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Original Research Paper

Dentistry

RATIONALE OF ANTIBIOTICS IN PERIODONTAL THERAPY

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ABSTRACT Periodontitis is an infection-driven inflammatory condition that leads to destruction of the attachment apparatus of the tooth where, the major etiological factor leading to the destruction is plaque. Plaque act as a reservoir for the complex subgingival microbiota. Therefore, an inference here could be drawn that with the overall reduction of micro-organism, disease progression could be halted. Periodontal therapy aims at restoring balanced periodontal health along with the compatible oral microbiota. Treatment of periodontal disease aims at achieving a healthy periodontium and preventing the risk of recurrence or disease progression. Due to specific properties of biofilm, the subgingival periodontal microbiota are more difficult to target which leads to dearth of clear protocols for the use of antibiotics and therefore, the development of specifically designed strategies to treat the subgingival microbiota, as a biofilm, is highly desirable. So, comes the use of antibiotics in periodontal therapy. Systemic antibiotics enter periodontal tissues via serum and can affect microorganisms outside the reach of adequate instrumentation and towards use of topical anti-infective chemotherapeutics. Antibiotic therapy delays subgingival recolonisation of the microbial pathogens by potentially suppressing the periodontal pathogens residing onto the oral surfaces. Antibiotic treatment strategies in conjugation with proper mechanical biofilm disruption, eventually helps in maintaining the periodontal health by minimizing and eradicating subgingival periodontal-pathogens and thereby, improves the status of clinical outcomes of periodontal therapy. This review henceforth, attempts to highlight the walk-on part of antibiotics in periodontal therapy.

KEYWORDS : Periodontal disease, antibiotics, antibiotic resistance, periodontal therapy, systemic drugs, local drug delivery.

INTRODUCTION

Since time immemorial, infections caused by microorganisms, have threatened human life. These have been a major concern in humans for the increased rate of mortality and morbidity, as the virulency of some organisms the one with high potency to spread infection may lead to worldwide pandemics, epidemics or outbreaks.

With the discovery of "the magic bullet" Penicillin- the first antibiotic, patients with different life-threatening infections were effectively cured. This approach brought a huge relief in the medical field to the medical practitioners. With this, the discovery and the evolution of a wide variety of antibiotic agents came into existence.[1]

Periodontal disease is a chronic inflammatory condition which leads to the formation of periodontal pockets and destruction of the tooth supporting tissues.[2] It occurs due to interaction between the host and bacteria, with the primary etiological factor being pathogenic bacteria present in the sub-gingival areas.[3-4] Bacteria adheres to the crowns of teeth soon after the teeth is cleaned. With time, this supragingival plaque becomes more complex, and it leads to succession of more pathogenic bacteria. Bacterial growth further precedes in apical direction and leads to subgingival plaque formation. Later on, these bacteria in the periodontal pocket forms a highly organised and complex biofilm, which eventually leads to bone destruction.[5]

Destructive periodontal disease is caused by subgingival infection due to specific microbial agent. Among all, Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans are considered as major periodontal pathogens resulting to destructive periodontal disease.[6]

Therefore, the goal of periodontal therapy aims at not only preventing, controlling or eliminating periodontitis, but also in restoring its lost form, function, patient's comfort and esthetics.[7] Traditional therapies aimed at elimination or suppression of subgingival microbiota via mechanical debridement which included scaling and root planning or surgical procedures in its the early stages, when the manifestations can be easily reversed. Further, standard periodontal therapy came into existence which aims at reduction of the bacterial load along with changing the environmental conditions of the microbial niches.[8]

Approach towards periodontal treatment ranges from non-surgical versus surgical, professional emphasis versus patient emphasis, ressective procedures versus regenerative procedures and mechanical versus chemical therapies.[9]

Although mechanical debridement reduces the level of subgingival bacteria, but it does not eliminate all the pathogens which reside deep into connective tissue which destroys the bone.[10] In order to prevail over the limitations of the conventional treatment, chemical agents such as antibiotics and antiseptics emanated and have been used successfully to treat moderate to severe periodontal conditions.[10]

