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A Systematic Review Evaluating Systemic Antibiotic Use and Resistance in Chronic Periodontitis: A Comprehensive Systematic Review

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ABSTRACT

Chronic periodontitis is a prevalent, multifactorial inflammatory condition that results in the progressive destruction of the supporting structures of the teeth. While conventional mechanical debridement remains the cornerstone of periodontal therapy, adjunctive use of systemic antibiotics has gained prominence, particularly in cases of aggressive disease, poor response to scaling and root planning (SRP), or compromised host immunity. However, the empirical use of antibiotics poses signifi cant risks, notably the emergence of antimicrobial resistance (AMR), which threatens the long-term efficacy of periodontal therapies. This systematic review aims to evaluate the rationale, efficacy, and patterns of systemic antibiotic use in the treatment of chronic periodontitis, with a focus on the development of resistance among key periodontal pathogens. A comprehensive literature search was conducted according to PRISMA guidelines, identifying eligible studies published between January 2010 and March 2025. Clinical and microbiological outcomes, antibiotic resistance mechanisms, and evidence-based recommendations were synthesized. The findings underscore the importance of judicious antibiotic prescribing and highlight the need for targeted antimicrobial regimens based on microbiological diagnostics and susceptibility profiles.

Keywords: Adjunctive Therapy, Antibiotic Resistance, Chronic Periodontitis, Clindamycin, Metronidazole, Periodontal Pathogens, Systemic Antibiotics, Tetracyclines

1 Introduction

CHRONIC periodontitis is a widespread and persistent inflammatory disease characterized by the progressive loss of supporting tooth structures, including the periodontal ligament and alveolar bone. If left untreated, the condition can ultimately lead to tooth mobility and eventual tooth loss. Its multifactorial etiology involves complex interactions between pathogenic bacteria in dental plaque biofilms and the host immune-inflammatory response. While early-stage periodontal diseases, such as gingivitis, are reversible with proper hygiene and intervention, chronic periodontitis often persists due to inadequate plaque control and host susceptibility [1].

Gingivitis and periodontitis represent the most prevalent periodontal infections, yet they differ markedly in terms of pathogenesis, clinical progression, and treatment requirements. Gingivitis is confined to the soft tissues of the gingiva, whereas periodontitis involves deeper periodontal structures and typically results in irreversible damage. Chronic periodontitis progresses in episodic bursts of activity and remission. It is influenced by individual variations in immune response, genetic predisposition, and environmental factors, including smoking and diabetes mellitus. However, gingivitis—the precursor to periodontitis—is reversible with proper hygiene and clinical intervention.

In contrast, chronic periodontitis often persists and progresses due to inadequate biofilm control and individual host susceptibility [2]. Importantly, periodontal infections are not restricted to oral complications alone. Emerging evidence has established significant associations between periodontitis and systemic diseases, including diabetes mellitus, cardiovascular disease, rheumatoid arthritis, and adverse pregnancy outcomes. Bacteremia induced by periodontal pathogens may contribute to systemic inflammation through the dissemination of inflammatory mediators and microbial by-products. Periodontal infections not only compromise oral health but also exert systemic effects. Numerous studies have linked chronic periodontitis to systemic conditions such as cardiovascular disease, diabetes mellitus, rheumatoid arthritis, and adverse pregnancy outcomes mediated through chronic low-grade inflammation and transient bacteremia [3].

The pathogenesis of periodontitis is closely associated with a specific group of subgingival Gram-negative anaerobic bacteria. Key periodontal pathogens include *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* [4]. These microorganisms colonize periodontal pockets, forming complex biofilms that are resistant to host defense mechanisms and mechanical debridement alone. Although scaling and root planning (SRP) remain the cornerstone of periodontal therapy, they may be insufficient in eradicating pathogens in deep pockets or anatomically inaccessible sites. These pathogens form tenacious biofilms within periodontal pockets, contributing to local tissue destruction and immune evasion [5].

Systemic antibiotics serve as adjuncts in the management of chronic periodontitis, especially in cases of aggressive disease, generalized involvement, or inadequate response to mechanical therapy. Their role includes targeting specific periodontal pathogens, reducing the bacterial load, and enhancing clinical outcomes when used appropriately. However, empirical and indiscriminate antibiotic use has raised concerns regarding the development of antimicrobial resistance (AMR), an escalating global health issue. While SRP remains the primary therapeutic modality, its limitations are increasingly acknowledged, particularly in anatomically complex areas or deep pockets where complete mechanical removal of biofilms is unfeasible. In such scenarios, systemic antibiotics serve as adjuncts to enhance bacterial eradication and improve clinical outcomes [6].

