

Antibiotic & Antiseptic Use in Periodontal Therapy

Microbial Etiology

- Bacterial is essential but insufficient for development of periodontitis, it depends on the host susceptibility - destructive immunoinflammatory response to subgingival plaque bacteria.
- There are over 600 species in subgingival flora, however only a few are associated with periodontitis
 - o Aggregatibacter Actinomycetemcomitans
 - o Porphyromonas Gingivalis
 - o Tannerella Forsythesis
 - o Treponema Denticola
- **Control of periodontal diseases:**
 - o Control host response
 - o Elimination of plaque retentive factors
 - o Disruption and reduction of plaque biofilm
 - o Shift of microbial flora composition
- **Limitation of treatment:**
 - o Local anatomy (root concavities, grooves & furcations)
 - o Bacterial invasion of gingival tissue
 - o Inability to disrupt biofilm and suppress bacteria to a level compatible with host
 - o Reduced treatment outcome associated with elevated periodontopathogen levels
 - o May experience ongoing periodontal breakdown
 - Requires adjunctive therapy (antibiotic therapy) which can be delivered systematically or locally.

Antibiotic Therapy

- Natural or synthetic substances that inhibit or kill selective micro-organisms.
- Poor antibiotic prescriptions have led to bacterial resistance (intrinsic, mutations or acquired).
 - o **MRSA:** Methicillin Resistant Staphylococcus Aureus
 - o **VRSA:** Vancomycin Resistant Staphylococcus Aureus
 - o **Prevotella (gram negative):** produce B-Lactamases which are resistant to tetracycline.

1. Antibiotics have the potential to cause harm

- Allergies and Hypersensitivities: Commonly penicillin, and has a risk of Anaphylaxis (0.04–0.011%) or Fatal Anaphylaxis (0.002%) which can develop at **any exposure** to drug
- Adverse Reactions: Nausea & Diarrhea
- Opportunistic Infections: Pseudomembranous Colitis & Candidiasis
- Drug Interactions: Warfarin & Alcohol
- Toxicity: Teratogenic effects & Breastfeeding

2. Antibiotics Should be used in limited clinical situations

Prophylaxis

a. Immunosuppressed Individuals

b. Infective Endocarditis

c. Prevention of postoperative infection

- Often for periodontal and implant surgery
 - Implant Surgery: Studies have shown no effect on postoperative infection, but a single preoperative antibiotic (2g of Amoxicillin 1hr preop significantly reduced early implant failures). Considerations:
 - Patient Factors
 - Level of asepsis
 - Prolonged procedures
 - Bone Grafting
 - Operative Experience (<50 implants)
 - CHX reduce infection and implant failure
 - Periodontal Regeneration: Improved clinical outcomes with e-PTFE membranes in patients using systemic antibiotics compared to patients not receiving antibiotics (Amoxicillin w/ Clavulanic Acid - Augmentin). No difference in clinical outcomes with Bioresorbable membranes and Emdogain (Amoxicillin and Metronidazole)
- No advantage in reducing postop infection after:
 - Gingivectomy
 - Osseous Resective Surgery
 - Mucogingival Surgery
 - Osseous Grafting
- Reduced infection rate when CHX used

d. Improve periodontal regenerative outcome

Therapy

- Antibiotics are used for treatment of:
 - NUG
 - Periodontal Abscess
 - Periodontitis (minimal benefit in chronic)
- Antibiotics may be useful in:
 - Localized & Generalized Aggressive Periodontitis
 - Refractory Disease
- Greatest improvements in sites >6mm

3. Antibiotics used as an adjunct, not replacement in periodontal therapy

Systemic antibiotics alone are insufficient due to:

1. Diverse microbial community
2. Increased antibiotic resistance
3. High GCF levels required for biofilm penetration (antibiotics may not penetrate biofilm)


Antibiotics should be used adjunct to subgingival debridement immediately after initial phase and at re-evaluation phase.

4. Different Agents for different situations

- Important Considerations:
 - Medical status and concomitant medications
 - Likely microbial specials
 - Lack an easy to use, cost-effective microbiological test
 - Not all etiological species are identified
 - Limited antibiotic agents available
 - Most regimes remain largely empirical
 - Limited evidence for optimal dosage and duration.