Due to specific properties of biofilm, the subgingival periodontal microbiota are more difficult to target which leads to dearth of clear protocols for the use of antibiotics and therefore, the development of specifically designed strategies to treat the subgingival microbiota, as a biofilm, is highly desirable.[11] Systemic antibiotics enter periodontal tissues via serum and can affect microorganisms outside the reach of adequate instrumentation and towards use of topical anti-infective chemotherapeutics.[12] Antibiotic therapy delays subgingival recolonisation of pathogens by potentially suppressing the periodontal pathogens residing on the oral surfaces.[13]

Even though systemic antibiotics presents with disadvantages like inability of drugs to achieve high gingival crevicular fluid concentration, increased selection of multiple antibiotic-

resistant micro-organisms an increased risk of adverse drug reactions, and uncertain patient compliance, which occurs as a result of use of large doses of systemic antibiotics.

Systemic antibiotics enables simple and easy administration of the drug along with they also help in eliminating or reducing periodontal pathogens from colonizing onto the oral mucosa and on the other extra-dental sites.

Thereby, reduces the chances of micro-organism translocation to periodontal sites and rekindle of the disease reduces.[6] The antibiotics used in periodontal therapy includes various types of agents like penicillins, quinolones, tetracycline, macrolides, nitroimidazole compounds and cephalosporins.[6,14-15]

The rapid emergence of bacterial resistant is occurring throughout the world, which endangers the efficacy of antibiotic use. The crisis of antibiotic resistance has been attributed to the misuse and overuse of the medications.[16-19] However, on the whole the use and misuse of antibiotics is leading to perseverance expansion of antimicrobial resistance, and thereby lowering the effectiveness of some drugs. Developing resistance has created demands for new treatment modalities, and so declines the development of new antimicrobial agents. Therefore, there is global priority in refinement in the thoughtful use of antimicrobials. Measures towards this should include rational use of antibiotic with proper incorporation of activities and programs with antimicrobial stewardship. Ultimately, improving the use of antibiotics involves actions at the national level to guide treatment decisions made by informed HCWs along with the awareness and cooperation of patients.[20]

Hence, the goal of this review article is to emphasis the use of antibiotics that are clinically relevant to the periodontist. This article focuses on antibiotics to be given with both surgical and nonsurgical procedures in periodontology.

Historical Background

1. The Ancient History

Historical evidences states about the ancient civilizations of naturally available treatment modalities as use of honey, herbs and animal faeces for curing infections and topical application of mouldy bread.

2. Renaissance And Enlightenment

In 1676, Antonie Van Leeuwenhoek (1632-1723) lead to the discovery of animalcules and in late 1800s, Robert Koch (1843–1910) and Louis Pasteur (1822–1895) established the association between individual species of bacteria and disease through its propagation onto artificial media and in animals.[21-22]

3. Dawn Of The Modern Era

1st antibiotic "Pyocyanase" was introduced for treatment of human infections. Later, Rudolf Emmerich (1856-1914) and Oscar Low (1844-1941) isolated green bacteria from injured patients, where they grew Pseudomonas aeruginosa and used its supernatant as medicine. Paul Ehrlich (1854-1915) further discovered an arsenic based chemical "Salvarsan" for treatment of syphilis.

Further, Paul Ehrlich (1854-1915) along with Robert Koch (1843-1910) and Emil von Behring (1854-1917) introduced Antitoxins. Later on, in the year 1928, Alexander Fleming (1881-1955) discovered penicillin.[22-23]

4. The Golden Age

Eli Lilly in the year 1952, grew Streptomyces orientalis, from which vancomycin was extracted, and in 1956, cycloserine the first antibiotic in the class of Oxazolidinones was investigated to treat TB. Beecham in the year 1959, developed the first penicillinase-resistant β-lactam antibiotic, Methicillin. Discovery of Cephalosporins was don in the year 1960's. further a year later, in 1961, Beecham introduced ampicillin. In 1967- Nalidixic acid was introduced for clinical use though it was limited to the treatment of uncomplicated urinary tract infections.

