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COMMENTARY

Concise evaluation and therapeutic guidelines for severe periodontitis: A public health perspective

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1 | INTRODUCTION AND BACKGROUND

Periodontitis is a worldwide health problem that can lead to tooth loss and increased risk for low-birth-weight infants, cardiovascular disease, cancer, and numerous other systemic diseases.[1] Comorbidity between periodontitis and serious systemic diseases provides a compelling argument for expanding periodontal health care to individuals of all income groups. However, periodontal treatment is beset by high cost and inequitable care. A population-wide approach to periodontal disease management needs to be low-priced with long-lasting impact.

Best practices for diagnosis, prevention, and treatment of periodontal disease remain important topics of research. Current therapies are proficient in controlling gingivitis and stable types of periodontitis, but despite skilled and dedicated professional care, patients with progressive/active periodontitis often experience further disease progression. Patients that fail to perform adequate oral hygiene are at elevated risk for continuing periodontal breakdown. However, progression of periodontitis can occur also in individuals who are committed to recommended oral hygiene procedures and regular supportive therapy.[2]

A cost-efficient treatment of severe periodontitis must target the etiology of the disease. Dental biofilms and calculus were traditionally thought to cause periodontitis, but an etiology based on biofilm accumulation alone cannot explain the site-specificity of periodontal breakdown, especially angular bony defects, which may approach the apex of one tooth while barely involving a neighboring tooth sharing the same interdental space. Such clinical observations led in the 1970s to a reappraisal of the etiology of periodontitis, from being a microbiologically nonspecific disease to a specific infection involving unique anaerobic bacteria. Herpesviruses became part of the etiology of periodontitis in the late 1990s, further underscoring the microbial specificity of the disease.[3] Targeted therapy against herpesviruses and key bacterial pathogens rather than against merely bacterial biofilms improves the management of severe periodontitis. This article reflects on current periodontal therapy and presents a pathogen-specific alternative treatment of severe periodontitis.

2 | EFFICACY OF CURRENT PERIODONTAL TREATMENTS

The overarching goal of periodontal treatment and the expectation of patients is the arrest of periodontal breakdown. Table 1 shows common periodontal treatments,[4–8] including highly comprehensive surgical and nonsurgical interventions with careful follow-up[4–6] and with the adjunctive use of single antibiotics.[5] Disappointingly, up to 39.1%[5] and 35.7%[6] of treated patients experienced progressive disease within a few years (Table 1). It is also unsettling that minimally treated or untreated periodontitis sites showed 5-year breakdown rates of 11.6% (>2.0-mm clinical attachment loss)[7] and 7.1% (1-mm probing alveolar bone loss),[8] which is a level of disease progression comparable with that of meticulously treated sites (Table 1). These findings are in contrast to the generally positive outcome reported for periodontal treatments.

The treatment failure probably relates to inability of scaling and flap surgery to reach billions of herpesviruses and bacterial pathogens within deep periodontal pockets and the inflamed gingiva of severe periodontitis lesions.[2] In contrast to purely mechanical intervention, systemic anti-infective drug treatment (or gingivectomy) can potentially suppress pathogens in the entire periodontium. Another problematic issue is the common use of average change in clinical variables to determine therapeutic outcome. Because the percentage of treated periodontal sites with 1 to 2 mm of probing attachment

gain (long-junctional epithelial attachment gain of uncertain clinical significance) greatly exceeds the proportion of deteriorating sites (Table 1), a dentition-wide average of attachment changes tends to overstate treatment efficacy. A better measure of therapeutic effectiveness would be the ability (or inability) to arrest or prevent disease progression in every single periodontal site of a dentition.

3 | PATHOGEN-SPECIFIC ANTI-INFECTIVE THERAPY OF SEVERE/PROGRESSIVE PERIODONTITIS

Table 2 presents an antimicrobial therapy that specifically targets periodontal herpesviruses (valacyclovir [Valtrex®]) and bacterial pathogens (amoxicillin-metronidazole, ciprofloxacin-metronidazole), and includes antiseptics (sodium hypochlorite [diluted regular household bleach]) and ultrasonic scaling. The two antibacterial drug combinations exert synergistically therapeutic effects and have a long history of use in periodontics.[9] Valacyclovir is a potent anti-herpesvirus drug that is widely used in medicine to treat herpesvirus infections. Valacyclovir inhibits herpesvirus DNA polymerase and is effective only against active (lytic) herpesviruses. Hundreds of millions of copies of active herpesviruses can inhabit a severe periodontitis lesion.[2,10] Valacyclovir monotherapy has produced impressive disease reversals in periodontics and endodontics. Sunde et al[11] treated Epstein-Barr virus-associated refractory periodontitis with 10 days of oral valacyclovir (500 mg twice daily). Posttreatment examination at 12 months revealed absence of periodontal Epstein-Barr virus and a "dramatically" improved periodontal health status. Sabeti et al[12] treated symptomatic apical abscesses with 3 days of

