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Review Article

Dental caries vaccine: A comprehensive review

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ABSTRACT:
Dental caries continues to be one of the most prevalent infectious diseases affecting humanity. Cariogenic microorganisms infiltrate the dental biofilm from an early age and can later proliferate under conducive environmental conditions, leading to disease manifestation. In response to these infections, adaptive host defenses are activated and can be detected in oral fluids, particularly in saliva and gingival crevicular fluid. This review aims to examine strategies for inducing mucosal host defenses through immunization to combat dental caries attributed to mutans streptococci.

Keywords: Vaccine, Dental caries, Cariogenic

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INTRODUCTION

Evidence suggests that dental practices existed as far back as 5000 B.C., though early theories attributed tooth decay to a mythical "tooth worm." The term "dental caries," derived from the Latin "caries" signifying decay, began appearing in written records around 1634, initially used to denote physical cavities in teeth.[1]Today, dental caries is recognized as a disease with a long history, affecting a significant portion of the global population. It is defined as a chronic infectious condition caused by cariogenic bacteria that adhere to the tooth surface, where they metabolize sugars to generate acids that progressively demineralize the tooth structure. Dental caries encompasses both the pathological process of tooth decay and the structural damage that results. This degradation occurs within the dental biofilm, a complex community of microorganisms. Remarkably, this biofilm maintains metabolic activity across fluctuating pH environments, ultimately causing the breakdown of the tooth's hard tissues.[2, 3]

ETIOLOGY

Onset of dental caries occurs when the microbial community within the oral biofilm, which usually maintains a balanced state, shifts towards a population that is acidogenic, aciduric, and cariogenic as a result of frequent sugar intake. This change may go unnoticed clinically or lead to a decrease in mineral content within the tooth's enamel and dentin.This mineral loss can eventually manifest as a visible cavity. It is essential to recognize that the caries process can progress without the presence of visible lesions. Consequently, dental caries is classified as a disease rooted in diet and microbial activity, requiring both a decay-promoting biofilm and a regular consumption of fermentable sugars, such as glucose, fructose, maltose, and sucrose, from dietary sources. Furthermore, complex inter-play of behavioral, psychological, and social elements significantly influence the advancement of this condition. The protective role of fluoride against caries is well-established means that inadequate exposure to fluoride should be recognized as a contributing factor in the development of tooth decay.

Bacteria that metabolize sugars into acids within dental plaque are classified as acidogenic, while those capable of withstanding acidic conditions are termed aciduric. Bacteria of both categories are integral to the development of dental caries. Acidogenic bacteria, which are often also aciduric, create an acidic environment, whereas aciduric bacteria contribute the biomass of plaque, allowing acids to remain in contact with the tooth surface. Continuous exposure to acids and insufficient plaque removal are significant contributors to the initiation of dental caries. Key bacterial and fungal species found in plaque that are implicated in the caries process include:

- Streptococcus mutans and other low-pH streptococci
- Rothia spp.
- Actinomyces spp.
- Lactobacillus spp.
- Bifidobacterium spp.
- Candida albicans
- Selenomonassputigena

Among these microorganisms, S. mutans is particularly notable for its role in dental caries. While S. mutans is often associated with dental caries, studies have shown that its presence is not a prerequisite for the development of cavities, as these lesions can occur even when the bacteria is not detected.[6- 9]

CARIES VACCINE

Extensive research, encompassing laboratory experiments, animal studies, and human clinical trials, has clarified crucial aspects of vaccine creation. Specifically, it has been demonstrated that significant virulence factors of Streptococcus mutans, such as Ag I/II (which aids in surface adherence), glucosyl transferase (responsible for glucan synthesis), and glucan-binding protein (which assists in glucan attachment to surfaces), are capable of triggering a targeted immune response. Furthermore, research indicates that utilizing multiple antigens or functional components of the genome associated with these virulence factors yields a more robust immune reaction in the host compared to a single gene vaccine or a complete genome of a singular antigen. To improve host responses, the incorporation of adjuvants has been explored, and various antigen administration routes have been examined. Recently, several promising vaccines, including pGJA-P/VAX, LT derivative/Pi39-512, KFD2-rPAc, and SBR/GBR-CMV-nirB, have shown promise in animal models. However, further investigation into novel virulence targets is necessary. To effectively tackle this issue, it is imperative to conduct joint research across multiple institutions and initiate human clinical trials. Furthermore, it is vital to garner the attention and financial support of funding agencies and public health experts. Dental caries represents an irreversible, complex opportunistic infection, with treatment costs contributing to its status as a public health concern. While extensive research has been conducted, a widely available vaccine remains undeveloped. Research objectives have evolved, informed by past experiences. Drawing on past research, future efforts should prioritize collaborative, multi-site studies focusing on multigene DNA or recombinant vaccines. These vaccines should incorporate optimal immune-boosting agents and delivery methods, such as nasal or under-the-tongue administration. Additionally, new vaccine targets should be identified, and stimulating interest from funders and public health stakeholders is necessary to overcome economic barriers.[10]

