State of the Art Review

Rationale for Use of Antibiotics in Periodontics

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The purpose of this review is to provide the clinician with some practical rationale for the selection and use of antibiotics in the treatment of destructive periodontal diseases. We have attempted to integrate approximately 20 years of periodontal literature describing antibiotic therapy with personal experience and 21st century ideas. This article addresses antibiotic use during treatment of aggressive periodontitis with emphasis on juvenile disease and adult refractory diseases. The literature review revealed few large, controlled studies that compared efficacy of adjunctive antibiotic use to mechanical therapy alone. Even fewer studies evaluated the efficacy of one antibiotic relative to another. However, based on the evidence available, certain conclusions were drawn. Adjunctive use of an antibiotic along with mechanical debridement is recommended for the treatment of Actinobacillus actinomycetemcomitans*-associated periodontitis as an acceptable therapeutic regimen. Due to the emergence of tetracycline-resistant* A. actinomycetemcomitans, *the combination of metronidazole and amoxicillin may be preferable. In aggressive refractory periodontitis, compelling evidence exists that the use of an appropriate adjunctive antibiotic frequently gives a more favorable clinical response than mechanical therapy alone. Unfortunately, the selection of antibiotic is not as clear and is probably case-dependent. Positive responses have been reported with amoxicillin/clavulanic acid, clindamycin, metronidazole, and the combination therapy metronidazole plus amoxicillin. The introduction of local delivery antibiotics specifically for the treatment of periodontitis offers a novel concept for the treatment of localized disease. The latter, in particular, may prove useful in the treatment of recurrent disease activity or where only a few individual sites are involved.* J Periodontol 2002;73:1188-1196.

KEY WORDS

Antibiotics/therapeutic use; periodontal diseases/drug therapy; periodontitis/drug therapy; review literature.

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An increased interest in antibiotic therapy as an adjunct to standard periodontal treatment regimens began in the late 1970s with the realization that certain bacteria were frequently associated with the disease process. The addition of antimicrobial control directed toward putative periodontal pathogens was thought to offer an opportunity to enhance the treatment of periodontal diseases. Mechanical and surgical treatments, combined with diligent oral hygiene measures, were usually successful in controlling periodontal destruction. However, over time clinicians found that certain patients continued to experience periodontal breakdown despite ideal care. In some instances, the combination of antibiotic therapy in conjunction with conventional periodontal treatment yielded a favorable clinical response not obtained with conventional therapy alone. Often, the antibiotic selected and the dosage administered, as well as the evaluation of clinical response, were empirically based. As a result, confusion developed as the practitioner considered antibiotic selection, risk/benefit ratio, dosing regimen, length of treatment, evaluation parameters, clinical outcome assessments, and short- and long-term benefits from adjunctive antibiotic therapy.

The treatment of periodontitis is quite different from the treatment of most bacterial infections. The bacterial flora present are always heterogeneous and relatively complex, and vary significantly from one patient to another. Rarely can the presence or absence of a single bacterial species be directly correlated with disease presence. In addition, the activity of the disease itself is not readily apparent.[1-4] Clinical diagnosis is based on presenting signs, symptoms, and history. Radiographs and periodontal probing can detect past destruction, but not necessarily when it occurred. Although there has been an enormous body of information generated over the past 30 years concerning the pathogenesis of periodontal infections, this information has not been integrated with clinical profiles of disease manifestations. Therefore, it is difficult, if not impossible, for the practitioner to consistently recognize patients presenting with periodontal diseases who may require, or benefit from, the adjunctive use of an antibiotic. Even when the practitioner thinks that an antibiotic may be indicated in the control of disease, there is no ready guidance

to help with the decision as to which antibiotic may be most beneficial. Unlike many medical specialties, laboratory analyses of the likely causative bacterial agent(s) and their susceptibility to various antimicrobial agents are either not readily available or utilized by the periodontal practitioner.

In the past, administration of antibiotics for the treatment of periodontitis has been almost exclusively systemic. Recently, several antibiotics have been refined for use as local delivery products aimed specifically at treatment of destructive periodontal diseases. The concept of administering an antibiotic to the immediate area of infection is attractive. It enables delivery of high drug concentrations directly to the infected site and eliminates, or decreases, the potential for creating antibiotic resistance. However, this adds another treatment decision: which is better, systemically delivered or locally administered antibiotic.

