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MINI REVIEW

Dental & Craniofacial Research

Periodontal vaccines: Need of an hour

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Abstract

Periodontal diseases are immune inflammatory responses induced by microorganisms in dental plaque which contributes to tissue destruction, bone loss and eventually tooth loss. Moderate to severe periodontitis affects more than 50 percent of population over the age of 65. It is also associated with diabetes, heart disease, rheumatoid arthritis, dementia and certain cancer. Current treatment modalities have resulted only in arresting the disease progression but have no solution for curing the disease or to prevent the recurrence. Hence there is a need for more sophisticated therapeutic modalities which may include vaccines targeting putative periodontal pathogens. Periodontal vaccines could emerge as an adjunct to mechanical therapy in future.

Keywords: *periodontal vaccine, pathogens,treatment modalities*

Introduction

Vaccines are generally prophylactic, i.e. they ameliorate the effects of future infection [1].Vaccination is induction of immunity by injecting a dead or attenuated form of pathogen [2]. One such vaccine considered here is the "**Periodontal vaccine**". Periodontitis is an infectious disease caused by predominantly gram-negative, anaerobic bacteria like *P. gingivalis, A. actinomycetemcomitans T. denticola* and *T. forsythus* etc. Various immunization approaches both as active and passive immunization, against periodontal pathogens have been explored either using the whole microorganism or their specific virulence factors. Till date, no preventive modality exists for periodontal disease and treatment rendered is palliative. The demanding primary role of any periodontal vaccine would be to eradicate the global periodontal disease burden with the ultimate purpose of lowering the prevalence of periodontal disease in practice. Moreover, recent findings linking periodontitis and systemic health concerns suggest that prevention of periodontal diseases is fundamental to the effective management of systemic diseases too [3].

Types of immunization

Active immunization: Individual immune system is stimulated by administrating killed or live attenuated products derived from micro-organisms. Eg: Whole bacterial cells, Sub unit vaccines, Synthetic peptidesas antigen [4].

Passive immunization: The antibodies formed in one individual are transferred to another. E.g: Murine monoclonal antibody, Plantibodies.

DNA vaccination: DNA plasmids encoding genes required for antigen production are transferred to an individual. E.g: Plasmid vaccines, Live, viral vector vaccines.

Types of immunization

In the early twentieth century, three periodontal vaccines were employed [5]:

- Pure cultures of streptococcus and other organisms
- Autogenous vaccines
- Stock vaccines

Examples: Vancott's vaccine and Inava endocarp vaccine

Up to now, however, no periodontal vaccine trial has been successful.

The development of vaccine is dependent on the identification of bacterial antigens that are expressed in vivo and induction of a protective response. DNA vaccines that were described <5 years ago have already progressed to Phase-I clinical trial in healthy humans [6]. Although success has been achieved in the case of animal models, there are several reasons which still have to be overcome to make the dream of periodontal vaccine for humans a reality. Some of the reasons include:

- periodontitis as a polymicrobial infection
- complexity and uncertainty of the different forms of periodontal diseases
- difficulty in accurately differentiating between primary colonizers and secondary invaders
- relative difficulty in growing and identifying many of the disease-associated microorganisms
- the variability of the plaque composition from one individual to the other and between sites in the same individual.

Thus, the current status of our understanding in the field of vaccines against periodontal disease is not complete, but extensive research in this direction may hold a promising future in the development of periodontal vaccine.

Target for periodontal vaccination

Porphyromonas gingivalis, A. actinomycetemcomitans, Treponemadenticola, Tannerella forsythia were implicated as the key pathogens in the etiology of periodontal disease. According to Loesche WJ in 1976, the specific plaque hypothesis states that only certain plaque is pathogenic, and its pathogenicity depends on the presence or increase in the specific microorganisms [6,7].

1. **Porphyromonas gingivalis whole cell as a target antigen**
   - Gingipains as target antigens Gingipains R (RgpA and RgpB) : cleaves proteins atarginine residues
   - Gingipain K (porphypain 2, Kgp): cleaves proteins at lysine residue.
   - HA2 domain as target antigen
   - Catalytic domain as target antigen
   - Fimbriae as target antigens
   - Capsular polysaccharide as a target antigen
2. **A. actinomycetemcomitans** is considered another important pathogen in human periodontal disease, especially in the localized form of aggressive periodontitis. Harano et al. prepared an antiserum against a synthetic fimbrial peptide of A. actinomycetemcomitans and found that it blocked the adhesion of the organism to saliva-coatedhydroxyapatite beads, to buccal epithelial cells, and to a fibroblast cell line.
3. **Plantibodies:** A very recent approach for vaccination strategies is molecular biological techniques to express bacterial or viral antigens in plants, which could be used as orally administered vaccines. This suggests the potential use of plants in synthesizing adjuvant fimbrial protein for the development of adjuvant mucosal vaccines against P. gingivalis.

Most periodontal immunization studies have targeted a single pathogenic species. However, a number of the potential candidate antigenic determinants may share a sequence homology with other periodontopathic bacteria. These antigens may include phosphorylcholine. In CPS and heat shock protein (HSP), Phosphorylcholine, however, would not be a suitable candidate antigen as it has not been identified in *P. gingivalis*. In addition, CPS is not a potent inducer of T-cell mediated immunity and would require protein conjugation in any vaccine design. Therefore HSP antigen, which has been identified in most putative periodontal pathogenic bacteria with a high level of sequence homology, may be a suitable candidate molecule.

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Future advancements

Vaccines using cross reactive immunodominant epitopes as antigenic molecules in an attempt to stimulate antigen–specific regulatory T-cells, secreting IL-10 and Transforming growth factor β, strategies to enhance immunogenicity of antigenic components of B or T lymphocytes [8].

Conclusion

Various forms of active and passive immunization methods have been tried. Although, most of these studies have yielded encouraging results, none of these modalities of immunization have been able to be incorporated as a sole or complete 'vaccine' against periodontal disease for use in thehuman population as yet. Extensive research in this direction may hold a promising future in development of periodontal vaccines [9]. Ongoing research and collaborative efforts can result in development of functional periodontal vaccine for human use in future.

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