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Does adjunctive antimicrobial therapy reduce the perceived need for periodontal surgery?

ANDREA MOMBELLI, NORBERT CIONCA & ADNAN ALMAGHLOUTH

Periodontal diseases are the result of an unsuccessful relationship between bacteria colonizing the surfaces of teeth and the tissues anchoring the teeth in the bone. Contemporary periodontal treatment generally aims at the removal of bacterial deposits (plaque and calculus) through a mechanical cleaning method termed 'scaling and root planing'. Scaling and root planing has limitations, particularly if the disease has led to the formation of pockets deeper than 5 mm around the affected teeth (5, 12, 73). To facilitate scaling and root planing, and to allow direct visual control in deep pockets, the soft tissues can be lifted back surgically for better access. In clinical practice, periodontal therapy is usually performed in two stages. An attempt to remove a maximum of bacterial deposits is made first without flap elevation. After 3–6 months, the case is re-evaluated, and, if deemed necessary, further root surface instrumentation follows, this time in the context of a local surgical intervention (Fig. 1, top). Two systematic reviews of numerous short- and long-term clinical trials have concluded that this way of dealing with periodontal diseases is efficacious (41, 89). However, it requires a considerable amount of active involvement of qualified personnel, extends over a long period of time, may induce notable loss of tooth substance, particularly if instrumentation is repeated several times, and may provoke gingival recession, leaving sensitive root surfaces exposed.

It would be unreasonable to suppose that mechanical cleaning of root surfaces alone can completely eliminate bacteria involved in the disease process. Bacteria are beyond the reach of mechanical instruments in dentin tubules, lacunae and concavities, and are inaccessible if they invade soft tissues. One frequent member of the subgingival microbiota,

Aggregatibacter actinomycetemcomitans (formerly known as *Actinobacillus actinomycetemcomitans*) (65), resists mechanical treatment particularly well (60, 63, 78). Longitudinal and retrospective studies have correlated persistence after therapy of *A. actinomycetemcomitans*, and a few other species, with continuing tissue destruction. Clinical results were better and more stable if such organisms were no longer detectable (10, 13, 14, 20, 31, 34, 36, 77, 98). Incomplete removal of pathogenic microorganisms should therefore be taken into account as a possible reason for an unsatisfactory treatment outcome.

Given the limitations of mechanical debridement, treatment protocols including antibacterial agents (antibiotics and antiseptics) may be more efficient than mechanical cleaning alone. Oral antibiotics are the most common approach for treating bacterial infections, and are the primary focus of this review. Local infections can also be treated with topically administered antimicrobials. Agents that are too toxic to be delivered by the systemic route, i.e. antiseptics, may be applied locally.

The literature on antimicrobial periodontal therapy has been thoroughly reviewed previously (23, 30, 86, 92). The aim of this review is to critically re-assess the strategies for using antimicrobial agents in periodontics, taking into account the literature summarized previously as well as the latest findings. In recent years, systematic reviews have become the preferred method of analyzing the available evidence because they search the literature using explicit procedures, appraise individual reports using pre-defined criteria, and combine the results of valid studies using appropriate statistical techniques. Where such systematic reviews are available, we do not cite individual trials in detail.

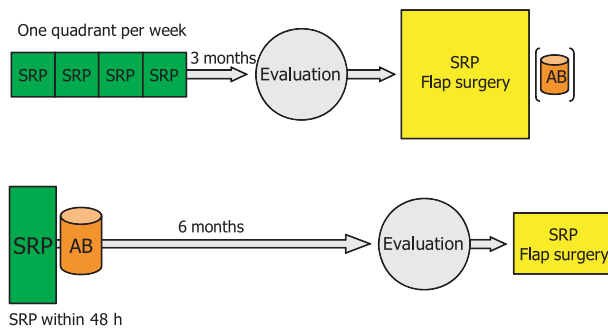


Fig. 1. Traditional (top) and alternative approach (bottom) to periodontal therapy. SRP, scaling and root planing; AB, adjunctive antibiotics.

