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REVIEW

Classical and alternative disinfection strategies to control the COVID-19 virus in healthcare facilities: a review

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Abstract
The coronavirus disease COVID-19 has spread throughout the world and has been declared as a pandemic by the World Health Organization on March 11th, 2020. The COVID-19 is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). One possible mode of virus transmission is through surfaces in the healthcare settings. This paper reviews currently used disinfection strategies to control SARS-CoV-2 at the healthcare facilities. Chemical disinfectants include hypochlorite, peroxymonosulfate, alcohols, quaternary ammonium compounds, and hydrogen peroxide. Advanced strategies include no-touch techniques such as engineered antimicrobial surfaces and automated room disinfection systems using hydrogen peroxide vapor or ultraviolet light.

Keywords COVID-19 · Chemical disinfectants · Virus inactivation · Ultraviolet light irradiation · Reactive oxygen species

Introduction

Healthcare-associated infections, also named hospital-acquired or nosocomial infections, are causing burden to the society by prolonging the stay in hospitals, which further increases the cost of healthcare (Ham et al. 2020; Nguemeleu et al. 2020). These infections are newly acquired infections by multidrug-resistant pathogens contracted within a healthcare environment. Rising pathogen resistance is explained by indiscriminate use of antibiotics and the lack of hygiene measures. In the USA, the number of hospitalized patients may reach 2 million per year soon. Contaminated healthcare surfaces and medical instruments are usually the main sources of pathogen transmission (Ogunsola and Mehtar 2020). Days to months survival on dry inert surfaces has been observed for bacteria, such as vancomycin-resistant *Enterococci*, *Pseudomonas spp.*, and methicillin-resistant *Staphylococcus aureus*; viruses such as hepatitis C virus, rotavirus, and norovirus, and spores such as *Clostridioides difficile* (Kramer et al. 2006).

Known pathways of virus transmission include direct contact, e.g., by hand shaking, with an infected individual, aerosol transmission involving air transmission of droplets from an infected person to healthy individuals, and surface transmission by touching contaminated surfaces (Fig. 1a; Bhattacharya et al. 2020; Garcia de Abajo et al. 2020; Rico et al. 2020). Viruses can be transmitted from an infected individual to a healthy person during speaking, sneezing, and coughing. Transmission of COVID-19 by food and particles emitted by laser printers are also likely (Han et al. 2020; He and Han 2020). Figure 1b–g presents the most common situations during which transmission may occur via airborne or surface-mediated processes. The magnitude of virus transmission is controlled by environmental factors such as indoor or outdoor, ventilation, humidity, wind, temperature, density of population, and infectiousness of

