



Intrapulmonary Use of Hydrogen Peroxide in Respiratory Obstruction: Initial Results Demonstrate the Possibility of Airway Recanalization and Blood Reoxygenation through the Lungs: An Update

Aleksandr Urakov ^{a*}, Petr Shabanov ^b,
Konstantin Gurevich ^c, Evgeny Fisher ^a,
Anastasia Stolyarenko ^a, Daria Suntsova ^a,
Ilnur Yagudin ^a and Nikita Muhutdinov ^a

^a Department of General and Clinical Pharmacology, Izhevsk State Medical Academy, Kommunarov Str., 281, 426034, Izhevsk, Russia.

^b Department of Neuropharmacology, Institute of Experimental Medicine, Acad, Pavlov Str., 12, 197022, Saint Petersburg, Russia.

^c UNESCO Chair "Healthy Lifestyle is a Key to Successful Development", Moscow State University of Medicine and Dentistry, Moscow, Russia.

Authors' contributions

This work was carried out in collaboration among all authors. Authors AU, PS and KG designed the study and wrote the protocol. Authors EF, AS and DS wrote the protocol and the first draft of the manuscript. Authors IY and NM managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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*Corresponding author: E-mail: urakoval@live.ru;

ABSTRACT

It is reported that the interaction of hydrogen peroxide and sodium bicarbonate solution with thick sputum, mucus, pus and blood clots leads to their rapid transformation into a fluffy oxygenated foam. This mechanism of action allows repurposing hydrogen peroxide from antiseptic to expectorant and oxygen forming antihypoxant, which can find application for recanalization of airways and increasing blood oxygenation in acute respiratory syndrome. It is reported that acute respiratory distress syndrome in COVID-19 can be caused by excessive accumulation of thick sputum, mucus and pus in the airways, which complicates intra-pulmonary oxygenation of blood, causes hypoxia and causes death, since there are no drugs for urgent recanalization of the airways today. At the same time, the first evidence emerged that alkaline hydrogen peroxide solution can claim to be an inhaled expectorant and oxygen-producing drug for urgent recanalization of the airways when they are blocked by mucus, sputum, pus, blood and other colloidal fluid containing the enzyme catalase.

Keywords: lung samples; respiratory obstruction; hypoxia; catalase; hydrogen peroxide.

1. INTRODUCTION

Hydrogen peroxide is an over-the-counter antiseptic that has been widely used topically for about 100 years to treat cuts, scratches, abrasions, burns and purulent wounds because it has a detrimental effect on pathogens, including coronaviruses [1-5]. A solution of 3-6% hydrogen peroxide solution is considered to be the most effective and safe preparation for external local application for medical purposes [6]. At the same time, hydrogen peroxide solutions continue to be used in various fields of medicine without regard to their physicochemical properties. In particular, the peculiarities of local interaction with sputum, mucus, pus and blood of hydrogen peroxide solution with changes in its acid (alkaline), osmotic, thermal and gaseous activity remain poorly studied [2,7-10]. Here we summarized the first data on the nonspecific local action of hydrogen peroxide solutions on biological tissues due to the value of its concentration, osmotic and alkaline activity, temperature and the ability to form gaseous oxygen. We sought to understand the basic laws of the mechanism of local non-specific action of hydrogen peroxide solutions on biological tissues containing the enzyme catalase in order to improve the effectiveness and safety of treatment of "purulent" diseases and complications caused by infectious processes of purulent-inflammatory nature [4,6,7,11,12]. According to international databases containing information on scientific articles and patents for inventions, the formulation and physical-chemical properties of hydrogen peroxide solutions have not been significantly altered for about last 100 years. Only in the last few years have the first proposals for radically changing the physical-chemical properties of hydrogen peroxide solutions to give

them new mechanisms of action begun to appear. The fact is that it was at this time that reports appeared on the possibility of transforming an "old" drug into a "new" one (a drug with new pharmacological activity) by means of a targeted change in its physical-chemical properties [13-15].

