

# To Prescribe or Not To: Systemic Antibiotics in Treatment of Periodontal Infections

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**Abstract:** *Periodontitis is a chronic infection induced by a mélange of microfloral aetiology. The first line of treatment by and large includes non-surgical mechanical debridement and regular periodontal maintenance care. In some cases surgical intervention may be indicated to improve access to the root surface for meticulous debridement. An array of systemic antibiotics available as adjuncts for treatment of periodontitis has been recorded. While some studies claim superior clinical outcomes following inclusion of these, others do not. A controversy was born as to question the role of systemic antibiotics in the treatment of periodontal diseases. Recent orderly reviews have bestowed an evidence-based assessment of the possible perks of adjunctive antibiotics in periodontal therapy. This review aims to provide an update on clinical issues of when and how to prescribe systemic antibiotics in periodontal therapy.*

**Keywords:** periodontitis, adjunctive therapy, systemic antibiotics, root planing.

## 1. Introduction

The objective of this review is to render the clinician an updated current literature regarding the use of systemic antibiotics in periodontal treatment. While the use of systemic antimicrobials for treatment of periodontitis has been controversial, the recent publication of two systematic reviews<sup>1,2</sup> has provided an even-handed evidence-based assessment of the possible advantages of systemic antibiotics. This paper will discuss some important clinical questions regarding when and how to use systemic antibiotics for the treatment of periodontal disease.

## 2. To Use Or Not To Use In The Treatment Of Periodontal Infections

A meta-analytical study indicated that systemically administered antibiotics provide a clear clinical benefit in terms of mean periodontal attachment level “gain” post-therapy when compared with groups not receiving these agents. Subjects with aggressive periodontitis showed greater benefit than subjects with chronic periodontitis.<sup>1,2</sup> The Sixth European Workshop of Periodontology concluded that there is no direct evidence to recommend a specific protocol for the adjunctive use of the antimicrobials.<sup>15</sup>

### 2.1 Are adjunctive systemic antibiotics expedient over surgical mechanical therapy alone?

Deficiency of access for effective mechanical debridement calls for surgical intervention. An additional clinical attachment level gain (weighted mean gain 0.6 mm) was reported in a systematic review by Haffajee et al. which encompassed prescribing systemic antibiotics as an adjunct to surgical mechanical debridement in deep pockets.<sup>2</sup> The results of three studies<sup>16-18</sup>, using different antibiotics (tetracycline, penicillin, amoxicillin plus clavulanate), were

merged in this meta-analysis comparing periodontal surgery plus adjunctive antibiotic versus periodontal surgery plus placebo.

However, Herrera et al., in his most recent review of the literature, concluded that there was deficient data supporting additional benefits of adjunctive antibiotics when combined with periodontal surgery.<sup>15</sup>

Hayes et al in 1992 stated the results of a meta-analysis, however, did not demonstrate an additional benefit of the systemic administration of tetracycline.<sup>3</sup>

Similarly, Elter et al. 1997 suggested that the additional benefit of the systemic metronidazole was not evident after a thirteen week follow-up period.<sup>4</sup>

Contrary to the above findings a recent systematic review and meta-analysis by Sgolastra F, et al. 2012 seems to support the combined systemic administration of amoxicillin and metronidazole adjunctively to scaling and root planning.<sup>5</sup> However, due to the small number and discrepancy regarding dosages of the included studies, no judgement could be made. Although the cost effectiveness of this therapeutic modality, the risk of inducing bacterial resistance should be taken seriously into considerations before antibiotics are prescribed as adjuncts of the nonsurgical periodontal therapy.<sup>6,7</sup>

Although an additional clinical benefit of adjunct systemic antibiotics has been described, it would be wise not to use this remedy routinely but only in cases of refractory or aggressive periodontitis so that the risk of developing antibiotic resistance is substantially reduced.

While these reviews indicate that, on average, the antibiotics contribute to therapeutic success, they fail to answer a number of critical questions.

- First, which patient would benefit most from systemic antibiotic administration?
- Second, which antibiotic or antibiotic combination is most appropriate for which form of periodontal infection?
- Third, what is the optimum dosage, duration and timing of antibiotic administration (in relation to mechanical debridement)?
- Fourth, is a poor treatment response due to the use of the wrong agent or failure of the agent to reach the site of action.
- Fifth, what is the “Negative Aspect” of antibiotic administration; i.e. the negative consequences of side effects and the development of antibiotic resistant species?