The purpose of this article is to examine the existing literature on the use of antibiotics in periodontitis, along with the authors' own work. Hopefully, this will provide the clinician with some rationale to help decide 1) whether an adjunctive antibiotic may be indicated; 2) which antibiotic might be the most efficacious; and 3) what dosage to prescribe. The authors are very aware that this is a formidable task.

It is not possible to include all of the existing literature on the use of antibiotics in periodontal therapy. We would like to recommend that the reader consult a number of excellent reviews that have addressed this subject.[1,5-10]

METHODS

Information presented in this review is based on a survey of the literature from around 1980 until the present date. The literature search was conducted primarily using the National Library of Medicine's Entrez PubMed search engine, both the journal browser and the MeSH browser, and was largely limited to papers and several abstracts published in English. Literature prior to 1980 was often obtained by reviewing the citations listed in previous review articles. Due to the diversity of the literature reviewed, no single set of criteria could be used for inclusion. Where possible, the decision to include a paper was based on the presence of adequate controls, a defined study population, the presence of active disease, and appropriate monitoring.

INDICATIONS FOR ANTIBIOTIC USE

In an evidence-based decision regarding when to use an antibiotic as an adjunct to periodontal therapy, a standard hierarchy of evidence is needed to support an efficacy claim. Ideally, this involves examination of data collected in clinical trials that compare the efficacy of adjunctive antibiotic treatment to conventional treatment without an antibiotic. Desirable endpoints might include effects on the periodontal flora, short- and long-term changes in clinical parameters, and length of treatment efficacy. Unfortunately, there are few well-controlled trials that directly compare the effects obtained by conventional periodontal therapy to conventional periodontal therapy in conjunction with an antibiotic. The reasons for this are fairly simple. Conventional periodontal therapy, whether it involves mechanical debridement usually thought of as deep subgingival scaling and root planing (SRP) or surgical involvement, is very effective for the vast majority of periodontal patients. Thus, to show an additive effect for the use of an antibiotic requires very large subject numbers to detect statistically significant differences. Studies of this magnitude are generally cost prohibitive. Even if statistically significant differences were detected, such differences may be so small that it would be questioned whether they constituted clinical significance. Thus, without these data, it is not surprising that the use of antibiotics in periodontal therapy remains highly controversial.

There is some strong evidence that supports the use of an adjunctive antibiotic in the treatment of certain forms of periodontal diseases. Aggressive forms of periodontal diseases frequently progress more rapidly than the more common, non-aggressive forms (chronic periodontitis); and as such, require more aggressive treatment. Patients presenting with aggressive periodontitis or with periodontitis that has not responded favorably to previous therapy; e.g., refractory disease, most likely will benefit from the additional use of an antibiotic along with conventional periodontal therapy.

It must be emphasized that the use of an antibiotic is not a replacement therapy for thorough instrumentation of the treatment site. Subgingival bacteria exist within a biofilm, which is relatively impervious to any antimicrobial agent unless it is first thoroughly disrupted. Using an in vitro biofilm model of the subgingival plaque, we have found that certain bacterial species survive antibiotic concentrations equivalent to 2 mg/ml (2,000 µg/ml).[11-13] This concentration is 500- to 1000-fold greater than can be achieved by systemic delivery. Similar results were obtained during a clinical trial evaluating the effect of a locally delivered doxycycline gel applied directly to the periodontal pocket. Viable bacteria were recovered from

the treated sites 7 days after placement of the gel.[14] Pharmacokinetic release data on the doxycycline gel indicated that doxycycline levels of 1,000 to 2,000 µg/ml were available for around 24 hours after placement and that concentrations in excess of 100 µg/ml were maintained for 2 weeks following placement.[15]

Thus, in the following discussion the use of an antibiotic is always considered as an adjunct to, not a replacement for, thorough instrumentation of the infected site(s).