General benefits of systemic antibiotics

A large number of reports have indicated beneficial effects of systemic antibiotics for patients with periodontal diseases in various clinical situations. Drugs investigated include amoxicillin (with or without clavulanic acid), azithromycin, clindamycin, doxycycline, metronidazole, spiramycin, tetracycline, and certain combinations thereof (85). In the context of consensus conferences issuing recommendations for periodontal care, two systematic reviews have been completed that assess the benefit of adjunctive systemically administered antibiotics (35, 43). Herrera et al. (43) included 25 controlled clinical trials of at least 6 months duration, in which systemically healthy subjects with chronic or aggressive forms of periodontitis had been treated with or without adjunctive systemic antibiotics. Patients treated with antibiotics generally showed better results than patients treated without. In deep pockets, a specific benefit of change in the clinical periodontal attachment level was found for the combination of amoxicillin and metronidazole. Haffajee et al. (35) included 27 controlled clinical trials, with a follow-up period of more than 1 month, that used mean attachment level change as primary outcome. Within the broad range of therapeutic protocols, metronidazole, alone or in combination with amoxicillin, was the most frequently used drug. In all studies, the antibiotic groups showed significantly greater changes in mean attachment level than the control groups. Trials allowing a more detailed analysis indicated that antibiotics had the greatest effect in sites with deep pockets (49, 50, 67, 68, 75, 81, 101, 102). However, specifically useful antibiotic regimes for distinct clinical or microbiological conditions could not be clearly identified based on the available evidence. Definite conclusions could also not be made con-

cerning the optimal dosage and duration of antibiotic therapy, the long-term benefits, and to what extent the antibiotics induced resistance or other changes in the oral microbiota.

Systemic antibiotics: early or late?

Although the benefit of systemic antibiotics is clear today in general, the specific relationship between benefit and risk in various clinical situations remains a subject of debate, especially with regard to individual prescription and combination with other procedures. Concerns have been raised that an extensive use of antibiotics in periodontics, particularly when administered to counterbalance incomplete mechanical debridement or poor oral hygiene, could contribute substantially to the development of bacterial antimicrobial resistance (3, 25, 33, 58, 80, 91, 95, 97). To limit the increase of antibiotic resistance and avoid unwanted systemic effects, it seems reasonable to adopt a precautionary, restrictive attitude to using antibiotics.

The optimal timing of antimicrobial drug administration is one subject for discussion, as it remains controversial whether adjunctive systemic antibiotics should preferably be administered during the initial non-surgical phase, or during a subsequent surgical treatment phase. A landmark study, published in 1992 by Loesche et al. (51), sparked this controversy by showing that systemic metronidazole, when given as an adjunct to scaling and root planing, reduced the need for surgical therapy in periodontitis patients with elevated levels of spirochetes in subgingival samples, thereby reducing the costs and the inconvenience for the patient. These findings were contrary to the opinion that mechanical therapy should be exploited to its limits before a decision is made to administer an antibiotic. Postponing antibiotic therapy to the surgical treatment phase may be defended for two reasons. First, it is known that scaling and root planing alone are able to resolve a considerable amount of periodontal pathology on their own (41, 89), and this strategy may help to keep the prescription of antibiotics to a minimum. Second, given the restricted effects of antibiotics on intact biofilm (84), and the known limitations of scaling and root planing (11, 73), surgical intervention may be necessary for complete biofilm disruption on all contaminated surfaces. Although this reasoning seems to make sense, it is – perhaps surprisingly – not supported by data from specifically designed controlled trials. As most available studies tested systemic antibiotics in

the context of non-surgical debridement, a systematic review that tried to assess the relative benefit of prescribing antibiotics either during the non-surgical or the surgical phase of therapy was inconclusive (42). One study (45), which was not included in that review, found that administration of amoxicillin and metronidazole immediately after initial scaling and root planing provided better clinical outcomes in deep sites than late administration in the context of rescaling after 3 months, corroborating the views expressed in 1992 by Loesche et al. (51).

