ORIGINAL RESEARCH PAPER

Dental Science

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PERIODONTAL VACCINE

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ABSTRACT

Periodontal disease though is multifactorial it is thought to be caused by group of gram negative anaerobic bacteria resulting in destruction of periodontal ligament and alveolar bone. The current treatment of periodontitis is non specific and is centered on removal of supragingival and subgingival plaque by mechanical debridement and surgical procedures. Due to its high prevalence rate this disease has created an innovative interest to find a solution in the form of vaccine. Vaccine is the name applied generally to a substance of the nature of dead or attenuated living infectious material introduced into the body with the object of increasing its power to resist or get rid of a disease. Vaccines are generally prophylactic, i.e. they ameliorate the effects of future infection. One such vaccine considered here is the "Periodontal vaccine". So the aim of this review is to describe in detail about periodontal vaccine.

Introduction:

Selected members of the periodontopathic bacteria play a role in destructive events of periodontitis. With transmission from gram positive to gram negative microorganism progression occurs from gingivitis to periodontitis. (Slots 1986) World workshop of periodontology 1996 has stated Porphyromonas gingivalis, aggregatibacter actinomycetemcomitans and Tanerrela forsythia as a periodontopathic bacteria. Host antibody response occurs to these bacteria in periodontitis. It is possible that immunization could have potential role in eliciting the antibody response against infection and provide benefits in preventing tissue destruction in periodontal disease. Edward Jenner in late 18th century developed and established principle for vaccination. Vaccination is a process that induces specific immune resistance to bacterial or viral infectious diseases. Various investigators have used selected group of periodontal pathogens like Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, whole cells or critical antigens of these bacteria for vaccine preparation. So the aim of the present review is to explain current advances in immunization against periodontal disease.

Immunization against periodontal pathogens:

Since ancient greek, it has been recognized that people who have recovered from plague, small pox, yellow fever rarely contact the disease again. Louis Pasteur to honor jenner's work gave the name vaccine to any preparation of a weakened pathogen that was used to immune against infectious diseases.

I. Active immunization:

Development of resistance by an individual as a result of a specific pathogen or antigen stimuli by active functioning of host immune system that leads to antibody formation and production of immunologically active cells. It sets after latent period. It is more effective and confers better protection than passive immunization. Active immunization has been studied against periodontal disease by using selected group of periodontal pathogens like porhyromonas gingivalis and aggregatibacter actinomycetem comitans using whole bacterial cells either live or killed or by using critical antigens.

Active immunization against selected group of periodontal pathogens:

Members of putative pathogenic subgingival microbiota including porhyromonas gingivalis aggregatibacter actinomycetem comitans, Tanerela forsythia, camphylobater rectus, Prevotella and other species. Periodontitis patients have elevated serum antibody levels to these microorganisms. Cox 1997, selected cell envelop 'ang' porhyromonas gingivalis, Prevotella intermedia and mixture of F. Nucleatum, camphylobater rectus and A. viscosus to activate acquired immunity causing interference with bacterial emergence and disease progression. It can be thus postulated that immunity with antigen cocktail resulted bin inhibition of clinical parameters and can act as a vaccine candidate.

Active immunization against P. gingivalis:

Slots 1985 stated that elimination of specific pathogens like P.gingivalis can control onset and progression of the disease. It has been shown that immunization with P. gingivalis resulted in increased levels of IgG antibody after subcutaneous immunization (McArthur 1989).

Whole cells or vaccine candidates:

Whole cell P.gingivalis either live (viable) or heat/formalin killed has been used as target antigen.

A. Live Whole bacteria:

It comprises of live or viable microorganisms. Bacteria can be attenuated so that they lose their ability to cause significant disease (pathogenecity) but retain capacity for transient growth. Bacause of this, the vaccine produces prolonged immune system exposure to individual epitomes, resulting in increased immunogenicity and production of memory cells. It requires only single immunization, no need of boosters. Clarke 1991, stated that it is possible to modulate infection by whole cell antigen.

Disadvantages:

1. Possibility that microorganisms can revert to virulent form.
2. Exacerbation of existing disease may occur.

Hence heat/formalin killed organisms were investigated.

B. Heat/formalin killed whole bacteria:

The bacteria is no longer capable of replicating in the host. The structure of epitome should be maintained during inactivation. Klausen 1991 had shown reduction in the P.gingivalis induced periodontal tissue loss in rats by heat killed P.gingivalis. Roberts 2004 had shown that heat killed immunization may be associated with the increase in PGE_2 levels.

Disadvantages:

1. Can cause extreme denaturation of protein.
2. Epitomes may be altered due to heat.
3. Chemical inactivation with formaldehyde or other alkylating agents has been shown to be successful.

Disadvantages of whole cell immunization:

1. Suppress overgrowth of P.gingivalis to a limited extend that too only in high titre animals.
2. Large number of P. gingivalis was still present.

Hence critical antigens were evaluated as candidates for vaccine.