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., 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.<sup>8</sup> 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<sup>9,10</sup>, and this strategy may help to keep the prescription of antibiotics to a minimum.
- Second, given the restricted effects of antibiotics on intact biofilm<sup>11</sup>, and the known limitations of scaling and root planing<sup>12</sup>, surgical intervention may be necessary for complete biofilm disruption on all contaminated surfaces.

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.<sup>15</sup>

One study, 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<sup>13</sup>, corroborating the views expressed in 1992 by Loesche et al. Slots *et al.* described a series of steps using anti-infective agents for enhancing regenerative healing. They recommend starting antibiotics 1-2 days before surgery and continuing for a total of at least 8 days, however, the value of this regimen has not been well documented.<sup>14</sup> Haffajee *et al.* concluded that data support similar effects for most antibiotics.<sup>2</sup>

## 2.2 Examples of antibiotic regimens documented for treatment of periodontitis

Antibiotic	Antibiotic regimen	Periodontal disease as described by authors	First author/year
Tetracycline	250 mg, 4 x day, 14 days	Advanced chronic periodontitis	Al Joburi, 1989 <sup>38</sup>
Doxycycline	200 mg, 1 x day, 8 days	Generalized rapidly progressive periodontitis	Sigusch, 2001 <sup>39</sup>
Spiramycin	1.5 UI, 2 x day, 14 days	Advanced periodontal disease	Bain, 1994 <sup>40</sup>
Azithromycin	500 mg, 1 x day, 3 days	Aggressive periodontitis	Haas, 2008 <sup>29</sup>
Metronidazole	250 mg, 3 x day, 7 days	Periodontitis > 10% spirochetes	Loesche, 1984 <sup>41</sup>
Clindamycin	150 mg, 4 x day, 10 days	Refractory periodontitis	Walker, 1993 <sup>42</sup>
Amoxicillin and Metronidazole	375 mg, 3 x day, 8 days	Chronic periodontitis	Flemmig, 1998 <sup>43</sup>
	250 mg, 3 x day, 8 days	presence of A.a, P.g	

## 3. Patient compliance : A crucial perspective

The concern of patient compliance has been intermittently documented in publications assessing the effects of systemic antibiotics. Some studies have demonstrated patient compliance, with antibiotic regimens prescribed, to be as little as 20 percent.<sup>19</sup>

Antibiotic azithromycin, due to its pharmacologic properties and long half life, may be advantageous over other antibiotic regimens as only one tablet (500 mg) per day during three consecutive days is required as opposed to one tablet three times a day for seven days with other antibiotic regimens.<sup>20</sup>

Significance of compliance as a part of oral hygiene and maintenance care should also be delivered. It should be noted

that, in studies where beneficial results following adjunctive antibiotics were reported, patients had received optimum maintenance care and had good plaque control. If a patient was belligerent with protocols of oral hygiene maintenance, then a benefic treatment causatum following adjunctive antibiotics was implausible. Prescription of antibiotics is no proxy for meticulous debridement, good oral hygiene technique and regular maintenance care.

## 4. Conclusion

The clinical diagnosis and situation dictate the need for possible antibiotic therapy as an adjunct in controlling active periodontal disease as the patient's diagnosis can change overtime. Continuing disease activity is an indication for periodontal intervention and possible microbial analysis

through plaque sampling. Also, cases of refractory or aggressive periodontitis may indicate the need for antimicrobial therapy. When used to treat periodontal disease, antibiotics are selected based on the patient's medical and dental status, current medications, and results of microbial analysis, if performed. Microbial samples may be obtained from individual pockets with recent disease activity or from pooled subgingival sites. A pooled subgingival sample may provide a good representation of the range of periodontal pathogens to be targeted for antibiotic therapy. Plaque sampling can be performed at the initial examination, root planing, reevaluation, or supportive periodontal therapy appointment. Systemic antibiotic therapy should be an adjunct to a comprehensive periodontal treatment plan. An antibiotic strength 500 times greater than the systemic therapeutic dose may be required to be effective against the bacteria arranged in the biofilms. Therefore, it is important to disrupt this biofilm physically so that the antibiotic agents can have access to the periodontal pathogens. Antibiotics have also been shown to have value in reducing the need for periodontal surgery in patients with chronic periodontitis. Risks and benefits concerning antibiotics as adjuncts to periodontal therapy must be discussed with the patient before the antibiotics are used.

