Should Antibiotics Be Prescribed to Treat Chronic Periodontitis?

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KEYWORDS

• Antimicrobials-systemic • Periodontitis microbiology • Oral biofilm
• Periodontitis therapy • Scaling and root planing • Clinical trials

KEY POINTS

- Although chronic periodontitis often responds to mechanical debridement alone, patients with progressive attachment loss, invasive subgingival pathogens, or multiple deep pockets may benefit from combining systemic antibiotics with mechanical therapy.
- Bacteria in subgingival biofilm are resistant to antibiotics. Antibiotics should only be prescribed after biofilm has been mechanically disrupted, not as the sole approach to treatment.
- Meta-analyses suggest that metronidazole (in combination with amoxicillin or alone) or azithromycin produce statistically significant adjunctive benefits in combination with mechanical therapy.
- When used to treat chronic periodontitis, the combination of mechanical therapy and antibiotics yields its greatest benefit at sites with deep initial probing depths.
- Systemic antibiotics have the potential to produce adverse reactions that must be considered in balance with their expected benefits.

INTRODUCTION

Periodontitis is a chronic inflammatory disease that leads to destruction of the supporting tissues of teeth and, if left untreated, tooth loss. Severe periodontitis was the world's sixth-most prevalent condition in 2010; its age-standardized prevalence

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between 1990 and 2010 among all countries was 11.2%.[1] Consistent with this estimate, a study based on data from the 2009 and 2010 National Health and Nutrition Examination Survey cycle reported prevalence rates of 8.7%, 30.0%, and 8.5% for mild, moderate, and severe periodontitis, respectively, in the United States.[2]

Studies from the past 3 decades have revealed that only a small subset of microorganisms from among the hundreds of species found in the oral cavity is highly associated with periodontitis.[3] Although specific biofilm-producing bacterial pathogens and other cooperative species are required, bacteria alone are not sufficient to induce periodontitis. The host immune-inflammatory response is a determinant of susceptibility to periodontitis and is responsible for most of the periodontal tissue destruction.[4] During persistent bacterial infection and prolonged homeostatic imbalance, cytokines and enzymes released by host leukocytes mediate destruction of periodontal connective tissue and bone. Systemic diseases (eg, diabetes), immune dysfunction, and environmental factors (eg, smoking) can also contribute to disruption of the homeostatic balance.[5] The goal of periodontal therapy is to preserve the natural dentition in stability, comfort, and function by eliminating pathologic biofilm and resolving inflammation.

Microbial complexes in subgingival biofilm have been recently characterized using molecular techniques. Individual species in these complexes have been assigned using a color-coded system that reflects community ordination and cluster analysis.[6] The red complex, consisting of *Tannerella forsythia*, *Porphyromonas gingivalis*, and *Treponema denticola*, is strongly associated with severe chronic periodontitis. The orange complex, which includes *Prevotella intermedia*, *Fusobacterium nucleatum*, *Campylobacter rectus*, and *Peptostreptococcus micros*, is closely associated with the red complex. The green complex includes *Aggregatibacter actinomycetemcomitans*, which has a strong association with aggressive periodontitis and a less frequent association with chronic periodontitis.[7] *Porphyromonas gingivalis*, *A actinomycetemcomitans* and other pathogens possess virulence factors that can overcome the host response and damage periodontal tissues.[8,9]

Porphyromonas gingivalis, *A actinomycetemcomitans*, and *Prevotella intermedia* are capable of invading the epithelium of periodontal pockets, which protects them from elimination by the host response, making them exceptionally difficult to eliminate by conventional periodontal scaling and root planing (SRP). Persistent infections by these bacteria are frequently associated with progressive chronic periodontitis.[10] Another limitation of SRP is that it is not effective in removing bacteria from deep pockets, furcations, dentinal tubules, and other subgingival sites where access is poor. The difficulties associated with eliminating bacteria that have colonized the soft tissue wall of the pocket and other inaccessible areas provide a rationale for incorporating systemic antibiotics into the treatment of periodontitis.

