CASE REPORT

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Neurotoxic effects of oxygen in hyperbaric environment: A case report

Neurotoksični efekat kiseonika u hiperbaričnim uslovima

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Abstract

Introduction. Oxygen is an essential element of life in aerobic organisms. However, if not controlled, inhalation of oxygen under increased pressure in conditions of hyperbaric oxygen therapy can lead to serious damage and even death. **Case report.** We presented a 20-year-old male who had begun exhibiting symptoms of epilepsy during diving test in a hyperbaric chamber while inhaling 100% oxygen. He was immediately taken off oxygen mask and started breathing air and began rapid decompression. He lost consciousness, began foaming at the mouth, and had a series of tonic spasms. The patient was previously completely healthy and not on any medications. He was admitted for emergency treatment in our hospital, where he was treated for epilepsy. On admission, he complained of muscle and joint pain, and had erythematous changes on the forehead, neck and chest. All these changes occurred after leaving the hyperbaric chamber. Bloodwork revealed leukocytosis with neutrophil (Leukocytosis 16.0 × 10^9/L (reference values 4.00–11.00 × 10^9/L), Neutrophili 13 × 10^9/L (reference values 1.9–8.0 × 10^9/L), with elevated enzymes aspartate aminotransferase (AST) 56 U/L (reference values 0–37 U/L), alanin aminotransferase (ALT) 59 U /L, (reference values 25–65 U/L), creatine kinase (CK) 649 U/L, (reference values 32–300 U /L), lactate dehydrogenase (LDH) 398 U/L (reference values 85–227 U/L). Because of pain and his condition we began treatment in a hyperbaric chamber at a pressure of 2.0 ATA for 70 minutes, resulting in a reduction of symptoms and objective recovery of the patient. Within 24 h, repeated laboratory tests showed a reduction of leukocytosis (13 × 10^9/L and neutrophils (7.81 × 10^9/L), and the gradual reduction of the enzymes AST (47 U/L), ALT (50 U/L, CK (409 U/L), LDH (325 U/L). Since head CT and EEG were normal, epilepsy diagnosis was ruled out. This fact, along with medical tests, facilitated the differential diagnosis and confirmed that this was a case of neurotoxic effects of oxygen while the patient was in a hyperbaric chamber, not epileptic seizures. **Conclusion.** This case report suggests that in patients with symptoms of epileptic seizures while undergoing treatment in a hyperbaric chamber, it is always important to think of neurotoxic effects of pure oxygen which occurs at higher pressures and with a longer inhalation of 100% oxygen. In these patients, reexposure to hyperbaric conditions leads to recovery. This effect is important in daily inhalation of 100% oxygen under hyperbaric conditions which is why the use of pure oxygen is controlled and diving is allowed in shallow depths and for a limited time.

Key words:
oxygen; epilepsy; skin manifestations; hyperbaric oxigenation; treatment outcome.

