the remission of withdrawal.^[9] A study from Romania shows the increased oxidative stress status in alcoholic patients and also significant decrease of the oxidative stress status one week and one month following the alcohol withdrawal.^[10]

The faster improvement of withdrawal symptoms can be explained by the actions of HBOT on cerebral vasculature like increasing the oxygen content by tenfold, reducing cerebral edema, increasing neuro-protective enzymes and proteins such as Superoxide dismutase (Mn-SOD) and heat shock protein 27 (HSP-27).^[11] HBOT helps to restore the brain connection and stimulates the inactive neurons by offering about ten times the normal oxygen amount, which enables the brain cells move to high-gear.^[12] Patients go into a pressurized chamber for 90 minutes and breathe pure oxygen through a mask. The result is a big increase in oxygen in the bloodstream. HBOT can help the body to overcome this stress, and may be a useful component of alcohol detoxification. Even though a study conducted in Russia, reports that HBOT reduced the duration of withdrawal symptoms significantly, there were no further literature in this area.^[13] So studying the effect of HBOT on alcohol withdrawal symptoms might lead us to a better treatment of ADS.

II. Materials And Methods

This is a prospective randomized study conducted in the de-addiction ward of Psychiatry department of a tertiary care teaching hospital in Thrissur, Kerala state. The study period was from 16th November 2014 to 30th April 2016 (17 months and 14 days). Male patients aged between 20-60 years with alcohol dependence as per the International Classification of Diseases and Related Health Problems (ICD-10:DCR-10), who presented with AW on admission or during the course in our ward were recruited in the study. Those patients suffering from severe physical illness incapacitating for psychiatric evaluation, who are mentally retarded, who have primary psychiatric disorders like psychosis, mood disorder and those with neurodegenerative disorders like Dementia, Cerebrovascular accidents were excluded. An informed consent for the study was obtained from the patient as well as the relatives. Each subject was evaluated by a proper history, general examination, systemic examination, detailed mental status examination, laboratory investigations and psychometric evaluation (if needed) at the time of admission. The severity of withdrawal symptoms was assessed using the Clinical Institute Withdrawal Assessment scale (CIWA-Ar). Before the hyperoxygenation therapy all patients had an ECG and a baseline echocardiography to assess their cardiac status. The echocardiography was repeated at the end of two weeks. Parameters studied included ejection fraction, and end systolic residual volume. All the patients had an ENT consultation to rule out any tympanic membrane pathologies.

The sample size in this study was calculated based on the mean and standard deviation observed in a previous publication with 95% Confidence level and 90% power.^[13] The required sample size was 10 (5 in each group).^[13] In the present study 30 patients were recruited (15 in each group). They were divided to **A**: HBOT group (15) and **B**: non-HBOT group (15) using simple randomization technique using random number generating software (ver. 1). Here the patients were not aware of which treatment they will receive (Single blinding method). **A**, received the Hyperbaric Oxygen therapy treatment at 2.4 ATA (Atmospheres Absolute) for 90 minutes each day. **B** were also taken inside the Hyperbaric Chamber, but received only normobaric oxygen therapy for the same period of time at 1 ATA. All of the cases received all standard medications like lorazepam, thiamine and antacids as per the symptoms. Hyperbaric oxygenation was done in a monoplace chamber (Oxicab, Hyperbaric SAC, Peru) at the same centre, where the patients were admitted. The entire session was carried out under the supervision of a Physician and a hyperbaric technician. Prior to this therapy the documentation of pulse rate, blood pressure and blood sugar were done as standard procedure. The Hyperbaric sessions were done for ten days in a row one time daily. Daily general examination, systemic examination, detailed mental status examination and administration of CIWA Ar scale were carried out till the day of discharge. The patients were discharged when the biological functions were adequate, physical and mental conditions were stable and when they were motivated to remain abstinent from alcohol. Parameters assessed in two groups were compared.

III. Statistical Analysis

The numerical variables were expressed as mean and standard deviation. The statistical significance was assessed by comparing the mean values of the study variables. Independent two sample t-test was applied for parametric variables and Independent Samples Mann-Whitney U test was applied for nonparametric variables.

IV. Results

There were no drop-outs in this study as all the patients were admitted in the ward during the treatment. The HBOT group and the non-HBOT group were demographically similar. The mean age of HBOT group was

42.60 and that for the non-HBOT group was 41.80, when we compared the duration of alcohol dependence syndrome in years (HBOT-7.87, non-HBOT-5.67) and the severity of withdrawal symptoms (CIWA) when the patients were recruited for this study (HBOT-28.27, non-HBOT-30.87), the variables were similar in both groups (Table 1). In this study the days required for the control of withdrawal symptoms of the HBOT group and the placebo group was compared using the CIWA scale, the mean period in days required for the HBOT group was 3.72 and for the non-HBOT group was 9.03 and the difference was statistically significant ($P < 0.001$) (Table 2).