Azithromycin

- Macrolide
- Few adverse effects
- Wide antimicrobial spectrum
 - Aerobic and anaerobic bacteria
 - Effective against *A. actinomycetemcomitans* and *P. gingivalis*
- High periodontal tissue concentrations for 5 days after administration
- Improved patient compliance



| Refractory Periodontitis | Aggressive Periodontitis (Grade C) | |
|---|---|--|
| | Localized (Molar Incisor Pattern) | Generalized |
| <ul style="list-style-type: none"> • Polymicrobial (A.a, P.g, T.f, P.i, Strep) • Considerations: <ul style="list-style-type: none"> ○ Number of unresponsive sites ○ Host response ○ Presence of modifying factors ○ Extended antibiotic duration in smokers | <ul style="list-style-type: none"> • A.a implicated • Considerations: <ul style="list-style-type: none"> ○ A.a not suppressed at all sites due to resistance and variable GCF concentration • Tetracyclines: <ul style="list-style-type: none"> ○ Tetracycline HCL 250mg 4 times daily (q.d.s) for 14 days | <ul style="list-style-type: none"> • Polymicrobial (P.g, T.f +/- A.a) • Tetracyclines: <ul style="list-style-type: none"> ○ Limited or no effect |
| <p><u>Azithromycin</u> 500mg once daily for 3 days Limited evidence Benefit in deep sites and smokers</p> | <p><u>Amoxicillin/Metronidazole</u> 250-500mg/200-400mg three times daily (t.d.s) for 5 days or <u>Azithromycin</u> 500mg once daily for 3 days Early evidence is promising</p> | |

5. Antibiotics can result in reinfection & recolonization

- Regular biofilm disruption is required during surgical periodontal therapy
- Reinfection of A.a, P.g, T.f, T.d
- Recolonization in:
 - Supragingival & Subgingival Plaque
 - Mucous membranes, tongue and tonsils

Conclusions

- Antibiotics are valuable therapeutic agents but are not magic bullets.
- The widespread use of antibiotics increases bacterial resistance → clinicians need to be responsible for sensible prescribing.
- Not an excuse for inadequate debridement or poor surgical technique
- Risks of complications may be greater than risk of postop infection

Antiseptic Therapy (Chemical Plaque Control - Mouthrinses)

- The concept of chemical plaque control is to improve plaque removal after mechanical plaque control to prevent gingivitis (It is assumed that gingivitis is precursor of periodontitis).
 - Gingivitis is a poor predictor for future periodontitis because the proportion of gingival lesions that convert to periodontitis is currently unknown and the factors that cause this conversion are not well understood. The most evidence that gingivitis do not progress to periodontitis comes from epidemiological studies on untreated populations in China, Kenya and Nigeria.

| Chemical Plaque Control Agents | | |
|--|---|---|
| First Generation | Second Generation (Agents of Choice) | Third Generation |
| Do not exhibit and substantivity (only minutes), can kill bacteria on contact but have limited abilities on oral flora after expectoration | Antimicrobial agents with high substantivity (hours). Have an immediate antibacterial effect and prolonged effect on oral flora | Moderate Substantivity (hours), characterized by an ability to inhibit or disrupt plaque formation with no effect on bacteria |
| <i>Cetylpyridinium Chloride, Sanguinarine</i> | <i>Chlorhexidine</i> | <i>Morpholinoethanol Derivative—delmopinol</i> |

- Generally, mouthrinses contain three basic ingredients:
 - Alcohol:** enhance flavor impact and solubilize the flavor and some active ingredients. Also acts as a preservative
 - Surfactants:** dual function: (1) assists in removal of debris from mouth and provide antibacterial effects (2) aid in solubilization of flavor and some active ingredients
 - Flavoring Agents:** breath-freshening properties

