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Clinical note

# Selection of antimicrobial agents in periodontal therapy

**Jørgen Slots**
University of Southern California School of Dentistry, Department of Periodontology, Los Angeles, CA, USA

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*Background:* The recognition over the past 3 decades of microbial specificity in periodontitis has afforded dental practitioners the ability to prevent and treat the disease with a variety of antimicrobial drugs. These include systemic antibiotics, topical antibiotics and topical antiseptics.

*Results:* Systemic antibiotic therapy can be essential in eliminating pathogenic bacteria that invade gingival tissue and in helping control periodontal pathogens residing in various domains of the mouth from where they may translocate to periodontal sites. Frequently used periodontal combination antibiotic therapies are metronidazole-amoxicillin (250–375 mg of each 3 × daily for 8 days) and metronidazole-ciprofloxacin (500 mg of each 2 × daily for 8 days). Microbiological analysis helps determine the optimal antibiotic therapy and effectiveness of treatment. Topical antibiotics that are commercially available as controlled release devices suffer from several potential problems, including insufficient spectrum of antimicrobial activity in some periodontal polymicrobial infections, risks of producing an antibiotic resistant microbiota, and high acquisition costs. Topical antiseptics of relevance in periodontal treatment include 10% povidone-iodine placed subgingivally by a syringe for 5 min, and 0.1% sodium hypochlorite solution applied subgingivally by patients using an irrigation device.

*Clinical implications:* The present paper recommends periodontal treatment that includes a battery of professionally and patient-administered antimicrobial agents (properly prescribed systemic antibiotics, povidone-iodine and sodium hypochlorite subgingival irrigants, and chlorhexidine mouthrinse). Available chemotherapeutics can provide effective, safe, practical and affordable means of controlling subgingival colonization of periodontal pathogens and various types of periodontal disease.

Jørgen Slots, University of Southern California School of Dentistry, Department of Periodontology, MC-0641, Los Angeles, CA 90089–0641, USA
Tel: +1 213-740-1091 (voice)
e-mail: jslots@usc.edu

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Destructive periodontal disease is a concern because of the potential damage to the dentition and the financial burden of treatment. It is generally agreed that microorganisms residing in periodontal pockets are responsible for periodontitis, but uncertainty exists regarding the exact mechanisms by which periodontal tissues are destroyed. Approximately 500 bacterial taxa inhabit periodontal pockets (1), which provide a moist, warm, nutritious and anaerobic environment for microbial colonization and multiplication. The abundance and diversity of periodontal pocket microorganisms depend upon several factors, including effectiveness of oral hygiene measures, pocket depth, degree of gingivitis, flow of gingival crevice fluid, type of interacting microbes and viruses, transmission rate of microbes from other individuals, and the antimicrobial efficacy of the host immune response. Most likely, some microorganisms produce gingivitis and some types of chronic periodontitis by their mere abundance ('non-specific' plaque hypothesis) and some microorganisms produce aggressive types of periodontitis

because of exceptionally high virulence ('specific' plaque hypothesis) (2). Important periodontal pathogens are *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis*, *Dialister pneumosintes*, *Bacteroides forsythus* and *Treponema denticola*. Other gram-negative anaerobic rods, some gram-positive bacteria and even enteric rods/pseudomonas may also play roles in the etio-pathogenesis of periodontitis (2).

Development of more effective diagnosis and control of periodontal infections and more cost-effective means of managing or curing severe types of periodontitis is urgently needed. Some periodontitis patients lose teeth from periodontal disease, despite regular maintenance appointments (3, 4), or derive little benefit from regular compared to less frequent maintenance appointments (5). Recently, Haffajee *et al*. (6) found ongoing loss of probing periodontal attachment in 18 of 57 (32%) adult patients who had received 3 h or more of initial scaling and root planing and then maintenance scaling and oral hygiene instruction every 3 months throughout a 9-month study period. Rosling *et al*. (7) were unable to prevent tooth loss in 64% of patients susceptible to periodontal disease over a 12-year period with maintenance therapy every 3–4 months. The relatively high level of ongoing disease is particularly disappointing given the generally low incidence of periodontal breakdown in untreated patients (8). The relevance of current periodontal antimicrobial therapy needs to be reevaluated. Thought must be given to the antimicrobial efficacy of initial periodontal therapy and to the reliance on frequent dental appointments, scaling and root planing, and plaque control by mechanical cleaning as virtually the sole modality of maintenance care.

