Adjunctive Periodontal Therapy: A Review of Current Techniques

Authored by Herbert I. Bader, DDS

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Adjunctive Periodontal Therapy: A Review of Current Techniques

LEARNING OBJECTIVES:
After reading this article, the individual will learn:
• The role of adjunctive therapy in periodontal disease management.
• Available adjunctive modalities from which the clinician can choose.

ABOUT THE AUTHORS

Dr. Bader practices periodontics and implant dentistry in Concord, Mass. He is a graduate of NYU College of Dentistry, and in 1966 completed a residency in periodontology at the Harvard School of Dental Medicine, where he currently serves as lecturer in postgraduate periodontology. He is a fellow of the American College of Dentists, International College of Dentists, and American Academy of Osseointegration. He has been published in the Journal of Dental Research, Journal of Periodontology, Journal of Clinical Periodontology, and the American Journal of Dentistry. He can be reached at via e-mail at redabsr@aol.com.

Disclosure: Dr. Bader is a dental consultant for Tolmar Pharmaceutical Co.

INTRODUCTION

There have been a number of critical findings with regard to the periodontal diseases which define our current understanding of the pathogenesis of these clinical entities. It is widely accepted that specific periodontal pathogens are included in the plaque biofilm.1,2 These organisms initiate a complex series of events resulting in an inflammatory response mediated by the host immune mechanism.3 When the balance of the pathogen-host equilibrium becomes tilted in favor of the invasive organisms, the immune response becomes exaggerated. The sequellae of the release of an overabundance of inflammatory mediators are loss of attachment and osseous destruction.4

Given the etiological factors contributing to inflammation and subsequent attachment loss, it has been widely accepted that mechanical disruption of the plaque biofilm via scaling and root planing (SRP) to reduce the pathogenic burden is the primary treatment of choice.5-9

The term “adjunctive therapy” applies to all additional or ancillary means of reducing the inflammatory burden by the use of anti-infectives (local or systemic) and/or host immune modulating agents. This includes such approaches as supragingival and subgingival irrigation.

This article reviews the current adjunctive periodontal therapy modalities available and discusses certain current research in this area.

IRRIGATION

Topical application of agents via irrigation has been discussed thoroughly in a position paper of the American Academy of Periodontology (AAP) in November 2005. The principal objective of irrigation is to reduce sulcular pathogens and potential pathogens coronal to the gingival margin. The conclusions of the paper state that irrigation (supragingival and subgingival) will continue to play a role in maintenance of periodontal patients, but the evidence for clinically relevant effects of a single episode of antimicrobial subgingival irrigation following SRP is lacking. There is some evidence that supragingival irrigation with pulsating instrumentation, especially with antimicrobial agents, may have some beneficial effects for the treatment of gingivitis.10-13 Repeated twice daily subgingival water irrigation following SRP was shown to significantly reduce the level of inflammatory cytokines in diabetic patients.14 Topical application of 0.12% chlorhexidine (CHX) with a rotary-powered brush was shown to be more effective for gingivitis control than a combination of manual brushing and irrigation, and especially useful in furcations (Figures 1a and 1b).15,16

There is emerging evidence that, in addition to CHX, topical application of agents such as anti-inflammatory histatin, cimetidine rinses, mercaptoalkylguanidines,
povidone iodine and others, especially the class of nonsteroidal anti-inflammatory drugs, can be useful when applied topically.\textsuperscript{17-20}

**ANTIMICROBIAL THERAPY**

*Local:* Over the past 3 decades a number of sustained release, anti-infective, site-specific vehicles have been developed as a means of improving the efficacy of SRP in terms of pocket depth reduction, attachment gain, and inflammatory reduction. Subsequent to Goodson, et al’s work\textsuperscript{21,22} with tetracycline impregnated ethylene acetate fibers, a variety of second generation applications were introduced in the late 1990s, all of which are biodegradable and do not have to be removed from the site of placement.