Groups of agents used to control plaque and/or gingivitis

1) Bisbiguanide antiseptics

| Chlorhexidine (CHX) Gold Standard Cationic (+ charge) antiseptic Broad spectrum antimicrobial | | | |
|--|---|---|-----------------------------------|
| Ingredients | Mechanism | Optimization | Side Effects |
| <ul style="list-style-type: none"> Water/alcohol base Glycerin Flavoring Agents | <ul style="list-style-type: none"> It is a positively charge compound → attracted to negatively charged bacterial cell wall - breaks down wall and causes cell death. It is absorbed to plaque, pellicle, oral mucosa, hydroxyapatite and these surfaces become reservoirs - slowly release active CHX for up to 12–24 hours “substantivity” Any bacteria adhering to tooth surface are either killed (bactericidal) or are prevented from multiplying (bacteriostatic) The bacteriostatic effect is what makes CHX the gold standard. Antiplaque (reduces by 45–61%) and antimicrobial (reduces gingivitis by 27–67%) | <ul style="list-style-type: none"> CHX should not be used before, or immediately after toothpaste (it will reduce the effective delivery of CHX to tooth surface) Limit intake of foods and beverages after CHX use | Shares some side effects with CPC |

2) Quaternary ammonium compounds

| Cetylpyridinium Chloride (CPC) | | | |
|---|--|--|--|
| Cationic (+ charge) antiseptic Broad spectrum antimicrobial Substantivity <3 hours Little evidence of any benefits to improve gingivitis | | | |
| Side Effects | | | |
| <ul style="list-style-type: none"> • Calculus Formation • Staining • Burning Sensation | | | |

3) Essential oils (EO)

| Listerine | | | |
|---|---|--|--|
| When used as an adjunct to unsupervised oral hygiene, it provides additional benefit regarding plaque and gingivitis reduction as compared to a placebo or control mouthrinse. | | | |
| Ingredients | Mechanism | Safety | |
| <ul style="list-style-type: none"> • Thymol • Eucalyptol | <ul style="list-style-type: none"> • Microorganisms are killed by disrupting their cell walls and inhibiting their enzyme activity • Reduces bacterial load | <ul style="list-style-type: none"> • Long-term use safe • Concerns about long-term use of high-percentage alcohol mouthrinse with oral cancer. • No evidence of cancer • Currently Listerine without alcohol is present in market. | |
| Triclosan (Trichloro-2-hydroxydiphenyl ether) - Colgate Plax/Total | | | |
| Can help reduce supragingival plaque/calculus & gingivitis but not as effective as CHx | | | |
| Ingredients | | | |
| <ul style="list-style-type: none"> • Triclosan (Antibacterial agent) • Copolymer [polyvinyl methyl ether maleic acid (PVM/MA) which helps retain triclosan on hard and soft tissues allowing for better plaque activity and "substantivity"]. | | | |

4) Natural products

- The blood root plant **Sanguinaria Canadensis** provides alkaloid "Sanguinarine" which is incorporated in mouthrinse formulations & zinc chloride salts to enhance the anti-plaque effect
 - It has limited benefit and might cause leukoplakia

5) Oxygenating agents

- H₂O₂ is most used in ANUG and pericoronitis.
 - Limited evidence to suggest use as anti-gingivitis or anti-plaque agent

6) Amine Alcohols

- Octapinol was withdrawn for toxicologic reasons
- Delmopinol followed at 0.1% and 0.2% concentrations in mouthwashes does not kill bacteria but disrupts the plaque matrix.
 - Many side effects; tooth discoloration, numbness of mucosa, taste disturbance and burning sensation.

7) Enzymes (Biotene, Zendium)

- Marketed for people with sensitive/dry mouths
 - No alcohol
 - Natural enzymes that are found in saliva - antibacterial effect
 - Glucose Oxidase, Lactoperoxidase, Lysozyme, Lactoferrin

8) Others

- **Povidone Iodine**: at 1% has a substantivity of only 1 hour; minimal plaque inhibitory activity.
 - Might affect thyroid function

Conclusion

- Mouthwash does not affect subgingival plaque or treat periodontitis (lack of subgingival penetration)
- CHX is the gold standard for mouthrinse
- Chemical plaque biofilm control has been shown to be effective for both plaque biofilm reduction and improved wound healing after periodontal surgery. Both CHX and essential oil mouthrinses have positive effects when used after periodontal surgery for 1–4 weeks.
- Mouthrinses have a role in gingivitis but considering gingivitis does not necessarily progress to periodontitis, we need to question whether use of chemical agents for general population is necessary.