Chemical Agents in Periodontal Therapy: Use or Misuse?

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Antimicrobial agents used to control opportunistic infections such as those that cause periodontal disease are capable of suppressing the oral microbiota. However, the effect is limited and transitory. The aim of this paper is to re-assess the current treatment modalities employed in plaque control and to analyse what advantages could be offered by chemical agents.

Over the past few decades, research has provided overwhelming evidence that micro-organisms are the primary aetiological agents in periodontal diseases. We have even gone as far as to associate aggregates of bacteria with specific clinical conditions. Several clinically and microbiologically distinct periodontal diseases are now recognized.

Treatment of any infectious disease is targeted towards the offending organism(s). It is not surprising, therefore, that the prevention and treatment of periodontal disease is based on the control of the oral flora, thereby limiting or minimizing the damaging effects of dental plaque.

Three approaches have been suggested for controlling plaque:

1. Eliminate all plaque.
2. Reduce plaque below an individual's threshold for disease.
3. Alter the microbial composition in such a way that health cannot convert to disease.

However, complete elimination of plaque is impossible, and may not be necessary. The second and third alternatives are therefore more practical. It is essential to consider the more important aspects of the microbiology of plaque, as this should enable us to act more rationally in our approach.

PLAQUE MICROBIOLOGY

Supragingival accumulation of plaque is characterized by a quantitative increase in plaque bulk, dominated by aerobic organisms (Actinomyces and Veillonella). The metabolism of aerobes and facultative anaerobes gradually decreases the level of oxygen in the plaque, favouring anaerobic growth, especially in the sheltered areas around the teeth (e.g. deeper layers of plaque, interdental space, gingival crevice) and even more so in the subgingival pocket. The nutrients available in the pockets, coupled with the reduced oxygen tension, reduced redox potential, protection afforded by the gingival tissues and increased gingival crevicular fluid flow support the growth of anaerobic periodontal pathogens.

The subgingival flora originates from the supragingival flora, but is not simply an apical down-growth of supragingival plaque. The growth of subgingival flora is characterized by a slow ingrowth of pioneer micro-organisms, followed by multiplication of those indigenous species that are particularly well adapted to the subgingival environment, thereby establishing a climax community of more than 100 different species. Of these only a handful have been implicated as putative periodontal pathogens, including:

- Porphyromonas gingivalis;
- Prevotella intermedia;
- Eikenella corrodens;
- Fusobacterium nucleatum;
- Wolinella recta;
- Treponema denticola; and
- Capnocytophaga species.

These organisms, which are capable of producing toxic substances, are recovered in higher percentages from periodontal pockets than anywhere else in the mouth. At this point it is critical to highlight two important points:

1. None of these organisms are foreign invaders. They are all members of the commensal oral flora and are present in healthy individuals, although their numbers increase significantly in disease.
2. They are probably not the only periodontal pathogens.

Therefore, in directing treatment specifically to these organisms we may fail to eradicate other important pathogens. Elimination of one or more of these species may induce a change in plaque ecology, resulting in the proliferation of other organisms capable of producing a destructive effect.

Cultural studies have revealed great complexity and variability of the predominant subgingival flora in periodontitis. Its composition varies from patient to patient, from site to site and also with time at the same site. Therefore it is still not possible to culture all the organisms within a subgingival plaque sample or to recover them in correct proportions. Of the 300 species of bacteria identifiable in oral microbiota only 30 are routinely observed and only 5% of these are considered strongly associated with periodontitis.
Further research is required before we are able fully to comprehend the subgingival environment. Insofar as treatment is concerned it is unlikely to undertake elimination of a specific pathogen as there is no evidence of such an organism.

Prevention and treatment of periodontal diseases aims at permanently reducing the indigenous species to a level conducive to periodontal health. This is achieved by establishing and maintaining a level of plaque control imnical to the survival of the suspected pathogens. The oral flora can be suppressed by both mechanical and chemical means.