Although mechanical debridement is essential in removing hard accretions on roots, subgingival scaling and root planing is time-consuming, unpleasant for patients, and technically difficult to perform, as shown in extracted teeth coated with fingernail polish (9). A review of studies evaluating the effectiveness of various subgingival debridement procedures showed that 5–80% of treated roots harbor residual plaque or calculus, and the deeper the pockets and furcation involvements, the more deposits are left behind (10). Up to 30% of the total surface area of treated roots may be covered with residual calculus following subgingival scaling (10).

The value of administering antimicrobial agents as a quick and inexpensive means of augmenting mechanical periodontal debridement is worthy of consideration. Periodontitis patients may benefit from systemic antibiotics, topical antibiotics and topical antiseptics. A debate is taking place about the utility of topical antibiotics in periodontal treatment. However, therapeutic success or failure depends not only on the intrinsic antimicrobial activity of chemotherapeutics but also on the clinical status of the patient (important with bacteriostatic drugs), the presence of foreign material (may include subgingival calculus) and the location of the infection (base of deep periodontal pockets and furcations that may be difficult to reach by topical therapy). This review highlights current approaches to antimicrobial periodontal therapy and aims to identify efficient chemotherapeutic means to control subgingival microbial colonization and periodontal infectious disease.

## Systemic antibiotics

During the past 2 decades, dentists and microbiologists have embraced periodontal antibiotic therapy, as evidence for bacterial specificity in periodontitis has accumulated and strengthened (2). Actively progressing periodontitis is virtually always associated with specific bacterial infections and often requires the adjunctive use of systemic antibiotic therapy. Antibiotics, defined as naturally occurring or synthetic organic substances that in low concentrations inhibit or kill selective microorganisms, are particularly useful in combating severe periodontal infections. Systemic antibiotics enter the periodontal tissues and the periodontal pocket via serum and can affect organisms outside the reach of cleaning instruments or topical anti-infective chemotherapeutics. Systemic antibiotic therapy has also the potential to suppress periodontal pathogens residing on the tongue or other oral surfaces, thereby delaying subgingival recolonization of pathogens (11). Systemic antibiotics may even be required for eradication and prevention of periodontal infections by *A. actinomycetemcomitans* and other pathogens that invade subepithelial periodontal tissue or colonize extra-dental domains from which they may translocate to periodontal sites (11).

Early approaches to systemic antibiotics in periodontal treatment included mainly single drug therapies with tetracyclines, penicillins, metronidazole or clindamycin. Recently, the gingival crevice fluid concentration of systemically administered tetracyclines was reported to be less than that of plasma concentration and vary widely among individuals (between 0 and 8 μg/ml), with approximately 50% of samples not achieving a level of 1 μg/ml, possibly explaining much of the variability in clinical response to systemic tetracyclines observed in practice (12). Since periodontitis lesions often harbor a mixture of pathogenic bacteria, drug combination therapies have gained increasing importance (11). Valuable combination therapies include metronidazole-amoxicillin (250–375 mg of each 3 × daily for 8 days) for *A. actinomycetemcomitans* and various anaerobic periodontal infections, and metronidazole-ciprofloxacin (500 mg of each 2 × daily for 8 days) for mixed anaerobic and enteric rod/pseudomonas periodontal infections (11). Because the periodontopathic microbiota includes a variety of microorganisms with differing antimicrobial susceptibility and clinical disease features can only rarely incriminate the offending bacteria, and because inappropriate antibiotic therapy may adversely affect human microbial ecology and give rise to resistance development among serious pathogens, microbiological analysis and antimicrobial susceptibility testing should ideally form the basis for selecting the optimal antimicrobial

therapy (11). Microbiological analysis is particularly advisable in periodontal lesions that are recalcitrant to conventional periodontal therapy and may harbor a great variety of periodontal pathogens.