TABLE 1 Appraisal of the efficiency of conventional (mechanical) periodontal therapy[a]

Study	Periodontal treatment	Periodontal outcome	Comments
Ramfjord et al.[4]	72 US adults with moderate-to-advanced periodontitis were each treated (in randomized quadrants) with: Group (i): SRP alone Group (ii): surgical pocket elimination/reduction Group (iii): MWF Group (iv): subgingival curettage Oral hygiene instructions and professional tooth cleaning every 3 mo Length of study: 5 y	CAL changes: % sites with gain (≥2 mm), % sites with loss (≥2 mm) 4-6 mm initial pocket depth: (i): 11.5, 21.1 (ii): 6.6, 29.3 (iii): 7.1, 27.9 (iv): 9.1, 22.6 7-12 mm initial pocket depth: (i): 29.5, 14.8 (ii): 18.5, 10.8 (iii): 22.6, 8.1 (iv): 32.7, 10.9	The difference in outcome among the 4 treatment groups was not statistically significant 4- to 6-mm pockets: 25% of sites lost CAL, mainly because of trauma from treatment 7- to 12-mm pockets: Patients showed average CAL gains of 0.43-1.04 mm. 63% of sites remained unchanged 11.2% of sites lost CAL (untreated periodontitis showed a similar CAL loss of 11.6%; see Lindhe et al. below)
Haffajee et al.[5]	92 US adults with moderate periodontitis were randomly assigned to receive: Group (i): SRP alone Group (ii): SRP + 500 mg azithromycin QD for 3 d Group (iii): SRP + 250 mg metronidazole TID for 14 d Group (iv): SRP + 20 mg doxycycline BID for 3 mo Each participant contributed with up to 168 periodontal study sites Length of study: 1 y	CAL changes: % sites with gain (≥2 mm), % sites with loss (≥2 mm) (i): 1.7, 0.8 (ii): 5.4, 0.2 (iii): 3.7, 0.2 (iv): 2.9, 0.7 % patients with loss of CAL: (i): 39 (ii): 32 (iii): 17 (iv):15	67 of the 92 study participants attended all dental visits Metronidazole + SRP provided clinical benefit over SRP alone ($P < .05$) No treatment regimen was able to prevent CAL loss in all patients 39.1% of the patients receiving SRP only showed additional attachment loss at 12 mo
Rams et al.[6]	56 US adults with generalized severe/refractory periodontitis and 1356 posterior interproximal sites Treatment included initial oral hygiene instruction, MWF, and repeated SPT for at least 1 y prior to entry into a 30-mo study, which, at every 3 mo, included SPT, full-mouth SRP, and clinical measurements. Periapical and bitewing radiographs were obtained at baseline and at the end of the study at 30 mo Length of study: 2.5 y	Progressive periodontitis was detected at 33 (2.4%) posterior interproximal sites in 20 (35.7%) patients Sites with angular bony defects developed progressive periodontitis more frequently (14.7%) than sites with a horizontal bone topography (1.8%) Periodontitis progression was not identified for 24 mo in sites showing intact radiographic crestal alveolar lamina dura or Class II and III furcation involvement at baseline	As many as 35.7% of adult periodontitis patients experienced ongoing periodontal breakdown over the 2.5-y study period despite careful SPT, full-mouth SRP, and initial flap surgery, performed by experienced and calibrated dental hygienists and periodontists Angular bony defects with no radiographic evidence of crestal alveolar lamina dura were particularly prone to additional breakdown

TABLE 1 (Continued)

Study	Periodontal treatment	Periodontal outcome	Comments
Lindhe et al.[7] Untreated patients	64 Swedish adults with mild-to-moderate periodontitis were monitored for CAL changes between baseline examination and 3- and 6-y follow-ups No periodontal treatment performed initially or during the 6-y study period. Length of study: 6 y	During the 6-y study, 523 sites (11.6%) showed additional CAL loss of >2 mm, and 11 sites (0.2%) showed >2 mm of CAL gain Risk of CAL progression was similar for sites with initially severe vs less severe disease	Progression of periodontitis was a relatively infrequent event (11.6% of sites) in patients with untreated disease Sites with initially moderate vs less severe CAL loss showed a similar rate of disease progression
Renvert et al.[8] Minimally treated patients	12 Swedish adults with moderate-to-severe periodontitis were initially treated with flap surgery (MWF, 21 defects) or SRP alone (SRP, 21 defects) and followed for 5 y SPT included oral hygiene instruction and tooth polishing every 6 mo, but no subgingival scaling An electronic pressure-sensitive probe with markings every 1 mm measured CAL and PBL Length of study: 5 y	≥1.0 mm PBL gain: 6 MWF-treated sites 2 SRP-treated sites 0.25-0.75 mm PBL "gain": 7 MWF-treated sites 6 SRP-treated sites 0 mm PBL changes: 2 MWF-treated sites 4 SPR-treated sites 0.25-0.75 mm PBL "loss": 4 MWF-treated sites 8 SRP-treated sites 1.0–2.0 mm PBL loss: 2 MWF-treated sites 1 SRP-treated site	In minimally treated subgingival sites of patients with moderate-to-severe periodontitis, 35% of sites experienced "loss" of PBL over a 5-y period Only 3 sites (7.1%) revealed a distinct additional loss of PBL (≥1.0 mm)

