Toxicology Reports 14 (2025) 101985

Contents lists available at ScienceDirect

Toxicology Reports

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

Blindness following hydrogen peroxide ingestion and recovery with hyperbaric oxygen therapy

Alexander R. Engelmann [a,b,c], Nutsa Pargalava [a,b], Alfredo A. Sadun [b,*]

[a] University of California Los Angeles, Jules Stein Eye Institute, Department of Ophthalmology, Los Angeles, CA, USA
[b] University of California Los Angeles, Doheny Eye Center, Department of Ophthalmology, Los Angeles, CA, USA
[c] Cleveland Clinic Foundation, Cole Eye Institute, Cleveland, OH, USA

ARTICLE INFO

Handling Editor: Prof. L.H. Lash

Keywords:
Hydrogen peroxide toxicity
Vision loss
Gas emboli
Hyperbaric oxygen therapy
Reactive oxygen species

ABSTRACT

Hydrogen peroxide (HP) poisoning is rare but potentially life-threatening. It can cause tissue damage through oxygen emboli and reactive oxygen species (ROS). This is the first reported case of blindness caused by cerebral infarctions involving the visual pathway due to oxygen emboli from HP ingestion. A monocular patient presented with profound vision loss and no apparent pharyngeal mucosal injury following ingestion of commercial-grade (35 %) HP. CT imaging revealed gastric wall edema and gas in the portal venous system, suggesting gas emboli. Post-treatment MRI of the brain and orbits with and without contrast confirmed multifocal embolic infarcts along the visual pathway, and transcranial doppler studies identified moderate right-to-left shunting to explain the paradoxical emboli. The patient received hyperbaric oxygen therapy, resulting in a rapid improvement in visual acuity from hand motion to 20/20 and near-total resolution of visual field loss. Remarkably, this recovery occurred despite treatment initiation more than 24 h after symptom onset. This case emphasizes the importance of timely recognition and management of HP poisoning. In the authors' minds it also raised questions about the routine use of 100 % oxygen in hyperbaric therapy due to potential additional oxidative stress. It is the authors' opinion that further research should be done to validate treatment protocols and further interrogate possible risks associated with reactive oxygen species and oxygen toxicity.

1. Introduction

Hydrogen peroxide (HP) may exert toxic effects on tissues either directly, by way of caustic corrosion and lipid peroxidation due to the effects of excess reactive oxygen species, or indirectly when tissue is infarcted by gas emboli which form as a result of rapid oxygen production creating bubbles in the vascular system [1]. Each of these mechanisms must be considered when assessing a patient with HP poisoning, as early intervention has the potential to produce a dramatically positive effect while failure to correctly diagnose and treat these individuals may lead to a poor outcome.

According to the Centers for Disease Control (CDC), less toxic exposures to HP are most commonly due to inhalation or skin exposure [2], but oral ingestion of higher strength (>10 %) solutions may cause severe morbidity or even death [3]. Vision problems associated with HP exposure are most likely related to cytotoxic injury of the ocular surface, as might occur with a splash of household strength solution (3 %) or rarely with use of a contact lens that has been cleaned with higher concentration (>3 %) HP [4]. Though HP is known to induce apoptosis in retinal ganglion cells (RGCs) and has been used as a model for optic nerve demyelination in vitro [5,6], only a single case report of HP associated optic neuropathy has been documented and it is unlikely that the case truly represented a causal relationship [7]. Tissue infarctions due to oxygen-emboli are a well-recognized byproduct of exposure to HP following oral ingestion or iatrogenic exposure [3]. With this manuscript we report the first case of blindness due to cerebral infarction by oxygen emboli as a result of industrial strength (>30 %) HP ingestion, as well as the dramatic improvement that followed hyperbaric treatment.

Case. Report

A 66-year-old right-handed man with a history of hyperlipidemia, hypertension, and phthisis bulbi of the right eye, following penetrating trauma during childhood, presented to the emergency department (ED) with severe vision loss which began 30 min to 1 h following oral ingestion of commercial grade 35 % HP solution 24-h prior to arrival. He reported ingesting about a quarter of a 16.9 oz/500 mL water bottle

* Correspondence to: University of California Los Angeles Doheny Eye Center, 625 South Fair Oaks Ave, Suite 227, Pasadena, CA 91105,USA.
E-mail address: alfredo.sadun@gmail.com (A.A. Sadun).

https://doi.org/10.1016/j.toxrep.2025.101985
Received 22 January 2025; Received in revised form 26 February 2025; Accepted 28 February 2025
Available online 1 March 2025

(approx. 125 mL = about 44 mL of HP), which was used to store HP for cleaning. He reported that he quickly regretted the mistake and expectorated the volume that was in his mouth before forcing himself to vomit.