Employment of systemic antibiotics can give rise to a number of adverse reactions and should be administered only after proper patient evaluation. Also, cost can be a determinant in selecting antimicrobial periodontal therapy. Antibiotics in the lower cost group include tetracyclines, amoxicillin and metronidazole. Antibiotics in the higher cost group include azithromycin, clarithromycin, ciprofloxacin, amoxicillin/clavulanic acid and clindamycin.

As discussed by Slots & Ting (11), systemic antibiotic therapy that is properly selected to patients with aggressive periodontitis can give rise to striking clinical outcome. In patients with chronic periodontitis, the utility of systemic antibiotics is not as clear.

## Topical antibiotics

Controlled release devices that contain tetracycline-HCl, doxycycline, minocycline, metronidazole or ofloxacin for direct pocket placement are commercially available in various countries. The usefulness of topical antibiotic therapy in periodontics is controversial. Most clinical studies have monitored the effect of controlled drug delivery on variables characteristic of gingivitis and not necessarily of periodontitis, and the adjunctive or alternative role of topical antibiotic therapies in short- and long-term management of periodontal disease has not been defined either.

Table 1 shows the ability of scaling and root planing alone and of various controlled antibiotic delivery devices to reduce periodontal pocket depth. Even after considering the difficulty in comparing studies involving non-calibrated clinicians and different clinical protocols, the clinical outcomes in Table 1 do not point to a significant utility of topical antibiotics in periodontal treatment, at least not when employed in conjunction with thorough mechanical debridement. A recent review by Quirynen *et al.* (20) also described only modest benefits of controlled antibiotic delivery in subgingival sites.

*Table 1.* Reduction of probing depth in 4–6-mm-deep pockets following periodontal therapy*

| Subgingival treatment | Authors | Average probing depth reduction in mm |
|---|---|---|
| Repeated scaling and root planing | Magnusson *et al.* (13) | 2.3 |
| Repeated scaling and root planing | Listgarten *et al.* (14) | 2.2 |
| Tetracycline fibers | Newman *et al.* (15) | 1.8 |
| Minocycline gel | Timmerman *et al.* (16) | 2.3 |
| Minocycline ointment | Van Steenberghe *et al.* (17) | 1.9 |
| Doxycycline gel | Garrett *et al.* (18) | 1.3 |
| Metronidazole gel | Stelzel & Flores-de-Jacoby (19) | 1.3 |

*Caution must be exercised in comparing treatment studies that are non-calibrated and differ in types of patients and clinical measurement techniques.

Considering potential problems with selectivity of antimicrobial action and possible development of resistant bacteria and adverse host reactions, topical antibiotic therapy seems to constitute a less desirable choice than the use of a broad-spectrum antiseptic agent with low potential for adverse reactions. Also, commercial topical antibiotic devices tend to carry high financial costs. When choosing between equally effective and safe drug therapies, preference should usually be given to the one having the lowest cost. If dental practitioners desire to utilize antibiotics topically in periodontal therapy despite the propensity of most antibiotics to induce bacterial resistance, then the choice of antibiotics should be restricted to those that are too toxic to be administered systemically (bacitracin, polymxyin B, neomycin) or are unlikely to develop resistance (metronidazole). Double or triple antibiotic combinations may then be used to provide an adequate spectrum of antibacterial activity. However, periodontal sites having yeast infections may respond adversely to antibiotic medications directed against bacterial pathogens.

## Topical antiseptics

An antiseptic is an agent that, applied to living tissues, is able to prevent or arrest the growth or action of microorganisms. Antiseptics have a considerably broader spectrum of activity than antibiotics and, in contrast to antibiotics, often have multiple intracellular targets which reduce the likelihood of resistance development. However, since antiseptics, unlike antibiotics, are potentially toxic to both infectious agents and host cells, their application in humans is limited to infected wounds, skin and mucosa.