Amoxicillin and metronidazole as adjunct to full-mouth scaling and root planing

Amoxicillin (recommended international non-proprietary name, sometimes previously referred to as 'amoxycillin') is a moderate-spectrum, bacteriolytic β -lactam antibiotic. Metronidazole is a nitroimidazole that is particularly active against anaerobic bacteria and protozoa. The combination of these two drugs has become a favorite choice for adjunctive antibiotic therapy in periodontics in the last two decades. Due to its proven ability to suppress *A. actinomycetemcomitans* from periodontitis lesions and other oral sites (7, 21, 27, 29, 62, 71, 72, 93, 94), the combination of amoxicillin and metronidazole initially appeared well suited especially to treat advanced *A. actinomycetemcomitans*-associated periodontitis. However, clinical trials have indicated that amoxicillin and metronidazole may also be very efficient in other situations (4, 7, 24, 32, 44, 52–54, 56, 57, 59, 79, 81, 88, 90, 102). Better clinical outcomes were reported if patients were treated with amoxicillin and metronidazole than if metronidazole alone was administered (56, 81). So far no comparative randomized clinical trial has demonstrated the superiority of any other regime over amoxicillin and metronidazole in any clinically or microbiologically defined variant of periodontal disease.

We have recently reported the results of a single-centre, double-blind, placebo-controlled, randomized longitudinal study of 6 months duration involving 51 patients with chronic periodontitis (15, 16). The aim of the study was to specifically evaluate the clinical benefit of amoxicillin and metronidazole when administered immediately after full-mouth periodontal debridement completed in 48 h. Twenty-five subjects received 375 mg amoxicillin and 500 mg metronidazole three times a day for 7 days and 26 received a placebo. The absolute number of sites per

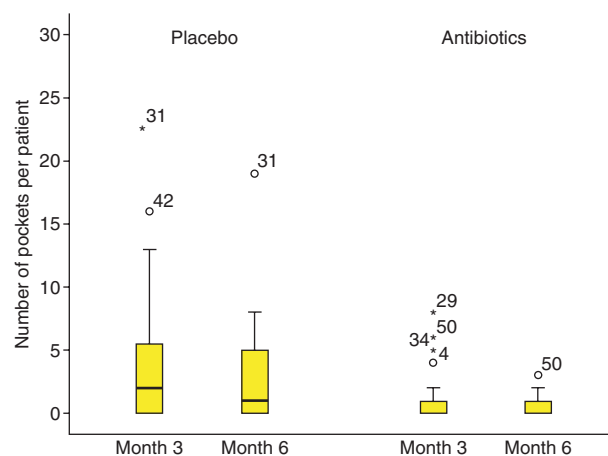


Fig. 2. Absolute number of sites with periodontal pocket depth > 4 mm and bleeding on probing per subject, 3 and 6 months after scaling and root planing (placebo, $n = 24$), or scaling and root planing plus amoxicillin and metronidazole (antibiotics, $n = 23$). Circles indicate mild outliers, and asterisks indicate extreme outliers (15).

subject with a pocket probing depth > 4 mm and bleeding upon probing was the primary clinical outcome measure, as persisting pockets > 4 mm that bled upon probing are commonly perceived as an indication for further treatment. All subjects were followed for up to 3 months, and 47 were followed for up to 6 months. Significant and clinically relevant improvements were observed in all subjects. An additional significant treatment effect was demonstrated in subjects treated with the antibiotics (Fig. 2). In the placebo group, a mean of 3.0 pockets > 4 mm that bled on probing were found per subject after 6 months, but only 0.4 sites that fall into this category were detected in the test group, and this difference was statistically significant ($P = 0.005$). The clearest advantage of antibiotics over placebo was noted in pockets that were initially deeper than 6 mm: in the test group, the mean pocket probing depth decreased from 7.3 ± 0.3 to 3.7 ± 0.6 mm, and that in the control group decreased from 7.2 ± 0.7 to 4.9 ± 1.4 mm ($P = 0.003$ for difference between groups). Using backward stepwise logistic regression, the impact of various variables on the persistence of more than one pocket > 4 mm per subject with bleeding on probing at 6 months was evaluated. The protective risk of the antibiotics for further periodontal therapy amounted to 8.85, meaning that every subject receiving amoxicillin and metronidazole was protected by a factor of 8.85 from further periodontal therapy.