AGGRESSIVE PERIODONTITIS IN CHILDREN

Based on the new periodontal classification system, previous definitions for periodontitis in young patients, including localized and generalized juvenile periodontitis and some forms of rapidly progressive periodontitis, are now classified under "aggressive periodontitis."[16] For the purpose of this discussion, we will refer to localized aggressive periodontitis in children as localized juvenile periodontitis (LJP) because considerable evidence indicates that LJP is frequently associated with the presence of the bacterium *Actinobacillus actinomycetemcomitans*.[2,4]

Localized juvenile periodontitis is clearly the easiest destructive periodontal syndrome to diagnose. The presence of periodontal lesions localized to the molar and/or incisor areas of the dentition in a young patient is readily apparent to any clinician. Successful treatment of this disease is one of the great success stories of periodontology. In the early 1980s, treatment consisting of SRP and the adjunctive use of tetracycline often resulted in amazing clinical improvement. Tetracycline-HCl, given as 250 mg qid (a gram a day) for 2 weeks, in conjunction with a thorough scaling resulted in the resolution of gingival inflammation and in the gain of clinical attachment and alveolar bone.[17-19] However, some patients failed to respond to this treatment regimen and continued to demonstrate attachment and bone loss. Renewed disease activity has been estimated to recur in about 25% of tetracycline-treated juvenile periodontitis patients despite regular supportive maintenance.[20]

One of the primary reasons for the failure of tetracycline therapy in these patients was likely due to the infecting organism's resistance to systemically delivered concentrations of tetracycline. Antibiotic resistance has become a major worldwide health care problem over the past 20 years. This is as true in the oral cavity as it is at other sites in the body. Our group has reported significant increases in the proportion of the periodontal flora with resistance to amoxicillin, tetracycline, doxycycline, and minocycline over a 10-year span from the mid-1980s to the mid-1990s.[21] Similar increases in resistance of *A. actinomycetemcomitans* to tetracycline have been reported.[22,23]

Metronidazole has been used in a few instances as an adjunct to scaling in the treatment of juvenile periodontitis. Saxén and Asikainen treated 27 localized juvenile periodontitis patients with mechanical debridement alone and with either a regimen of metronidazole (200 mg, tid, for 10 days) or a regimen of tetracycline (250 mg, qid, for 12 days).[24] At the end of 18 months, *A. actinomycetemcomitans* was eliminated or suppressed below detectable levels in all of the test sites in the metronidazole treated patients. By comparison, the bacterium was detected in 9 of 26 sites following tetracycline treatment.

Very good results have been reported in the treatment of juvenile periodontitis cases using the combination of metronidazole plus amoxicillin. Van Winkelhoff et al. have reported that use of metronidazole (250 mg, tid) and amoxicillin (375 mg, tid), simultaneously administered for a period of 10 days following periodontal scaling and root planing, eliminated *A. actinomycetemcomitans* in 97% or more of the patients and resulted in improved clinical status.[25,26] In a small clinical trial involving 25 patients with localized juvenile periodontitis, Tinoco et al. compared the effects of metronidazole plus amoxicillin as an adjunct to mechanical treatment to mechanical treatment alone.[27] After one year, *A. actinomycetemcomitans* was isolated from all of the patients who received only mechanical therapy but from only half of the patients receiving metronidazole plus amoxicillin. The latter group displayed better clinical results than the former relative to decrease in probing depth, gain in attachment level, and radiographic analysis of crestal alveolar bone mass.[27]

Some investigators think that the use of metronidazole in combination with amoxicillin and clavulanic acid (ACA)‡ might be preferable to metronidazole used in conjunction with amoxicillin for the adjunctive treatment of *Aa*-associated periodontitis. Currently, there are no documented studies comparing the effects of combination metronidazole-amoxicillin therapy to metronidazole ACA therapy. Generally speaking, amoxicillin is gentler on the stomach and is less expensive than ACA. A recent review article presents some evidence for the association of ACA with severe adverse events in older patients.[28]

‡ Augmentin, Smith-Kline Beecham, Philadelphia, PA.

While this may not be pertinent in the treatment of younger patients, there is no current indication to use ACA rather than amoxicillin in combination with metronidazole as an adjunct for *Aa*-associated periodontitis.

