Literature Review

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Application of adjunctive periodontal treatment modalities as part of non-surgical therapy of periodontitis

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Abstract

This manuscript aims to elucidate the importance of non-surgical periodontal treatment as a prerequisite for achieving periodontal health. To accomplish a local tissue environment related to periodontal health many clinical strategies for restoring the balance between bacteria and host are introduced. In this manuscript, we will provide a short description of the different possible adjunctive modalities that supplement the standard initial periodontal therapy.

Keywords: periodontitis, nonsurgical periodontal therapy, adjunctive periodontal treatment

Introduction

Periodontitis is a widespread disease characterized by gingival inflammation, periodontal pocket formation, clinical attachment loss, and bone loss. When untreated, periodontal disease leads to aesthetic and masticatory complications increasing the risk of tooth loss, affecting the patient's quality of life, and their self-esteem. Periodontitis is considered as a complex disease in which bacterial, environmental, and genetic components are involved (1-4). Many local and systemic factors are related to the periodontal disease manifestation. While the complex bacterial dental plaque consortium, especially the gram-negative anaerobic species including the red-complex bacteria (Porphyromonas gingivalis, Tannerella forsythia and Treponema denticola) initiates the inflammation, the host`s immunity is responsible for the further destructive response. The influence of tobacco smoking and systemic diseases, such as uncontrolled diabetes mellitus, on the development of periodontal disease has been thoroughly studied and analyzed.

Smoking has an adverse effect on neutrophils of the immune system, while a distinction is made with respect to quantity, with light and heavy smokers being at different yet higher risk from non-smokers for developing alveolar bone loss, with an odds ratio of 3.25 and 7.28 respectively. While patients with uncontrolled diabetes type 2 show an odds ratio of 3.43 for alveolar bone loss (5). Bacterial plaque accumulation leads to inflammatory changes in the gingiva, resulting in the reversible disease known as gingivitis. In susceptible individuals, gingival inflammation cannot be resolved successfully, thus resulting in periodontitis, an inflammatory and destructive disease with the potential for tooth loss or loss of entire dentition (6).

Regardless, of the fact that the treatment of periodontitis takes place in several phases, the initial therapy is the one that is always present in every treatment case. In most periodontitis cases, non-surgical treatment gives satisfactory results. However, with regards to advanced periodontal disease, often a surgical approach is required, with different levels of complexity, and the need to use various techniques (7,8). Prior to any surgical procedure, periodontal treatment usually starts with nonsurgical therapy. This aims to improve the patient`s personal plaque control and eliminate the inflammatory process in the gingiva. These goals are achieved through procedures facilitating personal dental care, but also professional treatment procedures which aim to eliminate the main etiological factor for the development of periodontitis, namely the pathogenic plaque biofilm.

The initial periodontal therapy, known as "Phase 1 therapy", "Nonsurgical therapy" etc. aims to control the dental plaque by removing the supra- and subgingival deposits located on the tooth surface – either in the enamel surface or on the root surface, and between the root surface and the soft tissue wall of the periodontal pocket. Both manual (hand instruments) and ultrasonic instrumentation produce similar clinical results, however, ultrasonic use creates a less rough root surface, with less root substance removal (9). Effective periodontal care includes both self-performed dental plaque control, combined with professional periodontal treatment. Considered as a gold standard in the periodontal treatment, scaling and root planning (SRP) are sufficient procedures for the majority of patients (4).

It is accepted that scaling and root planning on quadrants or sextants is sufficient to achieve smooth and bacterial-free root surfaces. Usually, beneficial results appear in both treatment options (10). Nevertheless, in some cases, the results after these procedures don`t give the desired results. Minimally invasive nonsurgical therapy represents a gentle approach to the periodontal tissues in mechanical therapy by involving instruments with a low potential for tissue trauma. It aids in tissue healing and reduces treatment time. Usually, it is performed by means of an endoscope mini curettes and ultrasonic devices (MINST – minimally invasive nonsurgical therapy) which allow precise vision and ultimately, better results from the debridement process. This approach is considered atraumatic and leads to more predictable treatment outcomes. Interestingly, it is a treatment option even in intrabody defects. It is suggested that MINST could represent an alternative to the surgical approach. This is further supported by the clinical study of Ribeiro et al. that used 2 groups performing MINST and MIST (minimally invasive surgical technique) at 3-, 6- and 12-month reevaluation, concluding in all periods to clinical stability and similar performance. Specifically, MINST promoted a PPD (probing pocket depth) reduction of 3.19 mm, CAL (clinical attachment level) gain of 2.58 mm, and GR of 0.58 mm, while MIST showed a PPD reduction of 3.50 mm, CAL gain of 2.8 mm, and GR of 0.59 mm, in the 12-month reevaluation (11).

