



RESEARCH ARTICLE

PERIODONTAL VACCINE- A REVIEW ARTICLE

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ABSTRACT

Vaccination is induction of immunity by injecting a dead or attenuated form of a pathogen. Periodontal diseases are one such group of infectious bacterial diseases, against which vaccine research is still going on. The complexities in the etiopathogenesis of the periodontal diseases have been the prime obstacle in the hunt for vaccine. The availability of periodontal vaccine would not only prevent or modulate the course of periodontal diseases, but also enhance the quality of life of people for whom periodontal treatment cannot be easily obtained.

Key words:

Periodontitis,
Vaccine,
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INTRODUCTION

Vaccination is a process that induces specific immune resistance to a bacterial or viral infection (Kudryar *et al.*, 2011). It had long been recognized that individuals who recovered from a disease developed subsequent resistance to the same. Simulating the above thought, it was seen that vaccines, which contain milder infectious agents when given, evoke an immune response and induce specific immunity and have successfully prevented several infectious diseases for many years, and are still being investigated for many others. Vaccination is induction of immunity by injecting a dead or attenuated form of a pathogen (Roderich, 2004).

Key Features of a Successful Vaccine

- It should be safe to administer
- It should induce the right sort of immunity
- Vaccine should be effective against the particular infectious agent and prevent the disease

- It should be stable and have a long shelf life.
- Vaccines should be affordable by the population at which they are aimed (Sharma N, Khuller, 2004).

Development of periodontal vaccine

Vaccination against bacterial/viral infectious diseases has progressed immensely throughout the 20th century. Periodontal diseases are one such group of infectious bacterial diseases, against which vaccine research is still going on. The complexities in the etiopathogenesis of the periodontal diseases have been the prime obstacle in the hunt for vaccine. Till date, no preventive modality exists for periodontal disease and treatment rendered is palliative (Malhotra, 2011). The mouth and the nose are the principal portals of entry of infectious agents and allergens into the human body. Approximately two thirds of all the pathogens infect humans via these routes. The combined mucosal surfaces of the body comprise a considerable area of some 400 m² to which mouth contributes about 240 cm², which must be protected from invasion by infectious agents and penetration by toxins and allergens. Though in humans a highly sophisticated and complimentary host defense system is present, there are some

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microorganisms that evade the host defenses and are responsible for disease production (Michael *et al.*, 2012). A new milestone was achieved after the prime pathogens, Porphyromonas gingivalis and Actinobacillus actinomycetemcomitans, were implicated in the etiology of periodontal disease. Now, the vaccine research has shifted toward identification of valid antigenic targets/molecules of P. gingivalis and A. actinomycetemcomitans involved and thus induction of suitable immune response. The availability of periodontal vaccine would not only prevent or modulate the course of periodontal diseases, but also enhance the quality of life of people for whom periodontal treatment cannot be easily obtained (Malhotra, 2011).

Types of periodontal immunization

Active immunization

- Whole bacterial cells
- Sub unit vaccines
- Synthetic peptides as antigens

Passive immunization

- Murine monoclonal antibody
- Plantibodies

Genetic immunization

- Plasmid vaccines
- Live, viral vector vaccines

Active Immunization

Active immunization has been studied using whole bacterial cells, outer components or synthetic peptides as antigens. The results showed that the progression of periodontal diseases could be prevented by immunization.

Whole bacterial cell

Klausen *et al* reported that the 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 the activities of collagenase and cysteine proteases in gingival tissues as well as periodontal tissue loss were decreased. In squirrel monkeys, immunization with whole cells of monkey isolates (P. gingivalis strain 1-372) increased the level of anti-P. gingivalis IgG antibody in serum and significantly reduced colonization in gingival crevice. Bone density was significantly decreased in ligated teeth from nonhuman primates immunized with whole cell antigens of P. gingivalis and Prevotella intermedia (Ishikawa *et al.*, 2000).