### Povidone-iodine

The antibacterial properties and uses of iodine-povidone in medicine are well established. The natural element, iodine, has been used for more than 150 years in mucosal antisepsis, in the therapy of skin infections and burns, and in wound management. Yet, only after the introduction of povidone-iodine in the 1960s, was it possible to employ this highly efficient microbicide to a wide variety of bacterial, fungal and viral infections. Short durations of povidone-iodine contact with various periodontopathic bacteria provides effective *in vitro* killing (21, 22). Also, povidone-iodine exhibits marked anticytomegalovirus activity (23), a herpesvirus implicated in the pathogenesis of periodontitis (24). Emergence of povidone-iodine resistance microorganisms has not been reported to have been detected to date. Despite its impressive antimicrobial properties, povidone-iodine is not widely used in the prevention and treatment of oral infections in the USA and Europe.

Povidone-iodine is water-soluble, does not irritate healthy or diseased oral mucosa, and exhibits no adverse side-effects, such as discoloration of teeth and tongue and change in taste

sensation, as seen with chlorhexidine. Blue povidone-iodine stains on starched linen will wash off with soap and water. Other types of povidone-iodine stains can be readily removed with 5% sodium thiosulfate solution. Povidone-iodine has the potential to induce hyperthyroidism due to excessive incorporation of iodine in the thyroid gland and should therefore be used only for short periods of time. Contraindications are patients with iodine hypersensitivity and thyroid pathosis, as well as pregnant and nursing women in order to protect the infant (25).

For subgingival irrigation, an effective concentration is 10% povidone-iodine applied repeatedly by an endodontic syringe to obtain a contact time of at least 5 min. This is generally performed upon completion of each session of scaling and root planing, but may also be done prior to mechanical debridement to reduce the risk of bacteremia, particularly in medically compromised individuals and in patients with severe gingival inflammation. For use in ultrasonic scalers, 10% povidone-iodine is diluted by mixing 1 part solution with 9 parts or less of water, dependent upon patient acceptance. A controlled release device for subgingival application of povidone-iodine has been developed (26); however, because of rapid microbial killing by povidone-iodine, a short-term application of the agent alone may produce an adequate antimicrobial effect.

Table 2 illustrates the ability of povidone-iodine to exert considerable antibacterial activity in the oral cavity, whether used to treat mild to severe periodontal infections or to prevent bacteremia after surgical procedures. Povidone-iodine mouthrinse/gargle has shown a reduction in gingival surface bacteria by about 33% compared to 8% by the control solution (47). Also, subgingival irrigation with povidone-iodine prior to tooth extraction has reduced the incidence of bacteremia by 30–50% (36, 38, 48–53), although not in all studies (54). The American Heart Association has suggested that antiseptic mouthrinses such as povidone-iodine applied immediately prior to dental procedures might reduce the incidence or magnitude of bacteremia (55).

Because of its antibacterial, antifungal and antiviral properties, povidone-iodine is potentially useful in treating HIV-related oral infections (34, 45, 56, 57). Investigators have also reported on favorable clinical outcome after treating advanced periodontitis with subgingival povidone-iodine and systemic antibiotics (58–61). In periodontal lesions exceeding 6 mm in probing depths, Christersson *et al.* (62) detected gain in probing attachment of 2 mm or more in 80% of sites treated with 0.5% povidone-iodine subgingival irrigation but only in 55% of placebo-treated sites. Rosling *et al.* (63) found that 0.1% povidone-iodine used as an irrigant with ultrasonic debridement caused significantly more decrease in probing pocket depth and more gain in probing attachment level during the first 12 months post-treatment and significantly less loss of attachment over the entire 13-year study period than ultrasonic scaling using water irrigation. However, relatively few studies on the utility of povidone-iodine in the treatment of oral infections have been carried out in the USA and Europe and none is a large multicenter investigation. The high costs of multicenter studies and the fact that a whole-mouth periodontal treatment by povidone-iodine has medication expenses of less than 20 cents may constitute impediments for obtaining research funding, at least from commercial sources.

