Chemotherapeutic Agents in Periodontics: A Review

Vasudha Gupta 1, Sameer Ahmed 2, Mayur Kaushik 3, Meenu Saleem 4

1 MDS-Postgraduate, Subharti Dental College & Hospital; Swami Vivekanand Subharti University- Meerut UP; 250005
2 Associate Professor, Subharti Dental College & Hospital; Swami Vivekanand Subharti University- Meerut UP; 250005
3 Associate Professor, Subharti Dental College & Hospital; Swami Vivekanand Subharti University- Meerut UP; 250005
4 Professor & Head, Subharti Dental College & Hospital; Swami Vivekanand Subharti University- Meerut UP; 250005

INTRODUCTION:

Periodontitis is a polymicrobial and inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or group of specific microorganisms, resulting in progressive destruction of the periodontal ligament & alveolar bone with increased probing depth formation, recession, or both.1

The microbial etiology of inflammatory periodontal disease provides the rationale for the use of antibiotic medication in periodontal therapy. This concept is based on the premise that specific microorganism causes destructive periodontal disease and that the antibiotic agent in vivo can exceed concentrations necessary to kill or inhibit the pathogens.2

Originally known as “antibiosis”, antibiotics were drugs that had action against bacteria. The term antibiosis which means “against life” was introduced by French bacteriologist “vuillemin” as a descriptive name of the phenomenon exhibited by these drugs.2

Antibiotics are now defined as naturally occurring or synthetic organic substances that in low concentrations can inhibit or kill selective microorganisms.3 The first antibiotic used in periodontal therapy were mainly systemically administered penicillin.4 The nitro-imidazoles were introduced into the periodontal field in 1962. Tetracycline-HCl became popular in the 1970s due to its broad-spectrum antimicrobial activity and low toxicity.

Antibiotic regimens in periodontal therapy can be single or combination antibiotic therapy. Tetracycline- HCl, minocycline, doxycycline which inhibit collagenolytic activity.5 The systemic use of antibiotics in the treatment of severe periodontitis has proven to be clinically advantageous. New and more effective antimicrobial treatments as well as better implementation of existing therapies have significantly improved the prognosis of periodontal disease and many oral infections. Currently, properly selected local antiseptic and systemic antibiotic therapies can provide periodontal treatment that is generally effective, low-risk and affordable.

SELECTION OF ANTIBIOTIC AGENTS:

Having established the need for using an antibiotic in a patient, it is often difficult to decide which to choose from the large number available. Therefore, the choice depends on the peculiarities of the patient, the infecting organism and the drug.6 Thus the various factors in regard to selection of antibiotic agents are:

1. AGE: Age may affect the kinetics of many antibiotics, e.g., Tetracyclines are contraindicated below the age of 6 years, as it
gets accumulated in the developing bone and teeth there by
discolouring the teeth and weakening the bones.

2. RENAL AND HEPATIC FUNCTION: Antibiotic are
contraindicated in renal insufficiency patients, under certain
conditions dose modification of antibiotic is required in renal
insufficiency individuals.

3. DRUG ALLERGY: If a drug has caused allergic reaction it has
to be avoided in that patient.

4. PREGNANCY: All Antibiotic should be avoided in the
pregnancy because of risk to the foetus. Penicillin, many
Cephalosporin and Erythromycin are safe. Tetracycline carries
risk of acute yellow atrophy of liver, pancreatitis and kidney
damage in the mother.

PATIENT SELECTION:

Antimicrobial therapy is expected to offer little to no additional
benefit over mechanical periodontal therapy and supragingival
plaque management for patients with gingivitis or stable
periodontitis. Antimicrobial therapy is necessary in situations of
periodontitis where bacteria have been shown to enter
gingival connective tissues (such as in cases of aggressive
periodontitis). Similar to individuals with acute abscess, severe
or rapidly progressing periodontal disease, systemic antibiotic
therapy may be beneficial in these cases as well.7

Sometimes serial and combination antibiotic is also used
because periodontal infections may contain a wide diversity of
bacteria, thus no single antibiotic is effective against all putative
pathogens. Thesis mixed infection can include a variety of
aerobic, micro-aerophilic and anaerobic bacteria as well as both
gram positive and gram-negative pathogens. In these cases, it
may be necessary to use more than one antibiotic either serially
or in combination, however before combination of antibiotic
are used the periodontal pathogens being treated must be
identified and antibiotic susceptibility test should always be
performed, as there can be resistance to antibiotics.