On presentation, his vision was limited to hand motions in all quadrants in his left eye. He had no light perception in the right eye, his baseline since childhood. His left pupil was round and reactive to light, with a dense afferent pupillary defect on the right. Intraocular pressure was normal in the left eye. Dilated fundus examination of the left eye demonstrated a nuclear cataract but otherwise clear media, and a normal appearing retina, without pallor, foveal darkening, vessel boxcarring, or other signs of a retinal vascular occlusion. The optic nerve appeared normal without any edema, pallor, hemorrhages, or cotton wool spots. Venous blood gas as well as laboratory testing for serum volatiles and osmolality were within normal range. The sedimentation rate and the c-reactive protein level were normal. Computed tomography (CT) of the brain and CT angiography of the head and neck did not reveal any acute findings. CT of the abdomen and pelvis demonstrated thickening of the gastric wall as well as a punctate focus of gas in the hepatic vein, and diffuse hepatic hypodensity. Magnetic resonance imaging (MRI) of the brain and orbits as well as transcranial dopplers were performed after treatment had been initiated. MRI of the brain and orbits with and without contrast demonstrated scattered foci of restricted diffusion on the surface of the cortices of the right medial occipital lobe, near the calcarine fissure, right superior frontal gyrus, precentral gyrus, bilateral inferior parietal lobules, and lateral occipital lobes (Fig. 1). The appearance was considered to be consistent with infarctions due to an embolic source. The optic nerves, the optic chiasm, and the tracts were without abnormal enhancement. Transcranial doppler with bubble study was performed, demonstrating a Spencer grade 4 right-to-left shunt, likely reflecting a patent foramen ovale or intrapulmonary arteriovenous malformation.

Upon arrival at the ED, the patient was evaluated by the emergency medicine, toxicology, neurology, gastroenterology, and ophthalmology services. Toxicology recommended hyperbaric oxygen therapy for treatment of possible infarctions due to arterial oxygen emboli. The first hyperbaric treatment was to a depth of 2.81 ATA consisting of a total of 143 min of compression, 113 min being bottom time, and 90 min of 100 % oxygen administration. The patient reported an improvement in vision 1–2 h following the first treatment and his corrected near vision was measured at J16 (20/200 Snellen distance equivalent). Given the measurable improvement, the patient received a second treatment session, this time to a depth of 2.36 ATA with a total of 67 min of compression, 59 min of bottom time, and again 90 min of 100 % oxygen

