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### *Aggregatibacter actinomycetemcomitans*: An orthodontic approach

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#### Abstract

**Introduction:** Orthodontic appliances may be associated with a worsening of preexisting periodontal diseases caused by *Aggregatibacter actinomycetemcomitans*.

**Objective:** To analyze the literature on the characteristics of *A. actinomycetemcomitans* and its relationship with orthodontics, particularly epidemiology, oral manifestations, diagnostic methods and treatments.

**Methodology:** Using the keywords “*A. actinomycetemcomitans*”, “orthodontics”, “oral manifestations”, “treatment” and “epidemiology”, the main public databases were searched, with emphasis on the last 5 years. It was evaluated with the PRISMA and AMSTAR-2 guidelines.

**Results:** Orthodontic treatment increase the prevalence of *A. actinomycetemcomitans*. Preexisting aggressive periodontitis is a great challenge to clinicians when providing orthodontic treatment due to *A. actinomycetemcomitans*. PCR is the technique of choice as a diagnostic method that is currently used most frequently in research centers. The removal of orthodontic appliances has shown a significant reduction in dentobacterial plaque, as well as proper oral hygiene and, if necessary, the use of alternative treatments such as moxifloxacin and antimicrobial photodynamic therapy.

**Conclusions:** Correct oral hygiene during orthodontic treatment is essential to reduce the presence of *A. actinomycetemcomitans*, thus diminishing cariogenic risk as well as a worsening of periodontal diseases.

**Keywords:** *A. actinomycetemcomitans*, orthodontics, oral manifestations, treatment and epidemiology

#### 1. Introduction

Orthodontic appliances may be associated with increased cariogenic risk and worsening of preexisting periodontal diseases. There is evidence regarding the association between orthodontic appliances and changes in oral microbiota, including *A. actinomycetemcomitans* [1]. First described in 1912 and variously named during the intervening years, *A. actinomycetemcomitans* was recognized as a member of the normal human oral microbiota in the 1950s [2]. Facultatively anaerobic, immotile, 0.4 to 0.5  $\mu\text{m} \times 1.0$  to 1.5  $\mu\text{m}$  in size. It grows poorly in ambient air, but well in 5% CO<sub>2</sub> [3, 4]. *Aggregatibacter actinomycetemcomitans* is a periodontal pathogen that colonizes the oral cavity of a large proportion of the human population [5]. It constitutes one of the leading causes of periodontal disease in young people and adolescents [6, 7]. This organism can induce bone resorption by various virulence factors in periodontal disease [6, 8]. Preserving the integrity of periodontal tissues is one of the main concerns of orthodontic specialists, which has led to the definition of specific hygiene protocols for orthodontic patients [1]. The application of orthodontic appliances makes oral hygiene difficult and increases plaque accumulation, which often leads to gingival inflammation [9, 10].

Currently there is no adequate review of *A. actinomycetemcomitans* in orthodontics, it is of vital importance that the orthodontist takes into consideration the patient's susceptibility to periodontal disease and during treatment takes the necessary measures to minimize the retention of bacterial plaque where we find *A. actinomycetemcomitans*.

In this work we analyzed the literature on the characteristics of *A. actinomycetemcomitans* and its relationship with orthodontics, particularly, the diagnostic methods, treatments, oral manifestations and epidemiology.

## 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 PRISMA guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews (AMSTAR-2). The search was performed using Boolean logical operators AND, OR and NOT. It was realized with the words “*A. actinomycetemcomitans*”, “orthodontics”, “oral manifestations”, “treatment” and “epidemiology”. The keywords were used individually, as well as each of them related to each other.

## 3. Results & Discussion

### 3.1 Diagnostic methods

To confirm the presence of *A. actinomycetemcomitans*, characteristic features of the colony were identified based on its typical “star-shaped internal structure” [11]. Different evaluation methods are available, namely, bacterial culture, PCR-based evaluation, hybridization techniques, pyrosequencing and transcriptomic analysis [12, 13]. Polymerase chain reaction (PCR) is frequently used for the identification and characterization of *A. actinomycetemcomitans* in clinical samples [3, 14, 15, 16, 17, 18, 19]. This is determined by occurrence of serotypes a-b-c-d-d-e-f-g and clone JP2 of *A. actinomycetemcomitans* [20, 21]. With the implementation of matrix-assisted laser desorption ionization-assisted laser desorption ionization time-of-flight mass spectrometry identification, less frequently encountered *A. actinomycetemcomitans* species will be increasingly identified in clinical microbiology practice [22]. Two-dimensional electrophoresis, MALDI-TOF mass spectrometry, and 2D immunoblotting have also been employed [23].

PCR is the technique of choice that is currently used more frequently, it is a technique of great applicability for having a high specificity, sensitivity, and safety because it offers a reliable diagnosis, faster and less laborious than normal cultures of this type of microorganisms.

