

Statins-based prophylactic mouthwash and nasal spray may protect against coronavirus disease 2019

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Abstract

The novel coronavirus 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused an unprecedented healthcare crisis. SARS-CoV-2 gets access into the human body mainly through the nose and the mouth and invades these mucosae in its destination to the pulmonary tissues. Thus, the oral and nasal mucosae serve as the main routes and reservoirs for aerosolized transmission of the viral particles to the external environment and hence infection transmission. Statins have been shown to have antimicrobial, antiviral, antifungal, anti-inflammatory, immunomodulatory, and antioxidant properties. Therefore, we hypothesize that using statins-based prophylactic mouthwashes will reduce COVID-19 transmission in dental settings.

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To the editor,

The novel coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused an unprecedented health-care crisis. By the date of writing this report, the pandemic has affected more than 20 million people and caused more than 740 000 associated deaths worldwide. SARS-CoV-2 gets access into the human body mainly through the nose and, to a lesser extent, through the mouth. The virus invades the nasal and oral mucosal cells, mainly through angiotensin-converting enzyme 2 (ACE2) receptors. In the following days, the virus progresses down through the pulmonary system triggering mostly mild respiratory symptoms, but it may trigger an intense inflammatory host response, sometimes leading to a life-threatening acute respiratory distress syndrome, in a fraction of individuals [1]. It is obvious by now that SARS-CoV-2 resides in the nasal and oral mucosal cells [1], rendering these anatomical areas sources of seeding the lower airways causing progression of pulmonary disease; and serving as the main routes and reservoirs for aerosolized transmission of the viral particles to the external environment [2]. Health-care workers, especially dentists and otolaryngologists, are at highest risk of becoming infected through droplet transmission or direct contact. In addition, WHO states that airborne transmission may be possible in specific circumstances and settings in which procedures that generate aerosols are performed. In dental settings, any dental procedure that can aerosolize contaminated saliva can significantly increase airborne contamination with microorganisms. All dental procedures involving the use of hand-pieces and air–water syringes produce aerosols and splatter, resulting in exposure of the clinicians, dental assistants and patients to a higher risk of being infected, and/or rendering them sources of infection transmission. We hypothesize that using a statins-based prophylactic mouthwash will reduce COVID-19 transmission in dental settings.

The statin family of drugs represent safe and effective therapeutic agents, indicated mainly to reduce cholesterol biosynthesis in the liver, and hence the levels of low-density lipoprotein cholesterol [3]. Apart from this main pharmacological property, statins have been shown to have antimicrobial, antiviral, antifungal, anti-inflammatory, immunomodulatory and antioxidant properties [4]. More specifically, several studies showed that statins inhibit Zika, Ebola, dengue and influenza viruses and cytomegalovirus [4,5]. There are many mechanisms (pathways) that may explain the antiviral property of statins. First, statins reduce serum cholesterol levels that facilitate binding of some viruses to the host cells result in lower viral titres. In fact, research showed that some viruses bind to the lipid rafts (rich in

cholesterol). Second, statins are believed to destabilize the lipid rafts, which constitute important pockets for virus replication [6]. Third, statins have been shown to interfere with ACE2 signalling and to promote ACE2 up-regulation, so reversing the action of SARS-CoV-2 [7].

A recent report based on molecular docking analysis showed that statins might inhibit SARS-CoV-2 entry into host cells through direct binding to its main protease [8]. Moreover, a more recent study, demonstrated that in-hospital systemic use of statins is associated with a reduced risk of mortality among individuals with COVID-19 [9].

From a dental perspective, several in vitro studies showed promising antibacterial effects of statins against periodontal pathogens [10,11]. One meta-analysis indicated that statins significantly improved periodontal parameters when used as sole adjuncts to mechanical periodontal treatment [12]. Recently, one study demonstrated a significant reduction in periodontal parameters and inflammatory biomarkers with the use of simvastatin gel and mouthwash in a 1% preparation [13].

It has been argued that the viral load in the oropharynx and nasopharynx with SARS-CoV-2 infection is as high in asymptomatic individuals as in those with symptoms [2]. Assuming that many asymptomatic and even symptomatic people may seek dental treatment, it is imperative to reduce the viral load in the oropharynx through adequate oral prophylactic measures to eliminate, or at least to minimize, the risk of SARS-CoV-2 transmission to dental personnel and patients.

To achieve this, we suggest: (a) pre-procedural use of mouthwashes and nasal sprays by dental patients, to reduce the risk that any aerosol-generating procedures will infect health-care workers, and (b) use of mouthwashes and nasal sprays by health-care workers pre- and post-exposure to patients with confirmed or suspected infection to reduce the risk of infection through their mouth or nose. We suggest the following formulation in the context of the currently discussed hypothesis: preparation of 1% simvastatin mouthwash by dissolving 20 mg simvastatin tablets in distilled water. Sodium benzoate is added as a preservative, followed by glycerin and natural food colour and flavour so that its taste will be tolerated. The final preparation will then be adjusted for pH by adding triethanolamine solution [13]. When considering use of a statins mouthwash, the suggested application time is 15–20 seconds [14].

Given the potential antiviral effect of statins, we hypothesize that the use of topical statins as a mouthwash or even as a nasal spray may minimize the risk of SARS-CoV-2 transmission in dental settings, and so will protect patients and health-care

providers during the COVID-19 pandemic. Clinical trials should be considered for this hypothesis.

Conflicts of interest

There is no conflict of interest.

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