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Porphyromonas gingivalis, an Orthodontic point of view

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Abstract
Introduction: Porphyromonas gingivalis (Pg) levels progressively increase in quantity and quality in the course of orthodontic treatment posing a risk to periodontal health.
Objective: To analyze the existing literature on the prevalence, clinical manifestations, diagnostic methods, treatment and prevention of Porphyromonas gingivalis from a systemic, oral and orthodontic point of view.
Methodology: A literature review was carried out by searching databases using the keywords: "Porphyromonas gingivalis", "prevalence", "orthodontics", "treatment", "prevention", "diagnosis", "levels", "systemic", "treatment" and "periodontitis".
Results: There is a 68.2% prevalence of Pg in periodontal pockets which increases during orthodontic treatment. Its main clinical manifestations in orthodontic treatment are increased depth and bleeding on probing, decreased level of clinical attachment and increased gingival and periodontal index. Pg is detected by measuring salivary MMP-9 levels by ELISA and intraoral clinical examination. Treatment for Pg infection includes mechanical therapy and adjuvant therapies such as the use of amoxicillin and metronidazole, chitosan and azithromycin or azithromycin alone. Toothbrushing and interproximal cleaning are the cornerstones of preventing the occurrence of Pg during orthodontic treatment, in conjunction with oral and periodontal hygiene education.
Conclusion: Pg levels increase during orthodontic treatment, which implies a risk for the development of periodontitis during and after treatment, its prevention is important at all stages of treatment.

Keywords: Porphyromonas gingivalis", "prevalence", "orthodontics", "treatment", "prevention", "diagnosis", "levels", "systemic", "treatment" and "periodontitis

1. Introduction
Orthodontic appliances are a risk factor for the development of periodontal disease due to the increase of periodontopathogenic microbes during treatment [1]. The decrease in the natural cleaning mechanisms by the tongue and cheeks, as well as the difficulty in brushing technique, favor the retention of dental plaque and produce a change in the population of bacteria in the oral cavity [2]. One of the periodontopathogenic bacteria associated with the imbalance of the microbiota during orthodontic treatment is Porphyromonas gingivalis (Pg) [3]. It is a gram-negative anaerobic bacterium found in subgingival dental plaque and highly associated with the onset and progression of periodontal diseases [4, 5]. It is present in subgingival biofilms causing progressive and irreversible destruction of periodontal supporting tissues [6]. It has been observed that Pg levels progressively increase in quantity and quality over the course of orthodontic treatment and remain for up to 6 months after removal of fixed appliances [7].
Currently, there are not enough research to evaluate the consequences of the presence of Pg in orthodontic treatment. The aim of this paper is to review the existing literature on the prevalence, clinical manifestations, diagnostic methods, treatment, and prevention of Porphyromonas gingivalis from a systemic, oral and orthodontic point of view.

2. Materials and Methods

A literature review was carried out by searching the PubMed, Scopus and Google Scholar databases, including articles from the last 5 years (January 2018 to January 2022). The keywords used for the search were: "Porphyromonas gingivalis", "prevalence", "orthodontics", "treatment", "prevention", "diagnosis", "levels", "systemic", "treatment" and "periodontitis". These terms were related in the search equation with the Boolean connector "AND". The selection of the articles was carried out by reading their abstract, title and evaluating their quality through the PRISMA guidelines. In addition, the quality of this systematic review was assessed using the Systematic Measurements Critical Appraisal Tool.

3. Results and Discussion

3.1 Epidemiology

3.1.1 Systemic

The oral microbiota is composed of about 770 species of microorganisms. When there is an imbalance in the composition of the microbiota, the levels of certain microorganisms that can cause oral pathologies with systemic repercussions increase. P. gingivalis has been described mainly in association with mammals and is involved in chronic oral infections and secondary systemic pathologies such as cancer or degenerative disorders [8]. High concentrations of Pg, the key pathogen of periodontal disease, have been identified in the brains of patients who have died of Alzheimer's disease [9].

3.1.2 Oral

Periodontal disease, caused by P. gingivalis infection, is a worldwide public health problem. It has been estimated to have a prevalence of 20% to 50% worldwide, being one of the main causes of tooth loss with compromised masticatory function, esthetics, self-esteem and quality of life [10]. A prevalence of 68.2% of Pg in periodontal pockets has been observed [11]. In addition, it exhibits higher abundance in the subgingival plaque of females, whereas, in males, it is found in higher levels in the supragingival plaque [12]. Tobacco and opium use have been associated with periodontal disease, suggesting a relationship between these habits and the presence of P. gingivalis [13].

3.1.3 Orthodontic

The use of fixed orthodontic appliances affects the composition of the subgingival microbiota from the early stages of treatment, which increases the prevalence of Pg and other periodontal pathogens [14]. The increase in Pg levels depends on the appliance used, as some types of brackets provide more retentive sites than others [15, 16]. More contamination of this bacterium has been observed in metal brackets than in clear aligners. In addition, it is more prevalent in lingually placed fixed appliances than in vestibularly placed ones [17].