### Sodium hypochlorite

Sodium hypochlorite (household bleach) has been used as a disinfectant for more than 100 years, as an antiseptic for more than 85 years, and as an endodontic irrigant for more than 75 years. Hecker (64) in 1913 used antiformin (concentrated sodium hypochlorite solution) as an epithelial-specific solvent in the treatment of periodontal disease. Sodium hypochlorite has many of the properties of an ideal antimicrobial agent, including broad antimicrobial activity, rapid bactericidal action, relative non-toxicity at use concentrations, no color, no staining, ease of access, and very low cost. The active species is undissociated hypochlorous acid (HOCl). Hypochlorite is lethal to most bacteria, fungi and viruses. Activity is reduced by the presence of organic material, heavy metal ions and low pH. Hypochlorite solutions will gradually lose strength, so that fresh solutions should be prepared daily, especially if the solution is not stored in closed brown opaque containers. Disadvantages include irritation of mucous membranes when used in high concentrations, bleaching of colored fabrics and corroding effect on some metals. No contraindications exist.

A sodium hypochlorite solution for subgingival irrigation can be prepared from household bleach that usually contains 5.25–6.0% of available chlorine. If 1 part bleach is combined with 49 parts water, the resulting solution will contain an appropriate working concentration of about 0.1% or 1000 p.p.m. of available chlorine. In actual use situations, a working bleach solution can be obtained by adding 1 teaspoon (5 ml) household bleach to 250 ml water (approximately 2 large drinking glasses), and deliver the bleach solution subgingivally via a commercial oral irrigator at a high pressure setting. The lowest concentration of chlorine that reliably inactivates test bacteria *in vitro* is 0.01% (65). In experimental biofilms with various endodontic/periodontal pathogens, the highest bactericidal activity was obtained with 2.25% sodium hypochlorite and 10% povidone-iodine followed by 0.2% chlorhexidine (66). At low concentrations, sodium hypochlorite can be used as a debriding and topical antibacterial agent for wounds and skin ulcers without inhibiting fibroblast activity (67).

Kalkwarf *et al.* (68) showed histologically that subgingival application of sodium hypochlorite solution might be adequately controlled to provide chemolysis of the soft tissue wall of a periodontal pocket with minimal effect upon adjacent tissues, and may exert no adverse effect upon healing. Kalkwarf *et al.* (68) recommended the use of subgingival sodium hypochlorite irrigation in the maintenance phase of periodontal therapy. That sodium

hypochlorite application might improve periodontal histological healing was suggested by Perova *et al.* (69) who found markedly better regeneration of connective tissue at the gingival base of sites that had received an application of 0.1% hypochlorite for 10 min during periodontal surgery than in control sites. However, dilute sodium hypochlorite treatment may not enhance the outcome of pedicle flap surgery for the coverage of gingival recession (70).

Lobene *et al.* (71) showed that subgingival irrigation with 0.5% sodium hypochlorite (Dakin's solution) caused significantly greater and longer lasting reduction in plaque and gingivitis than irrigation with water. In localized juvenile periodontitis lesions, gingival curettage with dilute sodium hypochlorite irrigation caused greater reduction in proportions of subgingival spirochetes than water irrigation (72). Dilute sodium hypochlorite applied to extracted teeth resulted in more than 80-fold less adherent endotoxin compared to water application (73). The American Dental Association Council on Dental Therapeutics proposed using dilute sodium hypochlorite as a topical antiseptic, for irrigation of wounds and as a mouthrinse (74). Considering sodium hypochlorite's significant antimicrobial properties and good safety profile and the promising research data, it seems rational to recommend hypochlorite subgingival irrigation as part of patients' oral self-care regimen.

### Chlorhexidine

Chlorhexidine is a diphenyl compound that is active mainly against bacteria and exhibits limited activity against viruses. Chlorhexidine demonstrates substantivity to tooth surfaces and oral mucosa and exhibits low irritability, even though adverse reactions after oral chlorhexidine rinsing have been described (75). It is cationic and, thus, incompatible with anionic compounds including some dentifrice ingredients that neutralize its action. Its activity is greater at alkaline than at acid pH and is reduced in the presence of organic matter. The latter feature may pose a problem with use in subgingival sites containing high levels of serumal proteins.