In this trial, antibiotics were not tested as an alternative, but rather as a supplement, to thorough debridement and proper oral hygiene. Guerrero et al. (32) used a similar protocol to evaluate the

adjunctive benefit of the same antibiotic regime in 41 patients with generalized aggressive periodontitis. The data from this trial demonstrate that the observations made in subjects with chronic periodontitis can be extended to subjects with aggressive forms of the disease. Shortly after our data were published, another group reported significantly better clinical results for full-mouth debridement using an ultrasonic scaler and limited to 45 min, if supplemented with adjunctive amoxicillin plus metronidazole (79).

Two systematic reviews (22, 48) concluded that the clinical outcomes for scaling and root planing without antibiotics differed little if treatments extended over several weeks (quadrant-by-quadrant treatment) or were completed within a few hours (full-mouth treatment). Nevertheless, if a short, intensive treatment phase is acceptable for the patient, and not contraindicated for medical or other reasons, it seems irrational to delay completion by fractionating and extending therapy.

Microbial profiling and antibiotic therapy

The results of these recent studies challenge the current prevailing opinion that the use of systemic antibiotics should be restricted to specific groups of periodontal patients, for example those with highly active disease or a specific microbiological profile (43). In a commentary (95) on our first paper presenting the clinical findings of this trial (15), it was stated that treatment of *Porphyromonas gingivalis*-negative patients with antibiotics may be considered over-treatment. This statement was based on results from a study from the same authors involving 49 subjects who were treated with full-mouth scaling and root planing, plus amoxicillin and metronidazole or placebo (102). In their trial, roughly half of the subjects in each group were culture-positive for *P. gingivalis*. When treated with antibiotics, *P. gingivalis*-positive patients did indeed show significantly better results than when treated with placebo. However, the percentage of pockets >4 mm decreased very similarly in *P. gingivalis*-negative subjects when treated with antibiotics (from 40 to 12% in *P. gingivalis*-negative subjects; from 46 to 11% in *P. gingivalis*-positive subjects). A study by another group (26) contradicts their statement as the results were interpreted to show that amoxicillin and metronidazole adversely affect the clinical outcome of patients harboring *P. gingivalis* but not *A. actinomycetemcomitans*.

Even though patient selection and treatment allocation were independent of microbiology, microbiological samples were in fact obtained from every participant in our study before and after treatment: pooled subgingival plaque was collected using paper points inserted into the deepest pocket in each quadrant (60, 61). Six periodontal marker organisms were detected and quantified using a commercially available real-time polymerase chain reaction-based method (Meridol® Perio Diagnostics; GABA International, Therwil, Switzerland). This gave us the opportunity of assessing whether patients with a particular microbial profile specifically benefited from adjunctive antibiotics (16).

