Available online on 15.05.2024 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

Chemotherapeutic Agents in Periodontics: A Review

Vasudha Gupta [1]*, Sameer Ahmed [2], Mayur Kaushik [3], Mehvish 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*

Article Info:

Article History:

Received 24 Feb 2024
Reviewed 09 April 2024
Accepted 26 April 2024
Published 15 May 2024

Cite this article as:

Gupta V, Ahmed S, Kaushik M, Saleem M, Chemotherapeutic Agents in Periodontics: A Review, Journal of Drug Delivery and Therapeutics. 2024; 14(5):194-197

DOI: http://dx.doi.org/10.22270/jddt.v14i5.6610

*Address for Correspondence:

Vasudha Gupta, MDS-Postgraduate, Department of Periodontology, Subharti Dental College & Hospital; Swami Vivekanand Subharti University-Meerut UP; 250005

Abstract

"Selman Waksman" first used the term "antibiotic" in 1942 to refer to any material produced by a bacterium that inhibits the growth of other micro-organisms in high dilution. The pathogenic bacteria, the patient, and the medication are the three main components of the antibiotic periodontal therapy idea. Patients with attachment loss or with aggressive types of periodontitis or those with periodontitis linked with underlying medical conditions are the best candidates for systemic antimicrobial therapy. The three main objectives of Periodontal Therapy are disrupting biofilms, suppressing potential periodontal pathogens throughout the entire oral cavity, and halting the illness. The microbial etiology of inflammatory periodontal disease provides the rationale for the use of antibiotic medication in periodontal therapy. This idea is predicated on the idea that a certain bacterium causes destructive periodontal disease and that antibiotic agents can be present in humans in doses greater than those required to kill or inhibit infections.

Keywords: Antibiotics, Systemic drug delivery, Local drug delivery, Periodontal therapy.

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.

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:

- Intrinsic 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[8], it is beneficial in treating periodontal disorders. It is applied to host modulation, refractory periodontitis, and aggressive periodontitis cases.[8] 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.[9]

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 microflora

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.[12] 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 micro-organisms 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.

A) Advantages of local drug delivery systems: 1. Avoidance of development of antibiotic resistance, 2. Elimination of systemic side effects, 3. Greater concentration of drug in diseased site, 4. Less overall dosage of drug, 5. Improved patient compliance. B) Disadvantages: 1. More expensive, 2. Does not penetrate deeply into soft tissues, 3. Little effects on potential reservoirs of infection.

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 12.7mg/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 ≥1γ00mg /ml is seen during the tenth day when it is removed, In contrast to 4-8 μ g/ml after systemic administration.[16]

It delivers drugs in a zero-order kinetics and 60% greater improvement in the pocket depth is seen when compared to scaling alone.[13]

2) SUBGINGIVAL DELIVERY OF DOXYCYCLINE (ATRIDOX)

It is a gel system containing 10% doxycycline in a syringable gel (fig.13B). Syrine A contains the delivery vehicle which is bioresorbable flowable polymeric formulation composed of poly (DL- lactide) dissolved in N –methyl -2 pyrrolidine. Syringe B contain 50 mg of DX, it is injected as a gel and solidifies within the pocket after the interaction with GCF and saliva. Attachment level gains and probing depth reduction were seen at nine months after therapy in the patients where it was used.[14]

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. gingival is and P. intermedia and *A. actinomycetemcommitans* were statistically significant.[15]

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.[15]

CONCLUSION:

Antibiotic therapy in periodontics is based on the premise that specific micro-organisms 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 for use of 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 complain

REFERENCES:

1. Kaur L, Kaushik M, Singh S, Arora G. Evaluation of healing and anti-plaque efficacy of antioxidant mouthrinse in patients with gingival inflammation. Int J Oral Health Dent 2021;7:14-19. https://doi.org/10.18231/j.ijohd.2021.004

2. Gould K. Antibiotics: from prehistory to the present day. J Antimicrob Chemother 2016;71:572-575. https://doi.org/10.1093/jac/dkv484 PMid:26851273

3. Slots J, Ting M. Systemic antibiotics in the treatment of periodontal disease. Periodontol 2000 2002;28:106-116. https://doi.org/10.1034/j.1600-0757.2002.280106.x PMid:12013339

4. Kapoor A, Malhotra R, Grover V, Grover D. Systemic antibiotic therapy in periodontics. Dent Res J 2012;9:505-515. https://doi.org/10.4103/1735-3327.104866 PMid:23559912 PMCid:PMC3612184

5. Caton JG, Ciancio SG, Blieden TM, Bradshaw M, Crout RJ, Hefti AF, et al. Sub antimicrobial dose doxycycline as an adjunct to scaling and root planing: post-treatment effects. J Clin Periodontol

2001;28:782-789. https://doi.org/10.1034/j.1600-051X.2001.280810.x PMid:11442739

6. Paterson L, David J, Stuart K. Looking for risk factors for the acquisition of antibiotic resistance: a 21st century approach. Clinical infectious diseases 2002;34:1564-1567. https://doi.org/10.1086/340532 PMid:12032890

7. Heitz-Mayfield LJ. Systemic antibiotics in periodontal therapy. Aust Dent J, 2009;54:96-101. https://doi.org/10.1111/j.1834-7819.2009.01147.x PMid:19737272

8. Newman, Takei, Klokkevold, Carranza. Carranza's Clinical Periodontology. 10th edition. 2006.

9. Dannewitz B, Lippert K, Lang NP, Tonetti MS, Eickholz P. Supportive periodontal therapy of furcation sites: non-surgical instrumentation with or without topical doxycycline. J Clin Periodontol 2009;36:514-522. https://doi.org/10.1111/j.1600-051X.2009.01414.x PMid:19508250

10. Cionca N, Giannopoulou C, Ugolotti G, Mombelli A. Amoxicillin and metronidazole as an adjunct to full-mouth scaling and root planing of chronic periodontitis. J Periodontol 2009;80:364-371. https://doi.org/10.1902/jop.2009.080540 PMid:19254119

11. Yashima A, Gomi K, Maeda N, Arai T. One stage full-mouth versus partial-mouth scaling and root planning during the effective half-life of systemically administered azithromycin. J Periodontol 2009;80:1406-1413. https://doi.org/10.1902/jop.2009.090067 PMid:19722790

12. Dannewitz B, Pohl S, Eickholz P, Kim TS. Clinical and microbiological effects of a combined mechanic-antibiotic therapy in subjects with Actinobacillus actinomycetemcomitans-associated periodontitis Am J Dent 2007;20:153-156.

13. Goodson JM, Cugini MA, Kent RL, Armitage GC, Cobb CM, Fine D, et al. Multicenter evaluation of tetracycline fibre therapy: II. Clinical response. J Periodontal Res 1991;26:371-379. https://doi.org/10.1111/j.1600-0765.1991.tb02076.x PMid:1831505

14. Singh P, Rana N, Kaushik M, Singh S. Role of antioxidants in Periodontal therapy. Int J Sci Res 2022;11:1-3.

15. Awartani FA, Zulqarnain BJ. Comparison of the clinical effects of subgingival application of metronidazole 25% gel and scaling in the treatment of adult periodontitis. Quintessence Int 1998;29:41-48.

16. Manini, Agarwal M, Kaushik M, Tomar N. Root Biomodification. J App Sci Comp 2020;7:230-238