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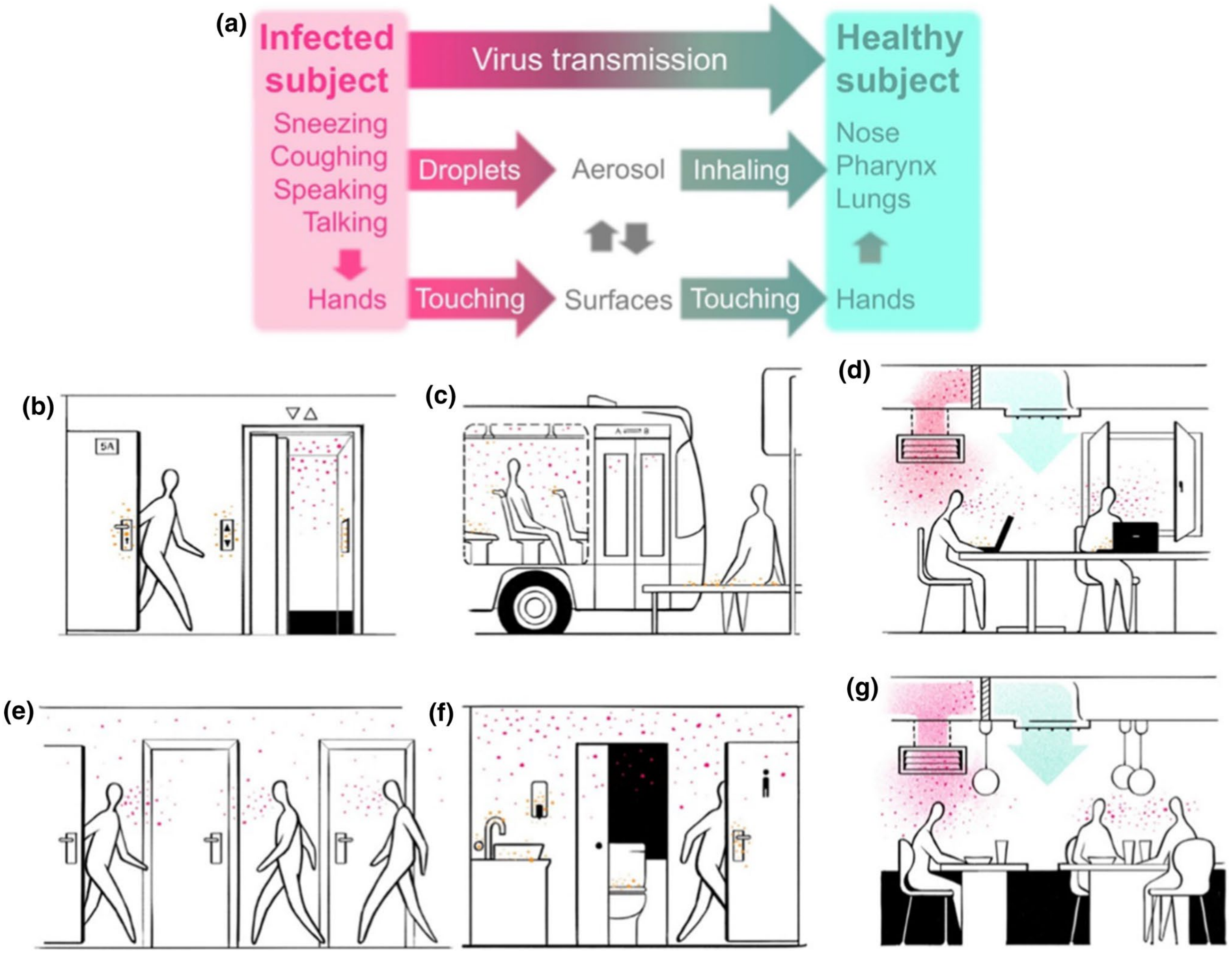

Fig. 1 Pathways of viral infection in everyday life. **a** Direct, aerosol, and surfaces act as pathways for virus transmission. Exposure to virus in everyday activities when **b** using elevators, **c** taking public transportation, **d** spending time in shared indoor spaces such as workplaces, schools, and centers for other social activities, **e** walking through corridors, **f** using common facilities such as toilets, office pantries, and storerooms, and **g** dining at restaurants or accessing other public services with high customer turnover. Colored items indicate airborne viruses (red dots), surface-deposited viruses (orange dots), contaminated-air flow (reddish arrows), and fresh/cleaned-air flow (blueish arrows). Reprinted from Garcia de Abajo et al. (2020) with permission from the American Chemical Society

the infected person (Lacotte et al. 2020; Paital et al. 2020; Sharma et al. 2020).

The coronavirus disease (COVID-19) has spread throughout the world and was declared as a pandemic by the World Health Organization on March 11th, 2020. This pandemic is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which originated in 2019 from Wuhan, China. This novel coronavirus pandemic has turned out to be one of the biggest threats of the century to the human well-being. Epidemiological studies have shown that human–human transmission through droplets is the main route of transmission of SARS-CoV-2 (Liu et al. 2020b). This highly contagious respiratory virus is causing huge burden to global public health, and there is a heightened risk of infection to healthcare workers within healthcare settings. One other possible route of transmission includes close contact of healthcare workers to the SARS-CoV-2-contaminated surfaces in the healthcare environment. Both porous surfaces, e.g., curtains, and nonporous surfaces, e.g., bed rails, nurses' stations, computers, sinks, and toilet seats, can be contaminated in healthcare facilities. Additionally, non-healthcare facilities may also serve as a potential source for transmission (Saravanan et al. 2020; Sun and Han 2020). Disinfection of healthcare surfaces is very important to prevent transmission of SARS-CoV-2 to healthcare workers and to other patients that occupy the facility (Totaro et al. 2020). Several approaches can be used for disinfection including chemical disinfectants, no-touch automated processes, enhanced coatings, and surfaces with antimicrobial properties.

