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NCT04027686

June 30, 2016

Research Proposal

Clinical Evaluation of WaterLase (iPlus) Laser Therapy used as an Adjunct to Non-Surgical Treatment of Chronic Periodontitis: A Randomized, Controlled, Split-Mouth Clinical Study

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Abstract

Laser use in dentistry has grown rapidly in recent years. This is especially true for the use of lasers in periodontics. Laser therapy is thought to provide marked improvement in non-surgical treatment outcomes resulting in a reduction in the need for surgery when compared to conventional periodontal therapy (scaling and root planing) alone. The research supporting these claims is limited to a few short-term studies and case reports. Questions remain regarding the long-term benefits of adjunctive laser therapy in the treatment of chronic periodontitis. However, if laser therapy proves to be advantageous, it has the potential to have a significant impact on the treatment of chronic periodontitis. Periodontal health and stability must be demonstrated over time to substantiate the claim of achieving successful periodontal therapy with a reduced need for surgery. The aim of this randomized, controlled clinical study is to examine the clinical efficacy of laser therapy as an adjunct to scaling and root planning in comparison to conventional non-surgical periodontal therapy alone. Clinical parameters including plaque index, gingival index, bleeding on probing, periodontal probing depth and clinical attachment levels will be measured at baseline and at 1, 3, 6, 9, and 12 months following treatment. Intraoral digital periapical radiographs and cone beam computed tomography scans will be taken at baseline, 6 and 12 months to evaluate changes in periodontal bone levels. This non-invasive method of evaluating changes in periodontal bone levels will serve as a surrogate indicator of periodontal bone regeneration.

Background and Significance

A substantially growing area of interest among clinicians is the use of lasers in the treatment of chronic periodontitis. Recently published data reveals a higher prevalence of periodontal disease in the US population than previously estimated, with approximately half of American adults suffering from varying forms of periodontal disease.[1] Periodontitis is a disease caused by bacterial pathogens that form a biofilm on the tooth / root surface, which elicits a host inflammatory response resulting in bone resorption, attachment loss, pocket formation and/or gingival recession. The diagnosis of periodontal disease is rendered by examination of the supporting tissues with a periodontal probe and evaluation of bone levels with radiographs.[2]

Non-surgical treatment of periodontitis with scaling and root planing (SRP) and ultrasonic scalers has been shown to be effective in removing subgingival calculus and increasing root surface smoothness to aid in the control subgingival bacterial biofilm. As a result, it reduces gingival inflammation, bleeding on probing and probing pocket depths.[2] Oral hygiene instruction with frequent reinforcement is also recognized as an important part of successful treatment.[3] However, SRP alone is not sufficient to treat all cases often due to instrument inaccessibility and clinician skill. It must be noted that significant limitations exist with conventional, non-surgical therapy due to the difficulty in accessing hard to reach areas such as furcations, root concavities, anatomical grooves and deep pockets, which ultimately justifies the need for surgical treatment.[4] Miniaturization and modifications of hand instrumentation have improved our ability to access difficult areas resulting in more effective treatment but challenges remain.

Surgery vs. Non-Surgical Therapy

Many studies have addressed the debate of whether to treat periodontitis with surgical or non-surgical methods. While both treatment modalities have been shown to be effective, surgical therapy initially demonstrates better pocket depth reduction in deeper

pockets.[5] This is likely due to the typical access limitations of traditional non-surgical treatment and the inability to effectively remove calculus in deep periodontal pockets.

Recently, lasers have been increasingly promoted as an adjunctive treatment to non-surgical therapy and an alternative to surgical therapy with some studies showing decreases in bacterial load, reduced inflammation and new-attachment/reattachment.[6, 7] Unfortunately, there is a paucity of published clinical studies to evaluate the effectiveness of laser therapy on chronic periodontitis. A significant problem with assessing the effectiveness of laser therapy is the variety of laser types, wavelengths and protocols used for the treatment of periodontal disease. Each laser has a specific medium and operating wavelength. The most common lasers used in dentistry today include the Nd:YAG laser (neodymium doped: yttrium, aluminum, and garnet), the Er:YAG laser (erbium doped: yttrium, aluminum, and garnet), the diode laser and the carbon dioxide (CO_2) laser. Wavelengths range from 635 to 10,600 nm.[8] The variability between laser units makes identifying an appropriate and effective protocol difficult. Consequently, numerous questions are raised regarding the efficacy of laser therapy in the treatment of periodontal disease.

The standard of care for the initial treatment of chronic periodontal disease has historically been non-surgical scaling and root planing. Laser therapy may augment non-surgical periodontal therapy by providing improved access to diseased root surfaces, improving the ability to remove calculus and enhance the reduction of oral pathogens found in the periodontal pocket. There may also be a stimulatory effect of laser therapy on periodontal wound healing and regeneration.