In 1998, Astra Pharmaceuticals introduced PerioChip, a 4 x 5 mm degradable chip in a gelatin matrix, containing 2.5 mg of CHX gluconate (Figure 2). The device was approved for room temperature storage in 2002. It remains in the pocket for 7 to 10 days, slowly releasing the antiseptic (40% initially),\textsuperscript{23} and is fully biodegradable. It may be placed every 3 months in residual pockets of 5 mm or more in depth. There are numerous published studies on efficacy, showing some gain in attachment level and pocket depth reduction as compared to SRP alone, along with some reduction in inflammatory mediators.\textsuperscript{24} The magnitude of change of probing depth and attachment gain has been demonstrated to average about 0.3 mm.\textsuperscript{25-28} It has been shown to be safe with minimal untoward side effects, and is easily inserted into the pocket.

The cost of the chips varies depending on the number of boxes purchased. Each box contains 20 chips at an average of $17.45 per chip. Generally, each surface of the tooth treated requires a single chip.

In 1998, Atrix Laboratories introduced Atridox, a thixotropic gel containing 10% doxycycline hyclate, a site-specific antimicrobial adjunct to SRP. The term “thixotropic” refers to the product’s conversion from a gel to a hard, plastic state when it comes in contact with moisture in the pocket. This allows the antibiotic-containing material to remain in place for 7 to 21 days. The flowable nature of the gel allows for the entire defect to be filled with the agent. Atridox is packaged in 2 syringes, which are mixed
thoroughly and then introduced into the pocket with a disposable cannula (Figures 3a and 3b). Each syringe contains enough material to treat 5 to 6 sites, making it a very cost effective approach to isolated residual pockets remaining after SRP. A box of 6 applications averages about $11.38 per site.

There is considerable evidence supporting the efficacy of Atridox. The report by Polson and colleagues on the initial clinical response to a subgingival, biodegradable doxycycline system in 1996 was an early study of clinical relevance. Perhaps the most interesting initial studies were multicenter, 3-armed protocols in which Atridox was compared to SRP, placebo control, and oral hygiene, and found to be equally effective to SRP, and in a subsequent study was equally effective in maintenance patients over a 9-month period. The system has been found to significantly reduce the anaerobic pathogens in the biofilm without an increase in resistant organisms or the development of antibiotic resistance. Figure 4 shows the effect on 2 critical periodontal pathogens over a 182-day period.

A recent study compared the effects of 3 local, sustained delivery systems: doxycycline hyclate 10% (Atridox), CHX gluconate 2.5 mg (PerioChip), and minocycline hydrochloride 1 mg (Arestin) on osteoblastic cell proliferation and differentiation, in terms of periodontal regeneration. The doxycycline hyclate did not have the cytotoxic effect exhibited by the 2 other agents, and in fact, appeared to enhance maturation and differentiation. The authors suggested that doxycycline hyclate may have an additional benefit other than its antimicrobial effect, and may help enhance periodontal regeneration.

The development of a technique for micro-encapsulating minocycline hydrochloride in a bioabsorbable polymer for site-specific subgingival delivery resulted in the introduction of Arestin in 2001. The system’s pharmacokinetics results in gradual hydrolyzation of the microspheres with sustained release over 14 days. It is delivered with disposable tips in a sterilizable syringe (Figures 5 and 6).

A large 18-site, multicenter study reported that SRP plus minocycline microspheres was more effective than SRP alone in reducing pocket depths in periodontitis patients.
This confirmed some of the findings from an earlier, well controlled study.35

Other reports in the literature attest to improvement in clinical parameters when using minocycline microspheres in addition to SRP. These include evidence that it can be an aid in peri-implantitis and improving surgical outcomes.36-39

Arestin is packaged in 2 foil wraps per box, each containing 12 disposable tips, for an average cost of $19.98 per application.

A thorough review of local drug delivery, also called locally applied antibiotics, by Greenstein13 suggests that while locally delivered agents have demonstrated clinical efficacy, they are not panaceas, and their use is based on clinical decisions taking into account the patient’s specific clinical situation. It is generally agreed that due to the nature of subgingival plaque biofilm, it must be disrupted by instrumentation prior to the use of antimicrobials.

