Efficacy of adjunctive Er,Cr:YSGG laser application following scaling and root planing in periodontally diseased patients

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A mis padres, Laura y Paco, por darme alas para volar

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GENERAL INDEX

General Index

1. INTRODUCTION

1. Introduction

1.1. Etiology and pathogenesis of periodontal disease

Periodontitis is an infectious disease, and today, the major pathogens have been identified. Even if bacteria are essential in the pathogenesis of periodontitis, they are insufficient to cause the disease. Research findings demonstrated the complexity of the interactions in multifactorial diseases and included roles for specific bacteria and host factors such as heredity and environmental factors (e.g. smoking) equally important as determinants of disease occurrence and severity of outcome (*for review see* 1).

The present introduction provides a short overview of the changing concepts in the etiology of periodontitis and summarizes the three main hypothesis that have been proposed over the years to explain the pathogenesis of periodontal disease (2).

1.1.1. Nonspecific plaque hypothesis

The nonspecific plaque hypothesis was an early concept based on the studies of Löe and collagues (3). It proposed that the accumulation of bacteria adjacent to the gingival margin led to gingival inflammation and subsequent periodontal destruction caused by toxic products of the bacteria. The basic thought behind the concept was the believe that the bacterial products of small amounts of plaque could be neutralized by the host. Greater amounts of plaque with their toxic products would eventually overwhelm the host defense mechanism and lead to chronic periodontitis.

While this concept is still valid for the development of gingivitis, it does not describe the development of periodontitis (1). Later on, this concept was questioned on the basis that not all gingivitis lesions progress to periodontitis. Additionally, it was noticed that bacterial sampling of periodontitis sites showed specific groups of bacteria (4). Furthermore, the concept failed to explain why some individuals accumulated high levels of plaque and demonstrated little overt periodontitis while other patients with very little plaque manifested with aggressive and advanced forms of periodontitis.

Recognition of differences in plaque at sites of health and disease resulted in an ongoing search for specific pathogens and a paradigm shift in thinking from the nonspecific to the specific plaque hypothesis.

1.1.2. Specific plaque hypothesis

This concept, first emerged in the 1970s (5), was based on the thought that specific bacteria may produce noxious products that mediate destruction of periodontal tissues. Subsequently,

specific bacteria were identified and associated with periodontitis (6) such as *Actinobacillus actinomycetemcomitans* (later renamed *Aggregatibacter actinomycetemcomitans*), a specific pathogen in juvenile periodontitis (7).

Through following the development and maturation of dental plaque, studies identified clear changes in plaque composition with a decrease in the number of beneficial commensal species and an increase in the number of specific pathogens eventually associated with periodontitis (8). These studies culminated with the identification of specific microbial groups within dental plaque (9). Six closely inter-related groups of microbes were reported, with the "red complex" consisting of *Bacteroides forsythus* (later *Tannerella forsythia), Porphyromonas gingivalis* and *Treponema denticola*, and these bacteria were significantly associated with the clinical features of periodontitis (pocket depth and bleeding on probing). It was noted that these groups of bacteria were interdependent and often could not exist in isolation. For example, the yellow, green and purple complexes are early colonizers of tooth surfaces and usually precede colonization with the orange and red complexes. It is unusual to find red-complex bacteria in the absence of the orange complex.

While the specific plaque hypothesis has provided an important conceptual framework for the microbiological etiology of periodontitis, it has been questioned in recent times. The fact that putative periodontal pathogens such as *Porphyromonas gingivalis* and *Tanerella forsythia* are frequently found in healthy periodontal sites argued against the case for them being true pathogens (10) and led to the replacement of the specific plaque hypothesis by the ecological plaque hypothesis.

1.1.3. Ecological plaque hypothesis

By the early 1990s, the ecological plaque hypothesis was proposed on the basis of the microbiological and pathogenesis data available at that time (11). In this hypothesis, it is proposed that the subgingival environment dictates or selects the specific microbial composition and this, in turn, drives the change from health to disease. More specifically, this hypothesis proposes that the nonspecific accumulation of plaque leads to inflammation within the gingival tissues and to the development of gingivitis. This again leads to

environmental changes within the gingival sulcus, which in turn favor the growth of Gram-negative and proteolytic species of bacteria. These changes all together lead to further inflammatory and immune-mediated tissue changes, further environmental changes and tissue destruction, culminating in a predominance of periodontal pathogens and a greater degree of tissue damage. Hence, the inflammation within the tissues drives the microbial changes and not vice versa, as in previous hypotheses (2).

The microflora associated with periodontal health appears to remain stable over time and exists in a state of dynamic equilibrium or "microbial homeostasis". In this context, the host is able to control the subgingival plaque through the innate immune system; there are low levels of gingival crevicular fluid relatively free of tissue-breakdown products that can be used as nutrients by the subgingival flora. However, the host inflammatory and immune response can be overwhelmed by excessive plaque accumulation (nonspecific), by plaque-independent host factors (e.g. immune disorders, changes in hormonal balance or systemic diseases such as diabetes) or by environmental factors (e.g. smoking, diet and stress). Consequently, tissue inflammation, with associated tissue degradation and increased gingival crevicular fluid rich in tissue-breakdown products and other bacterial nutrients, can lead to a shift in the subgingival plaque composition toward a more Gram-negative disease-associated flora, culminating in overt periodontitis.

The ecological plaque hypothesis is very compatible with reports that disease-associated bacteria are relatively minor components of the subgingival flora in health and increase significantly with the development of periodontal pockets and periodontitis (12, 13). In health, these organisms seem to be regulated by the interspecies competition of microbial homeostasis. It is also a question of nutrients. Many of the gram-negative anaerobes require amino acids or small peptides for growth. Gingival crevicular fluid enriched with collagen peptides from inflammation selects for these bacteria; therefore, disease is associated with an overgrowth of specific subsets of microbes within the subgingival dental plaque as a result of changes in the microenvironment.

1.2. The treatment concepts of periodontal disease in the course of time

The diagnosis and treatment concepts of periodontal disease have changed within the course of time. In the 16th century it was Bartolomeo Eustachi, who was the first to describe the removal of calculus and granulation tissue using scalers and curettes, in order to induce healing of the diseased periodontal tissues (14). Based on this pioneering work, Fauchard, a French surgeon presented a comprehensive manuscript about dentistry which

became the foremost book on dentistry. He postulated a humoral etiology of periodontal disease that is modulated by local factors like the calculus (15).

In the 19th century, thanks to the achievements in microbiology, the insights into periodontal diseases changed and consequently the treatment concepts as well. Two German physicians, Ficinus and Witzel, associated bacteria with periodontal disease and pointed out the cause-relation between the disease and tooth loss. Before, the latter has been believed to be an age-dependent, inevitable process. In the same period, the American dentist Riggs started to treat diseased pockets by calculus removal, curettage of soft tissues and implementation of oral hygiene rules to each patient (16).

In the early 20th century, peridontics began to attain the relevance of a true specialty and numerous practitioners started to limit their practice to it. Clayton Gracey from Michigan designed the curettes used by most clinicians today and Isador Hirschfeld became the leader in nonsurgical therapy. Born in 1882, he was the founder and first chair of the Department of Periodontics at Columbia University, New York.

Local mechanical debridement of teeth and root surfaces has been advocated for centuries as a treatment for periodontal disease. Some other treatment modalities have been proposed at various times and in various cultures. To these belonged cauterization, using thermal or chemical agents, the use of adstringents for hard and soft tissues and the removal of soft tissues using curettes or surgical blades.

Modern periodontics date back to the period after the second world war and it was Sigurd Ramfjord, a Scandinavian, who pioneered the use of controlled clinical studies, comparing on different quadrants of the same mouth the results obtained with different therapeutic modalities (17). In the second half of the 20th century, Löe et al. (3) demonstrated the cause and effect relationship between bacterial biofilms and gingivitis and the natural history of periodontal disease (18), and in this period most of the treatment research was focused on the therapy of gingivitis and the most common types of periodontitis.

While in the first half of the last century, the focus in the treatment of periodontal disease was directed to the eradication of the pockets, in the second half, the importance of the elimination of the inflammation moved into the center of attention.

The observation that nonsurgical mechanical therapy of chronic periodontitis was successful in the treatment of most of the patients, but not in all of them, led to the hypothesis of the host susceptibility (19). Nowadays, it is generally accepted that effective periodontal treatment has to be centered to mechanical and chemical modalities aiming for elimination of the bacteria in the periodontal pocket.

The main objective of the mechanical treatment is to minimize the bacterial load by removing deposits of plaque and calculus, and their supragingival and subgingival endotoxins. However, certain pathogens may not be accessible through mechanical interventions due to their ability to invade periodontal tissues, dentinal tubules and locations that are not accessible by periodontal instruments (20, 21, 22).

The use of antibiotics during the initial phase of the therapy as adjunct treatment to scaling and root planing has become the standard of care in aggressive and non-responsive forms of periodontitis. Clinical attachment level gains seem to bring a greater benefit in short-term studies of chronic and aggressive periodontitis, especially in deeper sites (23, 24). However, it has been pointed out that the use of systemically administrated antibiotics must be prescribed with caution, because it may increase the risk of developing bacterial resistance (25).

Due to the above-mentioned drawbacks of conventional scaling and root planing, the development of novel systems for subgingival debridement has been propagated and clinically evaluated. To these belong sonic and ultrasonic scalers and as a latest innovation, different type of laser devices. All these innovative technologies are aimed at overcoming the technical sensitivity of scaling and root planing, reducing the chair-side treatment time and improving the access to areas such as furcations, concavities and grooves which are difficult to debride with conventional curettes and scalers.

1.3. Epidemiology of periodontal disease

In the last half century, the focus of periodontal epidemiological research has been on providing data on the prevalence of periodontal diseases in different populations. Most of the studies aimed at evaluating the frequency of occurrence of periodontitis, as well as the severity of such conditions. Based on our current understanding of the etiological factors and the increased insights into the immune defense mechanisms of the human body, the task of periodontal epidemiology should be extended to the elucidation of aspects related to etiology and the determinants of these diseases (causative and risk factors). Additionally, population based epidemiological studies should provide documentation concerning the effectiveness of preventive and therapeutic measures aimed against these diseases.

Although numerous periodontal studies have been performed globally, there is still much unknown regarding risk susceptibility and prevention effectiveness and only limited data are available regarding current national estimates of periodontal disease. The most

frequently oral problems surveyed in the Spanish adult population are untreated caries lesions (18%), hypersensitivity (12%), gingivitis (9%) and tooth hypermobility (7%) (273). The reasons behind are the lack of standardized study design, the absence of uniform definitions of periodontal disease status and methods for disease detection. These factors all together, combined with inhomogenous criteria for subject selection, markedly limit the interpretation and analysis of available population based periodontal disease data from around the world.

1.3.1. Methodological issues

When first epidemiolgical studies have been performed in periodontology, the prevailing assumption was that periodontal disease was a gradually progressive disease, starting as gingivitis and ending with significant bone loss (26). The index system used in those times was based on numerical scores which increased as the periodontal conditions worsened from gingival inflammation to significant bone loss with tooth mobility (27). Early epidemiological studies and the results from World Health Organization surveys conducted in five Asian and African countries between 1957 and 1963 indicated an extremely high prevalence of periodontitis because many adults were suffering from gingivitis (28, 29). Additionally, the disease was believed to progress at a relatively even pace and continously (30). As a consequence of the mentioned surveys, it became widely accepted that the prevalence of periodontal disease was greater in the developing world compared to higher income areas.

As our understanding of the relationship between plaque, gingivitis and periodontitis has changed, so has our understanding of the global extent of periodontal disease. This change was a direct result of the changes in measurement methodology as the design of the index systems and the definition of the various scores inevitably reflects the knowledge of the etiology and pathogenesis of periodontal disease at the time these systems were introduced. In the late 1970's the Community Periodontal Index of Treatment Needs (CPITN) was introduced (31) to overcome the many limitations of the Russel's periodontal index (27) and Ramfjord's periodontal disease index (29). The CPITN was endorsed by the World Health Organization (WHO) and designed to facilitate performance of population based surveys under a variety of conditions (32). It was based on the division of the dentition into six sextants and recording of the treatment needs. For epidemiological surveys probing assessment was recommended to be performed around a limited number of index teeth. However, only the most severe measure in the sextant is chosen to represent the sextant.

The periodontal conditions are scored in four degrees. While code one and two characterize a periodontally healthy dentition, code three with pocket measurements of 4-5 millimeters represents a moderate and code four with pocket depths of six millimeters or deeper a severe periodontal disease.

A later modification of the CPITN, termed Community Periodontal Index (CPI) placed more emphasis on the assessment of periodontal conditions rather than the assessment of periodontal treatment needs (32). The CPITN methodology was quickly adopted by the periodontal research community and many epidemiological studies were reporting CPITN/ CPI results across a number of countries (33). Principal findings collected by the WHO are available online (34) and key studies showed that the global differences in the prevalence and severity of periodontal disease were not as evident as previously believed (35).

Since the beginning of epidemiological studies in periodontology, the key outcome for assessing periodontal disease was the presence or absence of periodontal pocketing. However, there has been growing concern that periodontal disease definitions should not be limited to pocket depth alone. Consequently, studies began to report periodontal disease in terms of a combination of attachment loss and pocket depth. A consensus report from the European Workshop on Periodontology in 2005 recommended that attachment loss in combination with probing depth and/ or bleeding from probing sites should characterize periodontal disease definitions (36). Additionally, the report proposed a two-tier case definition for disease based on both, the severity and the extent of attachment loss.

The newly postulated definition for periodontitis was soon confirmed by recommendations from a work group jointly sponsored by the Centers for Disease Control and Prevention and the American Academy of Periodontology (CDC/ AAP), emphasizing the use of a combination of attachment loss and pocket depth measurements for periodontal disease definitions (37).

Although these approaches are laudable attempts to use a more valid definition of periodontitis for dental and public health research, they also contribute to greater diversity in the disease definitions used. This lack of uniformity in application of case definitions for periodontal disease reduces the opportunities for comparisons across population-based studies and impedes the epidemiological and clinical research (38, 39, 40).

More epidemiological methods should be integrated into the translational process that can lead to improved periodontal health (41). Based on these requirements, the use of the CPITN/ CPI seems to fade out as the quantity and quality of studies utilizing these indexes continues to diminish (42). Furthermore, there are many examples of complaints regarding

the ability of epidemiological methods to accurately ascertain disease status, that means to measure the true prevalence of periodontitis in study populations. It has been suggested that serology could be useful for assessing periodontal status in epidemiological studies, and that serology may also be useful in investigation associations between periodontal infection and systemic health (43). This might be an interesting idea but the use of biomarkers as surrogates first has to be validated. Until then, the direct measurement of attachment loss, probing pocket depth and bleeding on probing remains the golden standard for evaluating periodontal disease.

1.3.2. Prevalence of periodontal disease in Europe

Periodontists in Europe have been at the forefront of epidemiological research. They have shown that although older people are more likely to have less periodontal support, advanced periodontal disease affects a relatively small proportion of the population, even if loss of bony support seems to be a common finding (44-47). The proportion of European 35-44 years old with shallow periodontal pockets (3.5-5.5 mm) ranges from 13% to 54% (48). The mean for East Europe was 45% and the corresponding number for West Europe 36%. The proportion of adults with deep periodontal pockets (> 5.5 mm) was below 10% in many West European countries but some East European countries had between 30% and 40% affected.

The proportion among European adults with a CPI score of 3 ranged from 13% (Ireland) to 57% (Norway). The estimated proportion of adults with a CPI score of 4 ranged from 3% (Malta) to 40% (Turkmenistan). The corresponding numbers for Spain are 21% (CPI score 3) and 18% (CPI score 4), respectively.

