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Tannerella forsythia: A periodontopathic pathogen review

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Abstract
Introduction: Periodontal disease impacts up to 50% of the population worldwide. *Tannerella forsythia* is a gram-negative anaerobic bacterium, which is part of the red complex that triggers periodontal disease.
Objective: To evaluate *T. forsythia* in relation to its epidemiology, diagnosis, treatment and oral manifestations, as well as its periodontal and systemic role.
Methodology: A search for information was carried out in databases such as PubMed, Scopus and Google Scholar, using logical operators AND, OR and NOT. We searched for the mention of *T. forsythia* bacteria related to the keywords: epidemiology, oral manifestations, diagnosis, and treatment.
Results: *T. forsythia* bacteria are present in the oral cavity, increasing their colonization in periodontal disease and endodontic lesions, as well as in cardiovascular and systemic diseases. Diagnosis can be made by molecular tests such as PCR and ELISA, or by clinical findings. Its treatment consists of the first two phases of periodontal treatment, hygienic and, if necessary, corrective for its elimination and regulation of colonization. In the oral cavity it can develop clinical attachment loss, bleeding on probing and increase in pocket depth, as well as loss in bone crest levels.
Conclusions: The knowledge of this bacterium as well as its effects are of high impact on the supporting tissues. Its control is the key to a successful periodontal treatment.

Keywords: *Tannerella forsythia,* epidemiology, diagnosis, etiology, treatment and oral manifestations

1. Introduction
Periodontal disease is estimated to impact 20-50% of the population worldwide, being considered as a chronic and progressive disease, mainly triggered by the presence of the red complex bacteria, a disease which has the potential to be involved in the development of other degenerative conditions of cardiovascular and systemic nature [1, 2]. Within the red complex we have *Tannerella forsythia*, gram-negative anaerobic bacteria in the form of a bacillus, which is considered periodonto-pathogenic in humans. This species was discovered by Dr. Anne Tanner in 1990 at the Forsyth Institute in Cambridge, Massachusetts [3]. It has been linked to atherosclerotic conditions, resulting in acceleration of atherosclerotic conditions due to lipid-lowering influence [4], as well as its presence and activity in bacterial vaginosis [5]. Within the oral cavity, *T. forsythia* has the potential to contribute to the pathogenicity of the microbiota in subgingival plaque, commonly associated with advanced periodontal disease, triggering clinical attachment loss of tooth-supporting tissues [6].
Early detection of this bacterium is important for an adequate diagnosis and treatment of periodontal disease, resulting in an adequate control of the oral microbiota to prevent the progression of the destruction of the supporting tissues [7]. As of today the information available regarding the bacterium is limited due to its difficult handling in laboratory tests, however, the objective of this article is to present the available information in a synthesized manner through a systematic analysis, making known its epidemiology, diagnosis, treatment and oral manifestations for easy understanding, and future research.

2. Materials and Methods

Information was collected from articles published in English and Spanish on PubMed, SCOPUS and Google Scholar servers, with emphasis on the last 5 years. The quality of the articles was evaluated based on the standard guidelines, i.e., identification, review, choice and inclusion. The quality of the review was assessed using the measurement instrument for evaluating systemic reviews. Boolean logical operators AND, OR and NOT were used in the search. It was performed with the words "Tannerella forshythia", together with the following terms: "epidemiology", "diagnosis", "treatment" and "oral manifestations".

3. Results & Discussion

3.1 Epidemiology

3.1.1 Incidence reported by the World Health Organization (WHO)

Currently in the year 2023, the WHO records a current net population of 1 billion presenting cases of periodontal disease in patients, this being 19% of the total adult population [8].

3.1.2 Percentage of *T. forsythia* in periodontal disease

This bacterium is present in 60.7% of the cases of patients with active periodontal disease, after the 85.7% of the bacterium "*Porphyromonas gingivalis*", considering *T. forsythia* as a secondary colonizer of the supporting tissues in the subgingival area of the teeth [9].

Similarly, the increased presence of *T. forsythia* within the sulcus and periodontal pocket is closely related to the depth of the sulcus, with similar percentages in terms of the presence of the other two bacteria that make up the red complex [10].

3.1.3 *T. forsythia* and its presence in root canals

The microflora that can form in root canals can be assimilated to that found in periodontal tissues, since both tissues can communicate with each other through the apices, accessory canals, dentinal tubules or fractures in the structure, leading to microleakage. In a study conducted in 2020, the microflora of 41 canals was analyzed, resulting in the presence of *T. forsythia* in 56.1% of them; with this we could conclude that the bacterium resides comfortably in the anaerobic environment that root canals provide [11].

In another study it was found that the presence of *T. forsythia* together with *T. denticola* within periapical lesions may be related to inflammation and pain in periapical lesions [12].

3.1.4 *T. forsythia* and its relationship with other diseases

3.1.4.1 Incidence in patients with cardiovascular conditions: Another study analyzed the colonization levels of bacteria residing in patients with cardiovascular conditions compared to healthy patients, resulting in a significant interrelationship between these patients with a 68% increase in the population of *Tannerella forsythia* in their oral cavity, concluding that patients in the study group tend to develop periodontal disease more easily [13].

3.1.4.2 Incidence in patients with atherosclerosis: *Tannerella forsythia* bacteria can be found in atherosclerosis, a disease consisting of the accumulation of plaque composed of different elements on the walls of blood vessels. In a study conducted in 2020, using the polymerase chain reaction (PCR) method, it is estimated that the presence of *T. forsythia* in periodontal pockets and atherosclerotic vessels is present in 75.6% and 53.3% of cases respectively, marking an intimate relationship between one condition and the other [14].

