

## Antibiotics in Periodontics - A Review

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### Abstract

Periodontitis and periodontal infections being chronic and multifactorial, needs a comprehensive way of treatment. Mechanical removal and debridement of calculus and granulation tissue might not be sufficient for the eradication of residual infection in the affected site. In such conditions, antibiotics usage comes handy. Treatment of compromised patients, acute periodontal infections often warrant use of antibiotics. Used in all phases of periodontal treatment in different modes, antibiotics are one integral part of our treatment. Selection of a bacteriostatic or bactericidal drug based on the activity of the disease helps in attaining expected success in periodontal treatment.

**Keywords:** Periodontitis; Antibiotics; Bacteriostatic; Bactericidal

### Introduction

Human race has fantasized a longer life span. Health and disease go hand in hand in everyone. Medical science has always saved the diseased days. Out of a variety of drugs used in medicine, with no doubt antibiotics top the table in frequent usage. The low molecular compounds produced by the wide variety of microbial world initiate the eukaryotic and prokaryotic world interactions. The intensity of the communications has lead to both well-being and ill-being. Antibiotic administration has been a major breakthrough in medical field. Wide variety of infections including orofacial infections are treated by antibiotics, starting from prophylaxis till treatment. Antibiotics prescriptions are beneficial under established systems. On breach of the regular protective protocols, antibiotic resistance is evident. In periodontics, antibiotics are used as an adjunctive therapy to phase 1 therapy. Antibiotics are used as both systemic and local administration.

### Forms of antibiotic usage

Antibiotics are used in various modes in periodontal treatment. Antibiotics usage can be seen in:

- Systemic administration
- Local drug delivery
- Host modulation.

### Systemic administration

#### Rationale of systemic antibiotic therapy

A thorough mechanical debridement mostly stands good for the successful periodontal treatment. But despite assiduous mechanical debridement, some patients experience progressive clinical attachment loss because of the periodontal pathogens which have the notorious ability to evade the host immune system. The red complex bacteria are prone to be attached to the soft tissue wall of the periodontal pocket which obviously makes it difficult to the patient to access during their supportive maintenance therapy phase [1].

Apart from the routine administration of antibiotics, the periodontal infections like periodontal abscess, acute necrotizing gingivitis etc. necessitates antibiotics prescription. Aggressive form of periodontitis, refractory periodontitis too demand antibiotic therapy. Systemically compromised patients need to be administered with antibiotics along with mechanical therapy for the achievement of significant amount of clinical attachment [3]. This administration of drug helps in the inhibition of anti-collagenase enzyme which is not feasible with mechanical debridement alone.

#### Determinants of antibiotics administration and dosage:

- Administer antibiotics based on their minimal inhibitory concentration (MIC) and the gingival fluid concentration.
- Always prescribe high dose for short duration.
- Attain 2 - 8 times of the MIC to recoup for the tissue barrier.
- Determine the duration of antibiotic dosage.

#### Commonly used antibiotics

Extensively used antibiotics in periodontics fall under the following broad category:

- Tetracycline
- Metronidazole
- Penicillin
- Cephalosporin
- Clindamycin
- Ciprofloxacin
- Macrolide
- Aminoglycosides.

Tetracycline is obtained from the natural sources of *Streptomyces* and can be prepared semi synthetically. They fall under the bacteriostatic group of drugs. The unique feature of tetracycline is its collagenase inhibition activity. They inhibit protein synthesis by 30S binding

in ribosome. Tetracycline, doxycycline, minocycline are widely used. Tetracycline is administered in 250 mg dosage, four times daily. Has a disadvantage of poor compliance with patients.

Spirochetes and rods are susceptible to the administration of minocycline. It is always administered in twice daily dosage. A better compliance of patients is always seen. Doxycycline has a periodontal favoring effect on administration. It has improvised anti-collagenase activity. It is usually administered as a once daily dose of 100 mg per day which favor compliance of patient. Metronidazole is the commonly administered antibiotics from the nitroimidazole group. They have bactericidal activity with mode of action of inhibition of DNA synthesis. Always used as an adjunct to mechanical therapy because monotherapy is always inferior [2].

Penicillin is bactericidal drug with major activity on gram positive organism. The bacterial cell wall synthesis is inhibited. Most commonly used drug, amoxicillin falls under this category. Beta lactamase enzymes produced by the microbes interfere with the antimicrobial activity of amoxicillin. To overcome this amoxicillin is commonly used in combination with clavulanic acid in the form of Augmentin. Cephalosporin is used similar to penicillin. They inhibit the cell wall synthesis. The most commonly used oral form of cephalosporin is cephalexin. It has ability to achieve high concentration in GCF. They are effective against the obligate gram negative anaerobes. Clindamycin is effective against anaerobic bacteria. They inhibit the protein synthesis of bacteria by binding to the 50s site [3].

### Combination therapy

Most commonly used combination of antibiotics in periodontics is the combination of amoxicillin and metronidazole. This combination has been found effective against A.a and P.G infections in periodontal therapy. Metronidazole is also prescribed in combination with ciprofloxacin and clindamycin [4].

### Local drug delivery (LDD)

Systemic antibiotic coverage comes with a huge catch of adverse reactions. The need of attaining the required concentration of the antibiotic in the crevicular fluid is arduous and the amount of drug to be administered systemically to achieve such concentrations is unfeasible. All patients might not be advised to follow the systemic administration of antibiotics. Based on the nature of the periodontal destruction and the condition of the patient, alternative mode of antibiotic administration like local drug delivery can be opted.

