Review Article

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Periodontal Vaccine: Unravelling An Enigma

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ABSTRACT

Background: Periodontal disease is polymicrobial, and the current treatment approach is centred on mechanical debridement of supragingival and subgingival plaque or surgical interventions. A new horizon needs to be developed in the form of a single vaccine which can act against all the periodontopathogenic bacteria preventing the disease onset and its progression. The periodontal vaccine is something which can meet our requirements as it aims to spot out the antigens involved in the destructive process of periodontitis against which antibodies would be educed for disease prevention.

Keywords: Periodontal disease, pathogens, vaccine.

INTRODUCTION

In adult population tooth loss is commonly caused by periodontal disease and being multifactorial in origin it is related to some systemic conditions also. Present treatment modality for such disease focuses on halting the progression of it, but the complexities in its etiopathogenesis have been the prime obstacle in the hunt for a deterrent therapy. As no preventive method exists yet, the introduction of a periodontal vaccine becomes necessary in the field. The vaccine is a name generally applied to the substance of nature of dead accentuated living infectious material introduced into the body with the objective of increasing its power to resist or get rid of a disease. The first vaccine was named after vaccinia, the cowpox virus; Sir Edward Jenner pioneered its use 200 years ago. The periodontal bacteria require an innovative strategy of vaccination developed in cellular biology. Availability of periodontal vaccine would not only prevent or modulate the course of periodontal disease but also enhance the quality of life of people for whom periodontal treatment cannot be easily obtained[1].

2. Fundamentals of vaccination

"Vaccination is the development of immunity or resistance to infection, after a secondary response (booster) that is adequate to consider the individual immune to a subsequent infection."

Types of vaccination[2]

Active immunization: Here, an individual immune system is stimulated by administrating killed or live attenuated products derived from micro-organisms.

Passive immunization: Here, the antibodies formed in one individual are transferred to another.DNA vaccination: Here, DNA plasmids encoding genes required for antigen production are transferred to an individual.

Characteristics of an effective vaccine[3]

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- Safety.
- Protectivity.
- The ability to provide sustained protection.
- The ability to produce neutralizing antibodies.
- Stimulation of protective t-cells.

Practical considerations

- Cost-effective.
- Biological stability.
- Access.
- Minimum contraindications and side effects.

Indication for periodontal immunotherapy[3]

- Severe periodontal disease with loss of bone around teeth.
- Inflammation and association with oral bacterial infection below the gum line.
- Exacerbated diabetes and CVD (cardiovascular disease).
- Where mouth rinses don't work.

History of periodontal vaccines[3]

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

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

Examples include Vancott's vaccine and Inava endocarp vaccine.

3. Why periodontal vaccine is needed

Eradicating the periodontal disease globally would be the primary demanding role of the periodontal vaccine. The role of any vaccine, however, should also be seen within the context of changes in lifestyle. Need for development of a periodontal vaccine is to lower down the incidence of periodontal disease by providing immunity against the bacteria having the ability to evade host immune response, thereby, invading the tissues. It is also needed because periodontal treatment puts a financial burden on the individuals suffering from it. Availability of vaccine for preventing or modulating periodontal disease would be of great benefit in both developing and developed countries[1].

4. Mechanism of action[3]

Types of periodontal immunization-

Active immunization

(a) Whole bacterial cells.
(b) Sub unit vaccines.
(c) Synthetic peptides.

Whole bacterial cells: Here, the entire cell with its components is inoculated into a host to bring about active immunization.

- Klausen; 1991[4] have shown that levels of serum antibodies to both whole cells and partially purified fimbriae from *P. gingivalis* were elevated in rats immunized with *P.gingivalis* cells and that the activities of collagenase and cysteine proteinases in gingival and periodontal tissues were decreased.

- Kesavalu; 1992[5] observed protection against invasion, but no colonization against *P. gingivalis* in a mouse chamber model by immunization with either killed heterologous Invasive or non-invasive *P. gingivalis* strains. The immune response to whole cells or selected envelope component did not completely abrogate lesions but eliminated mortality.

P. gingivalis has emerged as the leading candidate pathogen in the development of chronic periodontitis. It is a gram-negative, non-spore-forming, non-motile, assacharolytic, obligate anaerobic coccobacillus[6].

The virulence factors of P. gingivalis which have been used as subunits for the development of active immunization are[7]-

(a) Outer membrane protein.
(b) Gingipains.
(c) Fimbriae and
(d) Heat shock protein.

Outer membrane protein: part of a bacterial cell is used in this type for immunization; the part used is Fimbrae or the outer component.

Gingipains: Term coined by Travis and Colleague. Gingipain vaccines are mainly DNA vaccines. DNA vaccines induce both humoral and cellular immunity[8].

Fimbriae: Fimbriae from *P. gingivalis* play an important role in adhesion to oral tissues and are highly immunogenic[9].

Functions of fimbriae are the following:

(a) Adherence to host.