Antibiotic resistant bacteria:

Antibiotic resistant bacterial strains may develop as a result of
an antibiotic treatment plan, which cannot be discounted.
Bacterial drug resistance can happen in one of two ways:

- Intrinsinc resistance results from a cellular characteristic that
  is already present, typically a gene product such an active drug
  export mechanism.

- Acquired resistance is caused by the introduction of genetic
  sequences that code for antibiotic resistance or the mutation of
  pre-existing genetic material.

ANTIMICROBIAL AGENTS-

Numerous natural and semi-synthetic (antibiotic) substances
limit microbial development, but not all of them are effective as
chemotherapeutic medicines. A substance must be safe for the
host in addition to inhibiting microbial growth in vivo in order
to be useful therapeutically.

Antimicrobial substances work by obstructing one or more of
the following processes: 1. Protein production, 2. Creation of cell
walls, 3. Preservation of cell wall strength, 4. The structure and
use of nucleic acids, 5. The vital metabolic process of cells (such
as folic acid and lipid biosynthesis).

Antibiotics are frequently added to periodontal treatment as
adjuncts. Periodontal disease has been successfully treated
with a variety of antimicrobials. Below are some of the
commonly employed antimicrobials discussed:

TETRACYCLINES:

These are broad spectrum antibiotics active against both gram-
positive and gram-negative bacteria. These are a class of
antibiotics that are derived semi-synthetically or biologically
from specific species of Streptomyces. Due to their 2 to 10 times
higher concentration in the gingival crevice than in serum, it
is beneficial in treating periodontal disorders. It is applied to host
modulation, refractory periodontitis, and aggressive
periodontitis cases.9 For two weeks, tetracycline is
administered in a dosage of 250 mg four times each day.

MINOCYCLINE:

It works well against a variety of bacteria. Spirochetes and
motile rods are suppressed. It is taken daily in doses of 200 mg
for a week.

DOXYCYCLINE:

It may be equally as effective as minocycline and shares the
same spectrum of activity. 100 mg twice daily for the first day,
followed by 100 mg once daily.

METRONIDAZOLE:

This substance is a nitroimidazole. It prevents the synthesis of
bacterial DNA and is bactericidal to anaerobic organisms. When
combined with other antibiotics, it becomes effective against A.
actinomycetemcomitans.10 Moreover, it works well against
anaerobes such P. intermedia and P. gingivalis used combined
with amoxicillin in cases of gingivitis, acute necrotising
ulcerative gingivitis, chronic periodontitis, aggressive
periodontitis, and refractory periodontitis. 250 mg taken four
times daily orally for seven days.

BETA-LACTUM ANTIBIOTICS:

1- Penicillin: Penicillin works by preventing the bacterial cells
from producing cell wall. limited application in gum disease.
Amoxicillin is a semi-synthetic penicillin that has a wide range
of effectiveness against bacteria with gram +ve and gram -ve
chromosomes indicate periodontal abscess and severe
periodontitis.10 During eight days, the dosage is 500 mg three
times per day.

2- Cephalosporin:

The structure and mode of action of cephalosporins are similar
to those of penicillins. Cephalosporins aren’t typically used to
treat infections connected to the mouth. When it comes to the
range of action they have against periodontal pathogenic
bacteria, penicillins outperform cephalosporins. Cephalosporins exhibit cross-allergy to the penicillin class of
medications. Dosage: 250-500mg bid for 10 days.

3- Azithromycin:

It works well against gram-negative bacteria and anaerobes.
Azithromycin is present in tissue samples from periodontal
lesions at much higher levels than in healthy gingiva. According
to some theories, azithromycin has a concentration that
penetrates fibroblasts and phagocytes that is 100-200 times
higher than the extracellular compartment.11 Phagocytes
actively transport azithromycin to sites of inflammation, where
it is then released as the phagocytes burst during phagocytosis.11 After a 500 mg first loading dose, azithromycin
is taken at dosages of 250 mg once daily for 3 days or 500 mg
once daily for 3 days.

4- Ciprofloxacin:

It is a quinolone and is effective against all facultative and
several anaerobic suspected periodontal pathogens as well as
gram-ve rods. For streptococcus species, which are linked to
periodontal health, it has a negligible impact. A microlora
linked to periodontal health may be established more easily with the help of ciprofloxacin medication. All strains of *A. Actinomycetemcomitans* can now only be treated with ciprofloxacin in periodontal therapy. With metronidazole, it can be used in combination therapy. In situations of severe periodontitis, ciprofloxacin is administered twice daily for eight days at a dose of 500 mg.

