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Dental Caries Vaccine - A Current Update

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ABSTRACT

Dental caries is a bacterial infection that causes progressive demineralisation and destruction of the calcified structures of the teeth leading to cavitations. It is a multifactorial disease. Dental caries involves the formation of a biofilm around the tooth structure. Biofilm consists of cariogenic bacteria and the substrate upon which it acts. Cariogenic bacteria release acids during the process of fermentation of the substrate and these in turn cause demineralisation There are numerous intraoral microbes that play a key role in the development of dental caries or tooth decay. *Streptococcus mutans* are the most important group of cariogenic bacteria. The other bacteria playing key roles in caries development are *Streptococcus sobrinus* and *Lactobacillus* .The worldwide prevalence of dental caries is very high. The incidence of dental caries can be prevented to a certain extend by good oral hygiene habits, dietary modifications and fluoride application. Recent advances in immunology have raised a possibility for an effective vaccine against dental caries. Active immunisation, Passive immunisation and DNA vaccines for the prophylaxis of dental caries are under research. Active immunisation for dental caries utilizes the protective effect of salivary IgA antibodies to *S.mutans* or *S.sobrinus*. The *S.mutans* components that are involved in adhesion, glucan formation or binding, or in cell wall synthesis are targeted by the vaccine. Passive immunisation may be achieved by administration of pre-formed immune-reactive serum or antibodies. Murine monoclonal antibodies, egg-yolk and bovine milk immunoglobulins generated against *S.mutans* has been used to control the dental caries in humans. Research studies have shown that DNA vaccines are capable of inducing the synthesis of IgA antibodies against *S.mutans* which would further prevent the adhesion of the bacteria to the tooth surface .This article reviews the current status of dental caries vaccination.

Keywords: dental caries, vaccination, *S.mutans*, biofilm

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INTRODUCTION

Dental caries is a bacterial infection that causes progressive demineralization and destruction of the calcified structures of the tooth, which are enamel, dentin and cementum. Dental caries causes cavitation of the tooth structure as it progresses. The formation of a biofilm around the tooth structures is the first step in caries initiation. Biofilm comprises of various kinds of cariogenic bacteria and the substrate upon which it acts. Cariogenic bacteria release acids which causes demineralization of tooth. Over a period of time demineralisation leads to cavitation.

The cell surface of cariogenic bacteria contain polymer matrix of glucans and virulence antigens. These factors aid in their organization and adhesion within the biofilm. In addition, it makes these microbes resistant to antibodies and antimicrobials. Though there are wide variety of pathogens involved in carcinogenesis, the chief pathogen is *Streptococcus mutans*, as it predominates in the formation of caries. The other bacteria playing key roles in caries development are *Streptococcus sobrinus* and *Lactobacillus*. Advancements in immunology and microbiology lead to the evolution of numerous vaccines against many microbial diseases.

The idea of prophylactic immunisation against dental caries is in prevalence for past few decades. The researches aim at interfering the adhering mechanisms of the bacteria and in the development of DNA vaccines. Mucosal route is the most preferred route of administration. Meanwhile other routes of administration such as oral, intranasal, tonsilar, minor salivary glands, rectal, systemic and gingivo-salivary route are also under research.[1-5]

Active Immunisation

Active immunisation for dental caries utilizes the protective effect of salivary IgA antibodies to *S.mutans* or *S.sobrinus*. *S.mutans* components that are involved in adhesion, glucan formation or binding, or in cell wall synthesis are targeted by the vaccine. Three protein antigens are the focus of attention which are, the surface fibrillar adhesions (AgI/II also called Pac or antigen B and P1), the glucosyl transferases, and the glucan-binding proteins. These three proteins are associated with the virulence and surface adhesion of *S.mutans.*

Intact proteins, derived, recombinant or synthetic peptides and DNA vaccines that code for any of these antigens or their combinations were seem to be effective in generating adequate protection. Effective usage of these with suitable adjuvant through mucosal route showed to increase the antibody levels.[6] Mucosal immunisation stimulates common mucosal immune system and can induce salivary S-IgA antibodies.Immunisation at local lymphoid tissues including gut-associated lymphoid tissue and nasopharynx associated lymphoid tissue results in

synthesis of S-IgA antibodies. Intramuscular or subcutaneous immunisation leads to synthesis of serum antibodies which are of IgG type and they can reach the dental surface only through gingival crevicular fluid. They are more potent, efficient, and are more safe.

The introduction of virulent *Streptococci* and high sucrose diet following immunisation with these proteins have shown decreased colonization and caries incidence in animal models. Several human trials have shown that salivary S-IgA antibody synthesis is inducible and in some cases it was possible to interfere with the colonization of *S.mutans*.[7] Though, there is successful immunisation in rodents and primates, it has been shown that there may be cross reactivity between surface antigens of *S.mutans* and human cardiac tissue. This makes immunisation non-viable.[2,8-12]

Passive Immunisation

Passive immunisation may be achieved by administration of pre-formed immunoreactive serum or antibodies. The antibodies introduced may provide immediate protection. Murine monoclonal antibodies, egg-yolk and bovine milk immunoglobulins generated against *S.mutans* has been used to control the dental caries in humans. Monoclonal secretory antibodies of IgA type to adhesins of *S.mutans* have shown to prevent colonization of *S.mutans*.

It can be introduced locally and it is safe. These monoclonal antibodies bind to pellicle on the tooth surface. *S.mutans* which is getting bound over it, get phagocytosed, killed and removed by gingival neutrophils. The antibodies that are administrated remain within the oral cavity for a shorter duration of time and hence it is difficult to maintain effective levels of inhibitor antibodies in the biofilm.

The topical application of antibodies following oral prophylaxis is found to be more effective. Oral prophylaxis interrupts the biofilm and the antibodies would prevent the adhesion capacity of the bacteria to form a new biofilm. Passive immunisation is expensive method of immunisation.[13-17]

DNA Vaccines

DNA vaccines are made entirely of DNA. It is a bacterial plasmid which has been designed to express a gene for the antigen of interest in the host cell. They do not replicate in mammalian tissues. The signals contained in them allow them to be grown in targeted bacteria. Also, they have signals that allow inserted antigens to be expressed in mammalian cells.

Research studies have shown that DNA vaccines are capable of inducing the synthesis of IgA antibodies against *S.mutans* which would further prevent the adhesion of the bacteria to the tooth surface. Memory cells can be generated during the initial period following the immunisation.

They are considered superior to the protein based vaccines because of the ease in preparation and administration, ability to induce long-lasting immune response and the ability to induce both cellular and humoral immune responses. Though it has been found effective in rodents, monkeys and other experimental animals, it does not give that good results with larger animals including humans.[18-20]

CONCLUSION

Dental caries is a very common, multifactorial, irreversible, bacterial disease that causes demineralisation, cavitation and destruction of tooth. Prevention is better than cure. The developments in the fields of immunology and microbiology paved way for the evolution of a numerous vaccines. The inability of these vaccines to maintain elevated antibody levels for long duration has been one of the reasons why dental caries vaccines are not popular. [21]Research is in progress for an efficient vaccine for the prevention of dental caries. The appropriate usage of vaccines at an appropriate time in an appropriate individual can reduce the dental caries.

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