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Review Article

Caries Vaccine: A Promising Future or a Time-Consuming Gamble?

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ABSTRACT-
Tooth decay, a prevalent dental issue, results from the interaction of bacteria and fermented sugars. Conventional preventive strategies, including proper oral hygiene and fluoride applications, have demonstrated efficacy in reducing the incidence of cavities. Nonetheless, these methods face challenges regarding their overall effectiveness and accessibility. In this context, caries vaccination has emerged as a potentially transformative strategy for the prevention of dental caries, promising enduring protection against this condition. Although research and development in this field are ongoing, there are encouraging indications that this approach may significantly mitigate the risk of cavity formation. Continued investigation and assessment of caries vaccines are essential to comprehensively evaluate their benefits and risks, as well as to create safe and effective vaccines for widespread use in the prevention of dental caries.
Key words: Vaccine, Caries

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INTRODUCTION
Dental caries is still one of the most prevalent preventable diseases worldwide, with prevalence in some countries over 90% in adults and children of age 3-5 years. It is a chronic disease displaying drastic variations in its prevalence.[1,2]Traditional preventive strategies, such as fluoride treatments, daily oral hygiene, and dental sealants, have significantly reduced the incidence of tooth decay. However, these measures are not without their limitations. Fluoride resistance and the temporary nature of dental sealants highlight the need for more sustainable, long-term solutions. Now comes the development of a caries vaccine as a promising alternative. Preclinical studies of immunological interventions have shown that the disease can be interrupted. Clinical trials have indicated that a mucosal immune response to Streptococcus mutans (the primary bacteria responsible for caries formation, offering potential protection against tooth decay) crucial antigens can influence the pathogenesis of dental caries.[3] This article will focus on challenges in making of caries vaccine and also checking its status and whether the time and efforts are worth the wait by comparing it to existing preventive strategies.

BACKGROUND-
Role of S. mutans in dental caries:
The primary habitats for S. mutans are mouth, pharynx, and intestine. Several factors, such as adherence to enamel surfaces, production of acidic metabolites, the capacity to build up glycogen reserves and the ability to synthesize extracellular polysaccharides are present in dental caries. S. mutans and Streptococcus sobrinus have a central role in the etiology of dental caries, because these can adhere to the enamel salivary pellicle and to other plaque bacteria.[4, 5]

CURRENT PREVENTIVE METHODS FOR DENTAL CARIES:

The review answered the research question on the primary prevention of dental caries in adults. It permitted us to understand the improvement and maintenance of oral health at clinical and community levels, involving: (i) fluoride application in the office; (ii) recommending the use of fluoride toothpaste; (iii) performing mouth rinses with chlorhexidine at home; (iv) recommending the use of xylitol; (v) treatments with fluoride varnishes in dental pits and fissures; (vi) more frequent visits to the dentist; (vii) adopting a non-cariogenic diet, i.e., alerting patients to the frequency of sugar consumption; (viii) brushing correctly; and (ix) alerting patients to the protective role of saliva in dental caries.[6]

INTRODUCTION TO THE CONCEPT OF CARIES VACCINE:

Vaccines are immunobiological substances designed to produce specific protection against any given disease. They mainly act through stimulation for the production of a protective antibody and other immune mechanisms. They are mainly prepared from live-modified organisms, nonvital organisms, extracted cellular fractions, toxoids, or a combination of these substances. A caries vaccine is mainly designed to play protective role against the process of tooth decay.[7, 8]In 1924, J. Clarke isolated an organism from carious lesions and called it Streptococcus mutans, because he thought the oval-shaped cells observed were mutant forms of streptococci.[9] While caries is a polymicrobial disease, selective targeting of S. mutans in dental biofilms is viewed as a suitable approach for its prevention. This is mainly because the synthesis of insoluble glucans from sucrose by S. mutans is central for the formation of a stable biofilm matrix that facilitates bacterial colonization of the tooth surface and, at the same time, serves as a diffusion barrier helping to maintain the acidic milieu within which cariogenic bacteria thrive.[10]

NEED FOR CARIES VACCINE:

If compared with traditional strategies of prevention, caries vaccine could be cost-effective because it could prevent dental caries and associated health issues for a long time. It could provide a single dose of protection that can last for years or even a lifetime and also thirdly could reduce the risk of tooth decay in those at greatest risk, including newborns and those with weak immune systems.[11]

CURRENT PROGRESS AND RESEARCH ON TREATMENTS -

ACTIVE IMMUNIZATION

Only few clinical trials have been performed in this field. When humans are immunized with glucosyl-transferases from S. mutans or S. sobrinus, there is a formation of the salivary IgA antibody at modest levels. Enteric coated capsules with crude S. mutans GS-5 GTF antigen preparations which were contained in liposomes, orally immunized some adults.[11]