In late 1970s, the antipseudomonal third-generation agent ceftazidime came into existence. Bacterial β-lactamase inhibitorswere first identified as a by-product of Streptomyces clavuligerus culture in the year 1976. Later, from which clavulanic acid was derived, and its combination with amoxicillin forming co-amoxiclav & thienamycin. Ciprofloxacin got introduced in the mid1980s and in late 1980s Daptomycin was first evaluated. In 2000- Linezolid was approved for use because of its good oral availability.[24-26]

The End Of The Golden Age

In the year 2005, Tigecycline, a derivative of tetracycline, was introduced and further in 2010s, ceftobiprole and ceftaroline, were introduced.[27-29]

General Principle Of Antibiotics

1. Selecting And Initiating An Antibiotic Regimen For-

- **Obtaining An Accurate Diagnosis Of Infectious Disease-** Disease diagnosis is determined by the site of infection, the host status and if possible, with establishing a microbial diagnosis.
- **Time Of Initiation Of Antibiotic Therapy-** The urgency of the situation marks the timing of initial therapy.
- **Definitive Vs Empiric Antimicrobial Therapy-** Inadequate therapy for infections (in critically ill) or hospitalized patients is generally associated with poor outcomes, including greater morbidity and mortality rates. Therefore, the use of broad-spectrum antimicrobial agents as a common initial empiric therapy/ approach is initiated.
- **Interpretation Of Susceptibility Testing Results-** With the identification of the pathogenic microorganism in clinical cultures, the next step performed is antimicrobial susceptibility testing (AST).
- **Bacteriostatic Vs Bactericidal Therapy-** Bactericidal drugs, are those which cause the death and disruption of the bacterial cell. It include drugs that primarily acts on the bacterial DNA (e.g fluoroquinolones), the cell wall (eg, β-lactams) or on the cell membrane (e.g, daptomycin). Bacteriostatic agents are those that inhibit bacterial replication without killing the organism. It includes macrolides, sulfonamides and tetracyclines, and act by inhibiting protein synthesis. This distinction is not absolute, as some of the agents that are bactericidal against certain organisms may only be bacteriostatic against others and vice versa. Furthermore, bactericidal agents are preferred in the cases of serious infections to achieve rapid therapy results.

- **Use Of Antibiotic Combinations-** Combination therapy of 2 or more antimicrobial agents is recommended-

✓ **When Agents Exhibit Synergistic Activity –** when studied in vitro, the combined effect of the antibiotic agents is greater than the sum of their independent activities when measured separately.
✓ **To Extend The Antimicrobial Spectrum-** When the infection is considered to be caused by more than one organism, a combination regimen is initiated as it extends the antibiotic spectrum beyond that is achieved by any single agent.
✓ **To Prevent Emergence Of Resistance-** The use of combination therapy provides a better chance so that at least one of the administered drug will be effective, thereby preventing the resistant mutant population from emerging as the dominant strain and causing therapeutic failure.

- **Consideration Of Host Factors In Selection Of The Agents-** Different host factors such as, age of the patient, gender, genetic variations, immune response, history of allergy or any intolerance, pregnant or lactating women or any history of initial or recent use of antibiotic must be taken into account prior to the initiation of any antibiotic regimen, as they can lead to changes into treatment outcome.
- **Intravenous Vs Oral Therapy –** Hospitalized patients with infections are treated with intravenous antimicrobial therapy because of the severity of infection.

