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# Clindamycin in Periodontal Therapy - An Alternative Option?

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**Abstract:** ***Periodontal disease is an oral infectious and inflammatory disease caused by microorganisms. Antibiotic administration, either systemically or through local delivery, has been shown to improve the clinical outcomes in periodontitis cases after mechanical periodontal treatment. Clindamycin, a lincosamide antibiotic, has shown promise as an alternative treatment in periodontal therapy due to its broad - spectrum activity against Gram - positive and anaerobic bacteria. This review explores the pharmacological properties of clindamycin, its mechanism of action and its potential advantages over traditional antibiotics like amoxicillin and metronidazole. Additionally, the article discusses the use of clindamycin in systemic and local delivery, its efficacy in reducing periodontal disease symptoms and the associated risks of resistance and adverse effects. Overall, clindamycin presents a viable option in the management of periodontal diseases.***

**Keywords:** Antibiotic resistance; Amoxicillin; Metronidazole; Oral biofilm; Periodontitis; Tetracycline

## 1. Introduction

The initial form of periodontal disease, also known as gingivitis, is reversible in nature following the removal of dental plaque biofilm and usually needs no antibiotic therapy. Majority of the patients seek dental treatment only when the condition deteriorates further in the form of continuous tissue destruction and resorption of alveolar bone leading to periodontitis which eventually leads to tooth loss. [1] Surgical or non - surgical treatments combined with antibiotics are often required to control the disease process. The optimal antibiotic used in periodontal therapy should be bactericidal at therapeutic doses, have antimicrobial activity against a variable spectrum of pathogens specific to periodontal infections, should induce a minimal bacterial resistance, have good tissue penetration and be well tolerated. [2] The antibiotics traditionally used in periodontal therapy have been amoxicillin (with clavulanic acid), tetracycline, metronidazole either as monotherapy or in combination. With reports of antibiotic resistance, decrease in efficacy and introduction of newer antibiotics, it is time to look beyond the traditional drugs. The purpose of this review is to evaluate clindamycin as an alternative antibiotic in periodontal therapy, considering its pharmacological properties, efficacy and potential benefits over traditional antibiotics.

Clindamycin, originally derived from lincomycin is an antibiotic with a high activity against Gram - positive aerobic bacteria and a broad range of anaerobic bacteria, among which are pathogens that produce beta - lactamase. Orally administered clindamycin is absorbed very quickly, penetrates the supporting periodontium and remains at an optimum level for inhibiting microbial growth for at least six hours. [3] However clindamycin has a relatively short half - life and therefore requires administration every six hours to ensure adequate antibiotic concentrations. Orally administered clindamycin is absorbed by the small intestine after being hydrolysed. It is then distributed to the tissues, except the meninges; therefore, it is not used in brain infections. Clindamycin is metabolized in the liver primarily by the Cytochrome P450 3A4 enzyme and CYP 3A5, which oxidize the antibiotic into clindamycin sulfoxide (primary metabolite) and N - desmethyl clindamycin, respectively.

## 2. Mechanism of Action

Clindamycin inhibits the synthesis of microbial proteins by binding to the RNA, the 50S subunit of the bacterial ribosome and thus exerts its bacteriostatic property. [4] Besides targeting of ribosomal units, clindamycin is the only antibiotic that diminishes the adhesion of bacteria to epithelial cells on the mucosal surface by hindering the expression of virulence factors. [5] It impedes the manufacture of M proteins by group A b - hemolytic streptococci, thus stalling the creation of capsules by facultative species of Gram - positive streptococci. It also inhibits the bacterial proteins, enzymes, cytokines and toxins produced by *Clostridium* and *S. aureus* species. [5] Owing to a synergistic effect in the oxidative eradication mechanisms of clindamycin and neutrophils, the former accumulates in the neutrophil organelle and leads to intracellular killing of bacteria. [6] Clindamycin suppresses the release of proinflammatory cytokines, such as TNF - a and IL - 1b and thus plays an inhibitory effect on the inflammation. [7] Clindamycin enhances the killing capacity of polymorphonuclear neutrophils (PMNs). That PMNs play an important role in bacterial annihilation is a well - established fact in patients with dysfunctional neutrophil who show massive periodontal destruction. [8] Even sub - inhibitory doses of clindamycin can cause amplified bacterial opsonization and phagocytosis. It is achieved by upsetting the synthesis of bacterial proteins and altering the surface of the cell wall which eventually leads to a diminution in the adhesion of bacteria to the host cell. The drug can exert prolonged effects for some strains of bacteria, even after the end of treatment, an effect attributed to the persistence of the drug at the binding site of the ribosome. [9]

### Adverse effects of clindamycin

Clindamycin is considered safe for most people, except pregnant and breastfeeding women. Among the most common side effects are diarrhoea, nausea, loss of appetite, abdominal discomfort and increased risk of *Clostridium*