Systemic tetracycline usage has reported two types of resistance known as non-specific and specific resistance. The non-specific resistance is due to the reduction of tetracycline transport. Specific resistance is achieved by any of the following three mechanisms:

- Tetracycline removal from the bacterial cell through active pumps.
- Enzymatic inactivation of tetracycline drug molecules.
- Protection of ribosomes against the drug.

Local mode of administration is site specific and has the advantage of delivering adequate concentration of drug at the site, avoiding systemic side effects. The controlled release of the drug is achieved by the use of delivery vehicle. LDD is available in the following types like fibers, gels, films and microspheres. Tetracycline fibers (Actisite) are non-resorbable bio-inert fibers used with 25%w/w tetracycline HCL powder in a thread of 0.5 mm in diameter and 23 cm in length. An active drug concentration of 1000 µg/mL is achieved for 10 days. Another form of tetracycline fiber is Periodontal Plus AB is a biodegradable form with 1.7 mg of the drug embedded in type 1 collagen [5]. Atridox is the local drug form of doxycycline. Two syringes one containing the 450 mg of Atrigel a liquid based polymer with another

syringe which contains 42.5 mg of active doxycycline. The combined drug is filled in the periodontal pocket. The site is always covered with periodontal dressing. Microspheres formulation of minocycline with a diameter of 20 - 60 µm diameter under the name of Arestin is available for LDD. It affects the protein synthesis of bacteria by directly passing through the lipid bilayer. Arestin is a 1 mg formulation of minocycline. The microspheres are applied to the site as powders and on contact they aggregate and give a sustained release of the drug. Metronidazole is also used in the local form under the name Elyzol Dentagel which has a concentration of 25% corresponding to 1 mg of metronidazole. This is applied twice a week and this gel crystalize on contact with the gingival crevicular fluid [7,8].

### Host modulation therapy (HMT)

Host modulation therapy is the treatment concept which reduces destruction and stabilizes or even regenerates inflammatory tissue by modifying host response factors [9]. This concept focuses on two different categories of treatment modalities. They are either by the inhibition of the host inflammatory responses [10] or by the resolution [11]. Non-antibiotic tetracyclines are widely used in the modulation of host immune mechanism.

These non-antibiotic tetracyclines act by their pleiotropic mechanism of action [12]. They have extracellular mechanisms, intracellular mechanism and proanabolic effects. They are as follows [13]:

- a. Extracellular mechanisms of non-antibiotic tetracycline:
  - a. Inhibition of the activated matrix metalloproteinases in the connective tissue by binding of Zn<sup>++</sup> and Ca<sup>++</sup> binding sites.
  - b. Inhibition of the activation of proactive matrix metalloproteinases by the reactive oxygen species independent of cation binding.
  - c. Inactivation of the proactive matrix metalloproteinases by the partial proteolysis.
  - d. Indirect inhibition of serine proteinases.
- b. Cellular mechanisms by decreased expression of proactive matrix metalloproteinases by decreasing inflammatory cytokines, phospholipases A2 and nitric oxide.
- c. Proanabolic effect is by up regulation of collagen synthesis and osteoblastic activity and increased bone formation.

Doxycycline used in the form of SDD-Sub antimicrobial dose of doxycycline, 20 mg dosage is the only tetracycline based HMT drug approved to be used as adjunct in periodontal therapy by food and drug administration (FDA). Periostat (20 mg doxycycline) is used for 3 months with once daily prescription.

Chemically modified tetracyclines are used as potential host modulating agents. The carbon in the 4<sup>th</sup> position side-chain was reported for the anti-microbial property of tetracycline by Golub., *et al.* C-4 in the A ring of the four ring structure of tetracycline was produced. This chemically modified drug had anti collagenase activity and did not have the anti-microbial activity of tetracycline. CMT-1, CMT-3 and CMT-8 are used widely in host modulation. Host microbial interaction takes place by:

- Release of the reactive oxygen species
- Release of proinflammatory cytokines
- Release of matrix metalloproteinase.

The host response to the microbial insult results in a respiratory burst which releases the reactive oxygen species and reactive nitrogen species. Excess of this response results in oxidative stress. Oxygen derived free radicals like superoxides, hydroxyl, peroxy etc. and non-radical compounds like ozone, hypochlorous acid, singlet oxygen etc. stimulate the pro inflammatory cytokine pathways. Pro-inflammatory cytokines like interleukin-1, Interleukin-6, Interleukin-8 and Tumor necrosis factor- $\alpha$  etc. They are secreted by a wide variety of host immune cells like, macrophages, lymphocytes, monocytes, fibroblasts. The matrix metalloproteinase are the zinc- and calcium- dependent enzymes secreted by the PMNs and macrophages, osteoblasts and osteoclasts etc. they lyse extra cellular matrix components like collagen, gelatin, laminin etc. exaggerated activity of MMPs results in tissue destruction and is most commonly seen in periodontitis, rheumatoid arthritis, etc.

### Conclusion

Even though it is proved that non-surgical therapy is efficient in attaining clinical attachment gain and periodontal pocket reduction, the eradication of the periodontal pathogens is made feasible by the usage of antibiotics. Treating periodontitis in medically compromised and other forms as aggressive periodontitis is made possible with a predictable success rate by the adjunctive antibiotic therapy. Management of the pro-inflammatory cytokines, Reactive Oxygen species (ROS), Reactive Nitrogen Species (RNS) is achieved. Judicial usage of antibiotics on ethical background along with mechanical therapy will warrant a successful periodontal treatment. Prudent administration of antibiotics is significant in improving the periodontal treatment success rate.

### Conflicts of Interest

Nil.

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