Patients initially treated with parenteral therapy can be safely switched to oral antibiotics once they become clinically stable. When using oral therapy for invasive infections as abscesses antibiotic of choice is then one with excellent absorption and bioavailability

- **Efficacy Of The Drug At The Site Of Infection-** The efficacy of antimicrobial agents depends on the capacity of the antibiotic agent to achieve a concentration equal to or greater than the MIC at the site of infection.
- **Monitoring Therapeutic Drug-** Most of the antimicrobial agents have a wide therapeutic index, thereby allowing standard doses. However, certain antibiotic agents require monitoring of serum levels as their therapeutic window is narrow. This is either due to toxicity at high levels or therapeutic failure at low drug levels but is usually a combination of both.
- **Pharmacodynamics Of The Drug Used-** The pharmacodynamic properties helps in the determination of the dosing regimen. It relates to the concept of time-dependent verses concentration-dependent killing.

Drugs that exhibit time-dependent activity (β-lactams and vancomycin) presents with slow bactericidal action, and therefore, it is important that the serum concentration exceeds the MIC for the duration of the dosing intervals which can be achieved via continuous infusion or frequent dosing.

2. Considerations For Continued Use Of Antibiotic Therapy

which includes-

- **Duration Of The Therapy-** Deleterious effects have been reported with the prolonged courses of antibiotic agents, which includes selection of antibiotic-resistant organisms, cost-effectiveness, the potential of adverse reactions and the problems associated with adherence.

Therefore, the duration of the treatment must be carefully analysed on the basis of proper clinical and radiographic responses.

- **Assessment Of The Treatment Outcome And Related Adverse Effects-** Both clinical and microbiological parameters help in the assessment of treatment protocols. Clinical parameters of successful treatment outcome include signs and symptoms like decrease in fever or tachycardia, radiologic findings include decrease in the size of an abscess and laboratory values includes decreased leukocyte count.

Adverse effects include- Allergic or hypersensitivity reactions. These are either immediate (IgE-mediated) or delayed and usually manifest as a rash. Anaphylaxis is one of the most severe manifestation of IgE-mediated allergy.
In a recent national study, the prevalence of adverse reactions- antibiotics were implicated in 19% of all medical emergencies and 79% of the all antibiotic-associated adverse events were classified as allergic reactions. Nonallergic drug toxicity is generally associated with higher doses or prolonged use of the antibiotic therapy. The cases are prevalent in patients with poor kidney or liver function that results in impaired clearance.

Furthermore, Certain drug combinations can be one of the reason to cause additive toxicity.

3. Exceptional Situations In Infectious Disease Therapy

Which encompasses-

- **Antibiotic Therapy for associated infections in foreign body-**

With the increasing demand of Prosthetic implants and devices an unfortunate consequence is the emergence of infections associated with the placement of such devices.
One of the most important characteristics of these device-related infection is the formation of biofilms, "a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface."

The Bacteria residing in these biofilms are relatively protected from the antibiotic therapy, probably as a result of alteration of their metabolic state. Awareness towards the prolonged antibiotic treatment in these infections is necessary as it can be ineffective, and can also be associated with adverse effects, and can result in the emergence of resistant strains of organisms.

- **Use as Prophylactic or suppressive therapy –**

✓ **Presurgical Antibiotic Prophylaxis-** Antibiotic prophylaxis is used for the reduction of incidence of postoperative surgical site infections. Patients undergoing treatment procedures who are associated with high infection rates, or those requiring prosthetic implantation, and those with serious consequences of infection should receive perioperative antibiotics.

The antibiotic should cover the most of the organisms and should be present in the tissues when the initial incision is made, and adequate serum concentrations should be maintained throughout the procedure. For example- single dose cephalosporin (cefazolin) administered 1 hour before the initial incision is appropriate for most of the surgical procedures, as it targets the most likely organisms like skin flora, while avoiding unnecessary broad-spectrum antimicrobial therapy. prophylaxis duration for surgical site infection should not exceed more than 24 hours in most of the cases.