Chemical disinfectants often used in the healthcare facilities include sodium hypochlorite, potassium peroxymonosulfate, alcohols, quaternary ammonium compounds, and hydrogen peroxide (De Lorenzi et al. 2020; Juszkiewicz et al. 2019; Khokhar et al. 2020). In the current paper, we review the basic science involved in chemical and alternative disinfection strategies, followed by examples of their applications to prevent transmission of SARS-CoV-2.

Chemical disinfectants

Chlorine has been applied as a disinfectant for several decades (Deborde and von Gunten 2008, Silverman and Boehm 2020). Chlorine in aqueous solution exists in hypochlorite (HOCl) and its anionic form (OCl^-), which are in equilibrium (Carrell Morris 1966):

$$HOCl \rightleftharpoons H^+ + OCl^-; pK_a = 7.6$$

The disinfection with hypochlorite depends on the speciation, which is a function of pH (Fig. 2). HOCl and OCl^- are both present in the pH range of 6.0–9.0. Hypochlorite species exists predominately below pH 7.5, while OCl^- is the major species above pH 7.5. Chlorine has high reactivity with amino acids and proteins (Sharma 2013) and has a strong capability to inactivate virus (Khokhar et al. 2020). The standard redox potential E^o of hypochorite is + 1.48 V in acidic media and + 0.84 V in basic media. Therefore, HOCl is much more effective to inactivate virus than OCl^- species. This suggests that hypochlorite disinfection is more effective at neutral pH than at alkaline solution.

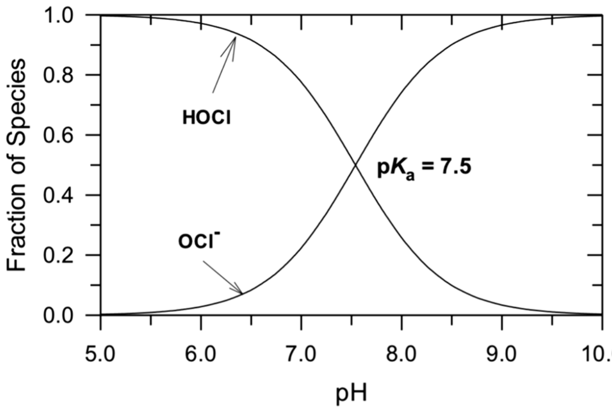

Fig. 2 Speciation of hypochlorite as a function of pH. This figure shows that hypochlorite is mainly present as HOCl below pH 6.0, as about half HOCl half OCl^- at pH 7.5, and as OCl^- above pH 9.0

Peroxymonosulfate has been used as a disinfectant because it generates reactive radicals. Peroxymonosulfate generates sulfate and hydroxyl radicals as the main reactive species (Lee et al. 2020). Sulfate radical $SO_4^{\bullet -}$ has redox potentials in the range of + 2.60 to + 3.1 V, while the redox potential of the hydroxyl radical $^{\bullet}OH$ is in the range of + 1.90 to + 2.70 V (Lee et al. 2020; Oh et al. 2016; Waclawek et al. 2017). Therefore, there is high capability of peroxymonosulfate to inactivate viruses (Delcomyn et al. 2006; Wallace et al. 2005). Examples include effectiveness of potassium peroxymonosulfate against African swine virus fvirus (ASF) (Juszkiewicz et al. 2019, 2020). Alcohols such as ethanol, 1-propanol, and 2-propanol have been applied to disinfect inert surfaces (Khokhar et al. 2020). Indeed, alcohols induce proteins denaturation, lipids solubilization, and membrane disruption (Boyce 2018; McDonnell and Russell 2001). Researchers have varied types and levels of alcohols to enhance the effectiveness of disinfection (Edmiston et al. 2020). Alcohols are flammable, and therefore, precautions should be maintained in their uses.

Compounds of quaternary ammonium are in use for surface disinfection (Diaz et al. 2019; Hora et al. 2020; Liu et al. 2020a; Schmidt et al. 2019). Examples include alkyl benzalkonium chlorides. These compounds are currently present in more than 200 disinfectants approved by the United States Environmental Protection Agency (US EPA). The disinfection by quaternary ammonium compounds involves cytoplasmic membrane adsorption and the leakage of cellular constituents (Edmiston et al. 2020). The use of hydrogen peroxide H_2O_2 as antiseptic has been known for more than a century (Haering et al. 2020; Khokhar et al. 2020; Totaro et al. 2020). H_2O_2 produces $^{\bullet}OH$ radicals under UV light irradiation and in combination with metal ions, e.g., Fe^{2+} and Cu^+; then, radicals cause disinfection (Nieto-Juarez and Kohn 2020; Ueno et al. 2020). The generated $^{\bullet}OH$ radicals react highly with proteins, lipids and nucleic acids to result in cleavage of RNA and DNA and destruction of sulfhydryl bonds in proteins and biological membranes (Arjunan et al. 2015; Lam et al. 2020).