MECHANICAL CONTROL
Mechanical control effectively suppresses the oral flora, keeping plaque to a minimum. It is the treatment instituted for preventing and treating gingivitis, the precursur of periodontitis. It also plays a critical role in the control of periodontal disease progression. Clinical and microbiological improvements have been observed following supragingival plaque control measures only. However, the effect is limited in more advanced cases and significant improvements in moderate and deep periodontal pockets should not be expected with home care procedures alone. Rather, a combination of home plaque control and instrumentation should be performed.

Supragingival Plaque
Supragingival plaque control is the patient’s responsibility, although the dental surgeon plays a pivotal role in imparting knowledge and motivating the patient. The major tool for plaque reduction is the toothbrush, which should be used in conjunction with other interdental cleaning aids (the actual aid used is not of particular importance). Effectiveness of plaque control depends on the attitude of operator and patient, as well as patient dexterity. Patient and dental surgeon work together as co-therapists.

Subgingival Plaque
Professional subgingival instrumentation disturbs the subgingival ecosystem, shifting the balance of flora towards one conducive to periodontal health. This must be accompanied by effective supragingival control and a careful recall programme, otherwise the subgingival flora will return to the original levels within a few weeks.

Unfortunately, the strict level of supragingival plaque control required by the patient is not invariably achieved. Therefore chemical agents have increasingly been used as adjuncts to mechanical plaque control. These are intended to augment, and not to replace, mechanical plaque control.

CHEMICAL CONTROL
Ever since the association between bacteria and periodontal disease was recognized, it seemed logical to resort to chemotherapeutic agents to treat this destructive process. To date the use of a wide variety of antiseptics and antibiotics has been explored.

Antiseptics
Chlorhexidine
Chlorhexidine is perhaps the most widely used chemical agent, although other compounds are used. It has been thoroughly investigated since Loe and Schiott discovered its antiplaque properties, and has not been superseded. This superiority above all other agents is attributed to its dicationic nature and prolonged substantivity, which is retained without loss of potency over a 12 hour period. Chlorhexidine Mouthwash. When used as a mouthwash (10 ml, 0.2% twice daily), chlorhexidine totally inhibits formation of new plaque and therefore prevents the development of gingivitis. However, it is not better than effective manual oral hygiene and has no effect on gingival inflammation adjacent to pockets that are deeper than 3 mm. This is because a mouthwash cannot penetrate periodontal pockets, leaving subgingival plaque undisturbed. Furthermore, the increased passage of exudate may prevent any agent entering the subgingival area. Significant reductions in plaque and gingivitis are observed following subgingival debridement, emphasizing the importance of professional instrumentation. Chlorhexidine is still beneficial for special category patients who find it difficult to achieve the necessary high standard of oral hygiene, e.g. handicapped patients, post surgery, etc.

Subgingival Application. Subgingival irrigation or slow release of chlorhexidine has shown to enhance the periodontal status, both clinically and microbiologically. However, these results are inconsistent with those obtained from other studies. This discrepancy may be explained by the difference in supragingival plaque control levels.

Cautions for Use. Chlorhexidine should be used with caution. Once its application is withdrawn plaque returns to pretreatment levels—prophylactic use therefore seems inappropriate as there is no logical endpoint for its withdrawal. In addition, prolonged exposure to chlorhexidine promotes growth of bacteria that are less sensitive to the drug.

Other Antiseptics
Quaternary Ammonium Compounds. These exhibit a moderate antiplaque effect. Cetylpyridinium chloride and benzalkonium chloride have oral retention properties that are better than, and antibacterial activity that is equivalent to, that of chlorhexidine. However, they are not as effective as chlorhexidine in inhibiting plaque and preventing gingivitis.

Fluridone: The use of fluridone is responsible for the decreased incidence of dental caries, but fluoride compounds do not seem to have any antiplaque properties. The modest plaque reductions achieved by the use of amine and stannous fluoride, have been attributed to the metal ion present. This is also true for zinc, copper and tin fluorides. The combination of zinc and triclosan in a dentifrice formulation has yielded encouraging results.

Oxygenating Agents. The effects of oxygen and hydrogen peroxide on plaque have been investigated. Application is based on the susceptibility of anaerobic organisms to oxygen. Some investigators have reported a beneficial effect when hydrogen peroxide is used alone or as a salt/peroxide solution; others have not show any significant therapeutic benefit of its use. One major disadvantage of hydrogen peroxide is that it produces toxic radicals—with possible deleterious effects.

