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A REVIEW ON THE EFFICACY OF MOUTHWASHES IN THE WAKE OF COVID-19

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ABSTRACT

In late 2019 a novel coronavirus, SARS-CoV-2 arose causing Coronavirus disease (COVID-19) with its epicenter in Wuhan China. In early experiments pertaining to the SARS-CoV-2 infection, viral titres borne in the saliva and nasal mucosa of infected individuals were greater than 10^7/ml. Reduction in the cross infections require the minimisation of these titres in two of the key areas from where droplets and aerosols containing the virus are expectorated, the first being the saliva and the second; the lower respiratory tract. It is therefore imperative to kill viruses entering the upper aerodigestive tract before it infects the host. Povidone-iodine (PVP-I) disinfectant has superior anti-viral activity in comparison to other antiseptics, proven in vitro to be an extremely effective virucide against severe acute respiratory syndrome and Middle East respiratory syndrome coronaviruses (SARS-CoV and MERS-CoV). Oxidising mouthwashes and Hydrogen peroxide weaken the infectivity of bacterial cells. Ongoing studies have hypothesized their efficacy against the viral load in the oral cavity. Chlorhexidine gluconate has always been the de-facto mouthwash in private dental practices. In, in-vitro studies Chlorhexidine was as efficacious as 70% ethanol though longitudinal studies are required to claim these hypotheses. The aim of this brief review is to highlight the efficacy of the commercially available mouthwashes and to ascertain their importance in minimizing the viral load in the oropharynx which would ensure a first step at personal hygiene maintainence and restrict droplet transmission.

KEYWORDS: Oxidising mouthwashes and Hydrogen peroxide weaken the infectivity of bacterial cells.

INTRODUCTION

SARS was first reported as a respiratory illness in Gangdong, China in November 2002. The epidemic expanded rapidly and was controlled during the summer of 2003. In March 2003, a distinct corona virus was identified as the probable etiological agent of SARS and referred to as SARS-CoV.[1,2,3]

In recent time, an outbreak of the virus has crippled the world. This strain was reported in late December of 2019 in Wuhan city, China, with no previous human identification. The International Committee on Taxonomy of viruses (ICTV) suggested the novel corona virus to be named as SARS Cov-2, due to phylogenetic and taxonomical analysis of the virus.[4]

Corona viruses are a genera of enveloped viruses with a positive sense, single-stranded RNA genome (26-32 kb). Four corona virus genera (α, β, γ, δ) have been identified, with human corona viruses (HCoVs) detected within the α coronavirus (HCoV-229E and NL63) and β coronavirus (MERS-CoV, SARS-CoV, HCoV-OC43 and HCoV-HKU1) genera. Coronavirus S protein has been reported as a major determinant of virus entry into host cells. The envelope spike glycoprotein binds to its cellular receptor, ACE2 for SARS-CoV and SARS-CoV-2, CD209L (a C-type lectin, also called L-SIGN) for SARS-CoV, DPP4 for MERS-CoV.[5,6,7]

COVID-19 patients exhibit an array of clinical symptoms which include fever, nonproductive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia. The lesser known symptom are inclusive of headache, hemoptysis and diarrhea. A vital mechanism for ARDS is the cytokine storm, an uncontrolled systemic inflammatory response ensuing from the discharge of enormous amounts of pro-inflammatory cytokines (IFN-a, IFN-g, IL-1b, IL-6, IL-12, IL-18, IL-33, TNF-a, TGF-b, etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10, etc.).[9]

AGENTS OF SPREAD

The oral cavity is the road to the entrance of pathogens into the body. The oral secretions - mainly saliva droplets along with nasal discharges – have been claimed by the WHO as the primary agents of transmissions of COVID-19.[10]

Saliva is a bio mixture which is additionally composed up of desquamated epithelial cells, crevicular fluid, microorganisms as well as respiratory secretions and food debris.[11]

A series of papers identify the presence of viral particle in the saliva of patients diagnosed with COVID-19, Khurshid et al 2020, Sabino Silva et al 2020, Xu et al 2020.[11,12,13] Report of one COVID-19 case in Germany indicates transmission occurring by asymptomatic patients.[14] To et al have reported the presence of the live viruses in the saliva of infected individuals by viral culture method.[15]

The entry of COVID-19 occurs through ACE-2 cell receptors which causes a cell invasion leading to human transmissions. ACE-2 cells are abundantly present throughout the respiratory tract, and are morphologically similar to the cells of the salivary gland. The ACE-2 cells have been nominated as early targets of SARS-COV infection.[16,17]