Critical Antigens:

A. Fimbriae:

The adhesive agent of P.gingivalis that can be important candidate is an effective vaccine antigen. Evans 1992 stated that fimbriae

induces strong immune response, thus may be helpful for better understanding of role of immune response. Thus fimbriae may be used as vaccine candidate.

B. Haemagglutinin:
Immune response against haemagglutinin can prevent colonization. Kohler 1998 stated that styphimurium satin can induce humoral response against hemagglutinins.. Thus heamagglutinins can be used as potential vaccine candidate.

C. Cysteine proteinases (Gingipains):
It has a highest potential to be used as a vaccine. Both Rgp-A and Rgp B and Kgp can act as vaccine candidate but it is not clear that which will be the best. Genco 1998 stated that antibody directed against catalyst domain may be useful. Nakagawa 2003 stated that opsonin targets on Rgp, Kgp can induce high titres of antibody.

D. Lipopolysaccharides :
Chen 1990 Lipopolysacchaides did not offers immunization against challenge from P.gingivalis.

E. Heat shock proteins:
It shares high sequence homology among periodontopathic bacteria. Choi 2005 stated that HSP-60 can be developed as vaccine against multiple periodontopathic bacteria.

F. Capsular polysaccharide:
Choi 1998 stated that candidate vaccine of capsular polysaccharide and fimbriae was shown to prevent P.gingivalis infection. Gonzalez 2003 immunization of mice with P.gingivalis capsular polysaccharide stimulates IgG response. Further studies should provide insight into important differences in host adaptive immune response to P.gingivalis capsular polysaccharide.

G. Protein Antigen:
It is an outer membrane protein that has coaggregation property. Protein antigen 75,57,41,46,35 Kda and 19 Kda are induced in coaggreagation and therefore in pathogenesis. Momoi 2008 has found that 40 Kda outer membrane protein are effective antigen for induction of protective immune response.

Active immunization against Aggregatibater actinomyce temcomitans:
Gram negative capnophilic AAC has been has been identified as a causative agent in localized aggressive periodontitis. In combination with other pathogenic bacteria it is also clearly related to disease activity in chronic periodontitis. A specific antibody reaction against fimbriae, leukotoxin and capsular polysaccharides has been found

A. Fimbriae:
Baiker 1999 found IgG_4 antibody reactivity against 110 Kda protein of AAC may have protective effect against periodontal disease progression. Engstorm 1999 found that salivary gingival crevicular fluid and serum specific IgG subclass antibodies against AAC leukotoxin.

II. Passive Immunization
Active immunization is specific immunization which confers specific immunity, which is long lasting but there is a risk of severe complications. It is doubtful that active immunization against periodontal disease can be used in humans in near future since it is difficult that layman will understand importance of oral diseases. Passive immunity is the transfer of humoral immunity is the form of readymade antibody from one individual to another. Natural passive immunity is when maternal antibodies are transferred to fetus through the placenta.

Advantages:
1. Immediate protection
2. Specificity and versality

Disadvantages
1. Short lived
2. No immunological memory
3. Risk of being infected by same pathogen later.

Specific antibodies are produced by injecting an antigen into a mammal such as rabbit, rat for small quantities of antibody or goat ,sheep and horse for large antibodies. Antibody secreting lymphocytes are isolated from animal and immortalized by fusing with other cell line know as Hybridoma. This hybridoma cells are cloned to generate same antibody known as monoclonal antibody (Kabir 2002).

Development of passive immunization:
Development of passive immunization system that blocks two colonization factors of P.gingivalis are monoclonal antibody neutralizing coaggreggation factor and monoclonal antibody neutralizing heamagglutinin.

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 Advantages:

1. Higher stability
2. Higher degree of functionality and
3. Protection against colonization by S mutans.

Genetic Immunization:
By the early 1990's, scientists had begun to study new approaches for the production of vaccines that differ in structure from traditional ones. The strategy involves genetic engineering or recombinant DNA technology

Plasmid vaccines:
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.

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.

Methods of DNA vaccine administration:
It can be administered through:
Intranasal
Intramuscular
Gene gun

Procedure:
Insert genes to be expressed (peptide antigen genes,GM-CSF genes, IL2 gene etc.,) into plasmid vector. Then prepare vaccine (usually an adjuvant of some type plus naked plasmid DNA). Genes are expressed in skeletal muscle cells or adipocytes where they facilitate an immunologic response.

Advantages of DNA vaccines
- The ease of manufacture
- Stable by nature
- Simple

Hurdles in periodontal vaccine development:
1. Periodontal disease is a multifactorial disease. Hence, elimination of certain bacteria may not prevent the onset and progression of the disease.
2. Problems such as maintaining adequate levels of antibodies for long enough, generating T-cell mediated response, multiple antigenicities of various microorganisms remain to

overcome.

3. The few similarities between the conventional animal models and human beings, and incidence of toxic reactions to inactivated whole cell vaccines add to our difficulties.

Conclusion:

Advances in our understanding of critical role of host response in the progression of periodontal disease and immunization strategies against periodontopathic bacterial infections might be feasible and may raise protective immunity against periodontitis. Thus periodontal vaccine which seems of distant dream today may be the reality of tomorrow.

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