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AN OVERVIEW OF PERSPECTIVES AND UPDATES IN IMMUNIZATION FOR DENTAL CARIES

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Abstract:
Dental caries is a non-reversible infectious condition caused by microorganisms. Streptococci mutans, S.sobrinus, and Lactobacillus are the main causative agents of dental caries. S.mutans adheres to the tooth pellicle via adhesions. This leads to the synthesis of GTF and subsequent glucan production, facilitating the colonization of new organisms. Consequently, the initiation of lactic acid formation occurs, resulting in the development of dental caries. To intervene in the immune response, one can inhibit the receptors that are essential for the bacteria's colonization or deactivate GTF. By implementing these strategies, it is possible to achieve immunization against dental caries.

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BACKGROUND:

Oral health is a crucial and indispensable aspect that reflects overall health, well-being, and quality of life. Regrettably, dental caries, an infectious microbial illness that impacts the teeth, continues to be a significant issue for oral health. It is not only limited to affluent countries but is becoming more widespread in impoverished nations worldwide. The World Health Organization has acknowledged the widespread occurrence of dental caries, affirming it as a significant global health issue [1]. As stated in the Oral Health Atlas published by the FDI World Dental Federation, the occurrence of untreated decay in permanent teeth affects approximately 40% of the global population, making it the most widespread condition out of 291 diseases studied in the Global Burden of Disease Study. This condition impacts an estimated 3.9 billion people worldwide [2]. Globally, dental decay affects between 60% to 90% of students and nearly all adults, resulting in frequent pain and suffering [3]. Hence, doctors are required to identify patients who are more susceptible to tooth decay or already have active tooth decay, and administer suitable interventions or preventative measures such as immunization, fluoride treatment, maintaining healthy saliva production, and using antibacterial agents [4].

Dental caries is a permanent microbiological illness that affects the hard tissues of the teeth. It is defined by the loss of minerals in the tooth's structure and the breakdown of its organic components, often resulting in the formation of cavities [5]. Dental caries is a complex disease that results from a combination of factors related to the individual, the causative agent, and the surrounding environment. Immunity is the host's ability to resist harm produced by microbes and their products. Immunity can manifest as either inherent immunity or acquired immunity. Acquired immunity can be obtained by active acquisition or passive acquisition. Saliva contains secreted IgA.

The results of a nationwide oral health study conducted in India indicate that the occurrence rate of dental caries among individuals aged 35-44 is between 80-95 percent. Based on the National Oral Health Survey, the occurrence of tooth decay among those aged 65-74 is approximately 70%. However, recent surveys conducted in several states report a range of 51-95% prevalence. Surveys indicate that caries are frequent in around 58 percent of school students in India. 90 percent of late adolescents and young adults in the United States were found to have dental caries, and 94 percent of all adults with teeth showed signs of either treated or untreated coronal caries[6].

Several caries prevention techniques are presently employed, such as oral health education, chemical and mechanical plaque protection, pit and fissure sealants, and fluoride utilization. Several of these tactics possess the capacity to be efficacious. Nevertheless, the persistence of economic, behavioral, or cultural obstacles has perpetuated the widespread occurrence of dental diseases among numerous youngsters worldwide [7].

DISCUSSION:

Tooth decay, also known as dental caries, is a complex process that occurs when the surface of the tooth interacts with dental plaque and carbohydrates derived from food. Approximately 700 distinct bacterial species have been identified inside the human oral microbiome. The bacteria that are particularly important in the process of cariogenesis are oral streptococci, specifically the mutans group, as well as lactic acid bacteria, such as species of Lactobacillus. In 1924, Clark discovered that Streptococcus mutans thrives in a media that mimics saliva and is present throughout the initial phases of the decay process [8]. In a study conducted by Meiers et al., water spray was collected during the restorative process of carious and noncarious lesions in navy recruits. The researchers discovered many species, among which S. mutans was the only bacterium that was substantially more abundant in carious lesions compared to noncarious lesions [9].