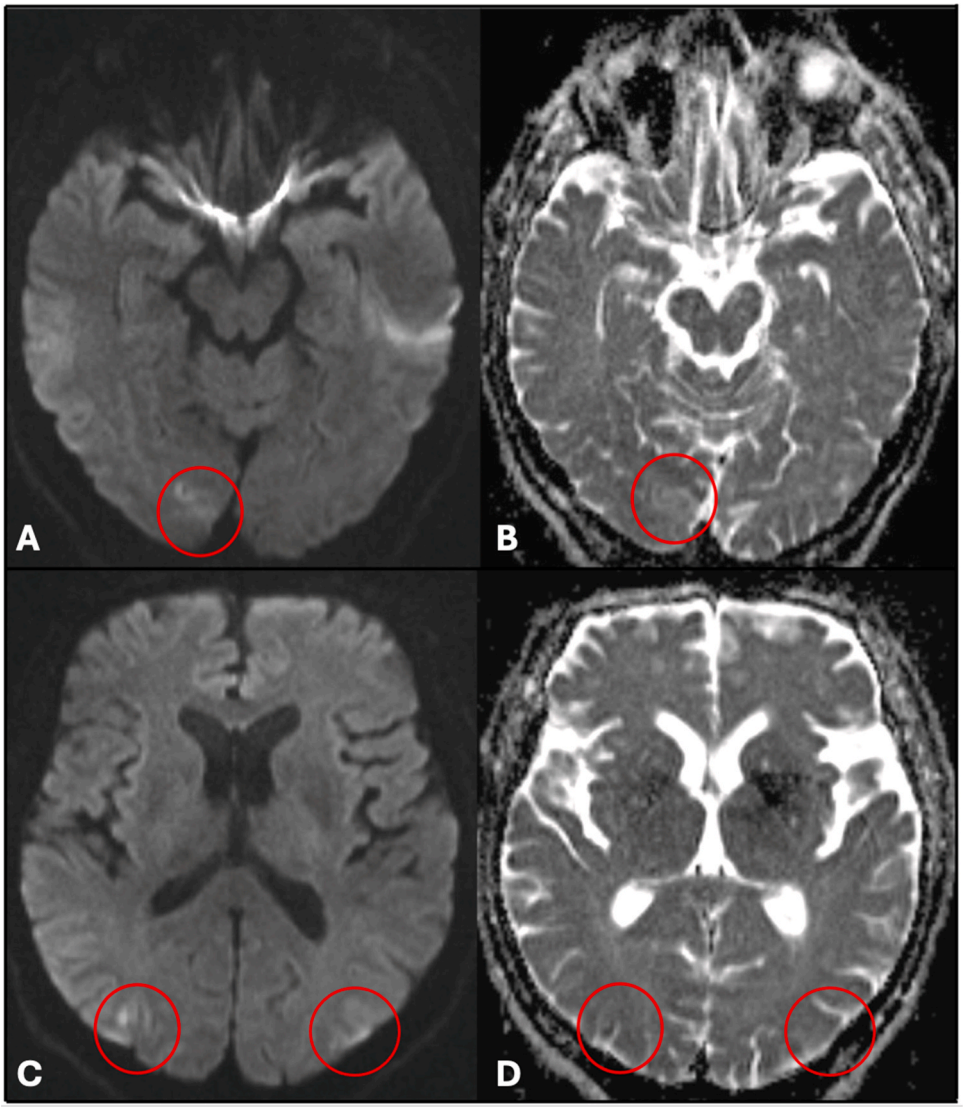

Fig. 1. MRI axial slices, DWI (A,C) and ADC (B,D) sequences demonstrating diffusion restriction in the right medial occipital lobe (A,B) and bilateral inferior parietal lobules (C,D).

administration. The following morning his corrected near vision measured J1 + (20/20 Sn. dist.) and subjectively he reported that his vision had returned to baseline. Given this success, treatment was discontinued. The patient was prescribed daily aspirin and atorvastatin, for stroke risk factor mitigation per his neurologist's recommendation, and discharged home to follow-up outpatient with neurology and neuro-ophthalmology.

At a follow-up visit 2 months after his hospitalization, the patient's uncorrected distance vision was 20/20 in the left eye. Testing was only possible for the left eye due to the aforementioned injury to the right eye. Standardized automated perimetry using the Humphrey Visual Field 30–2 SITA Standard strategy with a size III stimulus demonstrated mild depression centrally with a dense scotoma inferonasal to fixation and a mean deviation of −6.30 dB (Fig. 2A). Zeiss Cirrus optical coherence tomography of the retinal nerve fiber layer (RNFL) flagged normal RNFL and neuroretinal rim thicknesses, but closer inspection revealed wedges of RNFL thinning both nasally and superiorly (Fig. 2B).

2. Discussion

This case highlights the time sensitive challenges a physician may be faced with when treating a patient with vision loss following a toxic ingestion as well as a very intriguing set of pathophysiological mechanisms. Localizing the lesion in a case where the only manifestation is vision loss was made more challenging by the fact that our patient was monocular at baseline. In this case, the patient reportedly recognized his error and spit out a large mouthful of HP before inducing emesis. The apparent lack of pharyngeal mucosal injury made HP toxicity seem less likely initially, but the findings of edema of the gastric wall and gas in the portal venous system on the CT of the abdomen provided the evidence needed to suspect cerebral infarctions due to gas emboli and prompted emergent treatment. This was later supported by the multifocal embolic infarcts seen on MRI and moderate right-to-left shunt that was seen on the transcranial dopplers with bubble study, both of which were performed post-treatment to confirm the diagnosis of multifocal infarcts involving the visual pathway. One feature of this case, which may be more impressive than the rapid improvement in visual acuity from hand motions to 20/20, is the fact that he presented greater than 24 h after symptom onset and still experienced near total resolution of his visual field loss.