It has to be emphasized that the CPITN classification system was not designed as a measure of the disease and it is not surprising that it does not measure the extent of the periodontal disease accurately.There are some problems in adding up prevalence data from different studies from the WHO database. The heterogeneity of the epidemiological reports led to a modifed calculation for correction of the errors (49), nevertheless, considerable heterogeneity remains between and within the countries, and, therefore, caution should be exercised when interpreting these results.

In a recent review of global trends in periodontitis, Hugoson & Norderyd (50) suggested that a downward trend has been emerging over the last decades. However, more recent findings for Europe indicate a mixed picture, with periodontal health improving in the UK but worsening in Germany and Hungary.

1.3.3. Prevalence of periodontal disease worldwide

The percentages of people suffering from moderate or severe periodontitis for Non-European rich economies are similar to the ones reported for Europe. That means that the overall global prevalence of generalized severe periodontal disease among adults during the 1980 and 1990 appeared to be low, ranging from 5-15%. These numbers are regardless of geographical and economical considerations (51, 38).

Prevalence data for periodontitis exists from each of the world's five major geographical regions. In a review focusing on data from Asia and Oceania (52), it was reported that the number of adults aged 35-44 years with CPI score 3 ranged from 57% (Hong Kong) to 8% (Saudia Arabia). For a CPI score of 4, the percentages ranged from 28% (Nepal) to less than 5% (Sri Lanka, Syria, and New Zealand). Similar results were obtained for Africa: a CPI score of 3 was fairly frequent and a CPI score of 4 was more infrequent. The prevalence of a CPI score of 4 was reported to be > 30% in studies from Libya, Mauritius, Nigeria, Sierra Leone and South Africa.

The use of the CPITN/ CPI score has never really embraced in the USA. In the last decades national surveys used a partial-mouth periodontal assessment in which two measurements were made around each tooth in an upper and lower randomly selected quadrant (53). For younger adults living in the USA, the prevalence of attachment loss ≥ 4 mm resulted in 18-20% and for older adults (ages 60-74) in 47%. These number might be taken with caution as partial-mouth examinations underestimate disease prevalence (54, 55, 56).

The overall tendency of an increase in periodontal disease in the elderly could be ascribed to a greater retention of teeth and the tendency to treat teeth with alveolar bone loss more conservatively than in the past. Teeth lost due to the sequels of the disease are obviously not amenable to registration in epidemiological surveys and may, hence, lead to an underestimation of the prevalence and severity of the disease.

1.3.4. Risk factors for periodontal disease

Periodontitis is of multifactorial etiology like many other diseases (57). Consequently, in any particular situation when a causative relationship is investigated, the specifity of the relation between exposure to an etiologic agent and effect may be challenged. In the case of most infectious diseases it is known that the presence of the microbial agent is not always accompanied by signs or symptoms characteristic of that disorder (58). The disease depends on other influencing factors such as specific host reponses, toxic exposures, nutritional deficiencies, emotional stress and the complex impact of social influences.

These factors can be classified into 1) non-modifiable ones and 2) environmental, acquired and behavioural factors. It is important to mention that factors associated with the initiation of the disease may be different from the ones involved in its progression.

A major factor for onset of periodontitis is the specifity of the microbiota (59, 60) even if the prevalence of red complex bacteria (8) varies substantially in healthy subjects with race and ethnicity (41). Collectively, literature data has clarified the significance of bacterial load rather than that of the mere positive colonization in conferring risk for progression (61, 62, 63). Thus, an antimicrobial approach, including removal of subgingival plaque with or without adjunctive antiseptics, antibiotics or lasers followed by adequate maintenance care is the single most successful and consistent strategy in the treatment of periodontitis (64).

A second important risk factor that has been shown to be strongly associated with periodontal disease is cigarette smoking (65-67). It has been proven that smoking affects the vasculature, the humoral and cellular immune responses, cell signaling processes and tissue homeostasis (for review see 68, 69). Overall, it entails a statistically and clincially significant risk for severe disease with an estimated overall odds ratio of 2.82 (95% confidence limits 2.36-3.39) (70).

The third factor that is well established for increased risks for periodontitis is diabetes mellitus. Its association is especially pronounced in subjects with poor metabolic control and a long duration of the disease (71, 72). In contrast to the previous risk factors, several studies suggest a two-way relationship between diabetes and periodontitis, with more severe periodontal tissue destruction in people with diabetes but also a poorer metabolic control of diabetes in subjects with periodontitis (73, 74).

Other risk factors for periodontal disease are age (74), gender (76), ethnicity (77) and gene polymorphism (78), obesity (79, 80), osteoporosis (81, 82), human deficiency infection (83) and stress. However, its influences on periodontal disease have been challenged over the years or have been reduced after adjustment of the covariates such as oral hygiene levels or access to dental care services (84).

1.4. The impact of periodontal disease on general health

Based on the epidemiological evidence of risk factors for initiation and progression of periodontal disease, a plausible association between periodontitis and a number of systemic diseases gained the attraction of the researchers in the last decade.

Emerging evidence from epidemiologic studies indicates that periodontal infections have an impact on a host of peripheral blood markers that have been linked to cardiovascular diseases. In particular, periodontitis-affected patients have been shown to display higher white blood cell counts (85) and C-reactive protein levels (86). Other studies have investigated the association between periodontitis and subclinical atherosclerosis, measured by means of carotid artery intima media thickness. They confirmed a direct relationship between such intima thickness and an increased risk for myocardial infarction (87).

Within the context of the present work of laser application in nonsurgical periodontal therapy, interventional studies on surrogate markers of risk for cardiovascular diseases are of special interest.

In a trial including 94 systemically healthy patients with severe periodontitis, nonsurgical therapy and tooth extractions resulted in a significant reduction of C-reactive protein-levels six months after periodontal treatment (88). These results have been confirmed by several studies (89-91) and underlined the suggestion of a biologically plausible association between periodontal infections and the pathogenesis of atherosclerotic cardiovascular disease.

Another topic of periodontal medicine is focusing on pregnancy complications. Robust research data led to the hypothesis that preterm birth may be indirectly mediated through distant infections resulting in translocation of bacteria, bacterial vesicles or lipopolysaccharides in the systemic circulation (92). An interesting finding supports the hypothesis that periodontal infections may have an influence on maternal complications with regard to adverse birth outcome. Bacterial cultures of amniotic fluids from women with vaginosis have been showed to contain different bacteria than those usually present in the vaginal tract. Interestingly, more fusobacteria of the oral origin have been found leading to the conclusion that oral bacteria may reach the amniotic fluids and influence maternal fetal tissues via hematogenous spread (93). In fact, there is an accumulating body of evidence from human studies regarding a potential link between oral infections and adverse pregnancy outcomes (for review see 94, 95).

Impressive positive findings were reported from two randomized controlled clinical trials (96, 97). 400 pregnant women suffering from periodontitis were randomly assigned to a test or a control group. The test group patients received a periodontal treatment before 28 weeks of gestation while the control group received the periodontal therapy only after delivery. The incidence of low birth weight among the 351 women who completed the trial

was 1.8% in the treatment and 10.1% in the control group leading to an odds ratio of 5.5 (95% confidence interval 1.6-18.2, p=0.001). Even after correction of co-factors such as previous low birth weights, frequency of prenatal visits, maternal low weight gain in a multi-variante logistic regression model, periodontitis remained the strongest factor with an odds ratio of 4.7 (95% confidence interval 1.3-17.1), thus confirming peridontitis as a risk factor for preterm, low birthweight babies.

As previously mentioned, limited data seem to suggest that an inverse relationship may also be present for periodontitis being a risk factor for poor metabolic control of diabetes patients (98, 99). A follow-up study including 90 patients with moderate to severe periodontitis revealed that severe periodontitis at baseline was associated with an increased risk for poor glycemic control (100). However, further studies are needed to clarify the conditions under which periodontal treatment can contribute to improved metabolic control of diabetes mellitus.

2. FUNDAMENTALS

2. Fundamentals

2.1. Nonsurgical treatment of chronic periodontitis

Nonsurgical periodontal therapy aims to eliminate both the living bacteria in the microbial biofilm and calcified biofilm from the tooth surface and adjacent soft tissues. The goal is to restore a biological compatibility of the diseased root surface and to allow a re-adaptation of the junctional epithelium and to create an environment that favors the recolonization with less pathogenic and more aerobic species. Complete elimination of such pathogenic microflora seems to be too ambitious (105). However, the impact of subgingival debridement on the composition of subgingival plaque biofilms lasts more than one week even if has been documented that pre-debridement microbial counts are restored within 4-7 days post debridement (106). In equal measure like the decrease in the total number of microorganism, it is important that the relative proportion of different microbial species within the subgingival biofilm shifts towards Gram-positive cocci and rods. These species have been shown to be associated with periodontal health (106).

Microorganisms do never exist in isolation but rather as members of communites. Socransky et al. (8) identified groups of organisms which were commonly found together and subdivided microorganisms into complexes accordingly. Members of the red and orange complexes are most commonly identified at sites displaying signs of periodontitis.

Clinically, chronic periodontitis is strongly associated with the presence of calculus on the root surfaces. It has been shown that the deleterious effect of calculus is rather its rough surface that favors microbial colonization than the calculus composition itself (107). It has been demonstrated that even epithelial adherence can occur to subgingival calculus when it has been disinfected with chlorhexidine. Thus, the removal of calculus is the main goal of nonsurgical therapy and can be achieved with different treatment methods of instrumentation.

2.1.1. Scaling and root planing with curettes and hand instruments

Hand instruments such as curettes and scalers are used for more than 100 years and still are the "golden standard" for subgingival debridement (108). They allow a good tactile sensation but the same time hand instrumentation is technique sensitive and requires correct and frequent instrument sharpening. The inter-operator variability performing subgingival debridement was investigated for two levels of operator experience. It was found that the experienced clinician achieved a superior level of calculus removal than the less experienced one (109). Furthermore, studies proved that in more than 90% of the

cases, deposits of plaque and calculus remained in pockets deeper than 5 millimeters following scaling and root planing (107). These findings were supported by other authors who claimed that closed debridement resulted in 50% more residual calculus on the root surfaces than an open one (110). It is an interesting finding that more residual calculus was found on molar and premolar tooth surfaces (111), at molar teeth up to 60%. Some molar sites were so difficult to access that 50% or more of the surfaces with pocket depth > 7 mm showed deposits of calculus, indepently of the methodology (open or closed debridement). All these facts underline the increased diffculty in achieving successful root debridement in posterior areas of the oral cavities, in addition to the more complicated root anatomy of multi-rooted teeth.

2.1.2. Nonsurgical treatment with sonic and ultrasonic devices

Ultrasonic and sonic scalers are referred to as power scalers or power-driven scalers and have become a common alternative to hand instruments. Basically, the devices are causing microvibration which crushes and removes calculus under cooling water (112, 113). They can be subclassified into three groups, namely 1) sonic scalers that uses air pressure to create mechanical vibration which, in turn, causes instrument tip vibration. The frequencies of vibration ranges from 2000-6000 Hz (114). 2) Ultrasonic scalers that convert electrical current to mechanical energy in the form of high-frequency vibration at the instrument tip, ranging from 18'000-45'000 Hz. They can be further classified in magnetostrictive devices and piezoelectric scalers which are completey housing the transducer within the handpiece (115). The tip of the piezoelectric scaler is primarily linear in direction and its vibration can dislodge tenacious calculus from the tooth surface. 3) As a the latest generation, ultrasonic instruments, have been developed. They are working with frequencies of 25 kHz and a coupling at the head of the handpiece to transfer energy indirectly to the working tip. These instruments are cooled by a water-based medium and polishing particles of various sizes can be added to the coolig fluids (116).

The advantages of power-driven instruments are their simultaneous flushing effect by cooling. It has been shown that endotoxins just adhere to root surfaces without penetration into cementum (117) and lipopolysaccharides can be washed out easily from the non-shedding surfaces (118). Based on these findings, it is commonly accepted today that excessive removal of cementum during root planing in order to eliminate endotoxins from the exposed root is not justified. Thus, several studies suggest that almost complete

debridement of root surfaces might be achieved by relatively simple and minimal traumatic measures using power-driven instruments (119, 120, 121).

2.1.3. Limitations of nonsurgical periodontal treatment

Basically, both manual and ultrasonic scalings have been reported to be equally effective in subgingival plaque removal (122-124). Power-driven instruments may cause less operator fatigue than scalers and curettes. On the other hand they provide poor tactile sensation which is an important aspect to detect subgingival concrements. The reports regarding the amount of cementum removal are controversial. While some studies report about more root substance loss by using hand instruments (125-127), others come to an opposite conclusion (128, 129). In fact, in nonsurgical debridement, excessive cementum and dentin removal may be a risk factor for damaging the tooth unnecessarily. But again, much depends on the operator's expertise and diligence. First studies were reporting about a removal of 60 µm of root substance after 20 strokes with a curette (130). Subsequent studies corrected these numbers downwards to a substance loss of 3-9 µm by applying a lateral pressure of 750 g. In general, applied pressure and hand dexterity seem to be an important aspect and according to these studies, the root substance removal with one stroke was 1-20 µm, depending on the tooth aspect, the power of the sonic or ultrasonic scaler, the shape of the tip and whether the root surface was exposed or not.

Both therapy methods have been shown to cause pain sensation during treatment as well as in the postoperative period (131). That's why nonsurgical removal of subgingival deposits should be performed under local anesthesia. Pain from trauma peaks between 2 and 8 hours post treatment (132) but root sensitivity may be experienced for a longer period of time. Clinical trials have shown that psychosocial factors may influence anxiety, depression and stress, which, in turn, have a direct impact on pain perception (133). Additionally, it was demonstrated that pain experience during diagnostic instrumentation correlated significantly with pain experiences during root debridement (134). Therefore, pre-emptive analgesics may have a positive effect and help the patient to have a more positive experience during deep scaling (135).

Several studies have confirmed the difficulty to reach deeper portions of the pockets with scalers and ultrasonic instrument tips in nonsurgical periodontal therapy. As a consequence, deposits of calculus may remain on the root surface and impair the healing process. Pockets measuring less than 3 mm almost completely heal with reformation of a

junctional epithelium while pockets with a depth of 3 to 5 mm show a success rate of 39% and those deeper than 5 mm a corresponding one of just 11% of healing. Similarly, other studies reported about the inability to remove subgingival plaque and calculus from all tooth surfaces with more than 3.73 mm pocket depth (136).

Matsuo et al. (137) extracted 40 teeth after subgingival scaling and root planing using various instruments and evaluated the residual calculus on the surfaces. The amount of deposits were most pronounced on teeth with a previously measured pocket depth deeper than 5 mm. Pockets with less than 3 mm depth showed least amounts of residual concrements.

Once the attachment loss has progressed to the furcation area of multi-rooted teeth, microbial communities may develop undisturbed and the composition may shift to more anaerobic species. Furcation sites consistently demonstrated higher microbial counts and greater proportions of suspected periopathogens than comparable flat root surfaces after subgingival debridement (138). Generally, clinical improvement after nonsurgical debridement was found to be less pronounced in furcation sites than in other locations (139).

To summarize, both hand and sonic/ ultrasonic debridement in nonsurgical periodontal therapy seem to produce similar results with respect to probing pocket depths reduction, bleeding on probing and clinical attachment level gain (20, 140, 141). When pocket depths exceed five millimeters, the operator will be challenged with a nonsurgical approach. Anatomical limitations such as the depth of the pocket, root concavities and furcations impairs the access via a nonsurgical approach and represent a serious limitation to successful management of the disease. As the surgical approach has inherent shortcomings as well, the future of nonsurgical mechanical debridement is to create power-driven instruments whose tip dimensions or working mode provide access to the problematic sites.