Emphasis is placed on evidence-based antibiotic selection, judicious use to minimize resistance, and integration with conventional mechanical therapies to achieve optimal periodontal health outcomes. Periodontitis is a prevalent inflammatory condition marked by progressive destruction of periodontal support. If untreated, it may lead to tooth loss. The disease can often be prevented or managed through effective oral hygiene and professional care. However, poor hygiene can lead to gingivitis, which may progress to periodontitis if left unaddressed. Agents such as metronidazole, tetracyclines, amoxicillin, and clindamycin have demonstrated efficacy against anaerobic and facultative periodontal pathogens when used inappropriately in indicated cases [7].

Host response, rather than bacterial presence alone, determines disease severity. Inflammatory mediators, such as IL-1, TNF-α, and prostaglandins, activate tissue-degrading enzymes like matrix metalloproteinases [8].

Treatment generally involves mechanical debridement, patient education, and maintenance therapy. Nowadays, mechanical treatment alone may be insufficient, particularly in deeper pockets or advanced cases. Systemic antibiotics can play a vital role in such scenarios [9, 10].

Chronic periodontitis is a widespread and progressive inflammatory disease characterized by the irreversible destruction of periodontal ligament fibers and alveolar bone. If left untreated, this pathology culminates in tooth mobility and eventual tooth loss. The disease arises from a complex interplay between microbial biofilms and host immune responses, modulated by genetic, behavioral, and environmental factors, so this systematic review aims to evaluate the current evidence regarding the rational use of systemic antibiotics in chronic periodontitis, focusing on the efficacy of commonly prescribed agents, routes of administration, resistance profiles, and clinical outcomes.

2 Materials and Methods

A comprehensive and systematic literature review was performed in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to identify relevant studies on systemic antibiotic use and resistance patterns in chronic periodontitis. The search strategy was designed to include both clinical and microbiological studies that explored antibiotic efficacy and resistance trends among periodontal pathogens.

2.1 Study Design and Protocol

This systematic review was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A predefined protocol guided the selection, inclusion, and evaluation of relevant studies addressing systemic antibiotic use and resistance patterns in chronic periodontitis.

2.2 Search Strategy

A structured search was performed across four major databases—PubMed, Scopus, Web of Science, and the Cochrane Library—to identify peer-reviewed literature published between January 2010 and March 2025. The search combined Mesh terms and free-text keywords: "chronic periodontitis," "systemic antibiotics," "antibiotic resistance," "adjunctive therapy," "subgingival microbiota," and "clinical outcomes." Boolean operators (AND, OR) were used to refine the results. Manual searches of reference lists from relevant reviews and primary studies were also performed to identify additional sources.

A total of 2,118 articles were initially identified through systematic database searching. After removing duplicates and screening titles and abstracts, 103 full-text articles were assessed for eligibility. Following the application of inclusion and exclusion criteria, 34 studies were selected for qualitative synthesis. These included randomized controlled trials (n = 19), cohort studies (n = 8), and cross-sectional studies (n = 7). The included studies varied widely in terms of antibiotic type, dosage, administration route, duration of therapy, and clinical or microbiological endpoints assessed.

2.3 Study Selection and Data Extraction

Two independent reviewers conducted the initial screening of titles and abstracts to assess eligibility. Full-text articles of potentially relevant studies were retrieved and evaluated based on the inclusion and exclusion criteria. Discrepancies between reviewers were resolved through discussion or consultation with a third reviewer.

Key data extracted included study design, sample size, patient characteristics, type and dosage of antibiotics used, duration of treatment, clinical outcomes (e.g., probing depth (PD) reduction and clinical attachment level (CAL) gain), and reported antibiotic resistance patterns. Full texts of potentially relevant articles were retrieved for detailed assessment.

Discrepancies in selection were resolved through consensus or consultation with a third reviewer. A standardized data extraction form was used to collect:

- Study characteristics (author, year, country, design).
- Population demographics and sample size.
- Type, dosage, and duration of systemic antibiotics.
- Type of mechanical therapy used.
- Clinical outcomes (PD reduction, CAL gain, BOP reduction).
- Reported antibiotic resistance patterns among periodontal pathogens.