Chlorhexidine mouthrinsing to combat biofilms in supragingival and oral mucosal sites should be performed with 10–15 ml of a 0.12–0.2% solution for 30 s twice daily, and not in conjunction with brushing using a dentifrice. However, 0.2% chlorhexidine exhibits little bactericidal activity against various enteric gram-negative rods (76) and microorganisms of experimental biofims (77). Enteric rods and pseudomonas may be present in approximately 15% of advanced periodontitis lesions in the USA (78) and in higher proportions in developing countries (79). The propensity of chlorhexidine to dark-stain teeth and tooth-colored restorations is a significant adverse effect in some patients.

0.2% chlorhexidine is usually not efficacious for subgingival irrigation (20, 80), and causes less change in the subgingival microbiota than low strength (0.05%) povidone-iodine (81). Using 2% chlorhexidine, as in root canal (82) and wound (83) irrigation, may provide more effective killing of subgingival pathogens. However, even low concentrations of chlorhexidine may be toxic to gingival fibroblasts and reduce the production of collagen and non-collagen proteins, potentially impeding periodontal healing (84).

Chlorhexidine chips for subgingival placement are commercially available but they seem capable of reducing mean probing depth by less than 1 mm in 4–6 mm deep periodontal pockets (85) and may not cause noticeable reduction in periodontal pathogens compared to thorough scaling and root planing (86).

## Clinical protocol for effective antimicrobial periodontal therapy

Recent articles have outlined current concepts of initial (87) and maintenance (88) antimicrobial periodontal therapy. An effective antimicrobial therapy takes into account the periodontal status of the patient and the microbial ecology of the entire oro-pharyngeal cavity. The proposed antimicrobial strategy emphasizes intensive, professionally administered antimicrobial treatment using a battery a well-tolerated antimicrobial agents (systemic antibiotics (if needed), povidone-iodine for subgingival irrigation, chlorhexidine mouthrinse), each exhibiting high activity against various periodontal pathogens, and delivered in ways that simultaneously affect pathogens residing in different oral ecological niches, followed by maintenance care having a strong anti-infective emphasis (including dilute sodium hypochlorite subgingival irrigation by the patient).

Effective periodontal treatment gives rise to a plaque microbiota predominated by gram-positive and potentially cariogenic microorganisms as well as gingival recession that may expose root surfaces with little fluoride content. Therefore, it is prudent to instruct patients to apply, on a daily basis, 0.05% sodium fluoride rinse or 1.1% sodium fluoride or 0.4% stanous fluoride gels, delivered with a tooth brush or a custom tray.

The treatment strategy described above was applied to 35 adults with severe periodontitis who, despite periodontal surgery within the preceding 1–4 years, continued to experience periodontal breakdown at multiple sites (87). Patients received instruction in oral hygiene measures including home-irrigation with dilute sodium hypochlorite, scaling and root planing, subgingival povidone-iodine irrigation, chlorhexidine mouthrinse and systemic antibiotic therapy, and were enrolled in a meticulous 3–4-month recall program. After 4–6 years, no single periodontal site revealed additional loss in probing attachment, and approximately 6% of periodontal sites gained in excess of 2 mm in attachment and deep periodontal pockets showed considerably less probing depths. Periodontal pathogens dominating the pretreatment microbiota were either undetectable or markedly reduced at the end of the study. The study did not delineate the relative effectiveness of the various antimicrobial agents used.

In another study of refractory periodontitis, Collins *et al.* (61) found that systemic amoxicillin/clavulanic acid,