Although scaling and root planning are effective procedures in terms of reducing many clinical parameters of periodontitis such as pocket depth, bleeding on probing, etc. many adjunctive therapies have been introduced.

Host modulation therapy. Anti-inflammatory medicaments

In recent decades, the relationship between host response and clinical manifestation of periodontal disease has become a more focal point of investigation. From the many pharmacological medications used, the focus is pointed towards non-steroidal anti-inflammatory drugs (NSAIDs). Many clinical strategies for suppression of the destructive inflammatory response were introduced. The role of NSAIDs has been widely discussed, with an example of this being research conducted by Popova and Mlachkova. In their study, 14 patients with periodontitis were given systemic administration of Aulin for 14 days, twice daily x 100 mg. The results showed a significant reduction of the deep periodontal pockets, clinically confirmed with the rise of shallow pockets from 23.8% prior to treatment to 75.7% after the application (12).
The benefits not only restricted to pocket depth reduction and clinical attachment level gain but also to the reduction of the alveolar bone resorption process have been reported. The prolonged course of administration has risk of development of significant undesired side effects (13).
Clinical studies are showing conflicting data and although many promising results are achieved, further investigations are needed. Many studies are investigating the effect of NSAIDs on periodontal disease. Some researches are showing greater PPD reduction and CAL gain in patients undergoing supplementation of the non-surgical therapy with celecoxib compared to the placebo group. Aspirin, known for its analgesic and antipyretic properties, is a product also studied as a host modulation drug. However, the undesirable side effects of NSAIDs regarding the gastrointestinal tract, the increased risk of bleeding etc. are too many. Therefore, other alternatives are sought in modulating the host response (14-16).

Local and systemic antibiotics

In search of additional means to medical therapy, local and systemic use of various medications have been introduced. Different adjunctive methods like the local delivery of chlorhexidine, systemic antibiotics administration and local delivery of them. All the additional treatment modalities are applied in adjunct to SRP since the biofilm can protect its pathogenic bacteria from the antimicrobial effects of all these agents unless it is disrupted i.e. mechanically removed. The effectiveness of local delivery systems depends on whether the agent has reached the depth of the periodontal pocket, which enhances it due to its anatomy, and the gingival crevicular fluid concentration needs to be more than the minimum inhibitory concentration of the periodontopathogens in the area. Periochip delivers chlorhexidine subgingivally, it is a film containing 2.5 mg of chlorhexidine gluconate incorporated in a biodegradable matrix of hydrolyzed gelatine cross-linked with glutaraldehyde. In the evaluated literature, small samples were gathered between 30-45 people equally and randomly separated into 3 groups, for example group A the control group that receive only SRP, group B SRP and Glucosite gel topical application, and group C SRP and Periochip. According to the clinical comparative study of Mohammad et al., Periochip (2.5 mg CHX) was applied in the periodontal pocket with tweezers after SRP and then sealed with a suture. In the index used to monitor plaque accumulation (PI – plaque index), there was a reduction ($p<0.05$) one month after application, always with adherence to oral hygiene instructions. While for the same period, treatment was performed with multiple subgingival irrigations of periodontal pockets with 0.12% CHX gluconate after SRP, using a syringe with a blunted needle in the area of the bottom of the pocket. Irrigation was performed once a day for five days, which showed a significant reduction in plaque index and gingival index values, the clinical attachment level gain and pocket depth reduction, still with adherence to oral hygiene instructions. Chlorhexidine solution presents a higher impact on the treatment of patients with periodontitis over the Periochips, in comparison to all values used to evaluate the pocket (17,18).

However the study of Luchian et al, compared the use of Glucosite (0.2% CHX digluconate and 3% hydrogen peroxide in gel form) which was applied three consecutive times, every 24 hours, and Periochip application for both course after SRP, the group that received SRP + PerioChip treatment was the one that experienced the most significant drop in PD and PBI, even though both of them presented better results in comparison to control group, that only received SRP. This conclusion, because the parameters are close in both studies, might be the outcome of different consistency and application techniques of CHX solution and Glucosite, since for both agents the main component is CHX. Although, from both application modalities of CHX in different forms and protocols, we can report that the reduction of gingival inflammation is evident. This is furtherly supported by the evaluation of Sahmedin Saliu et al, which compares the influence of CHX application Gel and Periochip, on gingival inflammation in periodontitis cases and conventional methods (18,19).

