DENTAL CARIES: REVIEW OF MICROBIAL ETIOLOGY AND INNOVATIVE PREVENTION METHODS

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Abstract:
Background: The human oral cavity harbors a diverse array of microbial species, with around 700 to 1000 species residing in the mouth. Oral diseases such as dental caries, periodontal disease, and oral cancer are closely linked to these oral microorganisms. The economic burden of dental diseases is substantial, with direct and indirect costs estimated in billions of dollars. Dental caries, a biofilm-associated disease, is a prevalent global issue affecting a large percentage of the population, particularly children and adults. Prevention of caries is crucial in public health management, with a shift towards early detection and monitoring to preserve tooth structure and promote natural healing processes. **Objective**: This research aims to investigate the specific microbial species responsible for causing dental caries, explore their mechanisms in caries development, evaluate the effectiveness of current preventive measures like fluoride treatments, and identify new strategies targeting microbial etiologies for caries prevention. **Conclusion**: Dental caries remains a significant global public health concern, with microbial biofilms playing a crucial role in its etiology. While conventional preventive measures like fluoride treatments and dental hygiene practices have shown some efficacy, there is a growing interest in natural antimicrobial compounds from plants as potential alternatives for caries prevention. Incorporating microbiologically-based strategies and emphasizing prevention over treatment could lead to more successful outcomes in managing dental caries. Further research into the mechanisms of action of anti-caries compounds and optimal dosing schedules for fluoride treatments is essential to enhance preventive strategies against dental caries.

Keywords: dental caries, biofilm, cariogenic microorganisms, antimicrobial drugs

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Introduction:
The human body harbors a vast array of microorganisms, with the oral cavity serving as a significant reservoir of microbial diversity. Researchers have identified approximately 700 to 1000 different microbial species that inhabit the oral cavity, playing a crucial role in the onset and progression of oral diseases such as dental caries, periodontal disease, and oral cancer [1]. Moreover, the presence of oral microorganisms can lead to systemic complications as they may infiltrate the bloodstream through compromised oral mucosa, triggering an increase in systemic antibody levels and thereby elevating the risk of various cardiovascular diseases [2].

A study by Peres et al. highlighted the global impact of preventing and managing oral diseases, revealing staggering direct costs of $356.80 billion and indirect costs of $187.61 billion associated with dental diseases in 2015 alone [3]. In the same year, the top three diseases with the highest combined direct and indirect costs were ranked as diabetes (€119 billion), cardiovascular diseases (€111 billion), and dental diseases (€90 billion) [4].

Dental disease, particularly dental caries, represents a significant public health challenge and ranks among the most prevalent conditions worldwide. The World Health Organization reported that 60 to 90% of school children and nearly all adults globally suffer from cavities [6]. Thus, the prevention of dental caries assumes paramount importance in public health management.

The concept of minimal intervention dentistry, as defined by the Federation Dentaire Internationale (FDI) in 2002, underscores the importance of preserving healthy tooth structure through preventive measures [7]. Shifting from a surgical to a medical model, emphasis has been placed on early detection and monitoring of caries to increase the uptake of preventive oral healthcare services [8]. By preserving sound tooth structure, preventing enamel demineralization, and facilitating natural healing processes, caries prevention strategies aim to mitigate the risk of dental caries [9].

Caries risk assessment plays a crucial role in identifying protective factors against dental caries and determining the need for therapeutic interventions. Featherstone et al. highlighted indicators such as 'bad bacteria', inadequate saliva production, and poor dietary habits as key determinants of caries development. They underscored the role of saliva, sealants, antibacterial agents, fluoride, and dietary modifications in maintaining oral health and preventing dental caries [10].

The Alliance for a Cavity-Free Future has proposed comprehensive steps for caries prevention, including maintaining a balanced oral bacterial environment, regulating the consumption of sugary and starchy foods, and strengthening demineralized enamel through fluoridated products [11]. Enhancing the oral flora emerges as a promising strategy for caries prevention, particularly through the inhibition of dental biofilms. Dental biofilms, composed of cariogenic microorganisms, play a pivotal role in the etiology of dental caries. Studies have shown that the composition of pathogenic biofilms differs significantly from non-pathogenic biofilms, with a higher proportion of cariogenic microorganisms implicated in caries development [12].

