

# Systemic Antibiotics in Periodontal Therapy: A

## Double-Edged Sword

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### Abstract

#### BACKGROUND

The use of systemic antibiotics to treat periodontitis has been a much debated topic for years, which has led to a number of controversial conclusions. In most cases of patients diagnosed with periodontitis - nonsurgical periodontal therapy, meticulous personal oral hygiene and regular maintenance visits to a periodontist are a successful treatment approach. Globally, the issue of antibiotic resistance is increasingly being addressed, which raises the question - are systemic antibiotics really necessary for the treatment of periodontitis? The purpose of this review is to give doctors an overview of recent research on the application of systemic antibiotics in periodontal care.

#### REVIEW RESULTS

While most chronic periodontitis cases are managed without the use of systemic antibiotics as a supplement, recent meta-analyses have demonstrated the potential therapeutic benefits of some systemic antibiotics when combined with SRP. A wide range of antibiotics used in conjunction with nonsurgical and surgical periodontal therapy has been reported in the literature. The most commonly used antibiotics are penicillins, tetracyclines, metronidazole, macrolides, clindamycin and ciprofloxacin.

Today, it is unacceptable to prescribe systemic antibiotics as stand-alone therapy in patients with periodontitis. They would be beneficial in some single cases, with exacto non-surgical periodontal therapy necessarily performed beforehand, i.e. as an adjuvant.

#### CONCLUSION

The presented study shows that systemic antibiotics are currently finding their application in periodontal therapy. The notorious topic regarding antibiotic resistance is not to be underestimated, therefore antibiotic agents need to be judiciously prescribed only when necessary!

**Keywords:** Antibiotic, Adjunctive systemic antibiotics, antibiotic resistance, Periodontal disease

### Introduction

The use of systemic antibiotics to treat periodontitis has been a much-debated topic for years, which has led to a number of controversial conclusions (1, 2). There are not a few publications that present the possible positives of using systemic antibiotics in the treatment of periodontitis (3, 4, 5). Nowadays, the topic of

antibiotic resistance is becoming more and more frequent globally, which raises the question - are systemic antibiotics really necessary for the treatment of periodontitis? (1). The purpose of this review is to give doctors an overview of recent research on the application of systemic antibiotics in periodontal care.

We looked through the PubMed and Google Scholar archives to find relevant papers on the topic. All of the articles that are being examined were published between 1979 and 2024. Several keywords and their combinations, such as "systemic antibiotics", "periodontal therapy", "antibiotic resistance" and "periodontology", were used in the search.

## REVIEW RESULTS

### Systemic antibiotics in the treatment of periodontitis - why?

Periodontitis is an infectious disease leading to inflammation and destruction of all periodontal components - gingiva, periodontium, tooth root cementum and the alveolar bone itself. The etiological factor playing a major role in the development of this disease is the specific microorganisms in the dental biofilm (6). For this reason, a variety of systemic antibiotics have been used over the years as part of the treatment for periodontitis (3, 4, 5).

The dental biofilm has an extremely complex structure made up of multiple bacterial microcolonies arranged in an extracellular matrix (glycocalyx). It is now well established that physical, metabolic and molecular interactions exist between the microorganisms distributed in these bacterial microcolonies. This primitive communication system provides many positives for the microbial entities, one of the most significant being their unusual resistance to antibiotics (7). Therefore, currently the main, critical method by which periodontists deal with periodontopathogenic microorganisms is the mechanical removal (scaling and root planing) of their "home" - the dental biofilm (2, 6).

The goal of using supplemental systemic antibiotics is to decrease the bacterial load even more, which will allow the periodontal pocket infection to resolve (2).

In most cases of patients diagnosed with periodontitis - non-surgical periodontal therapy, meticulous personal oral hygiene and regular maintenance visits to a periodontist are a successful treatment approach (5, 6, 8, 9).

While most chronic periodontitis cases are managed without the use of systemic antibiotics as a supplement, recent meta-analyses have demonstrated the potential therapeutic benefits of some systemic antibiotics when combined with scaling and root planing. Nonetheless, a large range of systemic antibiotic treatments are currently in use (10).