Confirming the remarkable capacity of amoxicillin and metronidazole to suppress *A. actinomycetemcomitans* already recognized previously, *A. actinomycetemcomitans* was no longer detected in any subject in the test group after antibiotic treatment. However, 38 of the 47 subjects completing the trial (18 in the placebo and 20 in the test group) were already negative for *A. actinomycetemcomitans* at baseline. None of these subjects tested positive at months 3 or 6 either. Although these subjects were thus *A. actinomycetemcomitans*-negative throughout the study, they had a significantly better primary clinical outcome if they received the antibiotics than if they were treated with placebo. It was therefore concluded that, even though amoxicillin and metronidazole very efficiently suppressed *A. actinomycetemcomitans*, testing for *A. actinomycetemcomitans* among subjects with a clinical diagnosis of chronic periodontitis did not identify subjects who will specifically benefit from antibiotics (16). *A. actinomycetemcomitans* displays a broad genetic and phenotypic diversity and is heterogeneously distributed in various populations and cohorts worldwide (46). A large prospective study (40) has indicated that only one sub-population of *A. actinomycetemcomitans* (the 'JP2 clone') (87) displays the properties of a true pathogen. One may therefore suggest that patients should be tested specifically for presence of clone JP2. However, until an interventional study identifies a specific advantage of a treatment other than amoxicillin and metronidazole in *A. actinomycetemcomitans* JP2-positive cases, the utility of such a test remains hypothetical.

The same holds true in principle for any other specific test of particular properties of members of the subgingival flora and any other form of periodontitis. In our study, patients treated with amoxicillin and metronidazole tended to show better results irrespective of whether they tested positive or

negative for *P. gingivalis* before treatment. Treatment of all negative cases in the test group was clinically successful, whereas, of the four *P. gingivalis*-negative subjects in the control group, one still had five pockets needing further therapy 6 months later. These results are in agreement with a previous placebo-controlled study (81). Patients treated with amoxicillin and metronidazole showed significantly better clinical outcomes for non-surgical therapy than those treated with placebo, despite the fact that only 27% of the subjects were *P. gingivalis*-positive and only 11% were *A. actinomycetemcomitans*-positive.

Risks vs. benefits of systemic antibiotics

Amoxicillin and metronidazole have been prescribed widely for over three decades, and their effects and side effects are therefore well documented (1, 2). The most frequent adverse reactions to amoxicillin are sensitivity phenomena. These are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and in those with a history of allergies in general. Most reactions are mild, and limited to a rash or skin lesion in the head or neck region. More severe reactions may induce swelling and tenderness of joints. In highly sensitized patients, a life-threatening anaphylactic reaction may develop (2). Potential side-effects of metronidazole include nausea, headaches, loss of appetite, diarrhea, a metallic taste, and sometimes a rash. Alcohol consumption enhances these symptoms, because imidazoles affect the activity of liver enzymes. Peripheral neuropathies, characterized mainly by numbness or paresthesia of an extremity, have been reported in isolated cases. Metronidazole should be discontinued immediately if abnormal neurological signs appear (1). There is evidence of carcinogenic activity of metronidazole in studies involving chronic oral administration in mice and rats, but not in other species tested. Due to inadequate evidence, metronidazole is not considered a risk factor for cancer in humans (6). Previously unrecognized candidiasis may become clinically manifest during antibiotic therapy.

To put things into perspective, the frequency and potential negative effects of antibiotics have to be balanced against the potential health consequences of not rapidly suppressing a periodontal infection, and the inconvenience, discomfort and financial consequences of further therapy. The traditional

approach sometimes expands treatment over several months, while scaling and root planing plus amoxicillin and metronidazole may be able to resolve the infection within a few days. Scaling and root planing plus amoxicillin and metronidazole have been shown to decrease clinical signs of inflammation and inflammatory biomarkers in gingival crevice fluid stronger than scaling and root planing alone (28). Although not directly confirmed so far by a clinical trial, it seems preferable, from a general health point of view, to let patients benefit early from the positive systemic effects of successful periodontal therapy (18, 19, 64). Although the number of subjects complaining about gastrointestinal problems, notably diarrhea, was higher in the test group than in the placebo group in our study (15), tooth loss and suppuration despite therapy were exclusively noted in the control group. Furthermore, one-third of subjects who mentioned diarrhea upon questioning were actually treated with placebo.