Given that the accumulation of pathogenic biofilm represents a major contributor to dental caries, interventions targeting biofilm inhibition have shown efficacy in caries prevention [13]. Efforts to enhance oral health through the prevention of dental biofilms are crucial in combating the prevalence of dental caries and promoting overall oral health.

Objectives:
The main objectives of this review are:
1. To investigate the specific microbial species responsible for causing dental caries.
2. To explore the mechanisms by which these microbial species contribute to the development and progression of dental caries.
3. To evaluate the effectiveness of current preventive measures, such as fluoride treatments and dental hygiene practices, in reducing the risk of dental caries.
4. To identify potential new strategies for preventing dental caries based on targeting specific microbial etiologies.

Dental Biofilms:
The oral cavity harbors a diverse array of microorganisms, such as bacteria, yeasts, viruses, mycoplasmas, protozoa, and archaea, collectively forming the oral microbiota, which thrives in the warm and nutrient-rich environment of the mouth. This oral microbiota not only plays a crucial role in maintaining oral health but also regulates bacterial colonization to prevent the invasion of pathogenic microbes [14]. However, disruptions in the equilibrium of the host's commensal microbial

community by invading microorganisms can lead to dental diseases. Particularly on the surface of teeth, the oral microbiota tends to form complex polymicrobial communities known as dental biofilms [15]. It is now widely acknowledged that the extracellular polymers (EPS) within these biofilms create an environment conducive to cariogenic microorganisms, suggesting that dental caries is primarily a biofilm-induced disease rather than a simple infectious one [16].

The initiation of caries biofilm formation occurs when a salivary glycoprotein film, known as dental pellicle, coats the tooth surface, facilitating the adherence of Gram-positive bacteria, such as streptococci of the mitis and mutans species, which are considered initial colonizers of the biofilm. These bacteria produce EPS, which not only aid in the attachment of other microorganisms but also provide a platform for the colonization of acid-producing species like Veillonella, Scardovia, Lactobacillus, and Propionibacterium, contributing to the cariogenic conditions in the oral cavity. The EPS matrix not only offers protection and mechanical stability to the biofilm but also makes it resilient to antimicrobials and challenging to eliminate [17].

Further research has highlighted the significance of the structural and biochemical properties of EPS in the development of caries, emphasizing that microbial behavior within biofilm communities and the properties of EPS are crucial factors in caries etiology. Experimental biofilm models have been employed to simulate metabolic processes during carbohydrate exposure in the mouth, aiding in the evaluation of anti-caries agents and the understanding of the cariogenicity of dietary sugars [19].

While Streptococcus mutans biofilm has long been recognized for its cariogenic potential due to its acid production, acid resistance, and EPS synthesis capabilities mediated by glucosyltransferases, recent advancements in caries prevention and treatment have revealed the complexity of cariogenic biofilms. Targeting S. mutans and reducing sugar intake alone may not suffice to prevent caries, as other microorganisms like Lactobacillus, Bifidobacterium, Scardovia, as well as polysaccharides derived from various species contribute to the pathogenic flora within cariogenic biofilms [20, 21]. The microbial diversity within biofilms influences their susceptibility to antibiotics, preservatives, and anti-adhesion compounds, with cariogenic microorganisms outcompeting health-associated commensal species during biofilm maturation, leading to the dominance of caries-associated colonizers [22, 23].

In conclusion, the prevention of dental caries presents challenges due to the intricate nature of biofilm matrices and the abundance of cariogenic microorganisms, underscoring the importance of understanding the microbial dynamics and EPS properties in caries development and exploring novel strategies for effective prevention and treatment.

Microbial Etiology of Dental Caries:

Currently, it is widely acknowledged that the formation of dental caries is a multifaceted process involving the interplay of acid-producing microorganisms and fermentable carbohydrates over a period of time. While the oral microbiome plays a crucial role in the development of dental caries, various host factors such as teeth and saliva also contribute to the progression of caries, resulting in a condition that is typically chronic and gradually advancing. The dental biofilm is a significant factor in the origin of dental caries. The intricate nature of the biofilm matrix, the transfer of resistance genes, and the protective shield provided by extracellular polymeric substances (EPS) all serve as risk factors for caries. Numerous research studies have emphasized that managing the dental biofilm is pivotal in the prevention of tooth decay [24]. Furthermore, the absence of a singular evident target for therapeutic intervention and the limited retention of locally applied treatments present additional challenges in addressing this issue.