Classical strategies of disinfection

Typically, pre-cleaning of both organic and non-organic debris precedes disinfection events. Chemical disinfectants are effective to break the outer lipid layer of corona viruses. Due to acute shortage of commercial disinfectants during the early stages of the pandemic, alternate disinfectants such as 70% alcohol or 1/3 cup of 5.25–8.25% hypochlorite added to 1.0 gallon of water was recommended by the Center for Disease Control and Prevention, USA. The current guidelines for disinfection include a potassium peroxymonosulfate and sodium hypochlorite solution, listed in the US

EPA-approved chemical solvents. Potassium peroxymonosulfate and sodium hypochlorite are suitable for hard nonporous surfaces as recommended in the list of disinfectants for use against SARS-CoV-2 (List N, US EPA). Indeed, *Canine parvovirus* and *Adenovirus type 5* pathogens, which are harder to inactivate than SARS-CoV-2, could be killed by potassium peroxymonosulfate and sodium hypochloritie. Ethanol solution and dilute sodium hypochlorite disinfectant, sprayed electrostatically, have also been shown to be an effective form of disinfection and could be useful for portable equipment or large open spaces (Cadnum et al. 2020, US. Environmental Protection Agency List N: Disinfectants for Use Against SARS-CoV-2 (COVID-19)). Another commercial product containing liquid hydrogen peroxide with surfactants, (ACCEL TB, Unimed Corp), is effective at a concentration of 0.5% against HCoV-229E within a minute (Omidbakhsh and Sattar 2006). More studies are needed for hydrogen peroxide use on various other surfaces and conditions. List N on the EPA's website provides information on various disinfectants that are effective against SARS-CoV-2.

During the 2003 SARS-CoV-1 epidemic, studies have shown that four different types of quaternary ammonium-based surface disinfectants, i.e., benzalkonium chloride and laurylamine, benzalkonium chloride, glutaraldehyde and didecyldimonium chloride, magnesium monoperphthalate, and glutaraldehyde and ethylenedioxydimethanol had high effectiveness to destroy the virus after 30 min of contact time (Rabenau et al. 2005). Additionally, the biocidal agent ethanol was shown to effectively inactivate SARS-CoV-1 and MERS-CoV with an 80% solution after only 30 s (Kampf et al. 2020). More specifically, a disinfecting wipes containing quaternary ammonium solution have also been found to effective against SARS-CoV-2 (US. Environmental Protection Agency List N: Disinfectants for Use Against SARS-CoV-2 (COVID-19)).

No-touch strategies

Disinfection efficiency is limited by the fact that cleaning is done episodically in healthcare facilities. This limitation can be overcome by use of "no-touch" (automated) disinfection approaches such as hydrogen peroxide vapor and ultraviolet light (UV). Hydrogen peroxide vapor has been widely used for disinfecting coronaviruses (Carlos Rubio-Romero et al. 2020). Virucidal efficacy of hydrogen peroxide vapor has been demonstrated against SARS-CoV-2 surrogates such as feline calicivirus, human adenovirus type 1, transmissible gastroenteritis coronavirus of pigs, avian influenza virus, and swine influenza virus. This vapor was virucidal with more than 4 log reduction for structurally distinct viruses dried on surfaces, suggesting that the vapor can be considered for the disinfection of contaminated surfaces (Goyal et al. 2014).

UV disinfection devices contain either a mercury-based source or pulsed-xenon bulb source to generate UV rays. Inhibition of the Middle East respiratory syndrome coronavirus (MERS-CoV) was done by 5 min application of UV-C from an automated whole-room (Bedell et al. 2016). Far UV-C light at 207-222 nm induced 99.9% inactivation of the airborne βHCoV-OC43 strain in 25 min, and presumably would have a similar effect on the SARS-CoV-2 (Buonanno et al. 2020). Studies conducted with UV-C indicate that a dose ranging from 3.7 mJ/cm^2 to 10.6 mJ/cm^2 should inactivate the viruses in 5 min. Recently, a pulsed-xenon-based UV device demonstrated 4.2 $\log_{10}$ reduction on hard surfaces and 4.79 $\log_{10}$ and reduction on N95 respirators following 5 min of exposure (Simmons et al. 2020).