2.2. Chemotherapeutics in nonsurgical periodontal therapy

As previously described, the current etiological concept of chronic periodontitis is based on many variables that influence the occurrence and progression of the disease (see 1.1.3.). As a consequence, its treatment is different from the treatment of most other bacterial infections. Today, neither the identity of the causative organisms nor the microbial agent are readily available to the periodontal practitioner. Therefore, treatment with or without adjunctive antimicrobial agents is largely based upon somewhat ambiguous clinical

parameters. The vast majority of periodontitis cases respond well to conventional nonsurgical periodontal therapy, improved oral hygiene and supportive periodontal recall. However, certain patients, for various reasons, do not respond favorably to mechanical therapy alone. For these patients, the use of an appropriate adjunctive antimicrobial might be beneficial. The problem is how to recognize the patients that will benefit from adjunctive antimicrobial therapy and which antimicrobial agent is most likely to provide the beneficial response desired with minimal adverse effects. Many of the available chemotherapeutics have been evaluated as adjunctive therapy to scaling and root planing (142). The following section will provide an overview of the available chemotherapeutics and their application form in the treatment of chronic periodontitis.

2.2.1. Adjunctive use of antibiotics, systemically delivered

The resistant nature of periodontal bacteria in the biofilm to chemotherapeutics emphazises the necessity of thorough physical removal of subgingival plaque, along with plaque retention sites. For many of the patients these measures together with conscientious oral hygiene program achieve control of the disease. Undoubtedly, for some other patients, the adjunctive use of an antibiotic either concurrently with scaling and root planing or during another phase of therapy is necessary to achieve control of the disease.

It is well accepted that bacteria in a subgingival biofilm are considerably more resistant to antibiotics than the same bacteria grown as pure cultures (143). The scientific approach to selection of an antibiotic that might be useful in the treatment of periodontitis was to determine the concentration of the antibiotic achieved in the gingival crevicular fluid and compare this level to the concentration of the antibiotic necessary to kill the bacteria associated with the diseased periodontal sites (minimum inhibitory concentrations, MICs). Using this these criteria, various antibiotics were identified that achieved levels in the gingival crevicular fluid that exeeded the MICs of the target bacteria, e.g. amoxicillin and amoxicillin/ clavulanic acid (144), the tetracyclines (145), clindamycin (146) and metronidazole (147).

The *tetracyclines* are a broad-spectrum antibiotics active against both Gram-positive and Gram-negative bacteria. Suppression of the normal flora may occur, followed by overgrowth of resistant organisms. Tetracycline derivatives, primarily doxycycline and minocycline, differ from the parent compound by minor alterations in the molecular structure. These minor alterations make both doxycycline and minocycline more lipophilic than the parent compound, resulting in better adsorption following systemic delivery and

better penetration into the bacterial cell. Thus, lower and less frequent doses of doxycycline and minocycline can be given. A number of clinical trials using various designs have been conducted to evaluate the effectiveness of the adjunctive use of systemically administrated tetracyclines (*for review see* 148). As a conclusion, systemic administration of the tetracyclines as an adjunct to scaling and root planing may yield benefits in certain patients, particularly some with localized aggressive periodontitis and in some patients refractory to previous mechanical therapy. However, there currently seem to be better choices of an antibiotic for systemic use.

The *penicillins* are a broad class of antibiotics that inhibit bacterial cell wall synthesis and directly result in the death of the cell. Molecular modifications yielded a wide variety of different properties, including improved stability to gastric acid, improved absorption and higher serum concentrations, and activity against Gram-negative as well as Gram-positive bacteria. On the other hand, allergic hypersensitivity is the most common adverse reaction and caution is advised (*for review see* 149).

Clindamycin is bacteriostatic and inhibits bacterial protein synthesis. Clindamycin-HCl has been shown, following normal oral dosage, to penetrate into the gingival crevicular fluid and to achieve and maintain concentrations that exceed the MICs of the periodontopathic Gram-negative anaerobic bacteria (146). Unfortunately, a number of undesirable adverse effects such as diarrhea, abdominal cramping and stomach irritation have been associated with the use of clindamycin (*for review see* 149).

Azithromycin belongs to the same general class of macrolide antibiotics as erythromycin but differs in several important aspects. Unlike erythromycin, it has broad-spectrum activity against a number of bacteria including Gram-negative anaerobes and provides excellent and prolonged drug concentrations in tissue and serum. Convenient dosing is a major advantage. The drug is relatively nontoxic and only a few adverse side-effects have been associated with its usage. Azithromycin has been reported to penetrate both healthy and diseased periodontal tissues and to maintain chemotherapeutic levels in excess of the MICs of the majority of periodontopathogens thought to be involved in chronic inflammatory periodontal diseases (150). Due to its unique pharmacokinetic properties and its spectrum of activity, azithromycin may prove beneficial in certain circumstances.

Metronidazole targets anaerobic microorganisms but has essentially no activity against aerobic or microaerophilic bacteria. It is an attractive antibiotic for use as an adjunct to periodontal therapy as it readily penetrates into the gingival crevicular fluid (147) and achieves concentrations in excess of the MICs established in vitro for most putative

periodontal pathogens (151). The efficacy of metronidazole in the treatment of periodontitis has been tested in a relatively large number of clinical trials (*for review see* 148). However, a significant proportion of the *A. actinomycetemcomitans* isolates tested have demonstrated resistance to metronidazole (152). Therefore, combinations of systemically administrated metronidazole and amoxicillin as adjunctive agents in periodontal therapy have been described with promising results (for review see 148). For the most part, research supports the general consensus that systemic metronidazole and amoxicillin in conjunction with mechanical debridement provides a tangible benefit over mechanical debridement alone. Available data indicate that *Aggregatibacter actinomycetemcomitans* can be controlled, if not eradicated, by systemic incorporation of an appropriate chemotherapeutic agent in conjunction with mechanical instrumentation.

In patients with insufficient response of the infected area to mechanical instrumentation, the incorporation of an appropriate systemically administrated chemotherapeutic agent may provide an additional antimicrobial effect offering increased opportunity to control disease. At present, there is no single periodontal therapeutic regimen that will provide a beneficial response for all patients. It is very unlikely that there ever will be. Based on the current literature, the evidence seems to favor the use of metronidazole/ amoxicillin as an adjunct to mechanical debridement.

2.2.2. Adjunctive use of antibiotics, locally delivered

Microbiologically, the concept of treating only those sites that are deemed to be in need of treatment by mechanically removing subgingival plaque, then subsequently applying a locally delivered antimicrobial, appears ideal. In theory, mechanical debridement serves to disrupt and displace the biofilm. Locally administered antibiotics, at concentrations much greater than can be achieved systemically, aid in site-specific elimination of residual bacteria. Equally important, local delivery of an antibiotic exhibits a negligible impact on the microflora residing in other regions of the body. Within the past decades, several locally applied controlled delivery products have been made commercially available to the practioners for the treatment of periodontitis. These products contain either tetraycline, doxycyline or minocyline. However, the clinicians have been slow to accept these devices and the learning curve as well as the time required to treat multiple periodontal sites have certainly contributed to this.

However, it seems that the major factor has been the lack of sufficient clinical response. Both tetracycline (Actisite®) and doxycyline (Atridox®) have been subjected to extensive

testing and a number of clinical trials, have been demonstrated to give statistically significant improvements in clinical (attachment level and probing pocket depth) and microbial parameters over those obtained with mechanical debridement alone (153-155). It is perhaps unfortunate that most of the clinical trials were with nonaggressive periodontitis (chronic adult periodontitis) subjects. These subjects often respond so well to scaling and root planning that it is difficult to demonstrate additional significant clinical improvement when a locally delivered antibiotic is used.

Minocycline, the most lipophilic of the tetracyclines, has also been incorporated into a local delivery device consisting of minocycline-HCl microspheres (Arestin®). Although clinical trials have not been as extensive as with the other two, positive results from clinical testing support the use of minocyline as a local delivery device as adjunctive therapy in deep or recurrent periodontal sites (156, 157).

Given metronidazole's spectrum of activity against most periodontopathogenic bacteria, its incorporation into a vehicle for local delivery seems natural. Localized delivery of metronidazole to specific, diseased sites would allow minimal amounts of drug to achieve high concentrations, alleviating many adverse reactions and unpleasant side-effects associated with systemic administration. Several systems providing various mechanisms for local delivery of metronidazole into periodontal pockets have been tested (*for review see* 158). However, the majority were never made commercially available. An exception to the above is Elyzol®, which is commercially available in many European countries but not in the United States. The use of Elyzol® as an adjunct to scaling and root planing did not demonstrate significant clinical improvements over scaling and root planing as monotherapy (159).

Another chemical agent that has often been employed as an adjunct to mechanical debridement due to its broad-spectrum antimicrobial activity is *chlorhexidine*. Its substantivity in the oral cavity and ease of use during oral irrigation or gel placement has been been proven and biodegradable chlorhexidine-containing gelatin chip (PerioChip®) has received Food & Drug Administration approval in the United States for use as an adjunct to scaling and root planing. However, only minor clinical benefits have been obtained and the antimicrobial effects on the subgingival microflora were shown to be negligible (160).

To summarize, local delivery formulations of doxycycline and minocycline may prove useful as adjunctive site therapy for individuals not demonstrating adequate initial or long-term clinical response to mechanical debridement. The use of subantimicrobial

doxycycline as an adjunct to mechanical instrumentation with or without the adjunctive use of an antibiotic should be a consideration. The inhibition of the inflammatory process and the downregulation of matrix metalloproteinases may provide a quicker return to periodontal health.

2.2.3. Adjunctive use of antimicrobial agents

The periodontal pocket is colonized by a host of different bacteria and represent a unique ecosystem that impedes the effectiveness of antiseptic agents for several reasons. First, the antimicrobial must successfully reach the target microorganisms within the subgingival plaque and second, it must achieve a concentration sufficient to inhibit target microorganisms and this concentration must be maintained at a minimally sustained level for a sufficient period of time. During topical application or local delivery of an agent, gingival crevice fluid flow may dilute or completely wash the agent out of the periodontal pocket. Inflamed periodontal pockets exhibiting probing depths of 5–6 mm have been shown to have a gingival crevice fluid outflow equal to or greater than 20 µl/ hour. This is equivalent to a pocket volume turnover of around 40 times per hour (161). Gingival crevice fluid movement makes pocket penetration of antimicrobial agents from oral health products such as mouthrinses or toothpastes (e.g. chlorhexidine, essential oils, triclosan and others) highly improbable. However, these agents often provide excellent prevention of supragingival plaque accumulation, and serve important roles in individualized oral hygiene programs.

A special situation represents the period following periodontal surgery when mechanical tooth brushing must be avoided. The fact that the total infectious burden in the oral cavity may be the determining factor by which wound infections after periodontal surgery may develop, it is reasonable to apply an effective antiseptic agent, such as chlorhexidine digluconate 2-3 weeks to deplete the supragingival plaque reservoir. The beneficial clinical effects on wound healing of such measures have been well documented. Following gingivectomies, the rinsing twice daily with 0.2% chlorhexidine gluconate promoted wound healing significantly (162). Applying infection control with daily applications of chlorhexidine in a histometric wound healing study in dogs (163) documented significantly improved wound healing following standardized gingivectomies with only minor signs of inflammatory infiltrates in the biopsies up to 42 days. Hence, it is evident that the use of chlorhexidine rinsing following periodontal surgery when mechanical tooth brushing is not

possible represents a fundamental concept contributing to the reduction of the infective burden in the oral cavity and hence, the promotion of oral postsurgical health.

2.3. The application of laser in the treatment of chronic periodontitis

2.3.1. Historical overview

It has been shown that conventional initial therapy presents limitations as mechanical treatment cannot complete removal the bacterial deposits along the periodontal pockets neither in some areas like furcations, concavities and grooves and antibiotics administered into periodontal pockets have a potentital risk of producing resistant microorganisms (164). In 1960 Maiman introduced the first laser device and from that time, it has been used in various medical fields (165). The incorporation of laser technology in Periodontics was due to its ability for ablation altogether with its high bactericidal and disinfectant capabilities. Besides, lasers could also treat areas that present difficult access for conventional instrumentation. In the early nineties, it was observed that some types of lasers had applications in the periodontal treatment and periodontal maintenance.

Clinical studies have demonstrated the effectiveness of some laser systems (Nd:YAG, Er:YAG, Argon, CO2 y diode laser) when used in combination with scaling and root planing. Ben Hatit et al. compared the effects of periodontal treatment with Nd:YAG on the subgingival bacterial flora with results obtained with traditional scaling and root planing. They concluded that a combination of scaling and a treatment with Nd:YAG accompanied by an adequate information on oral hygiene caused a superior suppression and eradication of the three types of studied subgingival microorganisms than only with scaling and root planing alone (166). Simultaneously, Moritz et al. analyzed the effect of 805nm wavelength diode laser application in periodontal treatment and contrasted the obtained results with a control group. This showed a lower gingival inflammation and demonstrated the existence of a bactericidal effect of the laser treatment in periodontal therapy (167). Leyes et al. evaluated the clinical efficacy of InGaAsP diode laser application as an adjunctive therapy to the traditional scaling and root planing. After 6 weeks, results showed that the additional application of laser during scaling and root planing produced qualitative improvements in bleeding on probing compared to conventional treatment (168).

The lasers that are most promising for the treatment of hard tissue ablation are Er:YAG and Er,Cr:YSGG. The Er:YAG laser is well absorbed by all biological tissues containing

water molecules, this laser is indicated not only in the treatment of soft tissues, but also for hard ones. In 2001 the "Food and Drug Administration of USA" (FDA) approved the use of this laser for soft tissue treatment and in 2002 hard tissue therapy (169, 170). The Er,Cr:YSGG laser was later incorporated into the armamentarium of dental lasers. This laser shows higher absorption by OH ions than by water molecules and it was predicted to have similar applications to the Er:YAG (171). Some preclinical studies were made to check the safety of this type of laser before this was brought in clinical applications (172-180). However, there are few studies on the clinical effects of Er,Cr:YSGG as a adjunct to the scaling and root planing in patients with periodontitis (175, 181, 182).

Therefore, it has been shown that lasers can attain an excellent level of tissue ablation with intensive bactericidal and detoxification effects; they are standout amongst the most guaranteeing new specialized modalities for nonsurgical periodontal treatment. An additional benefit of lasers is that they can treat areas that conventional mechanical instruments cannot. The adjunctive or alternative utilization of lasers with conventional instruments may facilitate the treatment, and possesses the capability of enhance the healing process.

In relation to soft tissues in periodontal pockets, gingival curettage after the treatment of scaling and root planing using mechanical tools has been shown not to have an additional advantage over conventional scaling and root planing (183-185). Nonetheless, the poor clinical results of gingival curettage may have been caused by the absence of an adequate instrument for soft tissue debridement. Instead of mechanical treatment with routine instruments, the excellent ablation of tissue with laser treatment is expected to advance the healing process of periodontal tissues, ablating the inflamed wound and epithelium of the periodontal pockets.

During the laser irradiation into periodontal pockets, a portion of the laser wave scatters and enters. The weakened laser at a low energy level may then stimulate the cells of the encompassing tissue, inducing a diminishment of the inflammatory conditions (186-188), in the proliferation of the cell (189-191), and increasing lymph stream (192), enhancing the periodontal connective tissue capability and probably diminishing postoperative aching. Moreover, conventional mechanical treatment usually provokes a smear layer and, in some cases, profound depressions on the root surface. A smear layer may antagonistically influence the healing of periodontal tissues as it contains bacteria and inflammatory substrate such as debris of contaminated cementum and calculus (193). Numerous

specialists have inspected the consequences of root conditioning after mechanical debridement, utilizing chemical agents such as tetracycline, citric acid, and ethylenediaminetetraacetic acid (EDTA). Root conditioning has been indicated to evacuate the smear layer, and to uncover collagen strands and dentinal tubules, improving the histocompatibility and new connective tissue attachment with cementogenesis (194-196). Laser irradiation has been proved to display bactericidal and detoxification effects without creating a smear layer, and the laser- treated root surface may hence generate ideal conditions to the attachment of periodontal tissue (197).