A broad range of systemic antibiotics has been used to treat chronic periodontitis. The pharmacokinetic and antimicrobial properties of the agents used most commonly are presented in **Table 1** and information on dosage is detailed in **Table 2**. In general, amoxicillin, metronidazole, azithromycin, tetracycline, and doxycycline are capable of attaining levels that can effectively inhibit periodontal pathogens when they are growing as single (planktonic) cells in a periodontal pocket or the soft tissue wall of a pocket. The exception is metronidazole, which exhibits relatively poor activity against *A actinomycetemcomitans* at typical in vivo concentrations. However, it is important to remember that subgingival bacteria live in a biofilm, not as single cells. Bacteria growing in a biofilm are substantially more difficult to inhibit with antibiotics. For this reason, antibiotics should only be used to treat periodontitis in patients who have already had their subgingival biofilm disrupted by SRP.

Table 1
Characteristics of antibiotics used to treat chronic periodontitis

Agent	Half-Life in Serum (h)	Action	GCF Level (μg/mL)	MIC_{90} (μg/mL) for *Porphyromonas gingivalis*	MIC_{90} (μg/mL) for *T forsythia*	MIC_{90} (μg/mL) for *Prevotella intermedia*	MIC_{90} (μg/mL) for *A actinomycetemcomitans*
Amoxicillin	1–2	Bactericidal	3–4	<0.016	0.38	0.25–1.5	0.4–1
Metronidazole	6–12	Bactericidal	8–10	<0.016	0.005	0.032–0.25	64–96
Azithromycin	40–68	Bacteriostatic or bactericidal	3–10	0.094–0.5	0.5–1	0.25–0.4	0.875–4
Tetracycline	6–8	Bacteriostatic	5–10	0.023–0.25	0.19	2–4	0.2–1.5
Doxycycline	12–22	Bacteriostatic	2–8	0.047	0.38	0.05	1

Abbreviations: GCF, gingival crevicular fluid; MIC_{90}, minimal inhibitory concentration of an antibiotic at which 90% of bacterial isolates are inhibited.
Data from Refs.[11–19]

Table 2
Representative antibiotic regimens for adjunctive use in treatment of chronic periodontitis

Antibiotic	Prescription	Potential Adverse Reactions
Amoxicillin + Metronidazole	500 mg tid for 8 d 250 mg tid for 8 d	Hypersensitivity to amoxicillin, nausea, diarrhea, vomiting, altered taste sensations, Antabuse effect
Metronidazole	500 mg tid for 7 d	Nausea, vomiting, altered taste sensations, Antabuse effect
Azithromycin	500 mg qd for 3 d	Diarrhea, nausea, vomiting, abdominal pain, cholestatic jaundice, increased risk of serious cardiac arrhythmia (prolonged Q-T interval) Inhibition of bactericidal agents if used in combination
Doxycycline	200 mg initial dose, then 100 mg qd for 21 d	Photosensitivity, nausea, diarrhea, vomiting, and abdominal pain Inhibition of bactericidal agents if used in combination

Unlike the other agents in **Table 1**, azithromycin and doxycycline have relatively long half-lives and are normally administered in a single daily dose. Azithromycin and tetracycline compounds are actively taken up and concentrated inside oral epithelial cells,[20,21] whereas amoxicillin and metronidazole enter cells by passive diffusion.[22,23] This property may be useful for targeting periodontal pathogens that have invaded the pocket epithelium. When cultured gingival epithelial cells infected with *A actinomycetemcomitans* are incubated with physiologic concentrations of azithromycin (8 μg/mL), azithromycin accumulates inside the epithelial cells at levels that kill more than 80% of the intracellular *A actinomycetemcomitans* within 2 hours. In the same experimental conditions, treatment with amoxicillin at its peak therapeutic concentration (4 μg/mL) kills only 14% of the intracellular bacteria.[21]

PATIENT EVALUATION FOR POTENTIAL USE OF AN ANTIBIOTIC: OVERVIEW

Although it is difficult to completely remove subgingival biofilm and root deposits with SRP, most patients with chronic periodontitis respond favorably to treatment with conventional SRP without antibiotics. However, some cases can derive an additional increment of clinical attachment gain or probing depth reduction from combining systemic antibiotics with SRP. The literature provides guidance for predicting which patients could potentially benefit.

Characteristics of chronic periodontitis patients who may benefit from use of antibiotics

- Patients who exhibit a poor response to adequate SRP, with continuing loss of clinical attachment
- Patients who test positive for *Porphyromonas gingivalis* or *A actinomycetemcomitans* in their subgingival biofilm
- Patients with severe chronic periodontitis and generalized deep pocket depths.