Systemic antibiotics used in conjunction with scaling and root planing can provide a further benefit over scaling and root planing on its own with regard to probing depth reduction (0.4 mm, spiramycin) and clinical attachment level gain (0.5 mm, a mixture of amoxicillin and metronidazole) in pockets of 6 mm or deeper, according to a systematic review presented at the fourth European Workshop by Herrera et al. (3). Haffajee et al.'s systematic review revealed similar results (4).

In 2019, Pretzl et al. published a meta-review whose conclusion states that systemic antibiotics should only be used cautiously and appropriately as an adjuvant to non-surgical periodontal treatment. Only select groups of patients with periodontitis exhibit substantial and clinically relevant improvement after using systemic antibiotics throughout the periodontal therapy (5).

Antimicrobial resistance is an increasing global concern, thus systemic antibiotics are an excellent adjunct in the treatment of periodontitis, but their usage must be applied with caution (1, 5). Up until now, there hasn't been a specific guideline that converts the use of adjunctive systemic antibiotics and how they should be

implemented into evidence-based guidelines that are tailored to clinical needs using the data that is now accessible (5).

### **Systemic antibiotics as monotherapy in the treatment of periodontitis?**

Haffajee et al. (4) addressed the question of whether systemic antibiotics prescribed as monotherapy (without nonsurgical periodontal therapy) are effective in the treatment of periodontitis. The team concluded that systemically administered antibiotics with or without nonsurgical and/or surgical periodontal therapy provided better results regarding clinical attachment level.

Based on the findings of four trials assessing metronidazole by itself (11, 12) or metronidazole in combination with amoxicillin as monotherapy (13, 14), it was determined that the antibiotic's effect was negligible and temporary. The majority of studies on this topic do not support the concept of monotherapy in the treatment of periodontitis, due to inferior clinical outcomes compared to those with nonsurgical periodontal therapy (15, 16, 17).

A study published in 1990 concluded that monotherapy with broad-spectrum oral antibiotics (penicillins, tetracyclines) in patients with advanced periodontal disease can alter the subgingival microflora and lead to the development of multiple periodontal abscesses (18).

In 2006, a study was published that led to serious discussions among periodontists because it concluded that monotherapy with a combination of Amoxicillin and Metronidazole produced identical results to those of patients undergoing nonsurgical periodontal therapy alone (19).

#### **Use of systemic antibiotics in periodontology**

1) **Periodontitis with moderate to rapid progression** scaling and root planing in combination with systemic antibiotics leads to additional clinical effect compared to scaling and root planing alone in the treatment of periodontitis with moderate to rapid progression (20).

2) **In systemic diseases affecting the body's resistance**

##### **2.1.) Diabetes mellitus**

In 2015, a study was published that concluded that additional prescribed antibiotic therapy to scaling and root planing in patients diagnosed with diabetes mellitus - provided little benefit in terms of probing depth and BoP parameters (21).

A number of studies recommend antibiotic prophylaxis (AP) as a suitable preventive treatment for individuals with diabetes mellitus (DM) because of the higher risk of infections and poor wound healing following oral surgery. The current guidelines for prophylactic antibiotic use prior to surgery are based on expert judgment and are not conclusive (22).

In 2016, Grellmann et al. carried out a meta-analysis aimed at examining the systemic antibiotic use as an adjuvant to scaling and root planing (SRP) against SRP alone in diabetic people using a systematic analysis of randomized clinical studies. The team concludes that - regarding the probing depth indicator - patients' outcomes were better with additional antibiotic therapy (23).

A systematic review including 22 articles was published in 2022. The aim of the study was to review the literature on the need for systemic antibiotic administration as a preventive measure before surgical interventions (22).

##### **2.2.) Neutropenia**

Schmidt et al. performed a comprehensive evaluation in 2013 that included a patient with severe autoimmune neutropenia as well as the clinical presentations and management of individuals with periodontitis who also

had neutropenia. A total of twenty-four case reports detailing thirty-three patients were found. There was a broad or regional pattern to the indications and symptoms that were observed. Compared to 47% of patients who did not get further medication, 86% of patients who received adjuvant systemic antibiotics showed improvements in their periodontal status (24).