There have been no large-scale, multi-center clinical trials evaluating the effect of adjunctive antibiotic therapy to mechanical therapy alone in the treatment of *Aa*-associated periodontitis. Nor are there any large trials evaluating the effects obtained with different adjunctive antibiotics. Most periodontal investigators and many practitioners believe that to obtain the best results in the treatment of *Aa*-associated juvenile periodontitis, whether localized or generalized, the use of an adjunctive antibiotic along with mechanical therapy is necessary. A likely reason for this may be the ability of *A. actinomycetemcomitans* to penetrate the epithelial surface of the pocket.[29] Thus, regardless of how thoroughly instrumentation was carried out, some of these bacteria may remain within soft tissue, readily available to recolonize the pocket. Adjunctive use of a systemic antibiotic allows drug delivery to the entire pocket, with penetration of the epithelium and connective tissue regions, exposing the organism to the antibiotic.

This brings up the question of using one of the several local delivery antibiotics to eliminate *A. actinomycetemcomitans*. Unfortunately, there is not very much information on this subject. Goodson used tetracycline fibers to treat 12 sites in 4 patients with localized disease.[30] The organism remained detectable in the pockets 28 days later and actually increased significantly in some cases. It was not known if the sites in question were repopulated from the surrounding tissue due to the inability of tetracycline to sufficiently penetrate the tissue or if repopulation may have occurred from other potential reservoirs in the mouth. It is possible that the use of either doxycycline or minocycline, in local delivery formulations, may prove more beneficial since both of these antibiotics are more lipophilic than tetracycline and penetrate soft tissue more readily.

REFRACTORY PERIODONTITIS

Under the 1999 periodontal classification system, "refractory periodontitis" has been eliminated as a separate category.[16] This is not to say that refractory periodontitis does not exist but that it can, and likely does, occur in all periodontal disease categories. The American Academy of Periodontology defined "refractory" periodontitis as any destructive periodontal disease in patients who, on longitudinal monitoring, continue to demonstrate additional attachment loss at one or more sites.[31] By some estimates, this may include 10% to 20% of treated adult cases.[32]

In this review, we will continue to use the 1989 definition and apply it to adults who continue to demonstrate wide-spread periodontal destruction despite conventional periodontal therapy consisting of SRP and/or periodontal surgery followed by a documented maintenance program. Although we do not consider "recurrent" periodontitis to be synonymous with refractory disease, it is often difficult to differentiate the two. Both tend to result in the continued loss of attachment despite conventional therapy and constitute a major therapeutic challenge. Possibly the major difference is the extent of disease. In our studies of refractory periodontitis in adults, we found continuing disease to be relatively widespread, often affecting the entire dentition. Recurrent periodontitis, on the other hand, appears to be more limited and generally involves fewer sites. However, many of the reported studies involving "refractory" periodontitis probably included patients that would qualify for either of these categories.

Assuming appropriate treatment and an adequate recall and maintenance program, refractory periodontitis is probably due, in most part, to a number of host factors rather than to the presence of particular microflora. Our studies indicated the typical adult refractory periodontitis patient was often female, mid-40s to mid-50s years of age, under stress, and who often smoked.[3,33-37] It was unclear whether a stronger tendency toward refractory disease exists in females, or whether females tend to seek treatment more readily than males. However, stress and smoking appear to be risk factors for refractory periodontitis.

Several studies have investigated the use of an adjunctive antibiotic in the treatment of refractory periodontitis. Few have been fully randomized controlled trials. Inclusion criteria and designs have varied widely as have the criteria that have been applied to what constitutes refractory periodontitis. In the early 1980s, Gordon and Walker's clindamycin-HCl studies made no attempt to randomize subjects with respect to placebo or antibiotic.[33,34] Inclusion criteria required evidence of continued disease activity following treatment with SRP, periodontal surgery, and the adjunctive use of tetracycline. Each patient served as his/her own control. Subjects received clindamycin when SRP did not control advancing disease and clindamycin was indicated by culture/sensitivity testing. Additional disease activity was defined

as ≥3 mm loss in attachment and/or a periodontal abscess. Gordon entered 13 patients and treated them with a thorough scaling and a course of clindamycin-HCl, 150 mg qid for 7 days. The patients were monitored for up to 2 years following treatment. During the first year, the number of average sites in the 13 patients showing disease progression decreased from an annual rate of 10.7% to 0.5% with each patient demonstrating a decreased incidence of active sites following clindamycin treatment.