**SYSTEMIC ANTIMICROBIALS**

The literature on the use of systemic antimicrobials is quite extensive, and much of the current use of this modality is based on the seminal works by Haffajee, Socransky, Teles, and others.8,40-44 Antibiotics have been used for many years based on the accumulated evidence of periodontitis being an infectious disease,44 as an adjunct to improve the results of SRP. The AAP’s position on systemic antibiotics is: “They may be prescribed for periodontal patients who do not respond to conventional mechanical therapy, for patients with acute periodontal infections associated with systemic manifestations, for prophylaxis in medically compromised patients, and as an adjunct to surgical and nonsurgical periodontal therapy.”45 Of the hundreds of bacterial species identified within periodontal pockets, relatively few have been associated with chronic periodontitis, and the weight of evidence relative to their pathogenicity has been described (Table 1).44,46

Based on the susceptibility to various antibiotics and antibiotic combinations, a number of different strategies have been developed for adjunctive systemic antimicrobial use.8,47-50 The most commonly used antibiotics, as described by the AAP paper,45 are seen in Table 2. Again, they are selected according to bacterial susceptibility. A DNA-polymerase chain reaction has been marketed (MyPerioPath [OralDNA Labs]) which provides a clinical laboratory report on 13 pathogens based on salivary testing,51 and can be used as a guide for antibiotic selection based on the patient’s periodontal status and medical and family history.

As is the case with local antibiotic administration, it is essential that the biofilm be disrupted initially before the administration of systemic antibiotics.

**HOST MODULATION**

Given the protective aspects of the host immune system in the periodontal patient,3 a major thrust in research for more than 2 decades has been aimed at modulating or ameliorating the release of proinflammatory cytokines such as the matrix metalloproteinases.52,53 As a result of this work, a subantimicrobial dose doxycycline regimen has been in use for

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**Table 1. Pathogenicity of bacterial species in periodontal pockets [From: Hafajjee and Socransky,44 and Slots and Chen46]**

<table>
<thead>
<tr>
<th>Pathogenicity</th>
<th>Porphyromonas gingivalis</th>
<th>Prevotella intermedia</th>
<th>Campylobacter rectus</th>
<th>Gram-enteric rods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>Aggregatibacter actinomycetemcomitans</td>
<td>Eubacterium nodatum</td>
<td>Peptostreptococcus micros</td>
<td>Pseudomonas species</td>
</tr>
<tr>
<td>Moderate</td>
<td>Tannerella forsythia</td>
<td>Treponema denticola</td>
<td>Fusobacterium nodatum</td>
<td>Staphylococcus species</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Spirochetes of acute necrotizing gingivitis</td>
<td>Dialister species</td>
<td>Eikenella corrodens</td>
<td>Enterococcus faecalis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Selenomonas noxia</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Candida albicans</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Beta-hemolytic streptococci</td>
</tr>
</tbody>
</table>
some time. Periostat (doxycycline hyclate 20 mg) is given twice daily to inhibit host-derived matrix metalloproteinases (MMPs), including the collagenases. These results have no relation to the antimicrobial action of the drug, and in fact, are administered at levels below that which causes bacteriostasis. By acting to down-regulate the expression of the MMPs and their precursors, the collagen-building block of the periodontal connective tissues are spared. 54

A seminal study on the combined effects of host modulation and local antibiotic therapy was published in 2008. 55 The inclusion of SRP along with Atridox doxycycline thixotropic gel, and systemic low dose doxycycline hyclate, was shown to provide significantly greater clinical benefits than SRP alone, perhaps as a result of synergistic actions of the adjunctive antimicrobials.