Hydrogen peroxide readily crosses epithelial barriers. Catalase, an enzyme present in all aerobic cells, is responsible for converting HP to water and oxygen [8]. Just 1 mL of 3 % HP will produce 10 mL of oxygen gas, while 1 mL of 35 % will produce 100 mL of oxygen [3]. It's unlikely that he retained the full measure of HP he said he took (125 mL) as this would have produced over 10 liters of gas. This startling fact may explain why our patient experienced profound deleterious effects despite his immediate effort to regurgitate the toxin. HP is an odorless and colorless liquid, allowing it to be mistaken for water if placed in an unlabeled container. While the liquid's bitter taste will signal to a consumer that it is not safe for ingestion, the recognition at this point may be too late.

A systematic literature review of embolic phenomena due to HP exposure by King et al. found that time to symptoms of embolic phenomena in cases of HP ingestion has been reported as early as immediate and as late as 72 h from exposure, but in 90 % of cases the symptoms occur within 10 h [3]. Treatment with hyperbaric oxygen therapy is aimed at restoring blood flow to infarcted tissue by dissolving the gas emboli through increased pressure. Oxygen is sometimes used to increase oxygenation to the tissues, though it will aggravate ischemia-reperfusion. King et al. found that 56.5 % of patients treated with hyperbaric oxygen for portal venous gas or air-gas emboli saw full recovery compared with 41.8 % of patients not treated with hyperbaric oxygen [3]. Optimal recovery of function is expected with a shorter time to treatment. There were deaths in 4 of the 54 (7.4 %) patients treated with hyperbaric oxygen compared with 13 of 72 (18.1 %) of patients in the non-treated group. One significant bias with these comparisons is that sicker patients may be too unstable to be candidates for hyperbaric therapy. Interpretation is also limited by small sample sizes, diversity of treatment indications, and lack of standardization among treatment centers, but in addition to data from previous studies, hyperbaric oxygen therapy seems to improve likelihood of recovery and reduce mortality in patients treated for infarctions due to air-gas emboli versus the alternative. The efficacy of hyperbaric therapy at room air concentrations ("hyperbaric air") for treatment of arterial oxygen emboli has not been studied.

One question the authors raise is whether treatment with 100 % oxygen may pose an additional risk by increasing oxidative stress in patients with possible or known injuries due to increased activity of reactive oxygen species (ROS). HP generates ROS both in vivo and in vitro, and this is at least part of the mechanism by which neutrophils kill bacteria. Clearly, there are scenarios where the therapeutic value of hyperbaric oxygen is desired, as with decompression sickness or treatment of bacterial and especially anaerobic infections [9]. One of the proposed mechanisms by which hyperbaric oxygen treats infectious disease is the antimicrobial effect of increased ROS formation [10]. Several studies have demonstrated that hyperbaric oxygen therapy may have deleterious effects on mitochondrial function [11]. Indeed, there are models that use HP titration as a test of mitochondrial dysfunction as the cells with mitochondrial impairment are more sensitive to HP induced apoptosis [12,13]. Oxygen, and particularly ROS may aggravate any underlying mitochondrial impairment [14]. To take the point a step further, the opposite of hyperbaric oxygen, or therapeutic hypoxia, has been proposed as a treatment of mitochondrial dysfunction and has demonstrated remarkable beneficial effects in animal models of neurodegenerative diseases, diseases where ROS excess plays a major role in the pathophysiology [15–17].

