

Antibiotics and its relevance in periodontal disease

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Abstract

Periodontitis is a multifactorial disease occurring as a result of complex inter-relationship between infectious agents and host factors. Environmental, acquired, and genetic risk factors modify the expression of disease and may therefore affect the onset or progression of periodontitis.

Keywords: Antibiotics, Antimicrobials, Periodontitis, Periodontal pathogens.

Introduction

Plaque is the main etiological agent to cause gingivitis which is characterized by the inflammation of the gingiva. Removal of the plaque reverses this phenomenon and if it left untreated it will progress into periodontitis.¹ Periodontitis has been described as a

complex and multifactorial disorder associated with a dysbiotic plaque mass and characterized by progressive loss of tooth supporting apparatus.²

Periodontitis is a multifactorial disease occurring as a result of complex inter-relationship between infectious agents and host factors. Environmental, acquired, and genetic risk factors modify the expression of disease and may therefore affect the onset or progression of periodontitis.³

Moderate to severe cases of chronic periodontitis may warrant periodontal surgical procedures. Of the various factors that affect the outcome of periodontal surgical procedures, the most important aspect is prevention of infection during and following surgical procedure. As postoperative infection can have a significant effect on

the surgical outcome, preventive measures like strict aseptic protocol, anti-infective measures like proper sterilization, disinfection, barrier techniques, and other measures should be taken. If such measures are taken, there is a very low rate of postoperative infection following periodontal surgery. 4 Thereby obviating the need for using antibiotics as a prophylactic measure. However, in actual clinical practice, it has been observed that different types of antimicrobials are routinely prescribed following periodontal surgery.

Bacteria are the primary etiological agent in periodontal disease and it is estimated that more than 500 different bacterial species can colonise the adult mouth. Some of the most common microorganism associated with periodontal diseases are Porphyromonas gingival is, Prevotella intermedia, Tanner Ela forsythia, Campylobacter rectus, Actinobacillus actino my cetemcomitans.

Most of the periodontal pathogens are anaerobes and the key to successful periodontal therapy depends on complete elimination and reduction of pathogenic bacteria from the periodontal pocket. Although conventional mechanical debridement remains the gold standard for periodontal therapy, the tissue invasiveness of certain periodontal pathogens necessitates the need for antimicrobial therapy for the management of periodontitis. Various antibiotics and dosing regimens are available under use on the basis of evidence and guidelines for the periodontal surgical procedures (Slots and Ting, 2002).5 Therapeutic success of an antimicrobial agent depends on the activity of the antimicrobial agent against the infecting organisms. Although systemic antibiotic therapy can be considered as an adjunct to comprehensive periodontal treatment plan, the prevalence of postoperative infections following periodontal surgery is less than one percent.

This low risk does not justify the routine use of systemic antimicrobials just to prevent infections. Hence the use of antibiotics should be based on procedural outcomes and should not be generalized to all procedures. (Oswal et al., 2014). 6 In India, dentists have been known to prescribe antibiotics more than any other medical personnel, which is based totally on empiricism without any protocol or rationale.7-8 Indiscriminate use of antibiotics carry the risk of development of gastrointestinal tract problem, colonization of resistant or fungal strains, cross-reaction with other drugs, allergies, and increased cost of treatment.9 The most preferred antibiotic drug following periodontal flap surgery is amoxicillin 500mg. However Ong et al stated that Azithromycin was the most commonly prescribed system of antibiotic for the management of all periodontal conditions followed by amoxicillin and metronidazole. (Ong et al., 2019).10 They also mentioned that post flap surgical procedure the drug of choice was Amoxicillin.

Mode of Action

1. Amoxicillin is a natural and semi synthetic derivatives of broth cultures of the penicillium mould. It is narrow spectrum and bactericidal in nature, it possess substantial antibacterial antimicrobial activity for gram-negative species.¹¹ Interfere with the synthesis of bacterial cell wall, inhibit the transpeptidases so that cross linking does not take place.