### 3.2 Treatments

Moxifloxacin may be a promising antimicrobial agent against *A. actinomycetemcomitans* for the treatment of periodontitis [11, 24]. *A. actinomycetemcomitans* resists destruction by neutrophils and is inhibited by azithromycin and amoxicillin. Azithromycin is actively concentrated within host cells, while amoxicillin enters by diffusion [25]. This bacterium has demonstrated some level of antimicrobial resistance to amoxicillin, metronidazole and tetracycline [17, 26, 27, 28]. Scaling and root planing plus antibiotics decreases the response of IgG levels against Omp 29 and *A. actinomycetemcomitans* serotypes implicated in periodontal disease [21]. In a pilot clinical trial, it was proposed that the use of moxifloxacin and amoxicillin plus metronidazole improves clinical and microbiological parameters compared to mechanical therapy alone; however, the moxifloxacin protocol caused no adverse events and reduced subgingival *A. actinomycetemcomitans* to imperceptible levels [29, 30]. Removal of orthodontic appliances, along with professional prophylaxis and proper oral hygiene instruction, results in

significant reductions of *A. actinomycetemcomitans* from supragingival and subgingival plaque samples [31]. As an adverse method, blue dyes for antimicrobial photodynamic therapy, at high concentration (10 mg/ml), are able to eliminate *A. actinomycetemcomitans* without the use of light sources as adjuvants [32, 33].

The removal of orthodontic appliances has shown a significant reduction of dentobacterial plaque. The use of moxifloxacin would represent a good option in antimicrobial therapy as an adjunct to root planing and scaling due to its broad spectrum, high tissue penetration and good absorption. As an alternative method, antimicrobial photodynamic therapy can be an excellent alternative for the elimination of *A. actinomycetemcomitans*.

### 3.3 Oral manifestations

*A. actinomycetemcomitans* is a perio-pathogenic bacterium associated with localized aggressive periodontitis [5, 6, 34]. In daily clinical practice, orthodontic appliances may be associated with increased cariogenic risk and worsening of pre-existing periodontal diseases [1, 35, 36]. Orthodontic bands have a detrimental influence on the microbial population of the surrounding tissues, because this bacterium has been previously reported to be associated with gingival inflammation [31, 37]. It has been shown that the presence of this bacterium in the subgingival crevicular fluid of orthodontic patients increased 3 to 6 months after fixed appliance insertion compared to untreated patients [35]. Orthodontic treatment using fixed oral appliances induce a qualitative bacterial change, with an increased prevalence of periodontal pathogens such as *A. actinomycetemcomitans*, associated with an increased cariogenic risk and worsening of periodontal diseases such as gingivitis and periodontitis.

### 3.4 Epidemiology

Early colonization of *A. actinomycetemcomitans* in oral cavities could be evaluated as a risk marker for periodontal disease [38]. In fact, 21.5% of periodontitis is due to *A. actinomycetemcomitans* [39]. In other studies, it is detected in 87.6% samples of patients with aggressive periodontitis, in 92.4% samples of patients with chronic periodontitis and 7.0% samples of periodontitis healthy subjects [40]. Similarly, prevalence of *A. actinomycetemcomitans* in whole saliva of aggressive periodontitis patients was significantly higher than in subjects with no periodontitis (32% vs. 4%) and chronic periodontitis patients (32% vs. 15%) [41]. In other countries, the prevalence of patients who tested positive for *A. actinomycetemcomitans* with real-time PCR was comparable in both groups (Germans: 27.0%; Koreans: 22.2%) [42]. In periodontally healthy patients, an *actinomycetemcomitans* was detected at only 1 site (0.90%) of periodontally healthy subjects [43].

In different studies we can find significant increase in the percentage of buccal cells containing *A. actinomycetemcomitans* after the placement of orthodontic fixed appliances [44, 45, 46]. The presence of *Aggregatibacter actinomycetemcomitans* in the subgingival crevicular fluid of orthodontic patients increased 3 to 6 months after fixed appliance insertion compared to untreated patients. There was still a higher subgingival prevalence of *Aggregatibacter* [35]. Other studies revealed no significant changes at the end of therapy compared to a periodontally healthy control group [47, 48, 49]. Clinical and microbiological factors associated with orthodontic appliances during an episode of gingival

inflammation and the impact of appliance removal on periodontal health were evaluated. Periodontal pathogens were associated with gingival inflammation during orthodontic treatment. Improvement in periodontal health at 30 days was concomitant with a reduction in *A. actinomycetemcomitans* positive sites<sup>[31]</sup>.

There are no studies on the epidemiology of *A. actinomycetemcomitans* in orthodontics, the presence in fixed appliances influences the quantity and quality of the oral microbiota, this depending on the oral hygiene of each patient during their treatment. However, it was detected more frequently in periodontitis sites than in periodontally healthy sites.

#### 4. Conclusions

*A. actinomycetemcomitans* is a periodontal pathogen associated with localized aggressive periodontitis. PCR is the technique of choice as a diagnostic method that is currently used more frequently in research centers that have the appropriate infrastructure for its implementation. The removal of fixed appliances has shown a significant reduction of dentobacterial plaque, as well as a correct oral hygiene and, if necessary, the use of alternative treatments such as moxifloxacin and antimicrobial photodynamic therapy. Proper oral hygiene during orthodontic treatment is indispensable to reduce the presence of *A. actinomycetemcomitans* and the cariogenic risk as well as a worsening of periodontal diseases.

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