REVIEW ARTICLE

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Contents

- SUMMARY
- INTRODUCTION
- LITERATURE REVIEW
- CONCLUSION
- REFERENCES

SUMMARY

The microbiome of the human body is home to an extensive community of microorganisms that interact with the immunologically competent host, and may even favor its physiological actions. However, these microbial colonies have potential for harmfulness, including that present in the oral cavity, being able to express themselves intensely in cases of momentary or chronic misadjustment of the human defense system. The diseases with the highest incidence in the oral cavity, periodontitis and dental caries, are pathological processes with microbial involvement and have in the patient's immune system a great combatant to its development, either as a preventive barrier or with direct actions of defensive response. Both pathological conditions were pointed out in this article, extolling the need for the dentist to observe the immunological aspects of impact on oral health. A bibliographic survey was conducted delimited by the theme- the immunological aspects that impact dental practice, through the databases of the digital platforms Google Academic and PubMed; for the realization of this literature review. Based on the scientific notes raised by this work, we

suggest the perspective that; the analysis of immunological aspects associated with the proposed dental diagnoses and treatments may offer a complementation of arguments and approaches that could be much more assertive and effective in the clinical routine.

Keywords: immunology, dental immunology, oral microbiome.

INTRODUCTION

The microbiome of the human body is composed of a complexity of microorganisms that are located in the most diverse locations, with specific community characteristics (SHREINER; KAO; YOUNG, 2015). These communities of microbes are perceived in regions such as the skin, gastrointestinal tract, urinary tract and oral cavity (AGUIAR et al., 2016).

The microbiome of the oral cavity is composed of different microbes, including bacteria, which, in relation to mutualism with an immunologically healthy host, this complex of microbeings can offer benefits, such as facilitating digestion, resistance to untimely colonization and participation in vitamin synthesis (DAGLI et al, 2016).

The presence of dental biofilm can be a major facilitator of oral diseases, because they favor the interaction between microbes, host diet and the individual himself (FLEMMING et al., 2006). In addition to these factors, David et al. (2014) include others, such as systemic, immunological conditions or the use of drugs that would decrease salivation, enabling the propagation and adherence of microorganisms to biofilm.

The oral cavity has, in its lining epithelium, a physical barrier against aggressor agents, including microorganisms with harmful potential (CHUNG et al., 2004). If microbial invasion occurs, the healthy patient's immune system comes into action and through different strategies, fights and restricts the expansion of infection, containing the diseases to the body (DEAS; MACKEY and MCDONNELL, 2003).

The accurate survey and pointing of the microbiota involved in oral injury is fundamental for the clinical diagnosis of the patient and treatment proposal, besides allowing the interrelationship of pathogens with the biomarkers of the individual's defense system, aiming at screening and acting, based on these data, in the prevention of the disease, accurate

diagnosis and development of the specialized treatment plan (NAIFF; ORLANDI; SANTOS, 2012).

The current options of the majority of the population for carbohydrate-rich diets, therefore, of great cariogen potential, make the immune control and defense system virtually incapable of containing the development of caries disease (AKIYOSHI et al., 1998).

The immune system plays a key role in the development of periodontal diseases, with some of its mediators and defense cells present from the beginning of gingivitis (BARTOLD et al., 2010). There is also a large participation of the immune system in the cycle of bone remodeling in the healthy individual (LOPES et al., 2008).

LITERATURE REVIEW

The microbiomes found in different locations of the human organism are common and do not aggressively alter the physiology process, and each of these communities performs its aggregate functions, correlating with the patient's health status, diet and hygiene. The degree of complexity and correlation of this microbiome with the individual, under symbiosis regime, depends on factors, such as anatomical site base, aggregate functions (RENDINBO, 2014) and host age (LEUNG and POULIN, 2008). In this perspective, the presence of certain microorganisms in our physical structure is not harmful, besides bringing benefits to both involved in the mutualistic relationship, including the human relationship (URSEL et al, 2012).

Wang et al. (2017) point out that the micromicrocomponents of the various human microbiomes have harmful potential, and can be enhanced by sporadic or chronic incompetence of the immune system. In case of uncontrolof these complex colonies, the diseases caused by these pathogens have an opportunity to spread to other areas of the human body.

Diseases of the oral cavity of higher incidence are dental caries and periodontal disease, and can be found in fully or partially toothed patients and in all age groups (MARSH, 2000).

According to Zarco et al. (2012), dental caries has the highest incidence among oral diseases. It is also attributed to the most common symptoms in the mouth, such as spontaneous pain

and loss of function. Multifactorial and bacterial colonization, this pathology can affect toothed patients in all age groups and dentures present- deciduous, mixed or permanent, compromising structures of the crown or dental root (SELWITZ et al., 2007).

The nonspecific defense system in the oral cavity manifests itself through the interaction of proteins present in saliva. These proteins have immune memory capacity and control the presence of microorganisms, including bacterial colony (LOESCHE, 1993). These protective proteins act alongside other properties of saliva making it difficult to join bacterial biofilm. According to Tellefson and Germaine (1986), this immunoprotective action has been getting smaller and smaller, thanks to bacterial resistance, especially in individuals with carbohydrate-rich diets.

The resistant behavior of the biofilm microbiota to antimicrobials and the host defense system has been reported by Hobley et al. (2015). The properties of the mature biofilm matrix can provide protection for its bacteria, potentiating bacterial resistance (XIAO et al., 2012).

In the presence of biofilm on the dental structure and diet rich in sugars, the composition of the biofilm becomes more likely to favor the metabolization of carbohydrates by the colonies of microorganisms present in the area. The result of excessive processing of simple sugars is the elimination of acids that result in decalcification of the dental surface: initial stage of caries disease (PITTS, 2017).

An immune expression that can delay the development of the carious lesion is the presence of secretory IgA immunoglobulin (IgA-s). It is more resistant to proteolytic enzymes in the oral cavity (MORRIER and BARSOTTI, 1990). IgA-s covers the surface of the bacteria, preventing them from adhering to the acquired enamel film, in the potential early stage of biofilm development. (TENOVUO, 1997) However, according to Yazaki et al. (1999), when the bacteria are already adhered to the tooth, the protective action of IgA-s becomes insignificant.

Another possibility of immunological intervention to contain the development of caries was proposed by Sato et al. (2002), when proposing the study of antigen III (or antigen A), observed in the cell wall of *S. mutans*. The isolation of the action of this antigen could hinder

bacterial adhesion to the dental surface, an opinion shared by Koga et al. (2002).

Koga et al. (2002) also suggests that the chemical inactivation of antigen III may be a pathway for the development of the caries vaccine. Another probable vaccine agent is the group of glycotransferases that, in gtf-1 glycans of *S mutans*, seem to drastically reduce their virulence (MUNRO et al., 1993)

Periodontal diseases are bacterial infections that result in damage to the supporting tissues and support of the teeth in the oral cavity (FILOCHE et al., 2010). According to Zarco et al. (2012), after the formation of the periodontal scholarship, periodontitis evolves to an irreversible loss classification and its treatment becomes emergency. Other agents may interfere in the progression/development of periodontitis, such as physical agents, chemicals or even these factors associated with poor function of the individual's defense system. Poor hygiene and harmful habits, such as alcohol consumption and smoking, in addition to chronic diseases, favor the rapid progression of periodontal disease (NAIFF; ORLANDI; SANTOS, 2012). Cardoso et al. (2009) characterize periodontal disease as an exacerbated immune response in an attempt to combat aggression from high pathogenic bacteria to the periodontum.

In clinical cases of periodontitis, there is an immunological "start" of primary character, soon after colonization of the gingival groove by microorganisms that induce the development of the disease. At this point, immunological events are observed, such as the presence of inflammatory mediators, production of cytokines and chemokines, expression of adhering molecules and an evident increase in the caliber of peripheral capillaries. Because of the cascade of events of the primary response, there is a migration of inflammatory infiltrate to the region of the initial aggression (FORD; GAMONAL and SEYMOUR, 2010).

The relationship of neutrophils with periodontin was studied by Page (1992). Neutrophils have been reported to be known as the main cells involved in periodontal defense. They are present in the gingival sulcon and are a physiological protection barrier between the epithelium and the biofilm (ATTSTRÖM and SCHROEDER, 1979). If there is some disorder that would hinder neutrophil strain, the result would be some level of periodontal destruction. Neutropenia situations are reported by Nussbaum and Shapira (2011), reaffirming the periodontal condition resulting in destruction due to the absence of the main protective cells.

However; Kartarci, Oyaizu and Van-Dyke (2003) state that the hyper action of neutrophils in case of oral disease can produce cytotoxins that would stimulate bone resorption.

As the effectiveness of the response is variable in each individual, it may be that, if there is sufficient support of the primary immunological response to the containment of the initial aggression, followed by its progression, other defense mechanisms will be required, such as the action of plasmocytes in the production of antibodies for the control of the infectious process (FORD; GAMONAL and SEYMOUR, 2010).

According to Gemmel, Marshall and Seymour (1997), the advancement of periodontitis from stable and reversible to advanced and irreversible is characterized by a change in the inflammatory infiltrate, with a significant increase in the presence of B cells, in addition to T-cells - already present previously- due to the resistance of pathogens to the initial immunological response. Antibodies would be produced immediately, as an advance in the aggressiveness of the immune response.

In more advanced periodontitis, the presence of antibodies may undesiredly induce bone resorption. Still in this clinical situation, high rates of pro-inflammatory cytokines would be observed and, because of their presence, an exacerbated inflammatory symptomatology (ANDRUKHOV et al., 2011).

Lerner (2005) declares that the process of resorption and bone formation is continuous and, in a healthy individual, it remains balanced and regulated by some mediators present in the immunological action- cytokines (interleukins and tumor growth factor) and prostaglandins. The dynamic and balanced process of bone remodeling is controlled by the endocrine system and the immune system (LOPES et al., 2008).

In cases of pathologies that trigger the sudden increase of these mediators, the bone resorption/remodeling process would go into imbalance and, most likely, bone resorption would become greater. Bartold et al. (2010) also says that the large number of cytokines present and their molecules released, in addition to the chronic migration of inflammatory cells, potentiates the resorption of bone tissues.

Lins et al. (2007) states that osteoclasts are hyper stimulated by cytokines due to their

origin: formed by the fusion of the precursors of the monocytes/macrophages lineage. Another cytokine present is Interleukin 1 (IL-1), which stimulates osteoclast function and chemotaxis of neutrophils and macrophages. Lerner (2005) reports the abundant presence of cytokines in regions where gingivitis is clinically diagnosed and that prostaglandins can induce bone formation.

A direct relationship is observed between the degree of tissue destruction and the complex balance of cytokines present at the different levels of periodontitis progression. The trigger for the release of cytokines is related to the complexity and quantity of pathological agents present in the development of injury (FORD; GAMONAL and SEYMOUR, 2010).

An effective way to investigate and characterize the presence of inflammation mediators is through saliva collection (PAGE, 1992). Meanwhile, Teles et al. (2009) state that there is no specific direct relationship between the cytokines found in salivary collection and the degree of development of periodontal disease.

Despite studies on the subject, in the dental routine, the diagnosis of oral diseases seems restricted only to clinical parameters, which could be justified by the lack of knowledge of professionals about the complexity of external and internal elements related to these diseases and the unique character of expression in each individual.

CONCLUSION

In clinical practice, periodontitis and dental caries have as main diagnostic elements, clinical observation and history of the disease. Other possibilities of diagnostic complementation, such as the appointment of the specific microbial flora existing in that pathological process, are constantly neglected, which is proven to be an error. The research and survey of the microbial population present, as well as the immunological competence of the patient, would facilitate an accurate diagnosis and indicate notes for an assertive and individualized treatment plan. From the perspective of prevention, research on immunological aspects related to diseases with higher oral incidence could provide the development of definitive impediments to their development. Further studies and dissemination of the immunological scope is necessary among dental professionals.

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