2.4 Inclusion Criteria [11]

- Human studies (randomized controlled trials, cohort studies, and cross-sectional studies).
- Studies assessing systemic antibiotic use as an adjunct to mechanical therapy in patients with chronic periodontitis.
- Reports documenting antibiotic resistance patterns in periodontal pathogens.
- Articles published in English.

2.5 Exclusion Criteria [12]

- In vitro or animal studies.
- Case reports, reviews, editorials, or conference abstracts.
- Studies involving patients with acute necrotizing periodontal conditions exclusively.

2.6 Quality Assessment

The methodological quality of this systematic review was assessed using the Cochrane Risk of Bias Tool, while observational studies were evaluated with the Newcastle-Ottawa Scale. Studies scoring high on methodological rigor were prioritized in the synthesis of results.

A systematic search was conducted using PubMed, Scopus, Web of Science, and Cochrane Library with keywords including "chronic periodontitis," "systemic antibiotics," "antibiotic resistance," and "adjunctive treatment." Articles published between January 2010 and March 2025 were screened.

3 Results

From 2,118 initial records, 34 studies met the inclusion criteria. These studies varied in antibiotics used, dosage, duration, and microbial targets.

3.1 Antibiotic Resistance Trends

Out of the 34 studies reviewed, 15 explicitly investigated antibiotic resistance. Resistance to metronidazole and amoxicillin was most frequently reported, particularly in *P. gingivalis* and *T. forsythia*. Clindamycin resistance was rare but observed in a few cases involving prolonged prior antibiotic exposure. Doxycycline resistance remained relatively low, although its bacteriostatic nature may limit effectiveness in severe infections, as shown in Table 1.

TABLE 1. Systemic antibiotics in chronic periodontitis.

Antibiotic	Target Organisms	Dosage	Duration	Notes
Metronidazole	Anaerobes	250–500 mg TID	7–14 days	Often used with amoxicillin
Doxycycline	*A. actinomycetemcomitans*	100 mg QD	14–21 days	Anti-collagenase activity
Amoxicillin	Mixed flora	500 mg TID	7–10 days	Combination therapy common
Clindamycin	Gram-positive cocci	150–300 mg QID	7–10 days	Used for penicillin allergy

3.2 Interpretation of Results

Table 2 presents the outcomes of a representative review evaluating changes in probing depth (PD) and clinical attachment level (CAL). Most studies reported statistically significant improvements in both PD reduction and CAL gain when systemic antibiotics were used adjunctively with SRP. The combination of metronidazole and amoxicillin demonstrated the highest clinical improvement, with a mean PD reduction of up to 2.5 mm and a CAL gain of 2.1 mm. However, inter-study variability was significant due to differing baseline conditions, treatment durations, and follow-up periods.

Table 3 summarizes the most frequently reported systemic antibiotics used in adjunct to scaling and root planing (SRP). Metronidazole and amoxicillin, alone or in combination, were the most commonly prescribed due to their synergistic effects against anaerobes and mixed flora. Doxycycline was noted for its bacteriostatic and matrix metalloproteinase (MMP)-inhibitory effects. Clindamycin was primarily used in patients allergic to penicillins.

Figure 1 Description: A bar graph depicting resistance prevalence for metronidazole, amoxicillin, clindamycin, and doxycycline among key periodontal pathogens based on pooled data from included studies.

TABLE 2. Clinical outcomes associated with systemic antibiotic use.

Study	Antibiotic	PD Reduction	CAL Gain	Resistance Reported
Study A	Metronidazole + Amoxicillin	2.5 mm	2.1 mm	Yes
Study B	Doxycycline	1.8 mm	1.5 mm	No
Study C	Clindamycin	2.2 mm	1.9 mm	Limited data

The evidence from this review supports the adjunctive use of systemic antibiotics in managing chronic periodontitis, particularly in complex or refractory cases. However, the emergence of resistance, especially with commonly used regimens like amoxicillin-metronidazole, necessitates a more tailored and evidence-based approach. The variability in study methodologies, patient demographics, and microbial testing underscores the importance of incorporating diagnostic microbiology into treatment planning. Moreover, resistance data reveal the need for continuous surveillance and stewardship protocols within periodontal practice, as shown in Table4.