2. MODERNIZATION OF THE HYDROGEN PEROXIDE SOLUTION FORMULATION

Analysis of the available articles and inventions allows us to recognize that the indicated way of hydrogen peroxide solution modernization turned out to be correct. At the same time, it becomes clear that the most productive elements in the modernization of the hydrogen peroxide solution formulation, which gave it completely new and unique physical and chemical properties, were the additional introduction of sodium bicarbonate, oxygen gas under increased pressure and increasing solution temperature to +37 - +42 °C. The first report on the possibility of using hydrogen peroxide solution for a new purpose relied on its ability to replace oxygen gas and prevent death of aquarium fish from hypoxia in water without access to oxygen gas (patent RU No. 2563151, 20.09.2015). It was reported that the use of a calculated therapeutic dose of a hydrogen peroxide solution by enteral administration through a gastric tube, intramuscular injection, or injection into the water in which the fish swam, increased the survival time of fish in hermetically sealed containers similar to the reoxygenation of fish water and/or blood. Previously, there were no such proposals. Before that, the most reliable preservation was achieved only by cooling (US Patent No.

7429398, 23.08.2003) [16]. The next report on the possibility of using hydrogen peroxide solution for a new purpose was based on its ability to transform a portion of canned donor venous blood into arterial blood without using oxygen gas (Patent RU No. 2538662, 10.01.2015). In the same years it was shown that hydrogen peroxide, when interacting with blood, is split by the enzyme catalase into water and molecular oxygen, so that oxyhemoglobin is formed in erythrocytes (Patent RU No. 2589682, 10.07.2016). Therefore, the appearance of hydrogen peroxide in the blood increases blood oxygenation and eliminates hypoxia. In addition, it has been shown that the introduction of sodium bicarbonate into the hydrogen peroxide solution provides the drug with the "right" alkaline activity (Patent RU No. 2539380, 20.01.2015). The fact is that blood and most body tissues have alkaline rather than acidic activity, which is provided by sodium bicarbonate (Patent RU No. 2586276, 10.06.2016). Therefore, injection and enteral administration of hydrogen peroxide solutions has been recommended as a promising direction for the development of drug-assisted extrapulmonary blood oxygenation in the future.

3. ANTIHYPOXIC EFFECT OF THE HYDROGEN PEROXIDE

It was soon shown that the additional introduction of oxygen gas into the solution under excessive pressure increases the antihypoxic effect of the hydrogen peroxide solution (Patent RU No. 2604129, 10.12.2016; Patent RU No. 2639493, 21.12.2018; Patent RU No. 2634271, 24.10.2017). Moreover, it turned out that forced introduction of hydrogen peroxide gas into the hydrogen peroxide solution under increased pressure gives the drug the ability of rapid cold boiling with foam formation regardless of the presence of catalase and is little dependent on the concentration of hydrogen peroxide. In addition, it has been shown that increasing the temperature of the solution to +37 - 42°C potentiates the process of foam formation and simultaneously reduces the local irritating effect of the drug. It was also found that due to the controlled foaming activity hydrogen peroxide solutions can have a geyser-like, polylytic, mucolytic, hemolytic, decolorizing, oxygen-releasing and antihypoxic effect, which was recommended for recanalization of airways and elimination of hypoxia in respiratory obstruction caused by purulent obstructive bronchitis [17-19]. It has been reported that if the airways are filled

with thick sputum, mucus, pus and/or blood, traditional mucolytics and expectorants and their application techniques do not provide urgent airway recanalization and urgent blood oxygenation through the lungs. At the same time, if under these conditions, inhaled aerosol of warm hydrogen peroxide solution with pH 8.5 is applied, it quickly dissolves sputum, mucus, pus and blood clots and turns them into oxygen foam, thus providing easy and rapid removal of biological masses from the airways outward, increasing oxygen content in the airways and its absorption into the blood through the alveoli. In other words, inhalation administration of aerosol of warm alkaline hydrogen peroxide solution has been shown to restore airway patency for respiratory gas, increase lung airiness, oxygen content in the airways and blood oxygenation through the lungs when the airways are blocked with sputum, mucus, pus and blood. Due to the described mechanism of local action in the respiratory tract of an aerosol of antiseptic alkaline hydrogen peroxide solution, this medication has recently been recommended for use during a severe attack of bronchial asthma and/or obstructive bronchitis. Moreover, it has been suggested that intrapulmonary use of an upgraded hydrogen peroxide antiseptic with new physicochemical properties may soon become an alternative to extracorporeal membrane oxygenation, since the drug has high availability and also easily and easily provides urgent increase of blood oxygenation through the lungs in severe hypoxia caused by acute respiratory obstruction in new coronavirus infection [18].