ACTIVE IMMUNIZATION AGAINST DENTAL CARIES

Human studies investigating active immunity against mutans streptococci are relatively few, with most focusing on oral administration. Notably, Mestecky et al. observed that ingesting capsules containing Streptococcus sobrinus effectively triggered the production of secretory IgA.In contrast, Gahnberg and Krasse reported no salivary IgA response following oral administration of heat-killed S. sobrinus cells in a small group (six in number) of participants. Conversely, when seven individuals were orally immunized using enteric-coated capsules with 500 μg of S. mutansglucosyltransferase (GTF), they exhibited a rise in salivary IgA antibodies specifically targeting that antigen. Furthermore, intranasal or topical application of the same antigen to the tonsils also stimulated salivary IgA antibody production.[11- 14]

PASSIVE IMMUNITY AGAINST DENTAL CARIES

The use of localized passive immunization has recently become a focus of attention as a potentially secure and effective way to control S. mutans and prevent dental caries. Studies suggest that repeated topical application of anti-AgI/II monoclonal antibodies (through localized passive immunization) to the primary teeth of Rhesus monkeys significantly reduced bacterial colonization and the development of cavities. Furthermore, Ma et al. successfully isolated and produced a plant-based secretory antibody. By cross-pollinating genetically modified plants, they created a high-molecular-weight secretory immunoglobulin that remained in the oral cavity for an extended period, offering specific protection against S. mutans colonization in humans for a minimum of four months.Secretory monoclonal antibodies offer a distinct advantage due to their longer persistence in the oral cavity compared to IgA. Presently, localized passive immunization strategies, employing antibodies derived from diverse sources like mice, genetically modified plants, egg yolks, and cow's milk, are being implemented to target mutans streptococci antigens, thereby controlling bacterial colonization and preventing dental caries in humans.[15- 17]

RECENT STUDIES

The recombinant enolase from Streptococcus sobrinus (rEnolase) serves as a target antigen in this study. When rEnolase was administered alongside an alum adjuvant into the mouth of rats, there was a notable elevation in salivary immunoglobulin A (IgA) and immunoglobulin G (IgG) antibodies targeting the recombinant protein. These findings suggest that rEnolaseholds potential as a safe and effective component in future human trials for dental caries prevention vaccines. The efficacy of lozenges containing egg yolk antibodies (IgY) against Streptococcus mutans cell-bound glucosyltransferase

(CA-gtf) was investigated in a study involving healthy young adults. The findings revealed that these lozenges effectively prevented the establishment of S. mutans colonies in the oral cavity of the participants.Generally, vaccines, when properly formulated and administered, appear to pose minimal risks. However, a significant concern arises from the serological cross-reactivity observed in some patients with rheumatic fever, where antibodies against certain antigens from hemolytic Streptococci may react with heart tissue antigens. Studies using antisera from rabbits, where the rabbits were immunized with whole S. mutans cells and a high molecular weight protein from S. mutans, have shown that these antisera react with healthy heart tissue from both rabbits and humans. Additionally, elements within the cell walls of both S. mutans and Streptococcus ratti have been observed to react immunologically with human heart tissue and the myosin protein found in rabbit skeletal muscle.Understanding the signals that govern the colonization and proliferation of pathogenic Streptococci within dental biofilms could lead to the development of more targeted strategies to eliminate these harmful bacteria. In gnotobiotic rats, consuming whole S. mutans has been shown to selectively induce the production of secretory IgA (S-IgA). This increase in S-IgA levels was linked to a reduced occurrence of dental caries following vaccination.

