DENTOALVEOLAR SURGERY

Hypochlorous Acid: A Review

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The surgeon needs to have an inexpensive, available, nontoxic, and practical disinfectant that is effective in sanitizing against the COVID-19 (Coronavirus Disease 2019) virus. The purpose of this article was to review the evidence for using hypochlorous acid in the office setting on a daily basis. The method used to assemble recommendations was a review of the literature including evidence for this solution when used in different locations and industries other than the oral-maxillofacial clinic facility. The results indicate that this material can be used with a high predictability for disinfecting against the COVID-19 (Coronavirus Disease 2019) virus.

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COVID-19 (Coronavirus Disease 2019) Virus Structure and Mechanism of Infection

Coronavirus Disease 2019 (COVID-19) is a novel virus. It causes severe acute respiratory syndrome. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the agent responsible for a surface-to-surface communicable disease that had infected approximately 4.7 million persons as of May 17, 2020.[1] Health care providers need options to limit and control the spread of the virus between themselves 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 the angiotensin converting enzyme 2 (ACE2) receptor, which allows entry into the host cell.[2-4] COVID-19 infection creates a cytokine storm, severe pneumonia, multiple-organ failure, and acute cardiac injury.[5,6]

Transmission occurs through touch or aerosol spreading of the virus. A common pathway of spreading this virus is through respiratory aerosols from an infected person.[7] During speech, humans emit thousands of oral fluid droplets per second that can remain airborne for 8 to 14 minutes.[8] COVID-19 is detectable for up to 3 hours in surface aerosols, for up to 4 hours on copper, for up to 24 hours on cardboard, and for up to 2 to 3 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

On contact with the virus, a disinfectant agent changes the protective protein coat, which loses its structure and aggregates, forming clumps of proteins with other viruses.[9,10] Currently, the US Environmental Protection Agency has recommended numerous disinfectants against COVID-19 including hypochlorous acid (HOCl).[11] The mechanism of disinfection involves the destroying of the cell wall of microbes or viruses, allowing the disinfectant to destroy or inactivate them.[12-27] This article focuses on HOCl.

Hypochlorous Acid

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

HOCl is an endogenous substance in all mammals and is effective against a broad range of microorganisms. Neutrophils, eosinophils, mononuclear phagocytes, and B lymphocytes produce HOCl in response

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to injury and infection through the mitochondrial membrane–bound enzyme known as "respiratory burst nicotinamide adenine dinucleotide phosphate 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 that has maximal antimicrobial properties.[29,30]

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 1-L container that is filled with water, to which 1 g of non-iodized salt and 1 teaspoon of vinegar are added. The system has the ability to make concentrations of 50 to 200 ppm (in which 1 ppm is equal to 1 mg/L) depending on its 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 efficacy as a disinfectant include contact time and concentration.[32-34] The method of application also will affect its efficacy to disinfect.

STABILITY OF SOLUTION

Rossi-Fedele et al[35] investigated the shelf life of HOCl by being either exposed to or protected from sunlight. When the HOCl solution was exposed to sunlight, the chlorine reduction started on day 4. When it was sheltered from sunlight, the chlorine reduction started after day 14. The half-life increases with decreasing pH owing to the decreasing ratio of OCl^- to HOCl.[36] The parts per million (ppm) is the concentration of the –OCl, which is the active ingredient and is known as the available free chlorine (AFC) in the solution. HOCl solutions are less stable when exposed to UV radiation, sunlight, or contact with air or when the temperature of the solution is elevated greater than 25°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 organic and inorganic ion concentrations that are as small as possible.[37-40]

CONCENTRATION RELATED TO TIME NEEDED FOR VIRUCIDAL ACTION

At a concentration of 200 ppm, HOCl is effective in decontaminating 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

IMPORTANCE OF AEROSOL SIZE TO DISINFECTION AND APPLICATION

Individuals 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 μm 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 measure 2.5 to 10 μm; fine particles, 0.1 μm to less than 2.5 μm; and ultrafine particles, less than 0.1 μm. The nose typically filters air particles larger than 10 μm. If a particle is smaller than 10 μm, it can enter the respiratory system. If smaller than 2.5 μm, it can enter the alveoli. A particle smaller than 0.1 μm, or an ultrafine particle, such as the COVID-19 virus, can enter the bloodstream or target the lungs.

