Hydrogen Peroxide and Viruses

Milton V. Marshall, PhD, DABT, RQAP-GLP, CCRP*

Significant evidence exists for the antiviral activity of hydrogen peroxide toward coronaviruses. The US Environmental Protection Agency regulates disinfectants, and 0.5% hydrogen peroxide and other products are registered as a disinfectant for human coronaviruses (EPA List N). Inactivation of SARS-CoV- 2 on surfaces can occur with a variety of biocidal agents, including hydrogen peroxide (Kampf et al.). The FDA allows use of vaporized hydrogen peroxide for sterilizing respirators for reuse under the Emergency Use Authorization Act.

Hydrogen peroxide kills SARS-CoV-2 on surfaces. It likely disrupts the viral envelope by interacting with the spike protein or disrupting the envelope and attacking the viral RNA, either of which would prevent the virus from replicating. In the presence of iron (Fe^{2+}) or copper (Cu^{2+}), the hydroxyl radical is generated (Floyd, Zs-Nagy), which can form 8-oxoguanosine in the viral mRNA. The formation of 8- oxoguanosine leads to incomplete translation of the viral genome (Dai; Sims et al.). RNA is more reactive with reactive oxygen species than DNA (Hofer et al.).

Exposure to SARS-CoV-2 can occur via aerosolization (Bourouiba; Anfinrud et al., Lu et al., Santarpia et al., Meselson). SARS-CoV-2 can be detected in saliva and sputum (Wang et al.; Han et al.; To et al.; Sabino-Silva et al.). Salivary glands have ACE-2 receptors to which the SARS (SARS CoV-1) virus can attach and enter the cells (Liu et al.). It is reasonable to assume that SARS-CoV-2 will also infect the salivary gland cells that have ACE-2 receptors, in addition to cells with the ACE-2 receptor within the respiratory tract (Liu). To decrease the risk of viral transmission, the American Dental Association (ADA) recommends rinsing the mouth with 1.5% hydrogen peroxide prior to conducting procedures in a dental office (ADA COVID-19 Center). More detailed protective measures for dental clinical care are described in an article by Ather, et al.

Dental team exposure can occur from a variety of processes, including direct transmission of viral particles in saliva, by inhalation of droplets, and indirect transmission through contact with procedure tools or surfaces in the examining room (Peng et al.). The likelihood of developing COVID-19 symptoms and transmitting SARS-CoV-2 to additional patients would be reduced by preprocedural treatment with hydrogen peroxide. Although it has not been tested in clinical trials against SARS-CoV-2, hydrogen peroxide is recommended as a pre-procedural rinse (Peng et al.). A literature review of the use of hydrogen peroxide in protection against viral infections also recommends use of oral rinses of hydrogen peroxide (Caruso, et al.) Oral rinses that target the viral envelope include hydrogen peroxide, ethanol, and povidone-iodine (O'Donnell, et al.). Use of a mouthrinse with hydrogen peroxide or povidone-iodine are not intended to treat COVID-19, but to reduce exposure to dental personnel during procedures (Kirk-Bayley et al.).

A compelling link between oral hygiene and severity of SARS-CoV-2 infections has been postulated by Sampson, et al., in which bacterial superinfections can occur, leading to the development of respiratory distress and sepsis. Dysregulation of the immune system can also occur in SARS-CoV-2-infected patients (Zheng, et al.). The primary cause of death in Wuhan, China from persons infected with SARS-CoV-2 was acute respiratory distress syndrome (ARDS) where 41.8% of infected patients developed ARDS and 52.4% died of respiratory failure. In Italy, 96.5% of complications from SARS-CoV-2 infection were ARDS. The authors also note that during the 1918 influenza pandemic and the 2009 H1N1 influenza pandemic, the primary cause of death was from bacterial superinfections, which may have included dysregulation of the immune system. Other links between good oral care and reduced risk of acute viral respiratory infections are reported in the Sampson, et al., article. An increased risk of complications and death from COVID-19 are also associated with altered oral biofilms and periodontal disease (Sampson, et al.). These results indicate that not only an immediate benefit from oral treatment with hydrogen peroxide prior to dental procedures is important, but ongoing treatment with hydrogen peroxide may reduce the risk of complications associated with SARS-CoV-2 infection.

Hydrogen peroxide has a long history of use in dentistry and is considered safe for daily use at concentrations up to 3% (Marshall et al. 1995). Patients rinsing with hydrogen peroxide should not swallow the rinse; however, if they accidentally do swallow peroxide in a concentration of 3% or less, it poses very little risk (21 CFR Part 356. [Docket No. 81N-033P]; Mahoney, et al.).

