

The Relationship between Periodontal Disease and *Aggregatibacter actinomycetemcomitans*: Suggesting Potential Therapies

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Three different studies about *Aggregatibacter actinomycetemcomitans* and its association with periodontal diseases were reviewed. Each study was conducted at a certain geographical area, and on a wide range of age groups. In addition, the subjects had different medical histories. The studies indicated a strong relationship between *A. actinomycetemcomitans* and the periodontal disease aggressive periodontitis. The main aims of the three studies were to find an antibacterial that would inhibit the growth of *A. actinomycetemcomitans*, find antibodies against the leukotoxin that is produced by *A. actinomycetemcomitans*, and finally to discover potential therapies that would prevent oral and non-oral infections caused by *A. actinomycetemcomitans*. The studies ended with exciting conclusions for the future of periodontal diseases. Systemic antibodies against leukotoxin could make a great contribution in the future to limit systemic effects of periodontal infections. Garlic extract, allicin, and DAS inhibit the growth of *A. actinomycetemcomitans*. DAS has an antibacterial activity against *A. actinomycetemcomitans* and can be useful in treating oral and non-oral infections caused by *A. actinomycetemcomitans*.

Introduction

Periodontal disease is defined as an inflammatory condition caused by bacterial infections. Those infections result in the loss of tooth supporting tissue. *Aggregatibacter actinomycetemcomitans* is a gram-negative facultative anaerobe that colonizes the human oral cavity and has been reported to be the causative agent of aggressive periodontitis (Elamin et al). *A. actinomycetemcomitans* is known to possess several important virulence factors. One of these factors is the bacterium's ability to secrete a protein toxin called leukotoxin. Leukotoxin is a protein that forms large pores of the repeat in toxin (RTX) family that activates and lyses human leukocytes in specific (Brage et al). The aim of this article is to provide a better understanding of *A. actinomycetemcomitans* in terms of its several serotypes, specific clone known as JP2 and other genotypes. The article will discuss the humoral immune response to leukotoxin secreted by *A. actinomycetemcomitans*. The article will also review a number of studies pertaining to

aggressive periodontitis, serum antibodies, JP2 clone, non-JP2 clone genotypes, prevalence of disease in different populations, age groups, and health conditions.

Because *A. actinomycetemcomitans* has many virulence factors it can colonize and survive in the oral cavity. There is also a constant emergence of resistant strains that make the treatment of *A. actinomycetemcomitans* very difficult. Therefore, an alternative method has to be discovered to treat/prevent periodontal diseases caused by this bacterium. Garlic extract was tested as an antibacterial against *A. actinomycetemcomitans* along with allicin and DAS (Velliyagounder et al).

Recent Progress

A. actinomycetemcomitans' Association with Aggressive Periodontitis

A group of microbiologists and immunologists went to Khartoum, Sudan to test the prevalence of *A. actinomycetemcomitans* in Sudanese high school students suffering from aggressive periodontitis. The aim of this case-control study was to identify the prevalence of the JP2 clone and non-JP2 genotypes of *A. actinomycetemcomitans* in the subgingival plaque of aggressive periodontitis patients. The study consisted of 17 patients and 17 controls ages between 14-19 years. All of the subjects went through clinical periodontal examination, and subgingival dental plaque samples were collected using paper points. The *A. actinomycetemcomitans* JP2 clone and non-JP2 genotypes presence was evaluated using a loop-mediated isothermal amplification (LAMP) and the PCR. The case-study showed an association between the presence of *A. actinomycetemcomitans* and aggressive periodontitis. This finding implies that *A. actinomycetemcomitans* can be used as a marker of increased risk of aggressive periodontitis in the young Sudanese subjects (Elamin et al).

Systemic Antibodies and Leukotoxin

A recent study at the Umeå University, Sweden aimed to examine the presence and function of systemic antibodies to the leukotoxin relative to periodontal status and history of myocardial infarction as well as to serum levels of inflammatory markers. The study consisted of 197 Swedish adults between 52 and 62 years of age. One hundred of these participants were admitted to the hospital because of acute myocardial infarction. The remaining 97 participants were totally healthy and from the same geographical area. Titers IgA and IgG against *A. actinomycetemcomitans* were calculated by multi-serotype ELISA. X-ray was used to determine the percentage of bone loss among the participating individuals. 56% had minor bone loss, 24% had moderate bone loss, and 10% had severe bone loss.