*Table 2*. Efficacy of povidone-iodine in the prevention and treatment of oral infections

| Authors | Outcome variables | Patients | Treatment | Conclusion |
|---|---|---|---|---|
| Clark *et al*. (27) | Plaque and papillary bleeding | 101 subjects | Subgingival irrigation daily with povidone-iodine/hydrogen peroxide or with water for 6 months | Significantly more reductions in plaque and papillary bleeding scores with povidone-iodine/hydrogen peroxide |
| Wolff *et al*. (28) | Gingival bleeding | 74 patients with gingivitis or early periodontitis | 42 patients performed subgingival irrigation with povidone-iodine and 32 patients performed no subgingival irrigation | Significantly lower gingival bleeding scores at 8 weeks in the povidone-iodine group |
| Ueda *et al*. (29) | Clinical periodontal variables | 11 adult periodontitis patients treated in a split-mouth design | Ultrasonic scaling with 0.02% povidone -iodone irrigation or water irrigation | Significantly more reduction in bleeding upon probing with povidone-iodone |
| Cigana *et al*. (30) | Clinical and histological periodontal variables | 12 patients with advanced periodontitis | Subgingival irrigation with povidone-iodine or with water once a day for 15 days | Significantly more reductions in plaque, bleeding upon probing and inflammatory cell infiltrate with povidone-iodine |
| Maruniak *et al*. (31) | Gingival bleeding upon probing | 71 subjects with gingivitis | Supervised 14-day twice daily rinsing with povidone-iodine/hydrogen peroxide mouthrinse | Bleeding reduced more with povidone-iodine than with Listerine Antiseptic® or water |
| Forabosco *et al*. (32) | Periodontal pocket depth reduction | 8 adult periodontitis patients treated in a split-mouth design | Ultrasonic scaling with 0.5% povidone-iodine or Widman flap surgery | Similar clinical outcome after ultrasonic scaling and after periodontal surgery in pockets up to 7 mm depth |
| Okada *et al*. (33) | Gingivitis | 2 children with chronic neutropenia and gingivitis/periodontitis | Daily rinsing with 1% povidone-iodine, subgingival minocycline gel (1 child), and scaling and root planing | Improvement of gingival conditions |
| Chidzonga (34) | Acute phase resolution of cancrum oris | 8 HIV/AIDS patients having cancrum oris | Debridement of necrotic tissue and povidone-iodine lavage | Satisfactory resolution of the acute infection |
| Nakagawa *et al*. (35) | Subgingival total viable bacterial counts | 26 untreated periodontitis lesions and 15 untreated gingivitis lesions | Subgingival irrigation with povidone-iodine or saline | Levels of viable bacteria were reduced by 98% with povidone-iodine and by 83% with saline irrigation |
| Aguada *et al*. (36) | Subgingival microbiota and bacteremia | 26 patients | 13 patients received povidone-iodine oral rinse and subgingival irrigation and 13 patients received placebo prior to tooth extraction | Significant reduction in subgingival viable counts and in incidence of postoperative bacteremia with povidone-iodine compared to placebo |
| Okuda *et al*. (37) | Salivary microbiota | 3 subjects | Subjects rinsed the oral cavity with 0.2% povidone-iodine | Levels of viable anaerobic bacteria reduced by 99% |