2.3.2. Physical characteristics and operation mode of lasers

"LASER" is acronym for Light Amplification by Stimulated Emission of Radiation. Einstein developed the physical principle in the mid 19th, and the first device was presented in 1960 (165). From that point forward, lasers have been utilized as a part of a wide range of spheres in medicine and surgery. Laser light is the human creation of a single photon wavelength and procedure of lasing happens when an excited atom is stimulated to emanate a photon before the process happens in a spontaneous manner. Spontaneous discharge of a photon by one atom boosts the emission of another photon and so forth. This stimulated release creates a unique type of light which has some specific characteristics; it is uniform (synchronous waves), monochromatic (a single wavelength), and collimated structure (parallel beams) (197, 198). The characteristics of a laser depend on its wavelength (Table 1).

		Wavelength	Color
Excimer lasers	Argon Fluoride (ArF)	193 nm	Ultraviolet
	Xenon Chloride (XeCl)	308 nm	Ultraviolet
Gas lasers	Argon	488 nm	Blue
		514 nm	Blue-green
	Helium Neon (HeNe)	637 nm	Red
	Carbon Dioxide (CO_2)	10.600 nm	Infrared
Diode lasers	Indium Gallium Arsenide Phosphorus (InGaAsP)	655 nm 670 – 830 nm	Red Red-infrared
	Gallium Aluminum Arsenide (GaAlAs)	840 nm	Infrared
	Gallium Arsenide (GaAs)	980 nm	Infrared
	Indium Gallium Arsenide (InGaAs)		
Solid state lasers	Frequency-doubled Alexandrite	337 nm	Ultraviolet
	Potassium Titanyl Phosphate (KTP)	532 nm	Green
	Neodymium: YAG (Nd:YAG)		
	Holmium: YAG (Ho:YAG)	1.064 nm	Infrared
	Erbium, chromium: YSGG (Er,Cr:YSGG)	2.100 nm 2.780 nm	Infrared Infrared
	Erbium:YSGG (Er:YSGG)	2.790 nm	Infrared
	Erbium:YAG (Er:YAG)	2.940 nm	Infrared

Table 1 Type and wavelength of lasers

Lasers concentrate light energy and apply a controlled impact, targeting tissue at a lower level of energy than natural light. The photon released has a particular wavelength that depends on the state of the electron's energy at the time of photon's liberation. (Figure 1).

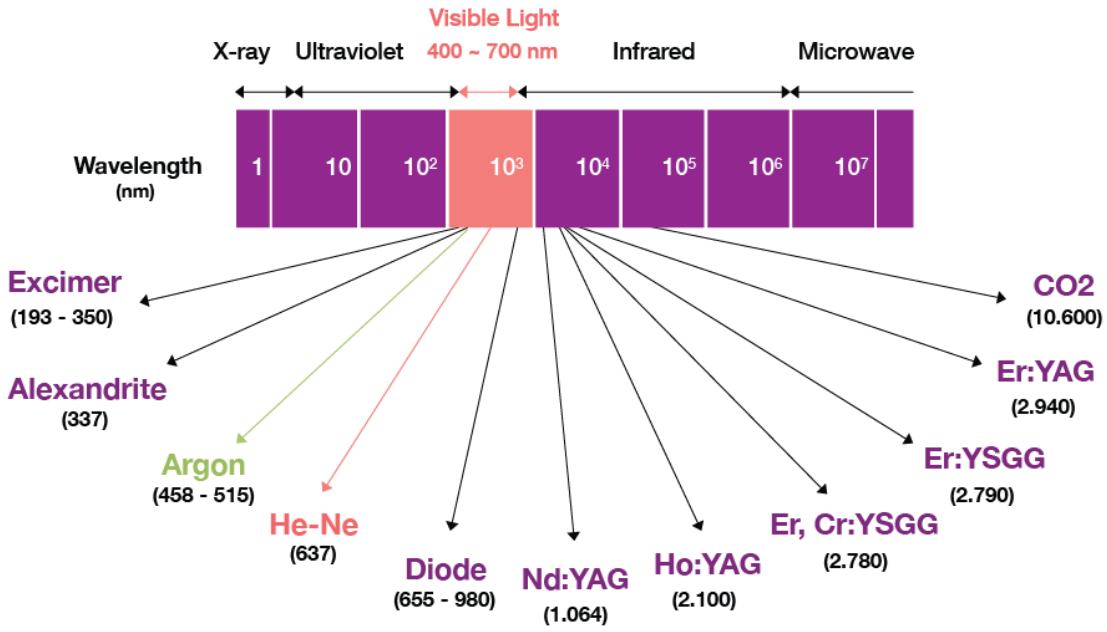

Figure 1 Electromagnetic spectrum and wavelength of lasers

The "waveform" of a laser depends on the manner how laser power is delivered over time. It can be a continuous or a pulsed beam emission. As long as the switch is turned on, an uninterrupted laser wave releases a continuous bundle at the output power set. The pulsed beam can be conveyed in two diverse manners: free-running pulse, in which pulsation happens inside the laser tube, and gated (chopped) pulse, in which the uninterrupted wave beam is stopped by a shutter at several rates. The gated pulse has the same power as that set on the laser control panel, while the free-running pulse is the consequence of power storage for certain periods of time (198, 199).

When reaching a tissue, laser light shows different effects; it can reflect, scatter, be absorbed or be transmitted to the neighbouring tissues (Figure 2).

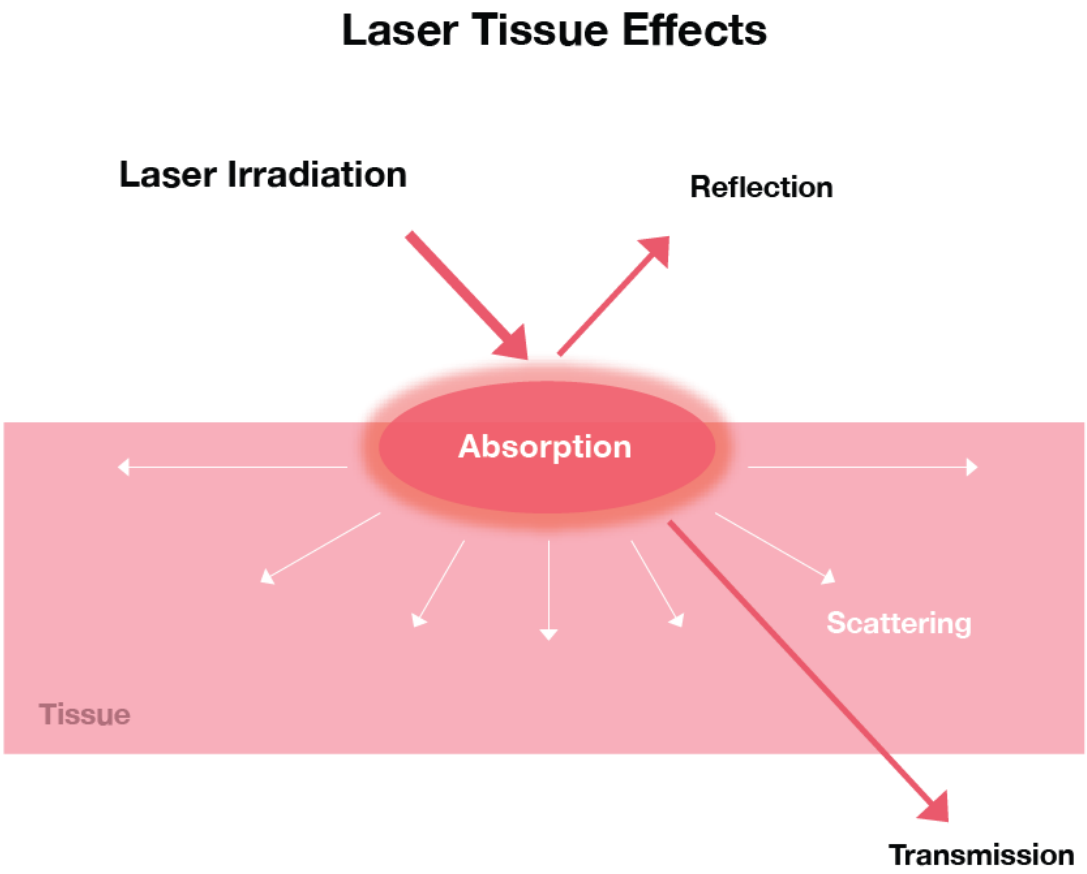

Figure 2 Effects of laser irradiation on tissue. When laser reaches a tissue, it can reflect, scatter, be absorbed or transmitted to the surrounding tissue

Absorption takes place in biological tissues thanks to the composition: free water molecules, proteins, pigments, and other macromolecules. The absorption coefficient depends on the wavelength of the laser and during thermal interaction, absorption by water molecules assumes an important function (200).

Lasers are generally classified into two types, depending on their wavelength: deeply penetrating type like neodymium-doped yttrium-aluminiumgarnet (Nd:YAG) and diode lasers, in which the laser light penetrates and scatters deeply into tissues, and superficially absorbed type such as carbon dioxide, Er:YAG and Er,Cr:YSGG lasers, in which the laser light is absorbed in the superficial layer and does not penetrate or scatter deeply (201).

2.3.3. Application of lasers in nonsurgical periodontal therapy

Nonsurgical mechanical debridement of periodontally affected root surfaces is one of the main parts in the initial phase of periodontal treatment. It has to be taken into account that

soft and hard tissues are constantly affected when utilizing lasers for the treatment of periodontal diseases since the periodontium is composed by gingiva, periodontal ligament, cementum, and alveolar bone.

For soft tissue ablation, some lasers like diode, CO2 and Nd:YAG are suitable and present an hemostatic effect. As the main beneficial effect is in soft tissues they are indicated in oral surgery to perform gingivectomies and frenectomies (199, 202, 203, 204). Nevertheless, these lasers are not approved for treatment of the root surface or alveolar bone, because of carbonization of these tissues and thermal consequences on the target and surrounding tissues (199).

In the early and mid 1990s, Nd:YAG laser was use to investigate the effects on pocket curettage and root surface debridement. The clinical use of the Nd:YAG laser had been tested out due to its advantageous, flexible fiber optic transmission system that made it adequate for utilization in periodontal pockets (205).

In 1965, the rubi laser was shown to be effectively for calculus removal along the root surfaces (206). Nevertheless, it was also pointed out that selectively vaporization of calculus was not possible without harming the underlying tooth substance. In the 80´s, some authors (207-210) reported dental hard tissue ablation by Er:YAG laser. From that point forward, various studies on hard tissue treatment utilizing the Er:YAG laser have demonstrated the capacity of this laser to ablate dental hard tissues and caries lesions avoiding undesired thermal side-effects. Encouraging results in basic and clinical application were exhibited in the field of caries treatment (211-217). Later, in the mid 1990s, Aoki et al. (218) and Keller et al (219) started to examine the utilization of the Er:YAG laser for periodontal hard tissue treatments, as for example, dental calculus elimination and the disinfection of the affected root surface and also demonstrated the safety for periodontal nonsurgical pocket treatment. Moreover, the use of Er:YAG laser for bone surgery has been investigated likewise in vitro and in vivo (172, 220-223). Advancement of this laser studies brought the possibility of hard tissue treatment in periodontics (224).

The Er:YAG laser is solid-state laser that generates a light with a wavelength of 2,940 nm. The absorption of the Er:YAG laser in water is the highest due to its 2,940 nm wavelength which corresponds with the large absorption band for water. Additionally, it is also well absorbed by the apatite component, despite the fact that the greatest absorption is around

2,800 nm (171). Therefore, the Er:YAG laser is well absorbed by all biological tissues that contain water molecules and is suitable for the treatment of soft tissues as well as for ablation of hard tissues . The high absorption of the Er:YAG laser into water diminish thermal impacts on the surrounding tissues during laser irradiation. Walsh et al. 1899 tested the termal changes in soft tissues while lasing; Er:YAG laser was utilized for an incision of pigskin in a noncontact mode and exhibited a thermally changed layer of just 10–50 μm (225). Nevertheless, when applying Er:YAG laser on hard tissues, some level of warmth generation is inexorable but it can be counteracted by the use of water coolant irrigation that produces less heat formation by cooling the targeted zone (226-228). The termal altered layer after Er:YAG laser irradiation while using water irrigation presents a width of 5–15 μm in width on cementum and dentin surfaces (211, 229, 230).

The Erbium, Chromium-doped: Yttrium-Scandium-Gallium-Garnet (Er,Cr:YSGG) laser with 2,780 nm wavelength which is greater absorbed by hydroxide (OH) ions than water molecules (171), was thought to have a similar applications as the one of the Er:YAG laser. The mechanism of tissue ablation by Er:YAG laser begins with thermal evaporation because the laser is easily absorbed in water and organic molecules within the biological tissues. During this process, water molecules within the hard tissues are vaporized as they absorb the laser energy and increase their intratissue pressure. After that, some vapor is produced within the tissue and provokes “micro-explosions” that cause mechanical break down of tissues and physically contribute to the ablation process (201).

Therefore, the erbium family of lasers has been shown to be capable of effectively ablating both soft and hard tissues without damaging deeper tissues (230).

2.3.4. Potential of Erbium lasers in nonsurgical therapy of chronic periodontitis

2.3.4.1. Basic studies

Some basic studies have demonstrated the security after use of Erbium lasers on root surfaces. Most of this basic research is done to respect to Er:YAG laser. The capability to remove calculus and root substance from the root surface, the surface modifications that take place after applying these laser wavelengths, the disinfection and detoxification effects as well as the thermal impact on the pulp tissue has been well investigated for this laser.

2.3.4.1.1. Removal of subgingival calculus

As it has been previously exposed, Erbium lasers are the most promising lasers for hard tissue ablation. The absorbance of the Er:YAG laser in water is about 2,5-times higher than

that of Er,Cr:YSGG laser as a result of the high absorption into water molecules. Dental calculus consists of water in its structural micropores and several studies have reported the capacity of the Er:YAG laser to remove subgingival calculus in vitro (216, 218, 23-234).

In 1994, Aoki et al. (218) presented the first study that indicated the potential for clinical use of the Er:YAG laser in subgingival scaling. It was demonstrated the capacity of the Er:YAG laser to eliminate subgingival calculus in vitro at 30mJ/pulse (10,6 J/cm2) in the contact mode, using a conventional cylindrical contact tip of 600 μm diameter with a perpendicular inclination to the root surface and water refrigeration. Nevertheless, some ablation of the root surface was observed after scaling. Soon after, it was (219) suggested that contact irradiation perpendicular to the root surface under water irrigation, an energy level of 50 mJ/pulse (tip diameter 600 lm, energy density 18 J/cm2 every pulse) should be utilized for successful calculus elimination and preventing any damage on the cementum. Moreover, few time after, new contact tips were developed to eliminate calculus from root surfaces and avoid damages in the cementum (Stock et al. 1996, Keller et al. 1997, Folwaczny et al. 2001).

When ideal contact tips were developed and energy outputs were defined, some studies were made to assess the effectiveness of Er:YAG laser scaling contrasted with conventional scaling therapies. On the one hand, Aoki et al. compared Er,YAG laser to ultrasonic devices. They (229) performed laser scaling at 40 mJ/pulse (14.2 J/cm2 every pulse) and 10 Hz with water spray, utilizing a conventional tip at 30° to the root surface in a sweeping movement. The level of calculus elimination accomplished by laser scaling was similar to the one achieved by ultrasonic scaling, despite the fact that the laser scaling was less effective. On the other hand, Schwarz et al. (235) compared the degree of calculus elimination with in vivo Er:YAG laser irradiation with scaling and root planing with hand instruments. The laser therapy was performed in a coronal to apical direction in parallel ways, with the fiber tip slanted 15–20° to the root surface. They concluded that Er:YAG laser treatment produced selective subgingival calculus elimination to a similar level than manual instruments.

2.3.4.1.2. Root substance removal during laser application

The average depth of cementum ablation is 40-136 μm after Er:YAG laser scaling in a perpendicular contact irradiation (218) whereas just 15-30 μm in oblique contact irradiation at 30º in a sweeping movement (229).