### 2.3.) Preventive measure after periodontal regenerative therapy

There are numerous studies evaluating the results of various regenerative methods (guided tissue regeneration, regenerative therapy using Emdogain, using platelet-rich plasma) combined with adjunctive antibiotic administration. The reason for prescribing an antibiotic regimen to these patients is in order to prevent postoperative infection (25, 26, 27, 28).

### 2.4.) In periodontal abscesses

Periodontal abscess is an acute localized infection in the periodontal area due to invasion of pyogenic bacteria. It is characterized by severe pain and swelling, which very often affect the general condition of patients (29, 30). One of the two etiologies—that is, non-periodontitis-related or connected to periodontitis—can account for the genesis of this entity. Abscesses caused by periodontitis usually appear as a side effect of periodontal therapy or as an exacerbation of the disease when left untreated. Abscesses that are unrelated to periodontitis can frequently occur as a result of abnormal root structure or the impaction of foreign objects, such as a piece of dental floss. (29, 31, 32, 33).

The benefit of taking systemic antibiotics in the presence of periodontal abscess is controversial. Some authors recommend prescribing systemic antibiotics after drainage and debridement of the involved area (34). Others recommend prescribing an antibiotic regimen only if the patient's general health is affected, as in most cases drainage and debridement in the area is quite sufficient (35).

### 2.5.) In necrotizing periodontal diseases

Necrotic periodontal diseases are the most severe inflammatory diseases that are caused by bacteria inhabiting the oral cavity. The most commonly isolated microorganisms from the lesions of these diseases are gram negative anaerobes (*Treponema Vincenti*, *Treponema Denticula*, *Tanarella forsythia*, *Porphyromonas gingivalis*). Clinically, the lesions are characterized by severe pain, spontaneous bleeding from the gingiva, increased salivation, and foetor ex ore (5, 36). The treatment includes debridement with mandatory anesthesia, chemical plaque control using oxidizing agents with gradual intensification of mechanical plaque control. Antibiotic therapy is prescribed in severe forms of necrotic periodontal swellings with lymphadenopathy, fever or malaise. A combination of a broad-spectrum antibiotic and metronidazole (targeting gram negative anaerobes) is usually prescribed (1).

## Choosing a systemic antibiotic

An antimicrobial's ability to treat a patient depends on how well it works against the organisms causing the infection. Since periodontitis is a mixed bacteria infection, selecting an antibiotic treatment can be challenging. Certain subgingival biofilm segments are the primary focus of particular antibiotics. For instance, *fusobacterium nucleatum*, *Tanerella forsythia*, *Porphyromonas gingivalis*, and *Treponema denticola* are among the gram-negative strict anaerobes from the red and orange Socransky complexes that are targeted by metronidazole; in contrast, the medication has little effect on members of the genera *Actinomyces*, *Streptococcus*, and *Capnocytophaga* (37, 38). Additionally, metronidazole has a minimal impact on the facultative anaerobe species *Aggregatibacter actinomycetemcomitans*, as opposed to the strict anaerobe

species. Amoxicillin has a wider range of effects, reducing the numbers of gram-negative anaerobes and Actinomyces species both during and after antibiotic treatment (38).

Microorganisms can be naturally immune to antimicrobials or may develop resistance through the development of resistant strains of bacteria that would normally be regarded as sensitive to the antimicrobial (1).

A wide range of antibiotics used in conjunction with nonsurgical and surgical periodontal therapy has been reported in the literature. The most commonly used antibiotics are penicillins, tetracyclines, metronidazole, macrolides, clindamycin and ciprofloxacin. The most commonly prescribed combination for periodontal disease is amoxicillin with metronidazole (1, 10).

In 2014, Keestra et al. published a meta-analysis concluding that when paired with scaling and root planing, systemic antibiotics provide further therapeutic benefits above scaling and root planing alone. There was a trend that metronidazole or metronidazole with amoxicillin led to more noticeable clinical improvements for initially moderate and deep pockets than either doxycycline or azithromycin, even though there were not any statistically significant distinctions. Furthermore, there was a tendency showing that the therapeutic benefit's magnitude decreased with time (1 year) (10).