✓ **Prophylaxis in Immunocompromised Patients-** Immunocompromised patients, the ones with HIV infection/AIDS, and those under chemotherapy, or receiving immunosuppressive therapy after organ transplant, are generally associated with increased risk of infection. In these specific settings, evidence supports the use of prolonged antimicrobial prophylaxis until immune markers are restored.
✓ **Prophylaxis Before Invasive And Dental Procedures In Patients Susceptible To Bacterial Endocarditis-**

Guidelines recommending antimicrobial prophylaxis in these settings have been recently updated and limits use to few very high-risk scenarios like prosthetic valves replacement, prior endocarditis, or congenital heart disease before surgical correction.

✓ **Traumatic Injuries Associated With Infectious Complications-** Certain injuries poses a high risk of infection because of the disruption of normal barriers or due to the delivery of high inoculum of pathogenic organisms. An example of inappropriate antimicrobial "prophylaxis" is the prolonged use antibiotic in those with open but non infected wounds, including surgical wounds.

- **Nonantibiotic Therapy For Infections-** One of the best-recognized example of nonantibiotic therapy in the treatment of infections is drainage or debridement. This procedure is recommended when the microorganism burden is high or in the cases of abscesses management, where the activity and penetration of antibiotic agent are inadequate.

Other nonantibiotic therapy involves modulating the host inflammatory response towards infection. Systemic corticosteroids, are administered that act by decreasing the deleterious effects of the host inflammatory response, have been found beneficial when used in conjunction with antimicrobial therapy for the treatment of bacterial infections.

4. Judicious Use Of Antibiotics

Incorporates-

- **Cost Deliberation And Antibiotic Stewardship -** The cost depends upon on many factors like in addition to the purchase price of any particular agent or can include administration charges, prolonged hospitalization due to adverse effects, the cost of serum concentration monitoring, and the clinical efficacy. The strategy that significantly reduces the cost is the switch to oral therapy from the intravenous. Oral therapy is generally less expensive, and is comparatively associated with less adverse effects. Cost considerations in the selection and continuation of appropriate antimicrobial therapy in acute care hospitals are part of a broader activity that is referred to as antimicrobial stewardship. Antimicrobial stewardship program aims at "optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection while limiting the unintended consequences, such as the emergence of resistance, adverse drug events, and cost."
- **Prevention For The Emerging Antibiotic Resistance -** The widespread inappropriate use of antibiotic agents is the only most important cause of the emergence of drug resistance. This emergence of antibiotic resistance can be prevented or delayed via judicious prescribing, which is characterized as

1. avoidance of antibiotic treatment for community-acquired infections
2. use of narrow-spectrum antibiotics whenever possible,
3. includes the use of antibiotics for the shortest duration that is effective for the treatment.[30]

Precis To Antibiotics Used In Periodontics

Minocycline

Minocycline is a semi-synthetic derivative of tetracycline used for the treatment of acne, chronic respiratory diseases, and rheumatoid arthritis. Minocycline has antibiotic properties, better absorption, increased antimicrobial activity, and negligible or no phototoxicity. Being lipid soluble, minocycline can easily penetrate into various body fluids, such as saliva and Gingival Crevicular Fluid, and can act locally at the site of infection.[31]

Metronidazole

Metronidazole offers high degree of efficacy and relatively few and/or mild adverse side effects. It is an antibiotic to which susceptible anaerobes have yet to develop clinical resistance. Therefore, it qualifies as the preferred drug against anaerobic infections under this combined treatment program.[32]

Azithromycin

Azithromycin is an azalide antibiotic with excellent in vitro activity against a wide variety of oral bacteria. It has a long half-life, good tissue penetration and is preferentially taken up by phagocytes and can be useful as an adjunct in the treatment of periodontal disease.[33]

Doxycycline

It is a prescription antibiotic medication, which belongs to a broad-spectrum tetracycline-class, generally used in the treatment of infections caused by bacteria and certain parasites. It inhibits the translation by binding to the 16S rRNA portion of the ribosome and further preventing the binding of tRNA to the RNA-30S bacterial ribosomal subunit, due to which the initiation of protein synthesis by polyribosome formation is blocked. This prevents the replication of bacteria and producing bacteriostatic effect.[34]