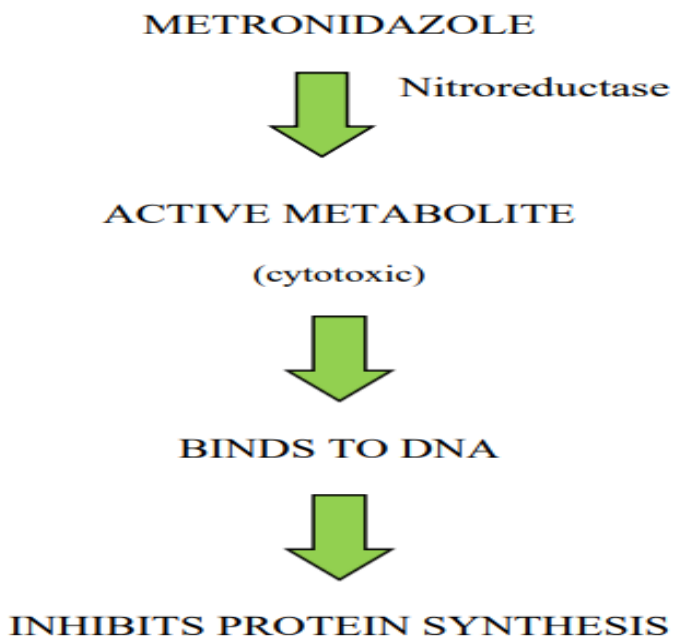
- Amoxicillin-Clavulanate (Augmentin) useful in the management of patients with refractory or localized aggressive periodontitis patients.
- In guided tissue regeneration, systemic amoxicillin-clavulanic acid therapy has been used to suppress periodontal pathogens and increase the gain of clinical attachment.¹²

- Amoxicillin is similar to penicillin in its spectrum of coverage against oral pathogens. The addition of a beta-lactamase inhibitor (such as clavulanic acid) makes amoxicillin active against most aerobic and anaerobic Beta-Lactamase-Producing Bacteria (BLPB)

2. Azithromycin like erythromycin, is usually bacteriostatic but can be bactericidal against very susceptible organisms. It inhibits many gram-positive aerobic and anaerobic species, a variety of intracellular pathogens, and several aerobic and gram-negative bacteria and acts by inhibiting protein synthesis by binding to the 50 S ribosomal subunits of sensitive microorganisms and interfere with translation.

- It is effective against anaerobes and gram-negative bacilli.
- Therapeutic use requires a single dose of 250 mg/day for 5 days after initial loading dose of 500 mg. After an oral dosage of 500 mg o.d for 3 days, significant levels of azithromycin can be detected in most tissues for 7-10 days.

Metronidazole



➤ Used in gingivitis, acute necrotizing ulcerative gingivitis, chronic periodontitis, and aggressive periodontitis.

➤ Metronidazole is inferior, should be used in combination with root planing, surgery or with other antibiotics. The most commonly prescribed regimen is 250 mg tid for 7 days.

Absolute Indication of Antibiotics

- When used to treat periodontal disease, antibiotics are selected based on the patient's medical and dental status, current medications, and results of microbial analysis, if performed.
- Microbial samples may be obtained from individual pockets with recent disease activity or from pooled subgingival sites. A pooled subgingival sample may provide a good representation of the range of periodontal pathogens to be targeted for antibiotic therapy.
- Plaque sampling can be performed at the initial examination, root planing, re-evaluation, or supportive periodontal therapy appointment.
- Antibiotics have also been shown to have value in reducing the need for periodontal surgery in patients with chronic periodontitis.
- Systemic antibiotic therapy should be an adjunct to a comprehensive periodontal treatment plan. An antibiotic strength 500 times greater than the systemic therapeutic dose may be required to be effective against the bacteria arranged in the biofilms. Therefore, it is important to disrupt this biofilm physically so that the antibiotic agents can have access to the periodontal pathogens.¹³
- Slots et al.¹⁴ described a series of steps using anti-infective agents for enhancing regenerative healing. They recommend starting antibiotics 1-2 days before surgery and continuing for a total of at-least 8 days, however, the value of this regimen has not been well documented.

Antibiotics are typically prescribed in dental practice for some of the following purposes:

- (a) as treatment for acute odontogenic infections;
- (b) as treatment for non-odontogenic infections;
- (c) as prophylaxis against focal infection in patients at risk (endocarditis and joint prostheses); and
- (d) as prophylaxis against local infection and systemic spread in oral surgery.

Rational antibiotic use is thus required in dental and oral clinical practice, to ensure maximum efficacy while at the same time minimizing the side effects and the appearance of resistances.

Commonly Prescribed Antibiotics in Periodontal Diseases for Adult and Pediatric Patients

ANTIBIOTICS	ADULT DOSAGE	PEDIATRIC DOSAGE
<ul style="list-style-type: none"> > AMOXICILLIN > METRONIDAZOLE 	500 Mg / t.i.d / 5 days 625 mg / t.i.d / 5 days	<ul style="list-style-type: none"> > AMOXICILLIN: Children > 3 months and 40 kg wt – 20-40 mg/kg/day in divided doses 8 hourly (2-3 days and maximum for 5 days) Children > 40 kg wt : 250-500 mg 8 hourly (2-3 days and maximum for 5 days) Children <12 yrs : 25-50/kg/day in divided doses 6 hourly Children > 12 yrs : 250-500 mg 6 hourly > AZITHROMYCIN: Children > 6 months upto 16 yrs : 5-12 mg/kg daily for (3 days) > METRONIDAZOLE: Children > 6 months upto 16 yrs in divided doses 6 hourly
> CLINDAMYCIN	300 mg / t.i.d / 8 days	
> DOXYCYCLINE / MINOCYCLINE	100-200 mg/ q.d / 21 days	
> CIPROFLOXACIN	500 mg / b.i.d / 8 days	
> AZITHROMYCIN	500 mg / q.d / 4-7 days	
> METRONIDAZOLE + AMOXICILLIN	250 mg / t.i.d / 8 days (each drug)	
> METRONIDAZOLE + CIPROFLOXACIN	500 mg / b.i.d / 8 days (each drug)	