Apstrakt

Uvod. Kiseonik je element od životne važnosti za aerobne organizme. Međutim, udisanje kiseonika pod povišenim pritiskom u uslovima hiperbarične oksigenoterapije može, ukoliko nije kontrolisano, da dovede do ozbiljnih oštećenja, pa i do smrti. **Prikaz bolesnika.** U radu je prikazan 20-godišnji muškarac koji je tokom testa za ronioca u hiperbaričnoj komori, prilikom udisanja 100% kiseonika, dobio simptome epilepsije. Odmah mu je skinuta maska sa kiseonikom, prešao je na disanje vazduha i započeta je brza dekompresija. Kod bolesnika je došlo do gubitka svesti, do pojave pene na ustima i serije toničkih grčeva. Bolesnik je ranije bio potpuno zdrav i nije koristio nikakvu medikamentoznu terapiju. Primljen je na lečenje u našu ustanovu kao hitan slučaj, i lečen kao da je imao epileptični napad. Na prijemu je zapaženo da se žali na bolove u mišićima i zglobovima i da ima eritematozne promene na čelu, vratu i grudima koje su se javile posle izlaska iz hiperbarične komore. Laboratorijski nalazi pokazali su da u krvnoj slici postoji leukocitoza sa neutrofilijom (leukociti 16,0 × 10^9/L (referentne vrednosti 4,00–11,00 × 10^9/L), neutrofili 13,0 × 10^9/L (referentne vrednosti 1,9–8,0 × 10^9/L), uz povišene enzime aspartat aminotransferazu (AST) 56 U/L; (referentne vrednosti 0–37 U/L), alanin aminotransferazu (ALT) 59 U/L, (referentne vrednosti 25–65 U/L,), kreatin kinazu (CK) 649 U/L (referentne vrednosti 32–300 U/L) laktat dehidrogenazu (LDH) 398 U/L (referentne vrednosti 85–227 U/L). Zbog bolova i opšteg stanja bolesnik je podvrgnut tretmanu u hiperbaričnoj komori na pritisku od 2.0 ATA u trajanju od 70 minuta, nakon čega je došlo do nestanka tegoba i objektivnog oporavka. Ponovljene labora-

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torijske analize posle 24 časa pokazale su sniženje leukocita na 13 × 10^9/L, neutrofila na 7,81 × 10^9/L, kao i na postepeno smanjenje aktivnosti enzima u serumu (AST 47 U/L, ALT 50 U/L, CK 409 U/L, LDH 325 U/L). Budući da su multislajsni skener (MSCT) glave i elektroencelafogram (EEG) bili uredni, isključena je dijagnoza epilepsije. Uz ostale nalaze, to je olakšalo diferencijalnu dijagnozu i potvrdilo da se radilo o neurotoksičnom efektu kiseonika koji je pacijent imao u hiperbaričnoj komori, a ne o epileptičnom napadu. **Zaključak.** Prikazani bolesnik upućuje na zaključak da bi u slučaju sa razvojem stanja epinapada u toku tretmana u hiperbaričnoj komori, trebalo uvek razmišljati o prouzrokovanom neurotoksičnom delovanju kiseonika koje se javlja pri većim pritiscima i kod duže inhalacije 100% kiseonika i da ponovno izlaganje hiperbaričnim uslovima kod takvih bolesnika dovodi do oporavka. Ovaj efekat je važan kod svakodnevnog udisanja 100% kiseonika pod hiperbaričnim uslovima zbog čega se kontroliše njegova upotreba i dozvoljava ronjenje na malim dubinama i na ograničeno vreme.

Ključne reči:
kiseonik; epilepsija; koža, manifestacije; hiperbarička oksigenacija; lečenje, ishod.

Introduction

People's attempts to stay under water while breathing air go back to the distant past. Throughout history there have been many attempts to create machines that would enable people to stay under water with more or less success. There also was always a desire to treat patients with many diseases under these conditions.

In 1662, British doctor Henshaw [1] constructed a ball-shaped chamber into which he pumped air using two organ bellows, and tried to cure a number of diseases. The idea was that breathing compressed air has the therapeutic effect.

A Frenchman, Antoine Lavoisier (1743–1794), even though he was not a doctor, came to the conclusion that gas exchange takes place in the lungs. He was sure that the oxygen in the body converts into carbon dioxide, and that the nitrogen which he discovered is removed from the body unchanged.

Following the discovery of oxygen, Joseph Priestley (1733–1804) was the first to raise the question about the possibility of harmful effects of this gas on the body [2]. Oxygen was called "a vital gas" at that time, and Lavoiser described changes in the lungs caused by its inhalation. Only in 1899, after several experiments, Lorain -Smith found that breathing oxygen at a pressure greater than 0.6 bar after a prolonged exposure causes irreversible pathological changes in the lungs. In his honor, this phenomenon is called the Lorain -Smith effect.