Sotiriou et al[42] showed that the concentrations of small particles (<0.5 μm) generated during dental drilling procedures were much higher than the concentrations of larger particles (>1 μm). 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/ft^3 with aerosolization of up to 6 ft and, if improper air current is present, microbes can last anywhere from 35 minutes to 17 hours.[44]

MOUTH RINSE

If HOCl is 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 given free access to HOCl water as drinking water. No abnormal findings were observed in terms of visual inspections of the oral cavity, histopathologic tests, or

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 HOCl at 100 ppm, a greater than 99% reduction in the staphylococcal load was achieved.[46]

Biofilm

HOCl may be effective for cleaning biofilm-contaminated implant surfaces. HOCl significantly lowered the lipopolysaccharide concentration of *Porphyromonas gingivalis* when compared with sodium hypochlorite 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 underwent lavage of the peritoneal cavity with 100-ppm HOCl and washing of the wound with 200 ppm.[49] No adverse effects were observed.

HOCl has been shown to be an effective agent in reducing wound bacterial counts in open wounds.[50] In irrigation solution in an ultrasonic system, HOCl lowered the bacterial counts by 4 to 6 logs. By the time of definitive closure, the bacterial counts were back up to 10^5 for the saline solution–irrigated control wounds but remained at 10^2 or lower for the HOCl-irrigated wounds. Postoperative closure failure occurred in more than 80% of patients in the saline solution group versus 25% of those in the HOCl group.

Hand Sanitizing

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

Surface Application

A study looked at disinfecting outpatient surgical centers using HOCl.[55] After cleaning, the rooms in the HOCl cleaning and disinfection study arm had significantly lower bacterial counts than the rooms that underwent standard cleaning and disinfection.

HOCl Applied by Spray or Fogger

A fogger takes a solution and creates a small aerosol area. HOCl fogs are highly effective in the microbial disinfection of surfaces. The fogging process can alter the physical and chemical properties of the disinfectant. It was found that fogging reduced the 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-fogging adjustment of the concentration and pH of the solution makes it possible to control the concentration levels to the desirable range to inactivate pathogens after fogging.[40] When the appropriate concentrations are used, a study found 3 to 5 $\log_{10}$ reductions in both the infectivity and RNA titers of all tested viruses on both vertical and horizontal surfaces, suggesting that fogging 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.[59] The 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 $\log_{10}TCID_{50}$/mL) within 5 seconds, with the exception of the 50-ppm solution harvested after spraying at a distance of 30 cm. When HOCl solutions were sprayed directly onto sheets containing the virus for 10 seconds, the solutions of 100 and 200 ppm inactivated AIV immediately. The 50-ppm solution required at least 3 minutes 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 into contact with the AIV. It required at least 10 minutes of contact to be effective.[61]

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

Discussion

The coronavirus pandemic has caused both a massive health care and economic disruption across the world. The current unavailability of an effective antiviral drug or approved vaccine means that the implementation of effective preventive measures is necessary to counteract COVID-19. Oral-maxillofacial surgeons are high-risk providers providing needed

open during reopening in the United States and elsewhere in the world, the need to reduce the 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, there is a low probability of becoming infected. The goal of this article is to provide information regarding disinfection in the clinical office setting using HOCl, a relatively inexpensive, nontoxic, noncorrosive, and well-studied compound.

HOCl has uses in many industries from farming and restaurants, regarding food, to health care applications, including chronic wound care and disinfection.[34,36,43,45,46,63] In addition to the use of HOCl as a liquid-based disinfectant, fogging with hypochlorous vapor has shown virucidal activity against 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.[42,44,64] In terms of particle size, oral-maxillofacial surgeons may be at a slightly lower risk than their dental counterparts because 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 on some surfaces for days, and the disinfection of all surfaces of an operatory is important to reduce transmission.[9,10]

Many properties of HOCl contribute to why it may be the disinfectant of choice in the OMS setting. Although 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 HOCl 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 costing less than $275 are available on the market.[66] By combining non-iodinated salt, water, and electricity,[33] 1 L of HOCl can be made in 8 minutes and the process can be repeated many times throughout the day. By comparison, a pack of common disinfecting wipes containing quaternary ammonium compounds costs between $4 and $15 for a pack containing 80 sheets. 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 in the form of wipes for disinfecting, using HOCl vapors through a fogging machine is an economical way to disinfect a large operating room or suite in which aerosols were produced during surgery. Foggers or misting machines are handheld machines and can be purchased for a reasonable

important to note that the fogging process can alter the physical and chemical properties of the disinfectant, making it more dilute and basic. As mentioned before, the 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 effects; the surfaces are then wiped clean and dry after a few minutes and, for a more dilute solution, after 10 minutes.

HOCl is one disinfectant that, when combined with adequate personal protective equipment, screening and social-distancing techniques, hand washing, and high-volume evacuation suction, may help reduce the transmission of COVID-19 in the outpatient OMS setting. It comprises many of the desired effects of the ideal disinfectant: It is easy to use, is inexpensive, has a good safety profile, and can be used to disinfect large areas quickly and with a broad range of bactericidal and virucidal effects.

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