The ability of an upgraded hydrogen peroxide solution, when administered intrapulmonary, to dissolve and turn thick sputum, mucus, pus and blood clots into oxygenated foam and to increase blood oxygenation through the lungs has been shown in laboratory and experimental conditions. It was reported that the above results were obtained from *in vitro* laboratory studies using isolated portions of pus, mucus, sputum and blood of the patient, as well as in experiments with isolated rabbit lungs and in experiments on awake rabbits with simulated airway obstruction performed by artificial filling of the airways with artificial sputum (Patent RU No. 2748999, 02.06.2021). It was shown that a single aerosol and/or injected solution of 0.3-0.5% hydrogen peroxide and 1.2- 10% sodium bicarbonate quickly (within seconds) turns pus, blood, thick sputum and mucus into an oxygenated foam in local interaction with them (Fig. 1).

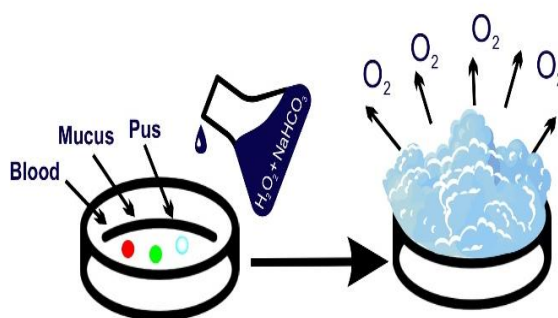


Fig. 1. A solution of hydrogen peroxide and sodium bicarbonate immediately turns thick mucus, pus and blood into fluffy oxygen foam.

In addition, at the same time the intrapulmonary application of the specified modernized antiseptic hydrogen peroxide urgently increased blood oxygenation through the lungs and eliminated hypoxia in the rabbit, caused by previously filled his airways with artificial sputum [19]. The protocol of the study on experimental animals (rabbits) corresponded to the principles set out in the Helsinki Declaration of the World Health Organization, and was approved by the Ethics Committees at the Institute of Thermology in Izhevsk (Protocol No. 3 of February 7, 2019).

4. CONCLUSION

Thus, the first reports on aerosol inhalation and/or intrapulmonary injection of an upgraded solution of the "old" antiseptic hydrogen peroxide, which show a previously unknown non-specific biological activity of hydrogen peroxide, and which can be used for effective airway recanalization and blood reoxygenation through the lungs during airway obstruction and acute hypoxia, appeared. Analysis of the first results shows that intrapulmonary application of alkaline hydrogen peroxide solution in the role of recanalizing and reoxygenating drug can optimize treatment of patients with severe hypoxia complicating severe bronchial asthma, lung diseases caused by infection, worm invasion, lung injury and/or congenital pathology like cystic fibrosis, etc. [20]

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance [published correction appears in *ClinMicrobiol Rev* 2001 Jan;14(1):227]. *ClinMicrobiol Rev*. 1999;12(1):147-179. DOI:10.1128/CMR.12.1.147.

2. Hosseini MA. Hydrogen Peroxide. *Encyclopedia of Toxicology (Third Edition)*. 2014;967-970.
3. Smith SR, Tying SK, Grande KK, Schlessinger J, Gold MH, Shanier SD. Hydrogen Peroxide Topical Solution, 45% for Common Warts: Phase 2 Efficacy and Safety Trial Results. *J Drugs Dermatol*. 2020;19(10):969-976. DOI:10.36849/JDD.2020.50544.
4. Zhu G, Wang Q, Lu S, Niu Y. Hydrogen Peroxide: A potential wound therapeutic target?. *Med Princ Pract*. 2017;26(4):301-308. DOI:10.1159/000475501U.
5. Rozman U, Pušnik M, Kmetec S, Duh D, Šostar Turk S. Reduced susceptibility and increased resistance of bacteria against disinfectants: A Systematic Review. *Microorganisms*. 2021;9(12):2550. Published 2021 Dec 10. DOI:10.3390/microorganisms9122550.
6. Mahran AM, Twisy HO, Elghazally SA, Badran AY. Evaluation of different concentrations of hydrogen peroxide solution (3% and 6%) as a potential new therapeutic option of nongenital warts: A randomized controlled triple-blinded clinical trial. *J Cosmet Dermatol*. 2020;19(2):416-422. DOI:10.1111/jocd.13021.
7. Thomas EL, Milligan TW, Joyner RE, Jefferson MM. Antibacterial activity of hydrogen peroxide and the lactoperoxidase-hydrogen peroxide-thiocyanate system against oral streptococci. *Infect Immun*. 1994;62(2):529-535. DOI:10.1128/iai.62.2.529-535.1994.

