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Review Article

Newer Developments in the field of Caries Vaccine- A Review

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***ABSTRACT*:**

A Caries Vaccination is a programmed approach to pre immunized and protect caries prone people mainly children by using proteins present on oral flora bacterial surfaces mainly Streptococcus mutans (antigens) themselves for inducing human body to produce antibodies against these antigens naturally. For decades, a dental vaccine has been the topic of mucosal immunology and infectious disease research. Apparently, the main focus of the dental research is on the development of safe and efficacious oral anti-mutant vaccines. Vaccination against caries is based on the idea that the same principles that apply to mucosal immunity are applicable to protection against caries.

Keywords: Caries vaccine, dental caries, streptococcus mutans, immunity.

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INTRODUCTION:

Dental caries is a disease caused by a group of oral streptococcal micro-organisms, comprised primarily of S. mutans, that occurs in three phases: 1) initial interaction with the tooth surface mediated by adhesins; 2) accumulation of the bacteria in a biofilm and the production of glucose and glucans by the bacterial enzyme glucosyl transferase; and 3) the formation of lactic acid.[1]

Currently various caries preventive strategies are in use like oral health education, chemical and mechanical control of plaque, use of fluorides, application of pit and fissure sealants etc. Many of these approaches can be broadly effective. However, economic, behavioral, or cultural barriers to their use have continued the epidemic of dental disease in the mouths of many people on a global level.[2]

The traditional way of managing dental caries was by a surgical approach of drill and fill. This approach has slowly evolved into a more conservative mode. Various preventive measures have been implicated for the prevention of dental caries, among which is immunization of the population against the disease.[3] The latest approach for combating dental caries is through the development of an effective vaccine that is well suited for public health applications especially in environments that do not lend themselves to regular health care.[2]

Vaccines are an immuno-biological substance designed to produce specific protection against a given disease. It stimulates the production of a protective antibody and other immune mechanisms. Vaccines are prepared from live modified organisms, inactivated or killed organisms, extracted cellular fractions, toxoids, or a combination thereof.[1] As dental caries is multifactorial and occurs as a result of the activity of members of a normal commensal oral microbiota, the development of a vaccine against this disease includes a high level of complexity. Furthermore, due to dental caries not being a fatal disease that can be prevented, developing a vaccine for this pathology requires that the immunogen has extreme effectiveness and does not cause any adverse effects.[4] Hence the present paper focused more on the recent developments on caries vaccine.

RECENT ADVANCES IN CARIES VACCINE PRODUCTION:

1. Sub Unit Vaccines:

Previously, the whole vaccine was introduced into the host to produce an antibody response. This had a potential disadvantage of cross-reaction with heart muscle. To overcome this, Sub unit vaccines are introduced. Here a particular protein antigen of the organism is used as an antigen. Synthetic peptide vaccines based on putative functional domains of glucosyl -transferase developed as sub unit vaccines. They have the advantage of specifically attacking the antigenic surfaces. Antigenic proteins of a different disease causing organism can also be joined together so that, these vaccines can be designed to induce immunity to more than one infection'.[5,6]

2. DNA Vaccines:

The genetic sequence of some oral microorganisms such as *S. mutans* UA159[7] made possible the knowledge of the most important regions of the major antigens that can induce an adequate immune response. Molecular genetics techniques have been applied in the construction of hybrid molecules for this purpose. Thus, new ways of presenting these immunogens have been developed, including DNA vaccines, in which a specific gene is injected and its product generated within the organism. The DNA of *S. mutans* used for the development of this type of vaccine is extracted by mechanical or chemical lysis, and its genetic material there is the encoding gene of the antigenic protein, which will be used for immunization.[8] The immune response induced by DNA vaccines is initiated with the activation of antigen-presenting cells (APCs), and they play a critical role in the induction of this response.

3. Adjuvants:

Adjuvants are molecules to which antigenic peptides are added to achieve a potent immune response. Adjuvant enhances the antigenicity of the antigen by the following ways.

1. It acts as a deposit or reservoir, whereby the antigen can be released progressively.
2. The adjuvant is able to present the antigen directly to the immune competent cells.
3. Some adjuvant acts as chemical immune stimulators of lymphoid cells.