PASSIVE IMMUNIZATION

When mouse monoclonal IgA or the transgenic plant secretory IgA/G antibody was topically applied, recolonization of the mutans Streptococci did not occur at least for two years after the treatment. Monoclonal antibodies, in the secretory form, are more effective, because they have increased survival times in the oral cavity as compared to IgA. Young children who are not infected with S. mutans during the window of infectivity remain undetectably infected for several years. The Sinche niche in the dental biofilm was filled by other indigenous flora. Experimentally, this could be achieved with the use of the antibody to GTF or GbpB.[12, 13]

THE ROUTES OF ADMINISTRATION

The oral route was used earlier, but it was not effective due to the determinantal effects of the stomach acidity on the antigen and as the inductive sites were far away. The intranasal route targets the nasal associated lymphoid tissues. With the S. mutans antigen, AgI/II12 and the glucan-binding domain of S. mutans, GTF-B11, a protection could be demonstrated. The tonsillar vaccine can induce an IgA response. The tonsillar application of a particular antigen can induce IgA production in both the major and minor salivary glands of rabbits. A labial application of GTF on the minor salivary glands resulted in a lower proportion of indigenous Streptococci/total Streptococcal flora in the whole saliva in next 6 weeks period. The rectal route remotely induces salivary IgA responses to the S. mutans antigen such as GTF.[14]The Cholera and E. coli heat liable enterotoxins, liposomes, microparticles and macroparticles act as adjuvants and help in delivering the dental caries vaccine.[15]

RECENT STUDIES

The S.sobrinus recombinant enolase (rEnolase) is used as a target antigen. rEnolase plus an alum adjuvant was delivered into the oral cavity of rats. It increased the levels of salivary IgA and the IgG antibodies which were specific for this recombinant protein. These results indicated that rEnolase could be a promising and a safe candidate for testing in the trials on vaccines against dental caries in humans.[13- 16]

EVALUATING THE VIABILITY OF CARIES VACCINE-

The primary aetiologic agents for dental caries are Streptococci mutans, S. sobrinus and Lactobacillus.

Through adhesions, S. mutans attaches to the dental pellicle and through the formation of GTF and then glucan, more organisms colonize and lactic acid formation is initiated, thus causing dental caries. An immune intervention can be undertaken by blocking the receptors which are necessary for the colonization of these bacteria or by inactivating GTF. Through these measures, the immunization against dental caries can be achieved. Preclinical studies of immunological interventions have shown that the disease can be interrupted. Clinical trials have indicated that a mucosal immune response to Streptococcus mutans crucial antigens can influence the pathogenesis of dental caries. The dental caries vaccine, when it is used in appropriate individuals at the appropriate time, can reduce the reemergence of the disease.[14- 16]

NANOPARTICLE-BASED ANTICARIES VACCINE

Zeoliticimidazolate framework-8 (ZIF-8) nanoparticles represent a specific category of metal-organic framework (MOF) nanoparticles, distinguished by their remarkable pH sensitivity, biodegradability, and a range of additional beneficial properties. These nanoparticles have found applications in the domain of vaccine adjuvants. Research conducted by Luzuriaga et al. demonstrated that ZIF-8 effectively safeguards the tobacco mosaic virus from denaturing conditions, thereby enhancing its immunogenicity and resulting in elevated antibody titers in mice, without causing any noticeable damage to the skin or vital organs. Furthermore, Zhang et al. developed ZIF-8-based nanoparticles aimed at targeting dendritic cells (DCs) to elicit robust immune responses, thereby establishing a potent platform for combating invasive malignancies and recurrent tumors. Additionally, ZIF-8 nanoparticles have been functionalized with various agents, including poly(ethylene glycol), aluminum, cytosine-phosphate-guanine oligodeoxynucleotides (CpG), and peptides, which have been employed to encapsulate a variety of antigens, such as tumor-associated antigens, bacterial antigens, and viruses, serving as a vaccine delivery system to bolster antigen-specific immune responses. Nonetheless, there has been limited application of ZIF-8 nanoparticle-based adjuvants for encapsulating the PAc antigen from Streptococcus mutans to stimulate an immune response and provide protection against dental caries.[17- 19]

CONCLUSION

Caries development is initiated by the colonization of Streptococcus mutans on the dental surfaces, which subsequently leads to acid-mediated demineralization and the formation of cavities. The expansion of these bacterial colonies is facilitated by the interaction of S. mutans with Antigen I/II receptors, as well as the enzymatic activities of glycosyltransferases, glucan-binding proteins, dextranases, and adhesins. The primary objective of this vaccine is to obstruct the functions of these four key molecules, thereby preventing bacterial colonization and ultimately reducing the incidence of dental caries.

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