Tetracycline

Tetracyclines are members of the tetracycline family are among the most important broad-spectrum antibiotics. The antibiotic spectrum and the chemical properties of tetracycline HCI and its semi-synthetic long-acting analogues, doxycycline and minocycline, are comparable, but not identical. They are generally well-tolerated, have few serious side-effects, and are the most commonly prescribed antibiotics. However, one important limitation to the continued widespread use of tetracyclines is the emergence of resistant oral flora.[35]

Chlorhexidine

Chlorhexidine is a broad-spectrum antimicrobial with activity against both gram-positive and gram-negative bacteria, yeasts, and viruses. Antimicrobial activity is dose-dependent - chlorhexidine is bacteriostatic at lower concentrations (0.02%-0.06%) and bactericidal at higher concentrations (>0.12%). Pharmacokinetic studies of oral chlorhexidine rinses indicate that approximately 30% of the active ingredient is retained in the mouth following rinsing, which is subsequently slowly released into oral fluids. This ability to adsorb to dentine, shared with tetracycline antibiotics such as doxycycline, is known as "substantivity" and is the result of chlorhexidine's positive charge - it is likely that this substantivity plays at least some role in chlorhexidine's antimicrobial activity, as its persistence on surfaces such as dentine prevent microbial colonization.[36]

Timing Of Systemic Antibiotic Therapy

➢ In clinical practice, periodontal therapy is performed in two stages-

- First, an attempt to remove the bacterial deposits without elevation of flap. Re-evaluation of the case is done after 3–6 months.
- If deemed necessary, further root surface instrumentation is performed, as local surgical intervention.

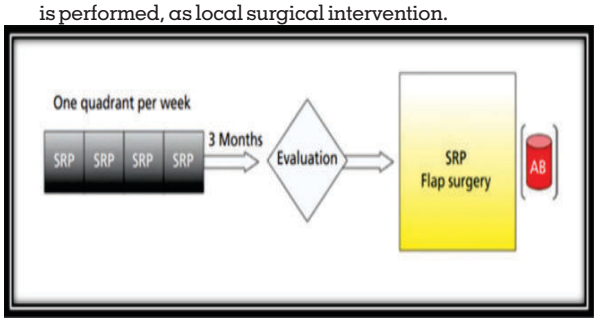


Figure 6. Traditional approach to periodontal therapy

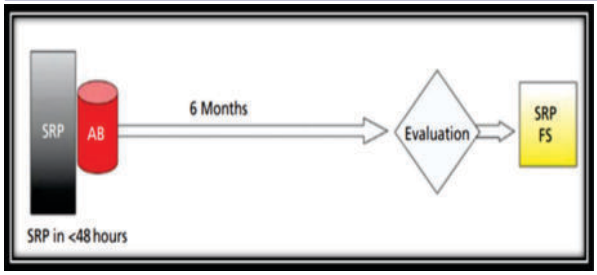


Figure 7. Alternative approach to periodontal therapy, Adapted from Mombelli et al. 2011 (AB, adjunctive antibiotics; FS, flap surgery, SRP, scaling and root planning)

Early Or Late Adjunctive Antimicrobial Therapy (mombelli, 2012)

- **Early (initial/non-surgical Treatment Phase)-**

BENEFIT- Shorter anti-infective treatment, with reduced need for surgical interventions.

RISKS- Incomplete removal of subgingival biofilm and calculus

- **Late (secondary Treatment Phase)-**

BENEFITS- Constrains prescription of antibiotics to cases that cannot be resolved by scaling and root planing alone

RISKS- Benefits of antibiotics used as adjunct to surgical procedures unclear.