Stock et al. (234) reported that the maximum depth of ablation was around 100 μm after Er:YAG laser scaling at 20° inclination of the chisel tip to the root surface. Folwaczny et

al. (232) analyzed root substance elimination while irradiating root surfaces with or without calculus with the Er:YAG laser with a chisel contact tip in oblique contact irradiation at 30°. They concluded that the root substance elimination with the Er:YAG laser at lower energy densities up to 100 mJ/pulse was similar to that after traditional root surface instrumentation with curettes, and that selective calculus elimination may be feasible utilizing lower radiation energies. Additionally, Folwaczny et al. (236) reported that the angulation of the application tip to the root surface has an important influence on the amount of root substance eliminated during Er:YAG laser irradiation. The angulation of the application tip is a key factor for diminishing root substance elimination.

Nevertheless, Frentzen et al. (233) noted that, in spite of the fact that Er:YAG laser scaling attained complete debridement clinically, laser scaling at a panel setting of 160 mJ/pulse with water spray generated an increased loss of cementum and dentin in vitro compared to mechanical scaling. They considered that this loss ought to be considered in the clinical circumstance. The crater profundity of the treated root surface was aproximately 40 and 80 μm. With respect to these results, Ishikawa (237) pointed out that Frentzen et al. used a relatively high energy output for Er:YAG laser scaling, and remarked that despite the fact that the productivity of laser scaling can be easily enhanced by utilizing a higher output power, caution ought to be taken when choosing the energy output, considering a balance between effectiveness and unnecessary tissue elimination. Enhancement of the effectiveness of laser scaling ought to depend on different variables, for example, pulse repetition rate and pulse duration, instead of just on an increment of energy output.

Schwarz et al. (238) reported interesting discoveries. They performed in vivo Er:YAG laser scaling on periodontally unhealthy roots of hopeless teeth considered for extraction. This was continued by in vitro Er:YAG laser scaling to diverse surfaces of the same roots after extraction. Then, the Er:YAG laser-treated root surfaces after in vitro and in vivo laser scaling were contrasted. The root surfaces after clinical utilization of the Er:YAG showed a smooth morphology, even at higher energy settings, which were not comparable to the marked morphologic changes that were generated in vitro. Therefore, they proposed that calculus elimination could be possible selectively in vivo.

Typical root defects caused by hand instrumentation with scaling and root planing have been also compared to Er,Cr:YSGG lasing (175, 179). It has been shown that irradiation with Er,Cr:YSGG laser creates less cracks on the root surfaces than by hand scaling but more craters compared with the ultrasonic instrumentation. The laser treated root surfaces

have generally been rougher in comparison with other treatment modalities. (175-177, 180) However, it does not interfere with the adhesion of blood components to the root surfaces (176, 177, 180) and it seems that Er,Cr: YSGG treated root surfaces present a suitable environment for cell adhesion and growth (178, 179). Hakki et al. in in vitro studies, compared hand instrumentation to two different settings with Er,Cr:YSGG laser for removing calculus from the root surfaces regarding root surface morphology. They tested two laser pulse modes: short mode at 140 ms pulse length and long pulse at 400 ms pulse length. They concluded that both settings were suitable to remove calculus and provide a biocompatible surface for survival of periodontal ligament fibroblast on diseased root surfaces, but the 140 ms pulse length setting was more suitable with respect to the root surface morphology (178, 179).

2.3.4.1.3. Root surface modification after laser application

The Er:YAG laser application does not result in carbonization of the irradiated root surface, however it has been proved that the ablated surface becomes chalky after drying because of micro-irregularities on the lased surface (218, 229, 230, 239). Er:YAG laser-treated surfaces after calculus removal under water coolant, shows a micro-irregular appearance without melting and carbonization (Aoki et al. 2000). Israel et al. (239) informed that the root surface showed an etched appearence after being treated with the Er:YAG laser in the noncontact irradiation mode. Fujii et al. (230) demonstrated a microstructured root surface with denaturation of collagen filaments up to a profundity of 15 μm in cementum, after applying a single-pulse of Er:YAG laser on perpendicular contact under water spray.

Aoki et al. (229) observed that various rounded or sharp pointed projections were evident on the root surfaces after Er:YAG laser scaling with water spray. They also reported that the superficial layer of the root surface ablated by Er:YAG laser irradiation showed minimal changes. They could be subdivided histologically into two different layers: a superficial, significantly altered layer and an underlying, less affected layer. The superficial layer demonstrated a delicate structure with micro-anomalies and degradation while the underlying subsurface layer was influenced just by thermal denaturation, but not degraded structurally.

Sasaki et al. (222) reported that the Er:YAG laser with water coolant did not induce major compositional changes or chemical harmful changes in the root cementum and dentin. Nevertheless, laser irradiation without water coolant created cyan-derived toxic substances. Sasaki et al. also (240) observed that the surface lased by Er:YAG under water irrigation

showed slight melting with cluster formation of expanded microparticles of inorganic components in scanning electron microscope observation. The utilization of water spray while Er:YAG laser irradiation generated a cleaner and less porous surface.

The influence of the microstructurally and thermally changes on root surfaces and the attachment of soft periodontal tissues has also been investigated. Benthin et al. (241) noticed a reduction of in vitro fibroblast attachment after Er:YSGG laser irradiation on intact root surfaces compared to attachment on a mechanically treated surface, despite the fact that the root surface irradiated with water cooling generated more favorable fibroblast attachment than that treated without water cooling. Schoop et al. (242) showed in a in vitro study that the surface structure of periodontally infected root after Er:YAG laser irradiation at 100 mJ/ pulse with water spray provided superior conditions for the adherence of fibroblasts than a root surface after mechanical scaling only. Schwarz et al. (243) completed in vivo Er:YAG laser irradiation at 160 mJ/pulse with water spray or scaling and root planing with hand instruments on periodontally damaged root of hopeless teeth, and cultured fibroblasts on the treated teeth after extraction. They noticed significantly greater cell attachment in vitro in the laser treatment group than in the hand scaled treatment group.

Root substance modification after laser irradiation has also been investigated with Er,Cr:YSGG laser. Kimura et al. (173) showed in a morphological and atomic analytical study that the Er,Cr:YSGG laser, used at high output settings in combination with water-air spray presented a good cutting effect on root surfaces and did not cause any burning or melting symptoms after laser irradiation. They examined by stereoscopy root surfaces of extracted human premolar and molars teeth after having been irradiated at 5.0 W for 5 seconds with water spray while moving. They observed craters having rough but clean surfaces and no melting or carbonization in the samples (173). Ting et al. also studied the appropriate power output setting for an Er,Cr:YSGG laser with regard to morphologic alterations of the root surface and the efficiency of calculus removal in extracted human teeth. The specimens were divided into 3 groups: a control group, an irradiation group without water, and an irradiation group with water. The power output settings for laser irradiation were 0.5, 1.0, 1.5, and 2.0 W for each group. In the group with irradiation without water carbonization was observed, and the degree of carbonization was dependent on the laser power. Although no carbonization was observed in any of the specimens irradiated with water at any power level, conspicuous ablation of the root surface was found with 1.5 and 2.0 W. Therefore, they suggested the use of Er,Cr:YSGG laser at 1.0 W

power output level to efficiently remove calculus without producing morphologic alterations in the root surface (174).

To summarize, Er:YAG laser and Er,Cr:YSGG laser can be applied on hard tissues with an extremely low thermal effect when used with water cooling (201).

2.3.4.1.4. Thermal impact on pulp tissue by laser application

Thermal side-effects could represent a major problem when applying lasers for hard tissue ablation. Aoki et al. (218) showed that the utilization of water coolant prevented thermal generation during laser scaling without decreasing the effectiveness of laser scaling. They analyzed the temperature on the pulpal wall of adjacent surfaces of mandibular incisors while Er:YAG laser scaling for 20 s with and without water coolant, at 30 mJ/pulse directed perpendicular to the root. They noticed that the greatest temperature ascend without water coolant was approximately 39 °C in the root surface and 18.4 °C in the pulpal wall, while with water coolant was 2.4 °C in the root surface and 0.8 °C in the pulpal wall. The tip angulation to the root surface seems to be a key factor in increasing the pulpal temperature. Keller et al. (216) noted that the greatest temperature increment of the pulpal tissues was 4°C during Er:YAG laser scaling at 120 and 150 mJ/pulse under water irrigation utilizing a tip at 20 or 40° to the root surface. Hence, temperature rise in the pulpal wall while Er:YAG laser scaling with these laser angulations and using water coolant would be restricted inside the physiologically tolerable level.

Consequently, the use of Er:YAG laser to subgingival scaling at a low energy level, particularly with the contact tip aimed obliquely or parallel to the root surface, does not create any major harmful results in the pulp tissue.

2.3.4.1.5. Disinfection and detoxification of root surfaces

As it has been previously exposed, conventional therapies for the treatment of periodontitis are not completely effective in eliminating all kind of bacteria. Although, systemic and local antibiotics are used to increase the disinfection of the periodontal pockets, the frequent use of this molecules can increase the risk of producing resistant microorganisms. Due to this limitations, the use of novel technologies with additional bactericidal effects, like lasers have been proposed. The Er:YAG laser shows a high bactericidal effect againts periodontopathic bacteria (244, 245) and the potential to eliminate toxins like bacterial lipopolysacharides (246).

Er:YAG laser may provide different antimicrobial benefits over conventional mechanical scaling, because of its valuable characteristics, for example, bactericidal impact (244, 245), degradation and elimination of bacterial endotoxins (247, 248) and ablation impacts

without creating a smear layer (249).

Part of the disinfection capacity of the erbium lasers is thanks to the specific wavelength. The infrared spectrum of bacterial lipopolysaccharide presents a peak at a 2940nm, which corresponds to the wavelength of the Er:YAG laser. Ando et al. (244) reported that the Er:YAG laser displays a high bactericidal potential against periodontopathic bacteria, for example, P. gingivalis and Actinobacillus actinomycetemcomitans at a reduced energy level of 0.3 J/cm2. Folwaczny et al. (245) reported that Er:YAG laser light at 60 mJ/pulse could decrease bacteria on root surfaces in vitro without a complete removal of the bacterias. Yamaguchi et al. (248) indicated that Er:YAG laser application at 100 mJ/pulse and 1 Hz (35.4 mJ/cm2) could successfully and quickly eliminate in vitro the vast majority of the lipopolysaccharide that had been coated on extracted root surfaces. Sugi et al. (247) reported that the quantity of endotoxins on damaged root surface treated by Er:YAG laser at 30 mJ/pulse was less than that on control diseased root surfaces treated by hand scaler. Likewise, Sasaki et al. (222) informed that root cementum and dentin treated with the Er:YAG laser utilized with water coolant was free of generating toxic substances, like cyanate and cyanamide that were seen on surfaces irradiated by CO2 and Nd:YAG lasers. Thanks to all this studies, enhanced disinfection and detoxification may be expected after using Er:YAG laser.

2.3.4.2. Clinical studies of Erbium lasers in periodontal therapy

According to the results of some of the previouly mentioned basic studies of Er:YAG laser, Watanabe et al. (250) tested clinically Er:YAG laser for scaling in 1996. The laser scaling was completed under water coolant aiming to remove the supra- and subgingival calculus on the root surfaces of 60 teeth in 60 patients. They found that the Er:YAG laser could eliminate calculus from root surfaces in 95% of cases. Even though scaled areas presented some irregularities, they were not clinically significant in 98% of cases, and a reduction of pocket profundity was achieved. Therefore, they recommended that laser scaling was secure and effective, and also clinically useful.

Lately, Schwarz et al. (238) reported interesting clinical information of nonsurgical periodontal therapy, comparing Er:YAG laser irradiation to traditional scaling and root planing in a randomized, controlled clinical study utilizing a split-mouth design in 20 patients. Periodontal pockets of 110 teeth having subgingival calculus with moderate to advanced periodontal disease were treated with either the Er:YAG laser or scaling and root planing utilizing hand instruments. Er:YAG laser therapy was completed utilizing chisel type contact tips with water coolant. The laser application was implemented in a coronal to

apical direction in parallel paths, with an inclination of the fiber tip at 15–20° to the root surface. The laser treatment lasted less time than the conventional scaling and root planing treatment. At a 6-month after treatment the laser treatment group exhibited similar or superior results than the conventional treatment in terms of bleeding on probing, pocket depth, and clinical attachment level. Specifically, the laser group showed a significant decrease of bleeding on probing and higher clinical attachment level gain in comparison to the hand instruments scaling and root planing group. Moreover, the difference between laser and hand instrumentation in treatment results was substantially more pronounced in deeper pockets. This study concluded that the Er:YAG laser may exhibit an adequate alternative for traditional mechanical debridement in nonsurgical periodontal treatment. The same researchers demonstrated that the clinical attachment gain achieved after lasing with Er:YAG in nonsurgical periodontal therapy was maintained over a 2-year period (235).

Schwarz et al. (235) likewise examined the effect of adjunctive scaling and root planing following Er:YAG laser therapy. They designed a clinical study similar to the previously mentioned study (238), and reported no additional improvement in clinical results for the laser treatment followed by scaling and root planing compared with laser treatment alone. Rotundo et al. also performed a randomized split-mouth clinical trial to test the adjunctive benefit of Er:YAG laser in non-surgical periodontal therapy. Four modalities of treatment were tested: supragingival debridement, Er:YAG laser application plus scaling and root planing as adjunct, Er:YAG laser alone and scaling and root planing alone. The clinical outcomes were evaluated at 3 and 6 months. They came to the conclusion that adjuntive use of Er:YAG laser to conventional scaling and root planing did not reveal a more effective result than scaling and root planing alone. Moreover, the sites treated with Er:YAG laser showed similar results of the sites treated with supragingival scaling (251). Sculean et al. (116) compared the effectiveness of an Er:YAG laser to that of ultrasonic scaler for nonsurgical periodontal therapy. Twenty patients with moderate to severe periodontal disease were randomly treated in a split-mouth design with a single episode of subgingival debridement utilizing either an Er:YAG laser device or an ultrasonic instrument. Six months after the treatment, there was a statistically improvement in the mean values of bleeding on probing, probing pocket depth, and clinical attachment level in both groups. Nevertheless, no signigicant or clinically differences were detected between the treatment groups.

In 2002, a new subgingival calculus detection system with fluorescence was included in a

Er:YAG laser device (241). It was expected to remove the calculus more effectively from the root surface compared with hand instruments and therefore achieve more predictable results (252). Nevertheless, the clinical efficacy of Er:YAG laser as an alternative therapy to scaling and root planing for the treatment of chronic periodontitis is still questionable. Up to now, three systematic reviews centred on Er:YAG laser therarpy (253, 254, 255).

Schwarz et al. concluded that Er:YAG laser produced similar clinical outcomes compared with mechanical debridement, both in short- and long-term evaluations (253). Nevertheless, Zhao et al. recently reported that Schwarz´s review was inadequate because within a limited number of studies and high heterogeneity, the authors could not perform a comprehensive meta-analysis (255). According to the sixt European workshop on periodontology consensus report, stronger evidence is needed to support the clinical recommendation of this novel intervention (101). Sgolastra et al. in their review came to the same conclusions as the could not find any significant difference between Er:YAG laser and scaling and root planing in any of the investigated clinical parameters (254). Nevertheless, Zhao et al. claimed that the findings from Sgolastra and Schwarz reviews might be interpreted with caution because none of them included a subgrop and a sensitivity analysis and performed a new systematic review of all eligible sudies about Er:YAG laser published since the date of publication (255). They evaluated the clinical outcomes of the Er:YAG laser as an alternative to scaling and root planing for chronic periodontitis at 3,6 and 12 months, they also evaluated if the adjuntive application of Er:YAG laser to scaling and root planing presented any additional advantage for chronic periodontitis. They concluded that there was no difference in clinical outcomes between Er:YAG laser and scaling and root planing for chronic periodontitis in the 3-month follow-up. The evidence related to clinical outcomes evaluated at 6 and 12 months postoperatively remained insufficient. Moreover, clinical benefits of Er:YAG laser as adjuntive therapy to scaling and root planing were still lacking (225).