With regard to the development of bacterial resistance in general, it should be remembered that systemic antibiotics are taken in thousands of subjects with untreated periodontitis worldwide every day without subgingival debridement. This happens whenever physicians prescribe antibiotics to persons with untreated periodontal disease for medical reasons. As an example, in a cohort of over 12,000 persons with destructive periodontal disease, more than 70% received at least one course of antibiotics over a 3-year period (17). The true contribution to the problem of resistance by a dentist treating once in the life of a patient a periodontal infection with adjunctive amoxicillin and metronidazole, in a controlled situation following thorough mechanical debridement, and by administering at the same time two drugs with different antimicrobial action, is unknown and warrants future research. This contribution may be minor compared to the effects of the frequent prescription of antibiotics by dentists and other healthcare providers for other therapeutic and prophylactic purposes.

Local antibiotics and antiseptics

A variety of methods to deliver antimicrobial agents into periodontal pockets have been devised and subjected to numerous experiments. They include pocket irrigation, application of drug-containing ointments and gels, and devices for sustained drug release.

A systematic review (38) that analyzed the literature in an effort to determine the effect of subgingival irrigation concluded that irrigation with chlorhexidine provided no additional benefit to conventional mechanical debridement. Another systematic review found no significant benefit of supplementing full-mouth debridement with chlorhexidine irrigation (48). A recent systematic review specifically addressed rinsing with povidone-iodine during non-surgical periodontal therapy (82). A small but statistically significant beneficial effect of pocket rinsing was found in terms of reduction of probing depth.

The efficacy of several commercially available local-delivery systems as adjuncts to scaling and root planing was compared in two trials (47, 74, 83), including patients with persistent periodontal lesions. One systematic review attempted to evaluate the combined literature-based evidence to determine the relative effect of local controlled-release anti-infective drug therapy in patients with chronic periodontitis (39). A meta-analysis that included 19 studies comparing scaling and root planing plus local sustained-release agents with scaling and root planing alone confirmed the clinical advantages of minocycline gel, microencapsulated minocycline, doxycycline gel and chlorhexidine chips over scaling and root planing alone. However, due to the heterogeneity of the material, the authors could not make any firm statements regarding the superiority of one system. A further systematic review looked at the relative adjunctive benefits of various locally applied agents (9). A statistically significant mean advantage was found for four agents in terms of additional attachment gain, and this advantage was greatest for minocycline, followed by tetracycline, chlorhexidine and metronidazole. The findings reported in this review must be interpreted with caution as data were combined from studies that explored various modes of local treatment, including irrigation, impregnated strips and pastes. Differences in the outcomes may reflect the dissimilarity in modes of application and study populations, rather than the potency of the agents.

Over the recent years, the practical value of local antibiotic therapy has decreased, as a majority of adequately tested formulations have been withdrawn from the market for economic reasons (not enough opportunity to make a profit), due to administrative obstacles (obligation to re-register products as drugs rather than as medical devices), or a combination of both (too expensive to fulfill the requirements for continued approval). Although local antibiotics may have the potential to reduce the perceived need for

periodontal surgery, discussion of this possibility will be limited to two specific examples. In the first example, the effect of a two-syringe mixing system for controlled release of doxycycline (Atridox®; Tolmar Inc., Fort Collins, CO, USA), applied after no more than 45 min of debridement without analgesia, was compared to 4 h of thorough scaling and root planing in a study involving 105 patients with moderately advanced chronic periodontitis in three centers. Interestingly, clinical parameters indicated a better result for the pharmaco-mechanical treatment approach after 3 months, although considerably less time had been invested than for conventional mechanical therapy (99). In the second example, the efficacy and safety of locally administered microencapsulated minocycline (Arestin®; OraPharma, Warminster, PA, USA) were shown in a multicenter trial that included 748 patients with moderate to advanced periodontitis. Minocycline microspheres plus scaling and root planing provided a substantially greater reduction in probing depth than either scaling and root planing alone or scaling and root planing plus the drug. The probability for reducing probing depths from ≥ 6 mm to < 5 mm was nearly three times greater for scaling and root planing plus local antibiotics than scaling and root planing alone (70, 100).

