Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Brain Research

Research Report

A comparison of factors involved in the development of central nervous system and pulmonary oxygen toxicity in the rat

Mirit Eynan, Nitzan Krinsky, Adi Biram, Yehuda Arieli, Ran Arieli*

Israel Naval Medical Institute, Israel Defense Forces Medical Corps, Box 22, Rambam Health Care Campus, P.O. Box 9602, 3109601 Haifa, Israel

ARTICLE INFO

Article history:
Accepted 30 May 2014
Available online 11 June 2014

Keywords:
CNS-oxygen toxicity
Antioxidant enzymes
Hyperbaric oxygen

ABSTRACT

Central nervous system oxygen toxicity (CNS-OT) can occur in humans at pressures above 2 atmospheres absolute (ATA), and above 4.5 ATA in the rat. Pulmonary oxygen toxicity appears at pressures above 0.5 ATA. We hypothesized that exposure to mild HBO following extreme exposure might provide protection against CNS, but not pulmonary oxygen toxicity. We measured the activity of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX), and nitrotyrosine and nNOS levels in the brain and lung in the following groups: (1) Sham rats, no pressure exposure (SHAM); (2) Exposure to 6 ATA oxygen for 60% of latency to CNS-OT (60%LT); (3) Exposure to 6 ATA for 60% of latency to CNS-OT, followed by 20 min at 2.5 ATA for recovery (REC); (4) Exposure to 6 ATA for 60% of latency to CNS-OT, followed by 20 min at 2.5 ATA oxygen and a subsequent increase in pressure to 6 ATA until the appearance of convulsions (CONV); (5) Control rats exposed to 6 ATA until the appearance of convulsions (C). SOD and CAT activity were reduced in both brain and lung in the REC group. GPX activity was reduced in the hippocampus in the REC group, but not in the cortex or the lung. nNOS levels were reduced in the hippocampus in the REC group. Contrary to our hypothesis, no difference was observed between the brain and the lung for the factors investigated. We suggest that at 2.5 ATA and above, CNS and pulmonary oxygen toxicity may share similar mechanisms.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Central nervous system oxygen toxicity (CNS-OT) represents a major risk for combat divers. It is characterized by convulsions similar to epileptic seizures and sudden loss of consciousness, sometimes without any warning symptoms. CNS-OT can occur in humans at pressures above 2 atmospheres absolute (ATA) (Hampson and Atik, 2003; Yildiz et al., 2004), and above 4 ATA in the rat (Arieli et al., 2001; Pilla et al., 2013). Pulmonary oxygen toxicity appears in humans at pressures above 0.5 ATA

*Corresponding author. Fax: +972 4 8693258.
E-mail addresses: estie@mail.idf.il, emirit@netvision.net.il (M. Eynan), k_nitz@walla.com (N. Krinsky), adi.biram@gmail.com (A. Biram), yarieli@netvision.net.il (Y. Arieli), rarieli@netvision.net.il (R. Arieli).

http://dx.doi.org/10.1016/j.brainres.2014.05.051
0006-8993/© 2014 Elsevier B.V. All rights reserved.

(Jackson, 1985) and in rats above 1 ATA (Harabin et al., 1990). One difference between these two toxicities is the latency to their appearance. Whereas CNS-OT can appear within minutes, the development of pulmonary oxygen toxicity takes several hours, depending on the ambient pressure.

In a study that screened over 2500 dives with closed-circuit apparatus, Arieli et al. (2006) found that symptoms related to CNS-OT were reported during dives to 3–6 m sea water, but not at 2 m. They suggested that in man, recovery from CNS-OT may take place at a level of hyperoxia where there is a continued risk of pulmonary oxygen toxicity. Arieli et al. (2002) and Arieli (2003) proposed an algorithm to calculate the risk of CNS-OT while diving with closed-circuit oxygen rebreathers. This algorithm was calculated using a rat model, based on the increase in the cumulative oxygen load index at a PO_2 in excess of the threshold for steady state production and removal of reactive oxygen species (ROS) (Arieli and Hershko, 1994). The underlying assumption was that recovery of the factors leading to the development of CNS-OT will take place during the steady state. To validate this assumption, Arieli et al. (2008) investigated whether recovery from CNS-OT would take place at a PO_2 higher than normoxia. It was found that recovery from CNS-OT in rats takes place at a PO_2 between 0.21 and 3 ATA. This later investigation was conducted on a rat model, and was defined as a pioneer study with a view to establishing the hypothesis.