In cases of air-gas emboli, the therapeutic purpose of hyperbaric treatment is to reduce the size of the emboli in accordance with Boyle's law and thereby restore blood flow to infarcted tissues. While the oxygen window effect explains the unmistakable benefit of treating nitrogen and inert gas emboli with 100 % oxygen [18], hyperoxygenation may have less therapeutic value in cases of pure oxygen emboli, as increasing the oxygen content in the blood would theoretically reduce the gradient which is otherwise leveraged to shrink nitrogen and inert gas bubbles [19]. Hyperoxygenation is also known to induce vasoconstriction of neurovasculature, which may be counterproductive in these cases [20]. Previous study does not support the use of hyperbaric oxygen or hyperoxygenation therapy for stroke patients [20,21]. Such concerns might lead one to consider whether treatment with hyperbaric air (21 % oxygen, 79 % nitrogen) would be preferable to hyperoxygenation, as it would be expected to produce fewer ROS, the byproducts of oxygen metabolism. It may be useful to investigate this idea by indirectly assessing systemic ROS production in patients undergoing hyperbaric oxygen therapy using serum-based testing such as derivatives-oxygen metabolites (d-ROMs) [22].

In conclusion, this is a report of blindness caused by cerebral infarctions involving the visual pathway due to oxygen emboli subsequent to ingestion of commercial grade (35 %) HP. The patient's profound blindness resolved shortly after treatment with hyperbaric oxygen therapy. We wish to highlight the importance of recognizing and treating patients with sequelae of possible oxygen emboli, the effects of which may be pleotropic. The beneficial effect of hyperbaric treatment in this cases was undoubtable, but in the authors' opinion there may be reason to reconsider the standard practice of treating patients exposed to HP with 100 % oxygen. Though the tremendous benefit of hyperbaric treatment alone may render the point moot, the authors express concern that treating patients with oxygen emboli due to HP ingestion with hyperoxygenation may place them at increased risk of adverse effects or tissue injury due to increased free radical production or delayed bubble dissolution, ideas which require validation with dedicated investigation.