In the excellent book "La pression barométrique", French physiologist Paul Bert in 1878, pointed out that breathing oxygen pressurized above 2 absolute bar causes convulsions similar to epilepsy. In deference to him, such cases are referred to as "Paul Bert effect" or neurotoxic effects of oxygen [2]. Others, starting with Berta, have proposed to replace air with oxygen during treatment process [4]. Behnke and Shaw [5] were the first to try this. Their work resulted in a recommendation of therapy based on the severity of the condition and first application of mixtures of oxygen and nitrogen different than normal air. Paul Bert effect is important in daily inhalation of oxygen, which is why its use is limited and diving is allowed in shallow depths and for a limited time. The most accepted mechanism is that oxygen inactivates ferments necessary for the performance of normal processes in nerve cells [6].

Bert [4] also noted that rapid transition from higher to lower pressure leads to sickness and even fatality, so he suggested the prevention of decompression sickness by gradually decreasing pressure (gradual decompression). This is actually the first introduction of the prophylactic decompression procedure based on the principle of slow and continuous emergence. An important aspect of this early work was the recognition of safe limits of exposure to oxygen in relation to dose and time, and the highest possible oxygen pressure and the longest exposure time with the minimum possible risk of oxygen toxicity to the central nervous system [7, 8]. Later, navies became interested in oxygen and expanded its use, speeding up the process of decompression and improving the efficiency and treatment of divers [9, 10].

Bert's other significant contribution to the practice of hyperbaric medicine was the recognition of oxygen toxicity to the central nervous system with application of oxygen under high partial pressures [6, 7]. Oxygen toxicity on the central nervous system was not significant for many years as it was mainly related to diving until the use of sufficiently high partial pressures of oxygen in the clinical setting [11]. The mechanism of oxygen neurotoxicity explans that hyperbaric oxygen inactivates ferments responsible for bioregulation of vital processes in nerve cells, but there is also a view that dissolved oxygen disrupts a regular transport of oxygen and removal of carbon dioxide [6].

Case Report

A 20-year-old male, a diver candidate became ill during testing in the hyperbaric chamber, and admitted to our hospital as an emergency case. The patient's history and medical records indicated that previously he was a healthy person who did not take any medication. While breathing 100% oxygen at the depth of 18 m for 60 minutes in the chamber, he developed problems that were manifested as the loss of consciousness, foaming at the mouth, and a series of convulsions of the entire body and limbs.

A companion in the chamber reacted by removing the mask and the patient began rapidly to ascent, and from that moment he stopped breathing 100% oxygen and breathed air during the ascent. After surfacing and exiting the hyperbaric chamber the patient was confused, he had nausea and queasiness, and within the next 50 minutes, he developed redness on the forehead, neck and chest, and conjunctival suffusion, with pain in the shoulders and muscles (Figure 1).

Post-admission laboratory analysis and blood work showed leukocytosis with neutrophilia (leukocytes 16.0 × 10^9/L, neutrophils 13.0 × 10^9/L), with elevated aspartate ami-