Outer components

In this type, a part of the bacterial cell is used for immunization. Either the outer component or the fimbriae is used. Fimbriae from P. gingivalis play an important role in adhesion to oral tissues and are highly immunogenic. Evans in 1992 reported that immunization with highly purified P. gingivalis fimbrial preparations as well as whole cells and soluble antigens of P. gingivalis protected against periodontal destruction induced by P. gingivalis in gnotobiotic rats. They suggested that fimbrial protein might serve as a model of effective vaccines against periodontitis.

Bird in 1995 showed that immunization of experimental animals with an outer membrane preparation isolated from P. gingivalis induces elevated levels of specific antibody and provides protection against the progression of periodontal disease. Chen in 1995 demonstrated that immunization with a purified outer membrane protein reduces the activities of collagenase, gelatinase and cysteine proteases in gingival tissues. However, it did not prevent periodontal bone loss (Gupta *et al.*, 2016).

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 antibody response.

Two ways of developing synthetic peptide vaccines are as Follows

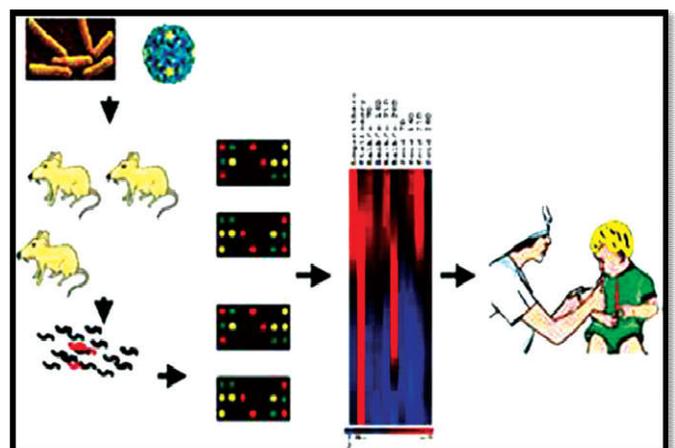
- By deduction of the protein sequence of microbial antigens from RNA sequence data.
- By testing overlapping peptides and by mutational analysis
- Genco; 1992 found that synthetic peptides based on the protein structure of fimbriin inhibit the adhesion of Pg to saliva-coated hydroxyapatite crystals *in vitro*.⁷

Passive Immunization

Murine monoclonal antibodies

In this, the antibodies are obtained by inoculating the antigens into mice. These antigens are 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.

Passive immunization of humans utilizing P. gingivalis monoclonal antibodies temporarily prevents colonization of P. gingivalis. Kaizuka *et al* (2003) showed that a human monoclonal antibody (Hu MAb – HMGD1) that is capable of recognizing the 43 and 49 KDa proteins from P.gingivalis and inhibiting the haemagglutinating ability of P.gingivalis may prove useful in passive immunization against periodontitis, with safety and efficacy studies pending (Kudiyar, 2011).



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 delivered vaccines. A recent approach using plantibodies has been suggested for vaccination strategies. It utilizes molecular biological techniques to express bacterial or viral antigens in plants, which could be used as orally administered vaccine candidates. Lehner *et al* (1995) in a study created secretory antibodies with heavy and light chains, J Chain and secretory components. Ma *et al* (1998) have characterized a secretory IgG antibody produced in transgenic plants (such as plantibodies) that was more stable and exhibited a higher functional affinity than the native antibody as well as affording protection against *Streptococcus mutans* colonization (Kudryar, 2001).



Genetic Immunization

This strategy involves genetic engineering or recombinant DNA technology

There are two types:

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 non-disease 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 (Barry, 1997).

Limitations of periodontal vaccines

The development of vaccines is a complex process that requires substantial resources over a long period of time. Currently, approximately 40% of vaccine projects are directed towards bacterial pathogens.

Additionally, development of vaccines takes approximately 9-10 years, which is comparable to other biopharmaceutical agents. Human periodontal disease is multifactorial caused by manifold pathogens. The multiplicity of pathogenic organisms indicates that vaccine design against periodontitis is very complex. Bacterial whole cells or crude extracts preparation for vaccination is not desirable because the antigenic determinants of bacteria potentially possess a high risk of cross reactivity with human counterparts. Finally, animal models for vaccine trials may pose inconsistencies with human models in major histocompatibility complex restriction of antigens presented by antigen presenting, thus obscuring the immunodominant epitope(s).

