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Exploring the Potential of Periodontitis Vaccines: A Comprehensive Review and Analysis

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OKU Sutro Excellence Day Project Cover Sheet

Project Title

Exploring the Potential of Periodontitis Vaccines: A Comprehensive Review and Analysis

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P. gingivalis, a prevalent bacteria in the oral cavity of patients with active periodontitis, presents a persistent challenge. Patients often receive root debridement therapy to manage disease progression, however, it merely addresses symptoms without curing or reversing the condition. Therefore, there is a pressing need for more sophisticated therapeutic approaches, such as vaccination, targeting the pathogen directly. Although comprehensive research involving human clinical trials are pending, the aim of this invention is to introduce specific antigens of periodontitis to stimulate the targeted antibodies. The periodontitis vaccine has the potential to become a supplement to mechanical therapy. The comprehensive literature review from peer reviewed PubMed resources will determine if immunization with a P. gingivalis vaccine has the potential to reduce progression of periodontal disease in adults with active periodontal disease during a four to six-week recall period. This can minimize the morbidity that is linked to periodontitis in adults and mitigate the impact of the disease. Examining existing studies for periodontal vaccinations and delving into potential future developments, the research provides insights to advancements for effectively managing the significant concern in periodontal health, providing patients with a more comprehensive treatment approach.

Exploring the Potential of Periodontitis Vaccine: A Comprehensive Review and Analysis

Dr. Eric Salmon, DDS, Jenny Choi, Lena Nguyen, DH 2024

Abstract

P. gingivalis, a prevalent bacteria in the oral cavity of patients with active periodontitis, presents a persistent challenge. Patients often receive root debridement therapy to manage disease progression, however, it merely addresses symptoms without curing or reversing the condition. Therefore, there is a pressing need for more sophisticated therapeutic approaches, such as vaccination, targeting the pathogen directly. Although comprehensive research involving human clinical trials are pending, the aim of this invention is to introduce specific antigens of periodontitis to stimulate the targeted antibodies. The periodontitis vaccine has the potential to become a supplement to mechanical therapy. This can minimize the morbidity that is linked to periodontitis in adults and mitigate the impact of the disease. Examining existing studies for periodontal vaccinations and delving into potential future developments, the research provides insights to advancements for effectively managing the significant concern in periodontal health, providing patients with a more comprehensive treatment approach.

Objective

The objective of this literature review is to combine different studies to provide a comprehensive summary of the current understanding of periodontitis vaccine. This study aims to collect relevant and up-to-date research on the development and potential implementation of vaccines targeting *P. gingivalis*. It will determine if immunization with a *P. gingivalis* vaccine has the potential to reduce progression of active periodontal disease in adults during a four to six-week recall period.

Methodology

Previous dental literature has been reviewed with randomized and controlled trials. Peer reviewed PubMed resources have been utilized on this topic. All journal articles used are written by professionals and published through reliable journals and have been mentioned in the resources section.

Background

Bacterial accumulation initiates host immune system responses, triggering gingival inflammation. Out of the red-complex bacteria, the main bacterium that takes the role in periodontal disease development are *Porphyromonas gingivalis. P. gingivalis* is the core pathogen that disrupts the oral microbiome resulting in a human immune response resulting in pathogen colonization and pathogenesis. This bacteria occupies in low amounts and still may lead to periodontitis (Olsen 2017). Once *P. gingivalis* is introduced, it attaches to tooth surfaces, ultimately invading gingival epithelial cells. *P. gingivalis* suppresses neutrophils and macrophages as they invade the epithelial cells.

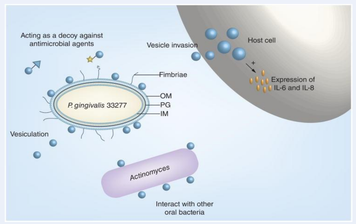

Figure 1. Structure of *P. gingivalis* with virulence factors interacting with host cells

Current therapeutic treatments for periodontitis include mechanical debridement called scaling and root planing and antimicrobials. However, the effectiveness of these treatments are still variable and the progression of this disease is difficult to manage. Therefore, there is a developing acknowledgement of the need for targeted and preventive measures to address the specific pathogenic factors leading to the disease progression. In the recent past, the investigation of vaccination systems targeting the periodontal pathogens has gained attention as a potential method for new therapeutic interventions.

The research aims to investigate the capability of immunization against *P. gingivalis* in adults with active periodontitis. By researching the effect of the vaccine, this study expects to add to the developing landscape of periodontal therapeutics. The purpose is to observe whether inoculation can effectively modify the host response and hinder the progression of the disease. By targeting the *P. gingivalis* which plays an important role in pathogenesis of periodontitis, this study strives to offer insights that may guide the trajectory of preventive measures and redefine the view of periodontitis.

Virulence factors of *P. gingivalis* contribute to the destruction of the periodontium. Major virulence factors of this bacteria include: gingipains, fimbriae, lipopolysaccharide (LPS), capsule, heme acquisition systems, and proteinases (Ahamed, 2016). Gingipains are cysteine proteases that degrade host proteins to disrupt host cell pathways. These proteases cleave host proteins such as immunoglobulins and cell adhesion molecules. Fimbriae work with adhesion to host cells and help initialize *P. gingivalis* colonization on tooth surfaces. Lipopolysaccharide or LPS are stimulators of the host's immune system response, like IL-6 and IL-8. These stimulators react like toll-like receptors which produce pro-inflammatory cytokines resulting in tissue inflammation. The capsule of the bacterium protects the bacteria from host immune responses.