The microbial community in dentinal lesions is highly diversified, consisting of both facultatively and obligately anaerobic microorganisms. These microorganisms belong to many genera, including Actinomyces, Eubacterium, Parvimonas, Bifidobacterium, and Rothia. Dental decay can also result from the presence of many bacteria, including Streptococcus groups mitis, anginosus, and salivarius, as well as Propionibacterium, Enterococcus faecalis, and Scardovia [10].

S. mutans is the primary bacteria responsible for dental caries globally and is regarded the most cariogenic of all oral streptococci [11]. S. mutans is a term used to describe a cluster of seven closely related species that are commonly known as mutans streptococci. Dental caries formation is influenced by various factors, including the ability to stick to tooth surfaces, the creation of acid, the accumulation of glycogen reserves, and the synthesis of extracellular polysaccharides. The bacteria alter the environmental circumstances of the oral flora, facilitating the colonization of other organisms that have specific requirements and promoting the production of dental

plaque. Specialized receptors possessed by S. mutans enable them to adhere to the surface of teeth, resulting in the formation of a viscous environment. After adhering to the enamel salivary pellicle, acidogenic bacteria like mutans streptococci and Lactobacillus produce strong acids, which provide an acidic environment that facilitates the creation of cavities [10,12].

The cariogenic potential of S. mutans is mostly attributed to its distinctive virulence factors, which play a crucial role in the production of dental caries. Moreover, it generates lactic acid through metabolic processes and possesses the capacity to stick to tooth surfaces when sucrose is present, achieved by creating water-insoluble glucans. These glucans, which are polysaccharides, aid in the attachment of bacteria to the tooth surface. The ability of mutans streptococci to produce significant quantities of lactic acid quickly, as well as their ability to withstand severe levels of sugar concentration, ionic strength, and pH, contributes to their effectiveness in developing dental caries [13].
The primary cause of dental decay is the erosion of enamel and dentin minerals in teeth by organic acids, particularly lactic acid, which is produced by microorganisms found in plaque. Taubman and Nash [14] categorized the molecular etiology of dental caries associated with mutans streptococci into three distinct phases. During the first stage, the bacteria attaches to the tooth pellicle through the action of adhesin produced by mutans streptococci, specifically known as antigen I/II. In the second phase, accumulation occurs based on the presence of sucrose, glucosyl transferases (GTFs), and glucan-binding proteins (GBPs) from mutans streptococci. Following the hydrolysis of sucrose into glucose and fructose, mutans streptococci's GTFs produce glucans with diverse α-1,3-linkages and α-1,6-linkages, resulting in varying solubilities in water. During the third and final stage, glucans that were generated engage with GBPs and the glucan-binding domain of GTFs on the surface of mutans streptococci [15,16,17].

In addition, the colonization and proliferation of these bacteria contribute to the buildup of biofilms, which in turn cause the development of dental plaques characterized by substantial quantities of mutans streptococci. When there is a significant buildup of bacteria, together with enough carbohydrates present, it causes the formation of substantial quantities of lactic acid. This acid then causes the breakdown of the enamel structure, resulting in tooth decay [12].