More recently, a randomized clinical trial has been performed by Sanz-Sanchez et al. 2015. They tested the efficacy of a treatment protocol combining full mouth ultrasonic subgingival debridement with the application one week later of Er:YAG laser only in initially deep periodontal pockets and compared to conventional ultrasonic debridement without the Er:YAG laser application in patients with moderate chronic periodontitis. The results of their research have demonstrated that both non-surgical periodontal protocols were effective in significantly improving the clinical outcomes of periodontal depth and bleeding on probing for at least one year. Nevertheless, the trial failed to demonstrate any

clinically significant benefit when the adjunctive laser therapy was added to ultrasonic root debridement (256).

According to the current literature, just two clinical studies are published about the effects of Er,Cr:YSGG laser application in addition to scaling and root planning (SRP) (181, 182). Kelbauskiene et al. in their first clinical study included 130 teeth and 6 sites per teeth were analized. In each patient two quadrants were treated using Er,Cr:YSGG laser plus SRP and two quadrants with SRP alone. They reported that both treatments led to significant improvements in clinical parameters including probing depth, and clinical attachment level. The combined treatment using laser as an adjunct to SRP seemed to be advantageous compared to SRP because of more efficient attachment level restoration (181). In the second study performed by the same group of researchers, they included 278 single rooted-teeth and 1088 sites were analyzed. They concluded that treatment using Er,Cr:YSGG laser as an adjunct to SRP appeared to be more advantageous when compared to SRP in all the investigated clinical parameters. Moreover, they bring to the conclusion that combined therapy, using SRP plus Er,Cr:YSGG laser appeared to have a prolonged clinical improvement throughout the study period (12 months) when compared to SRP (182). To obtain a more rigorous evidence about Er,Cr:YSGG laser, new randomized clinical studies are needed.

2.4. Rationale for the present study

Periodontal disease appears to be a major, global public health problem affecting the majority of the adult population (see 1.3.3.). Left untreated, the disease might lead to progressive destructive periodontitis with tooth loss as a consequence (see 1.1.). More than 90% of the variance of the periodontal disease severity in the population can be explained by age and oral hygiene. Moreover, a history of ongoing periodontitis must be considered as a risk factor for systemic diseases (see 1.4.) which not only have an impact on the individual but on public health service as well.

Reliable clinical concepts for treatment of periodontal infections do exist and the successful outcome has been documented in long-term follow-up studies on a high level of evidence (see 1.2. and 2.1.). The removal of subgingival deposits (plaque and calculus) with or without adjunctive antiseptic or antibiotics followed by adequate maintenance care is the most successful and consistent strategy in the treatment of periodontitis.

Nevertheless, the commonly applied technique performed with curettes and scalers is technically demanding and time consuming. Additionally, sites in furcations, concavities, grooves and distal aspects of molars are difficult to access. Therefore, lasers have been suggested as an alternative treatment modality to overcome the shortcomings of the conventional approaches (see 2.3.3.).

The clinical efficacy of laser application compared to mechanically treated root surfaces has been intensively evaluated in the literature, both as a monotherapy or as an adjunctive treatment to mechanical debridement (see 2.3.3.). Despite the numerous publications, it is a fact that most of the available studies lack from adequate randomization methods and sample size calculations and, as a consequence, the different study designs complicate a comparison between them.

The Consensus Report of the Sixth European Workshop on Periodontology (101) suggested that well-designed randomized controlled clinical trials using a larger number of patients are needed to further assess the scientific evidence of the efficacy of laser application in the treatment of chronic periodontitis. Based on these recommendations (102), the present study evaluates the therapeutic efficacy of laser application as an adjunctive treatment to subgingival debridement compared to subgingival debridement alone.

3. HYPOTHESIS

3. Hypothesis

Hypothesis:

Adjunctive laser therapy (Er,Cr:YSGG laser, 2.78 µm wavelength) immediately applied after scaling and root planing results in a gain of clinical attachment compared to scaling and root planing alone (superiority).

Null hypothesis:

The application of laser Er,Cr:YSGG after initial scaling and root planing does not produce additional gain of clinical attachment (CAL gain) compared to scaling and root planing (non inferitority).

4. OBJECTIVES

4. Objectives

4.1. General objective

To assess the efficacy of two different nonsurgical approaches, subgingival debridement performed as scaling/ root planing (SRP) and a combination of scaling/ root planing with Er,Cr:YSGG laser (SRP+laser) at 6 weeks and 6 months, in patients suffering from moderate to advanced chronic periodontitis. Laser irradiation (2.78 µm wavelength) will be applied as adjunctive treatment to subgingival debridement immediately after SRP.

4.2 Specific objective

To evaluate the periodontal clinical status with the most reliable and sensitive variables that can be clinically measured: probing pocket depth (PPD), gingival recession (GR) and clinical attachment level (CAL) together with the bleeding scores (BoP). Based on these key variables the early healing response after therapy of chronic periodontitis will be evaluated, comparing two treatment modalities.

5. MATERIAL & METHODS

5. Material & Methods

5.1. Study population

The protocol of the study was approved by the Ethical Committee of the International University of Catalonia with number PER-ELC-2013-07 (Annex 1). Patients suffering from chronic periodontitis, were consecutively selected for the study. After a screening visit, including a full-mouth periodontal evaluation, all patients fulfilling the following inclusion criteria were asked to participate:1) age ≥ 18 years, 2) no systemic diseases, 3) no pregnancy, 4) no active periodontal treatment and systemic antibiotic therapy in the last six months 5) presence of at least one incisor, one premolar and one molar in each quadrant, 6) diagnosis of moderate to advanced chronic periodontitis and the presence of at least two teeth with at least one site with probing pocket depth (PPD) that ranged between 4 and 9 mm in each quadrant with bleeding on probing (BoP).

The sample size calculation was based on detecting a difference between groups of 0.5 mm in the main outcome variable (CAL gain) with an assumption of a common standard deviation (SD) of 0.6 mm, an α error of 0.05 and a β error of 0.20. This analysis resulted in 30 patients (n=30 patients), which were included and randomized, assumed that no patient would drop out. In this split-mouth study, each patient presented two contralateral quadrants, one in the maxillar and one in the mandibular jaw that were assigned to the test group and two contralateral quadrants, one in the maxillar and one in the mandibular jaw, to the control group.

The patients were informed about the laser treatment (Annex II) and oral and written consents were obtained (Annex III).

5.2. Study design

5.2.1. Clinical measurements and data collection

The following parameters were recorded at baseline (0), 6 weeks and six months thereafter: Plaque Index (PlI) (259), probing pocket depth (PPD), gingival recession (GR), bleeding on probing (BoP) and the clinical attachment level (CAL). All measurements were taken by the same calibrated examiner, who was blinded to the treatment and was different from the clinician performing the periodontal treatment.

Probing pocket depth (PPD) was measured from the gingival margin with a pressure-sensitive plastic periodontal probe standardized at 0.25 N (Vivacare TPS® probe, Ivoclar, Schaan, Liechtenstein). Gingival recession (GR) was measured from the cemento-enamel

junction (CEJ) to the gingival margin (GR was equal to 0 whenever the CEJ was covered). Clinical attachment level (CAL) was calculated by adding the values of GR and PPD. All measurements were made at six sites per tooth: mesio-vestibular (mv), central-vestibular (cv), disto-vestibular (dv), mesio-lingual (ml), central-lingual (cl), and disto-lingual (dl). Additionally, adverse effects and complications during or after treatment were noted.

5.2.2. Clinical procedure

Two weeks prior to treatment, all patients were scheduled for oral hygiene instructions as well as for professional supragingival debridement according to individual needs. Supragingival plaque was recorded at baseline and patient's abilities to maintain optimal oral hygiene standards were checked.

Control group

In the control group, a subgingival mechanical instrumentation was performed as deep scaling and root planing (SRP) with the help of Gracey mini five curettes 1/2, 7/8, 11/12, 13/14 (Hu-Friedy® Mfg. Co., Chicago, IL) and the end point of mechanical debridement was achieved when the clinicians were unable to detect any remnants of calculus on the treated root surfaces. During treatment the inspection of the treated sites was carried out periodically with a periodontal probe (probe tip PCP-UNC 15, Hu-Friedy® Mfg. Co., Chicago, IL).

Test group

In addition to SRP, according to the control group and in the same treatment session, the subgingival root surfaces in the test group were treated by application of Er,Cr:YSGG laser.

An Er,Cr:YSGG device (Waterlase MD Turbo™, Biolase Technology, Irvine, CA) with a wave length 2,78 µm was used in the present study (Figure 3).

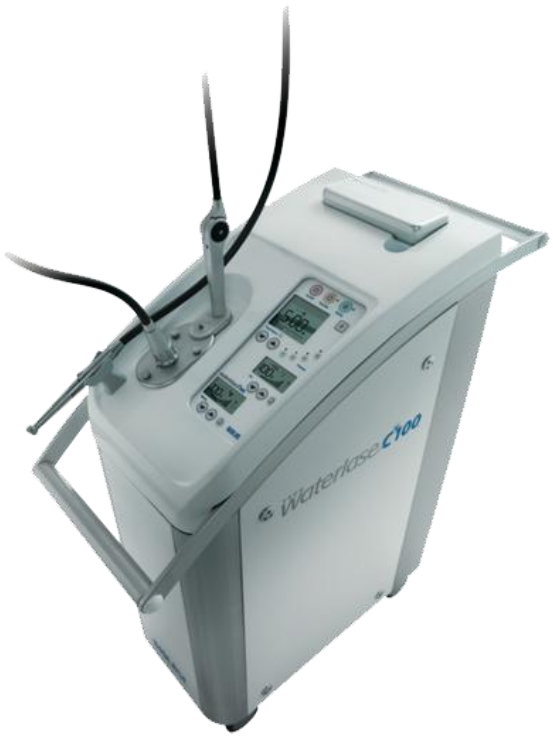

Figure 6 Er,Cr :YSGG device with 2780 nm of wave length used in the present study

The laser system used had a pulse duration of 140 to 200 μs with a repetition rate of 20 Hz. The average power output could be varied from 0 to 6 W (300 mJ/ pulse). The delivery system consisted of a fiber-optic tube terminating in a handpiece with a tip bathed in an adjustable air-water spray. The power output of the Er,Cr:YSGG laser was set to 1.0 W (50 mJ/pulse), a repetition rate of 20 pulse/second and an air-water spray ratio of 10% air and 15% water. A Z-6 series tip of 600 μm in diameter and 9 mm in length was used (Figure 4). Laser irradiation was applied for 60 seconds on each tooth surface from coronal to apical aspects of the pocket (Figure 5). The fiber optic tip was led in parallel paths with an inclination of 5-15° towards the root surface (Figure 6). The sequence of the clincial steps performed in the test group (SRP+laser) is depicted in Figure 7.

To avoid any operator bias, all patients were treated under local anaesthesia by the same experienced clinician.

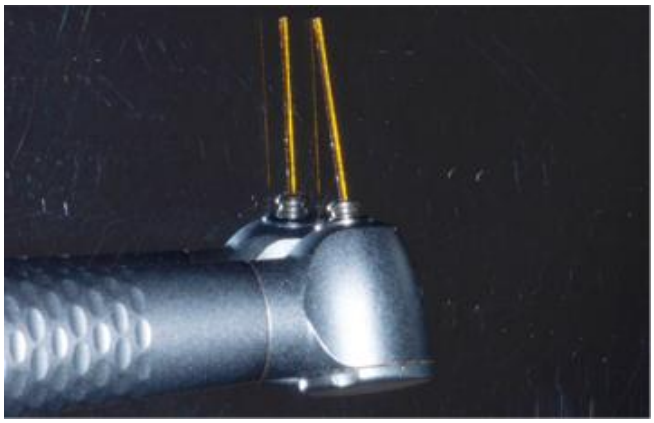

Figure 4 Er,Cr :YSGG laser handpiece with Z-6 tip with 600 μm in diameter and 9mm in length.

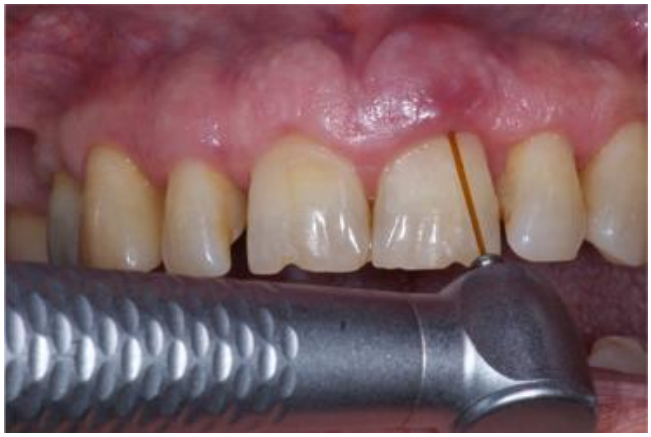

Figure 5 Insertion of the tip from coronal to apical aspects of the pocket in the test group.

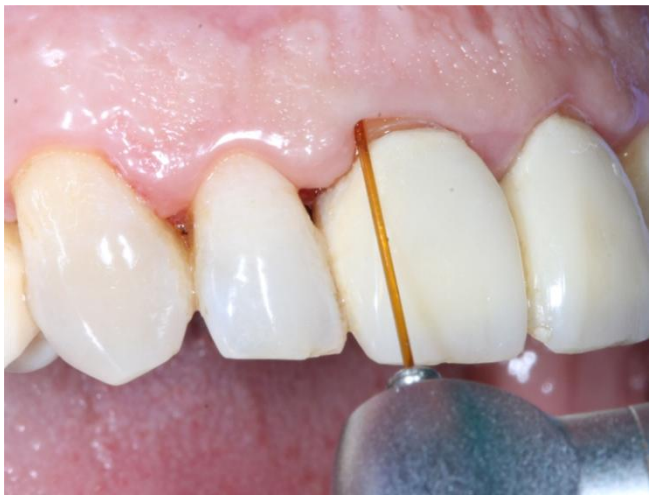

Figure 6 Tip inserted with an inclination of 5º-15º towards the root surface

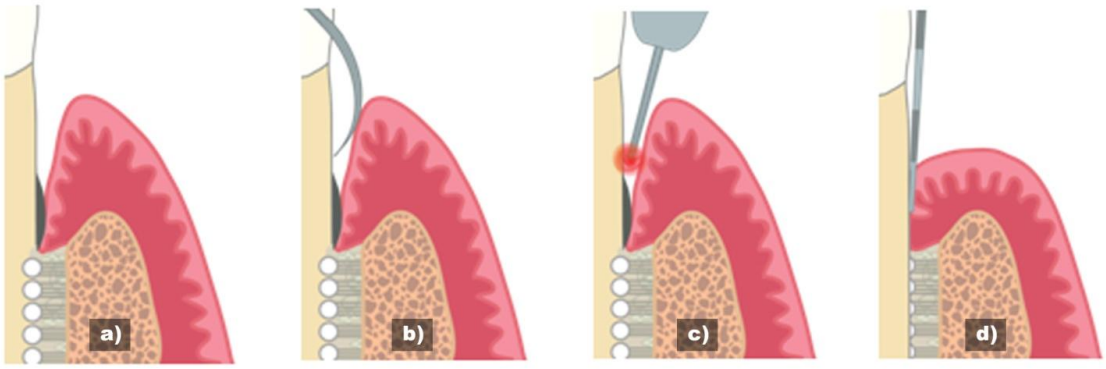

Figure 7 Consecutive treatment steps in the test group. a) baseline situation, b) initial scaling and root planing, c) adjunctive laser application, d) clinical evaluation by measuring pocket depths and bleeding scores

5.3. Methodology

The statistical analysis was intention to treat and the site was considered as the statistical unit and each outcome variable was reported at every visit by means and standard deviations. The primary outcome variables were probing pocket depth (PPD) and clinical attachment level gain (CAL gain). Only sites with PPD ≥ 4 mm at baseline were considered eligible, and therefore included for the analysis. The secondary outcome variables were the changes in gingival recession (GR) and bleeding on probing (BoP). Plaque scores were considered as confounding variables.