ROS and reactive nitrogen species (RNS) such as peroxynitrite, produced by the reaction of NO with superoxide, are both factors that play a major role in the generation of oxygen toxicity (Bitterman and Bitterman, 1998; Bitterman et al., 1994; Demchenko and Piantadosi, 2006; Elayan et al., 2000; Ohtsuki et al., 1992; Oury et al., 1992; Torbati et al., 1992). Living cells have developed a number of mechanisms for coping with continuous exposure to ROS, among others antioxidant enzymes and low molecular weight antioxidants such as vitamin C, vitamin E and glutathione, which scavenge the ROS. The antioxidant enzymes include three types of superoxide dismutase (SOD), which transform the superoxide ion into hydrogen peroxide (H_2O_2). Catalase and glutathione peroxidase catalyze H_2O_2 to O_2 and H_2O. Under normal conditions, there is a state of equilibrium between ROS generation and ROS scavenging. In oxidative stress, however, this equilibrium is disturbed, and an increase in the level of ROS may result in cell injury (Ames et al., 1993; Davies, 1987; Halliwell, 1992).

The cumulative oxygen load index may not be the same in the brain and the lung at different oxygen pressures. Demchenko et al. (2007) demonstrated in a rat model that at 2–2.5 ATA and above pulmonary injury is largely due to a non-inflammatory process, whereas at lower pressures it is due to a direct inflammatory process. In addition, at hyperbaric pressure a neurogenic CNS affects the development of pulmonary oxygen toxicity. This phenomenon was initially described by Bean and Rottschafer (1938), Bean and Smith (1953), and Bean and Johnson (1955); Demchenko et al. (2011, 2012) continue to search for its specific underlying mechanism. It should be pointed out that no neurogenic component has of yet been reported as part of the role played by the sympathetic nervous system in the generation of pulmonary oxygen toxicity in humans (Winklewski et al., 2013).

We suggest it may be possible to use the finding that CNS-OT recovers in a rat model at a PO_2 of 2–3 ATA to differentiate between the processes leading to CNS and pulmonary oxygen toxicity. We hypothesized that after exposure to 6 ATA, even without reaching the point of convulsion, a reduction of the HBO pressure to 2.5 ATA will bring about recovery of the CNS-OT, whereas the inflammatory processes leading to pulmonary oxygen toxicity may continue to develop.

2. Results

2.1. *Antioxidant enzyme activity*

Total SOD activity was significantly reduced in the brain (predominantly in the hippocampus, $p<0.01$) and the lung ($p<0.05$) in the REC group, compared with the other groups (Fig. 2). The same pattern was obtained in the brain for catalase ($p<0.05$), while in the lung, catalase activity was reduced in the REC group compared with the 60%LT group and with the CONV and C groups ($p<0.05$, Fig. 3). There was no significant difference in the activity of SOD and catalase between the CONV and C groups. GPX activity was reduced in the hippocampus in the REC group compared with the 60%LT group ($p<0.01$), but did not change in the cortex. In the lung, GPX activity increased in the REC and CONV groups compared with 60%LT group (Fig. 4).

2.2. *Nitrotyrosine and nNOS immunoblotting*

Using Western blot technique, we found differences between the groups for proteins labeled by an antibody specific to nitrotyrosine. In the cortex and the hippocampus we observed nitrotyrosylation of proteins at 65 kDa and 75 kDa (Fig. 5a), whereas in the lung nitrotyrosylation was observed only at 65 kDa (Fig. 5b). NT levels at 75 kDa in the cortex were elevated in the REC group compared with the other groups ($p<0.01$, Fig. 6). No changes in NT at 75 kDa levels were observed in the hippocampus. No significant change was observed in the cortex or the hippocampus at 65 kDa. NT levels at 65 kDa in the lung were reduced in the REC group compared with the C group ($p<0.05$, Fig. 7).

nNOS levels were significantly reduced in the hippocampus in the REC group compared with the SHAM

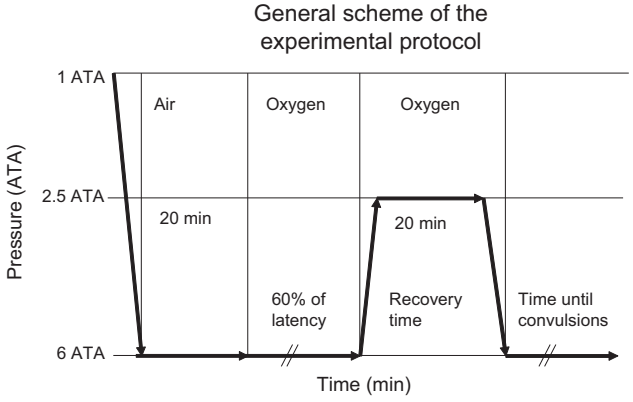

Fig. 1 – General scheme of the experimental protocol.

Download English Version:

https://daneshyari.com/en/article/4324202

Download Persian Version:

https://daneshyari.com/article/4324202

Daneshyari.com