5- Clindamycin:

It works well against aerobic bacteria. In cases where the patient has a penicillin allergy, it works. Recommended for people who are allergic to penicillin. Clindamycin has shown clinical efficacy in patients with refractory periodontitis. It is given for eight days; the dosage is 300 mg twice daily.

### LOCAL DRUG DELIVERY:

Local drug delivery system is the application of anti-microbial or anti-infective agent that would target pathogenic microorganisms by delivering it at the base of the pocket yielding a stable and good clinical outcome along with mechanical debridement.

Primarily by DR. Marx Goodson in 1979 and his first delivery device involved hollow fibres of cellulose acetate filled with tetracycline. In this device 95% of the drug was released within 2 hours and the therapeutic level was maintained for 24 hours.


### Different types of Local Drug Delivery systems include:

1) **TETRACYCLINE CONTAINING FIBRES** *(Periodontal Plus AB)*

This was the first local drug delivery system available in U.S.A. It is an ethylene vinyl acetate copolymer fibre of 0.5mm in diameter containing TC 12.7 mg/9 inches.

When packed in pocket, it is needed to be applied in successive layers to completely fill the pocket. It is basically a non-resorbable cylindrical monolithic fibre with 25% Tetracycline hydrochloride Concentration of ≥1 μg/ml after 16 hours; it is seen during the tenth day when it is removed. In contrast to 4-8 μg/ml after systemic administration. It delivers drugs in a zero-order kinetics and 60% greater improvement in the pocket depth is seen when compared to scaling alone.

2) **SUBGINGIVAL DELIVERY OF DOXYCYCLINE (ATRIDOX)**

It is a gel system containing 10% doxycycline in a syringable gel (fig.13B). Syringe A contains the delivery vehicle which is bioresorbable flowable polymeric formulation composed of poly (DL- lactide) dissolved in N – methyl -2 pyrolidone. Syringe B contain 50 mg of DX, it is injected as a gel and solidifies within 30 minutes. The device involved hollow fibres of cellulose acetate filled with doxycycline hydrochloride that delivers drugs in a zero order kinetics and 60% greater improvement in the pocket depth is seen when compared to scaling alone.

3) **SUBGINGIVAL MINOCYCLINE (ARESTIN)**

Minocycline microsphere can be used for sub gingival placement as an adjunct to SRP. In a four-centre double blind randomized trial patient with at least 5mm deep periodontal pocket were selected and 2% Minocycline gel or vehicle were applied once every two weeks after initial Scaling & root planning (SRP) and reduction in P. gingivalis and P. intermedia and *A. actinomycetemcomitans* were statistically significant.

4) **SUBGINGIVAL METRONIDAZOLE** *(Elyzol Dental Gel)*

A topical medication containing an oil-based metronidazole 25% dental gel. It is applied in viscous consistency to the pocket where it is liquefied by the body heat and hardens again forming crystal in contact with water. It's application at a 1-week interval is generally recommended. Studies have shown that metronidazole gel is equivalent to SRP but have not shown adjunctive benefit with SRP.

### CONCLUSION:

Antibiotic therapy in periodontics is based on the premise that specific microorganisms initiate destructive periodontal disease and that the antibiotic agent in vivo can exceed concentrations necessary to kill or inhibit the pathogens. Periodontal antibiotic therapy aims to reinforce mechanical periodontal treatment and to support host defences in overcoming the infection by killing subgingival microorganisms that remain after conventional mechanical periodontal therapy.

Combination drug therapies aim at enlarging the antibiotic spectrum and exploiting synergy between antibiotics and may be indicated with complex mixed subgingival infect ion. Thus, the microbial etiology of inflammatory periodontal diseases provides the rational use for antibiotics in periodontal therapy. Antibiotics remain an important adjunctive therapy in the treatment of periodontal diseases, and the use of host modulating drugs as supplemental agents in the management of periodontal diseases continues to grow. Considering the dramatic progress in the past decade in understanding the cause and pharmacological management of periodontal diseases, the twenty first century holds great promise for development of magic bullets.

### Author’s contribution-

Concept and design- Vasudha Gupta, Sameer Ahmed
Drafting of the manuscript- Vasudha Gupta, Sameer Ahmed
Acquisition, Analysis or interpretation of data- Vasudha Gupta, Mayur Kaushik
Critical review of the manuscript for important intellectual content- Vasudha Gupta, Sameer Ahmed, Mehvish Saleem
Supervision - Vasudha Gupta, Sameer Ahmed, Mayur Kaushik

### Conflict of interest:

Authors have no complaint.

### REFERENCES:


