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Porphyromonas: A dental approach

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Abstract
Introduction: Periapical lesions are characterized by the destruction of the periapical bone and occur as a result of local inflammatory responses of root canal infection by microorganisms.
Objective: To analyze the literature on Porphyromonas bacteria, which is one of the most relevant bacteria in root canal treatment and periodontal disease, and to investigate information on epidemiology, diagnostic methods, treatment and clinical manifestations.
Methodology: Research was carried out in PubMed, SCOPUS and Google Scholar, using the following words, Porphyromonas, epidemiology, diagnostic methods, oral manifestations, treatment.
Results: Porphyromonas bacteria are widely associated with the presence of dentobacterial plaque in different areas of the oral cavity. These tend to be concentrated in a higher percentage in the tongue. Diagnostic methods are obtained by saliva collection or PCR bacterial cultures. Treatment includes the use of vitamin D, chitosan gel, chlorhexidine and povidone, which have been studied to counteract the presence or inhibition of this bacterium. Manifestations associated with this bacterium are linked to oral cavity cancer and presence and increase of dentobacterial plaque.
Conclusions: Gran-negative bacteria in their anaerobic environment can cause different oral manifestations, mainly periodontal and endodontic, which have different methods for their detection. Currently, research continues on methods to obtain more effective treatments against this type of bacteria.

Keywords: Porphyromonas, root canal, periodontal disease, epidemiology, diagnostic methods, treatment, clinical manifestations

Introduction
Increased knowledge of polymicrobial synergy and the development of sequencing techniques have led to the discovery of new potential periodontal pathogens [1].
The host immune response against the periodontal pathogenic bacterial challenge causes severe destruction of dental supporting tissues including cementum, periodontal ligament and alveolar bone [2].
Virulence factors promote congregation of Porphyromonas with other bacteria and the formation of dental biofilm. These virulence factors also modulate a variety of host immune components and subvert the immune response to evade bacterial clearance or induce an inflammatory environment [3]. Inflammatory and host immune responses to microbial communities change the subgingival environment, causing low abundant key opportunistic pathogens such as P. gingivalis to become the dominant bacteria in the biofilm [4]. Bacteria enclosed in the biofilm structure are highly resistant to attack by the host immune system and antibacterial agents, allowing persistent infection [5]. A dense infiltration of lymphocytes, macrophages and dendritic cells is also observed in the surrounding connective tissue, suggesting a robust immune response to these bacteria [6]. P. gingivalis has been shown to survive within macrophages and myeloid dendritic cells where it reprograms them to induce an immunosuppressive T-cell effector response [7]. Accurate identification and culture of many anaerobic microorganisms is difficult. Molecular genetic methods have recently been used in endodontic infections to identify microorganisms [8].

Within the oral cavity there are various bacteria present in certain oral diseases, an example is the bacterium Porphyromonas and its derivatives, which have different ways of acting in the face of infection. Therefore, the aim of the study is to analyze the literature on Porphyromonas bacteria since it is one of the most relevant in root canal treatment and periodontal disease, as well as to investigate information on epidemiology, diagnostic methods, treatment, and clinical manifestations.

2. Materials and Methods

Articles on the subject published through the PubMed, SCOPUS and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews. The search was performed using Boolean logical operators AND, OR and NOT. The search was performed using Boolean logical operators AND, OR and NOT; with the keywords: "Porphyromonas", "root canal", "periodontal disease", "epidemiology", "diagnostic", "treatment", "clinical manifestations". The keywords were used individually, as well as each of them related to each other.

3. Results and Discussion

3.1 Epidemiology

P. gingivalis is a gram-negative, anaerobic, non-motile, asaccharolytic bacillus that produces brown pigmented colonies on blood-agar culture medium.

The oral cavity and associated structures provide ideal conditions for bacterial growth [9]. This is achieved primarily through a reasonably stable temperature (35-37 °C) and pH value (6.5-7.5) with minor fluctuations, providing an ideal environment for most microbial species [10].

Microbes on the tongue facilitate the colonization of bacteria in other regions of the oral cavity through saliva. Changes in environmental conditions increase the potential for pathogenic bacteria to create oral disease [11].

Bacteria in root canal samples from teeth with apical periodontitis in order of prevalence are; P. endodontalis (59%), Fusobacterium nucleatum (55%), Dialister invisus (50%), Olsenella uli (49%) and Parvimonas micra (48%) [12].

In apical lesions, the detection frequencies (%) and median bacterial loads (DNA copies/mg) respectively were 70.8% and 4521.6 for total bacteria; 21.5% and 1789.7 for Porphyromonas endodontalis; and 18.4% and 1493.9 for Porphyromonas gingivalis [13].

Recent studies have revealed that the oral microbiota harbors a decrease in overall microbial diversity in parallel with an alteration of the microbial consortium, such as an enrichment of Porphyromonas [14]. In a study carried out in Chile, P. endodontalis was detected in 41.5% (22 patients) of the microbiological samples obtained from teeth diagnosed with asymptomatic apical periodontitis [15].

The main cause of dental abscess is poor hygiene together with uncontrolled dental caries. The damage produced in the enamel will cause the oropharyngeal bacteria to penetrate the dental cavity, causing a local infection, which will subsequently evolve towards the development of a dental abscess [16].

Porphyromonas bacteria are widely related to the presence of dentobacterial plaque present in different areas of the oral cavity. These tend to be present in a higher percentage on the tongue and generate infections that can trigger different conditions. They can manifest themselves in periodontal disease, which can connect with the supporting tissues of the tooth, and can enter the dental pieces through periapical lesions.

3.2 Diagnostic Methods

Mouthwash samples were originally collected in both cohorts, instead of blood samples, in order to obtain oral cell DNA. Mouthwash samples containing the broad spectrum of oral bacteria are suitable for testing some hypothesis [17]. Future studies should focus on evaluating sites with different diagnoses for the same patient and investigate the complex host-biofilm interaction [18]. They should include microbiota obtained from oral cavity samples; have data from cohort or observational studies or randomized controlled trials, including gastrointestinal (GI) cancer cases. And they should report the results of oral microbiota differences between GI cancer patients and healthy controls, or oral microbiota detection capabilities for GI cancer [19].

On the other hand, prediction models based on oral microbiome profiles are generated using five machine learning algorithms and their ability to predict patient status is validated [20].

Another diagnostic method used in endodontics is to collect samples from the apical third of the roots using a #10 K file and then amplify them using multiple displacement amplification and by PCR with universal primers [21]. In vitro studies have been evaluated using Minimum Inhibitory Concentration and Minimum Bactericidal Concentration on planktonic cultures of Porphyromonas gingivalis and Porphyromonas endodontalis. In addition, gas chromatographic analyses were performed to measure the concentration of volatile sulfurized bodies, bacterial cultures and to characterize the components of alternifolia oil [22].

Subgingival biofilm samples were collected as follows: I) group pH - from the mesial / buccal side of each tooth in two randomly chosen contralateral quadrants; II) group with three sites in each of the following probing depth categories: superficial (≤3 mm), moderate (4-6 mm) and deep (≥7 mm). Checkerboard DNA hybridization was used to analyze the samples [23].

Conventional 16S rRNA gene sequencing is sometimes a useful alternative technique for bacterial identification, but is confused with polymicrobial infection [24].

There are several diagnostic methods that can be performed for the detection of P. gingivalis. The method is developed according to what each study requires, either by saliva collection or by PCR bacterial cultures. These studies carry a complex evaluation and diagnosis, as they are especially used in randomized controlled studies.

3.3 Oral Manifestations

Porphyromonas gingivalis is one of the most commonly detected pathogens in periodontal disease and root canal infections. Its viability and pathogenicity are greatly increased in plaque biofilms [25].

P. endodontalis and its main virulence factor, lipopolysaccharide (LPS), are associated with the development of periapical lesions and alveolar bone loss [26]. P. gingivalis and F. nucleatum in the presence of ATP, may play a significant role in IL-1β-induced pulpal inflammation by deregulating inflammasomes and act as regulators [27]. Porphyromonas gingivalis and other pathogenic bacteria, implicated in periodontal disease, induce reactions that have repercussions at the systemic level and can even generate or

exacerbate pathognomonic processes that would affect not only oral health, but also the general health of the host [28].

Porphyromonas gingivalis is one of the bacteria involved in the formation of bacterial plaque biofilms and plays an important role in the progression of periodontal disease [29]. The microbiota of persistent infection is polymicrobial with predominance of P. gingivalis in all phases of endodontic retreatment, regardless of the method used for microbial identification. Associations between specific bacteria were found [30].

Infection by parasites linked to periodontal disease is strongly implicated in the pathogenesis and its development. Their relationship is linked to the citrullination process and production of anti-citrullinated peptide antibodies [31]. The relationship of Porphyromonas gingivalis and oral squamous cell carcinoma has been studied for several years. Previous studies have focused on the direct effect of P. gingivalis on the activities of primary epithelial cells and squamous cells in the oral cavity. In vitro and in vivo data suggest that P. gingivalis may promote oral cancer immunoevasion by protecting the cancer from macrophage attack [32].

The literature review describes the relationship of Porphyromonas bacteria in periodontal disease. These bacteria are the first line in the formation of dentobacterial plaque, which initiates the different manifestations, such as apical lesions caused by the proliferation of bacteria that lead to infections. There are studies on the relationship between these bacteria and oral cancer.

3.4 Treatment

Active form of vitamin D (calcitriol, 1α,25-dihydroxyvitamin D3, 1α,25 (OH)2D3, 1,25D). Treatment with 1,25D decreased the number of live P. gingivalis in KB cells and U937 cells in a dose-dependent manner [33]. In a study conducted in 2020, mouthwash containing chlorhexidine digluconate (0.1%) was used. A numerical decrease was observed, however, not statistically significant (P = 0.066), in the number of live bacteria in the group treated with the PVP-iodine solution, compared to the control group [34]. Cinnamon (Cinnamomum zeylanicum) bark essential oil and its main constituent cinnamaldehyde against Porphyromonas gingivalis inhibited P. gingivalis biofilm formation by 74.5% [35]. A new dysfunctional zinc coordination polymer has been hydrothermally synthesized from tetrabromoterephthalic acid. The potential anti-infective mechanism was further studied by using molecular docking technique [36]. Akkermansia muciniphila is a beneficial intestinal commensal whose anti-inflammatory properties have recently been demonstrated. One study aimed to evaluate the effect of A. muciniphila on inflammation caused by Porphyromonas gingivalis, A. muciniphila decreased inflammatory cell infiltration and bone destruction [37]. Metronidazole with gingival epithelial cells present in a report reveals that persisters of P. gingivalis induced by lethal antibiotic treatment were able to maintain their ability to adhere to and invade human gingival epithelial cells [38]. Ginger exosomes (GELN) are selectively taken up by the periodontal pathogen Porphyromonas gingivalis in a phosphatidic acid-dependent manner. Upon binding the pathogenic mechanisms of P. gingivalis, they were significantly reduced after interaction with GELN cargo molecules. Previous reports have shown that GELNs have anti-inflammatory effects [39].

The effect of chitosan gel on total oral bacteria, Porphyromonas gingivalis, Tannerella forsythia and Treponema denticola, was evaluated during orthodontic treatment with mini-implants. The total number of bacteria was reduced after application of chitosan gel. The greatest decrease in the proportion of P. gingivalis was observed in the chlorhexidine gel application group, which showed a value of 70.86% [40].

Throughout the literature review, different treatments such as the use of vitamin D, chitosan gel, chlorhexidine, and povidone, have been studied to counteract the presence or inhibition of this bacterium. In some studies, favorable results have been obtained, while in others it has been proven that they are not effective in reducing gram-negative bacteria. The discovery of products, ranging from gels to essential oils, which could help reduce the activity in the oral cavity, is still in progress.

4. Conclusions

Gram-negative bacteria in their anaerobic environment can cause different oral manifestations, mainly periodontal and endodontic. It is closely related to the presence of microfilm found in the mouth and causes its proliferation. There are different methods for its detection, although currently methods are still being investigated to find a treatment with a higher percentage of effectiveness to help inhibit this type of bacteria.

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