There is agreement that patients who fail to respond favorably to SRP, especially those with progressive attachment loss, can benefit from treatment with antibiotics.[24] As previously mentioned, progressive chronic periodontitis is often associated with persistent infections by *Porphyromonas gingivalis*, *A actinomycetemcomitans*, and *Prevotella*

intermedia,[10] which invade the soft tissue wall of the periodontal pocket and are difficult to eliminate with SRP. Consistent with this recommendation, patients with chronic periodontitis who have undergone microbiological testing and are positive for *Porphyromonas gingivalis* or *A actinomycetemcomitans* in their subgingival plaque can be expected to benefit from use of antibiotics.[25] Finally, patients with generalized severe chronic periodontitis and multiple deep periodontal pockets may also benefit.[26,27] The common thread in these guidelines is an acknowledgment that SRP has limited ability to eliminate invasive pathogens and remove biofilm from inaccessible sites.

Smokers typically exhibit a less favorable response to periodontal therapy than nonsmokers. There is evidence that subgingival pathogens are more difficult to eliminate in smokers.[28,29] Although some studies have suggested that adjunctive systemic antibiotics can improve the responses to periodontal therapy in smokers,[30] a recent systematic review concluded that additional well-designed randomized clinical trials are needed to provide sufficient evidence to support the use of adjunctive antibiotics in the treatment of periodontitis in smokers.[31]

EFFICACY OF SCALING AND ROOT PLANING AS THE SOLE TREATMENT OF PERIODONTITIS

Although SRP is regarded as the gold standard of nonsurgical periodontal treatment, it is a highly demanding therapy. Its effectiveness is limited by anatomic factors (furcation involvement, tooth type, and surface) and the experience of the operator.[32] As previously mentioned, SRP loses some of its ability to eliminate subgingival biofilm as pocket probing depths increase.[33,34] Despite this, the magnitude of probing depth reduction and clinical attachment gain resulting from SRP is greatest at periodontal sites with deep pretreatment probing depths (**Table 3**).[35]

In pockets deeper than 6 mm, SRP provides a mean clinical attachment gain of 1.19 mm and a mean probing depth reduction of 2.19 mm. In pockets of moderate (4–6 mm) depth, the respective values are 0.55 mm and 1.29 mm. SRP also reduces clinical signs of inflammation. As an example, it reduces bleeding on probing to approximately 43% of baseline levels.[35] These outcomes can be consistently achieved with chronic periodontitis patients, independent of the types of instruments used (power-driven or manual).[36,37] Patients with poor oral hygiene, smoking habits, or poor glycemic control exhibit a less favorable response to SRP.

EFFICACY OF SYSTEMIC ANTIBIOTICS AS THE SOLE TREATMENT OF PERIODONTITIS

In patients with advanced chronic periodontitis, diligent treatment with SRP requires a substantial amount of time and effort. It may seem reasonable to consider using systemic antibiotics as a cost-effective alternative to SRP for eliminating subgingival

Table 3
Summary of clinical outcomes achieved with scaling and root planing when used to treat nonmolar sites

Pretreatment Status	Number of Clinical Studies Surveyed	Mean Clinical Attachment Level Gain	Mean Probing Depth Reduction
Shallow pockets (1–3 mm)	9	−0.34 mm	0.03 mm
Moderate pockets (4–6 mm)	27	0.55 mm	1.29 mm
Deep pockets (>6 mm)	18	1.19 mm	2.19 mm

Data from Cobb CM. Non-surgical pocket therapy: mechanical. Ann Periodontol 1996;1:443–90.

bacteria. Although this question has been examined in several reviews,[27,38,39] relatively few studies have been specifically designed to address it. As a monotherapy for chronic periodontitis, metronidazole can reduce probing depths, induce modest attachment gains, reduce bleeding on probing, and suppress spirochetes in subgingival biofilm.[38] Comparisons of the efficacy of metronidazole alone with SRP have demonstrated that metronidazole is inferior or, at best, equivalent in improving periodontal status.[40–42] Moreover, a meta-analysis of 4 clinical trials that compared attachment level changes in subjects with untreated periodontitis with that of subjects treated with metronidazole alone or metronidazole in combination with amoxicillin failed to show a statistically significant difference between groups. Thus, there is not sufficient evidence that systemic antibiotics, when used as a monotherapy, are beneficial in the treatment of periodontitis.[27]

