Molecular and Cellular Neuroscience 83 (2017) 74–82

Contents lists available at ScienceDirect

Molecular and Cellular Neuroscience

journal homepage: www.elsevier.com/locate/ymcne

Immediate and delayed hyperbaric oxygen therapy as a neuroprotective treatment for traumatic brain injury in mice

Renana Baratz-Goldstein [a,*,1], Shlomi Toussia-Cohen [a,1], Aviya Elpaz [a,b], Vardit Rubovitch [a], Chaim G. Pick [a,b,c]

[a] Department of Anatomy and Anthropology, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv 69978, Israel
[b] Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv 69978, Israel
[c] The Dr. Miriam and Sheldon G. Adelson Chair, Center for the Biology of Addictive Diseases, Tel-Aviv University, Tel-Aviv 69978, Israel

ARTICLE INFO

Article history:
Received 2 April 2017
Revised 19 June 2017
Accepted 19 June 2017
Available online 8 July 2017

ABSTRACT

Background: Traumatic brain injury is the most common cause of death or chronic disability among people under-35-years-old. There is no effective pharmacological treatment currently existing for TBI. Hyperbaric oxygen therapy (HBOT) is defined as the inhalation of pure oxygen in a hyperbaric chamber that is pressurized higher than 1 atm. HBOT offers physiological and mechanical effects by inducing a state of increased pressure and hyperoxia. HBOT has been proposed as an effective treatment for moderate traumatic brain injury (mTBI), yet the exact therapeutic window and mechanism that underlies this effect is not completely understood.
Methods: HBOT was administrated for 4 consecutive days, post a mouse closed head weight drop moderate TBI (mTBI) in 2 different time lines: immediate treatment - initiated 3 h post-injury and delayed treatment - initiated 7 days post-injury. Behavioral cognitive tests and biochemical changes were assessed.
Results: The results were similar for both the immediate and the delayed treatments. mTBI mice exhibited impairment in learning abilities, whereas mTBI mice treated with HBO displayed significant improvement compared with the mTBI group, performing similar to the sham groups. mTBI mice had a decline in myelin basic protein, an increase in neuronal loss (NeuN staining), and an increase in the number of reactive astrocytes (GFAP). The HBO treated mice in both groups did not exhibit these changes and remained similar to the sham group.
Conclusions: The delayed HBOT has a potential to serve as a neuroprotective treatment for mTBI with a long therapeutic window. Further research is needed for fully understanding the cellular changes.
© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Trauma is a major cause of morbidity and mortality in young people and in military personnel, with traumatic brain injury (TBI) being one of the most common causes of death and chronic disabilities in the under-35-year-old age group. Consequently, there is an increasing concern among parents and health care providers, regarding the prevalence of brain injuries in commonly practiced sports, car related accidents, work place injuries and injuries in combat soldiers (Chua et al., 2007).

Approximately 1.7 million Americans will experience a brain injury annually, with nearly 80% of those patients diagnosed with mild-to-moderate TBI (mTBI). The morbidity caused by mTBI carries a tremendous burden for families and for society as a whole (Bazarian et al., 2005; Faul et al., 2010). The Department of Defense of the United States has defined and developed criteria for the diagnosis of mTBI. mTBI is generally characterized by a traumatic-concussive event that causes a brief period of unconsciousness lasting <30 min, or a period of confusion, amnesia or alteration in the mental state lasting no longer than 24 h. Transient neurological deficits may appear as well. Clinical findings may be transitory, and late abnormalities that are not explainable by other means may qualify an individual for the diagnosis of mTBI (Assistant Secretary of Defense for Health Affairs 2007, 2014).

The symptoms of mTBI are variable and may include headaches, impulsivity, irritability, anger, a cognitive impairment, loss of memory, difficulties in executive functions and sleep disturbances (Arciniegas et al., 2005). The medical treatment of mTBI is somewhat inadequate; Drug treatments have been lacking in the ability to provide a significant recovery, and surgical treatment is used for saving lives but cannot improve the prognosis. Thus, the limited medical and technological tools to address this urgent concern have created a strong need to develop new approaches of treating mTBI sufferers (Narayan et al., 2002; Chua et al., 2007).

Hyperbaric oxygen therapy (HBOT) has been in use for over 50 years, safely treating a variety of medical conditions, and recently has emerged as an attractive and effective alternative for the existing insufficient treatments for mTBI (Ding et al., 2013). HBO is currently indicated as therapy for several different approved medical treatments,

* Corresponding author at: Department of Anatomy and Anthropology, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel.
E-mail address: renanaba@post.tau.ac.il (R. Baratz-Goldstein).
[1] Equal contribution.

http://dx.doi.org/10.1016/j.mcn.2017.06.004
1044-7431/© 2017 Elsevier Inc. All rights reserved.

such as air embolism or carbon monoxide poisoning, as listed in the Undersea and Hyperbaric Medical Society (UHMS) committee report (Hampson, 1999). Other current suggested indications for HBOT, though not UHMS approved, include acute cerebrovascular incidents, cerebral edema, head injuries, ischemia-reperfusion injury, a spinal cord injury and an acute central retinal artery insufficiency (Nighoghossian et al., 1995; Gill and Bell, 2004). HBOT is defined as the inhalation of pure oxygen in a hyperbaric chamber that is pressurized to >1 atm. HBOT offers physiological and mechanical effects by inducing a state of increased pressure and hyperoxia (McDonagh et al., 2003). High concentrations of oxygen in the blood may decrease brain tissue hypoxia, thus preventing neuronal cell death.