Abbreviations: BID, twice daily; CAL, clinical attachment level; MWF, modified Widman flap surgery; PBL, probing bone level; QD, once daily; SPT, supportive periodontal therapeutic maintenance program; SRP, scaling and root planing; TID, thrice daily.

[a]Data compiled from renowned research groups in clinical periodontology.

TABLE 2 Treatment of severe/progressive periodontitis

Treatment	Purpose/comments
Antiseptic treatment using 0.1%-0.2% sodium hypochlorite (dilute regular household bleach)	a. Cooling spray in ultrasonic scalers using sodium hypochlorite[13] or 1% povidone-iodine (Betadine®)[14] to reduce pathogenic viruses and bacteria and minimize aerosolization of infectious agents b. Flosser fluid in oral irrigators in patient self-care: newer types of oral irrigators tolerate dilute sodium hypochlorite c. Mouthrinse in patient self-care[15,16]: freshly prepared 0.1%-0.2% sodium hypochlorite for a 30-s oral rinsing at 2-3 times weekly. Dilute sodium hypochlorite is safe and effective in reducing dental biofilm build-up and gingival inflammation (bleeding). Sodium hypochlorite is readily available as household bleach. Adding one teaspoon (5 ml) of 6%-9% common household bleach to a large glass (250 ml/8.5 oz) of water produces a 0.1%-0.2% sodium hypochlorite solution
Mechanical treatment	a. Ultrasonic scaling: scaling only periodontal sites with confirmed or suspected calculus and performed in 1 or 2 office visits depending on the amount of calculus and gingival bleeding. Antiseptics and antibiotics control periodontal pathogens in nonscaled sites b. Instruction in traditional oral self-care
Systemic anti-infective treatment after having established pharmacotherapy eligibility	a. Valacyclovir: 1000 mg BID on day 1 (baseline), and 500 mg BID on day 2 and on day 3. For systemically healthy adults b. Amoxicillin-metronidazole: 250 mg of each, TID for 4 d. For systemically healthy adults c. Ciprofloxacin-metronidazole: 500 mg of each, BID for 4 d. For immunosuppressed (old) individuals and for patients exposed to contaminated water and poor sanitation The drug doses are the lowest perceived to be effective against severe periodontitis Treatment: (a) + (b) or (c) - see text for details
Follow-up and recall appointments	Individualized scheduling according to periodontitis severity, efficacy of self-care, and environmental and medical risk factors

Abbreviations: BID, twice daily; TID, thrice daily.

oral valacyclovir (2 g at day 1 [baseline] and 500 mg, twice daily, at day 2 and day 3). On the first day following baseline treatment, the valacyclovir group ($N = 10$) showed two patients with moderate pain and one patient on pain medication, whereas an amoxicillin "placebo" group ($N = 10$) revealed as many as eight patients with pain and nine patients on pain medication. These findings lend credence to a major pathogenic role of active herpesviruses in periodontal pathosis.

Adverse drug-to-drug interactions among the proposed antiviral and antibacterial agents are rare and unremarkable, but out of an abundance of caution, the anti-infective medications might be taken successively, starting with valacyclovir, followed by a 3-day drug-free period, and ending up with one of the antibacterial regimens. In addition, to avoid excessive use of systemic antimicrobials, the recommended drug doses are the lowest perceived to be effective against severe periodontitis. For patients who show moderate levels of dental calculus and gingival bleeding and are capable of self-managing the drug prescription, perhaps with the help of day-to-day written instructions, one office visit may suffice to complete the treatment. As recognized in medicine, the more efficient a treatment is, the less need exists for routine follow-up appointments.

4 | CONCLUDING REMARKS

Conventional (mechanical) treatment of periodontitis can be prohibitively expensive and may not cure severe disease, as evidenced in Table 1. The obstacle is inability of mechanical instrumentation to reach billions of herpesviruses and bacterial pathogens in deep periodontal pockets and inflamed gingiva. By contrast, systemically delivered anti-infective drugs gain access to the entire periodontium, including tissue-invading pathogens. The treatment outlined here includes four common anti-infective medications, which are reasonably safe and have demonstrated effectiveness in managing periodontitis. The suggested therapy can help retain teeth that otherwise might have been extracted because of focal infection concerns. Also of importance, the present low-cost periodontal treatment, made possible by limited dental office visits and low-priced generic drugs, may benefit particularly underserved individuals in economically disadvantaged communities.

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