TABLE 3. Types of systemic antibiotics and their mechanism in treating chronic periodontitis.

Antibiotic	Target Organisms	Mechanism of action
Metronidazole	Obligate anaerobes	Often combined with amoxicillin for synergy
Doxycycline	A. actinomycet-emcomitans	Inhibits collagenase enzymes
Amoxicillin	Mixed flora	Broad-spectrum enhances the metronidazole effect
Clindamycin	Gram-positive cocci, anaerobes	Reserved for penicillin-allergic patients

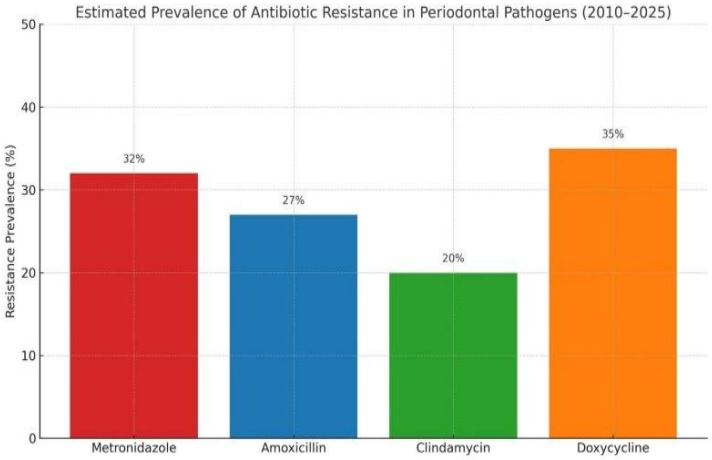

Fig. 1. Estimated prevalence of antibiotic resistance in periodontal pathogens (2010–2025).

TABLE 4. Reported resistance patterns in periodontal pathogens.

Antibiotic	Primary Resistant Species	Resistance Rate (%)	Mechanism Noted
Metronidazole	P. gingivalis, T. forsythia	20–35%	Efflux pumps, reduced uptake
Amoxicillin	A. actinomycetemcomitans, P. intermedia	15–28%	β-lactamase production
Clindamycin	P. gingivalis, S. intermedius	<10%	Ribosomal methylation
Doxycycline	*F. nucleatum*	<8%	Tet(M) gene expression

4 Discussion

Systemic antibiotics provide substantial clinical benefits in managing chronic periodontitis, particularly in cases that are unresponsive to mechanical therapy alone. Yet, the threat of resistance underscores the need for individualized, evidence-based protocols. Sustainable periodontal care must combine patient compliance, mechanical therapy, and cautious antibiotic use. Metronidazole, tetracycline, clindamycin, and amoxicillin remain frontline choices, but their use should always consider potential adverse effects. Systemic antibiotics have been demonstrated to provide measurable clinical benefits in the treatment of chronic periodontitis, particularly when used as adjuncts to conventional mechanical debridement. Their efficacy lies in their ability to achieve therapeutic concentrations in periodontal tissues via systemic circulation and gingival crevicular fluid, thereby targeting both accessible and inaccessible subgingival sites [13]. However, their use must be balanced against potential risks such as resistance, fungal overgrowth, and allergic reactions. The rational prescription should consider patient history, microbial profile, and local resistance patterns. Metronidazole and amoxicillin are most frequently used due to their synergy, while tetracycline offers anti-inflammatory benefits but faces resistance challenges [14].

Short, targeted antibiotic courses and culture-based selection are increasingly advocated. Antibiotic stewardship and clinician education are essential for sustainable use [14].

When metronidazole and amoxicillin are used in combination, they have consistently shown synergistic effects in reducing anaerobic bacterial load and improving clinical outcomes, such as reduced probing depth and increased clinical attachment levels. This combination is particularly effective against P. gingivalis and A. actinomycetemcomitans, two keystone pathogens in periodontitis. Tetracyclines, including doxycycline, offer additional benefits due to their anti-collagenase and anti-inflammatory properties, although rising resistance levels have limited their routine use [15]. Clindamycin is another potent antibiotic that penetrates bone and periodontal tissues effectively. It is often reserved for patients who are allergic to penicillin or in cases of refractory periodontitis.