Essentially this same design was applied to the treatment of refractory periodontitis by the Florida group.[3,36,37] However, a placebo group was added. Patients with a history of continued periodontal destruction despite conventional periodontal treatment, which included the adjunctive use of a tetracycline and/or a penicillin, were entered into a monitoring phase of up to one year. Subjects initially received a thorough subgingival SRP and instructions in oral hygiene. All sites were monitored at monthly intervals. Subjects with documented continued destruction were randomly assigned to a placebo or an adjunctive antibiotic group, either amoxicillin plus clavulic acid or clindamycin-HCl. Antibiotic selection was based upon the susceptibility of the subgingival flora. Treatment consisted of SRP in conjunction with clindamycin-HCl, 150 mg qid for 10 days, or amoxicillin plus clavulic acid, 250 mg tid for 10 days, or placebo. The subjects were evaluated at 3-month intervals for up to 2 years or until additional destruction was detected. No additional maintenance treatment was given during the post-treatment monitoring period unless additional disease activity was detected. All subjects entered into the SRP/placebo group demonstrated additional destruction within the first year. Seven of the 9 clindamycin-treated subjects demonstrated no additional breakdown for up to 2 years. Two of 9 ACA-treated patients required additional treatment within the first year and an additional subject required treatment after 21 months. Interestingly, the microflora associated with the group assigned to receive clindamycin and the group assigned to receive ACA were very different. The former consisted of the expected Gram-negative anaerobic bacteria and contained a high proportion of spirochetes, *Prevotella intermedia, Porphyromonas gingivalis,* and other Gram-negative anaerobic rods. Prior to treatment with clindamycin, the subjects were characterized by a rapid loss of attachment. Subjects assigned to receive ACA contained primarily a Gram-positive flora in which the predominant microorganism was *Streptococcus intermedius*. These subjects demonstrated a much slower rate of attachment loss.

McCulloch et al.[38] conducted one of the first placebo-controlled randomized trials using SRP and an adjunctive antibiotic. Fifty-five subjects were enrolled. Inclusion criteria required a recent history of a periodontal abscess and/or loss of ≥2 mm of gingival attachment during a specified monitoring period. Doxycycline, 100 mg/day, or placebo was given for 3 weeks following periodontal scaling and tooth polishing. Within 7 months, 15 (79%) of the 19 subjects receiving the placebo exhibited additional disease activity compared to 13 (45%) of 29 subjects who received doxycycline. Subjects who exhibited additional disease activity were retreated using metronidazole.[39] Metronidazole was found to be very effective at arresting additional disease activity and appeared to be more effective than doxycycline. However, the results obtained may have been due to consecutive use of the 2 antibiotics rather than only to metronidazole.

Loesche et al. have presented some very interesting data using metronidazole in a group of patients simply defined as "adult periodontitis."[40-42] In these studies, the outcome was defined as a reduced need for periodontal surgery. Metronidazole clearly showed improvements in outcome greater than scaling alone. Winkel et al.[43] used metronidazole (500 mg, tid, for 7 days) as an adjunct to debridement in the treatment of 27 refractory periodontitis patients. All patients had detectable levels *of Bacteroides forsythus*. Mean probing depth, attachment level, and bleeding index all showed significant improvement following metronidazole treatment. Maximum improvement was seen in those patients who were negative *for B. forsythus, P. gingivalis,* and *P. intermedia* after treatment.

Several studies have addressed the treatment of advanced periodontal diseases utilizing a combination of metronidazole and amoxicillin. Although the patients were not defined as "refractory," data obtained may be pertinent to the treatment of patients who continue to demonstrate periodontal breakdown despite adequate care. Winkel et al.[43] utilized a double-blind, placebo-controlled study to test the effectiveness of this drug combination in a group of 49 adults with generalized severe periodontitis. Twenty-six subjects received treatment consisting of SRP and antibiotics (375 mg amoxicillin plus 250 mg metronidazole, tid, for 7 days). Twenty-three received SRP and placebo. The results indicated that metronidazole/amoxicillin in conjunction with SRP gave significantly

better clinical and microbiological results than SRP alone.