Regeneration vs. Repair

Studies evaluating conventional periodontal therapy have shown that both periodontal regeneration and repair can result from mechanical therapy and that both can be maintained to achieve stability and health.[9] The question that is of particular interest to many is whether laser therapy has the ability to induce or facilitate periodontal

regeneration. True periodontal regeneration, often considered the ultimate goal in periodontal therapy, occurs when there is regeneration of the periodontal attachment apparatus including new inserting connective tissue fibers into the previously diseased root surface with new cementum, alveolar bone and periodontal ligament.

To date, only two human clinical studies have attempted to evaluate the potential of laser therapy on periodontal regeneration. Specifically, these two studies tested LANAP® (Laser Assisted New-Attachment Procedure), using an FDA approved laser (PerioLase, Millennium Dental Technologies, Inc.) and patented protocol marketed for the treatment of chronic periodontitis.[7, 10] In 2007, Yukna et. al., published human histological results of a small clinical study using the LANAP protocol. Six pairs of single rooted teeth with subgingival calculus in six patients (three men and three women) were scaled and root planed with ultrasonic and hand scalers. One tooth of each pair was also treated with the LANAP® protocol. Three months after treatment, all treated teeth were removed en bloc for histologic processing. The authors reported periodontal regeneration with new cementum and new connective tissue attachment in all six of the LANAP® treated specimens, whereas five of the six control specimens had a long junctional epithelium with no evidence of new attachment or regeneration.[7] In 2012, Nevins, et. al., published histological findings of 10 teeth removed en bloc nine months after treatment with the LANAP® protocol.[10] They reported that five teeth showed evidence of some periodontal regeneration with new cementum, periodontal ligament and alveolar bone. One tooth showed evidence of new attachment with new cementum and inserting collagen fibers, and four teeth showed healing via long junctional epithelium. Critically, there were no controls in this study. Subsequently in 2014, Nevins, et. al., published the nine month clinical findings of the above study.[11] There were eight patients with a total of 930 sites treated with full-mouth LANAP® at a single clinical center. Briefly, the authors reported a mean probing depth reduction from 4.62 ± 2.29 mm to 3.14 ± 1.48 mm after nine months ($p < 0.05$). Recession increased from 0.86 ± 1.31 mm to 1.52 ± 1.62 mm. Analysis revealed that 73% of all sites decreased probing depth, 21% of sites had no change and 6% of sites increased probing depth; 58% of

sites gained attachment, 24% of sites showed no change in attachment and 18% of sites lost clinical attachment. Again, there were only eight patients in the study and there were no controls.

Clearly, well-designed, controlled clinical trials are needed to evaluate the effectiveness of lasers as an adjunctive therapy in the non-surgical treatment of chronic periodontitis.

Specific Aims

The purpose of this study is to evaluate whether adjunctive laser therapy will yield more favorable clinical results than conventional therapy alone in the treatment of chronic periodontitis. The laser to be evaluated in this study is the Waterlase iPlus (Er,Cr:YSGG) laser.

The specific aims of this research are to:

1. Evaluate the effect of adjunctive laser (Er,Cr:YSGG) therapy on periodontal disease resolution using clinical parameters to assess improvement in periodontal health.

2. Evaluate the effect of adjunctive laser (Er,Cr:YSGG) therapy on periodontal regeneration using radiographic imaging to assess changes bone levels (as a surrogate marker of regeneration).

Hypothesis

Laser therapy, used as an adjunctive treatment with conventional non-surgical therapy, improves the short- and long-term clinical and radiographic results of periodontal treatment as compared to conventional non-surgical therapy alone and reduces the need for surgical intervention in patients with moderate to severe chronic periodontitis.

Materials and Methods

This study will be a single center, prospective randomized, controlled clinical trial. Thirty-Five (35) patients with moderate to severe chronic periodontitis (affecting at least two quadrants, each with two or more sites probing ≥ 5mm) will be included in the study. The research will be conducted in the Postgraduate Periodontics and Implant Surgery Clinic at the UCLA School of Dentistry.