(b) Invasion of oral epithelial cells and fibroblasts.

(c) Modulation of inflammation by the release of interleukin (IL)-, IL-, tumour necrosis factor (TNF).[10] Five types of P. gingivalis fimbriae (TYPE I-V) have been explained recently, depending on their antigenicity.

Heat shock proteins: They have an important role in an inflammatory mechanism, autoimmune disease and atherosclerosis. Homologues of specific stress protein families have been demonstrated to be present in oral bacteria including Fusobacterium nucleatum, Prevotella intermedia, Prevotella melanogenic, A. comitans and P. gingivalis. Rats immunized with P. gingivalis HSP60 showed a decrease in bone loss induced by infection with multiple periodontopathic bacteria. The significant association between HSP90 concentration and microbial colonization has been observed[11].

Synthetic peptides: These require synthesis of linear and branched polymers of 3-10 amino acids based on the known sequences of microbial antigens. Such peptides are weakly immunogenic by themselves and need to be coupled to large proteins to induce an antibody response.

Two ways of developing synthetic peptide vaccines are as follows:

• By deduction of the protein sequence of microbial antigens from RNA sequence data.

• By testing overlapping peptides and by mutational analysis.

Genco; 1992 found that synthetic peptides based on the protein structure of fimbrillin inhibit the adhesion of Pg to saliva-coated hydroxyapatite crystals in vitro[3].

Passive immunization

Passive immunization is short-lived because the host does not respond to the immunization, and the protection lasts only as long as the injected antibody persists.

(a) Murine monoclonal antibody: In this, the antibodies are obtained by inoculating the antigens into mice. These antigens are then injected into the host that brings about passive immunization. Booth,1996 developed a murine monoclonal antibody to P.gingivalis that prevented recolonization of deep pockets by this pathogen in periodontitis patients[12]. It is important to realize that for vaccination to be successful, it should limit the transmission and/or intraoral dissemination of periodontopathic bacteria, and it would appear advantageous for an effective vaccine to induce immunity at three levels[3].

(b)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[13]. Ma; 2000, characterized a secretory IgG antibody against *Streptococcus mutans* produced in transgenic plants.

Genetic immunization

Gene therapy is the insertion of genes into individual cells and tissues to treat a disease. The strategy involves genetic engineering or recombinant DNA technology[3]. They are of two types-

(a) Plasmid vaccines[3]: DNA does not have the ability to grow, whereas plasmids have the ability to grow. With this ability of the plasmids, they are fused with the DNA of a particular pathogen of interest and inoculated in an animal for the production of antibodies. This is then transferred to the host for immunization.

Disadvantages of plasmid vaccines are that in some cases, it may lead to oncogenesis.

(b) Live, viral vector vaccines: A variety of infectious but nondisease, causing DNA or RNA viruses or bacteria have been engineered to express the proteins of a disease-producing organism. The vector enters the body cells where the proteins are generated and then induce humoral or cellular immune responses[14].

Methods of DNA Vaccine administration

(i) Intranasal
(ii) Intramuscular
(iii) Gene gun

Advantages of DNA vaccines

(i) Ease of manipulation

(ii) Stable by nature

(iii) Simple

5. Human Periodontal Vaccines

Three types of vaccines are employed for the control of periodontal disease[15]:

(i) Pure culture of streptococci and other oral organisms.

(ii) Autogenous vaccine: Prepared from dental plaque samples of patients with destructive periodontal disease. Plaque samples are removed from the diseased site. They are sterilized by heat or by immersion in iodine or formalin solution and reinjected into the same patient either locally or systemically.

(iii) Stock vaccine such as vancott's vaccine or Inava Endocarps Vaccines: Prepared from stock microbial stain.

6. Obstacles in the development of the periodontal vaccine

As periodontal disease is multifactorial in origin; eliminating some specific bacteria may not prevent the onset and halt the progression of the disease. Problems such as maintaining adequate levels of antibodies for long enough, generating a T-cell mediated response, multiple antigenicities of various microorganisms remain to overcome. Incidence of a toxic reaction to inactivated whole-cell vaccines[3]. Till now, most of the periodontal immunization studies have targeted on a single pathogenic species. However, a number of the potential candidate antigenic determinants may share sequence homology with other periodontopathic bacteria. These antigens may include phosphorylcholine[16], CPS[17] and heat shock protein (HSP) [18, 19]. The few similarities between the conventional animal models and human beings and the incidence of toxic reactions to inactivated whole-cell vaccines add to our difficulties in developing a single vaccine against all periodontal microbial species.

CONCLUSION

Mechanical debridement and antimicrobial therapy as an adjunct is the current treatment modality available for treating periodontal diseases; development for a new method targeting particular site colonization is an innovative approach towards treating a disease. Though the current status of the periodontal vaccine is unaccomplished, extensive research in the field is expected to develop an effective and safe periodontal vaccine in the near future.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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