Common adjuvant that has been tried for a long lime is

1. Freund's incomplete Adjuvant- aluminium hydroxide or phosphate.
2. Freund's complete Adjuvant - Freund's incomplete Adjuvant with a suspension of killed tubercle bacilli.
3. Silica particles, Beryllium sulfate
4. Endotoxins

However, important adjuvants used with caries vaccine antigens in the recent research are

1. Mucosal adjuvants eg. Cholera toxin A1 subunit of cholera toxin is replaced with chosen protein antigen segment and cholera toxin becomes a chimeric immunogen.
2. Coupling with carrier microparticles
3. Live bacterial vectors eg attenuated Salmonellal BCG, normal oral-flora
4. Oral administration with recombinant-streptococcus lactis ILl403 carrying S.mutans MT8l48 surface protein antigen gene has been tried in mice.
5. Live viral vectors eg Vaccinia, adenovirus, polio replicons

Thus the addition of adjuvant and antigen together are a significant improvement in the caries vaccination research.

4. Liposomes:

Liposomes are lipid vesicles lined by external liposomal membranes composed of same lipids as the cell membrane (100nm). Any liposoluble antigen can be incorporated to the lipid membrane and any hydro soluble antigen can be included in the internal cavity of the liposome. Studies in rats show doubling in the efficacy of orally administered vaccine from 40% to 80 % with the use of liposomes. Changing lipid composition can modify particle size of liposomes. A first population of small liposome can deliver the antigen rapidly, while a second population of larger liposome delivers antigen slowly. Thus sustained release of antigen can be achieved.[6]

5. ISCOM:

ISCOM are solid particles generated by combining an antigen with a biocompatible detergent and adjuvant, giving rise to minute structures of 35nm. Protein antigens of caries vaccine can be incorporated in them.[6]

6. Biodegradable Micro Spheres:

Composition of microspheres is similar to surgical sutures. Antigens can be incorporated in to microspheres and released by non-enzymatic rapid hydrolysis. Micro spheres can be placed inside the host tissue and sustained long-term release of antigen can be obtained.[6]

7. Bio Adhesive:

Bio adhesive poly D, L- lactide- co-glycolide (PLGA) microparticles can also be used to Incorporate antigens. Liposomes, biospheres and bioadhesives have emerged out as effective method to deliver antigen to the host system.

8. Edible Vaccines:

Creating edible vaccines involves introduction of selected desired genes into plants and then inducing these altered plants to manufacture the encoded proteins. This process is known as “transformation” and the altered plants are

called" transgenic plants". Like conventional subunit vaccines, edible vaccines are composed of antigenic proteins and are devoid of pathogenic genes. Thus, they have no way of establishing infection, assuring its safety, especially in immunocompromised patients. Conventional subunit vaccines are expensive and technology-intensive, need purification, require refrigeration and produce poor mucosal response. In contrast, edible vaccines would enhance compliance, especially in children, and because of oral administration, would eliminate the need for trained medical personnel. Their production is highly efficient and can be easily scaled up. They exhibit good genetic stability. They are heat-stable; do not require cold-chain maintenance; can be stored near the site of use, eliminating long-distance transportation. Non-requirement of syringes and needles also decreases chances of infection. Fear of contamination with animal viruses - like the mad cow disease, which is a threat in vaccines manufactured from cultured mammalian cells – is eliminated, because plant viruses do not infect humans.[9]

ADVANCES IN ROUTE AND TIME OF VACCINE ADMINISTRATION:

Previously the exact time at which caries vaccine could be administered remained confusion. Now it is proposed that Caries vaccines are better given at 6 months to one year of age after teeth have begun to emerge but before the mutans streptococci bacteria have begun to colonize. Present studies state that mucosal immunization with antigens (active) administered through oral or intra-nasal routes and passive immunization with topical application and use of transgenic plants can be effective in protection against and eradication of dental Caries.[6,10]

CONCLUSION:

Preventive part of Paediatric Dentistry has taken long strides in the direction of eliminating dental diseases, especially dental caries. it is like, imagine never having to face your dentist's drill again. Among the numerous studies going on regarding the above, the first and the most important could be caries vaccine. A vaccine is a preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms that is administered to produce or artificially increase immunity to a particular disease. It is basically a Mutant bacteria used against an existing bacteria, to seize its existence.

Vaccines are particularly well suited for public-health applications in environments that do not lend themselves to regular health care. But, at present, initiatives for developing a vaccine against dental caries seem to be stymied, with major research resources directed to other agendas. Few, if any, issues in oral health research could be as compelling as the eradication or the reduction of dental caries.

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