However, its use is limited by potential adverse effects, including the risk of Clostridioides difficile infection [16]. Despite their benefits, the use of systemic antibiotics in periodontics must be approached with caution. Overuse or inappropriate selection contributes to the global challenge of antimicrobial resistance (AMR), which compromises the effectiveness of standard treatments and poses a serious public health risk. Therefore, the selection of systemic antibiotics should be guided by microbiological testing where possible, patient-specific risk factors, and adherence to established treatment protocols. Short, targeted courses are preferable over prolonged empirical regimens [17].

Antibiotic stewardship in dentistry is essential to mitigate resistance development. This involves clinician education, updated prescribing guidelines, and the integration of rapid microbial diagnostics to facilitate tailored therapy. Future periodontal care may increasingly shift toward adjunctive approaches such as host modulation therapy, probiotics, or antimicrobial peptides to minimize reliance on antibiotics [18].

Systemic antibiotics have long been recognized as valuable adjuncts in the management of chronic periodontitis, particularly in cases where conventional mechanical debridement, such as scaling and root planning (SRP), fails to achieve optimal therapeutic outcomes. Their principal advantage lies in their ability to reach subgingival areas that may remain inaccessible to mechanical tools, thereby improving microbial control in deep periodontal pockets [19]. These agents reach the periodontal tissues via systemic circulation and gingival crevicular fluid, delivering therapeutic concentrations directly to the infection site. However, their use must be weighed against potential risks, especially in the context of increasing antibiotic resistance [20].

The strategic and selective use of antibiotics is essential to achieving a favorable risk-benefit balance. Current best practices advocate for short-term, high-efficacy regimens, targeting specific periodontal pathogens without contributing excessively to the burden of antimicrobial resistance (AMR) [14]. Furthermore, antibiotic prescriptions must be personalized, taking into account the patient's

systemic health, microbial profile, disease severity, and local resistance patterns. Antibiotics are not a substitute for mechanical therapy but rather a supplement in select cases, particularly in aggressive or refractory forms of periodontitis, immunocompromised patients, or those with systemic dissemination of infection.

5 Risks and the Importance of Antibiotic Stewardship

While antibiotics can enhance clinical outcomes when used appropriately, their indiscriminate or empirical use poses significant risks, most notably the acceleration of antimicrobial resistance. AMR not only limits the effectiveness of conventional periodontal therapies but also has broader public health implications. The overuse of antibiotics in dental settings contributes to the emergence of multidrug-resistant organisms, making future infections more difficult and expensive to treat [21].

To mitigate these risks, antibiotic stewardship must be an integral component of periodontal care. This involves rigorous clinician training on evidence-based prescribing, adherence to established guidelines, and the use of microbiological diagnostics to guide targeted therapy. Where available, culture and sensitivity testing can inform the selection of the most effective antibiotic, reducing unnecessary exposure to broad-spectrum agents. Short, targeted courses, typically. Systemic antibiotics continue to play a critical adjunctive role in the management of chronic periodontitis, especially in patients who exhibit inadequate response to non-surgical mechanical debridement alone. Their value lies in their ability to reach the periodontal tissues via systemic circulation and gingival crevicular fluid, achieving therapeutic concentrations in both supragingival and subgingival sites [22]. This systemic penetration allows them to combat pathogens in deep periodontal pockets and inaccessible areas that may not be fully reached by local instrumentation.

However, while systemic antibiotics can enhance clinical outcomes such as reductions in probing pocket depth (PPD), bleeding on probing (BOP), and gains in clinical attachment levels (CAL), their use must be guided by a thorough risk-benefit assessment. Inappropriate or empirical use contributes to microbial resistance and adverse effects, including gastrointestinal disturbances, fungal overgrowth, allergic reactions, and the disruption of host microbiota [20. 21]. Therefore, systemic antibiotic administration should always be reserved for specific clinical indications and implemented within the context of a comprehensive periodontal care protocol.

6 Key Antibiotic Agents and Their Clinical Roles

Among the antibiotics commonly used in periodontal therapy, metronidazole and amoxicillin stand out for their synergistic effects against anaerobic gram-negative species such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans—two of the primary pathogens implicated in the etiology of periodontitis. Studies have consistently shown that their combination leads to significant reductions in probing pocket depth (PPD) and improvements in clinical attachment levels (CAL), particularly when used as an adjunct to SRP [14]. Metronidazole is particularly effective against strict anaerobes due to its mechanism of disrupting bacterial DNA synthesis, while amoxicillin offers broader coverage against facultative anaerobes and gram-positive cocci [19].