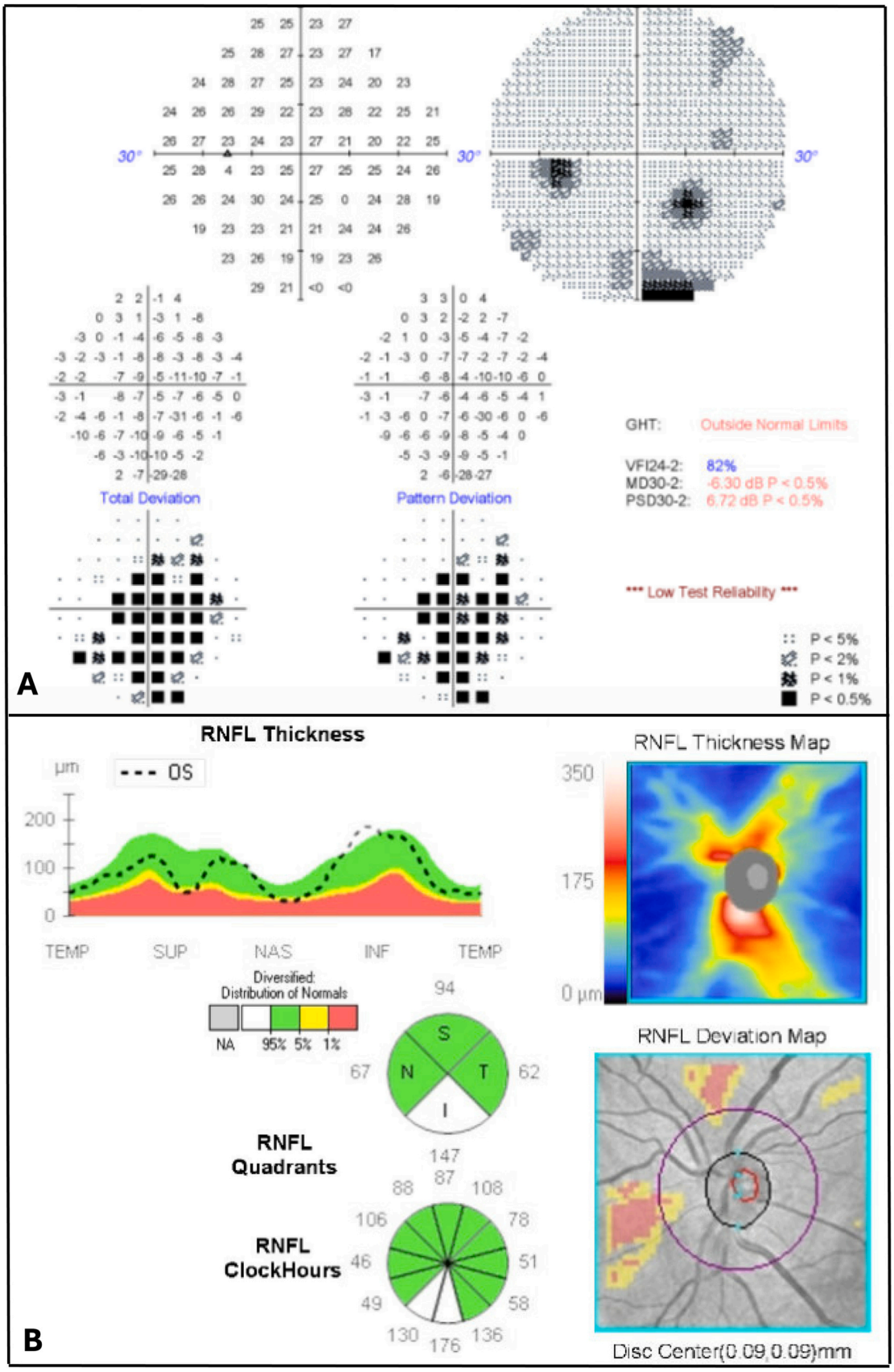

Fig. 2. Humphrey Visual Field 30–2 SITA Standard strategy with a size III stimulus (A) demonstrating mild depression centrally with a dense scotoma inferonasal to fixation in the left eye. Zeiss Cirrus optical coherence tomography of the RNFL (B) demonstrating wedges of RNFL thinning nasally and superiorly in the left eye.

Financial disclosures

None to report.

CRediT authorship contribution statement

Pargalava Nutsa: Writing – review & editing, Writing – original draft. **Engelmann Alexander:** Writing – review & editing, Writing – original draft, Conceptualization. **Sadun Alfredo A.:** Writing – review & editing, Supervision, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data was used for the research described in the article.