Antibiotic systemic administration as an adjunct to mechanical debridement should be reserved and considered sensibly before selection. Clindamycin is considered a treatment choice, represents a lincosamide with broad-spectrum activity, meaning it can eliminate aerobic, anaerobic, and even β-lactamase-producing bacteria. It offers several advantages and can be used in periodontal treatment both systemically and locally with various degrees of success. However, it also has disadvantages that should not be underestimated due to their severe impact on the human organism as well as bacterial evolution, which may also dictate the treatment application. Clindamycin should not be given to those that are breastfeeding or pregnant, but even in healthy individuals, the most significant adverse effect is C. dificille-associated diarrhea, which could range from a mild form to fatal colitis. According to B. Pretzel, the age of the patient plays a significant role in the progression of CAL, in young patients with former aggressive periodontitis there was an additional benefit with the use of systemic antibiotics rather than mechanical debridement alone. Also, there are not any specific antibiotic recommendations for diabetic patients or for the ones regularly consuming tobacco. The regular ones are applied: Clindamycin or a combination of Metronidazole and Amoxicillin. According to Karrabi et al, Amoxicillin and Metronidazole combination can yield a satisfactory short-term outcome (3 and 6 months reevaluation), in cases of aggressive periodontitis, and even with CAL gain with increased dosage of Metronidazole (400-500mg). This combination, which is dose-dependent, is deemed superior for aggressive periodontitis cases, given the fact that different causal microorganisms thrive in these cases, compared to chronic periodontitis (20-23).

From comparing systemic to local application, the disadvantages of the first counteract its use, when the last could be applied as well. Cases which are refractory to treatment could be aided with adjunctive local use of clindamycin. In the local delivery system, we should have proven biocompatibility, a biodegradable substance and they should not irritate the tissues that are exposed to the antimicrobial agent. Local systems are available in a variety of forms such as gels, fibres and micro or nanoparticles. Because of the aforementioned side effects of antibiotic use, we could also consider the choice of other modalities such as photodynamic therapy (22).

Laser treatment – antimicrobial photodynamic therapy (aPDT)

Antimicrobial photodynamic therapy (aPDT) represents another additional treatment option in nonsurgical periodontal therapy, which intends to eradicate the resident microorganisms in the periodontal pocket. It is performed by activation of a photo-sensitizing agent that stimulates the formation of free radicals or singlet oxygen that eliminates bacteria. Usually Toluidine blue O or methylene blue are applied, both showing convincing results both in planktonic bacteria and bacterial biofilm. This type of treatment is orientated mainly to targeted therapy and is less invasive compared to systemic antibiotic treatment. Some studies have evaluated the benefits of non-surgical periodontal treatment combined with photodynamic therapy

compared to non-surgical periodontal treatment alone. A greater pocket depth reduction and clinical attachment gain is observed when both modalities are combined. According to the clinical study of Aykol et al., where LLLT (low-level Laser therapy) was applied as an adjunct to non-surgical periodontal therapy, the improvement was clinically significant, in all measured values compared to control groups, concluding that LLLT aids in periodontal healing (24-26).

Supplements

As with any chronic disease, periodontitis is characterized by dysbiosis changes with a prevalence of inflammation. It is known that some fatty acids (omega-6 and omega-3) can inhibit tissue inflammation, especially the leucocyte chemotaxis process, adhesion molecule expression etc. (27).
Aiming to reinforce the benefits of non-surgical periodontal treatment some additional aids can be administered. Recently scientific data highlighted the importance of reduced carbohydrate intake on periodontal tissue health. This statement is based on the importance of supplement intake in regulation of the oxidative stress. Omega-3 fatty acids are not synthesized in the human body, they include α-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid, which are acquired through the consumption of fish products oil and walnut oil (28). Many researchers have highlighted the benefits of Omega – 3 fatty acids on periodontal health - as they can control cell signalling, gene expression and inflammatory processes, leading to its anti-inflammatory action (29-31).
In their pilot study, Woelber et al. hypothesized that the low carbohydrate diet combined with rich in Omega – 3 fatty acids, vitamins C and D, antioxidants and fibres has positive impact on periodontal health which is evaluated by a significant reduction of gingival bleeding, probing pocket depths and bleeding upon probing. This outcome is obtained due to the nature of carbohydrates which increase gingival inflammation, contrary to the positive role of Vitamins C, D, and Omega 3 acting to resolve the inflammation (32). These results are supported by another study trying to provide data about the effectiveness of Omega-3 supplements as a complementary treatment in the initial periodontal therapy. Maybodi et al. included 30 patients with stage II-IV (moderate and severe) periodontitis in their study. They suggested that the intake of 1000 mg natural fish oil soft gels daily (300 mg Omega-3 marine triglycerides, 180 mg Eicosapentaenoic acid and 120 mg Docosahexaenoic acid) compared to soybean supplements results in a greater reduction of pocket depths and clinical attachment loss (4). The results of the above-mentioned studies are supported by many clinical investigations - In all the studies no side effects were reported in general, although some authors reported nausea and mouth malodor in some patients (6,33,34).