Future Considerations

There is a need for a better understanding of the infections in periodontitis. The majority of studies that can be linked to vaccine trials have been focused on *P. gingivalis*. Although it appears clear that this pathogen is involved in periodontitis, other pathogens may be more critical in the early development of the biofilm resulting in periodontitis. The foremost area of concern is the development of a vaccine that is an admixture, targeting multiple bacterial antigens. Vaccines targeting the specific periodontal pathogen involved or the antecedent plaque organisms may be the best approach possible. Further studies are needed to develop scientific models for studies of naturally occurring periodontitis. The effect of trauma induced by ligature placement alone will, in itself, cause an inflammatory response with bone loss. Thus, the induced mechanical trauma from ligatures will mask any positive impact of infection prevention in a vaccine project. Additional studies are, however, necessary to find a suitable model for vaccine trials. Recent advent of nanotechnology opens an entire array of nanospheres and liposomes for controlled release of protein or nucleic acid for the delivery of vaccine in adequate amounts. Delivery routes, such as oral drops, nasal spray, dermal patch and subcutaneous or intramuscular injections are to be studied. Local delivery of vaccine is also another option. Plantibodies that can be used orally could also evolve as one of the major modes of administration due to its ease of development and efficacy.

Conclusion

Major efforts have been dedicated to the development of vaccines against serious diseases, highly prevalent diseases, and diseases without effective treatments. With regard to periodontitis, there are well-established treatment modalities for chronic periodontitis, the most common type of periodontitis. Whether there is merit in developing a periodontal vaccine for the prevention of periodontitis in general, and for special risk populations, must be considered before major efforts can be pursued in periodontal vaccine development. Recent findings of associations between periodontitis and other systemic diseases may provide a rationale for the development of a vaccine against periodontitis, especially a vaccine that could have additional benefits and reduce risks for other diseases (Gupta, 2016).

REFERENCES

Barry MA, Johnston SA. 1997. Biological features of genetic immunization. *Vaccine* 15:788-91.

- Evans RT, Klausen B, Sojar HT, Bedi GS, Sfintescu C, Ramamurthy NS, *et al.* 1992. Immunization with *Porphyromonas (Bacteroides) Gingivalis fimbriae* protects against periodontal destruction. *Infect Immun*; 60:2926-35.
- Gupta C, Deepa D. 2016. Periodontal vaccine: A new vista in periodontology - A review. *J Curr Res Sci Med.*, 2:10-3.
- Ishikawa I, Nakashima K, Koseki T, Nagasawa T, Watanabe H, Arakawa S, *et al.* 1997. Induction of immune response to periodontopathic bacteria and its role in pathogenesis of periodontitis. *Periodontology* 200014:79-111.
- Kudiyar N, Dani N, Mahale S. 2011. Periodontal vaccine: A dream or reality. *J Indian Soc Periodontol*, 15:115-20.
- Maheaswari R, Sivasankar K, Subbarayan S. 2014. Toll gates: An emerging therapeutic target. *J Indian Soc Periodontol.*, 18:686-92.
- Malhotra R, Kapoor A, Grover V, Tuli AK. 2011. Periodontal vaccine. *Indian J Dent Res.*, 22:698-705.
- Michael CL, Peter LM. 2012. Oral microbiology and the immune response. In: Richard LJ, Robert BA, Martilyn LS, Donald J. LeBlanc, editors. *Oral Microbiology and Immunology*. 1st ed. 2006. p.
- Reid R, Roberts F. 2005. Textbook of pathology illustrated. 6th Ed. Churchill Livingstone.
- Roderich N. Immunology. In: Brooks GF, Butel JS, Morse SA. editors. 2004. Javetz, Melnik and Adelberg's Medical Microbiology. 23rd ed. p. 121.
- Sharma N, Khuller N. 2010. Periodontal Vaccine: A New Paradigm for Prevention of Periodontal Diseases. *J Oral Health Comm Dent.*, 4:23-8.