Clarke was the initial individual to separate streptococcus from decayed lesions and recognized its correlation with illness. He subsequently designated his newly discovered species as S. mutans [8]. Subsequently, doubts were raised about its involvement in the development of tooth decay, which resulted in the omission of S. mutans from scientific literature. After about 40 years, the significance of mutans streptococci in the development of tooth decay was once again recognized, confirming its infectious and easily spreadable characteristics. In addition, Heremans et al. [18] and Tomasi et al. [19] discovered and characterized the secretory form of immunoglobulin A (IgA), known as S IgA, in saliva, which offered more detailed understanding of specific immunological components. Bowen established the concept of immunization against tooth decay, demonstrating that monkeys who received immunization with S. mutans had reduced caries compared to those who did not get vaccine. Subsequently, numerous authors in the early 1970s carried out experiments on animals to investigate the effectiveness of immunization against tooth decay. They showed that caries can be prevented by stimulating a specific immune response in the salivary gland region, namely the production of salivary IgA antibodies [21,22]. The continuous flow of saliva, which contains the main immunoglobulin S IgA, helps to cleanse the tooth surfaces. By stimulating the production of salivary S IgA against mutans streptococci, we can establish a primary defense mechanism to prevent the formation of bacterial colonies on the teeth [23]. Subsequent research conducted on rats employed local immunization to stimulate the production of salivary S IgA. This resulted in a decrease in mutans streptococci and the severity of dental caries [22]. Russell et al. have elucidated the potential processes by which salivary IgA antibodies can impede the binding of mutans streptococci to tooth surfaces, both in the presence and absence of sucrose [24].

Commencing immunization against dental caries in the second year of life is advisable, since individuals in this age bracket are at a typical risk for this infection. Both aggressive and passive strategies have demonstrated efficacy in animal models and human clinical studies. Gaining insight into the colonization cues and proliferation of cariogenic Streptococcus in dental biofilms is crucial for developing a precise method to eradicate or immobilize pathogenic bacteria. The components of vaccines consist of the structural elements of the Ag I\II adhesin family, GTFs or Gbp B [25].

Monoclonal antibodies are generated in synthetic peptide vaccines through immunization with the entire

Ag I\II, which interacts with the proline rich segment and experimentally prevents the onset of dental caries [26]. Antibody preparations, both monoclonal and polyclonal, that target multiple N-terminal GTF proteins, effectively suppress the GTF activity [26]. Synthetic peptides were also employed for constriction. These findings indicated that immunization with specific epitopes, which were linked to various virulence traits, could potentially provide protection.

The recombinant vaccine expresses a significant portion of the functional domains. The 42 kDa salivary binding receptor (SBR) of S mutants, AgI\II, which is genetically connected to the A2 and B subunits of cholera toxin, was used to create a chimeric protein. When this protein was administered intranasally, it effectively reduced dental cavities in Fischer rats [27]. Conjugate vaccines are created by combining bacterial polysaccharides with proteins or peptides that have a functional relationship.

Active immunization and passive immunization are two methods of acquiring immunity against a certain disease.

There have been a limited number of clinical trials conducted in this area.Immunizing humans with glucosyl-transferases from S. mutans or S. sobrinus leads to the production of salivary Ig A antibodies at moderate levels. Oral immunization of adults was conducted using enteric coated capsules containing liposomes that contained crude S. mutans GS-5 GTF antigen preparations [28]. The re-emergence of mutan Streptococci in young people after a dental prophylaxis was impacted by a mucosal immunization with GTF [29]. Topical application of GTF on the lower lip resulted in a delayed appearance of S mutans. Application of mouse monoclonal IgA or transgenic plant secretory IgA/G antibodies on the surface prevented the regrowth of mutans Streptococci for a minimum of two years following the treatment. Monoclonal antibodies in their secretory form are more efficient due to their extended lifespan in the oral cavity compared to IgA [29]. Young children who do not contract S.mutans within the critical period of susceptibility remain asymptomatic carriers for several years. The vacant ecological niche in the dental biofilm was occupied by other native vegetation. Practically, this might be accomplished by utilizing the antibody to GTF or GbpB [30].

Previously, the oral route was employed, but it proved ineffective due to the deleterious impact of stomach acidity on the antigen, as well as the considerable distance between the inductive sites. The intranasal administration specifically targets the nasal related lymphoid tissues [31]. A demonstration of protection was achieved using the S. mutans antigen, AgI/II12, and the glucan-binding domain of S. mutans, GTF-B11. The tonsillar vaccination has the ability to elicit an IgA immune response. Applying a specific antigen to the tonsils can stimulate the synthesis of IgA in both the major and minor salivary glands of rabbits [32]. Applying GTF to the small salivary glands on the lips led to a decrease in the ratio of native Streptococci to the total Streptococcal population in the entire saliva throughout the following 6-week period. The rectal administration elicits salivary IgA immune responses to the S.mutans antigen, specifically GTF. Heat-labile enterotoxins of Cholera and E.coli, along with liposomes, microparticles, and macroparticles, function as adjuvants to facilitate the administration of the dental caries vaccine [32].

