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Hypochlorous acid – a review - Hypochlorous acid may be the disinfectant of choice for coronaviruses in an oral and maxillofacial surgery (OMS) office

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Abstract

CoVID-19 virus structure and mechanism of infection

Coronavirus -19 (CoVID-19) is a novel virus. It causes Severe Acute Respiratory Syndrome. Coronavirus-2 (SARS-CoV-2) is the agent responsible for a surface to surface communicable disease which has infected approximately 4.7 million people as of May 17th, 2020 ([1]). Healthcare providers need options to limit and control the spread of the virus between each other and patients.

CoVID-19 is an enveloped, positive-sense, single-stranded RNA virus approximately 60 to 140 nm in diameter. The virus's Spike glycoprotein S1 firmly binds to angiotensin converting enzyme 2 (ACE2) receptor which allows entry into the host cell ([2, 3, 4]). CoVID-19 infection creates a cytokine storm, severe pneumonia, multiple organ failure, and acute cardiac injury ([5, 6]).

Transmission of this virus occurs through touch or aerosol spreading of the virus. A common pathway of spreading this virus is through respiratory aerosols from the infected person ([7]). During speech, humans emit thousands of oral fluid droplets per second which can remain airborne for 8 to 14 minutes ([8]). CoVID-19 is detectable in surface aerosols for up to three hours, up to four hours on copper, up to 24 hours on cardboard, and up to two to three days on plastic and stainless steel ([9, 10]). There is a need to disinfect surfaces potentially exposed to CoVID-19 to prevent transmission.

Use of disinfectants

A disinfectant agent upon contact with the virus changes the protective protein coat, which loses its structure and aggregates, forming clumps of proteins with other viruses ([9, 10]).

Currently, the United States Environmental Protection Agency (USEPA) has recommended numerous disinfectants ([11]) against CoVID-19 which includes hypochlorous acid ([11]). The mechanism of disinfection involves the destroying of the cell wall of microbes or viruses, allowing the disinfectant to destroy or inactivate them ([12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27]). This paper focuses on hypochlorous acid.

Hypochlorous Acid (HOCl)

An ideal disinfectant and sanitizer must be non-toxic to surface contact, non-corrosive, effective in various forms, and relatively inexpensive. Hypochlorous acid may be the disinfectant of choice for coronaviruses in an oral and maxillofacial surgery (OMS) office.

Hypochlorous acid (HOCl) is an endogenous substance in all mammals and it is effective against a broad range of microorganisms. Neutrophils, eosinophils, mononuclear phagocytes, and B lymphocytes produce HOCl in response to injury and infection through the mitochondrial-membrane–bound enzyme known as respiratory burst NADPH oxidase ([28]). HOCl selectively binds with the unsaturated lipid layer and subsequently disrupts cellular integrity. Between pH levels of 3 and 6, the predominant species is HOCl which has maximal antimicrobial properties ([29, 30]).

Hypochlorous acid (HOCl) is a powerful oxidizing agent. In aqueous solution, it dissociates into H^+ and OCl^- , denaturing and aggregating proteins ([30]). HOCl also destroys viruses by chlorination by forming chloramines, and nitrogen-centered radicals resulting in single- as well as double-stranded DNA breaks rendering the nucleic acid useless and the virus harmless ([31]).

How is HOCl made? HOCl can be made on site combining non-iodinated salt, water and electrolysis. The system to make HOCl on site is a one-liter container which is filled with water. A gram of non-iodized salt and 1 teaspoon of vinegar is added to the water. The system has the ability to make 50 ppm (1 ppm = 1 mg/L) to 200 ppm concentrations depending on use which is chosen by pressing a button on the instrument. The electrolyzed solution is completed in 8 minutes, when it is ready for use.

The parameters that contribute to HOCl's disinfectant's efficacy include contact time and concentration ([32, 33, 34]). The method of application will also affect its efficacy to disinfect.

Stability of solution: Rossi-Fedele et al investigated the shelf-life of hypochlorous acid by being either exposed to or protected from sunlight. When the HOCl solution is exposed to sunlight, chlorine reduction starts at day 4. When sheltered from sunlight, the chlorine reduction started after day 14 ([35]). The half-life increases with decreasing pH due to the decreasing ratio of OCl^-/HOCl ([36]). The parts per million (ppm) is the concentration of the –OCl which is the active ingredient and is also known as the available free chlorine (AFC) in the solution. HOCl solutions are less stable when exposed to UV radiation, sunlight, contact with air, or when the temperature of the solution was elevated greater than 25 degrees centigrade (C). HOCL solutions should be stored in cool, dark places, and contact with air should be minimized. The water for fabrication should be water that contains as small as concentration as possible of organic and inorganic ions ([37, 38, 39, 40]).

Concentration related to time needed for virucidal action: HOCl has been shown to inactivate a variety of viruses including coronaviruses in less than one minute ([39]). At a concentration of 200 ppm, HOCl is effective to decontaminate inert surfaces carrying noroviruses and other enteric viruses in a 1-minute contact time. When diluted 10-fold, HOCl solutions at 20 ppm were still effective in decontaminating environmental surfaces carrying viruses in a 10-minute contact time ([40]).