Two contralateral quadrants per patient, one in the maxillar and one in the mandibular jaw, were randomly assigned to the SRP (control) and two quadrants to the SRP+laser (test) group by tossing a coin for the first quadrant.

5.4. Statistical analysis

After checking normality using the Kolmogorov-Smirnov test, continuous variables were compared between groups by ANOVA, using the treatment group as the factor. All comparisons were analysed using two tails and a significance level of < 0.05; for an adequate interpretation of the data, since multiple comparisons were carried out, the level of significance for changes between visits and for visits was adjusted (Bonferroni correction).

A software package Statgraphics® (Statpoint Technologies Inc., Virginia, USA) was used for the statistical analysis. The significance level for rejection of the null hypothesis was set at $p < 0.05$. Differences between baseline, 6 weeks and 6 months postoperatively were

analyzed for PPD, CAL, GR, PlI and BoP by means of analysis of variance (ANOVA) for repeated measurements.

6. RESULTS

6. Results

6.1. Patient characteristics at baseline

A total of 30 patients, including 752 teeth or 4512 sites were examined. The mean age of the patients was 48.5±9.4 years and 20 out of 30 were females. Only 4 patients were smokers (< 10 cigarettes/day) (Table 2).

Number of patients	**30**
Age [mean±SD (years)]	**48.5±9.4**
Gender (female / male)	**20 / 10**
Smokers (< 10 cigarettes / day)	**4**
Total number of teeth included	**752**
Total number of sites examined	**4512**
Total number of sites with PPD ≥ 4 mm	**3654**

Table 2 Patient characteristics at baseline

The clinical measurements recorded in the sites with PPD ≥ 4 mm at baseline are reported in Table 3. All patients included in the study completed the treatment and both, 6 weeks and 6 months follow-up evaluations. None of the teeth included in the study were lost during the follow-up period.

At baseline, no differences could be found between test and control group regarding PPD, CAL and GR (Table 3).

	SRP (control group)	**SRP + laser** (test group)
Number of sites ≥ 4 mm	1'759	1'895
PPD (probing pocket depth in mm)	5.6±1.3	5.5±1.1
• vestibular sites (cv)	5.4±1.1	5.3±1.3
• lingual sites (cl)	5.5±1.0	5.2±1.2
• interproximal sites (mv,dv, ml, dl)	5.9±1.3	5.9±1.3
CAL (clinical attachment level in mm)	6.5±1.2	6.5±1.4
• vestibular sites (cv)	6.6±1.1	6.4±1.3
• lingual sites (cl)	6.4±1.3	6.3±1.0
• interproximal sites (mv,dv, ml, dl)	6.6±1.3	6.8±1.2
GR (gingival recession in mm)	1.2±1.2	1.1±1.0
• vestibular sites (cv)	1.2±0.9	1.0±1.2
• lingual sites (cl)	0.9±0.7	1.0±1.0
• interproximal sites (mv,dv, ml, dl)	0.7±1.1	0.9±1.0
BoP (bleeding on probing)	71%	69%
PlI (plaque index)	42%	37%

Table 3 Measurements at baseline, calculated on 30 patients (752 teeth, 4512 sites), 3654 sites with PPD ≥ 4 mm (cv=central-vestibular, mv=mesio-vestibular, dv=disto-vestibular, cl=central-lingual, ml=mesio-lingual, dl=disto-lingual)

6.2. Results at six weeks follow-up

A total number of 3654 sites could be analyzed at baseline and both follow-up evaluations times. No complications such as abscesses or infections were observed throughout the study period.

In general, adequate oral hygiene practices could be maintained throughout the whole follow-up period, documented by mean plaque scores. In both groups a slightly decrease of percentages in PlI was recorded between baseline and 6 weeks evaluation and between 6 weeks and 6 months evaluation (Table 4).

The mean bleeding scores significantly decreased between baseline evaluation and 6 weeks follow-up in both groups from 69% to 39% in the test, and from 71% to 36% in the control group, respectively.

Table 4 shows the measurements of the variables PPD, BoP, PlI, GR and CAL recorded 6 weeks after therapy. The variations of the variables CAL, PPD and GR have been considered as CAL gain, PPD reduction (PPD red) and GR reduction (GR red). Although a significant mean PPD reduction could be observed for both test (SRP+laser) and control group (SRP) between baseline and 6 weeks follow-up (0.7±1.4 mm versus 0.9±1.2 mm, respectively), no statistically significant difference could be noticed between the two treatment modalities. When PPD changes were analyzed separately for vestibular, lingual and interproximal sites, again, no additional efficacy could be detected for laser application in the test group. For both treatment modalities, the PPD reduction was more pronounced at interproximal sites than at vestibular and lingual surfaces.

At six weeks follow-up, the mean CAL in the test group yielded a gain of 0.1±1.1 mm, which was statistically significant less than in the control group with 0.5±0.4 mm, respectively ($p<0.05$). Regarding site-specific evaluations, the results for CAL gain (both treatment modalities) were similar to PPD reduction with statistically significant better outcomes at interproximal than vestibular or lingual sites.

The differences in gingival recessions (GR red) between the two treatment groups at six weeks follow-up did not reach statistical significance. In contrast to the variables PPD and CAL, the gingival recession changes (GR red) did not differ between interproximal and vestibular or lingual sites.

Compared to SRP (control group), the adjunctive laser application (test group) did not improve the results regarding PPD reduction. On the contrary, with regard to CAL gain, the outcome in the test group was even slightly inferior compared to the control group.

6.2. Results at six months follow-up

Descriptive statistics at 6 months after therapy are reported in Table 4. The variation of the variables CAL, PPD and GR has been considered as CAL gain, PPD reduction and GR reduction.

It is possible to observe that the variable plaque index showed a continuous decrease along with the follow-up time in both treatment procedures.

Regarding the variable CAL gain 6 months after therapy, the SRP group showed a greater gain value (0.6±1.2 mm) than the SRP+laser group (0.1±1.9 mm). A similar but less

pronounced effect could be noted for the PPD reduction (1.1±1.4 mm and 0.8±1.6 mm, respectively).

	SRP (sites no=1'759)		**SRP + laser** (sites no=1'895)	
	6 weeks	**6 months**	**6 weeks**	**6 months**
PPD (in mm)	4.7±1.1	4.5±1.3	4.8±1.3	4.7±1.1
• vestibular sites (cv)	4.9±0.9	4.6±1.2	4.8±1.6	4.6±1.8
• lingual sites (cl)	4.9±1.0	4.8±1.0	4.7±1.6	4.7±1.4
• interproximal sites (mv,dv, ml, dl)	4.2±0.9	4.0±1.1	4.8±1.2	4.7±1.2
CAL (in mm)	6.0±1.4	5.9±1.2	6.4±1.3	6.4±1.0
• vestibular sites (cv)	6.3±0.8	6.1±1.0	6.2±1.2	6.1±1.1
• lingual sites (cl)	6.0±1.1	5.9±1.0	6.3±0.9	6.4±0.6
• interproximal sites (mv,dv, ml, dl)	5.7±1.4	5.7±0.8	6.7±1.1	6.8±1.2
GR (gingival recession in mm)	1.3±1.1	1.4±1.4	1.6±0.9	1.8±0.9
• vestibular sites (cv)	1.4±0.8	1.5±0.9	1.4±1.0	1.5±1.4
• lingual sites (cl)	1.1±1.0	1.1±1.4	1.6±1.1	1.7±1.6
• interproximal sites (mv,dv, ml, dl)	1.5±1.0	1.7±1.1	1.9±1.1	2.1±1.2
BoP (bleeding on probing)	36%	34%	39%	36%
PII (plaque index)	39%	37%	36%	34%

Table 4 Clinical outcomes at 6 weeks and 6 months, calculated on 30 patients, 3654 sites with PPD $\geq$ 4 mm (cv=central-vestibular, mv=mesio-vestibular, dv=disto-vestibular, cl=central-lingual,ml=mesio-lingual, dl=disto-lingual)

7. DISCUSSION

7. Discussion

7.1. Discussion of the study design

The adjunctive effect of laser treatment to mechanical debridement has been intensively investigated in the literature. Due to the heterogenity of the protocols, the outcomes substantially differed and the results were difficult to compare with each other.

Two systematic reviews compared the additional benefit of either photodisinfection (260) or Nd:YAP laser application (261) with conventional manual debridement. Both studies included a sufficient number of subjects and the patients were followed-up 12 weeks postoperatively. While photodisinfection resulted in a significant improvement of the clinical parameters compared to SRP alone, no differences could be detected between test and control group in the second study. As no initial therapies were performed in none of the studies nor hygiene instructions were given, the results must be taken with caution. It is well documented that supragingival debridement and plaque control affect the results of subgingival scaling (262, 263). Therefore, one might speculate that the beneficial effect of the photodisinfection could be compensated by improving hygiene levels of the patients before starting the treatment.

In another trial, similar to the present study, the additional benefit of Er,Cr:YSSG laser application was compared to mechanical subgingival debridement alone (181). The protocol of the systematic review consisted of a one stage treatment in the control group (SRP), while the laser application was repeated in the test group once per week for the duration of 3-4 weeks. The authors concluded that the combined therapy was superior to SRP alone. Taken into account that the laser treatment has been performed repetitively and the sample size consisted of the limited number of 10 subjects, the study design seems at least to be questionable.

Neill & Mellonig (264) evaluated the effect of Nd:YAG laser therapy in addition to Sc/ RP compared to a conventional mechanical treatment. After the follow-up period of six months, findings exhibited a slightly inferior outcome for clinical attachment gain in the control group and suggested a longer lasting effect for the laser therapy in altering the microflora. Again, with 10 patients included, the sample size was small and the benefit of the adjunctive laser application minimal.

Based on the recommendations of the Consensus Report of the Sixth European Workshop on Periodontology (101) for an appropriate sample size calculation, a systematic review was initiated to compare four treatment modalities, namely 1) professional supragingival prophylaxis, 2) laser treatment followed by SRP, 3) laser treatment alone and 4) SRP alone

(265). The follow-up period went up to 6 months and clinical measurements were taken as well as patient's subjective opinion evaluated. The results will be discussed further down. In contrast to the present study, the Er:YAG laser treatment was the basic therapy in the combined test group followed by adjunctive mechanical scaling. From our point of view it seemed likely to choose SRP as primary therapy and restrict the laser use for the remaining sites that are difficult to access with scalers and curettes.
In the present study the laser application was chosen as adjunctive therapy to SRP and not vice versa. As the trial was aiming at evaluating the early and late healing responses of initial periodontal therapy, the follow-up periods were chosen at 6 weeks and 6 months interval from subgingival debridement.

7.2. Discussion of the results

The present study was aimed at investigating the efficacy of Er,Cr:YSGG laser application in addition to conventional SRP. 30 patients affected by moderate to advanced chronic periodontitis were enrolled for this study. They showed a high level of plaque accumulation and bleeding scores, and needed periodontal causal therapy.
In split-mouth design, mechanical debridement with curettes was compared with an approach consisting of SRP, followed by adjunctive laser treatment.

The results of the present randomized clinical trial have shown that both treatment protocols were efficacious in the therapy of patients suffering from chronic periodontitis, resulting in a significant improvement of the main measurement variables (PPD and CAL changes). Comparing the outcomes of the two treatment modalities, no significant differences could be noticed between control and test group regarding PPD changes. In other words, the clinical use of an Er,Cr:YSGG laser in addition to SRP did not improve probing pocket depth reduction at the end of the six months healing period. On the contrary, with respect to CAL gain, the conventional approach with SRP achieved slightly better results compared to the combined therapy with the laser.

In the present study, the better results of SRP as a monotherapy regarding CAL gain at 6 months follow-up are difficult to explain. It can be speculated that a delayed periodontal wound healing after laser application in comparison to healing after conventional mechanical debridement (267) might have had an influence. In vitro studies have shown a decreased periodontal ligament cell attachment on the surface of intact roots treated by

Er:YAG laser under water irrigation, compared to mechanically treated root surfaces (164). Even though previous studies have demonstrated that Er:YAG laser radiation was not associated with major compositional or chemically deleterious changes on the root surface (268), it might be difficult to estimate to what extent a reduction of organic components is capable to influence the detachment of newly formed cementum (222).

The clinical effect of laser application compared with mechanical debridement in nonsurgical periodontal therapy in patients with chronic periodontitis has been intensively evaluated in the literature. Up to now, four systematic reviews centered on Er:YAG lasers have been published (253, 254, 255, 268). The included studies either described a comparison of laser radiation applied as a monotherapy with SRP alternatively, or lasers in addition to SRP as an adjuvant treatment with SRP alone. However, the review articles published in 2008 (253, 268) are based on a limited number of studies with a high heterogeneity and hence, no meta-analysis could be performed. Therefore, as a conclusion of the Sixth European Workshop on Periodontology, stronger evidence was required to support the clinical recommendation of the use of lasers in the treatment of chronic periodontitis (101).

Sgolastra et al. (254) systematically assessed the scientific evidence for the efficacy of Er:YAG laser compared to SRP in the treatment of chronic periodontitis. Based on a specific search strategy (quality assessment according to the CONSORT guidelines and the systematic review according to the QUORUM statement and Cochrane Collaboration recommendations) five out of 1282 publications fulfilled the required inclusion criteria. A total of 85 patients and 3564 sites were entered in the meta-analysis to investigate the CAL gain and PPD reduction. All studies reported significant intragroup improvements in clinical parameters in patients treated with the Er:YAG laser. However, three studies (116, 269, 265) did not report a significant difference between Er:YAG laser and SRP groups in CAL gain, PPD reduction or GR changes.

The results for the latter two variables, but not for CAL gain, are in accordance with the findings of the present study. The different outcomes regarding attachment level gain might be explained by two aspects: First, despite the strict selection criteria for inclusion in the meta-analysis , there was a significant heterogeneity between the studies with an inherent high risk of bias. The included studies even differed in the treatment modalities. In three of them (270, 243, 116) laser application was compared with Sc/RP as a monotherapy while the use of the laser as an adjunctive intervention following Sc/RP, similar to the present setting, was just evaluated in one study (269). A second reason for

the variable outcomes in CAL gain might be the differences of healing times, consisting of 6 months in the present study compared to 6 months or more in the articles included in the systematic review (254).

In another recent systematic review (255), twelve eligible randomized clinical trials were included. Four of them highlighted short-term evaluations regarding Er:YAG laser adjuvant to SRP. The pooled results revealed that both of the treatments were equally effective with respect to CAL gain 3 months postoperatively. However, comparisons of the two treatment modalities indicated a significant reduction in PPD within the combined therapy group (laser followed by SRP) compared to SRP alone. Again, the controversies concerning divergent results might be attributed to different selection criteria and design methodology. In our study the laser debridement was used as the additional adjuvans while the test groups in the above-included trials differed in their designs (269, 265, 271, 272). Rotundo et al. (265) applied a combination of laser treatment, followed by SRP. In particular, mechanical scaling was performed after the laser application while Yilmaz et al. (271, 272) used ozone or metronidazole as comparative treatments in the test groups.

Summarizing, the use of lasers as an alternative or adjunct to conventional periodontal treatment is well investigated in the current literature. There is evidence that Er:YAG lasers are as effective as SRP alone (254, 255). If lasers are used in addition to SRP, the literature does not support the hypothesis for the superior effectiveness of a combined therapy (254, 255, 268). Most of the available studies have in common that they lack from adequate randomization methods and sample size calculations. Additionally, the different study designs complicate a comparison between them and therefore, well-designed RCT's are needed to assess the scientific evidence of laser efficacy.