In contradistinction to these studies, a more recent study concluded that a combination of metronidazole and amoxicillin as the sole therapy for periodontitis produces changes in clinical and microbiological parameters that are similar to those obtained from conventional SRP.[43] However, every subject in this study received supragingival scaling to facilitate periodontal probing. Thus, the group treated with antibiotics did not actually receive a monotherapy because removal of supragingival biofilm has been shown to alter the number and composition of subgingival bacteria.[44]

Consistent with most clinical studies, microbiological studies have shown that bacteria living in biofilms are more resistant to antimicrobial agents than single, dispersed (planktonic) bacteria.[45–47] This may be related to impairment of antibiotic diffusion into biofilms or to the slower bacterial growth rate secondary to deprivation of nutrients within the biofilm[44]; however, there are other contributing factors. The close association of bacteria living in biofilms facilitates horizontal transfer of genetic information that confers resistance to antibiotics.[48,49] In vitro studies have shown that the antibiotic concentrations found in gingival crevicular fluid (GCF) have limited impact on periodontal pathogens living in biofilms.[50,51] For these reasons, there is a consensus that antibiotics should only be prescribed after biofilm is mechanically disrupted.

EFFICACY OF SCALING AND ROOT PLANING COMBINED WITH SYSTEMIC ANTIBIOTICS

Several comprehensive reviews have evaluated the efficacy of a combination of SRP and systemic antibiotics in treatment of chronic periodontitis.[26,27,39,52–55] Their general conclusions are summarized below:

- Combining systemic antibiotics with SRP can provide a greater therapeutic benefit than SRP alone.
- The combination of antibiotics and SRP provides a greater benefit to patients with aggressive periodontitis than to those with chronic periodontitis.
- The combination of SRP and antibiotics yields its greatest benefit at sites with deep initial probing depths.
- Several different antibiotic regimens are capable of enhancing the treatment response to SRP. Meta-analyses support the use of metronidazole (alone or in combination with amoxicillin) or azithromycin.
- Indirect evidence suggests that antibiotics should be started on the day SRP is completed and that SRP should be completed within a short period (ideally, less than a week).

Meta-analysis is a useful statistical technique for combining results from different studies to achieve higher statistical power. This approach has been used to analyze

the benefits of combining antibiotics with SRP. **Table 4** summarizes data from several meta-analyses of the overall effect of combined treatment of chronic periodontitis with SRP and adjunctive antibiotics in comparison with treatment with SRP alone. These studies examined treatment effects throughout the mouth, including sites with only minor attachment loss and shallow probing depths. Based on 2 meta-analyses that considered the effects of a broad range of different antibiotic regimens on treatment of chronic periodontitis, combined therapy can enhance clinical attachment gain by 0.20 to 0.24 mm and decrease probing depth by a mean of 0.28 mm in comparison with SRP alone.[27,54] Neither of these analyses could identify an antimicrobial regimen that was clearly superior to the others. Adjunctive antibiotics seem to consistently enhance the clinical response to SRP for both aggressive and chronic periodontitis patients but patients with aggressive periodontitis seem to derive greater benefit. The mean clinical attachment gain observed in studies of subjects with aggressive periodontitis patients is nearly 3 times greater than that observed in studies of chronic periodontitis.[27]

Regarding the effects of specific antibiotic regimens, treatment with SRP combined with amoxicillin and metronidazole can enhance overall clinical attachment gain by 0.16 to 0.21 mm, and overall probing depth reduction by 0.29 to 0.43 mm, in comparison with SRP alone (see **Table 4**).[52,54] Similarly, the adjunctive benefits of combining metronidazole with SRP correspond to an additional 0.1 mm of attachment gain and 0.15 to 0.18 mm of probing depth reduction.[54,55] The combination of SRP and azithromycin yields a mean attachment gain of 0.11 mm (not statistically significant) and a mean probing depth reduction of 0.39 mm in comparison with SRP alone.[54] Meta-analysis of studies using an adjunctive doxycycline regimen failed to demonstrate a significant overall enhancement of attachment gain or probing depth.[54]