Arguments About Postponing Antibiotic Therapy To The Second Surgical Treatment-

1. Heitz-Mayfield et al. 2002, van der Weijden & Timmerman 2002, stated that SRP alone can resolve a considerable amount of periodontal pathology, so this restricts the prescription of antibiotics to a minimum.
2. Sedlacek & Walker 2007-stated about the restricted effects of antibiotics on intact biofilm, and, about the limitations of non-surgical mechanical debridement the known limitations of non-surgical mechanical debridement, Rabbani et al. 1981, Buchanan & Robertson 1987- surgical intervention may be needed for access to assure complete removal of subgingival biofilm and calculus.[37]

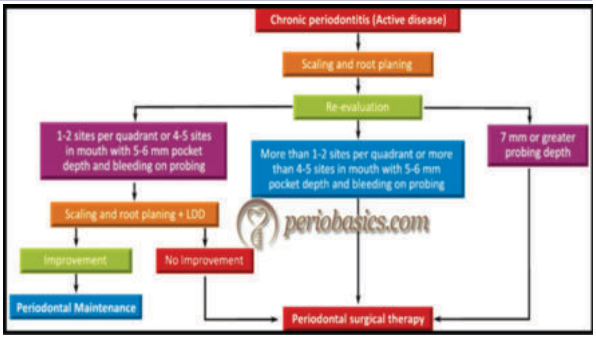
Systemic Antibiotics Regimen Used In Periodontal Therapy

Usage of antibiotics in conjugation with periodontal therapy has always been perplexing. The below listed figure demonstrates different systemic antibiotics, their route alongwith their doses and duration.[38]

Systemic Antibiotics	Route	Primary Excretion	Doses and Duration
Penicillin group			
Ampicillin	Oral	Renal	250mg-500mg/6h/5-7 days
Amoxicillin	Oral	Renal	500mg/8h/8 days
Augmentin	Oral	Renal	250-500mg/6h/5-7 days
Penicillinase – resistant penicillin Group			
Cloxacillin	Oral	Renal	500mg/6h/
Dicloxacillin	Oral	Renal	500mg/6h/
Cephalosporins			
Cephalexin	Oral	Renal	250-500mg/6h/5-7days
Tetracycline group			
Tetracycline HCL	Oral	1°Renal 2°Bilary	250mg/6h/2-7 years
Minocycline	Oral	1°Renal 2°Bilary	200mg 1st day then, 100mg/12h/ 21 days
Doxyclinie	Oral	1°Renal 2°Bilary	200mg 1st day then, 100mg/12h/21 days
Erythromicin group			
Clindamycin	Oral	Hepatic	300mg 1st day, then 150mg/8h/8days
Metronidazole	Oral	Renal	500mg/8h/8days
Azithromycin	Oral	Hepatic	500 mg/qid./3-7 days
Combination therapy of antibiotics (synergism)			**Dosage**
Metronidazole + amoxicillin			250mg/t.i.d./8 days of each drug
Metronidazole+ciprofloxacin			500mg/b.i.d./8 days of each drug

Topical Use Of Antibiotics In Periodontal Pockets

Local delivery of an antibiotic into the periodontal pocket helps in achieving a greater potent concentration of drug than available via systemic delivery. This local route of antibiotic delivery accomplishes 100-fold greater therapeutic doses in the subgingival sites as compared with systemic therapy. Disadvantage of local administration includes difficulty in placing therapeutic concentration of antimicrobial agents into deeper parts of periodontal pockets and furcation lesions respectively.



Pharmacokinetics Of Chemotherapeutic Agents In Gingival Sulcus

- The gingival sulcus is filled with gingival crevicular fluid, which is constantly replaced by new GCF formed at the base of the gingival sulcus.
- Hence, if the chemotherapeutic agent is placed in a periodontal pocket, it shall get flushed out due to continuous flow and renewal of GCF.
- The expected elimination half-time of the drug in the gingival sulcus is around 1 minute which limits the efficacy of the drug in sub-gingival environment.

