Immunology of Dental Caries

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ABSTRACT

Dental caries is the most widespread diseases in humans. In modern times, it has reached epidemic proportions. Dental caries is a microbiologic infectious disease of the teeth that ends in localized dissolution and destruction of the calcified structure of the teeth. Dental caries is a multifactorial disease that is caused by the host, agent, and environmental factors. The time factor is significant for the initiation and progression of dental caries. A wide group of microorganisms is established from carious lesions. S. mutans, Lactobacillus acidophilus, and Actinomyces viscosus are the main pathogenic species involved in the inception and development of dental caries.

Key words: Dental caries, streptococcus mutans, Glucosyltransferase.

INTRODUCTION

Dental caries is an infectious microbiologic disease of the teeth that results in sectorial dissolution and destruction of the calcified tissue. Dental caries is one of the most common diseases in humans. In modern times, it has reached epidemic proportions. The prevalence of dental caries in developed countries varies highly and can reach over 90%. The rate of Caries has been increasing in developing countries with the increase in the popularity of highly refined sugars. The human oral cavity is colonized by about 300 to 500 microorganism species. Most of them involve commensal and opportunistic bacteria. The relations between the host (human organism) and bacteria commenced in the oral cavity are dynamic and subject to many conditions. They are representative of the virulent efficiency and properties of bacteria as well as defensive forces of the host.

The development of dental caries requires the existence of cariogenic bacteria that are capable of producing acid and a sugar present in the diet which favors the colonization of these bacteria to form acid. Dental caries appears to be a major public health problem which if left untreated can cause ample pain, discomfort, and treatment costs are very high. Dental caries results from the interaction within the host, the hosts diet, and the microflora on the tooth surface bounded by the time factor. A wide group of microorganisms are determined from carious lesions of which Streptococcus mutans (S. mutans), Lactobacillus acidophilus, and Actinomyces viscosus are the main pathogenic species involved in the initiation and development of dental caries. Colonization by S. mutans occurs after tooth eruption, and if the fissures become colonized in their depths, then decay may be unavoidable. However, if this colonization is delayed until the fissure depths are occupied by other bacteria, there is feasibility that decay will not occur or its occurrence will be greatly reduced.

The immune response

The primary response

When an antigen is administered for the first time to an animal or human, there is a latent
course of induction of 3 to 10 days before antibodies appear in the blood. The antibody that is first obtained is entirely of the IgM type. The IgM antibody titer rises steadily during the next 2 to 3 days, reaches a crest level, and then declines almost as fast as it developed. Meanwhile, if the antigenic stimulus was sufficient, the IgG antibody emerges in a few days. IgG reaches a peak in 7 to 10 days and then gradually falls over a period of weeks or months. A significant outcome of the primary antigenic challenge is the education of the reticuloendothelial system of the body. Both B and T lymphocytes produce what are known as memory cells or primed cells. These cells are culpable for the immunological memory that is established after immunization.

Secondary (Booster response)

The response to a booster dose varies in a number of ways from the primary response. The secondary response also involves the synthesis of IgM and IgG antibodies. A collaboration between B and T cells is necessary to initiate a secondary response. There is an abrupt production of the IgM antibody and a much larger and more prolonged production of the IgG antibody. This accelerated response is associated to immunological memory. The immune response (primary and secondary) and immunological memory are the bases of vaccination and revaccination.¹

Immunology of the oral cavity

Antigens and antibodies of the oral cavity

The application of natural immune responses to caries producing organism and the development of a vaccine involves the knowledge of the antigenic properties of the organism. The cell surfaces of S. mutans possess many antigens. The cell wall enzyme glucosyltransferase (GTF), responsible for the synthesis of insoluble extracellular mutans, has been largely studied as it has the serotype-specific polysaccharide containing glucose, rhamnose, and occasionally galactose and galactosamine. In addition, the cell wall contains lipoteichoic acid (LTA), a polymer of glycerol and phosphate covalently linked to a glycolipid, which is found virtually in all Gram-positive organisms. This antigen may be accountable for some immunological cross-reactions between bacterial species.

Immunological microenvironments in the mouth

The cervical region and root surface plaques in older subjects are thus subjected to the influence of SIgA, serum immunoglobulins, complement factors and PMNLs from the gingival crevice. IgA, IgG, IgM, and the third component of complement can be detected in plaque extracts, and in the free aqueous phase of plaque (plaque fluid) separated from the solid phase by centrifugation.

Plaque in the fissures and more coronal parts of the smooth surfaces of the teeth is probably influenced only by salivary antibodies. PMNLs survive for a very short time in human saliva, although in monkeys their survival may be more prolonged and in the gingival crevice they may persist for long periods.

Antibodies or oral bacteria including S. mutans can be detected in human serum and saliva. In order to see where or not these antibodies might play a part in natural caries immunity, numerous comparisons of caries experience, and levels of immunoglobulin or specific antibody have been carried out, but consistency in the results of such experiments is not apparent. Various small-scale human trials in adults have shown that it is feasible to increase levels of salivary S-IgA antibodies to mutans streptococci, and in some cases to interfere with mutans streptococcal colonization.⁴

The Relationship Between Caries and sIgA

IgA deficiency is a relatively common disease afflicting 1:1000 individuals which have been associated with dental caries. It was found that subjects with IgA deficiency fell into two groups in terms of oral antibody: ie., those with compensatory IgM antibodies against S. mutans in saliva and those without.