8. Courtois P. Oral peroxidases: From antimicrobial agents to ecological actors (Review). *Molecular Medicine Reports*. 2021;24:500. DOI: 10.3892/mmr.2021.12139.
9. Ashby MT. Inorganic chemistry of defensive peroxidases in the human oral cavity. *J Dent Res*. 2008;87(10):900-914. DOI:10.1177/154405910808701003.
10. Herrero ER, Boon N, Bernaerts K, et al. Clinical concentrations of peroxidases cause dysbiosis in in vitro oral biofilms. *J Periodontal Res*. 2018;53(3):457-466. DOI:10.1111/jre.12534.
11. Rai S, Gupta TP, Shaki O, Kale A. Hydrogen Peroxide: Its Use in an extensive acute wound to promote wound granulation and infection control - Is it Better Than Normal Saline? [published online ahead of print, 2021 Aug 2]. *Int J Low Extrem Wounds*. 2021;153473462-11032555. DOI:10.1177/15347346211032555.
12. Smith SR, Xu S, Estes E, Shanler SD. Anatomic Site-Specific Treatment Response With 40% Hydrogen Peroxide (w/w) topical formulation for raised seborrheic keratoses: pooled analysis of data from two phase 3 studies. *J Drugs Dermatol*. 2018;17(10):1092-1098.
13. Urakov AL, Urakova NA, Stolyarenko AP. How to turn an old medicine into a new medicine. *J.Bio.Innov*. 2020;9:774-777. DOI:10.46344/JBINO.2020.v09i05.13.
14. Urban MV, Rath T, Radtke C. Hydrogen peroxide (H₂O₂): A review of its use in surgery. *Wasserstoffperoxid (H₂O₂) – eine Übersicht zur Verwendung in der Chirurgie*. *Wien Med Wochenschr*. 2019; 169(9-10):222-225. DOI:10.1007/s10354-017-0610-2.
15. Murphy EC, Friedman AJ. Hydrogen peroxide and cutaneous biology: Translational applications, benefits, and risks. *J Am Acad Dermatol*. 2019;81(6): 1379-1386. DOI:10.1016/j.jaad.2019.05.030.
16. Zhu CD, Wang ZH, Yan B. Strategies for hypoxia adaptation in fish species: a review. *J Comp Physiol B*. 2013;183(8): 1005-1013. DOI:10.1007/s00360-013-0762-3.
17. Fisher E, Urakov A, Svetova M, et al. COVID-19: Intrapulmonary alkaline hydrogen peroxide can immediately increase blood oxygenation. *Med. Cas* 2021;55:135-138. DOI:10.5937/mckg55-35424.
18. Urakov AL, Urakova NA. COVID-19: Intrapulmonary injection of hydrogen peroxide solution eliminates hypoxia and normalizes respiratory biomechanics. *Russian Journal of Biomechanics*. 2021; 25:350-356. DOI: 10.15593/RJBiomech/2021.4.06.
19. Urakov AL, Urakova NA, Yagudin II, Svetova MD, Suntsova DO. COVID-19: Artificial sputum, respiratory obstruction method and screening of pyolitic and antihypoxic drugs. *Bioimpacts*. 2022;12(4) :393-394. DOI:10.34172/bi.2022.23877.
20. Servello FA, Fernandes R, Eder M, et al. Neuronal temperature perception induces specific defenses that enable *C. elegans* to cope with the enhanced reactivity of hydrogen peroxide at high temperature. *Elife*. 2022;11:e78941. Published 2022 Oct 13. DOI:10.7554/eLife.78941.

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