REVIEW ARTICLE

AODMR

Caries Vaccine

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ABSTRACT:

Dental caries is an infectious microbiologic disease of the calcified tissues of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic substances of the tooth.Various preventive measures have been implicated for the prevention of dental caries, among which is immunization of the population against the disease.

Keywords: Caries, Dental Caries Vaccine, Vaccine.

INTRODUCTION

Dental caries is an infectious microbiologic disease of the calcified tissues of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic substances of the tooth.[1] This condition is caused by the production of acids by the bacteria in the biofilm-tooth interface, through the metabolization of carbohydrates, especially sucrose.[2] Although several micro-organisms like S. sobrinus and Lactobacillus, are associated with dental caries[3], streptococcus mutans which is a Gram positive, acidophillic and acidogenic bacterium, is the primary microorganism causing dental caries.[4]

The traditional way of managing dental caries was by a surgical approach of "drill and fill". However 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.[5]

VACCINES

Vaccines are an immune-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.[6]

DENTAL CARIES VACCINE

An interference in the interaction between the bacterial attack and host defense is responsible for dental caries.[3] The development of a vaccine against dental caries includes a high level of complexity as dental caries is a disease resulting due to involvement of many factors and occurs as a result of the change in activity of normally present commensal oral microflora.[7,8,9] 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.[8]

The concept of vaccination against dental caries has existed almost from the time that dental caries was recognized to result from colonization of the teeth by acidogenic bacteria, even though the etiological agents were originally thought to be lactobacilli. Since then, Streptococcus mutans and Streptococcus sobrinus and their relatives, collectively known as mutans streptococci, have become recognized as the principal

organisms responsible for initiating caries in humans.[4]

The search of developing a vaccine against dental caries needs to target the virulence factors of S. mutans as the colonization of S. mutans is the first step in the induction of dental caries.[8]

HISTORY OF VACCINES

Edward Jenner was the pioneer in the field of immunization after he invented vaccine for the small pox virus from the cowpox disease. The term **"vacca"** means **"cow"** and since the cow pox sample was taken from a cow, the name stuck. Louis Pasteur eventually succeeded in developing a vaccine against anthrax and rabies.

Based on the concept of immunization against caries, a vaccine for caries was also tried out. The caries immunization experiments were performed in the 1930s. Lactobacillus was used as an antigen. Immunization against lactobacillus was only partially successful and could not provide adequate protection against caries. This was because it was a mere consequence of caries initiation and was not present in deep carious lesions.

Hence streptococcus mutans became the target in virtually all immunization experiments after their redetection in 1960. S. mutans was recognized as the major pathogen because of its colonizing ability in dental plaque.[10]

TYPES OF CARIES VACCINES

1.Based on active immunization which stimulate secretory IgA (SIgA) production

Mucosal immunization involving direct topical application of immunoglobulins stimulates the production of secretory immunoglobulin A (SIgA) which is specific in saliva, whereas systemic immunization involving intramuscular or subcutaneous application of immunoglobulins induces the production of serum antibodies (IgG), which reaches the dental surface by means of crevicular gingival fluid. The SIgA prevents adhesion of microorganisms to the tooth surface, avoiding the onset of bacterial colonization. If purified antigens of S. mutans are incorporated in the mucosal immune system, the microorganism surface receptors can be blocked and the metabolic functions of bacterial enzymes can be modified. In this way antibodies will be able to significantly reduce biofilm formation and, consequently, the development of caries. The SIgA specific for the antigen I/II interferes with this virulence factor by inhibiting the adhesion capacity of S. mutans and thus their colonization and dental biofilm formation.[11]

2. Based on passive immunization which acts by introduction of specific antibodies to S.mutans in the oral cavity.

Passive immunization against dental caries involves the development of antibodies which can be suitable for topical application. Passive immunization has the advantage of completely avoiding any risk that might arise by active immunization, preventing application of the microorganism or their antigens in the host to achieve immunization. However, in the absence of any active response by the host, there is no immune response induction.[12]

In passive immunization, a preformed antibody which may be taken from immunized bovine milk, eggs, monoclonal antibodies produced in culture and recombinant antibodies produced by transgenic bacteria is introduced orally.[3,13]The administered antibodies are not able to maintain a sufficient levelof inhibitor antibodies in the biofilmas they remain in the mouth only for a few hours.[3]As such a prophylaxis is performed prior to topical application of antibodies against S. mutans, disrupting the biofilm. The antibodies thus applied would act topically on these microorganisms and prevent their adhesion capacity to form a new biofilm.[12]

3.Nucleic acid-based vaccines (DNA)

In DNA vaccines, a specific gene is injected and its product generated within the organism.[14] 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 is the encoding gene of the antigenic protein, which is used for immunization.[15]

Activation of Antigen-presenting cells (APCs)plays a critical role in the induction of immune response induced by DNA vaccines.[16,17,18] DNA vaccines can directly transfect somatic cells in vivo. The antigens expressed by the transfected cells are captured, processed and submitted by APCs via MHC (major histocompatibility complex) as peptides to T lymphocytes in regional lymphoid organs, where antigen-specific T cells are activated.[19]

A DNA vaccine has many advantages which include easy preparation and administration, ability to induce an effective immune response, with stable and persistent expression of antigens in their native conformation.