When used as a topical agent in the oral cavity, concerns have been raised regarding free oxygen radicals. Any peroxide product will initiate the production of free radicals, but this is not necessarily harmful. Peroxide is generally present in the human mouth. Active inflammatory cells, like pulmonary alveolar macrophages, release peroxide in the lungs and it is carried into the mouth in exhaled breath (Teng et al.; Olin et al.). In the oral cavity, the enzyme catalase breaks down hydrogen peroxide into oxygen and water very quickly. Salivary peroxidase and glutathione provide additional protective properties. Some products, like Perio Gel®, are also formulated with free radical trapping agents.

Humans make hydrogen peroxide in the liver (Chance et al.) and it is used by white blood cell for phagocytosis. In the body, phagocytic cells release active oxygen species and use reactive oxygen species internally to destroy phagocytized pathogens, including bacteria and viruses, as a normal part of the host defense system against pathogens. In treatment for oral health, the oxidizing elements of peroxide help debride bacterial cell walls. (Schaudinn et al.; Dunlap et al.) The oxygenating effects are multiple but the most important for long-term gingival health is the modification of the microenvironment of the periodontal pocket or sulcus so that healthy bacteria repopulate at the expense of pathogens. This is possible when hydrogen peroxide gel is administered with a Perio Tray® (Schaudinn et al.; Keller and Cochrane; Putt et al., 2012-2014). Against viral agents, the oxidizing properties of hydrogen peroxide are the most important against viral agents.

Although the FDA has not approved any hydrogen peroxide product for treatment or prevention of SARS-CoV-2, the preceding information provides compelling evidence for use of hydrogen peroxide in patients who present for treatment in a dental office to protect dentists, hygienists, and dental assistants from exposure to persons who may be infected with SARS-CoV-2 but are asymptomatic. Hydrogen peroxide is more stable in the oral cavity when delivered as a gel in a tray, rather than rinsing as a liquid or delivery without a tray (Marshall MV unpublished observations), including brushing with a gel (Marshall et al. 2001).

In summary, hydrogen peroxide can inhibit virus replication through a number of different mechanisms – altering the viral envelope, which can decrease binding of a virus to cells leading to reduced infectivity, alteration of nucleic acids, leading to reduced protein synthesis, and alteration of viral and intracellular proteins, leading to enzyme inactivation. On surfaces, levels of hydrogen peroxide as low as 0.5% are effective in decontamination. In the presence of iron (Fe^{2+}) or copper (Cu^{2+}), hydrogen peroxide can form the hydroxyl radical, which greatly increases potency as a decontaminant. Following the recommendation of the ADA to rinse with 1.5% hydrogen peroxide prior to procedures, use of a delivery tray to apply hydrogen peroxide gel will enable extended release of hydrogen peroxide, which should provide a more effective pretreatment to avoid exposure to dental office personnel to SARS-CoV-2.

* Milton Marshall received a PhD from the University of Texas Health Science Center at Houston. His PhD dissertation was, "The mengovirus replicative form RNA: Properties and possible role in inhibition of host protein synthesis". Mengovirus is in the family of picornaviruses in a subgroup called enteroviruses that includes poliovirus, and it has the same type of genetic material as SARS-CoV-2, a positive strand of RNA that acts like a messenger RNA, which produces an enzyme that replicates the viral RNA in a duplex (double-stranded) form; these RNAs are further replicated and proteins are translated from the positive strand. SARS-CoV-2 is an enveloped virus that contains elements of the host cell in its viral envelope, along with the spike protein that attaches to acetylcholinesterase-2 (ACE-2) receptors to gain entry into susceptible cells. Mengovirus and other picornaviruses have a capsid rather than an envelope. Although viruses must gain entry into a cell for replication to occur, disruption of the ability to enter cells is more likely to occur in enveloped viruses than capsid-containing viruses after hydrogen peroxide exposure..

Milton Marshall has also worked on hydrogen peroxide-containing or -generating products to ensure their safety, presenting safety data on hydrogen peroxide to the FDA (Final Monograph for Over-the-Counter Drug Products for the Reduction or Prevention of Dental Plaque and Gingivitis, Docket No. 81 N-033P). He was also involved in establishing safety testing recommendations for peroxide-containing or -generating products that were developed by the ADA (ADA Council on Dental Therapeutics, Guidelines for the Acceptance of Peroxide-Containing Oral Hygiene Products. JADA 125(8): 1140-1142, 1994).

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