In Panhypo- or agammaglobulinemia, increased caries activity have been reported. It has been shown that human parotid sIgA antibodies against surface antigen I/II of S. mutans could block S. mutans adhesion to saliva-coated hydroxyapatite suggesting that there is a mechanism of protection available to the host against certain cariogenic bacteria. Serum antibodies, intragingival
antibodies, complement, and granulocytes are constantly extravasating from the periodontal crevice and into the oral environment. These components may confer modest protection to the tooth in the cervical area, but they are not likely to be significant in coronal portions of the teeth.5

Caries vaccines and its role in immunology of dental caries

Bacteria passing through the mouth into the stomach and intestine come in contact with specialized lymphatic tissue located in Peyer’s patches along with intestinal walls. Certain T (Thymus) and B (Bone marrow) cells in Peyer’s patches become sensitized to these microorganisms. These sensitized T and B cells migrate through lymphatics to the blood stream and eventually settle in glandular tissues including the salivary glands. These sensitized cells produce IgA that are secreted in the saliva, which are capable of agglutination of oral bacteria, reduce adherence and easy clearance. Immunization of dental caries should begin early in the second year of life. Both active and passive approaches have shown success in human clinical trials. Signals and growth of cariogenic streptococcus in dental biofilms.4

The S. mutans present a set of virulence factors that enables them to adhere to and accumulate in the dental biofilm. Three main groups of Ags associated with the surface of these microorganisms participate in the process of adhesion and accumulation of S. mutans in the biofilm. These Ags are the main targets for the development of caries vaccine: the glucosyltransferases (Gtf), antigen adhesin I/II (Ag I/II), and glucan-binding proteins (Gbp). One of the major virulence characteristics of S. mutans is precisely its ability to produce Gtfs, enzymes that synthesize intracellular polysaccharides (ICP) and extracellular polysaccharides (ECP) from sucrose of the diet.6 Thus, the various antigenic components against which immune responses are produced are Adhesins, Glucosyltransferases, and Glucan-binding proteins.7 8 9

Adhesins

Effective antigenic components have been obtained from S. mutans and S. sobrinus in the form of intact proteins and subunit vaccines. These single polypeptide chains are approximately 1600 residues in length. S. mutans Ag I/II contain an alanine-rich tandem repeating region in the N-terminal third, and a proline-rich repeat region in the center of the molecule. These regions have been associated with the adhesin activity of Ag I/II. Immunological approaches support the adhesin-related function of the AgI/II family of proteins and their repeating regions. Abundant in vitro and in vivo evidence indicates that antibody with specificity for S. mutans AgI/II or S. sobrinus SpaA can interfere with bacterial adherence and subsequent dental caries. Furthermore, numerous immunization approaches have shown that active immunization with intact antigen I/II or passive immunization with monoclonal or transgenic antibody to putative salivary-binding domain epitopes within this component can protect rodents, primates, or humans from dental caries caused by S. mutans.

Glucosyltransferase (GTF)

S. mutans that have lost the ability to produce GTF are unable to produce disease in animal models. S. mutans has basically three forms of glucosyltransferases-GTF 1, GTF-S-1, GTF-S and respective genes are GTF-B, GTF-C, and GTF-D. An antibody directed to native GTF or sequences associated with its catalytic or glucan-binding function interfere with the synthetic activity of the enzyme and with in vitro plaque formation. Since GTFs from the two major cariogenic streptococcal species in humans, S. mutans and S. sobrinus, have very similar sequences in the functional domains, immunization with GTF protein or subunit vaccines from one species can induce a measure of protection for the other species.

Glucan-binding protein (GBP)

Various proteins with glucan-binding properties have been identified in S. mutans and S. sobrinus which are described elsewhere. S. mutans secretes at least, three distinct proteins with glucan-binding activity: GbpA, GbpB, and GbpC. GbpA has a deduced sequence of 563 amino acids. The molecular weight for the processed protein is 59.0 kDa. The expressed GbpB protein is 431 residues long and has a calculated molecular weight of 41.3 kDa. The third S. mutans nonenzymatic glucan-binding protein, GbpC, is composed of 583 amino acids. This protein has a
calculated molecular weight of 63.5 kDa. Of the three S. mutans glucan-binding proteins, only GbpB has been shown to induce a protective immune response to experimental dental caries. It can either be achieved through a subcutaneous injection of GbpB in the salivary gland region or by mucosal application by the intra-nasal route.

**Dextranases**

Dextranase, an important enzyme produced by S. mutans, destroys dextran which is an important constituent of the early dental plaque so that the bacterium can easily invade dextran-rich early dental plaque. Dextranase, when used as an antigen, can prevent colonization of the organism in early dental plaque. 7,8,9

**CONCLUSION**

_S. mutans_ and _Streptococcus sobrinus_ are closely associated with dental caries. Fluoride treatment used abroad has successfully limited caries progression but was not sufficient to control this infectious disease even when used together with professional tooth cleaning and dietary counseling in populations highly exposed to this cariogenic microbiota. Along with established methods of caries prevention, caries vaccines have the potential of making a highly valuable contribution to disease control. Regardless of the mechanism by which immune protection against dental caries is achieved, further advances to make immunization against caries practical will depend upon clinical trials aimed at establishing whether the findings from animal experiments can be transferred to humans.

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