Inclusion criteria

- Age 18 years old or older (male or female)
- Healthy without systemic diseases that may adversely effect healing
- Not pregnant and no current plans to become pregnant
- No periodontal treatment in the previous 6 months
- No systemic antibiotic therapy in the previous 6 months
- At least two quadrants with chronic periodontitis (ideally opposite side same jaw)
- Each quadrant must have two or more sites with probing pocket depths ≥ 5mm
- Presence of interproximal intrabony defect(s) in each quadrant

Exclusion criteria

- Any systemic disease, medication, or habit known to adversely influence bone metabolism and/or wound healing:
    - Poorly controlled diabetes (HbA1c > 7%)
    - History of bisphosphonate medications
    - History of radiation therapy affecting the proposed treatment site(s)
    - History of immunosuppressive medications (e.g. corticosteroids)
    - History of tobacco use (current or past tobacco use within the past 1 year)
    - Immune compromise caused by disease, treatment or other condition
- Recent history of periodontal surgery (within the previous 2 years)
- Recent history of scaling and root planing (within the previous 1 years)
- Any condition that contraindicates periodontal therapy including surgery

Instrumentation. The laser to be used in this protocol is the Waterlase iPlus Er,Cr:YSGG laser manufactured by Biolase (Irvine, California, USA).

Laser specifications as described by the manufacturer:

- Model: Waterlase iPlus
- Operating Voltage: 100 VAC ± 10% / 230VAC ± 10%
- Frequency: 50 / 60 Hz
- Current Rating: 15.0 A / 8A
- Laser classification: Class 4 (Er,Cr:YSGG), Class 1 (635nm red Aiming Beam)
- Type of laser: Er,Cr:YSGG
- Wavelength: 2780 nm
- Type of operation: Pulse
- Laser energy: 0- -600 mJ
- Aiming Beam: 635nm (red)
- Cooling method: Water cooling (built-in reservoir)
- Outer dimensions (WxDxH): 11” x 19” x 33” (246mm x 585mm x 1057mm)
- Weight: Approx. 75 lb. (34 kg)

Operator training. A training session offered by Biolase and The World Congress for Laser Instruction (WCLI) for the use of the Waterlase iPlus Er,Cr:YSGG laser has been completed by the principal investigator and will be completed by all co-investigators participating in this study.

A pressure sensitive Florida Probe will be used to standardize and calibrate examiners. A UNC-15 periodontal probe will also be used in this study to evaluate the clinical parameters. It has markings in 1 mm increments up to 15 mm.

Non-surgical instrumentation will include the use of a Symmetry IQ 3000 Piezo Scaler (Hu-Friedy) with fiber optic light and various tips, Universal and Gracey curettes (Hu-Friedy).

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Protocol Summary. Following a thorough review of the patient's health history, clinical and radiographic examination, qualified subjects will sign an informed consent to be enrolled in the study. Treatment will be randomly assigned to quadrants and implemented according to the following standardized protocol:

1. Participants will be provided with oral hygiene aids and receive standardized oral hygiene instructions.
2. One week following oral hygiene instruction participants will return for collection of baseline clinical data including:
    a. Plaque index
    b. Gingival index
    c. Bleeding on probing
    d. Probing pocket depth
    e. Gingival recession
    f. Clinical attachment levels (calculated)
3. Each qualifying quadrant will be randomly assigned to scaling and root planing alone or scaling and root planing with adjunctive laser treatment.
4. At the time of treatment, occlusal contacts will be evaluated and appropriate occlusal adjustments will be made if deemed necessary (i.e. adjustment of occlusal interferences and/or fremitus).
5. Each quadrant will be treated, according to assigned group, at separate visits that are at least two weeks apart.
6. A plaque sample (biofilm) will be collected from selected sites in each qualifying quadrant prior to treatment for microbial analysis. This will be repeated at the re-evaluation appointments.
7. A visual analog scale will be used to assess pain during the first 24-48 hours.
8. Subjects will keep a log of the type and amount of analgesics taken.
9. Subjects will be evaluated at 3, 6, 9 and 12 months after therapy.
10. Periodontal recall maintenance will be provided, as needed, at 3, 6, 9 and 12 months. Oral hygiene instructions will be reinforced at each visit.

11. Radiographic imaging (intraoral digital periapical radiograph and cone beam computed tomography scan) will be taken of each quadrant/treatment site at baseline, 6 and 12 months.
12. Subjects will complete a written survey to answer questions about their satisfaction with the treatment provided.

Treatment Groups. Each subject must have at least two qualifying quadrants. One quadrant will be randomly assigned to one of the two treatment groups (control or test) and the second quadrant will be assigned to the other group. Every subject will have at least one quadrant assigned to the control group and one quadrant assigned to the test group and will thus serve as their own control. Each additional qualifying quadrant in the same individual will be assigned to the next treatment group (i.e. if the second quadrant was assigned to the test group, then the third quadrant will be assigned to the control group and the fourth quadrant will be assigned to the test group). Treatment of multiple quadrants in the same group for the same subject will be treated on the same visit in order to maintain a reasonable follow-up / data collection schedule. All treatment will be completed with local anesthesia.

Group 1 (control):

- Non-surgical, mechanical scaling and root planing with hand instruments and ultrasonic device.