Evidence suggests that the benefits of combining antibiotics with SRP are more substantial at sites with initial probing depths of greater than 6 mm (**Table 5**). At deeper sites, treatment with SRP combined with amoxicillin and metronidazole can enhance clinical attachment gain by 0.45 to 0.67 mm and reduce mean probing depth by 0.92 mm in comparison with treatment with SRP alone.[26,54] Combining metronidazole with SRP results in an additional attachment gain of 0.55 to 0.66 mm and an additional probing depth reduction of 0.83 mm in comparison with SRP alone.[26,54] Use of azithromycin as an adjunct to SRP enhances mean attachment gain and probing depth reduction by 0.43 mm and 0.52 mm, respectively, over SRP alone.[54]

Because many different protocols have been used in studies that evaluated the benefits of combining antibiotics with SRP, there is a lack of evidence pointing to a specific protocol. However, there is indirect evidence that antibiotic therapy should immediately follow the completion of SRP and that SRP should be completed within a reasonably short time (ideally, within 1 week).[39]

TREATMENT COMPLICATIONS AND RESISTANCE

Systemic antibiotics have the potential to produce adverse reactions that must be considered in balance with their expected benefits (see **Table 2**). Direct toxic effects of amoxicillin, metronidazole, doxycycline, or azithromycin are rare. However, all have the potential to induce nausea, vomiting, diarrhea, and abdominal pain in a small percentage of patients.[56] The most common adverse effects associated with amoxicillin and other penicillins are allergic reactions, including skin rashes; serum sickness; and, rarely, anaphylaxis.[57] Patients taking metronidazole often report altered taste sensations and can experience Antabuse effects in response to alcohol ingestion.[38] Photosensitivity can occur in individuals taking doxycycline.[56] In rare instances,

Table 4
Meta-analyses of clinical outcomes associated with combining systemic antibiotics with scaling and root planing to treat chronic periodontitis (overall effects at all sites)

Reference	Dates and Number of Included Studies	Antibiotics Studied	Observation Time (mo)	Mean Clinical Attachment Level Gain (*P* Value)	Mean Probing Depth Reduction (*P* Value)
Haffajee et al,[27] 2003[a]	1983–2001 n = 17	MET, SPIR, AMX + MET, AMX + CA, TET, DOX	>1, most ~6	0.24 mm (0.001)	Not analyzed
Keestra et al,[54] 2015[b] (main analysis)	1994–2012 n = 35	AMX, AMX + CA, AMX + MET, MET, AZM, CLR, DOX, SDD, ORN, SPIR, TET, MOX	3	0.20 mm (0.0004)	0.28 mm (<0.00001)
Sgolastra et al,[52] 2012	2001–2011 n = 4	AMX + MET	≥3	0.21 mm (0.03)	0.43 mm (<0.0001)
Keestra et al,[54] 2015 (subanalysis)	1998–2012 n = 7	AMX + MET	3	0.16 mm (0.05)	0.29 mm (0.003)
Sgolastra et al,[55] 2015	1998–2012 n = 6	MET	≥3	0.10 mm (<0.00001)	0.18 mm (0.0001)
Keestra et al,[54] 2015 (subanalysis)	2004–2012 n = 5	MET	3	0.10 mm (0.12)	0.15 mm (0.004)
Keestra et al,[54] 2015 (subanalysis)	2005–2012 n = 6	AZM	3	0.11 mm (0.32)	0.39 mm (0.004)
Keestra et al,[54] 2015 (subanalysis)	1999–2008 n = 4	DOX	3	0.09 mm (0.34)	0.11 mm (0.15)

Abbreviations: AMX, amoxicillin; AZM, azithromycin; CA, clavulanic acid; CLR, clarithromycin; DOX, doxycycline; MET, metronidazole; MOX, moxifloxacin; ORN, ornidazole; SDD, subantimicrobial-dose doxycycline; SPIR, spiramycin; TET, tetracycline.

[a] Main meta-analysis included 3 studies that examined the effect of the antibiotic as a sole treatment.

[b] Main meta-analysis included 9 studies that examined the effect of adjunctive subantimicrobial-dose doxycycline.