The controversial results of studies investigating Er,Cr:YSGG laser application as an adjunct to SRP can be explained by the different protocols. While in most of the studies the adjunct treatment consisted of a single dose of laser application, in some studies the affected sites were treated in several subsequent appointments (182, 182).

8. CONCLUSIONS

8. Conclusions

Based on an appropriate sample size calculation and with adequate power, the present study clearly demonstrated that the adjunctive use of an Er,Cr: YSGG laser did not improve the results regarding PPD reduction and GR changes at 6 weeks and 6 months re-evaluation after initial therapy. In contrary to expectations, the CAL gain at 6 months evaluation was slightly increased in the control compared to the test group.

These results are in accordance with most of the recent randomized controlled studies evaluating the efficacy of Erbium lasers as adjunct to traditional subgingival debridement. Thus, the clinical use of lasers in the treatment of chronic periodontitis is still questionable and supported by weak evidence in the current literature.

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10. ANNEXES

Annex I Document for the protocol approval by the Ethical Committee of the International University of Catalonia

CEIC Comitè Ètic d'Investigació Clínica

CUO Clínica Universitària d'Odontologia | Universitat Internacional de Catalunya

CARTA APROVACIÓ ESTUDI PEL CEIC

Número de l'estudi: PER-ECL-2013-07
Versió del protocol:1.3
Data de la versió:02/04/2014
Títol:"Efectos clínicos tras la aplicación de láser Er-Cr: YSGG durante la fase higiénica de tratamiento periodontal"

Sant Cugat del Vallès, 08 d'abril de 2014

Dr.Antonio Santos/Dr.Federico Hernández

Referència: "Efectos clínicos tras la aplicación de láser Er-Cr: YSGG durante la fase higiénica de tratamiento periodontal"

Benvolgut Doctor,

Els membres del CEIC de la Clínica Universitària d'Odontologia, els hi agraeixen l'aportació científica en el camp de la investigació i la presentació del Protocol en aquest Comité per a la seva avaluació.

Valorades les noves aportacions realitzades a l'estudi, sol.licitades pel nostre CEIC, el passat dia 02 d'abril de 2014, li comuniquem que el dictamen final ha sigut FAVORABLE.

Li recordem que, segons la Normativa del Real Decret 223/2004 art. 27, s'haurà de presentar al Comitè d'Ètica d'investigacions clíniques de la CUO, i a través de la Comissió Científica, un informe preliminar mensual del seguiment de l'estudi i un informe final un cop finalitzat aquest.

1

Annex II Information document for patients enrolled in the study

CEIC Comitè Ètic d'Investigació Clínica

DOCUMENTO DE INFORMACIÓN AL PACIENTE PARTICIPANTE EN EL ESTUDIO DE INVESTIGACIÓN

Número de protocolo de investigación: PER-ECL-2013-07

Investigador/a principal: Antonio Santos Alemany/ Federico Hernández Alfaro

Investigador/a secundario/a (alumno/a): Vanessa Ruiz Magaz

Tutor/a / monitor/a: Jose Nart Molina

Departamento: Periodoncia

Línea de investigación: Láser

Título de la investigación: Efectos clínicos tras la aplicación de láser Er-Cr: YSGG durante la fase higiénica de tratamiento periodontal.

CEIC Comitè Ètic d'Investigació Clínica

He solicitado su participación en un estudio de investigación. Antes de decidir si acepta participar, es importante que comprenda los motivos por los que se lleva a cabo la investigación, cómo se va a utilizar su información, en qué consistirá el estudio y los posibles beneficios, riesgos y molestias que les pueda conllevar.

En el caso de participar en algún otro estudio, deben comunicarlo al responsable para valorar si pueden participar en éste. Un paciente sólo puede participar en un estudio clínico.

¿CUÁLES SON LOS ANTECEDENTES Y EL OBJETIVO DE ESTE ESTUDIO?

Actualmente se está popularizando el uso de láser en diferentes disciplinas médicas. Se ha comprobado científicamente que su uso es seguro y no presenta efectos dañinos para la salud del paciente. En relación a la piorrea o enfermedad periodontal, se ha visto en varios estudios que parece que su aplicación puede hacer mejorar el estado de salud de las encías y hueso que sujeta los dientes gracias al poder bactericida, entre otros, ***de esta luz láser.*** Es por este motivo que deseo realizar un estudio en el que añado una luz láser al tratamiento convencional y de este modo puedor observar, gracias a una mediciones, en que medida es positiva su aplicación y cómo nos podemos beneficiar.

¿TENGO LA OBLIGACIÓN DE PARTICIPAR?

La decisión sobre participar o no en la investigación es suya. En el caso de no querer participar o bien de querer abandonar, la calidad de la asistencia que recibirán, no se verá afectada y se seguirán los protocolos médicos habituales de cada departamento. Si decide participar, se le entregará el formulario de consentimiento informado para que lo firmen.

Asimismo, el/la doctor/a que se encarga de dirigir el estudio, Vanessa Ruiz Magaz, podrá considerar que su participación ya no les reporta ningún tipo de beneficio. Además, en caso de no seguir las instrucciones de la doctora del estudio, o por cualquier otro motivo justificado, se dará por concluida su participación sin la necesidad de su consentimiento.

Finalmente, una vez haya concluido su participación, deberán seguir los procedimientos indicados por la doctora para garantizar su seguridad.

CEIC Comitè Ètic d'Investigació Clínica

¿QUÉ PASARÁ SI ACEPTO PARTICIPAR?

Se le realizará el tratamiento covencional de fase higiénica para el tratamiento de la periodontitis con raspados y alisados radiculares en dos cuadrantes de su boca con curetas y ultrasonidos y los dos restantes recibirán tratamiento adicional con láser

¿CÚALES SON MIS OBLIGACIONES?

Cepillarse adecuadamente los dientes y pasar el hilo de seda a diario para obtener una higiene oral adecuada y debe venir a las 6 semanas de haber realizado el tratamiento para realizar una reevaluación.

¿CUÁLES SON LOS POSIBLES EFECTOS SECUNDARIOS, RIESGOS Y MOLESTIAS ASOCIADOS A LA PARTICIPACIÓN?

El láser Er-Cr:YSGG se trata de un producto que ya se ha aplicado en humanos, y no presenta efectos adversos sobre las raíces dentales ni tejidos periodontales cuando se aplica con los parámetros que se usan en este estudio.

¿CUÁLES SON LOS POSIBLES BENEFICIOS DE PARTICIPAR?

Pretendo demostrar que la utilización adicional del láser Er-Cr:YSGG mejora significativamente los parámetros relacionados con el estado de salud periodontal como por ejemplo el sangrado gingival.

¿CÓMO SE VAN A UTILIZAR MIS DATOS DEL ESTUDIO?

Según el artículo 3.6 del RD 223/2004, de 6 de febrero, por el que se regulan los ensayos clínicos con medicamentos, el tratamiento, la comunicación y la cesión de los datos de carácter personal de los sujetos participantes en el ensayo, éste se ajustará a lo dispuesto en la Ley orgánica 15/1999, de 13 de diciembre, de protección de datos de carácter personal.

La doctora del estudio utilizará sus datos personales para la administración y dirección del estudio, la investigación y los análisis estadísticos.

Estos datos, no incluye su nombre ni su dirección, sino que la doctora del estudio le asignará un número de código. Únicamente la doctora del estudio y mi equipo investigador, tendrán acceso a la clave del código que permite asociar los datos del estudio con usted. No obstante, autoridades reguladoras, el comité de ética independiente u otras entidades de supervisión podrán revisar sus datos personales, el objetivo de dichas revisiones es garantizar la dirección adecuada del estudio o la calidad de los datos del estudio.

CEIC Comitè Ètic d'Investigació Clínica

Cualquier uso continuado de los datos del estudio por parte de la doctora del estudio tendrá los fines que se describen en este formulario. Si retiran el consentimiento de utilizar sus datos del estudio, no podrán seguir participando en la investigación. ***Debe*** tener en cuenta que los resultados del estudio podrán aparecer publicados en la bibliografía médica, si bien su identidad no será revelada. En caso de que deban tomarse fotografías de la cara y/o el cuerpo completo, se garantizará la protección de su identidad.

Se han de poner en conocimiento del Ministerio Fiscal, los ensayos clínicos que incluyen a menores; por tanto, es posible que el Ministerio Fiscal se ponga en contacto con ustedes a fin de obtener información sobre la evolución del estudio.

¿CÓMO PUEDO ESTABLECER CONTACTO SI NECESITO OBTENER MÁS INFORMACIÓN O AYUDA?

Mediante la firma de este formulario, usted asienta que han estado informado de las características del estudio, han entendido la información y la doctora ha clarificado todas sus dudas.

En caso de sufrir un daño relacionado con el estudio o para obtener respuesta a cualquier pregunta que pueda surgir durante la investigación, pónganse en contacto con:

Dr. Antonio Santos Alemany y Dr. Federico Hernández Alfaro
Vanessa Ruiz Magaz
Clínica Universitaria de Odontología
Universitat Internacional de Catalunya
Dirección: C/ Josep Trueta, s/n-08195, Sant Cugat del Vallés
Num. de teléfono: 93 504 20 30
Mail: cec.cuo.ceic@uic.es

Annex III Document for the informed consent

CEIC Comitè Ètic d'Investigació Clínica

CONSENTIMIENTO INFORMADO

Número de protocolo de investigación: PER-ECL-2013-07

Investigador/a principal: Antonio Santos Alemany/ Federico Hernández Alfaro
Investigador/a secundario/a (alumno/a): Vanessa Ruiz Magaz
Tutor/a / monitor/a: Jose Nart Molina
Departamento: Periodoncia
Línea de investigación: Laser
Título de la investigación: Efectos clínicos tras la aplicación de laser Er-Cr: YSGG durante la fase higiénica de tratamiento periodontal.

CEIC Comitè Ètic d'Investigació Clínica

Yo, Sr./Sra.: .....

- He recibido información verbal acerca del estudio y he leído la información escrita que se adjunta, de la que he recibido una copia.
- He comprendido lo que se me ha explicado.
- He podido comentar el estudio y realizar preguntas al profesional responsable.
- Doy mi consentimiento para tomar parte en el estudio y asumo que mi participación es totalmente voluntaria.
- Entiendo que podré retirarme en cualquier momento sin que ello afecte a mi futura asistencia médica.

Mediante la firma de este formulario de consentimiento informado, doy mi consentimiento para que mis datos personales se puedan utilizar como se ha descrito en este formulario de consentimiento, que se ajusta a lo dispuesto en la Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal.

Entiendo que recibiré una copia de este formulario de consentimiento informado.

_____ _____

Firma del paciente o la paciente — Fecha de la firma
N.° de DNI

CEIC Comitè Ètic d'Investigació Clínica

DECLARACIÓN DEL INVESTIGADOR O LA INVESTIGADORA

El paciente o la paciente que firma esta hoja de consentimiento ha recibo, por parte del profesional, información detallada de forma oral y escrita del proceso y naturaleza de este estudio de investigación, y ha tenido la oportunidad de preguntar cualquier duda en cuanto a la naturaleza, los riesgos y las ventajas de su participación en este estudio.

_____ _____

Firma del investigador o investigadora Fecha de la firma
Nombre:

Annex IV Letter of acceptance for publication in *The International Journal of Periodontics and Restorative Dentistry*

Manuscript title: Efficacy of adjunctive Er,Cr:YSGG laser application following scaling and root planing in periodontally diseased patients

Dear Dr Ruiz Magaz

It is a pleasure to inform you that the above manuscript is acceptable for publication.

Thank you for taking the time and making the effort necessary to accomplish such a fine result. I hope that you will continue to consider The International Journal of Periodontics & Restorative Dentistry for publication of your studies in the future.

In order to publish your article, we will require high-resolution digital image files. For more information about image quality requirements, please see the Guidelines for Authors.

Please email image files to Dojna Shearer, Managing Editor, at dshearer@quintbook.com or upload to a file transfer service of your choice, such as wetransfer.com or hightail.com. If necessary, mail a disk containing the image files to:

Managing Editor
Quintessence Publishing Co Inc.
4350 Chandler Drive
Hanover Park, IL 60133

Yours sincerely

Myron Nevins

Annex V Summary

El acúmulo de bacterias sobre tejidos duros orales es la causa básica del desarrollo de gingivitis y periodontitis. Por ello que es fundamental eliminar de forma mecánica y regular la placa bacteriana que se ha depositado sobre las superficies no descamantes. Sin embargo, ciertos patógenos como *A.actinomycetemcomitans* pueden ser inaccesibles a estas intervenciones mecánicas debido a su capacidad para invadir los tejidos periodontales o los túbulos dentinarios o porque residen en localizaciones de difícil acceso para instrumentos periodontales como pueden ser las concavidades radiculares o las furcas.

A finales de 1930 cambió el enfoque de tratamiento de las infecciones bacterianas gracias a la introducción de quimioterápicos potentes. Estos productos eran capaces de destruir o invalidar las bacterias causantes de infecciones. A pesar de ello, a lo largo de las siguientes décadas se ha observado que estos productos presentan limitaciones y pueden producir efectos indeseables como el desarrollo de resistencias a antibióticos .

A principios de la década de los noventa, se observó que algunos tipos de láseres tenían aplicaciones en el tratamiento y mantenimiento periodontal. Los láseres más prometedores para el tratamiento de tejidos duros eran Er:YAG (2,94 μm de longitud de onda) y Er, Cr:YSGG (2,78 μm de longitud de onda). El láser Er:YAG es bién absorbido por todos los tejidos biológicos que contienen moléculas de agua, este láser está indicado no sólo en el tratamiento de tejidos blandos, sino también duros. El láser Er-Cr:YSGG es una incorporación posterior al armamentario de láseres de uso odontológico. Presenta una longitud de onda que es más altamente absorbido por los iones de OH que por las moléculas de agua y tiene unas aplicaciones similares a las del láser Er:YAG. La presente tesis presenta un estudio realizado con el láser de Er,Cr.YSGG.

Numerosos estudios clínicos han demostrado la eficacia del uso del láser de Er:YAG cuando se utiliza en combinación con el raspado y alisado radicular y existen estudios básicos que avalan la seguridad de uso del láser de Er,Cr:YSGG sobre superficies radiculares. Sin embargo, el número de estudios sobre los efectos clínicos del láser Er,Cr:YSGG como complemento del raspado y alisado radicular en pacientes con periodontitis es muy limitado.

Actualmente es necesario establecer protocolos críticos de uso que demuestren su efectividad basándonos en la evidencia. Siguiendo las recomendaciones del "Consensus Report of the Sixth European Workshop on Periodontology" se elaboró un protocolo de estudio en el que se incluyeron 30 pacientes para evaluar la eficacia terapéutica de la aplicación adicional de láser Er,Cr:YSGG durante el desbridamiento subgingival comparándolo con el desbridamiento convencional. Las variables clínicas evaluadas fueron la profundidad de sondaje (PPD), recesión gingival (GR) y el nivel de inserción clínica (CAL) junto con el índice de sangrado (BoP).

Basándonos en un cálculo muestral apropiado y con una potencia adecuada, los resultados de este estudio demuestran que la irradiación complementaria con láser de Er,Cr:YSGG durante el tratamiento convencional de raspado y alisado radicular no aporta beneficios en relación a la reducción de la profundidad de bolsa ni cambios en la recesión gingival a las 6 semanas ni a los 6 meses de la reevaluación de los valores iniciales. En cambio, el nivel de inserción clínica mejora discretamente en el grupo de tratamiento convencional si se compara con el grupo test en el que se aplica adicionalmente láser Er,Cr:YSGG.

Estos resultados están en concordancia con la mayoría de estudios clínicos randomizados y controlados que evalúan la eficacia de los láseres de Erbio como complemento del desbridamiento subgingival tradicional. Por tanto, el uso de este tipo de láser es aún cuestionable en el tratamiento de la periodontitis crónica.