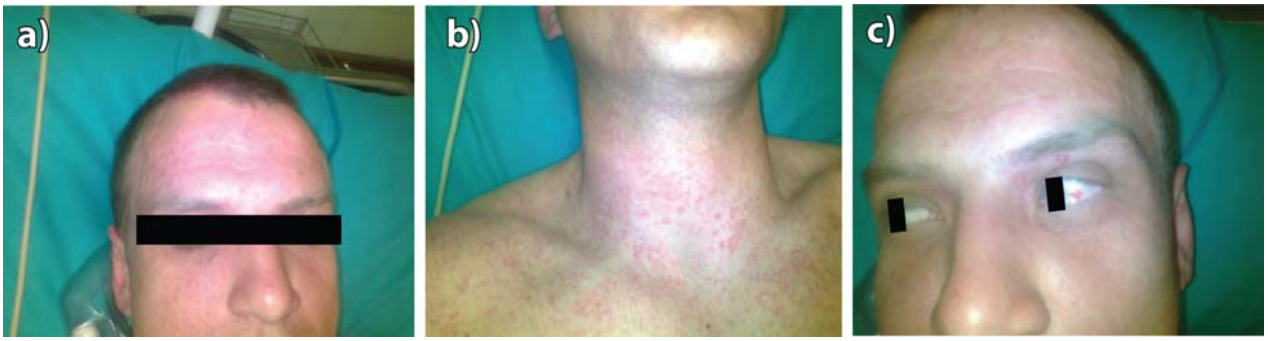

Fig. 1 – Appearance of the patient before treatment with hyperbaric oxygen therapy: a) Changes on the skin of the face; b) Changes on the skin of the neck; c) Changes on the conjuctive (conjuctival suffusion)

notransferase (AST) 56 U/L, alanine aminotransferase (ALT) 59 U/L, creatine kinase (CK) 649 U/L, lactate dehydrogenase (LDH) 398 U/L. Other laboratory tests were within the normal range. Radiography of the heart and the lungs, and head computed tomography (CT) were also normal (Figure 2), as were cardiological and neurological examinations. Head magnetic resonance imaging (MRI) with contrast was also normal. Despite the demonstrated symptoms that resembled the epileptic seizure, the tests confirmed that it was the neurotoxic effect of oxygen. Despite the manner of onset of the disease and the findings that were suggestive of neurotoxic effect of oxygen, the patient was treated in a hyperbaric chamber for 70 minutes at the pressure of 2.0 ATA, primarily due to the redness of the forehead, neck and chest, conjunctival suffusion, and pain in the shoulders, muscles and joints.

During the treatment in the hyperbaric chamber, within 30 minutes the patient's condition improved, skin redness and muscular and joint pain disappeared, and conjuctival suffusion became less pronounced (Figure 3).

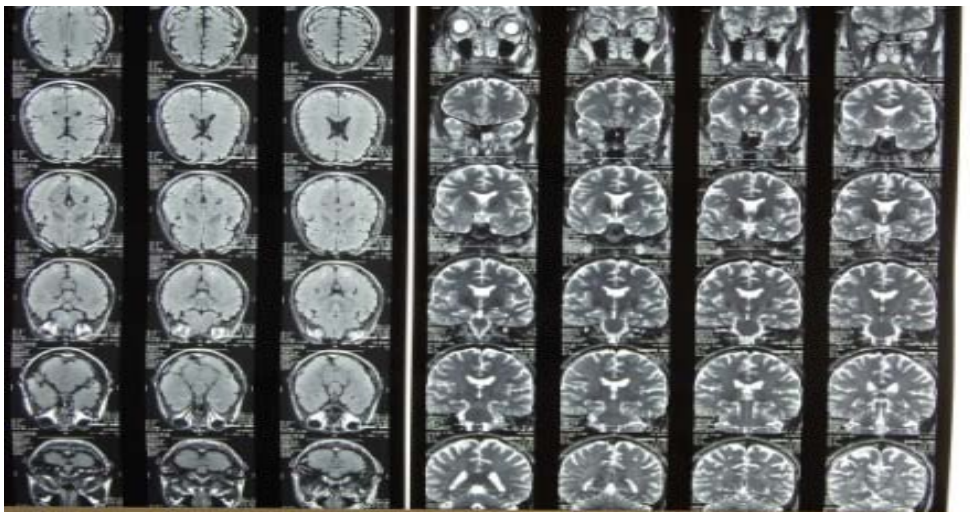

Fig. 2 – Computed tomography (CT) scan of the head – normal findings.

