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Review

Etiology and microbiology of periodontal diseases: A review

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Nowadays, there is a high prevalence of periodontal disease worldwide, and knowing the etiology is basic for its control. Biofilms that colonize the oral cavity are among the most complex of nature. Besides pathogenic microorganisms, genetic and environmental factors contribute to the development of this disease. Periodontal disease can be increased by several risk factors such as smoking, systemic diseases, medications such as steroids, antiepileptics, drugs for cancer therapy, poor placement of dental bridges, dental crowding, lack of teeth, pregnancy and contraceptive use. The objective of this review is to provide an overview of periodontal disease, as well as the microbiology aspects of this worldwide prevalent oral infection.

Key words: Periodontal disease, oral microbiology, periodontitis.

INTRODUCTION

Periodontal disease and dental caries are the most prevalent infections affecting the human dentition (Brown et al., 1996). Periodontal disease is a chronic bacterial infection characterized by persistent inflammation, connective tissue breakdown and alveolar bone destruction (Yamamoto et al., 2011).The term periodontal disease refers to gingivitis and periodontitis as well. Gingivitis is a reversible dental plaque induced inflammation of the gingiva, is a common occurrence in children as young as 5 years old.

Periodontitis, which is bacterially induced, can be defined as a chronic inflammatory disease initiated by dental plaque biofilm and perpetuated by a deregulated immune response (Suvan et al., 2011) usually accompanied by gingivitis resulting in irreversible destruction of the supporting tissues surrounding the

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tooth, including the alveolar bone (Yamamoto et al., 2011). Periodontitis generally is defined as a condition where the supporting tissue of the teeth is destroyed (Reeves et al., 2006) and which leads to gingival recession (Saini et al., 2010), gingivitis (Lopez et al., 2005), loss of alveolar bone or teeth at the last stage of periodontal disease (Nesbitt et al., 2010), besides the loss of gingival collagen (LeRoy et al., 2010) and degradation of the periodontal ligament (Bonifait and Grenier, 2010). The hard and soft tissues of the oral cavity are colonized by bacterial biofilmscomposed by proteins epithelial cells, food residues, enzymes, plus different species of bacteria responsible for causing dental caries and periodontal disease (Bonifait and Grenier 2010). The gingiva, periodontium, alveolar bone and cement are structures that provide support to the tooth. Any pathological process affecting periodontum is defined as periodontitis. For a long time, it was thought that gingivitis and periodontal disease appeared as a result of aging of the periodontal tissues that gave rise to inflammation and recession of the gingival tissues bone and finally tooth loss. However, several studies have indicated that this is not just an adult disease, but also appears frequently in children (Escudero et al., 2008).

In latest research, 800-1,000 species that colonize the oral cavity were identified, nevertheless only about 50 species are strongly related to periodontal disease (Colombo et al., 2009). The metabolic action of early bacterial colonizers in the gingival crevice alters the environment and facilitates colonization by secondary organisms. These secondary colonizers are more pathogenic and when they exceed threshold levels, disease can occur, although, the presence of periodontopathic bacteria itself does not necessarily result in disease (Socransky and Haffajee, 2002). The concordance of a variety of bacterial virulence factors, the activity and composition of the commensal microbiota, and host immune factors, are required for the initiation of the disease process (Lamont and Jenkinson, 2010).

The objective of this review was to provide an overview of periodontal disease, as well as the microbiology aspects of this worldwide prevalent oral infection.

RISK FACTORS FOR PERIODONTAL DISEASE

Besides pathogenic microorganisms, genetic and environmental factors contribute to the development of this disease. The risk of periodontal disease increases with several factors as smoking, systemic diseases, medications such as steroids, antiepileptics, drugs for cancer therapy, poor placement of dental bridges, dental crowding, lack of teeth, pregnancy and contraceptive use. In addition to these factors, any health condition that triggers bacterial defense mechanisms such as human immunodeficiency virus (HIV), diabetes and neutrophils disorders can cause periodontal disease. The risk factors for periodontal disease are shown on Table 1.