Few studies have addressed the issue of selection of a local or systemic route when use of antibiotics

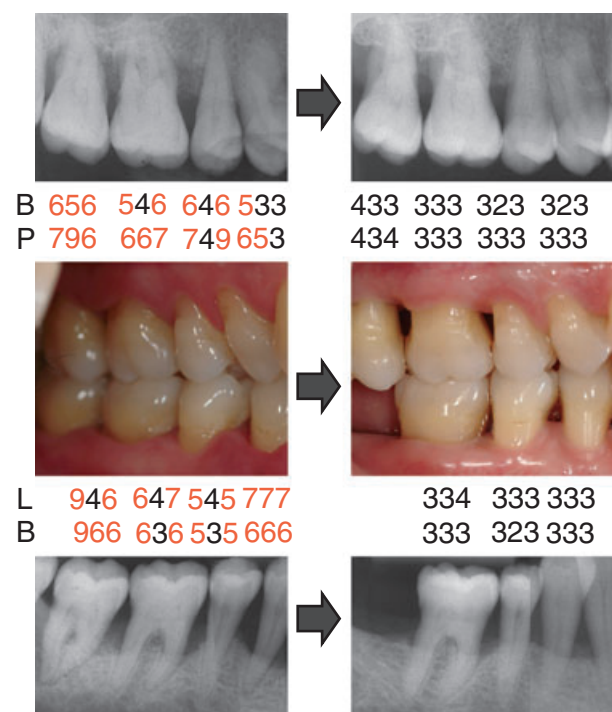


Fig. 3. Advanced chronic periodontitis treated with scaling and root planing plus amoxicillin and metronidazole before (left) and 12 months after therapy (right).

Table 1. Protocol for the treatment of chronic or generalized aggressive periodontitis. Adapted from the protocols of two randomized controlled clinical trials (15, 32) demonstrating efficacy. Not validated for subjects below age 16 years or above age 70 years, with systemic illnesses, or pregnant or lactating women

Procedure	Action
Preparatory procedures	
Clinical assessment	Full-mouth plaque score (presence or absence of plaque) (four surfaces per tooth) Pocket probing depth, recession and bleeding on probing (six sites per tooth) Pulp vitality test
Imaging	Take radiographs of teeth with clinical signs of disease or unclear status (e.g. negative pulp vitality test)
Case presentation and motivation	Explain disease status and describe the planned therapy to the patient Motivate patient for self-performed oral hygiene Obtain written informed consent
Supragingival debridement	Remove supragingival calculus and plaque (ultrasonic and / or hand instruments) Eliminate obstacles for mechanical plaque control and remove plaque-retentive elements Extract teeth that are unreasonable to treat
Oral hygiene instructions	Instruct and train in oral hygiene procedures (toothbrush, interdental cleaning device, other)
Oral hygiene controls	Record plaque score within 10 days after instructions If plaque score > 20%, provide additional instructions Repeat this step until plaque score <20%
Subgingival debridement (within 1 month)	
Scaling and root planing	Thorough scaling and root planing of all teeth with pocket probing depth > 3 mm to the depth of the pocket with ultrasonic instruments and hand curettes (carried out under local anesthesia in one or two sessions within 48 h)
Chemical plaque control	Instruct patient to rinse the mouth twice daily with 0.2% chlorhexidine for 10 days
Adjunctive antibiotics (immediately after subgingival debridement)*	
Standard protocol (amoxicillin and metronidazole)	500 mg metronidazole and 375 mg amoxicillin, 3 times per day, for 7 days (corresponds to 20 mg / kg metronidazole and 15 mg / kg amoxicillin, per day, for a subject weighing 75 kg)
Alternative protocols	Monotherapy with azithromycin (37, 55), or metronidazole combined with cefuroximaxetil, or ciprofloxacin (76, 96), depending on type of intolerance. The equivalence of these protocols to amoxicillin and metronidazole has not been established
Post-treatment controls (at months 1 and 3)	
Oral hygiene control	Record plaque score If plaque score > 20%, review and reinforce oral hygiene