The primary approach in many experiments has involved initially immunizing animals withS. mutans antigen, combined with an adjuvant and administering it repeatedlyto achieve elevated antibody levels. Subsequently, the same bacteria are introduced into the animal's oral cavity, along with a diet high in sucrose. Given that dental caries exhibits characteristics of an infectious disease, researchers have explored the potential for its prevention through vaccination. The underlying hypothesis is that immunizing against S. mutans would elicit an immune response that prevents the bacteria from colonizing tooth surfaces, thus averting decay. This vaccine could be administered concurrently with those for diphtheria and tetanus, with periodic boosters thereafter to ensure long-lasting immunity.[18- 20]

CONCLUSION

REFERENCES

1. Rathee M, Sapra A. Dental Caries. [Updated 2023 Jun 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551699/
2. Kidd EA. Clinical threshold for carious tissue removal. Dent Clin North Am. 2010 Jul;54(3):541-9.
3. Schwendicke F, Frencken JE, Bjørndal L, Maltz M, Manton DJ, Ricketts D, Van Landuyt K, Banerjee A, Campus G, Doméjean S, Fontana M, Leal S, Lo E, Machiulskiene V, Schulte A, Splieth C, Zandona AF, Innes NP. Managing Carious Lesions: Consensus Recommendations on Carious Tissue Removal. Adv Dent Res. 2016 May;28(2):58-67.
4. Pitts NB, Zero DT, Marsh PD, Ekstrand K, Weintraub JA, Ramos-Gomez F, Tagami J, Twetman S, Tsakos G, Ismail A. Dental caries. Nat Rev Dis Primers. 2017 May 25;3:17030.
5. Reisine S, Litt M. Social and psychological theories and their use for dental practice. Int Dent J. 1993 Jun;43(3 Suppl 1):279-87.
6. Campbell K. Oral microbiome findings challenge dentistry dogma. Nature. 2021
7. Robinson C, Shore R C, Brookes S J, Strafford S, Wood S R, Kirkham J. The chemistry of enamel caries. Crit Rev Oral Biol Med. 2000;11(04):481–495.
8. Daculsi G, LeGeros R Z, Mitre D. Crystal dissolution of biological and ceramic apatites. Calcif Tissue Int. 1989;45(02):95–103.
9. LeGeros R Z.Chemical and crystallographic events in the caries process J Dent Res 199069(Spec No):567–574., discussion 634–63
10. Patel M. Dental caries vaccine: are we there yet? LettApplMicrobiol. 2020 Jan;70(1):2-12.
11. Mestecky J, McGhee JR, Arnold RR, Michalek SM, Prince SJ, Babb JL, et al. Selective induction of an immune response in human external secretions by ingestion of bacterial antigen. JClin Invest. 1978;61:731–7.
12. Gahnberg L, Krasse B. Salivary immunoglobulin A antibodies and recovery from challenge of Streptococcus mutans after oral administration of Streptococcus mutans vaccine in humans. Infect Immun. 1983;39:514–9
13. Childers NK, Zhang SS, Michalek SM. Oral immunization of humans with dehydrated liposomes containing Streptococcus mutansglucosyltransferase induces salivary immunoglobulin A2 antibody responses. Oral MicrobiolImmunol. 1994;9:146–53.
14. Childers NK, Tong G, Li F, Dasanayake AP, Kirk K, Michalek SM, et al. Humans immunized with Streptococcus mutans antigens by mucosal routes. J Dent Res. 2002;81:48–52.
15. Lehner T, Caldwell J, Smith R. Local passive immunization by monoclonal antibodies against streptococcal antigen I/II in the prevention of dental caries. Infect Immun. 1985;50:796–9.
16. Ma JK, Lehner T, Stabila P, Fux CI, Hiatt A. Assembly of monoclonal antibodies with igG1 and igA heavy chain domains in transgenic tobacco plants. Eur J Immunol. 1994;24:131–8.
17. Ma JK, Hikmat BY, Wycoff K, Vine ND, Chargelegue D, Yu L, et al. Characterization of a recombinant plant monoclonal secretory antibody and preventive immunotherapy in humans. Nat Med. 1998;4:601–6.
18. Honda O, Kato C, Kuramitsu HK. Nucleotide sequence of the Streptococcus mutansgtfD gene encoding the glucosyltransferase-S enzyme. J Gen Microbiol. 1990;136:2099–2105. J ClinImmunol. 1990;10:273–81.
19. Hajishengallis G, Nikolova E, Russell MW. Inhibition of Streptococcus mutans adherence to saliva-coated hydroxyapatite by human secretory immunoglobulin A (S-IgA) antibodies to cell surface protein antigen I/II: reversal by IgA1 protease cleavage. Infect Immun. 1992;60:5057–64.
20. Shiroza T, Ueda S, Kuramitsu HK. Sequence analysis of the gtfB gene from Streptococcus mutans. J Bacteriol. 1987;169:4263–70