The inclusion of amoxicillin–clavulanic acid has also been explored, particularly in combination with metronidazole. Clavulanic acid, a beta-lactamase inhibitor, extends the spectrum of amoxicillin by preventing enzymatic degradation, making this combination highly effective against beta-lactamase-producing anaerobes [23].

Tetracyclines, particularly doxycycline, provide both antimicrobial and host-modulating benefits. In addition to their inhibitory effects on A. actinomycetemcomitans, tetracyclines suppress matrix metalloproteinases (MMPs) involved in connective tissue destruction and bone resorption, thereby offering anti-inflammatory and anti-collagenase activity [15]. Despite these advantages, their use is increasingly limited due to widespread resistance and the potential for photosensitivity and gastrointestinal disturbances. Tetracyclines, including doxycycline and minocycline, have been used due to their broad-spectrum antimicrobial properties and unique host-modulating effects. Tetracyclines inhibit collagenase activity, thereby reducing connective tissue breakdown and exerting anti-inflammatory effects by suppressing cytokine production [15]. However, their clinical utility has been limited by widespread resistance among periodontal pathogens and patient compliance issues due to dosing frequency.

Clindamycin is another potent antibiotic with excellent tissue penetration, including bone and periodontal connective tissue. It is particularly useful in patients with beta-lactam allergies or cases of refractory periodontitis unresponsive to other antibiotic regimens. Clindamycin is effective against anaerobic cocci and various gram-positive pathogens. However, it must be used cautiously due to its association with severe gastrointestinal side effects, including Clostridioides difficile-associated diarrhea and colitis. Clindamycin represents another potent systemic antibiotic, particularly effective against anaerobic cocci and gram-positive organisms. It has demonstrated high penetrability into bone and periodontal tissues, making it valuable in cases of refractory periodontitis or patients with penicillin allergy [16]. Nevertheless, its association with serious adverse events, including the risk of Clostridioides

difficile-associated diarrhea, has restricted its use in carefully selected cases [22].

7 Clinical Rationale for Antibiotic Use in Periodontitis

Clinical studies have consistently shown that the use of systemic antibiotics in combination with scaling and root planning (SRP) results in statistically significant improvements in periodontal outcomes compared to SRP alone. For instance, the synergistic combination of metronidazole and amoxicillin has been particularly effective in eradicating anaerobic pathogens such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans, which are strongly implicated in chronic and aggressive periodontitis [17]. This combination has been shown to reduce pathogenic bacterial load, improve clinical parameters, and delay disease progression.

8 Rationale for Short, Targeted Regimens

Antibiotic stewardship in dentistry is crucial to mitigate the growing threat of antimicrobial resistance (AMR). Current evidence supports the use of short, targeted antibiotic regimens tailored to microbial culture results and susceptibility patterns [18]. This approach ensures that antibiotics are only used when the bacterial etiology has been confirmed and when local debridement alone is insufficient.

Clinician education plays a central role in promoting responsible prescribing practices. Adherence to evidence-based protocols and updated treatment guidelines helps ensure that antibiotics are used judiciously, thereby preserving their long-term effectiveness. Dental practitioners should be trained to recognize clinical scenarios that warrant antibiotic use and to integrate microbiological diagnostics wherever feasible.

Ultimately, successful periodontal treatment requires a multidisciplinary approach that involves effective mechanical therapy, patient education, maintenance care, and the judicious use of systemic antibiotics to achieve long-term disease control and minimize the development of resistance.

Systemic antibiotics remain a valuable adjunct in the treatment of chronic periodontitis, especially in patients who do not respond adequately to mechanical therapy alone. When prescribed appropriately, they offer significant clinical benefits by reducing microbial burden, improving periodontal indices, and enhancing healing outcomes [24]. The distinct mechanisms, indications, and safety considerations.

However, the rising threat of antimicrobial resistance demands the judicious use of systemic agents. Empirical or routine antibiotic use without confirmed microbial diagnosis contributes to resistance development and compromises therapeutic efficacy. Therefore, antibiotic prescriptions in periodontology should be evidence-based, individualized, and protocol-driven, considering microbial susceptibility, patient-specific risk factors, and overall disease severity.