P. gingivalis causes periodontal disease, which has a prevalence of 20% to 50% worldwide. In addition, there is a 68.2% prevalence of Pg in periodontal pockets, which increases during orthodontic treatment, with lingual fixed metal appliances having the highest levels.

3.2 Clinical Manifestations

3.2.1 Systemic

Porphyromonas gingivalis is the main pathogen contributing to the onset and progression of periodontal disease. However, several systemic pathologies have been associated with Pg infection, such as cardiovascular disease, rheumatoid arthritis, pancreatic cancer, hepatitis, oral cancer and neurodegenerative diseases, among others [18, 19]. Pg infection results in the release of inflammatory mediators and toxins into the bloodstream, causing systemic manifestations or aggravating pre-existing conditions [20]. In addition, it has been detected outside the oral cavity in synovial fluid and plasma, confirming its correlation with systemic diseases [21]. People with diabetes and cardiovascular disease are more susceptible to an infection, and in addition, the presence of P. gingivalis during these diseases worsens the patient's situation [22]. Finally, Pg is associated with the development of adverse effects of pregnancy such as preeclampsia, preterm delivery, spontaneous abortion, gestational diabetes and fetal growth restriction [23].

3.2.2 Oral

The main oral manifestation of Porphyromonas gingivalis infection is the development of periodontitis, characterized by gingival inflammation, bleeding and bone loss [24]. After prolonged inflammation, the attachment of the junctional epithelium to the root surface is disrupted, resulting in the formation of a periodontal pocket colonized by P. gingivalis and other periodontal pathogens. In this new environment, Pg releases toxins as by-products of its metabolism and contributes to the progression of alveolar bone loss [25]. In addition, it has also been found in the microscopic gaps between dental implants and their attachments, favoring the development of peri-implantitis [26].

3.2.3 Orthodontic

Orthodontic treatment favors the accumulation of dental plaque, thus increasing the transport and amount of subgingival P. gingivalis, causing increased gingival inflammation. The amount of Pg remains high for 6 months after appliance removal, which implies a potential risk for the development of periodontitis during and after orthodontic treatment [27]. In addition, subgingival Pg accumulation induces increased bleeding on probing, changes in probing depth, level of clinical attachment, and increased gingival and periodontal index [28].

The presence of P. gingivalis increases in orthodontic treatment and leads to increased bleeding on probing, increased probing depth, decreased clinical attachment level and increased gingival and periodontal index. In addition, it is related to systemic diseases such as diabetes, cardiovascular diseases, rheumatoid arthritis, pancreatic cancer, hepatitis, oral cancer and neurodegenerative diseases.

3.3 Diagnostic Methods

3.3.1 Systemic

One way to detect it is by analyzing the immunogenicity of its virulence factors, which indicates the host response to infection by this bacterium [29]. Kgp12 is an epitope of the virulence factor Lys-gingipain (Kgp) of P. gingivalis, which causes immunoglobulin G (IgG) immunoreactivity, the levels of which can be measured in serum by enzyme-linked immunosorbent assay (ELISA) and thus, detect the presence of chronic periodontitis [30]. In addition, it has been found that the N-terminal end of the RgpA epitope, which is a domain of a protein called gingipain, is also an antigen recognized by IgG in P.gingivalis infection, and can be used for the development of a rapid diagnostic "kit" for periodontal disease [31]. On the other hand, Botelho *et al.* found a

relationship of higher white blood cell levels, higher neutrophil levels, higher erythrocyte sedimentation rate and lower mean blood platelet volume during an infection [32].

3.3.2 Oral

The easiest way to achieve a diagnosis of periodontal disease, which implies the presence of Pg, is through intraoral clinical examination by periodontal probing, which indicates the appearance of periodontal pockets, but does not provide detailed information on the structural changes taking place in the underlying tissues [33]. In the latest 2017 global consensus, the diagnosis of periodontitis was defined as clinical attachment loss greater than 3 mm with periodontal pockets greater than 3 mm in 2 or more teeth [34]. In addition to clinical examination, metalloproteinases 8 and 9 (MMP), tissue inhibitor of metalloproteinase 1, and myeloperoxidase are important biomarkers found in saliva samples for the diagnosis of P. gingivalis infection [35, 36].

3.3.3 Orthodontic

Metalloproteinase 9 (MMP-9) is an enzyme involved in collagen degradation present in the crevicular fluid during periodontal disease and is detectable by enzyme-linked immunosorbent assay (ELISA). This enzyme also increases during orthodontic treatment, making it a viable diagnostic tool for the presence of P. gingivalis and the levels of inflammation and periodontal involvement during the course of orthodontic treatment [37].

Pg screening is performed by ELISA-type serum tests that detect a protein called gingipain, which is an antigen recognized by IgG in P. gingivalis infection. In orthodontic treatment, it is detected by salivary MMP-9 levels and intraoral clinical examination.