Table 1. (Continued)

Procedure	Action
Debridement	Remove supragingival calculus, if detected
Re-evaluation and further therapy (after 3–6 months)	
Clinical assessment	Record plaque score, pocket probing depth, bleeding on probing, suppuration, furcation involvement
Further therapy	Plan and carry out additional therapy as needed (e.g. open flap debridement, furcation therapy, tissue regeneration, implant therapy)

*Adjunctive antibiotics are indicated for subjects fulfilling the following conditions: (i) presence of at least four teeth with a pocket probing depth > 4 mm, clinical attachment loss of at least 2 mm, and radiographic evidence of bone loss, (ii) no confirmed or suspected intolerance to 5-nitroimidazole derivatives or penicillins, and (iii) willingness to strictly follow prescription and to abstain from alcohol consumption during treatment.

seems indicated. In one investigation, carried out in patients with rapidly progressing periodontitis (8), no significant differences were noted between scaling and root planing supplemented with either systemic amoxicillin/clavulanic acid or application of tetracycline using a local-delivery device. For patients with adult periodontitis, two studies reported better results for scaling and root planing supplemented with locally applied metronidazole than with adjunctive systemic metronidazole (66, 69). So far, no non-antibiotic antimicrobial alternative has proven to be equally efficient or better than systemic amoxicillin and metronidazole. One of the few studies that really evaluated this possibility concluded that adjunctive placement of chlorhexidine chips was less efficacious in the treatment of aggressive periodontitis than amoxicillin and metronidazole (44).

Conclusions and recommendations

Adjunctive antibiotics can enhance the clinical outcome of non-surgical mechanic debridement, thereby reducing the need for further therapy, which is frequently surgical in nature (Fig. 3). Full-mouth scaling and root planing combined with amoxicillin and metronidazole has the potential to resolve the periodontal infection within a few days. However, the available evidence does not justify the indiscriminate use of just any antibiotic in any patient, and should not be interpreted as a recommendation for prescription of antibiotics to all periodontal patients.

A treatment protocol implementing the recent evidence is shown in Table 1. In summary, mild cases can, and should, be treated non-surgically

and without antibiotics. In deep pockets, non-surgical, non-antibiotic treatments alone resolve the bacterial infection less predictably than open flap debridement (41). It is suggested that cases with multiple deep pockets should first be treated by thorough scaling and root planing and adjunctive amoxicillin and metronidazole. The initial treatment plan should be reviewed and adapted after 3–6 months on the basis of a clinical re-examination. Surgical interventions may be necessary to further reduce persisting pockets, for the treatment of furcations, or to regenerate periodontal tissues. Should such therapy be indicated, this sequence allows invasive interventions to be performed only in tissues with minimal persisting pathology, and without antibiotic coverage.

In its strictest sense, the statement that ‘systemic antibiotic therapy in periodontics aims to eliminate or markedly suppress specific microorganisms with the potential of causing breakdown of periodontal attachment in susceptible patients’ (92) is no longer tenable. Although it is known that some antibiotic regimes are able to specifically suppress certain organisms, it has not been proven that selective suppression of specific members of the subgingival microbial complex is the key element for success. Bacteriological efficacy (suppression of a target organism) is not proof of clinical efficacy, and vice versa. Given the large diversity of the microbiota associated with all forms of periodontitis and the multiple synergistic and antagonistic interactions among the members of the flora, the concept of specifically identifying and eradicating a particular pathogen may be illusionary. The combination of amoxicillin and metronidazole appears to have an impact on factors beyond those that have been studied using bacterial culture and currently available tests.

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