Various Drugs/agents Used In The Local Drug Delivery System

1. Tetracycline
2. Doxycycline
3. Minocycline
4. Metronidazole
5. Chlorhexidine
6. Other drugs like clarithromycin, Alendronates, ofloxacin, clindamycin, etc.[39]

Table 50.1 Various commercially available products for local drug delivery in periodontal pocket.

Product	Name of agent and Manufacturer	Dosage form	Mechanism of action
Atrigel®	Doxycycline, Atridox (atrix Lab)	Gel	Inhibits protein synthesis
Periochip®	Chlorhexidine Gluconate (Adrian Pharmaceuticals, LLC)	Films	Bactericidal action via destroying the integrity of the cell wall and precipitation of cytoplasmic contents
Periochip®	Chlorhexidine Gluconate (Dexcel Pharma Inc, Jerusalem)	Biodegradable device	-do-
Periocol-CG®	Chlorhexidine	Type-I collagen membrane	-do-
Chlo-Site®	Chlorhexidine	Xanthan gel	-do-
Actisite®	Tetracycline (Alza Corp. Palo Alto, CA,	Non resorbable fiber	Inhibits protein synthesis
Elyzol®	Metronidazole (Dumexpharma)	Gel	Interferes with nucleic acid metabolism
Metrogene®	Metronidazole	Sponge	-do-
Dentomycine®	Minocycline (Sunstar corp., Tokyo, Japan)	Biodegradable mix in syringe	Inhibits protein synthesis
Arestin®	Minocycline (Oropharmacorp Warminster)	Microsphere	-do-
Dentomycin®	Minocycline (Henry Schein UK Holdings Ltd, Medcare House, Centurion Close, UK)	Gel	-do-
OnSite®	Antibiotics (Alza Corp. Palo Alto, CA, USA)	Fiber	Multiple mechanisms

Figure Flowchart For The Application Of Surgical And Non-surgical (LDD) Therapies.

CONCLUSION

Majority of destructive periodontal disease is caused due to the presence of pathogenic periodontal microorganisms, which colonises the subgingival biofilm. The eradication of microorganism results in the improvement of the status of periodontal health. Traditional therapy of the removal of the subgingival plaque helps in the reduction of the bacterial load. However, due to anatomical variations, in certain situations, mechanical therapy alone is not sufficient enough for the control of disease progression, and so comes the need for the use of antibiotic therapy. Antibiotics is boon to the society which when systemically or locally administered, has the ability to enhance the effect of periodontal therapy. In order to limit the increasing antibiotic resistance and its ineffectiveness, due to inappropriate use of antibiotics, and to circumvent the associated risk of systemic effects of antibiotics, a restrictive attitude towards the prevention on the usage of antibiotics is indicated.

Therefore, to restrict the overuse of antibiotics, a proper

diagnosis is needed, as whenever there is ample evidence stating that a thorough non-surgical mechanical debridement alone can resolve the problem, antibiotic prescription should be avoided.[40]

Providing additional treatment benefits for SRP in deep pockets, systemic antibiotics can reduce the need for further surgical therapy. Systemic antibiotics are useful as an adjunct in the retreatment of cases with unsatisfactory response to mechanical therapy.

Locally delivered antibiotics can be used in the areas with localized non-responding sites/localized recurrent disease. Alongwith thorough mechanical debridement (SRP), antimicrobial therapy should be preceded, for proper treatment outcomes and after resolution of the periodontal infection, the patient should be placed on tailored maintenance care program to prevent re-infection.

At present, the most appropriate documented way of using antibiotics in periodontal conditions is SRP with adjunctive oral amoxicillin and metronidazole. In patients with chronic periodontitis, other protocols, including SRP with metronidazole or SRP with azithromycin may be considered as treatment. It must be kept in consideration that antibiotics are not a panacea for all types of non-responsive conditions. An appropriate, efficacious and judicious use of antibiotic agent, makes them an important agent, in the treatment of periodontal diseases.[40]

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