| | | | | |
|---|---|---|---|---|
| Rahn *et al.* (38) | Bacteremia | 120 patients (40 patients in each group) receiving either intraligamentary injection or extraction of a molar | Subgingival irrigation with 10% povidone-iodine, 0.2% chlorhexidine or sterile water | Lowest levels of incidence of bacteremia and total number of organisms in blood after povidone-iodine irrigation |
| Redleaf & Bauer (39) | Clinical wound healing | 106 consecutive patients undergoing head and neck surgery | Oral rinse with povidone-iodine or no rinse | Significantly more favorable wound healing with povidone -iodine |
| Rahn *et al.* (40) | Presence, degree and duration of oral mucositis after antineoplastic treatment | 40 patients undergoing radiochemotherapy of the head and neck region | 20 patients rinsed the oral cavity 4 times daily with povidone-iodine and 20 patients rinsed with sterile water | In the povidone-iodine group, oral mucositis was seen in 14 patients (mean grade 1, mean duration 2.75 weeks). In the control group, oral mucositis was seen in all 20 patients (mean grade 3.0, mean duration 9.25 weeks). All differences were statistically significant |
| Kovesi (41) | Prevention of infections after surgical interventions | 25 patients with periodontal disease and other oral infections | Povidone-iodine oral rinse | Povidone-iodine showed excellent action against bacterial and fungal infections in the oral cavity |
| Summers *et al.* (42) | Oral microbiota | 30 patients receiving maxillofacial surgery | Preoperative oral rinse with povidone-iodine (10 patients), saline (10 patients), or no preparation (10 patients) | Significant and sustained reduction of anaerobic and aerobic bacteria with povidone-iodine but not with saline |
| Domingo *et al.* (43) | Microbiota of cheek mucosa and saliva | 20 patients | Patients rinsed the oral cavity with 20 ml of 1% povidone-iodine for 30 s | Significant reduction in total viable counts for up to 4 h (end of study) |
| Lopez *et al.* (44) | Incidence of early childhood caries | 31 subjects aged 12–19 months | Every 2 months for 5–7 months subjects had 10% povidone-iodine (test) or instant tea (control) applied to their dentition | 0 of 15 test subjects but 5 of 16 control subjects experienced dental caries (statistically significant) |
| Rahn (45) | Periodontal disease and wound infections in immunocompromised patients | Review | | Subgingival irrigation with povidone-iodine will reduce gingival inflammation and progression of periodontal disease, as well as prevent wound infections following surgical interventions in patients having leukemia, AIDS and immunosuppressant therapy |
| Bouchlariotou *et al.* (46) | Periodontal disease and bacteremia | Review | | Subgingival irrigation with povidone-iodine is recommended to reduce pathogenic bacteria and to decrease bacteremia after dental procedures |

along with subgingival povidone-iodine application, resulted in probing attachment gain of at least 1 mm in 41% of deep sites at 3 years post-treatment. They also showed that the combined mechanical and therapeutic intervention reduced subgingival *P. gingivalis* to below detectable levels in 10 of 11 culture-positive patients. Since systemic amoxicillin/clavulanic acid may cause only minor changes in the subgingival microbiota (89), most of the clinical and microbiological benefits observed were probably due to the mechanical debridement and the subgingival povidone-iodine irrigation.

Recently, Hoang *et al.* (90) showed that subgingival irrigation with 10% povidone-iodine, together with scaling and root planing, was able to reduce total subgingival counts of periodontal pathogens at 5 weeks post-treatment by more than 95% in 44% of sites exhibiting pocket depths ≥6 mm and radiographic evidence of subgingival calculus. In contrast, scaling and root planing alone, povidone-iodine irrigation alone and water irrigation alone caused a 95% reduction of periodontal pathogens in only 6–13% of study sites ($p = 0.02$). Periodontal sites treated with povidone-iodine and scaling and root-planing showed an average reduction of 1.8 mm in probing pocket depth. Evidently, subgingival irrigation with povidone-iodine can help control periodontal pathogens but should be performed in conjunction with mechanical debridement, at least in deep and calculus-affected periodontal pockets.

Clearly, dental practitioners and patients can benefit significantly from not relying solely on mechanical periodontal therapy but on a combination of mechanical debridement, possibly in conjunction with surgery, systemic antibiotics when indicated, subgingival application of effective and safe antiseptics by dental professionals and patients, and patients' oral hygiene efforts.

## Concluding remarks

It is relevant to employ antimicrobial medications to control effectively various types of periodontal disease. Combating periodontal infections is best accomplished by combined mechanical and chemotherapeutic efforts of the dental professional and the patient. It can be concluded that properly used systemic antibiotics and subgingival irrigation with 10% povidone-iodine (dental professionals) and 0.1% sodium hypochlorite (patients) along with oral rinsing with 0.12–0.2% chlorhexidine constitute effective, essentially safe and inexpensive antimicrobial therapies that can readily be incorporated into the current armamentarium for periodontal treatment. An effective anti-carious fluoride treatment should constitute an integrated part of periodontal therapy. Continued research into anti-infective agents to prevent and treat periodontal diseases will undoubtedly lead to even more effective therapies. With the improved knowledge of the periodontopathic microbiota and with various safe and affordable, yet effective, periodontal antimicrobial agents and therapies, the future looks bright for patients at risk of or suffering from destructive periodontal disease.

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