Recommendations for office use

The importance of aerosol size to disinfection and application: Those working in the dental and medical field using surgical and high-speed handpieces are at risk from aerosolization. Aerosols are defined as particles less than 50 micrometers in diameter. Particles of this size are small enough to stay airborne for an extended period before they settle on environmental surfaces or enter the respiratory tract ([41, 42]). Additionally, a true aerosol or droplet nuclei may be present in the air of the operatory for up to 30 minutes after a procedure ([41]).

Particles are classified based on size: coarse particles are 2.5–10 microns, fine particles are less than 2.5 microns, and ultrafine particles are less than 0.1 micron. The nose typically filters air particles above 10 microns. If a particle is less than 10 microns, it can enter the respiratory system. If it is less than 2.5 microns, it can enter the alveoli. A particle less than 0.1 micron, or an ultrafine particle like the COVID-19 virus, can enter the bloodstream or target the lungs.

Sotiriou et al. demonstrated that the amounts of small particles (<0.5 μm) generated during dental drilling procedures were much higher than the amounts of larger particles (>1 μm) ([42]). Ultrasonic and sonic transmission during nonsurgical procedures had the highest incidence of particle transmission, followed by air polishing, air/water syringe, and high-speed handpiece aerosolization ([43]). One study found that ultrasonic instrumentation can transmit 100,000 microbes per cubic foot with aerosolization of up to six feet, and, if improper air current is present, microbes can last anywhere from 35 minutes to 17 hours ([44]).

Mouthrinse: If used as a mouth rinse, one must assume that a portion of the rinse will be swallowed. The systemic and gastrointestinal effects of ingesting HOCl, from the perspective of its use in mouthwash, was evaluated in an animal study ([45]). Seventeen mice were used given free access to HOCl water as drinking water. No abnormal findings were observed in terms of visual inspections of the oral cavity, histopathological tests, or measurements of surface enamel roughness showing no systemic effect.

Other Clinical applications:

***Ophthalmology*:** HOCl is used in the treatment of blepharitis by reducing the bacterial load on the surface of the periocular skin. Twenty minutes after application of a saline hygiene solution containing 100 ppm HOCl, a >99% reduction in the staphylococcal load was achieved ([46]).

Biofilms: HOCl may be effective for cleaning biofilm-contaminated implant surfaces. HOCl significantly lowered the lipopolysaccharide concentration of *P. gingivalis* when compared with NaOCl and chlorhexidine, and was well tolerated by the oral tissues ([47]). HOCl significantly reduced bacteria on toothbrushes. It was effective as a mouthwash and for toothbrush disinfection ([48]).

***Wound care*:** In a clinical study on intraperitoneal wound care, patients had their peritoneal cavity lavaged with 100 ppm HOCl and their wound washed with 200 mL ppm. No adverse effects were observed ([49]).

Hypochlorous acid has been shown to be an effective agent in reducing wound bacterial counts in open wounds ([50]). In the irrigation solution in the ultrasonic system, HOCl lowered the bacterial counts by 4 to 6 logs. By the time of definitive closure, the saline-irrigated control wounds had bacterial counts back up to 10^5 whereas the HOCl irrigated wounds remained at 10^2 or fewer. More than 80% of patients in the saline group had postoperative closure failure compared with 25% of patients in the HOCl group.

***Hand sanitizing*:** Hand antiseptics are alcohol-based or are non-alcohol based containing antibiotic compounds ([51]). Chlorine-based sanitizers, at a concentration of 50–100 ppm, are effective against bacteria and viruses ([52]). HOCl specifically used for hand sanitizers are effective with 100-200 pm strengths ([53, 54]).

Surface application: A study looked at disinfecting outpatient surgical centers using HOCl. After cleaning, the HOCl cleaning and disinfecting study arm had significantly lower bacterial counts compared to the standard cleaning and disinfecting rooms ([55]).

HOCl Applied by a spray or fogger

A fogger takes a solution and creates a small aerosol mist ideally less than 20 microns in size, to disinfect an area. HOCl fogs are highly effective in the microbial disinfection of surfaces. The fogging processing can alter the physical and chemical properties of the disinfectant. It was found that fogging reduced the available free chlorine (AFC) concentration by approximately 70% and increased the pH by approximately 1.3 making the solution slightly more basic. It is speculated that the loss of chlorine resulted from evaporation of chlorine gas ([56, 57]). Because the changes in the properties of hypochlorous fogs are predictable, pre-adjustment of the concentration and pH of the solution prior to fogging makes can control the concentration levels to the desirable range to inactivate pathogens after fogging ([40]). When used in the appropriate concentrations, a study found a 3 $\log_{10}$ reductions to 5 $\log_{10}$ reductions in both the infectivity and RNA titers of all tested viruses on both vertical and horizontal surfaces, suggesting that it is an effective approach to reduce viruses on surfaces ([40, 58]).