Table: 1

Maximum Recommended Doses
<ol style="list-style-type: none"> 1. Maximum Amoxicillin dosage is 4000 mg/day (80-90mg/kg/day) for targetting high dose. 2. Azithromycin 500-2000 mg/day once a day or 250-500 mg/day for several days. 3. Metronidazole 1600 mg/day.

Table: 2

In a knowledge, attitudes, and practices (KAP) study done by Esamhalboub et al in Saudi Arabia they found that the most commonly preferred drug was a

combination drug of amoxicillin with clavulanic acid followed by amoxicillin stand-alone (Halboubet al., 2016).¹⁶

In a study done by Hai et al it was found that practitioners preferred prescribing antibiotics after using bone graft to avoid post-operative infection which might affect the regenerative potential of the graft material (Hai et al., 2020).¹⁷ It was seen that combination regimen was preferred among periodontists rather than standalone drugs. Because they reduce adverse effects of single drugs and the effect of the standalone drug was minimal and short term. (Heitz-Mayfield, 2009).

Various guidelines for prescription of drugs such as Grading of Recommendation Assessment, Development and Evaluation (Grade) are available. Though these guidelines are not specific to periodontal surgery as such, practitioners should make use of these guidelines while prescribing drugs. The American Academy of Periodontology published a position paper in 2004 outlining the efficacy and practical aspects of antibiotics in periodontal therapy.

Literature suggest that amoxicillin has been used in the treatment of periodontal disease because of its considerable activity against several periodontal pathogens. It has excellent activity against gram positive and negative bacteria, but long-term usage of single drugs may lead to development of drug resistance. Antibiotic resistance can be more prevalent where antibiotic consumption is found to be higher and the antibiotic resistance is accelerated by the misuse and overuse of antibiotics. Development of some resistance is almost certainly an inevitable consequence of the clinical use of antimicrobial drugs. Feres et al in their demonstrated that a large number of bacterial strains of subgingival plaque belonging to various species were resistant to amoxicillin and metronidazole.

Hence it is important to consider the benefits and disadvantages of antibiotic drugs so that appropriate use of antibiotics can lead to decreased rate of drug resistance. Further longitudinal and interventional studies assessing different types of antibiotics for various periodontal surgical procedures can be performed to evaluate the role of antibiotics for the success of periodontal therapy.¹⁸

Problem Due to Excessive Application of Antibiotics

- ❖ Increase of antimicrobial resistance
- ❖ Increase of more severe diseases
- ❖ Increase of the length of disease
- ❖ Increase of the risk of complications
- ❖ Increase of the mortality rate
- ❖ Increase of healthcare costs
- ❖ Increase of the risk of adverse effects, some being life-threatening
- ❖ Increase of re-attendance due to infectious diseases
- ❖ Increased medicalization of self-limiting infectious conditions.¹⁹

Conclusion

Periodontal surgery done under strict surgical protocol did not result in postoperative infection, irrespective of whether antibiotics were prescribed or not. Hence, it is concluded that prophylactic medication of patients with antibiotics who are otherwise healthy following routinely properly performed periodontal surgery is unnecessary and has no demonstrable additional benefits. Further studies need to be conducted in different clinical settings before recommending changes in the antibiotic policy for surgical procedures.

Based on this hospital-based assessment, it was found that the most commonly prescribed antibiotic was amoxicillin 500 mg, followed by a combination of

amoxicillin and metronidazole for flap surgical procedures like Open flap debridement, resective osseous surgery and regenerative osseous surgery. The least preferred antibiotics were azithromycin and doxycycline. There was statistically significant association between gender and type of antibiotic given, with a higher percentage of males receiving a combination of amoxicillin and metronidazole than females. There was no significant difference between the antibiotics prescribed for patients who underwent respective or regenerative flap surgery. Thus, Amoxicillin is the most preferred, cost-effective and less toxic drug which acts against both aerobic and anaerobic microorganisms. Care must be taken in administering antibiotics since they tend to develop drug resistance on use for longer time and larger bases.

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