Result

Multiple studies have been conducted on mice, each altering a specific virulence factor of *P. gingivalis.* From serum levels testing for antibodies and evaluating bone loss levels, each study found various ways to create a periodontal vaccine. The method that utilized fimbriae proteins that were injected intramuscularly into mice showed the antibody IgG was prevalent within the body. Mice present were divided into five groups which included group 1 with no oral challenge and no immunization, group 2 with *P. gingivalis* oral challenge but no immunization, and group 3, 4, 5 with *P. gingivalis* oral challenge and immunization of Mfa1, *P. gingivalis* minor fimbriae protein, HA1&2, gingipain hemagglutinin domains. The mice in group 3, 4, and 5 had a total of three vaccinations in the span of six weeks. As a result, ELISA test method was used to measure the level of IgG antibody. With IgG present in group 3, 4, and 5, bone loss from *P. gingivalis* was prevented (Huang 2019).

Although other routes of administration such as mucosal, oral, and sublingual vaccinations were introduced, the limitations on the trials remained the same. This includes periodontitis complexity, possible toxic responses and contamination, and sustaining sufficient antibody levels (Kohli, 2023). Periodontitis involves several bacteria such as *P. gingivalis, T. forsythia*, and *T.denticola.* However, the vaccinations under development only target one bacteria. The selective focus may limit the efficacy of the immunization in preventing all features of periodontitis because of its multifaceted nature. No vaccinations in trials were conducted on the human body and therefore, the potential for toxic responses or adverse reactions have not been assessed. Lastly, sustaining sufficient antibody levels is challenging due to chance of antibody response decreasing over time, variability in every individual, and difficulty in maintaining mucosal immunity. This will also require human trials to provide comprehensive assessment.

The use of periodontal vaccines and traditional treatment has come up for debate on how the vaccine should be utilized. As root debridement therapy has the current and traditional way to treat periodontal disease, the potential of a vaccine may aid in the healing process of the patient. However, though the potential is there for a vaccine, it was stated a vaccination alone would not be sufficient in eliminating the disease (Kudyar 2011). The formulation of the periodontitis vaccine denotes a significant progress in the ongoing pursuit of preventive strategies against the widespread concern of oral health. In this research, an immunization was intended to target a specific pathogen, *P. gingivalis*, that causes periodontitis. It demonstrates that the inoculation of the vaccine can decrease measurement of alveolar bone loss. This evidence provided potential possibilities of developing vaccines for the prevention and management of periodontitis in adults.

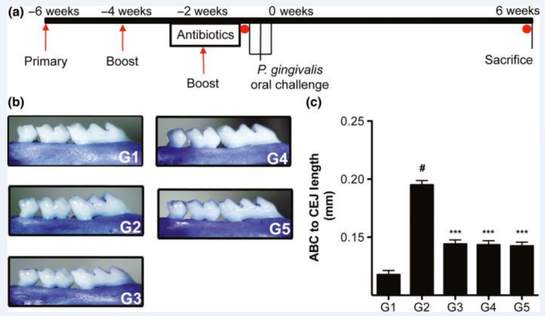

Figure 2. Evaluation of bone loss.
(a) This was the timeline in which the mice were given their booster vaccinations. Each mouse was given 3 intramuscular injections with their respective antibody combinations as indicated by the red arrows on the timeline. Antibiotics were given for 10 days and were taken off antibiotics 3 days before group G1 for evaluation of oral challenge and *P. gingivalis* oral challenge (Groups G2-G5). Each red dot indicated when the mice were sacrificed to evaluate oral health.
(b) Oral evaluation of each group stained with methylene blue.
(c) This graph shows the average distance between the cementum-enamel junction and alveolar bone crest. G2 had the furthest distance.

Conclusion

The current therapeutic treatments for periodontitis include antimicrobials and mechanical debridement that removes subgingival plaque. These methods can be highly priced, painful, and the result can be variable due to different compliances of patients. In several preclinical trials, significant reduction in periodontitis progression could be observed in rodent models by having less *P. gingivalis* antigens and bone loss after receiving the vaccination.

The *P. gingivalis* vaccine demonstrates encouraging results, as evidenced by the preservation of clinical attachment from the CEJ to the alveolar bone crest following three booster injections (Figure 2). Given that the studies have exclusively involved mice, which serve as model organisms, it hints promising outcomes once human trials begin. The vaccination can possibly be a supplement intervention to current treatments, however, there are no trials that were successful in meeting the criteria such as preventing colonization of multiple pathogens and obtaining enough immunoglobulins to opsonize and phagocytose the invading microorganisms.

Using a combination of proteomic, genomic, and immunologic approaches due to periodontal disease being a multifactorial and polymicrobial disease. With the evidence that periodontitis significantly increases the risk of systemic health such as coronary heart disease or diabetes mellitus, the invention of vaccines can have health benefits far surpassing the prevention of periodontitis.

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