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Editorial

# Systemic antibiotics and periodontal diseases

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Dr. Robert Genco once made the profound statement that we were 'at the end of the beginning of research into human periodontal diseases' (13th International Congress on Periodontal Research, Osaka Japan, 1992). Despite huge advances in the last 18 years, we still remain at the end of the beginning, rather than at the beginning of the end. Although a tremendous amount of effort has been expended over the past 30 years to elicit the causative agents of periodontitis, rarely has a single bacterial species been directly linked to periodontal diseases as its single etiologic factor.

Mechanical debridement remains the cornerstone of periodontal treatment. This is an absolutely essential step in any form of periodontal therapy and is often sufficient to control the progress of periodontal disease in a majority of patients. However, for some patients, mechanical instrumentation of the infected area is not sufficient to control disease progression. Failure to obtain a favorable response may be due to inadequacy of the host's immune response, the ability of the pathogen(s) to escape, either by invading gingival tissue or finding shelter in an unreachable site, limited access, instrument availability, operator skill, or a host of other possible factors. Nonsurgical scaling and root planing may remove subgingival Campylobacter rectus, but is frequently ineffective against Porphyromonas gingivalis, Prevotella intermedia, Bacteroides forsythus, staphylococci and enteric rods, and may not significantly reduce Actinobacillus actinomycetemcomitans[1]. Often, incorporation of an appropriate chemotherapeutic agent in conjunction with mechanical instrumentation provides an additional antimicrobial effect offering increased opportunity to control disease.

Antibiotics, defined, as naturally occurring or synthetic organic substances that, in low concentrations, inhibit or kill selective microorganisms, are particularly useful in combating severe periodontal infections. The wholesale misuse of these drugs has led to the emergence of resistant strains. Antibiotics are valuable and, in some instances, life saving drugs. They can only retain this position in both medicine and dentistry if used with care and prescribed appropriately.

Management of severe types of periodontitis should not rely solely on systemic antibiotics but upon a combination of mechanical debridement possibly in conjunction with surgery, subgingival administration of antiseptics by dental professionals and patients, patients' oral hygiene efforts and effective and safe systemic antibiotics in certain cases.

There is currently strong enough evidence to implicate three microorganisms as etiologic agents of periodontal diseases: A. actinomycetemcomitans, Porphyromonas gingivalis and Tannerella forsythia. Periodontitis can and does occur in the absence of any of the aforementioned three identifiable periodontal pathogens. Associative evidence has linked a number of different bacterial species with destructive disease like Prevotella intermedia, Fusobacterium nucleatum, Eikenella corrodens, Campylobacter rectus, Eubacterium nodatum, Peptostreptococcus micros, and various spirochetes. There is some recent evidence that implicates certain viral agents e.g. cytomegalovirus, Epstein–Barr virus, papillomavirus, and herpes simplex virus, may have a role in the initiation of periodontitis, most likely by affecting the host response to the bacterial challenge. Nevertheless, the primary host challenge and disease initiator continues to appear bacterial in nature.

### Role of Systemic Antibiotics in Periodontal Diseases

Systemic antibiotics enter the periodontal tissues and the periodontal pocket via serum and can affect organisms outside the reach of cleaning instruments or topical anti-infective chemotherapeutics. Systemic antibiotic therapy can also potentially suppress periodontal pathogens residing on the tongue or other oral surfaces, thereby delaying subgingival recolonization of pathogens[2]. Systemic antibiotics may even be required for eradication of periodontal infections by A. actinomycetemcomitans and other pathogens. Actively progressing periodontitis

is virtually always associated with specific bacterial infections and often requires the adjunctive use of systemic antibiotic therapy. Single drug therapies with penicillins, tetracyclines, metronidazole or clindamycin have been used frequently in periodontal practice. However, since periodontitis lesions often harbor a mixture of pathogenic bacteria, drug combination therapies have gained increased importance[3]. Valuable combination therapies include metronidazole–amoxicillin for A. actinomycetemcomitans and various anaerobic periodontal infections and metronidazole–ciprofloxacin for mixed anaerobic and enteric rod/Pseudomonas periodontal infections. The tetracyclines have the additional advantage of inhibiting collagenases.

There is no single periodontal therapeutic regimen that will provide a beneficial response for all patients. It is very unlikely that there ever will be. Prescription of systemic antibiotic therapy in periodontics should be based upon scientific data and not upon personal biases. Empirical antibiotic therapy may be used for periodontal diseases with known microbial causes, such as acute necrotizing ulcerative gingivitis, which is caused by anaerobic organisms and can be cured by metronidazole, and early localized aggressive periodontitis, mostly involving A. actinomycetemcomitans, which can be controlled or eradicated by systemic metronidazole–amoxicillin combination therapy.

Wherever microbiological testing is unavailable, metronidazole–amoxicillin combination therapy (250–500 mg of each, three times daily for 8 days) may be a reasonable antibiotic first choice in periodontics. The metronidazole–amoxicillin combination is an appropriate choice in about 70% of advanced periodontitis patients[4]. However, the metronidazole–amoxicillin combination does not affect Pseudomonas or enteric gram-negative rods that inhabit approximately 14% of advanced periodontitis lesions. The combination of metronidazole and ciprofloxacin (500 mg of each, twice daily for 8 days) can cure anaerobic, enteric rod and A. actinomycetemcomitans periodontal infections and promote subgingival overgrowth of streptococci able to inhibit gram-negative pathogens[5].

The evidence seems to favor the use of metronidazole/amoxicillin. However, this is not a panacea for all patients. Metronidazole has a number of unpleasant side effects that are not well tolerated by some patients. Amoxicillin is definitely contraindicated in patients with penicillin hypersensitivities. Potentially pathogenic bacteria, such as E. corrodens, may be resistant to both metronidazole and amoxicillin. Other antibiotics clearly provide significant benefits for specific situations. Clindamycin-HCl remains effective against classic gram-negative anaerobic rods associated with periodontitis refractory to conventional therapy[6]. However, due to its propensity for severe adverse effects, clindamycin-HCl should only be prescribed following culture and sensitivity testing. Many microorganisms continue to demonstrate sensitivity to tetracyclines, particular doxycycline and minocycline. The use of subantimicrobial doxycycline as an adjunct to mechanical instrumentation with or without the adjunctive use of an antibiotic should be a consideration. The inhibition of the inflammatory process and the downregulation of matrix metalloproteinases may provide a quicker return to periodontal health[7].

Comprehensive treatment of periodontitis is very different from the treatment of most bacterial infections. It is important to realize that growth of bacteria in pure cultures is very foreign to the way that the vast majority of bacteria naturally grow. Growth of bacteria in the biofilm is very different than the growth of a single pure culture in a test tube or on an agar plate. The aggregation of bacteria in a biofilm impairs the diffusion or may even inactivate antimicrobial agents. High concentrations of the active ingredient are needed before a beneficial effect can be expected. Biofilm experiments indicate that the necessary minimum inhibitory concentrations of antimicrobial agents are at least 50 times (or even 210,000 times) higher than for bacteria growing under planktonic conditions[8].

The evidence available suggests that disadvantages and safety aspects of systemic antimicrobial use in the management of periodontal diseases significantly outweigh the benefits. Antibiotic prescribing should be the exception rather than the rule and, in the majority of cases, only considered after conventional therapies have been unsuccessful. Recommendations for periodontal anti-infective therapy will undoubtedly be continually revised along with the development of even better understanding of the pathogenic periodontal microbiota and the availability of new and more effective drugs to control or possibly cure periodontal infections.

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