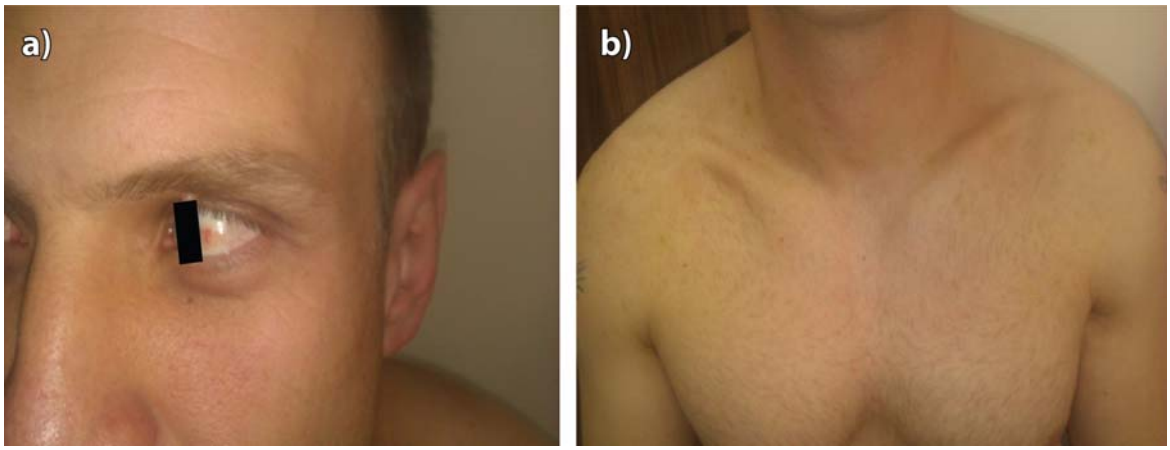

Fig. 3 – The patient after first treatment in the hyperbaric chamber: a) A significant reduction in conjunctival suffusion; b) A significant regression in skin changes.

The next day, laboratory analysis was repeated, revealing a reduction in leukocytes count to 13×10^9/L, neutrophils to $7{,}81 \times 10^9$/L, as well as a gradual reduction in serum enzymes activities (AST 47 U/L, ALT 50 U/L, CK 409 U/L, LDH 325 U/L).

Discussion

Occurrence of neurotoxic effects of oxygen has been described in divers who do not comply with the depth of dive, and time for inhalation of 100% oxygen in a closed apparatus [12]. This effect can occur in a hyperbaric chamber in the event of inhalation of 100% oxygen over 2.0 ATA pressure in people who are particularly sensitive to elevated partial pressure of oxygen.

In this case report, we presented healthy person who had been tested in a hyperbaric chamber. While breathing 100% oxygen at the pressure of 2.8 ATA he exhibited a neurotoxic effect, with the appearance of clinical symptoms that resembled epileptic seizures .

This effect is not unknown in the literature and is also called oxygen epilepsy or Paul Bert effect [2]. The clinical picture is consistent with epileptic seizure and may represent a major differential diagnostic problem to clinicians who are not familiar with diving diseases. Only later, as in the case of our patient, after neurological examination (EEG, CT and MRI of the head) neurotoxic effect of oxygen that the patient breathed at high pressure, and not epileptic seizure, was confirmed.

Also, with pressure reduction in the chamber and cessation of breathing 100% oxygen, symptoms disappear spontaneously and there is no need for further treatment in most cases.

However, immediately upon admission and after examination and the diagnosis, we placed our patient in a hyperbaric chamber where he was treated for pain in the muscles, joints, and erythema which appeared at the head, neck and chest and conjunctival suffusion. We did that at the pressure of 2.0 ATA for 70 minutes. Already in the course of treatment in the hyperbaric chamber, the patient's condition objectively and subjectively improved which was confirmed by laboratory findings.

Conclusion

We presented a case with neurotoxic effects of oxygen that occurred in the hyperbaric chamber. Such cases occur frequently when diving in a closed type apparatus. In particular, in such cases we emphasize the need to carefully and quickly perform a differential diagnosis to severe neurological diseases, but taking into account inhalation of 100% oxygen, which precedes the condition. The diagnosis is easy to establish following normal EEG, CT and MRI of the head findings, unlike a true epileptic attacks.

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