*difficile* infection. Clostridium difficile - associated diarrhoea (CDAD) due to clindamycin can vary from mild diarrhoea to fatal colitis, rarely even two months after discontinuing the antibiotic. [10] This risk occurs when the balance of the bacterial flora in the intestine is significantly altered thus necessitating the co - prescription of probiotics. [11] Other reported adverse reactions include eosinophilia, skin rash, oesophagitis, in rare cases, rheumatoid arthritis, Stevens–Johnson syndrome and hypotension. [12] Hematologically, increased serum transaminases, neutropenia, leukopenia, agranulocytosis and thrombocytopenic purpura have also been reported. In rare cases, renal changes such as proteinuria or azotemia may occur. In conclusion, considering its associated risks, clindamycin should be used with caution and when less toxic antimicrobial agents are inefficient.

**Resistance**

Clindamycin belongs to $MLS_B$ class (macrolide–lincosamide–streptogramin B) of antibiotics that are known for inducing resistance to pathogens which may increase the risk of clinical failure. Previous studies have shown the involvement of four ermA, ermB, ermC and ermF genes frequently associated with $MLS_B$ resistance. [13] The fact that each class is relatively specific, but not strictly limited to a bacterial gene reflects the easy exchange of genes. These genes produce methylase, an enzyme that alters the target site on ribosomes, thus preventing antibiotic binding, leading to both constitutive and inducible resistance. [14] However, previous studies demonstrated that among several antibiotic options used in the treatment of periodontal disease, clindamycin was the most efficient, mainly due to its reduced bacterial resistance. [14]

**Clindamycin in Periodontal Disease Therapy**

Successful periodontal disease treatment utilizing anti - microbial drugs depends upon several factors like selecting the proper agent, its correct dose and proper route of administration. Clinical studies have tested many antimicrobial agents, such as amoxicillin, metronidazole, clindamycin, spiramycin, azithromycin, tetracycline, doxycycline and their effects have been assessed for the treatment of aggressive and chronic periodontitis in several systematic reviews and meta - analyses. [15 - 19] Several bacterial species notably *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans* among many others have been isolated in periodontal disease. [20] While enzymes released from the former cause the destruction of the supporting connective tissue, those from the latter can damage the PMNs. [21, 22]

Eick et al. (2000) reported from their study that the use of clindamycin resulted in a significant increase in phagocytosis and intracellular elimination of *P. gingivalis* and *A. actinomycetemcomitans* in patients with aggressive periodontitis. [23] When comparing systemic clindamycin with tetracycline and metronidazole treatment, both treatments increased Immunoglobulin - G levels in aggressive periodontitis subjects, highlighting an improved immune reaction in this condition. [24] Dubey et al (2019) compared clindamycin with minocycline in order to assess the angiogenic potential and cytocompatibility and noted that even at higher concentrations, clindamycin had a lower cytotoxicity when compared to minocycline thus suggesting the replacement of minocycline with clindamycin for the beneficial effects in the overall regenerative outcome. [25] Gomez - Sandoval et al. who showed that the administration of clindamycin for seven days to diabetic patients with periodontal disease has similar effects to a combination of amoxicillin and metronidazole in reducing probing depth, the bacterial plaque index and the degree of bleeding during probing. [26] Currently, there is no consensus on whether one antibiotic is superior over another, as they all exert similar clinical parameter improvements. However, the benefits of using antibiotics for pocket reduction and clinical attachment gain are evident, especially in more severe, progressive forms of the disease. [27]

Clindamycin can also be used in local drug delivery. Hasan et al. (2019) prepared positively charged and non - charged clindamycin - loaded nanoparticles in order to investigate their effect on bacteria adhesion in the treatment of infected wounds with methicillin - resistant Staphylococcus aureus. Both systems had a sustained drug release, but the clindamycin nanoparticles were able to bind to the bacteria surface, enhancing the bactericidal potency when compared to the non - charged specimen, increasing the healing and wound re - epithelialization. [28]

Besides systemic and local drug delivery, the advances in periodontal therapy include Antimicrobial Photodynamic Therapy (aPDT) and laser therapy. [29] Whether or not the local delivery of clindamycin associated with aPDT or laser therapy can significantly improve the clinical periodontal parameters is not clear yet. Similarly further research is needed to determine whether replacing amoxicillin with clindamycin may improve implant prognosis. [27]

## 3. Conclusion

In conclusion, clindamycin offers a valuable alternative in periodontal therapy, particularly in cases where traditional antibiotics may fail. Its broad - spectrum activity, both in systemic and local applications, makes it a versatile option. Despite its potential, careful consideration of resistance and adverse effects is essential. Further research is needed to solidify its role in periodontal treatment and to explore its potential in combination therapies.

**Conflict of interest:** NIL

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