Data from Refs.[26,52,54,55]

Table 5
Meta-analyses of clinical outcomes associated with combining systemic antibiotics with scaling and root planing to treat chronic periodontitis (effects at sites with initial probing depths >6 mm)

Reference	Dates and Number of Included Studies	Antibiotics Studied	Observation Time (mo)	Mean Clinical Attachment Level Gain (*P* Value)	Mean Probing Depth Reduction (*P* Value)
Herrera et al,[26] 2002 (subanalysis)	1998 n = 2	AMX + MET	12–24	0.45 mm (0.001)	Not analyzed
Keestra et al,[54] 2015 (subanalysis)	2008–2012 n = 4	AMX + MET	3	0.67 mm (0.02)	0.92 mm (0.0003)
Herrera et al,[26] 2002 (subanalysis)	1983–1984 n = 2	MET	2–12	0.55 mm (0.057)	Not analyzed
Keestra et al,[54] 2015 (subanalysis)	2004–2012 n = 5	MET	3	0.66 mm (<0.00001)	0.83 mm (<0.00001)
Keestra et al,[54] 2015 (subanalysis)	2002–2012 n = 5	AZM	3	0.43 mm (0.03)	0.52 mm (0.0003)

Abbreviations: AMX, amoxicillin; AZM, azithromycin; MET, metronidazole.

Data from Herrera D, Sanz M, Jepsen S, et al. A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. J Clin Periodontol 2002;29(Suppl 3):136–59; and Keestra JA, Grosjean I, Coucke W, et al. Non-surgical periodontal therapy with systemic antibiotics in patients with untreated chronic periodontitis: a systematic review and meta-analysis. J Periodont Res 2015;50(3):294–314.

azithromycin may induce angioedema or cholestatic jaundice. In addition, azithromycin can contribute to cardiac arrhythmias and slightly increase the risk of cardiovascular death in individuals with a high baseline risk of cardiovascular disease.[58] Patients should be informed of the potential for adverse reactions; however, these effects typically present as gastrointestinal upsets and most are not serious.[27,39]

Several fundamental issues can, individually or in combination, undermine the therapeutic benefits associated with use of adjunctive antibiotics in periodontal therapy. Lack of patient compliance (adherence) with the prescribed dosage regimen is a major concern. If the antibiotic does not reach optimal concentrations at the infection site or the duration of treatment is too short because the patient does not follow directions, its therapeutic benefit will be compromised. Studies have shown that compliance can be poor with complex regimens that require patients to take multiple doses per day.[59] Thus, it is reasonable to expect that compliance with a combined regimen of amoxicillin and metronidazole will be lower than with a once-a-day azithromycin regimen.

Prescribing an antibiotic will not predictably enhance treatment outcomes if the subgingival biofilm is not thoroughly disrupted before antibiotic treatment or if patients fail to inhibit biofilm reformation by maintaining good oral hygiene.[39,60] An antibiotic's minimal inhibitory concentration (MIC) for bacteria living in a biofilm can be 10 to 1000-fold higher than for bacteria growing in a planktonic state,[61,62] and typically exceeds the concentration that the antibiotic can attain in GCF. In effect, disruption of subgingival biofilm decreases the MIC values and renders the bacteria more susceptible to antibiotics at concentrations found in GCF.[63] There is evidence to suggest that the red complex of subgingival bacteria associated with chronic periodontitis is relatively susceptible to antibiotics.[27] However, other subgingival pathogens found in chronic periodontitis patients, including *Prevotella intermedia*, *Prevotella nigrescens*, and *A actinomycetemcomitans*, are often resistant to doxycycline, amoxicillin, or metronidazole.[64] Failure to eliminate these pathogens could limit the success of SRP combined with an adjunctive antibiotic regimen.

If examination reveals that inflammation has not resolved or attachment loss has not been arrested by treatment with a combined regimen of SRP and antibiotics within 2 to 3 months, 2 different approaches can be used to address resistance to treatment. Microbiological testing could help explain why the original treatment failed and guide additional nonsurgical therapy. Subgingival plaque samples should be collected from progressive disease sites with sterile paper points and shipped to a laboratory that has the specialized expertise needed to identify pathogens that have not been eliminated. Based on this information, an alternative regimen that is appropriate for targeting the remaining pathogens can be selected. Because the subgingival environment progressively recolonizes with bacteria after SRP, subgingival biofilm must be disrupted and dispersed again before administering the alternative antibiotic. At the time the clinical response is reexamined 2 to 3 months later, it may be prudent to conduct another microbiological test to confirm that pathogens have been eliminated. As a second option, periodontal surgery may be used to address persistent pocketing and attachment loss.