References

[1] B.E. Watt, A.T. Proudfoot, J.A. Vale, Hydrogen peroxide poisoning, Toxicol. Rev. 23 (2004) 51–57, https://doi.org/10.2165/00139709-200423010-00006.
[2] Agency for Toxic Substances and Disease Registry (ATSDR), Managing Hazardous Materials Incidents. Volume III - Medical Management Guidelines for Acute Chemical Exposures: Hydrogen Peroxide. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, 2002.
[3] A. King, M. Fee, E. McGlynn, B. Marshall, K.G. Akers, B. Hatten, Timing of embolic phenomena after hydrogen peroxide exposure – a systematic review, Clin. Toxicol. 61 (1) (2023) 12–21, https://doi.org/10.1080/15563650.2022.2144745.
[4] B.J. Tripathi, R.C. Tripathi, C.B. Millard, N.S. Borisuth, Cytotoxicity of hydrogen peroxide to human corneal epithelium in vitro and its clinical implications, Lens Eye Toxic. Res. 7 (3-4) (1990) 385–401.
[5] X. Xi, J. Ma, Q. Chen, X. Wang, Y. Xia, X. Wen, J. Yuan, Y. Li, Acteoside attenuates hydrogen peroxide-induced injury of retinal ganglion cells via the CASC2/miR-155/mTOR axis, Ann. Transl. Med. 10 (1) (2022) 5, https://doi.org/10.21037/atm-21-5630.
[6] J. Guy, E.A. Ellis, R. Mames, N.A. Rao, Role of hydrogen peroxide in experimental optic neuritis. A serial quantitative ultrastructural study, Ophthalmic Res. 25 (4) (1993) 253–264, https://doi.org/10.1159/000267321.
[7] F.M. Domaç, A. Koçer, R. Tandr, Optic neuropathy related to hydrogen peroxide inhalation, Clin. Neuropharmacol. 30 (1) (2007) 55–57, https://doi.org/10.1097/01.WNF.0000240948.34068.FF.
[8] G.P. Beinert, J.K. Schjoerring, T.P. Jahn, Membrane transport of hydrogen peroxide, Biochem. Et. Biophys. Acta Biomembr. (8) (2006) 994–1003, https://doi.org/10.1016/j.bbamem.2006.02.015.
[9] D. Muroya, S. Nadayoshi, K. Yamada, Y. Kai, N. Masuda, T. Nishida, M. Shimokobe, T. Hisaka, Effects of hyperbaric oxygen therapy for *Clostridioides difficile*-associated colitis: a retrospective study, J. Anus Rectum Colon 7 (4) (2023) 264–272, https://doi.org/10.23922/jarc.2023-033.
[10] M.Y. Memar, M. Yekani, N. Alizadeh, H.B. Baghi, Hyperbaric oxygen therapy: Antimicrobial mechanisms and clinical application for infections, Biomed. Pharm. 109 (2019) 440–447, https://doi.org/10.1016/j.biopha.2018.10.142.
[11] N. Schottlender, I. Gottfried, U. Ashery, Hyperbaric oxygen treatment: effects on mitochondrial function and oxidative stress, Biomolecules 11 (12) (2021) 1827, https://doi.org/10.3390/biom11121827.
[12] A. Wong, G. Cortopassi, mtDNA mutations confer cellular sensitivity to oxidant stress that is partially rescued by calcium depletion and cyclosporin A, Biochem Biophys. Res. Commun. 239 (1) (1997) 139–145, https://doi.org/10.1006/bbrc.1997.7443.
[13] V. Carelli, F.N. Ross-Cisneros, A.A. Sadun, Optic nerve degeneration and mitochondrial dysfunction: genetic and acquired optic neuropathies, Neurochem. Int. 40 (6) (2002) 573–584, https://doi.org/10.1016/s0197-0186(01)00129-2.
[14] S.J. Spiegel, A.A. Sadun, Solutions to a radical problem: overview of current and future treatment strategies in Leber's hereditary opic neuropathy, Int. J. Mol. Sci. 23 (21) (2022) 13205, https://doi.org/10.3390/ijms232113205.
[15] I.H. Jain, L. Zazzeron, R. Goli, K. Alexa, S. Schatzman-Bone, H. Dhillon, O. Goldberger, J. Peng, O. Shalem, N.E. Sanjana, F. Zhang, W. Goessling, W. M. Zapol, V.K. Mootha, Hypoxia as a therapy for mitochondrial disease, Science 352 (6281) (2016) 54–61, https://doi.org/10.1126/science.aad9642.
[16] R.S. Rogers, H. Wang, T.J. Durham, J.A. Stefely, N.A. Owiti, A.L. Markhard, L. Sandler, T.L. To, V.K. Mootha, Hypoxia extends lifespan and neurological function in a mouse model of aging, PLoS Biol. 21 (5) (2023) e3002117, https://doi.org/10.1371/journal.pbio.3002117.
[17] T. Ast, H. Wang, E. Marutani, F. Nagashima, R. Malhotra, F. Ichinose, V.K. Continuous Mootha, but not intermittent, regimens of hypoxia prevent and reverse ataxia in a murine model of Friedreich's ataxia, Hum. Mol. Genet 32 (16) (2023) 2600–2610, https://doi.org/10.1093/hmg/ddad091.
[18] H.D. Van Liew, J. Conkin, M.E. Burkard, The oxygen window and decompression bubbles: estimates and significance, Aviat. Space Environ. Med. 64 (9 Pt 1) (1993) 859–865.
[19] C.M. Muth, E.S. Shank, Gas embolism, N. Engl. J. Med. 342 (2000) 476–482, https://doi.org/10.1056/NEJM20000217342070.
[20] O.M. Ronning, B. Guldvog, Should stroke victims routinely receive supplemental oxygen? A quasi-randomized controlled trial, Stroke 30 (1999) 2033–2037, https://doi.org/10.1161/01.STR.30.10.2033.
[21] M.H. Bennett, J. Wasiak, A. Schnabel, P. Kranke, C. French, Hyperbaric oxygen therapy for acute ischaemic, Stroke Cochrane Database Syst. Rev. 3 (2005) CD004954, https://doi.org/10.1002/14651858.CD004954.pub2.
[22] F. Pigazzani, D. Gorni, K.A. Dyar, M. Pedrelli, G. Kennedy, G. Costantino, A. Bruno, I. Mackenzie, T.M. MacDonald, U.J.F. Tietge, J. George, The prognostic value of derivatives-reactive oxygen metabolites (d-ROMs) for cardiovascular disease events and mortality: a review, Antioxidants 11 (8) (2022) 1541, https://doi.org/10.3390/antiox11081541.