Group 2 (test):

- Non-surgical, mechanical scaling and root planing with hand instruments and ultrasonic device including the use of adjunctive WaterLase iPlus (Er,Cr:YSGG) laser therapy according to the following REPaiR protocol. See Attachment 1.

Post-treatment Instructions. All patients will be provided with specific oral hygiene instructions. From day two until day seven, patients will be instructed to brush with a

manual soft or extra-soft toothbrush and to use interproximal cleaning aids. Patients will return for postoperative evaluation at week 2 and months 1, 3, 6, 9 and 12.

Recall Maintenance Cleanings. Supportive periodontal therapy (recall maintenance cleanings) will be completed, as needed, at 3, 6, 9, and 12 months after treatment. Recall maintenance therapy will be limited to supragingival scaling and prophylaxis.

Data Collection. Data will be collected in a standardized, de-identified fashion and will be stored in a locked file cabinet at the study site. Data will be entered into a password-protected database. At the completion of the study including analysis and publication, the data sheets will be destroyed.

Clinical Measurements. The following clinical measurements will be recorded at the initial baseline examination (0), 3, 6, 9, and 12 months after treatment:

- Probing depth (PD) at six sites for each tooth
- Bleeding on probing (BOP) at six sites for each tooth
- Plaque index (PI) at six sites for each tooth
- Gingival index (GI) at six sites for each tooth
- Gingival recession at six sites for each tooth
- Clinical attachment level (CAL) at six sites for each tooth (calculated)
- Plaque score % (calculated)
- Bleeding score % (calculated)

Data Analysis. A biostatistician will be consulted for data analysis. Comparative evaluation of radiographic imaging will be analyzed with an experienced consultant.

Patient Compensation. Subjects will not receive financial compensation for participation in this study. Subjects will be provided with non-surgical periodontal treatment including laser therapy as well as 1 year post-initial therapy maintenance associated with the study at no cost to them. Periodontal therapy will include scaling

and root planing with or without adjunctive laser therapy and periodic periodontal recall maintenance over the course of 12 months while enrolled in the study. Any other non-periodontal dental treatment needs that may be deemed necessary will be the patient's responsibility.

Human Subjects and Privacy. This study proposal is being submitted to the UCLA Human Research Protection Program (HRPP) for IRB approval. A similar protocol using an Er:YAG laser has been approved. It is anticipated that this protocol will be approved.

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ATTACHMENT 1

REPaiR Protocol (**R**egenerative, **Er,Cr**:YSGG, **P**eriodontitis, ai, **R**egimen)

1) Surgical preparation: Following patient identification, review of health history and checking vital signs, local anesthesia is applied to the area.
2) Outer pocket de-epithelialization: The outer pocket gingival epithelium is removed (and gingivectomy performed if pseudopocket) with laser. Setting: RFTP5, 1.5W, 15% air, 15% water, 30 Hz, H mode (iPlus preset).
3) De-epithelialization and retraction: The inner pocket epithelium is removed from the free gingival margin to the level equal with the pocket depth. Setting: MZ6, 1.5W, 11% air, 20% water, 30 Hz, H mode (iPlus preset).
4) Scaling and Root Planing: Conventional treatment with hand instruments and ultrasonics to remove root surface accretions /calculus, and to smooth root surface cementum/dentin.
5) Sulcular Debridement / Degranulation: The purpose of this step is to remove smear layer from root surface, to completely remove pocket lining and to degranulate the pocket. Setting: RFPT5, 1.5W, 20% air, 40% water, 30 Hz, H mode (iPlus preset).
6) Bone Decortication: The purpose of this step is to recontour osseous defects and to stimulate bone regeneration. The tip is held parallel to the root surface while gently tapping all the way down to bone at the base of the defect. The laser slightly penetrates the bone at each point as this step is repeated stepwise around the tooth. The angle of the tip maybe changed to treat the walls of the intrabony defect. Setting: MZ6, 2.5W, 70% air, 80% water, 30 Hz, H mode (iPlus preset).
7) Sulcular Debridement: The purpose of this step is to remove the residual debris while inducing blood coagulation. The laser tip is gently brushed through the entire periodontal pocket in a sweeping motion from the base to the top of the pocket. Setting: RFPT5, 1.5W, 10% air, 10% water, 30 Hz, H mode (iPlus preset).
8) Compress: The surgical site is compressed with moistened 2 x 2 gauze using finger pressure for five minutes to achieve hemostasis.
9) ~~*Optional -Biostimulation: Application of the 940nm diode laser with pain therapy handpiece. Setting: 3.0W for 30 seconds directed toward the apices and another 30 seconds directed toward the gingival margins. THIS OPTIONAL STEP WILL NOT BE INCLUDED IN THIS STUDY – CONSIDER FOR FUTURE STUDIES.*~~