MECHANISM OF ACTION OF VACCINE

Of the 1-3% of immunoglobulins present in saliva, majority is of Secretory IgA. Other immunoglobulins like IgG and IgM which are derived from the gingival circular fluid are also present. Various cellular components of the immune system like lymphocytes, macrophages and neutrophils are seen in gingival sulcus. Salivary IgA antibodies act against mutans streptococci in the ways given below.[20, 21]

1. The salivary IgA may interact with the bacterial surface receptors as a specific agglutinin,and thus inhibit colonization and subsequent caries formation. Surface glucosyl transferase (GTF) may also be inactivated by interference with one or more of the functional activities of the enzyme resulting in reduced amount of the plaque.

2.By direct immunization of the gut associated lymphoid tissue (GALT), the salivary glands produce secretory IgA antibodies from where sensitized B-cells may be home to the salivary glands. By inhibiting the activity of glucosyl transferase (GTF), the salivary IgA antibodies may prevent S. mutans from adhering to the enamel surface.

3.Gingival cervicular level which involves humoral and cellular components of the systemic immune system mayalso exert its function at the tooth surface. Sufficient amount evidence has shown that the organism is phagocytized after a subcutaneous immunization with S. mutans and it undergoes antigenic processing by macrophages. Macrophages in the lymphoid tissue sensitize T and B lymphocytes preventing the antigen HLA Class complex and releasing IL-1. This induces CD-4 helper and CD-8 cytotoxic suppressor cell response to take place. This interaction plays an essential part in modulating the formation of IgG, IgA and IgM antibodies and lymphocytes.[20-24]

VACCINE ROUTES

Various routes in the body have been used to introduce protective immune responses to dental caries:

ORAL

Many of the earlier studies relied on oral induction of immunity in the gut-associated lymphoid tissues (GALT) to elicit protective salivary IgA antibody responses system. Oral route is not ideal for reasons including the detrimental effects of stomach acidity on antigen, or because inductive sites were relatively distant.[20]

INTRANASAL

Intranasal installation of the antigen, the nasal associated lymphoid tissue (NALT), has been used to induce immunity to many bacterial antigens including those associated with mutans Streptococcal colonization and accumulation.[25]

TONSILLAR TISSUE

Tonsillar tissue shows a dominant immune response to IgG rather than IgA. The palatine tonsils, mainly the nasopharyngeal tonsils, contribute precursor cells to mucosal effector sites such as the salivary glands.[26]

MINOR SALIVARY GLAND

The minor salivary glands populate the lips, cheeks and soft palate. Short, broad secretory

ducts which facilitate retrograde access of bacteria and their products along with the lymphatic tissue aggregates make salivary glands as potential routes for mucosal induction of salivary immune responses. In experiments, those who received labialapplication of GTF had a significantly lower proportion of indigenous S. mutans/total Streptococcal flora in their whole saliva during a 6-week period following adental prophylaxis, compared with a placebo group.[20]

RECTAL

Secretory IgA antibodies have been seen in distant salivary sites following rectal immunization with non-oral bacterial antigens such as Helicobacter pylori or Streptococcus pneumonia. The colo-rectal region has the highest concentration of lymphoid follicles in the lower intestinal tractand as such is considered as an inductive location for mucosal immune responses in humans. Preliminary studies have indicatedthat this route could also be used to induce salivary IgA responses to streptococcal mutans antigens such as GTF.[26]

FUTURE OF VACCINES FOR DENTAL CARIES

The immunization against dental caries should begin as early as the second year of life, as this age group is at a greater risk of developing dental caries. To develop a refined technique for clearing or locking harmful bacteriathe colonization signals and the growth of cariogenic Streptococcus in dental biofilms needs to be understood. The subunits of vaccines contain the structural elements of the Ag I\II adhesin family, GTFs or Gbp B.[20]In synthetic peptide vaccines, caries are inhibited by an immunization with the intact Ag I\II that react experimentally with the proline rich fragments.[27]Conjugate vaccines are produced by conjugating bacterial polysaccharides with functionally associated proteins /peptides.

CONCLUSION

As dental caries is a multifactorial disease, various modalities exist to prevent it like use of fluorides, mechanical and chemical control of plaque, pit and fissure sealants etc. The primary etiologic agents for dental caries are Streptococci mutans, S.sobrinus and Lactobacillus. Streptococcus mutans play a key role for the development of dental caries and a vaccine directed against this microorganism could be a valuable adjunct to existing preventive measures. However further studies need to be done to validate the use of caries vaccine in humans.

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