The serum antibodies with specific reactivity to *A. actinomycetemcomitans* leukotoxin were detected by western blot analyses. The purified leukotoxin were separated and cut into strips and tested for detection of serum antibodies against *A. actinomycetemcomitans*. The proteins that were immunoreactive were enhanced by chemiluminescence technique. The intensity of leukotoxin was classified as weak or strong in relation to a standard human serum with known immunoreactivity to leukotoxin. Sera with equivalent or stronger reactivity were classified strong, and sera weaker than the standard were classified weak.

Detection of neutralizing capacity in serum was done as a reduction of leukocyte damage and subsequent leakage of lactate dehydrogenase upon exposure to purified leukotoxin. Positive serums inhibited the lactate dehydrogenase released by the toxin with 50% or more;

and were further analyzed. The end of the study revealed high prevalence (57%) of antibodies against *A. actinomycetemcomitans* leukotoxin in the studied population. These antibodies were associated with leukotoxin neutralizing capacity and ELISA titers of *A. actinomycetemcomitans*-specific IgA and IgG. Increasing levels of leukotoxin were related to increasing age as well. Periodontal disease parameters and cardiovascular risk factors were not related to the high levels of leukotoxin. The study concluded that systemic antibodies against leukotoxin produced by *A. actinomycetemcomitans* were prevalent among Swedish adults; these very antibodies might make a contribution in the future to limit the systemic effects of the infection (Brage et al).

Antimicrobial Effects on A. actinomycetemcomitans

A recent study in the University of Medicine and Dentistry of New Jersey aimed to evaluate the antimicrobial effects of diallyl sulfide (DAS) treatment on *A. actinomycetemcomitans*. The study also provided an understanding of DAS potential as therapeutic agents for treatment of periodontal disease. *A. actinomycetemcomitans* has many virulence factors that enable it to colonize and survive in the oral cavity. This bacterium has the ability to invade tissues and cells, so it is very difficult to be eradicated from the oral cavity. *A. actinomycetemcomitans* also has many resistant strains that complicate the treatment process of aggressive periodontitis; antimicrobial agents and antibiotics do not treat LAP efficiently. That is why an essential therapy is needed to prevent the disease. Recently, garlic extract was shown to have effective broad spectrum antimicrobial activity against numerous bacteria including bacteria found in the oral cavity. *A. actinomycetemcomitans* was treated with garlic extract, allicin (oxygenated sulfur compound), or DAS. The antimicrobial effects against *A. actinomycetemcomitans* were evaluated. Garlic extract, allicin, and DAS inhibited the growth of *A. actinomycetemcomitans* significantly. DAS treated *A. actinomycetemcomitans* cells showed complete inhibition of glutathione (GSH), S-transferase (GST) activity. Those results suggested that DAS-induced GST inhibition is probably involved in *A. actinomycetemcomitans* cell death. The results also indicated that DAS shows antibacterial activity against *A. actinomycetemcomitans*, thus the properties of DAS might be used for discovering a therapeutic potential in the treatment of *A. actinomycetemcomitans* associated oral and non-oral infections (Velliyagounder et al).

Discussion

The revision of the above three studies confirmed that there is a strong association between *A.*

actinomycetemcomitans and aggressive periodontitis. So in the future the presence of *A. actinomycetemcomitans* can be used as a marker of an increased risk of aggressive periodontitis infection. Systemic antibodies against the protein toxin leukotoxin produced by *A. actinomycetemcomitans* were common between the Swedish subjects, which implies that those antibodies can contribute in the future to limit systemic effects of oral infections, specially, aggressive periodontitis.

A more recent study found that the growth of *A. actinomycetemcomitans* could be significantly inhibited by treating the bacterium with garlic extract, allicin, and DAS. Furthermore, complete inhibition of GSH, GST activity was found when *A. actinomycetemcomitans* cells were treated with DAS. Therefore, there is probably an association between DAS and *A. actinomycetemcomitans* cell death, or even a direct involvement. DAS also showed an antibacterial activity against *A. actinomycetemcomitans*. Hence, DAS suggests a potential therapeutic treatment of *A. actinomycetemcomitans* oral and non-oral infections. There is a lot of potential for finding a treatment or an antibacterial that will inhibit the growth of *A. actinomycetemcomitans*, and hopefully prevent periodontal infections.

References

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