There continues to be a large body of ongoing research on various forms of host modulating therapy. 56 Research extends into inhibition of osteoclasts with bone sparing agents such as bisphosphonates and cathepsins, 57 affectin prostaglandin formation. 58 With a greater understanding of the sequence of events related to inflammation and its resolution, researchers are beginning to look at drugs that may have been heretofore overlooked. 59

**ADJUNCTIVE LASER THERAPY**

A number of different types of laser engines have been used in dentistry for many years, and published papers have exhibited some controversy 60 over usefulness in adjunctive treatment of periodontitis. A review of the literature by Cobb, 61 commissioned by the AAP, is very comprehensive on this subject. There is current evidence as to the positive effect of the Nd:YAG and Er:YAG lasers in reducing probing depths and altering the subgingival microbiota, 61 and recent work by Yukna, et al 62,63 describe the laser assisted new attachment procedure with promising results.

Photodynamic laser therapy (PDT) is another adjunctive laser approach that is receiving much attention. PDT is based on the principle that a photosensitizer (methylene blue, phenothiazine, tolamine chloride [TBlue; Zila]) is absorbed onto the surface of the target cell (Gram-negative pathogens), is activated by a diode laser (660 nm wavelength), and is then toxic to the cell. While there is evidence that there is a reduction in inflammatory mediators (TNF-alpha, and crevicular RANKL), the effects are similar to SRP in order of magnitude. 64

It is generally agreed that more detailed, controlled clinical research studies are necessary, especially long-term designs looking at clinical outcomes, for complete validation of this form of adjunctive therapy.

**SUMMARY**

This paper has reviewed the different types of adjunctive therapeutic approaches used in the control of periodontitis. While there are many avenues of current clinical use and research, it is generally agreed that all of the modalities reviewed are adjunctive to basic mechanical control of the root surface environment in the form of SRP.

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### Table 2. Commonly used antibiotics and dosages

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Metronidazole</th>
<th>Amoxicillin</th>
<th>Tetracycline</th>
<th>Ciprofloxacin</th>
<th>Azithromycin</th>
<th>Clindamycin</th>
<th>Clarithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doses</strong></td>
<td>500 mg twice a day or 3 times a day</td>
<td>250 to 500 mg 3 times a day</td>
<td>100 to 200 mg once a day</td>
<td>500 mg 2 times a day</td>
<td>250 to 500 mg once a day</td>
<td>300 mg 3 times a day or once a day</td>
<td>500 mg 2 times a day</td>
</tr>
<tr>
<td><strong>Time (days)</strong></td>
<td>8 to 10</td>
<td>8 to 10</td>
<td>8 to 14</td>
<td>8 to 10</td>
<td>5 (Z-pack)</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

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For more information on the use of these therapies, see the references and guidelines provided by the American Academy of Periodontology.
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REFERENCES


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1. The term “adjunctive therapy” is used to describe:
   a. Pocket reduction surgery.
   b. Ancillary or additional means of reducing the inflammatory burden.
   c. Osseous regeneration using guided bone regeneration.
   d. Scaling and root planing.

2. Topical application of anti-inflammatory agents has been shown to be effective. These agents include:
   a. 0.12% chlorhexidine.
   b. Saline solution.
   c. Peroxide.
   d. Chloramphenicol.

3. Second generation sustained release systems are:
   a. Antiseptics.
   b. Alcohol based.
   c. Biodegradable.
   d. Elastomeres.

4. Periochip is an:
   a. Antibiotic.
   b. Antiseptic.
   c. Anti-inflammatory cytokine.
   d. Immune regulator.

5. Atridox is doxycycline as a:
   a. Reversible colloid.
   b. Irreversible colloid.
   c. Thixotropic gel.
   d. Anionic gel.

6. The American Academy of Periodontology states that antibiotics may be prescribed for:
   a. Pocket depths greater than 5 mm.
   b. Use instead of SRP.
   c. Patients older than age 21 years.
   d. Nonresponsive patients.

7. Host modulation refers to:
   a. Antimicrobial suppression.
   b. Altering a patient’s genotype.
   c. Altering the immune response.
   d. Eliminating the immune response.

8. Current literature supports the use of lasers to:
   a. Regenerate bone.
   b. Reduce probing depths.
   c. Create osteotomies for implant placement.
   d. Increase anti-inflammatory matrix metalloproteinases.
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3. ☐ a  ☐ b  ☐ c  ☐ d  7. ☐ a  ☐ b  ☐ c  ☐ d
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