Table 1 Comparison of demographic variables

Variables	HBOT group (n=15)		non-HBOT group (n=15)		P-Value
	Mean	SD	Mean	SD	
Age	42.60	10.95	41.80	9.18	0.830
Duration of alcohol dependence in years	7.87	6.86	5.67	4.98	0.369
Severity of withdrawal symptoms (CIWA score)	28.27	13.90	30.87	12.04	0.588

Table 2 Comparison of time required for control of withdrawal symptoms

Groups	n	Time required for control of withdrawal symptoms in days		P-Value
		Mean	SD	
HBOT	15	3.72	1.51	< 0.001
non-HBOT	15	9.03	3.29	

V. Discussion

In this study, the utility of HBOT was evaluated as an adjunct in the detoxification of alcohol-dependent patients. The effects of adjunctive HBOT alcohol withdrawal symptoms of alcohol-dependent patients were studied. The HBOT group had a better rate of improvement of withdrawal symptoms and the difference was statistically significant ($P = 0.0001$). The result was similar to a previous study on HBOT, according to which the period necessary for the control of withdrawal syndrome decreased at an average of two times ($P < 0.001$).^[13] The role of Hyperbaric Oxygen therapy (HBOT) in the management of ADS patients which may decrease the oxidative stress during the AW should be further studied. It may help us to manage the AW in a better way. Further studies are needed to assess the effects of HBOT on the hematological system of alcohol dependent patients.

VI. Limitations

The funds available for this project and the time frame for the completion of the project were also determinants in the small sample size, as there was not always a continuous flow of patients requiring this form of therapy within this hospital. Hence obtaining the study sample size also took a considerable period of time.

VII. Conclusion

The promising results in this study with regard to faster recovery from withdrawal symptoms suggests that the effect of HBOT as an adjunct to the current detoxification regime should be evaluated in a larger sample with a longer period of follow-up. When we consider the quantum of disability and morbidity suffered by alcohol dependent individuals and the amount of stress and financial burden their family have to imbibe, even a small improvement in the existing de addiction treatment is going to be a great blessing to our society.

7.1 Conflict of Interest: There is no conflict of interest.

Funding: Funded by Department of Biotechnology, Govt. of India. Under INCRE Fellowship (No NBRC/ Acad /INCRE/2014-2015/3110 dated 28th Oct, 2014) & Jubilee Mission Medical College & Research Institute, Thrissur, Kerala.

Acknowledgement

We extend our sincere gratitude to faculty members of Jubilee Center for Medical Research for editing this article.

References

- [1]. World Health Organization (WHO). Global Status report on Alcohol and Health. Geneva, Switzerland; 2014.
- [2]. Sassi. Tackling Harmful Alcohol Use: Economics and Public Health Policy. Paris: OECD Publishing; 2015.
- [3]. Benjamin J. Saddock, M.D, Virginia A. Saddock, M.D, Pedro Ruiz, M.D. Kaplan & Saddock's Comprehensive Textbook Of Psychiatry. 9th edition. Philadelphia. Lippincott Williams & wilkins; 2009.
- [4]. Caetano R, Clark CL, Greenfield TK. Prevalence, trends, and incidence of alcohol withdrawal symptoms: analysis of general

- population and clinical samples. *Alcohol Research and Health*. 1998 Jan 1;22(1):73.
- [5]. Sanna E, Mostallino MC, Busonero F, Talani G, Tranquilli S, Mameli M, Spiga S, Follesa P, Biggio G. Changes in GABAA receptor gene expression associated with selective alterations in receptor function and pharmacology after ethanol withdrawal. *Journal of Neuroscience*. 2003 Dec 17;23(37):11711-24.
- [6]. Nutt D. Alcohol and the brain. *Pharmacological insights for psychiatrists*. *The British Journal of Psychiatry*. 1999 Aug 1;175(2):114-9.
- [7]. Lingford-Hughes A, Nutt D. Neurobiology of addiction and implications for treatment. *Br J Psychiatry* 2003; 182:97–100.
- [8]. Huang MC, Chen CH, Peng FC, Tang SH, Chen CC. Alterations in oxidative stress status during early alcohol withdrawal in alcoholic patients. *Journal of the Formosan Medical Association*. 2009 Jul 1;108(7):560-9.
- [9]. Parthasarathy R, Kattimani S, Sridhar MG. Oxidative stress during alcohol withdrawal and its relationship with withdrawal severity. *Indian journal of psychological medicine*. 2015 Apr;37(2):175.
- [10]. Alexinschi O, Chirita R, Ciobica A, Manuela P, Dobrin R, Prepelita R, Serban IL, Chirita V. The relevance of oxidative stress status in one week and one month alcohol abstinent patients. *Journal of Medical Biochemistry*. 2014 Jul 1;33(3):284-90.
- [11]. Dirk Jan Bakker, MD, PhD, Frederick S. Cramer, MD. *Hyperbaric Surgery*. USA: Best Publishing Company; 2002; 89-91.
- [12]. Efrati, S., Fishlev, G., Bechor, Y., Volkov, O., Bergan, J., Kliakhandler, K., et al. HyperbaricOxygen Induces Late Neuroplasticity in Post Stroke Patients – Randomized, *PloS one*. 2013 Jan 15;8(1):e53716.
- [13]. Epifanova NM. Hyperbaric oxygenation in the treatment of patients with drug addiction, narcotic addiction and alcoholism in the post-intoxication and abstinence periods. *Anesteziologiya i reanimatologiya*. 1995(3):34-9.

*Geomy George Chakkalakkudy. "Hyperbaric Oxygenation in Treatment of Alcohol Withdrawal."
IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.12 (2017): 80-83