Further studies are needed to fully assess the antiplaque properties of phenolic compounds and natural products such as sanguinarine.

Antibiotics
The antiplaque properties of several antibiotics have been studied. Although topical application may reduce supragingival plaque in some patients, antibiotics should not be used for this purpose—the bulk of plaque should be kept in check by routine homecare procedures. In chronic periodontitis pockets provide a protected environment for pathogenic
organisms and restrict access for mechanical procedures. Antibiotics are increasingly being used with the aim of facilitating treatment and improving the chances of success. The antibiotics most often used in periodontal practice are metronidazole or tetracycline, applied systemically or locally.

A fundamental principle in antibiotic therapy is that the drug must reach its site of action in sufficient concentrations and for sufficient time to have a full effect.

Systemic antibiotics are excreted in gingival crevicular fluid, which means that high concentrations of the drug are achieved subgingivally, limiting the organisms at the advancing front of the lesion. A number of clinical studies have been performed to assess the benefits of their use, alone or in addition to scaling and root planing.

However, the therapeutic benefit of any systemically administered antibiotic must be weighed against its adverse side effects. Tetracycline and metronidazole have been used for a number of years and both are not without limitations. The potential risks of resistance developing, of superinfection by fungal organisms, patient hypersensitivity and systemic side-effects must obviate their routine use.

Systemically Applied Tetracycline

Tetracycline and its semi-synthetic derivative minocycline accumulate in higher concentrations in the subgingival region than in serum. The tetracyclines work by:

- Enhancing spread and attachment of fibroblasts;
- Inhibiting tissue collagenase and;
- Inhibiting parathyroid hormone-mediated bone resorption.

They are absorbed onto teeth and soft tissues and are released in active form over a long period of time.

A number of short- and long-term studies have monitored the clinical and microbiological effects of tetracycline, with and without scaling. In the absence of mechanical therapy systemic tetracycline suppresses the oral flora but its effect is short-lived and not sufficient to eliminate clinical signs of disease. When used in addition to scaling and root planing, tetracycline appears to have no clinical benefit over scaling and root planing alone; it does, however, virtually eliminate suppuration from periodontal pockets. In conjunction with surgery, tetracycline seems to have no effect on pocket depth or healing of intrabony defects.

If the antibiotic is administered in low doses, Gram-negative organisms develop resistance to it. This could be of some concern because Gram-negative organisms have been particularly implicated in the aetiology of periodontal diseases.

The routine use of systemic tetracycline in chronic periodontitis seems to offer no significant therapeutic benefit and cannot be recommended.

In contrast, tetracycline may be beneficial in treatment of specific periodontal conditions such as localised juvenile periodontitis, rapidly advancing or refractory periodontitis. In juvenile periodontitis, mechanical therapy alone does not reduce the proportions of causative organisms, especially Actinobacillus actinomycetemcomitans, which is capable of invading the periodontal tissues. Systemic tetracycline significantly suppresses this organism and may be useful in the non-surgical treatment of juvenile periodontitis.

Systemically Applied Metronidazole

The nitroimidazole group of drugs, which includes metronidazole, is very effective against anaerobic bacteria and spirochaetes. The microbial activity of metronidazole does not disturb the commensal oral flora or facultative anaerobes. An important advantage of its use is that susceptible organisms rarely develop resistance.

When used as the sole source of treatment, systemic metronidazole has an antimicrobial effect similar to that obtained after mechanical debridement only.

Clinical trials using systemic metronidazole as an adjunct to scaling and root planning have given somewhat inconsistent results. Some studies have demonstrated no significant clinical benefit over scaling and root planing alone; others showed marked clinical and microbiological improvements.

The greatest improvements were observed in patients with advanced or refractory forms of periodontitis and high spirochaete counts. These results were significantly better than those achieved with metronidazole therapy alone, emphasizing the importance of combining metronidazole therapy with mechanical debridement in patients with advanced or refractory periodontitis (which are ideally diagnosed by high spirochaete counts). There seems to be a critical level of spirochaete count beyond which anaerobic infections may be diagnosed: 20% spirochaetes form a single site and 15% from pooled samples of subgingival plaque.