A review of the existing literature on the treatment of refractory periodontitis leaves the impression that the adjunctive use of antibiotics in combination with mechanical treatment provides a better therapeutic result than mechanical treatment alone. The initial question still remains "Which antibiotic is best?" There is no clear cut answer. There is not now, nor is it likely there will ever be, a "silver bullet" to use in the treatment of periodontal diseases. The microflora associated with refractory periodontitis varies significantly from patient to patient.[3,44,45] Therefore, the response to an antibiotic can be expected to vary as well.

LOCAL DELIVERY OF ANTIBIOTICS INTO THE PERIODONTAL POCKET

Up to now, this review has concentrated on the systemic delivery of antibiotics. Within the past decade, several locally applied controlled delivery products have been approved by the Food and Drug Administration for the treatment of periodontitis. The concept that local delivery of an antibiotic into the periodontal pocket achieves a greater, more potent concentration of drug than available with systemic delivery is very attractive. The amount of drug delivered often exceeds the equivalent of 1 mg/ml (1000 µg/ml). This level is considered bactericidal for most bacteria that exhibit resistance to systemically delivered concentrations. Equally important, local delivery of an antibiotic would have a negligible impact on the microflora residing in other regions of the body.

In the United States, 3 local delivery antibiotic-containing products have received FDA approval for use in the treatment of periodontitis. These include 12.7 mg tetracycline-HCl in an ethylene/vinyl acetate copolymer periodontal fiber,§ 10% doxycycline hyclate in a gel delivery system,‖ and minocycline-HCl microspheres.¶ Tetracycline-containing controlled release fibers were the first local delivery system available and have been subjected to the most extensive testing. For a review of the literature describing their efficacy on clinical and microbial parameters, see Rams and Slots.[46] In most cases, all 3 products have been tested primarily in the treatment of "chronic periodontitis" either as an adjunct to SRP or as an alternative to SRP. However, tetracycline fibers have had limited testing in both juvenile periodontitis[47] and refractory periodontitis.[48] Positive clinical results were reported in each study. Currently, sufficient data are not available to evaluate the potential efficacy of these systems in the treatment of refractory periodontal disease. Intuitively, these systems would seem to be ideal for the treatment of recurrent periodontitis or for the treatment of individual sites that have not responded as well as the practitioner might desire.

We would like to comment briefly on another FDA-approved drug for the treatment of periodontitis, the subantimicrobial dose of doxycycline hyclate (SDD).# Prescribed at a dosage of 20 mg, bid, doxycycline has no detectable antimicrobial efficacy on the oral flora[14,49] or on the flora in other regions of the body.[50] A 20 mg dose exerts its effect not as an antibiotic, but as a collagenase inhibitor as well as an anti-inflammatory agent. This product has been extensively tested as an adjunct to SRP in multi-centered, double-blind, placebo controlled studies.[51-54] Significant improvements in clinical attachment level and probing depth were present at 3, 6, and 9 months of treatment in the SDD/SRP subjects relative to SRP alone, with more severely diseased sites showing the greatest improvement.[53]

ANTIBIOTIC SELECTION

Once a patient has been diagnosed with periodontitis, treated and evaluated appropriately, and has not responded favorably to conventional therapy, the adjunctive use of an antibiotic may be indicated. In the case of classical *Aa*-associated juvenile periodontitis, the practitioner might choose tetracycline-HCl, or one of its derivatives, in conjunction with conventional therapy. If a favorable response is not obtained with tetracycline or if the disease appears to be particularly aggressive, the combination of amoxicillin and metronidazole (250 mg and 375 mg, respectively, given 3 times a day for 7 days) would be suggested.

