

Hyposalivation as a potential risk for SARS-CoV-2 infection: Inhibitory role of saliva

Dear Editor,

Human saliva is an inquisitively complex fluid and has an imperative role for prevention and protection from viral infection, particularly through innate immune system, which is a prominent first-line defense against viral infection (Dawes et al., 2015; Malamud et al., 2011).

Despite the clear role of saliva in the continuous cleansing of oral cavity, we focus on proteins that illustrate anti-viral activity, particularly against coronaviruses. The results of a study (Iwabuchi, Fujibayashi, Yamane, Imai, & Nakao, 2012) have suggested that hyposalivation could lead to acute respiratory infection. There are two potential reasons for increasing the incidence rate of this infection. First, reduced saliva secretion may impair the oral and airway mucosal surface as a physical barrier, which consequently enhances the adhesion and colonization of viruses. Second, this reduction may also impair the secretion of antimicrobial proteins and peptides (Iwabuchi et al., 2012).

Saliva contains a large number of proteins and peptides, which have exhibited anti-viral effects. Cathelicidin (LL-37), lactoferrin, lysozyme, mucins, peroxidase, salivary agglutinin (gp340, DMBT1), sIgA SLPI, α , β defensins, and cystatins are the known proteins in the oral cavity that demonstrate anti-viral activity for at least one virus. Salivary gp340 demonstrated anti-viral activity against HIV-1 as well as influenza A (Dawes et al., 2015; Malamud et al., 2011).

Cystatin type II is present in saliva and possesses anti-viral activity (Magister & Kos, 2013). It was determined although cystatins C, SN, and S are inactive against bacteria; they found to be more efficient toward parasites and viruses (Magister & Kos, 2013).

Salivary cystatins may have a role in the host defense mechanism against virus infections as they can interfere with events in viral replication. The anti-viral effect of cystatin C against herpes and coronavirus is documented. Moreover, cystatin D has been reported to inhibit the replication of coronavirus potentially at its physiologic concentration (Magister & Kos, 2013), and the presence of cystatin D in saliva may play a protective anti-viral role (Collins & Grubb, 1998).

Moreover, anti-viral activity of saliva may arise from salivary microvesicles that contain at least 20 microRNAs (miRNAs), which can limit the replication of certain virus types (Dawes et al., 2015; Irmak, Erdem, & Kubar, 2012). The miRNAs in saliva have established anti-viral activity, and saliva has been employed as a treatment of

ophthalmic herpes zoster (Dawes et al., 2015; Irmak et al., 2012). It is reported that unstimulated submandibular saliva has been shown to inhibit the HIV-1 virus, even when diluted several-fold (Dawes et al., 2015).

Considering the presence of many proteins with established anti-viral properties in saliva, some of which can potentially inhibit virus replication especially coronavirus, it gives the impression that the protective effect of these salivary proteins against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be the same.

On the other hand, concerning the endurance of infectious viruses in the oral cavity despite the potential anti-viral properties of saliva and other compartments, it is essential to remind that most of anti-viral proteins of saliva have rather limited effectiveness and a narrow range of pursuit (Malamud et al., 2011).

Hyposalivation could be a potential risk factor for acute respiratory infection (Iwabuchi et al., 2012). It may expose patients at high risk of getting coronavirus disease (COVID-19). However, further investigations are crucial to prove this hypothesis.

CONFLICTS OF INTEREST

None to declare.

AUTHOR CONTRIBUTION

Nima Farshidfar: Conceptualization; Investigation; Methodology; Project administration; Validation; Visualization; Writing-original draft; Writing-review & editing. **Shahram Hamedani:** Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Validation; Visualization; Writing-original draft; Writing-review & editing.

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