The timing of metronidazole administration relative to mechanical debridement is also important—should it be given during or after scaling and root planing?

Concurrent antibiotic therapy and mechanical debridement improves the clinical signs of disease by reducing pocket depths and increasing attachment levels about the most severely involved teeth (pockets deeper than 6 mm) and is more effective than debridement and placebo. Combined therapy is also capable of reducing the need for periodontal surgery and improving the prognosis of otherwise ‘hopeless’ teeth (2.6 teeth per patient). These results were confirmed and further improved upon by giving metronidazole after completing scaling and root planing (8.4 teeth per patient). The findings revealed significantly lower proportions of the putative pathogens, including spirochaetes and improvements were maintained for up to 18 months, confirming that systemic metronidazole is effective in treating advanced periodontal infections. The diagnosis should ideally be made by the presence of elevated spirochaetes in two or more subgingival plaque samples.

Locally Administered Antibiotics

The adverse effects of antibiotics are minimized if they are used at the lowest effective concentration. This is achieved by administering the drug locally through the pocket orifice in gel form or following absorption onto a carrier system which allows a slow but sustained delivery at the site of action. Maximum chemotherapeutic levels are obtained with minimal dose of antibiotics. The subgingival concentrations established by the controlled delivery of antibiotic are between 10 and 1000 times those achieved with even gram dose of systemic antibiotics. The levels are maintained for longer periods and are capable of completely inhibiting growth of several of the bacteria isolated from periodontal pockets.

Clinical trials of the effects of topical tetracycline and metronidazole on chronic
periodontitis have shown clinical and microbiological improvements. In spite of achieving pronounced reductions in the clinical signs of periodontal pathology and a marked change in the composition of the subgingival flora the effects are not as good as the results achieved by conventional scaling and root planing. Also, once their use is discontinued the pocket flora returns to baseline values within a few weeks. The use of topical antibiotics is therefore recommended only as an adjunct to scaling and root planing.

Although intrapocket delivery devices will not replace conventional periodontal therapy, these devices seem to offer an attractive alternative in situations when the level of conventional therapy cannot be achieved (e.g. when access is limited).

CONCLUSIONS

Plaque control constitutes a major step towards the success of periodontal therapy. Most cases of adult periodontitis can be treated with conventional mechanical therapy (scaling and root planing for as long as 2 years) provided that strict supragingival plaque control is achieved.

Antiseptics (the most effective being chlorhexidine) are known to be safe and effective in reducing plaque-forming bacteria, but should be used on a short-term basis in conjunction with scaling and root planing. Prophylactic use of such agents seems inappropriate.

Antibiotic therapy is useful in special-category patients, such as those with juvenile periodontitis, advanced or refractory periodontitis.

All chemical agents should be considered as adjuncts to, and never as substitutes for, conventional scaling and root planing and meticulous homecare procedures.

References

33. Williams BL, Osterberg SKA, Jorgensen
Computer Assisted Learning (CAL) Programmes for GDPs

The following CAL programmes have been developed with Section 63 funding, and are available free of charge to GDPs working in the GDS in England. They may be obtained from Postgraduate Dental Deans Directors or their Administrators.

1. Orthodontic Diagnosis
   (in MS DOS format)
   Developed by Professor C. Stephens of Bristol University Dental School. (This programme also requires a manual and sets of orthodontic study casts which are not provided free.)

2. Aspects of Partial Denture Design
   (Windows format)
   Developed by Dr J. Davenport and Mr D. Pollard of Birmingham University Dental School.

3. Minimal Preparation Resin Retained

Bridgework (Windows format)
   Developed by Dr N. Meredith of Bristol University Dental School.

4. Molar Endodontics (Windows format)
   Developed by Dr N. Meredith of Bristol University Dental School.

5. The Management of Patients with Special Needs (Windows format)
   Developed by Dr R. Bedi and Mr D. Pollard of Birmingham University Dental School.

The following programmes are under evaluation or development and should be available later on this year:

- The Oral Manifestations of AIDS
- Introduction to Occlusion
- Aspects of Oral Surgery
- Copy Technique for Complete Dentures