3.1.4.3 Interrelation with bladder cancer: The relationship between the level of antibodies to *Tannerella forsythia* and the risk of developing different types of cancer, including bladder cancer, was studied. ELISA tests showed that *T. forsythia* antibodies can inversely predict this type of cancer within 95%, concluding that the reduced immune response in periodontitis is related to a risk factor for the development of cancer [15].

3.2 Diagnosis: Depending on the type of study, a variety of diagnostic methods can be used to identify this bacterium. Molecular biology tests can be used, such as the polymerase chain reaction (PCR), as well as the ELISA test. On the other hand, taking into account that periodontal disease is strictly developed by the presence and interaction of *T. forsythia* together with the others, clinical diagnostic methods are also taken into account, such as gingival bleeding rates, pocket depth and in periapical lesions the presence of inflammation and pain [11, 16].

In a study carried out in pregnant women to study the presence and activity of periodontopathogenic bacteria, saliva samples were taken from the patients and then PCR tests were performed on each of them to quantitatively detect the amount of the 4 periodontopathogenic bacteria studied. In this study, *T. forsythia* was found to be related to patients with poor hygiene habits [17]. In another study, using the polymerase chain reaction, the interrelation of high levels of *Tannerella forsythia* presence with the risk of triggering the fever stage in patients in a nursing home was discovered [18]. As mentioned above, there are studies that use enzyme-linked immunosorbent assay (ELISA) to measure their results.

In a study conducted in 2020, the interaction of low immunoglobulin production due to immune deficiency in the presence of *T. forsythia* and other bacteria with the development of cardiovascular disease is inversely related to the aforementioned test [15]. In another study, the presence of immunoglobulin Y (IgY) was observed which has affinity for carylysin, a protein found in the membrane of *T. forsythia*, resulting that IgY-based ELISA immunoassay may be useful as part of the detection of protein-based biomarkers of periodontopathogenic bacteria in the clinic or at the point of care [19]. In the following article, clinical and molecular biology techniques were combined to arrive with the result of the presence of *T. forsythia* in areas classified with peri-implantitis; mechanical debridement was performed using titanium curettes to then analyze by RNA sequence the types of bacteria present, resulting in a positive result of *Tannerella forsythia* activity in peri-implantitis [20]. Finally, another article analyzed antibiotic resistance in patients with peri-implantitis, including amoxicillin, azithromycin and moxifloxacin against many bacteria of the gingival sulcus and pocket, including *T. forsythia* [21].

3.3 Treatment: The treatment of choice for the control of *Tannerella forsythia* is based on the hygienic and corrective phase of periodontal treatment, since this consists of removing fomites to improve periodontal health [22].

Emphasizing the importance of the hygienic phase in our patients is relevant since with proper plaque control and hygiene instructions appropriate to the patient's needs we can regulate the homeostasis of a healthy environment in the oral cavity, remembering our biannual interventions at least to perform an adequate detartration and monitor oral tissues and structures [23].

In cases where bleeding, deep pockets and levels of clinical

attachment loss are present, we will proceed with scaling and root planing to remove foci of infection below the gingival margin. The removal of calculus together with the smoothing of root surfaces is considered a fundamental step for the reduction of bacterial load and regulation of a healthy microflora [24]. In the event that scaling and root planing is insufficient, it will be necessary to proceed with surgical intervention in areas where recurrent pockets are present after the revision appointment. The debridement flap is the treatment of choice for adequate access to instrumentation of the root surfaces, as well as implant surfaces; in the latter case it is recommended to perform an implantoplasty to smooth the implant surface [25, 27].

There are adjuvants in the process of regulating the bacterial environment, such as the use of mouthwashes based on chlorhexidine and chitosan, and the use of antibiotic therapy such as amoxicillin and metronidazole [28, 29].

We must take into account that there may be cases in which the root canals present lesions of periodontal origin, allowing *T. forsythia* to colonize the internal surfaces of the root canal. In this case, matching the symptomatology and clinical findings, endodontic treatment is performed to control the infection and eliminate the microorganisms [21, 30].

3.4 Oral Manifestations: In a state of disrupted homeostasis, the expansion of periodontopathogenic bacteria begins to mark a turning point for the potential development of imbalance, since it is unlikely that host homeostasis can be restored without thinking of a robust and tissue-destructive inflammatory response [31, 32]. For this reason *T. forsythia* is intimately related to periodontal disease, however, it should be taken into account that in healthy conditions it can also be present, only at lower rates [33]. When the homeostasis of the balance in the microflora is altered, it is the perfect moment for this bacterium to reproduce more rapidly [34], and when clinically loss and destruction of supporting tissues can be recorded, this means that *T. forsythia* increases its virulence factors until it becomes pathogenic [35]. To identify the elevated presence of *T. forsythia* in the mouth, the presence of bleeding on probing, loss of attachment levels, as well as deep pockets can be taken into account [36]. In studies in rats, loss of the bone crest level related to this bacterium has been observed radiologically [37].

Finally, we must keep in mind that no bacteria act alone, there must be a synergy with their ecology, propagated by bacteria working together, available substrate and the right environment [38].

4. Conclusions

Tannerella forsythia is one of the three bacteria that compose the red complex, which triggers the progression of periodontal disease, leading to the destruction of supporting tissues. In addition to occurring in the oral cavity, it can be involved in the progression of autoimmune and cardiovascular diseases. The oral manifestations produced by this bacterium are loss of clinical attachment level, deep pockets and bleeding on probing, as well as loss of bone crest level. Its treatment consists of the implementation of the hygienic and corrective phase of periodontal treatment to reduce its levels in the mouth.

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