MICROBIOLOGY OF PERIODONTAL DISEASE

Infectious diseases have in common, the fact that they are necessarily associated with the presence of bacteria that colonize the sub gingival niche (Escribano et al., 2005). The mouth facilitates the growth of a characteristic resident microbiota. The composition of the oral microbiota is influenced by temperature, pH and atmosphere, as well as by the host defences and host genetics (Marsh and Devine, 2011). The subgingival microbiota involved in periodontal disease has been a mayor research topic for more than 40 years (Contreras et al., 2000).

Recently, published studies show the association between certain families of virus and periodontal disease. Contreras et al. (2000) demonstrated the presence of some virus like Epstein-Barr type 1, cytomegalovirus and human herpes in crevicular fluid of Nigerian children with necrotizing ulcerative gingivitis. This pathogenicity is attributed to the degradation of the host defense mechanisms due to viral infection of the gingiva, favoring the bacteria colonization (Ling et al., 2004). In latest research, they identified 800-1,000 species that colonize the oral cavity, nevertheless only about 50 species are strongly related to periodontal disease (Colombo et al., 2009). However, a major portion of this species remains incompletely characterized, that is why their virulence and immunobiology are still unknown.

Bacteria are responsible for stimulating the host response, which define tissue changes causing periodontal lesions (Ling et al., 2004). Such bacteria are in communities within a glycocalyx forming a biofilm, which allows microorganisms to join and multiply on different surfaces (Lamont et al., 2013). The biofilm protects the microorganisms from toxic substances in the environment; it also facilitates the uptake of nutrients, the cross-feed, the elimination of metabolic products and the development of an appropriate environment with suitable physicochemical condition for their growth (Socransky and Haffajee, 2002).

Biofilms that colonize the oral cavity are among the most complex of nature, as in the mouth, there are 4 different niches: masticatory mucosa, tongue dorsum, saliva and hard surfaces such as tooth surfaces and restorative materials (Escribano et al., 2005).

Bacteria that cause periodontal disease can be classified according to their function in the associations between them when colonizing the gingival sulcus (Socransky and Haffajee, 2002). In Table 2, the Socransky classification is shown.

Microbiology related to periodontal disease has been a subject of discussion, although Lamont et al. (2013) identified specific bacteria related to gingivitis and periodontitis as shown in Table 3. Of all the bacteria forming biofilm, there are three that are particularly relevant in the initiation and progression of periodontal disease: *Actinobacillus actinomycetemcomitans* (Aa), *Porphyromonas gingivalis* (Pg) and *Tannerella forsythensis*

Table 1. Risk factors for periodontal disease.

Risk factor	Description	Author(s)
Oral microorganisms	- More than 500 different microbial species in the mouth - Most pathogenic are: *Tanerella forsythia, Porphyromona gingivalis, Treponema denticola*	Sockransky et al., 2000; Listgarten, 1976; Moore and Moore, 1994; Kroes et al., 1999; Tanner et al., 1998
Genetics	Syndromes that affect phagocytes, ephitelial structure, connective tissue or teeth like: Haim-Munk; Papillon Lefevre; Chédiak-Higashi; Ehlers-Danlos (types 4 & 8); Kindlers	Hart et al., 1999; Hewitt et al., 2004
Tobacco and alcohol	Smokers more likely to develop periodontitis; Negative effect in response to periodontal treatment and surgical interventions; Association between alcohol consumption and loss of periodontal support	Modeer et al., 1980; Johnson and Slach, 2001; Robertson et al., 1990; Tomar and Asma, 2000; Tezal et al., 2004
Hiv and aids	Necrotising/ulcerative gingivitis and periodontitis	Robinson et al., 2002; Glick et al., 1994; Ramirez et al., 2003
Nutrition	- Vitamin C deficiencies associated with periodontal disease - Noma (Cancrum Oris) more common in malnourished individuals	Enwonwu et al., 2000
Osteoporosis	- Raises susceptibility to periodontal disease - Periodontal attachment loss	Yoshihara et al., 2004; Ronderos et al., 2000
Diabetes	- Impaired wound healing, exaggerated monocyte response to dental plaque antigens, impaired neutrophil chemotactic responses. - Local tissue destruction - Progressive bone destruction	Tervonen and Oliver, 1993; Karjalainem et al., 1993; Soskoln and Klinger, 2001; Taylor, 2001; Enwonwu et al., 2000; Lalla and Papapanou, 2011
Stress	Emotional and psychosocial stress can cause periodontal disease, although the precise role is still unknown.	Silva et al., 1995; Hugoson et al., 2002