3.4 Treatment

3.4.1 Systemic

As mentioned above, it is implicated in a wide variety of systemic diseases, so its treatment will depend on the organ affected. Toxic proteins of this bacterium, called Gingipains, have been found in the brain of Alzheimer's patients. Therefore, inhibition of this protein has been a therapeutic target to reduce the Pg load in the brain, reduce neuroinflammation, block the production of beta-amyloid and rescue hippocampal neurons [38, 39]. On the other hand, it has been shown that control of P. gingivalis by root planing has an impact on metabolic control and reduction of systemic inflammation in patients with type 2 diabetes and cytokines involved in cardiovascular diseases [40, 41].

3.4.2 Oral

Clinical practice guidelines for the treatment of clinical manifestations of P. gingivalis establish different levels of intervention depending on the severity of the infection. The first step consists of supragingival plaque removal and control of risk factors; followed by supra- and subgingival instrumentation with or without the use of adjuvant therapies; the next step consisting of different types of periodontal surgery; and finally, frequent periodontal maintenance [42]. The use of amoxicillin and metronidazole in conjunction with periodontal therapy has been indicated for better restoration of clinical parameters such as bone loss and probing depth [43]. Additionally, the use of antimicrobials such as chlorhexidine, zinc and chitosan have been proposed to decrease host levels of P. gingivalis [44, 45, 46]. Finally, new experimental therapies have been developed using the algae Spirulina maxima or the commensal bacterium Akkermansia muciniphila as natural adjuvants in periodontal treatment [47, 48].

3.4.3 Orthodontic

It has been suggested the use of orthodontic mini-implants coated with chitosan, chitosan and azithromycin or azithromycin alone, to suppress P. gingivalis colonization around them [49]. On the other hand, the use of probiotic mouth rinses has been suggested as an adjunct to tooth brushing to decrease P. gingivalis levels during orthodontic treatment with fixed appliances [50]. Finally, orthodontic treatment has been shown to result in an improvement in all clinical parameters of periodontal disease (probing depth, clinical attachment level, bleeding on probing and plaque index) 4 months after the end of treatment [51].

Treatment for Pg infection includes supragingival and subgingival plaque removal, periodontal surgery and hygiene maintenance. In addition, there are adjunctive therapies such as the use of amoxicillin and metronidazole, chitosan and azithromycin, or azithromycin alone and probiotic rinses during orthodontic treatment.

3.5 Prevention

3.5.1 Systemic

The World Health Organization reported that periodontitis is one of the main causes of tooth loss and, subsequently, can worsen a person's quality of life. In addition, it affects the progression of some diseases, such as diabetes mellitus, kidney disease, premature birth, aspiration pneumonia and arteriosclerosis. Therefore, prevention of P. gingivalis infection is important to maintain both systemic and oral health [52]. Nutrition is an important modifiable parameter, which can have a major impact on oral health and be reflected in good systemic conditions and quality of life [53]. Deficiencies of vitamins A, C, E, folic acid and calcium have been associated with the progression of periodontal disease [54]. In addition to tooth brushing and other oral hygiene practices, there are other important factors for the prevention of P. gingivalis infection such as education, motivation, manual dexterity, socioeconomic status and control of risk factors [55].

3.5.2 Oral

Tooth brushing and interproximal cleaning are the cornerstones of periodontal disease prevention. The main prophylactic approach requires personalized instruction in the implementation of a systematic oral hygiene regimen by a dentist [56]. There are ancillary devices to tooth brushing for oral hygiene such as dental floss, interdental brushes, and oral irrigators. It has been suggested that the use of oral irrigators has a positive effect on gingivitis scores and probing depth. For plaque removal, adjunctive use of interdental brushes is significantly more effective than manual tooth brushing alone [57].

3.5.3 Orthodontic

The finding that increased gingival inflammation implies greater intensity and duration of pain during orthodontic treatment shows that oral hygiene instructions and periodontal care are of great importance before and during treatment in both periodontally compromised and healthy individuals [58]. In addition, it has been proposed that the use of antibacterial stainless steel is effective in reducing the incidence of P. gingivalis and may be a more suitable material for orthodontic attachments than conventional stainless steel in orthodontic

treatment [59]. Oral hygiene instructions and topical application of fluoride every 6 months have been shown to be effective measures for plaque control and reduction of Pg in patients with fixed appliances [60].

Tooth brushing and interproximal cleaning are the cornerstones of preventing the occurrence of Pg during orthodontic treatment, in conjunction with oral and periodontal hygiene education.

4. Conclusions

There is a 68.2% prevalence of Pg in periodontal pockets which increases during orthodontic treatment. The presence of Pg in orthodontic treatment produces greater depth and bleeding on probing, a decrease in the level of clinical attachment and an increase in the gingival and periodontal index. It is detected by measuring salivary MMP-9 levels by ELISA and intraoral clinical examination. Treatment for Pg infection includes mechanical therapy and adjuvant therapies such as the use of amoxicillin and metronidazole, chitosan and azithromycin, or azithromycin alone. Toothbrushing and interproximal cleaning are the cornerstones of preventing the occurrence of Pg during orthodontic treatment, in conjunction with oral and periodontal hygiene education.

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