The therapeutic effects of HBOT on mTBI are attributed to several pathophysiological mechanisms; HBOT increases arterial oxygen pressure and consequently also brain tissue oxygen levels, it increases diffusion rate and an effective diffusion distance of oxygen, it reduces brain tissue edema and intracranial pressure thus improving consciousness, it protects neurons from ischemic death by collateral circulation acceleration, stimulates angiogenesis and neurogenesis accompanied by repair of damaged microvessels, and it prevents large micro-thrombi formation (Gill and Bell, 2004; David et al., 2012; Abraini, 2013; Sánchez, 2013; Wang et al., 2014; Chazalviel et al., 2016) through prothrombolytic mechanisms (David et al., 2012; Abraini, 2013; Chazalviel et al., 2016). In addition, studies have shown that repetitive HBOT applied after mTBI attenuates reactive astrogliosis and glial scarring and reduces expression of inflammatory mediators (Lavrnja et al., 2015). Furthermore, studies done on mTBI induced rat models treated with HBOT, showed improvement in spatial learning and memory, as well as a significant increase in Nissl bodies in the hippocampal CA3 region, and a decrease in glial fibrillary acidic protein positive cells (Su et al., 2013).

Determination of the therapeutic window for HBOT is a major part in the assessment of the efficacy of the treatment. Studies have shown that HBOT administered within several hours of the trauma had a significant neuroprotective effect, improving cognitive functioning and decreasing neuronal cell death. No such effect was observed when the treatment was applied 60 days after the trauma (Yang et al., 2014). Our time points for HBOT intervention were selected, in order to define the optimal therapeutic window for the treatment, based on previous work done with rodent mTBI models and HBOT time frames.

In this study, we aimed to evaluate the efficacy of HBOT on recovery from mTBI. We examined the impact of HBOT on spatial learning abilities and memory, as well as conducted brain tissue immunofluorescence analysis. We were interested in assessing the efficacy of HBOT in two different scenarios: the first, applying HBOT immediately after the brain injury has occurred, and the second, applying HBOT a whole week after the brain injury has occurred.

2. Materials and methods

2.1. Animals

Male ICR mice (6–8 weeks old, 30–40 g weight) were purchased from HSD Jerusalem, Israel, and then bred and raised within the vivarium of Tel Aviv University, Israel. Mice were housed 4–6 per cage with free access to food and water on a 12:12 light/dark cycle at 22 ± 1 °C. Lighting during the light phase kept constant. All experimental procedures took place during the light phase of the cycle. All efforts were made to minimize potential suffering; a minimum number of animals were used throughout the study and each animal was used for only one experiment. Experimental manipulations and housing conditions were approved by the Institutional Animal Care and Use Committees of Tel Aviv University (M-14-049).

2.2. Procedure

In the first experiment, mice were treated with HBOT for 1 h daily for 4 consecutive days, starting 3 h post-injury. 72 h after last HBOT (a week from the impact), mice were assessed in behavioral tests or brains were removed for immunofluorescence. Another group was assessed in the behavioral tests 30 days after the injury. In the second experiment, mice were treated with HBOT beginning 7 days post-injury. HBOT protocol was identical to the first experiment - 1 h/day for 4 consecutive days. 72 h after last treatment mice were assessed in behavioral tests or brains were removed for immunofluorescence. For each experiment, we compared 4 different groups: Sham, mTBI, HBOT and mTBI + HBOT.

2.3. Moderate traumatic brain injury

Mice were subjected to mTBI using the weight drop device, a vertical metal guide tube (13 mm in diameter and 80 cm long), through which a 70 g. cylindrical–shaped piece of metal with a slight spherical tip, was dropped. Mice were anesthetized with Isoflurane and then placed on a supportive sponge under the weight drop device with the right temporal side of their head, between the corner of the eye and the ear, facing the opening of the tube. The weight was then released from the top of the tube and the sponge supported the head of the mouse, allowing some anterior/posterior motion in the absence of any rotational head movement at the moment of impact (Zohar et al., 2003; Milman et al., 2005; Baratz et al., 2011). Sham mice were subjected to an identical procedure as described for mTBI, but without the dropped weight.

2.4. Hyperbaric oxygen therapy

For the HBOT, animals were administered 100% oxygen at a pressure of 2 ATA in a custom-made monochamber intended for small animals for 60 min daily for 4 consecutive days. In the first stage of our study, treatment was first initiated 3 h post-injury, whereas on the second stage treatment was first initiated 7 days post-injury. 100% oxygen was administered 5 min prior to the compression of the monochamber for oxygen content enrichment. Compression and decompression were executed progressively within 5 min. The oxygen level inside the monochamber after compression reached saturation of ≥96%, as measured by an oxygen analyzer (320BRC model, Teledyne Analytical Instruments). The animals in the control, non-HBO treated group were placed inside the monochamber at 1 ATA for 60 min without additional treatment. Temperature in the monochamber, measured with a temperature controller (N322, Novus), was similar for all groups during every session. After every session the monochamber was washed with water and soap.

2.5. Blood oxygen saturation

Oxygen saturation was determined using a noninvasive pulse oximeter for laboratory animals (Mouse Vent G500, Kent Scientific Corporation) following manufacturer's instructions. The oxygen saturation was measured for 1 min because mice were moving and the range of reading was recorded. We evaluated Oxygen saturation 1 h post-mTBI/ first treatment of HBO.

2.6. Behavioral tests

7 days or 30 days post-injury mice were assessed via 3 behavioral tests: First, the elevated plus maze, for the evaluation anxiety like behavior. Second, the Y-maze test, for the evaluation of spatial learning and third, the novel object recognition test for the evaluation delayed learning.

Download English Version:

https://daneshyari.com/en/article/5534406

Download Persian Version:

https://daneshyari.com/article/5534406

Daneshyari.com