(Tf) (Sanz et al., 2000), this bacteria are designated major pathogens or “red complex” bacterias, as shown in Table 4.

Microbiological diagnosis

There are several methods developed for microbiological diagnosis in recent times. Which are shown in Table 5.

Treatment

Nowadays, periodontal disease has a variety of possible treatments depending on the stage of the disease, the way the patient respond to previews treatments and the patient oral health.

Some of these treatments are: Professional dental cleaning, scaling and root planing, antibiotic therapy and surgical procedures.

Lately, the dental community was in search of new non-invasive treatments to restore oral health like the use of natural products such as plants; their components have been in use for treatment and cure of diseases all around the globe from ancient times much before the discovery of the current modern drugs (Dua et al., 2015).

Hambire et al. (2015) tested 60 children of ages 9-14 with mouthwash of *Camellia sinesis,* obtaining as a result, an improvement in the children gingiva as well as the antiplaque effectiveness of this plant. Also, Hussain et al. (2015) demostrated in their *in vitro* test, the inhibition of three periodontopathic bacteria such as: *Aggregatibacter actinomycetemcomitans, Prevotella intermedia and P. gingivalis* with ethanolic extracts of *Citrus sinesis*, reporting a minimum inhibitory concentration of 12-15 mg/ml.

On the other hand, some researchers are interested in the application of phytomedicine as a possible treatment for dental decay and other oral health conditions. Jain et al. (2015) tested the antimicrobial activity of six plant extract against *Streptococcus mutans*, concluding that garlic, amla and ginger contains certain compounds that inhibit this cariogenic pathogen, reporting a zone of inhibition between 18.76-24.62mm. Ardakani et al. (2014) also tested mouthrinses of green tea against *S. mutans*, *Streptococcus sanguis*, *Enterococcus faecalis*, *Pseudomonas aerogenosa* and *Escherichia coli,* and obtaining a larger zone of growth inhibition with green tea

Table 2. Current classification system of bacteria responsible of periodontal disease (Socransky and Haffajee, 2002).

Complex	Bacteria	Role in periodontal disease
Yellow	- *Streptococcus sanguis* - *Streptococcus gordonii* - *Streptococcus intermedius*	Early colonizers
Green	- *Capnocytophaga gingivalis* - *Capnocytophaga ochracea* - *Capnocytophaga sputigena* - *Campylobacter concisus*	Secondary colonizers
Orange	- *Fusobacterium nucleatum* - *Prevotella intermedia* - *Prevotella nigrescens* - *Peptostreptococcus micros* - *Streptococcus constellatus* - *Eubacterium nodatum* - *Campylobacter showae* - *Campylobacter gracilis* - *Campylobacter rectus*	Secondary colonizers Precede colonization by bacteria of the “Red complex”
Purple	- *Veillonella párvula* - *Actinomyces odontolyticus*	Bridge species between “Orange complex” and “Red complex”
Red	- *Tannerella forsythia* - *Porphyromona gingivalis* - *Treponema denticola*	Secondary colonizers Main pathogens, associated with bleeding on probing

Table 3. Bacterial colonizers during gingivitis and periodontitis (Lamont et al., 2013).