Probiotics, prebiotics and symbiotics

The pathogenesis of periodontal disease highlights the importance of balance between the pro- and anti-inflammatory host response. The imbalanced environment caused by dysbiosis changes the immune response to the bacterial challenge. Research based on probiotic intake in relation to gingivitis has shown promising results. According to the study of Hailstorm et al. performed on experimental gingivitis, GCF (gingival crevicular fluid) volume increase, appeared significant only in the group not receiving the probiotics lozenges, however, they concluded that the daily application did not seem to achieve an important action over biofilm composition and concentration under experimental conditions in gingivitis (35,36).
Prebiotics and probiotics are mostly introduced in the initial periodontal treatment as lozenges that support the main procedures performed in the Phase 1 therapy. The effects of probiotic intake along with SRP

improve the results of SRP alone by reducing the bacterial load and controlling the inflammatory mediator's expression (37,38).

Some of the most studied prebiotics include polydextrose, inulin, fructooligosaccharides, galactooligosaccharides and xylooligosaccharides, due to their beneficial effects on the immune system of humans and animals. Their general benefits include improving digestion, especially of lactose, upgrading general resistance to bacterial infection and assisting the improvement of the host`s immune response (26,39). The prebiotics can stimulate the growth of beneficial bacterial species, including lactobacilli and bifidobacterial species (40).

Many studies have been carried out about the influence of beta-methyl-D-galactoside, N-acetyl-D-mannosamine and β-glucans fibre from Saccharomyces cerevisiae. They have shown a positive impact on biofilm composition by stimulating the population of beneficial microorganisms. During the in vitro study of Slomka et al., it was proven that biofilm composition reached 96.8% ± 3.5%, instead of 72.7% ± 7.7% in the control treatment (41,42). Some studies have noted that the lactobacilli species (L. gasseri, L. salivarius and L. fermentum) and Bifidobacterium species are corresponding to periodontal health, and have abilities to maintain microflora related to periodontal health. Some bioactive molecules – small peptides, produced from Lactobacillus helveticus can increase the osteoblast activity thus promoting the bone formation (43).

In other studies, the intake of Lactobacillus reuteri as a supplement to conventional non-surgical periodontal therapy including scaling and root planning in patients with periodontitis discusses its effectiveness especially in deep periodontal pockets, however, the results are similar to other adjunctive methods (44). A study conducted by Krasse et al. shows that Lactobacilli reuteri intake has a beneficial effect against gingivitis (45).

Teughels et al. recommended the use of probiotics as adjunctive care together with scaling and root planning, especially in patients with a high risk of progression of periodontal disease and even in some sites with potential need for surgical treatment. They also enhance P. Gingivitis reduction, which is one of the most significant pathogens, enhancing the dysbiotic phenomenon between biofilm and the host organism (46).

Since antibiotic resistance represents a fundamental problem in modern-day society, many therapies are targeted to use probiotics and prebiotics that have the potential to modify the oral microbial environment.

Conclusion

The initial phase in periodontal treatment is administered in every patient suffering from periodontal disease, regardless its severity. From the information provided above, we can see that non-surgical approaches are becoming a more popular modality of therapy. It is also clear that non-surgical means of treatment are ever expanding into new areas, which incorporate the overall health of the individual, not only the health of their periodontal tissues. Since not all patients respond well enough to non-surgical therapy, it is necessary to develop additional methods that support its effectiveness. Scientific research is aimed at developing strategies that guarantee additional effectiveness of periodontal treatment. Many of them with proven effectiveness, while others require further research and study.

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ABBREVIATIONS:
SRP – scaling and root planning
MINST – minimally invasive nonsurgical therapy
MIST - minimally invasive surgical technique
PPD - probing pocket depth
CAL - clinical attachment level
NSAIDs - non-steroidal anti-inflammatory drugs
PI – plaque index
aPDT - antimicrobial photodynamic therapy
LLLT - low-level Laser therapy
GCF - gingival crevicular fluid

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