## References

- [1] Herrera D, Sanz M, Jepsen S, Needleman I, Roldan S. A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. *J Clin Periodontol* 2002;3:136–159; discussion 160-132.
- [2] Haffajee AD, Socransky SS, Gunsolley JC. Systemic anti-infective periodontal therapy. A systematic review. *Ann Periodontol* 2003;8:115–181.
- [3] Catherine Hayes, Alexia Antezak-Bouckoms, Elizabeth Burdick. Quality assessment and meta analysis of systemic tetracycline use in chronic adult periodontitis. *J Clin Periodontol* 1992;19:164-168.
- [4] John Elter, Herenia P Lawrence, Steven Offenbacher, James D Beck. Meta-analysis of the effect of systemic metronidazole as an adjunct to scaling and root planing for adult periodontitis. *J Periodontal Research* 1997;32:487-496.
- [5] Fabrizio Sgolastra, Ambra Petrucci, Roberto Gatlo, Annalisa Monaco. Effectiveness of systemic Amoxicillin/Metronidazole as an Adjunctive Therapy to full mouth scaling and root planning in the treatment of Aggressive periodontitis: A Systemic review and Meta-Analysis. *J Periodontol* 2012;83:731-743.
- [6] Joe W. Krayner, Renata S. Leite, Keith L. Kirkwood. Non-surgical Chemotherapeutic Treatment Strategies for the management of periodontal diseases. *Dent Clin N Am* 2010;54:13-33.
- [7] Peter A. Heasman, Chris R. Vernazza, Francesca L. Gaunt. Cost-effectiveness of adjunctive antimicrobials in the treatment of Periodontitis. *Periodontology* 2000, 2011;55:217-230.
- [8] Walter J. Loesch, James R. Giordano, Philippe Hujoel. Metronidazole in periodontitis : Reduced need for Surgery. *J Periodontol* 1992;19:103-112.
- [9] G.A. Van der Weijden, M.F. Timmerman. A systematic Review on the clinical efficacy of subgingival debridement in the treatment of chronic periodontitis. *J Clin Periodontol* 2002;29:55-71.
- [10] L.J. Heitz-Mayfield, L. Trombelli, F. Heitz, I. Needleman, D. Moles. A Systematic review of the effect of Surgical debridement for the treatment of chronic periodontitis. *J Clin Periodontol* 2002;29:92-102.
- [11] M. J. Sedlacek and C. Walker. Antibiotic Resistance in an In Vitro subgingival biofilm model. *Oral Microbiology and Immunology* 2007;22:333-339.
- [12] Sally A. Buchanan and Paul B. Robertson. Calculus Removal by Scaling/Root Planing with and without Surgical Access. *J Periodontol* 1987;58:159-163.
- [13] Dogan Kaner, Claudia Christan, Thomas Dietrich. Timing Affects the Clinical Outcome of Adjunctive Systemic Antibiotic Therapy for Generalized Aggressive Periodontitis. *J Periodontol* 2007;78:1201-1208.
- [14] Jorgen Slots, Erika Smith Mac Donald, Hessam Nowzari. Infectious Aspects of Periodontal Regeneration. *Periodontology* 2000,1999;19:164-172.
- [15] Herrera D, Alonso B, Leon R, Roldan S, Sanz M. Antimicrobial therapy in periodontitis: the use of systemic antimicrobials against the subgingival biofilm. *J Clin Periodontol* 2008; 5:45–66.
- [16] Palmer RM, Watts TL, Wilson RF. A double-blind trial of tetracycline in the management of early onset periodontitis. *J Periodontol* 1996; 23:670–674.
- [17] Kunihiro DM, Caine FA, Palcanis KG, Best AM, Ranney RR. A clinical trial of phenoxymethyl penicillin for adjunctive treatment of juvenile periodontitis. *J Periodontol* 1985;56:352–358.
- [18] Haffajee AD, Dibart S, Kent RL Jr, Socransky SS. Clinical and microbiological changes associated with the use of 4 adjunctive systemically administered agents in the treatment of periodontal infections. *J Clin Periodontol* 1995; 22:618–627.
- [19] Llor C, Sierra N, Hernandez S, et al. The higher the number of daily doses of antibiotic treatment in lower respiratory tract infection the worse the compliance. *J Antimicrob Chemother* 2009;63:396–399.
- [20] Foulds G, Shepard RM, Johnson RB. The pharmacokinetics of azithromycin in human serum and tissues. *J Antimicrob Chemother* 1990;25(Suppl A):73–82.