Natural Antimicrobial Compounds for the Prevention of Dental Caries:

There has been a noticeable increase in interest surrounding plants that possess a rich reservoir of natural antimicrobial compounds. Traditional dental healers have come to recognize the significance of medicinal plants as potent sources of therapeutic agents. Some of these plants, which are devoid of adverse effects, have demonstrated superior efficacy compared to synthetic drugs in combatting dental caries [25]. The World Health Organization has highlighted that approximately 80% of the global population relies on herbal remedies for treating various ailments, with most herbal medications containing at least one botanical constituent. It is noteworthy that extensive research has been conducted on the bioactivity and bioavailability of phytochemicals [26]. In a study by Malvania et al. (2019), it was observed that a licorice extract exhibited a significantly greater inhibitory effect on oral pathogens in comparison to sodium fluoride. Liquid or dried plant extracts are commonly incorporated into oral hygiene products such as toothpaste, mouthwash, and functional foods for oral care to bolster their anti-caries properties. Additionally, plant-derived ingredients are utilized in cavity fillings to alleviate caries-related discomfort [27]. The majority of antibacterial agents found in plants are secondary metabolites that are not essential for plant growth but serve specific physiological functions. These compounds typically encompass alkaloids, phenols, flavonoids, and organic acids. Further exploration is warranted on the mechanisms by which plant-derived compounds exert their anti-caries effects and their impact on the host's biology. Throughout history, plants have been harnessed as natural remedies beneficial for oral health, with some exhibiting antibacterial traits that help reduce infections [28]. Another notable function of anti-caries compounds is their ability to inhibit glucosyltransferase, a pivotal enzyme in the production of cariogenic biofilms, thereby impeding their formation [29]. Investigating plant extracts containing a diverse array of bioactive compounds is imperative. Studies have indicated that cinnamon, clove, and coriander are effective in preventing dental caries [30]. The antimicrobial potency of phenolic acids is influenced by the number and arrangement of substituents on the benzene ring, while the saturation and length of side chains may impact their effectiveness against oral pathogens [31]. One of the potential antibacterial mechanisms of xanthorrhizol involves the formation of hydrogen bonds between its hydroxyl groups and proteins in the cell membrane, ultimately disrupting the membrane integrity of pathogens like C. albicans [32]. Alkaloids are known to suppress pathogen cytokinesis as part of their antimicrobial action, while polyphenols are recognized for inactivating cellular enzymes in pathogens. Nevertheless, further investigations are needed to elucidate the precise mechanisms of action of bioactive compounds against dental caries. Apart from their antibacterial properties, plants often harbor natural antioxidants due to the presence of polyphenols and flavonoids, making them a valuable adjunct to mechanical dental biofilm control [33].

Prevention and Treatment:

In the realm of traditional dental treatment, there has been a notable absence of microbiologically-driven strategies within the arsenal of available approaches. Instead, the prevailing method has been one centered on reacting to symptoms rather than proactively addressing underlying microbial factors. The shortcomings of such an approach, rooted in outdated biological principles from the turn of the century, have been starkly illustrated in Scandinavian nations with their socialized dental care systems, which have democratized access to high-quality dental services for all. This emphasis on reactive treatment over preventive measures has only marginally extended the functional lifespan of teeth, yielding rather modest therapeutic outcomes [34].

Across the English healthcare landscape, a similar emphasis on treatment over prevention was evident, leading to a concerning statistic in the 1970s where half of individuals over 35 years old were completely edentulous. In contrast, Scandinavian countries, particularly Sweden, have adopted a paradigm shift towards implementing plaque prevention programs for both children and adults. This comprehensive approach involves regular dental cleanings using a 5% fluoride paste at intervals of 2 to 4 weeks, coupled with educational initiatives on oral hygiene. The results have been striking, with a reduction of dental decay in children by an impressive 80% to 90% compared to those receiving solely symptomatic treatment. Symptomatic treatment typically involves interventions like dental restorations for visibly decayed teeth or extractions. Similar success has been observed in adults, irrespective of the presence of periodontal disease [35].