The S sobrinus recombinant enolase (rEnolase) serves as the designated antigen of interest. Rats were administered with rEnolase together with an alum adjuvant via the oral cavity. The levels of salivary IgA and IgG antibodies specific to this recombinant protein were elevated. The results suggest that rEnolase shows promise as a safe option for testing in human trials for vaccinations against dental caries [33]. A study was conducted to investigate the inhibitory effects of lozenges containing egg yolk antibodies (immunoglobulin Y [IgY]) against the Streptococcus mutans cell-associated glucosyltransferase (CA-gtf) in healthy young individuals. The study's findings demonstrated that the lozenges containing anti-CA-gtf IgY were effective in inhibiting the oral colonization of mutant Streptococci in healthy young individuals. When vaccines are made and delivered correctly, they appear to have no associated dangers. An important concern arises when the sera of certain individuals with rheumatic fever exhibit a serological cross-reactivity between antigens found in heart tissue and specific antigens derived from haemolytic Streptococci. The investigations found that antisera from rabbits, which were immunized with both the entire cells of S. mutans and a high molecular weight protein of S. mutans, showed a cross reaction with normal rabbit and human heart tissues. Immunologically cross-reactive polypeptides, which resemble those found in human heart tissue and rabbit skeleton muscle myosin, are present in the cell membranes of S. mutans and Streptococcus ratti. Understanding the indicators of the colonization and proliferation of cancer-causing Streptococci in dental biofilms will assist us in developing more sophisticated and knowledgeable methods to prevent

the entry of these harmful bacteria. Gnotobiotic rats consuming intact S. mutans exhibit a specific production of S-IgA. The presence of secretory immunoglobulin A (S-IgA) was found to be associated with a decreased occurrence of dental caries following vaccination. The primary objective in the majority of the experiments was to initially vaccinate the animals with an antigen derived from S. mutans, which was combined with an adjuvant, as needed, to achieve elevated levels of antibodies. Subsequently, the same organism was introduced into the mouth and the animals were put on a diet rich in sucrose. Due to dental caries meeting the requirements of an infectious disease, efforts have been made to explore the potential of vaccination as a means of prevention. The justification is that immunization with S. mutans should stimulate an immunological response, thereby inhibiting the bacterium from establishing itself on the tooth surface and so preventing decay. The vaccine can be administered concurrently with the diphtheria and tetanus vaccines. Subsequent immunizations could be administered periodically to enhance and maintain lifelong immunity [34].

CONCLUSION:

The eradication of one of the symbiotic oral microbes is an additional significant challenge for the development of the caries vaccine. Advancements in technology, such as nano delivery technologies, along with enhanced understanding, have the potential to facilitate the development of vaccines, enabling their evaluation in human clinical trials. Prior to the distribution of any vaccination, it is imperative to carefully evaluate the potential long-term consequences of disturbing the commensal microbiota. The research substantiates the correlation between Streptococcus mutans and dental caries. Although the utilization of fluoride mouth rinses, varnishes, and professional cleaning has contributed to a significant reduction in dental caries, there remains a substantial likelihood of caries development, especially among individuals from lower socioeconomic backgrounds. Nevertheless, there have been no vaccinations that have been brought into the commercial market so far due to the challenge of stimulating and maintaining effective antibodies in oral fluids. The caries vaccine will have a significant impact in the future as it interferes with the metabolism of the primary causative agent. Therefore, a caries vaccine remains the most economically efficient strategy in the long run for addressing the issue of dental caries.

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