There is general agreement that selective, rather than routine use of antibiotics is the best practice. Commensal bacteria living in the intestinal tract contribute to the development, maintenance, and function of the immune system. By disrupting commensal microbiota, antibiotics can perturb host defenses in a detrimental manner.[65] Moreover, antibiotic resistance has become a serious public health issue in recent years. Its economic and social costs are significant. A recent study suggests that subgingival biofilm can serve as a reservoir of β-lactam resistance genes.[66] Dentists can help prevent these issues by prescribing antibiotics only when they are indicated, by

prescribing an appropriate antibiotic regimen, and by using antibiotics only after subgingival biofilm has been debrided. Patients can help reduce the risk of inducing resistance by complying with the recommended dosage and duration of the prescribed regimen.

EVALUATION OF OUTCOME AND LONG-TERM RECOMMENDATIONS

Increased tooth survival is one of the most relevant outcomes for reporting the effectiveness of periodontal therapy, and one that patients readily understand. It is rarely used, however, because exceptionally long study periods are required to obtain meaningful data.[26] As a practical matter, increases in clinical attachment level and reduction of probing depths are reasonable proxies for increased tooth survival. In absolute terms, a full-mouth attachment gain of only 0.10 to 0.24 mm (see **Table 4**) could be viewed as a modest benefit for using antibiotics in combination with SRP. Considering that patients who are highly susceptible to periodontitis experience a mean full-mouth attachment loss of 0.067 mm per year during supportive therapy after active periodontal treatment,[67] an attachment gain of 0.10 to 0.24 mm effectively offsets 1.5 to 3.5 years of disease progression.

At periodontal sites with deep (>6 mm) probing depths, combining an antibiotic with SRP can enhance attachment gain by 0.43 to 0.67 mm (see **Table 5**). Because SRP yields a mean attachment gain of 1.19 mm at sites with deep initial probing depths (see **Table 3**), the use of antibiotics in combination with SRP enhances attachment gain by 36% to 56% more than that obtained from SRP alone. In patients with many deep pockets, a benefit of this magnitude is cost-effective and clinically relevant because it could potentially decrease the need for periodontal surgical therapy.[68]

As mentioned previously, patients with mild-to-moderate chronic periodontitis usually respond favorably to initial treatment with SRP alone without adjunctive antibiotics. Patients with severe chronic periodontitis who have multiple deep pockets, progressive attachment loss, or test positive for invasive subgingival pathogens may benefit from an initial therapy that combines systemic antibiotics with SRP. Consistent with the meta-analyses detailed in **Tables 4** and **5**, a combination of amoxicillin and metronidazole is a reasonable choice for adjunctive use in patients who are not allergic to β-lactam antibiotics. This combination of 2 bactericidal agents has the potential to inhibit a broader spectrum of bacteria than a single agent and is less likely to induce resistance. In patients who are allergic to amoxicillin, an adjunctive regimen of metronidazole or azithromycin is a reasonable alternative. The response to initial periodontal treatment should be evaluated within 2 to 3 months and adjusted as necessary. If progression of attachment loss has been arrested and the outcome is generally favorable, it would be appropriate to treat persistent deep pockets with periodontal surgery. Most patients treated with surgical therapy do not require a postoperative antibiotic regimen.[68] Currently, there is not sufficient evidence to support the adjunctive use of systemic antibiotics in conjunction with periodontal surgery.[39]

SUMMARY

- Although chronic periodontitis often responds to mechanical debridement alone, patients who have progressive attachment loss, invasive subgingival pathogens, or deep pockets may benefit from combining systemic antibiotics with mechanical therapy.
- Bacteria in subgingival biofilm are resistant to antibiotics. Antibiotics should only be prescribed after biofilm has been mechanically disrupted, not as the sole approach to treatment.

- Meta-analyses suggest that metronidazole (alone or in combination with amoxicillin) or azithromycin produce statistically significant adjunctive benefits in combination with mechanical therapy.
- When used to treat chronic periodontitis, the combination of mechanical therapy and antibiotics yields its greatest benefit at sites with deep initial probing depths.
- Systemic antibiotics have the potential to produce adverse reactions that must be considered in balance with their expected benefits.

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