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REVIEW

Impact of COVID-19 vaccination on saliva immune barriers: IgA, lysozyme, and lactoferrin

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Abstract
Understanding the role of salivary constituents, such as lactoferrin, lysozyme, and secretory immunoglobulin A (sIgA), in immune protection and defense mechanisms against microbial invasion and colonization of the airways is important in light of the ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. The salivary immune barrier in individuals affected by COVID-19 may contribute to disease prognosis. Thus, the aim of the present review is to evaluate the effect of COVID-19 vaccines on the immunological composition of saliva. IgA antibodies generated by vaccination can neutralize the virus at mucosal surfaces, whereas antimicrobial peptides, such as lysozyme and lactoferrin, have broad-spectrum antimicrobial activity. Collectively, these components contribute to the protective immune response of the oral cavity and may help minimize viral transmission as well as the severity of COVID-19. Measuring the levels of these components in the saliva of COVID-19-vaccinated individuals can help in evaluating the vaccine's ability to induce mucosal immunity, and it might also provide insights into whether saliva can be used in diagnostics or surveillance for monitoring immune responses following vaccination. This also has implications for viral transmission.

Introduction

Diverse microbial communities present in saliva reflect dietary patterns and health conditions, and bacterial populations are thought to be key biological immune barriers. Numerous studies on the diversity of the salivary microbiome have focused on the changes caused by specific diseases, but the similarities and differences identified in healthy saliva have attracted less attention [34]. Salivary antibodies are reactive with the receptor-binding domain (RBD) and the S protein of the SARS-CoV-2 spike protein. A sustained presence of SARS-CoV-2 immunoglobulins (IgGs) for three months has been observed. Notably, the profiles of IgGs in salivary samples specific for the S protein and the RBD show greater consistency and higher antibody titers than secretory IgA [19, 20]. Antimicrobial peptides such as lysozyme and lactoferrin are part of the innate immune system and can be detected in a variety of host secretions, including saliva. These peptides have been shown to have antiviral properties, and some research suggests that they may play a role in protection against COVID-19 [6, 18, 36]. By hydrolyzing the 1,4-glycosidic bond between N-acetylglucosamine and N-acetylmuramic acid in the bacterial cell wall, lysozyme kills Gram-positive bacteria, but because of its cationic nature, which enables it to cling to negatively charged surfaces (as lactoferrin does), it possesses antibacterial qualities in addition to its enzymatic activity, extending its activity beyond Gram-positive bacteria [32, 42]. Secretory immunoglobulin A (sIgA), a component of the immune system, protects against infections through mucosal immunity. sIgA is composed of dimeric IgA, a J chain, and a secretory component that is secreted by the salivary and mammary glands to inhibit the entry of antigens from the mucosa [46]. The oral, nasal, and pulmonary cavities are entry sites for SARS-CoV-2 in humans [37]. Furthermore, saliva contains many anti-infective compounds (the most common of which are lactoferrin, lysozyme, and sIgA), which may help prevent the virus from entering the mouth [16].

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