Disease	Bacteria involved
Gingivitis	- *Actinomyces* - *Prevotella intermedia* - *Bacteroides* - *Fusobacterium nucleatum*
Periodontitis	- *Porphyromona gingivalis* - *Tannerella forsythia* - *Treponema denticola* - *Campylobacter rectus* - *Fusobacterium nucleatum* - *Eikenella corrodens* - *Selenomonas noxia*

Recently, Segura et al. (2015) reported that the extracts of *Quercus rubra, Carya illinoinensis* and *Smilax glyciphylla* with papin have an inhibitory effect on the dental biofilm formation, they also did an *in vivo* test with mouthrinses, proving once more the antibacterial activity of these extracts.

CONCLUSION

Periodontal disease is a worldwide health issue, but is particularly severe in individuals with low-income, mainly because they do not receive adequate dental care because of economic constrains and scarcity of affordable dental services.

The increasing evidence of the importance of periodontum health and its relation with other systemic diseases makes the dental community to develop safe and effective methods to control periodontal infections. pure extract than with 0.2% chlorhexidine.

Knowledge of basic periodontology, risk factors, classification and microbiology of periodontal disease are

Table 4. Main bacteria involved in periodontal disease.

Bacteria	Description	Virulence factors	Reference
Actinobacillus actinomycetemcomitans (Aa)	Gram-negative, facultative nonmotile bacteria. Associated with aggressive periodontitis.	- Immunosuppression factors (inhbit blastogenesis, antibody production and activate t-suppressor cells) - Lypopolysaccharides - Antimicrobial resistence - Leukotoxin, killd PMN and monocytes - Resistant to complement-mediated killing	Slots, 1976; Socransky and Haffajee, 1994
Porphyromonas gingivalis (Pg)	Gram-negative nonmotile, anaerobic, pathogenic bacteria	- Gingipain (collect nutrients for the Pg to survive) - Capsular polysaccharide - Evasion of host defenses and immune response - Fimbriae	Naito et al., 2008; Tsuda et al., 2005; Lin et al., 2006
Tannerella forsythensis (Tf)	Gram-negative anaerobic bacteria	- Apoptosis-inducing activity - Production of methylglyoxal - Trypsin-like protease	Cionca et al., 2010; Socransky and Haffajee, 1994

Table 5. Main methods for microbiological diagnosis, pros and cons.

Method	Description	Pros	Cons
Bacterial Culture	- Currently the gold standard. - Determines the presence of the different species	- Evaluates the antibiotic susceptibility - Estimates the number of isolated bacteria	- No culturable bacteria (T. denticola and T. Forsythensis)
Immunological diagnostic methods	- Direct immunofluorescence - Indirect immunofluorescence - Flow cytometry - Latex agglutination - Enzyme-linked immunoabsorbent assay (ELISA)	- Used to establish the nature of the bacterias in the biofilm - Calculates the percentage of bacteria - Greater sensitivity and specificity	- Cannot be used to assess bacterial susceptibilities
Enzymatic detection methods	- Doesn´t detect bacterias directly, determines the presence of enzymes that bacterias produce - BANA (benzoil arginine naftilamida)	- Enables detection of certain bacterial species capable of producing tripsyn enzymes as a virulence factor	- Low specificity and sensitivity - High concentrations of microorganisms
Molecular biology techniques of DNA and RNA	Polymerase chain reaction (PCR): amplifies DNA strands	- High specificity - Diagnosis of major periodontal pathogenic bacteria - Does not need living microorganisms	- Limited bacterial quantification - Ease of contamination in the process. - Inability to provide information on the sensitivity to antibiotics

critical for a successful periodontal therapy. The recent advances in molecular diagnosis will hopefully give new tools for the oral microbiota study, leading to a better understanding of the initiation and progression of periodontal disease.

Nowadays, the periodontal therapies mainly used are pocket debriment and the administration of antibiotics. However, some other equally effective treatments are being investigated lately, such as the phytomedicine.

Conflict of Interests

The authors have not declared any conflict of interests.

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