Selection of an antibiotic for adjunctive use in the treatment of refractory and/or recurrent periodontitis is more difficult. Culture and antibiotic sensitivity testing is strongly recommended. Such a test provides valuable information regarding the periodontal pathogens present and their predicted response to different antibiotics. Several laboratories across the country now offer this service on a fee basis. In a recent study by Cohen et al.,[55] microbial samples were collected from 25 adult patients, subdivided and sent to each of 3 commercial oral testing labs by overnight courier. The results obtained showed some minor differences in the quantity of a particular bac-

§ Actisite, ALZA Laboratories, Palo Alto, CA.
‖ Atridox, CollaGenex, Newtown, PA.
¶ Arestin, OraPharma, Warminster, PA.
# Periostat, CollaGenex.

Table 1.

Suggested Oral Antibiotic Dosages

Generic Name	Usual Adult Dosage	Length of Treatment	Maximum Child Dosage	Dosage Suggestions
Amoxicillin/clavulanic acid	250 or 500 mg, tid	10 days	Weight <20 kg: 20-40 mg/kg in divided doses, tid	Given without regard to meals (given with food helps eliminate some of the stomach distress)
Amoxicillin plus metronidazole	375 mg amoxicillin, tid, plus 250 mg metronidazole, tid	7 days	Not recommended forchildren under 16 years of age	Given without regard to meals
Clindamycin hydrochloride	150-300 mg, qid	10 days	8-12 mg/kg in 3-4 equally divided doses	Given without regard to meals (given with food helps eliminate some of the stomach distress)
Doxycycline hyclate	100 mg bid first day followed by 100 mg a day either as single dose or 50 mg, bid	10-14 days	Age >8 years: 4 mg/kg divided into equal doses, bid, on 1st day; followed by 2 mg/kg as single dose or divided into equal doses, bid	Given 1 hour before or 2 hours after meal
Metronidazole	250 mg, tid or qid	10 days	Not recommended for children under 16 years of age	Given without regard to meals
Minocycline hydrochloride	200 mg bid first day followed by 100 mg, bid	10-14 days	Age >8 years: 4 mg/kg divided into equal doses bid on 1st day; followed by 2 mg/kg, bid	Given 1 hour before or 2 hours after meal
Tetracycline hydrochloride	250 mg, qid	14-21 days	Age >8 years: 25-50 mg/kg in equal doses, bid	Given 1 hour before or 2 hours after meal

terial species recovered; however, overall, the results were highly similar and would lead to the same treatment recommendation.

When culture and sensitivity testing are not feasible, the practitioner has to make the choice of antibiotic based on patient presentation and history. If disease is limited to a minimum number of sites, local delivery of antibiotic placed immediately following SRP is suggested. The choice of which local delivery device to use would be based upon the practitioner's experience and preference.

Widespread disease may necessitate the need to incorporate systemic antibiotics into the treatment plan. Culture and sensitivity testing are strongly recommended to select the antibiotic regimen that will be the most efficacious. If culture and sensitivity is unavailable, the following approach is suggested. Patients without a previous history of antibiotic therapy may respond well to a tetracycline (tetracycline, doxycycline, or minocycline). Alternatively, for patients not allergic to penicillins, amoxicillin plus clavulic acid may be effective. The combination amoxicillin/clavulanic acid appears superior to amoxicillin alone. However, care should be utilized in its use for older patients on multi-drug regimens. A recent review article reports that severe adverse events, particularly drug-induced cholestatic hepatitis, may be associated with the use of ACA in such patients.[28]

When the disease process is considered extremely aggressive, the combination of amoxicillin plus metronidazole is suggested. Clindamycin-HCl has been shown to be very effective in the treatment of a subset of patients with refractory periodontitis. However, due to the potential for severe adverse effects, this drug should only be used if indicated by culture and susceptibility testing. Oral dosages, treatment regimens, and absorption suggestions for the administration of systemic antibiotics are summarized in Table 1. Please consult manufacturer's package insert for the use of local-delivery antibiotics.

In summary, the decision to incorporate adjunctive antibiotic therapy into the treatment protocol for periodontitis should be based on accurate scientific knowledge and sound clinical judgement. The need for an adjunctive antibiotic should be firmly established in the clinician's mind as well as the expected outcome of the therapy. Culture and sensitivity testing is strongly recommended as an aid in the selection of the most efficacious antibiotic.

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