The same year, Kolakovic et al. Determine the likelihood probabilities for the appropriate cut-off points of periodontal disease following mechanical treatment for periodontal disease, both with and without antibiotics (in particular the combination of amoxicilline and metronidazol) (39).

The dose and duration of antibiotic intake vary considerably in the literature to date. Another debated case is when antibiotic therapy should be initiated, with most studies on the topic suggesting that the most appropriate time is after completion of nonsurgical periodontal therapy (40, 41, 42).

It should be noted that it is extremely important that patients comply with all prescriptions of the antibiotic regimen. There are publications showing that only about 20% of patients strictly adhere to their antibiotic prescriptions (43).

In 2010, a systematic review was published on the efficacy of additionally included antibiotics to nonsurgical periodontal therapy in smokers diagnosed with periodontitis. The team concluded that the evidence for the benefit of additionally prescribed antibiotics in smokers was insufficient and inconclusive (44).

### **Common side effects after taking systemic antibiotics**

There is generally a shortage of information in the literature about the occurrence or non-occurrence of side effects after systemic antibiotic adjunctive treatment. Most of the side effects that have been documented are mild and connected to digestive issues like nausea and diarrhea (1).

However, while administering systemic antibiotics, patients should be made aware of the possibility of both minor and significant adverse effects. Serious adverse events include allergic and anaphylactic reactions, as well as pseudomembranous colitis. Roughly in every 10,000 courses given, anaphylactic reactions to penicillin occur, and 10% of them are deadly (45).

When using antibiotics, caution should be exercised in selecting drugs that optimize antibacterial activity while reducing the risk of adverse effects and medication interactions. A full health record should be obtained before prescribing antibiotics (1).

### **Antibiotic resistance**

Feres et al. found antibiotic-resistant species in subgingival biofilm and salivary samples of patients with periodontitis treated by nonsurgical periodontal therapy and a combination of amoxicillin and metronidazole. The level of antibiotic-resistant microorganisms returned to baseline after 90 days (46).

In 2005, a comparative assessment of microbial resistance in oral bacteria was made between the population of Spain, where systemic antibiotics are readily available and purchased over the counter, and the population of the Netherlands, where antibiotic use is limited. It appears that there has been a serious increase in patterns of microbial resistance in Spain, compared with that in the Netherlands (47).

In 2024, a study related to antibiotic resistance in the microflora of patients with periodontitis was published. *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella denticola*, *Prevotella melaninogenica*, *Fusobacterium nucleatum*, *Tannerella forsythia*, *Aggregatibacter actinomycetemcomitans*, *Streptococcus constellatus*, *Streptococcus intermedius*, and *Parvimonas micra* have all been linked to a substantial proportion of antibiotic-resistant isolates. However, in the majority of investigations, isolate resistance did not surpass 10% of isolates, with the exception of amoxicillin resistance in *Aggregatibacter actinomycetemcomitans*. Out of all the bacterial species, amoxicillin, clindamycin, and metronidazole had the highest frequency of resistance. The collective concludes that antibiotic resistance in the microflora of patients with periodontitis has not yet reached a critical level. However, it is extremely important not to abuse the use of antibiotics (1).

Clinicians and dentists should concentrate on preventing antibiotic resistance and any potential negative effects on the human microbiome. Therefore, it's imperative to administer antibiotics sensibly (5).

## Conclusion

The presented study shows that systemic antibiotics are currently finding their application in periodontal therapy. Today, however, it is unacceptable to prescribe systemic antibiotics as stand-alone therapy in patients with periodontitis. They would be useful in some single cases, with prior exact non-surgical periodontal therapy, i.e. they are used as an adjuvant. There is evidence of many adverse drug reactions to antibiotics. The notorious topic regarding antibiotic resistance is not to be underestimated, therefore antibiotic agents need to be judiciously prescribed only when necessary!

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