HOCl solutions appear to be virucidal based on concentrations above 50 ppm. HOCl was evaluated against a low pathogenic avian influenza virus (AIV), H7N1. HOCl solutions contained 50, 100 and 200 ppm chlorine at pH 6. Spraying with HOCl decreased the AIV titer to an undetectable level (< 2.5 $\log10TCID_{50}$/mL) within 5 sec, with the exception of the 50 ppm solution harvested after spraying at the distance of 30 cm. When HOCl solutions were sprayed directly on sheets containing the virus for 10 sec, the solutions of 100 and 200 ppm inactivated AIV immediately. The 50 ppm solution required at least 3 min of contact time. These data suggest that HOCl can be used in spray form to inactivate AIV ([59, 60]). When the aerosol was not sprayed directly onto an inoculated surface, a lower amount of solution had a chance to come in contact with the AIV. It required at least 10 min of contact to be effective ([61]).

The ability of a sprayer to make smaller particles may help solution's molecules to be suspended in the air for a longer period of time because of their low settling velocity rate. This may increase its chance to come in contact with pathogens and inactivate them. Thus, the fogger used should have an aerosol size less than 20 microns ([62]).

Discussion

The Coronavirus Pandemic has caused both a massive healthcare and economic disruption all across the world. The current unavailability of an effective antiviral drug or approved vaccine means that the implementation of effective preventive measures are necessary to counteract CoVID-19. Oral-maxillofacial surgeons are high risk providers providing needed care to patients. As more OMS and surgical offices open during reopening in the United States and elsewhere in the world, the need to reduce risk of transmission of CoVID-19 between patients and providers is necessary. It is widely believed that with proper screening and discretion, along with adequate personal protective equipment (PPE), there is a low probability of becoming infected. The goal of this paper is to provide information regarding disinfection in the clinical office setting using hypochlorous acid, a relatively inexpensive, non-toxic, non-corrosive, and well-studied compound.

HOCl has uses in many industries from farming and restaurants regarding food, to healthcare applications including chronic wound care and disinfection ([34, 36, 43, 45, 46, 63]). In addition to being used as a liquid based disinfectant, fogging with hypochlorous vapor has shown viricidal activity to numerous types of viruses and bacteria ([40, 56, 57]). This is of potential benefit to disinfect large spaces such as medical and dental offices where aerosols can be airborne for extended periods of time ([42, 44, 64]). Oral-maxillofacial surgeons may be at a slightly lower risk to their dental counterparts in terms of particle size as ultrasonic scaling and high speed handpieces create smaller particles that remain airborne longer ([42]). However, aerosols are still created with surgical handpieces. Additionally, the CoVID-19 virus can be present upon some surfaces for days and the disinfection of all surfaces of an operatory is important to reduced transmission ([9, 10]).

Many properties of HCOl contribute to why it may be the disinfectant of choice in the OMS setting. While the shelf-life of HOCl is relatively short, it is effective for up to 2 weeks under ideal conditions ([35]). It can be made on site inexpensively. A gallon of hypochlorous acid can be purchased from manufacturers but it is far more economical for an oral-maxillofacial surgeon to produce the solution on site in the office ([65]). A variety of HOCl systems on the market are available costing less than $275 ([66]). By combining non iodinated salt, water, and electricity ([33]) a liter of HOCl can be made in 8 minutes and the process repeated many times throughout the day. By comparison a pack of common disinfecting wipes containing quaternary ammonium compounds containing 80 sheets cost between $4 and $15 for a pack. These wipes may only last a day or two depending the size of the office and area to clean. Shortages of these products can occur making sourcing them difficult as well ([67]).

In addition to using HOCl as wipes for disinfecting, using HOCl vapors through a fogging machine is an economical way to disinfect a large operating room or suite where aerosols were produced during surgery. Fogger or misting machines are handheld machines and can be purchased for a reasonable cost ([68]). The aerosol mists should be ideally less than 20 microns in size to maximally disinfect an area. It is important to note that fog processing can alter the physical and chemical properties of the disinfectant making it more dilute and basic. As mentioned before, the available free chlorine (AFC) concentration can be reduced by approximately 70% and the pH can increase by about 1.3 ([40]). To make a vapor as effective as a solution containing 100 ppm of HOCl, the solution would need to be concentrated. The fine mist can be left in the empty surgical room without thought regarding harmful chemical affects and then surfaces wipes clean and dry after a few minutes and ten minutes for a more dilute solution.

Hypochlorous acid is one disinfectant which combined with adequate PPE, screening/social distancing techniques, handwashing and high-volume evacuation suction that may help reduce the transmission of CoVID-19 in the outpatient OMFS surgical setting. It comprises many of the desired effects of the ideal disinfectant: it is easy to use, inexpensive, has a good safety profile, can be used to disinfect large areas quickly and with a broad range of bactericidal and viricidal effects.

Footnotes

Disclosures: Dr. Block owns stocks with X-Nav, Inc. Dr. Rowan has no financial conflicts.

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