UV-A has been shown to have a weaker effect even after 15 min of exposure, suggesting that UV-C is more potent (Heilingloh et al. 2020). Additionally, simulated sunlight appeared to decrease the recovery of SARS-CoV-2 on nonporous surfaces after 20 min of exposure to 1.6 W/m^2 ultraviolet-B (UV-B) (Ratnesar-Shumate et al. 2020). Moreover, a recent study demonstrates the feasibility of passive heating of vehicles in parking lots under the sun to inhibit the virus because indoor car temperatures reach 52–57 °C in 90 min (Wang et al. 2020a): this is probably the most sustainable method because it requires no chemicals, no energy production, no human intervention, and it can be done when vehicles are not in use during parking time. These alternative methods could be used during commercial shortages of UV devices due to COVID-19.

UV application on aerosols using an AGI-30 liquid impinger showed that coronaviruses were more impacted than the bacteriophage MS2 virus and adenovirus (Walker and Ko 2007). UV germicidal devices also allow to decontaminate personal protective equipment, airport security bins and mobile phones. Viral survivability depends on many factors such as wavelength, dose, distance and duration of UV radiation, which should be studied and tuned prior to use in healthcare and other non-healthcare settings (Hessling et al. 2020). The combination of hydrogen peroxide and ultraviolet light that generates reactive hydroxyl radicals can be used to disinfect surfaces (Donskey 2019; Wallace et al. 2019). The lamps include mercury bulbs emitting continuous radiation (UV-C) and xenon gas bulbs. The mercury bulbs emit radiation in the wavelength of 200–270 nm, while xenon gas bulbs emit radiation with short high-intensity pulses consisting of both ultraviolet light in the range of 100–280 nm and visible spectra at 380–700 nm.

Antimicrobial surfaces

Using materials or coatings with antimicrobial properties is another approach to controlling the infection. Copper and copper-based alloys are known to possess antimicrobial properties. A rapid inactivation of coronaviruses has been observed for copper and brass alloys; this inactivation was proportional to the content of copper or brass in the material (Warnes et al. 2015). A combination of cuprous oxide and polyurethane coating that can adhere to both glass and stainless steel, is durable and can survive multiple cycles of disinfection even when immersed in water. Interestingly, doorknobs, credit card holders, and pens can be coated with cuprous oxide and polyurethane. Both glass and stainless steel coated with cuprous oxide and polyurethane were found to inactivate SARS-CoV-2 up to 99.9% (Behzadinasab et al. 2020). Viral inactivation of surfaces was also tested using single-wall carbon nanotubes (SWCNTs) decorated with Pt, Pd, Ni, Cu, Rh, and Ru for adsorption of hydrogen peroxide. Here, Pt and Cu displayed a longlasting shelf life (Aasi et al. 2020).

The Centers for Disease Control and Prevention has recommended high-touch surfaces be cleaned and disinfected repeatedly to continually prevent the spread of SARS-CoV-2. Many hospitals implement policies for more rigorous cleaning and disinfecting, especially on high-touch surfaces to prevent the transmission of virus (Kornack et al. 2020; Shabto et al. 2020; Wang et al. 2020a, b). Portable medical equipment like computer on wheels or pumps can also be considered as high-touch surfaces (Jinadatha et al. 2017). Apart from daily cleaning and disinfection strategies, no-touch technologies can be supplemented to achieve higher disinfection capabilities.

Conclusion

Generally, chemical disinfectants are widely used in hospitals, but thorough manual cleaning of surfaces may not be adequate to fully control pathogens or transmission of the virus. Increased cleaning and disinfection of healthcare surfaces is essential for effective prevention and control of SARS-CoV-2 infection. Results suggest that chemical disinfectants are efficient at reducing if not eliminating SARS-CoV-2 from the surfaces. In the future, the state-of-the art technologies involving no-touch approaches may be developed to fully disinfect the contaminated surfaces. The application of UV light as stand alone or in combination with oxidants would increase the chance of thorough surface disinfection. The use of innovative advanced materials such as nanomaterials are forthcoming, which may be applied with conventional disinfectants and UV light irradiation to enhance the efficiency with shorter contact time to fully disinfect the surfaces in the healthcare settings.

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