The meticulous cleaning regimen involving fluoride appears to foster the proliferation of beneficial bacterial strains, such as S. sanguis and S. mitis, on tooth surfaces, while inhibiting the dominance of less desirable strains like S. mutans. The frequent removal of plaque disrupts the conditions conducive to S. mutans' prevalence, as the low pH levels in undisturbed plaque that favor its growth are neutralized. Moreover, the immediate bacteriostatic effects of the 5% fluoride paste on plaque organisms further contribute to its efficacy [36].

The mechanisms through which fluoride confers protection against decay are multifaceted, with the predominant explanation attributing the 30% to 50% reduction in decay following water fluoridation to the formation of fluorapatite. This compound, resulting from fluoride replacing hydroxyl groups in tooth enamel, is less soluble in acidic environments compared to hydroxyapatite, the primary constituent of enamel. As a result, teeth containing fluorapatite dissolve at a slower rate in acidic conditions, facilitating faster remineralization between sugar exposures. While this explanation accounts for the efficacy of water fluoridation, questions persist regarding the precise modes of action of topically applied fluorides [37].

The fluoride ion (F–) exerts its protective effects by inhibiting the bacterial enzyme enolase, thereby disrupting the production of phosphoenolpyruvate (PEP), a crucial intermediate in the glycolytic pathway of many bacteria. This interference impedes the energy and phosphate acquisition necessary for sugar uptake by bacteria. The presence of 10 to 100 parts per million (ppm) of fluoride inhibits acid production by most plaque bacteria, a concentration easily achieved through prescription fluoride products, as demonstrated in Swedish studies. Notably, at acidic pH levels of 5.5 or below, lower fluoride concentrations (1 to 5 ppm) can inhibit oral streptococci, particularly in plaque-rich environments like those of individuals using fluoridated water or toothpaste. This suggests a potential antibacterial mechanism of action for fluoride, involving a depot effect conferred by systemic and topical fluoride administration [38].

The concept of a depot effect arises from the interaction between fluoride and tooth enamel. Water fluoridation promotes the formation of fluorapatite, while topical fluorides enhance the retention of fluoride by enamel, either as fluorapatite or more soluble calcium salts. Within the plaque microenvironment, microbial acid production may release this enamel-bound fluoride, which, at the acidic pH prevalent in plaque, could exhibit lethal effects on acid-producing microbes. This selective action could disadvantage aciduric bacteria like S. mutans and lactobacilli, which are typically the primary acid producers at the plaque-enamel interface. Consequently, fluoridated teeth harbor a reservoir of potent antimicrobial agents that are released and most effective in acidic conditions, potentially contributing to the success of water fluoridation and topical fluoride applications. This hypothesis underscores the potential antimicrobial benefits of fluoride and suggests that targeted use of topical fluorides could be particularly effective in individuals with high caries activity [39].

Despite these advancements, the optimal dosage and formulation of fluoride for maximum efficacy remain undetermined. For instance, in cases where individuals with xerostomia resulting from jaw cancer radiation therapy are predisposed to extensive caries, daily administration of neutral 1.0% sodium fluoride to adults has yielded remarkable outcomes, with few to no instances of caries reported [40].

Conclusion:

In conclusion, dental caries remains a significant public health issue globally, with a high prevalence among both children and adults. The microbial etiology of dental caries, particularly the role of pathogenic biofilms, has been well-established. Current preventive measures such as fluoride treatments and dental hygiene practices have shown some effectiveness in reducing the risk of dental caries. However, there is a growing interest in natural antimicrobial compounds derived from plants as potential alternatives for preventing dental caries. These compounds have shown promising results in inhibiting oral pathogens and preventing the formation of cariogenic biofilms.

Moving forward, incorporating microbiologically-based strategies into dental therapy and emphasizing prevention over treatment could lead to more successful outcomes in managing dental caries. The success of fluoride in preventing decay highlights the importance of targeting specific microbial factors in preventive interventions. Further research into the mechanisms of action of anti-caries bioactive compounds and optimal dosing schedules for fluoride treatments is necessary to improve preventive strategies against dental caries.

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