Thus it has been speculated that COVID-19 follows the same transmission route. The transmissions may vary either due to contact transmissions or direct transmission. These include airborne spread, contact spread or by contaminated surfaces.[10]

ORAL HYGIENE MEASURES

Oral self-care by patients have proven to cause alleviation in minor oral issues as well as perceivably noted successful treatment outcomes. Oral hygiene instructions rendered to a patient aims to induce behavioral changes in the regimen involving tooth brushing habits or the usage of mouth rinses.[18, 19] Kirk et al states the presence of a viral load of $1.2x10^8$ covid-19 species in the saliva as detected by PCR assay, while the nasopharynx accounts for an even higher count.[20]

POVIDONE-IODINE

Povidone- iodine was developed in 1955 (iodine with the water-soluble polymer polyvinylpyrrolidone, PVP-I) at the industrial toxicology lab in Philadelphia; as an anti-microbial agent. The release of free Iodine from the polymer complex was deemed to penetrate microbes and cause the disruption of proteins and oxidation of nucleic acid structures.[21]

In vitro studies by Eggers et al on SARS CoV during the 2002-03 epidemic have demonstrated its effectiveness at 99.99% antivirucidal activity when used at 1% concentration further in vitro studies established the lowest concentration of 0.23% to be adequately effective.[22,23]

Subsequent studies by Kariwa et al, 2020 recommended 0.5% PVP -1 standard aqueous PVP-1 antiseptic solution diluted with 1:20 with water administered in a dosage of 0.3 ml into nostril using an anatomizing device, for nasal lavage.[24]

9 ml of 0.5 % solution used as a mouth wash distributed evenly for 30 seconds and gargled at the back of the throat for 30 seconds, was efficacious as an antivirucidal.[25]

HYDROGEN PEROXIDE

Hydrogen peroxide function therapeutically based on its oxidizing nature by releasing nascent oxygen [O], which necrobiosis of obligate anaerobes. Seymour and Heasman,1992, initially demonstrated its cidal activity on the bacterial cell walls.

A pilot study by Ramesh et al, 2015 established the superiority of the adjunctive use of hydrogen peroxide solution as compared to the lone usage of chlorhexidine; in the reduction of CFU's caused by bioaerosols. 0.5% hydrogen peroxide solution has been established as an ideal concentration required to be virucidal to coronavirus.[27]

In a recent letter by Saravanamuttu, 2020 recommended the application of 1.5% hydrogen peroxide solution as a mouthwash to contain the transmission of the COVID-19 particles within the oropharyngeal complex.[28]

Oxidizing agents are employed in dentistry for several years .The magnitude of plaque reductions obtained with the peroxyborate and more so with peroxycarbonate rinses would suggest a necessity for further study of these preparations when used as adjuncts to normal toothbrushing.(Addy 1994)[30,31] Oxidising mouthwash has a highly effective oxidising action: this property has been shown in studies from Wuhan to be required for the effective killing of coronavirus within the mouth and in aerosols.

CHLORHEXIDINE

Chlorhexidine was developed as an antiseptic agent by imperial chemical industries in 1950's,[29] the potential use of chlorhexidine for the prevention and control of aerosol transmission in recent times has been noted (An et al,2020; Su 2020).[32,33] It has extensive substantivity against bacterial cells in bioaerosols by causing leakage of cytoplasmic components and irreversible precipitates with intracellular adenine triphosphate.(Shetty et al, 2013; Gupta et al, 2014; Santos et al, 2015; Saini, 2015; Mohan et al, 2016; Vardes et al, 2017).[34-39] Though it has poor virucidal activity (Faizan and Firozi, 2019; Kampf et al, 2020).[40,41]

A study conducted by Chin et al, 2020 at the Hong Kong university reported that 0.02% chlorhexidine gluconate is ineffective as surface disinfectant, however at an increased dosage of 0.05% it is as effective as 7.5% PVP-1 or 70% ethyl alcohol.[42]

Chitguppi, 2020 have concluded the effectiveness of chlorhexidine gluconate.[43]

TOOTHBRUSHING

The dentrifice works on the teeth like soap works on the hand. A microbial biofilm on the surface induces an inflammatory response (Marsh 1994) as well as harbors a variety of microflora.(Marsh 2006, Dalwai 2006) Toothbrushing is the main intervention preferred at home to control biofilm mechanically.