9 Specific Antibiotic Insights

- Amoxicillin-clavulanic acid: This broad-spectrum beta-lactam antibiotic, especially when combined with metronidazole, exhibits strong efficacy against gram-negative anaerobes. It is commonly prescribed in dosages of 500 mg thrice daily for 7–10 days, depending on clinical severity. Its mechanism includes cell wall synthesis inhibition, making it particularly effective against *A. actinomycetemcomitans* and *P. gingivalis* when used in combination therapy [21, 23].
- Metronidazole: Metronidazole is a nitroimidazole antibiotic with selective activity against obligate anaerobes. It is well absorbed, effective against anaerobes like P. gingivalis, achieves high concentrations in crevicular fluid, and is effective at 250–500 mg three times daily for 7–10 days. Often used in synergy with amoxicillin to target multiple bacterial strains involved in periodontal infections, P. intermedia reaches high crevicular concentrations and is mostly used with amoxicillin [23].
- Tetracycline: Broad-spectrum inhibits collagenase and protein synthesis, and it exhibits unique host-modulating properties. Doxycycline is often administered at sub-antimicrobial doses (20 mg BID) as a long-term adjunct for chronic inflammatory modulation. However, traditional tetracycline (250 mg QID) remains an option in bacterial eradication protocols, particularly against *A. actinomycetemcomitans* [15]. 250 mg QID for two weeks is effective against *A.* actinomycetemcomitans [15].
- Clindamycin: A lincosamide antibiotic effective against anaerobic cocci and gram-positive bacteria that binds to the 50S ribosomal subunit. Its ability to penetrate bone and soft tissues makes it useful in difficult-to-treat cases. The typical dosage is 300–450 mg every 6–8 hours for 7 days, but it is reserved due to the potential for gastrointestinal toxicity and *C. difficile* infection [16].

10 Challenges and Limitations in Current Literature

10.1 Challenges

Despite a growing body of research, considerable heterogeneity remains in clinical trial design, including variations in patient populations, antibiotic regimens,

treatment durations, and clinical endpoints. Many studies lack long-term follow-up data, making it difficult to assess the sustainability of clinical improvements or the risk of disease recurrence. Moreover, standardized diagnostic criteria and treatment protocols are lacking, which complicates comparisons across studies and hinders the development of universal guidelines.

Furthermore, most clinical trials focus on short-term microbial and clinical outcomes, whereas the impact of systemic antibiotics on host immune modulation, microbial recolonization, and resistance development over time remains under-investigated.

10.2 Limitations

- Heterogeneity in study design.
- The lack of long-term data limits definitive conclusions.
- Standardized protocols are needed for future research.

11 Conclusion

Systemic antibiotics remain valuable adjuncts in the management of chronic periodontitis, particularly in patients who do not respond adequately to mechanical debridement alone. Their appropriate use can lead to significant improvements in periodontal health by reducing pathogenic bacterial loads and enhancing tissue healing. Among the commonly prescribed agents, metronidazole, amoxicillin, tetracycline, and clindamycin have demonstrated clinical efficacy, albeit with varying resistance concerns and safety profiles.

However, the increasing prevalence of antibiotic resistance necessitates cautious, evidence-based use. Antibiotic prescriptions in periodontics should be individualized based on clinical indications, microbial susceptibility, and patient-specific risk factors. Routine and indiscriminate use must be avoided to preserve antibiotic efficacy and reduce public health risks associated with resistant infections.

12 Future Directions and Considerations

- Development of rapid diagnostics for targeted therapy
- Host modulation to reduce antibiotic reliance
- Regulatory policies for dental antibiotic use
- Exploration of alternatives like probiotics and peptides

Antibiotics should be reserved for specific cases where mechanical methods fail or systemic involvement warrants pharmacologic intervention.

- Development of rapid microbial diagnostics to allow personalized, culture-based antimicrobial selection.
- Integration of host modulation therapies, such as sub-antimicrobial dose doxycycline or NSAIDs, to reduce inflammation without relying solely on antimicrobials.
- Implementation of antibiotic stewardship policies in dental settings, including prescribing audits and clinician education programs.
- Research into novel therapeutic alternatives, including antimicrobial peptides, probiotics, and bacteriophage therapy, to reduce reliance on traditional antibiotics.

Ultimately, successful periodontal therapy will require a multifactorial approach, integrating effective mechanical debridement, antimicrobial precision, maintenance therapy, and patient education. Only through such a comprehensive model can long-term periodontal health be maintained while minimizing the risk of antibiotic resistance and associated complications.

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