Addy, in a very recent paper, emphasized the neglection on the importance of tooth brushing within the wake of this pandemic. As observed by him, dentrifices contain detergents and surfactants which eliminate a good array of microbes on a daily basis.[44] Most dentrifices comprise of antibacterial agents like triclosan, which in various trials have removed plaque effectively.[45]

However in these troubled times we are in an urgent need for studies to assess the connection between toothbrushing and therefore the viral salivary load.

CONCLUSION

Researchers theorize that the fatty shell encasing the coronavirus are often softened by certain mouthwash ingredients — including grain alcohol; chlorhexidine, a long-lasting kind of iodine; and hydrogen peroxide. Presently there are no definitive studies in reference to the virucidal efficacy of oral mouthwashes against SARS-CoV2. It has been hypothesized that both povidone-iodine and hydrogen peroxide substantially exhibit more virucidal activity than chlorhexidine (Log10 reduction factor of 0.6) against respiratory viruses by an element of 8000 times (Kampf et al., 2020). It must even be borne in mind that apart from chlorhexidine the other mouthwashes have poor substantivity allowing the oral microflora to reestablish within several minutes (Addy and Wright, 1978; Lafaurie et al., 2018). To conclude, most of these studies enumerate the individual effects of the components against the salivary viral titres of COVID-19, till the time their substantivity lasts; but furthermore they do not talk of preventing the virus transmission from the infected to the susceptible.

	SUMMARY
Addy & Wright 1978	Stated that 1 % povidone iodine exerts an immediate antibacterial effect while 0.2 % chlorhexidine, is retained at antibacterial levels within the oral cavity after expectoration.
Moran et al.1995	Compared 2 mouthrinses containing peroxyborate and peroxycarbonate with a chlorhexidine rinse for their ability to inhibit plaque reformation.
Kariwa et al. 2006	Inactivated SARS Coronavirus by Povidone-Iodine of an equivalent of 70% ethanol, by heating the virus at 56^{o}C for 60 min and by fixation of SARS-CoV-infected Vero E6 cells with formalin, glutaraldehyde, methanol and acetone for 5 min.
Riley & Lamont 2013	Reviewed that toothpastes containing triclosan/copolymer, and fluoride, reduced plaque, gingival inflammation, gingival bleeding as well as root caries and calculus.
Shetty et al. 2013	Advocated the usage of preprocedural antimicrobial rinses during aerosol generating dental procedures, to reduce the risk of crosscontamination due to infectious agents.
Gupta et al. 2014	Suggested that 0.2% chlorhexidine gluconate preprocedural mouthrinse could majorly eliminate bacterial aerosols.
Santos et al. 2014	Assessed that the prior use of 0.12% chlorhexidine mouthwash in vitro, significantly reduced the contamination caused by aerosolized sodium bicarbonate.
Romesh et al. 2015	Evaluated the superiority of the adjunctive use of 1.5% hydrogen peroxide with 0.2% chlorhexidine compared to the lone usage of chlorhexidine against dental aerosols.
Saini et al. 2015	Compared the efficacy of preprocedural mouthrinses containing 0.2% chlorhexidine (CHX) gluconate, chlorine dioxide (ClO_2) mouthwash, and water in reducing the levels of viable bacteria in aerosols.
Mohan et al. 2016	Analyzed that the use of chlorhexidine pre-procedural mouthrinse can significantly reduce the levels of viable microbial content in dental aerosols.
Retamal-valdes et al. 2017	Conducted a randomized, single blinded clinical trial and evaluated the effectiveness of a cetylpyridinium chloride (CPC), zinc lactate (Zn) and sodium fluoride (F) containing pre-procedural mouthwash to reduce bacteria in aerosols.
Eggers et al. 2018	In a test series; evaluated the virucidal efficacy of 7.5% PVP-I against murine norovirus (MNV) while PVP-I and CHG 4% were bactericidal against E. coli.
Eggers et al. 2018	Acknowledged the in vitro virucidal efficacy of 7% (At a dilution of1:30) povidone-iodine mouthwash/ gargle in inactivating SARS-CoV, MERS-CoV, within a 15 s exposure.
Farzan & firoozi, 2019	In a systematic review concluded that PVP-I gargle/mouthwash is the only approved mouthwash for pre-procedural rinsing in dental practice to eliminate coronaviruses according to the available literature.
Bayley et al. 2020	proposed a protocol of intra-nasal and oral application of PVP-I for patients and their attendant healthcare workers (HCWs) during the COVID-19 pandemic to limit the transmission of SARS-CoV-2
Kampf et al. 2020	Elucidated that surface disinfection with ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite, benzalkonium chloride or 0.02% chlorhexidine digluconate helped inactivate microbial agents.

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