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Evaluation of Effectiveness of Photodynamic Therapy With Low-level Diode Laser in Nonsurgical Treatment of Peri-implantitis

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Abstract

Introduction: Side effects related to antibiotic therapy for peri-implantitis are rare in laser therapy (LT); therefore, the aim of this study was to evaluate the effectiveness of LT and photodynamic therapy (PDT) on patients with primary peri-implantitis.

Methods: In this randomized clinical trial, 40 implants presenting primary peri-implantitis in 20 patients with a mean age of 52.6 years old were included using the simple sampling technique. Periodontal treatment comprising scaling and root planing (SRP) was accomplished for the whole mouth while mechanical debridement with titanium curettes and air polishing with sodium bicarbonate powder was accomplished around the implants. The implants were randomly divided into two groups and treated with LT (control) and PDT (test). The clinical indices were measured at baseline, 6 weeks and 3 months after treatment. Real-time polymerase chain reaction (PCR) was used for analysis of microbial samples at baseline and 3-month follow-up. Data were analyzed with SPSS 20, using repeated-measures analysis of variance (ANOVA) and Friedman's and Mann-Whitney tests ($\alpha = 0.05$).

Results: Both groups showed statistically significant improvements in terms of bleeding on probing ($P < 0.001$), probing pocket depth (PPD) ($P = 0.006$) and modified plaque index ($P < 0.001$), with no significant differences between the 2 groups ($P > 0.05$). The number of *Aggregatibacter actinomycetemcomitans* ($P = 0.022$), *Tannerella forsythia* ($P = 0.038$) and *Porphyromonas gingivalis* ($P = 0.05$) in the test group and *Porphyromonas gingivalis* ($P = 0.015$) in the control group significantly decreased.

Conclusion: The results suggested that LT and PDT have significant short-term benefits in the treatment of primary peri-implantitis.

Keywords: Laser; Photosensitizer; Photodynamic therapy.

Introduction

Peri-implantitis is defined as the inflammation of supporting tissues of dental implants in association with bone loss, which will result in the progressive destruction of bone around the implant, if left untreated.[1] Peri-implantitis is treated through mechanical and chemical techniques. Usually, mechanical techniques alone cannot eliminate microorganisms from the major parts of pockets around the implants. In addition, after mechanical debridement with carbon fiber curettes alone, without any adjunctive treatment, pocket depth improves but not significantly.[2] In addition, various systemic and local chemical antimicrobial agents have been introduced for the treatment of peri-implantitis, which suppress periodontopathogens more effectively compared to mechanical techniques, and improve the results of conventional mechanical therapeutic techniques.[3-7] Some disadvantages of antimicrobial agents' use, (such as antibiotics) include an increase in the counts of bacteria resistant to these agents, the need for the use of different antibiotics due to the diversity of periodontopathogens, an increase in the number of immunosuppressed patients and the incidence of unfavorable reactions. Considering the complications above, it is necessary to expand research

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in an attempt to find alternative antimicrobial techniques. One of them is the application of lasers and photodynamic therapy (PDT), which might be effective in eliminating microbes in local and superficial infections.[8-11]

Nowadays, treatments with laser alone or PDT in association with photo-sensitizers have become popular as new therapeutic techniques in dentistry, and are used in a large number of dental procedures, including treatment of periodontal diseases,[12] peri-implant infections[13,14] and endodontic infections.[15] Given the non-invasive and local nature of lasers, the incidence of many side effects associated with the use of antibiotics, including injuries to the gastrointestinal mucosa and occurrence of drug allergies, are improbable with the use of lasers. In addition, since the photodynamic technique exerts its bactericidal effect through free oxygen species and hydroxyl radials, it appears that it is rare for resistance to occur against PDT.[16-19] A review study evaluated the results of several studies in an attempt to evaluate the effect of PDT on periodontal diseases, concluding that the use of photo-sensitizing dyes followed by their activation with visible light can effectively destroy periodontopathogens.[20]

Of all the lasers available, diode laser is used for the debridement of periodontal pockets and removal of the epithelial lining, including the granulomatous tissues.[21,22] This laser has a superb hemostatic effect and can be applied for cutting and coagulating gingiva and mucosa.[23] In addition, this laser can contact the implant surface without melting, cracking or making it concave.[1] Therefore, the aim of the present study was to evaluate the clinical and microbiological effects of the use of EmunDo dye as a photosensitizer, in association with the applications of 810-nm diode laser beams and to compare it with the application of laser alone for the treatment of peri-implantitis.

Methods

Subjects

The patients were selected from those referring to the Department of Periodontics, Faculty of Dentistry, Isfahan University of Medical Sciences, during 2014-2015. Twenty patients (10 males and 10 females) with an age range of 20-67 years and a mean age of 36.6 ± 9.7 years were selected. The subjects were selected using convenient sampling technique and signed informed consent forms after receiving explanations about the study procedures. The inclusion criteria consisted of age over 18, systemic health, no tobacco use and consent to be included in the study. The exclusion criteria consisted of use of alcohol or tobacco, pregnancy or breastfeeding, use of antimicrobial agents during the previous 2 months and a history of periodontal surgery during the previous year. Finally, a total of 40 sites with primary peri-implantitis in 20 patients were included in the study.

Study Design

The present double-blind randomized clinical trial had a 3-month follow-up design. Microbial samples were taken from the deepest part of each peri-implant pocket at the beginning of the study and 3 months after treatment. Microbial genome was evaluated using the real-time polymerase chain reaction (RT-PCR) technique. The clinical parameters of probing depth, papilla bleeding index[24] and modified plaque index (PI)[25] were determined at four points around each implant: distobuccal, mesiobuccal, distolingual and mesiolingual areas.

In the first stage, ultrasonic devices were used to carry out scaling and root planing (SRP) in all the oral cavity areas for every patient (Piezoscaler, Mectron, Carasco GE, Italy). In addition, mechanical debridement was carried out with a carbon fiber curette (Hu-Friedy, Chicago, USA) and air polishing was carried out with a Prophy-Jet (NSK, Tokyo, Japan) and sodium bicarbonate powder around the implants with peri-implantitis. Then all the patients were instructed in oral hygiene, including brushing with modified Bass technique and flossing.

Two weeks after completion of phase I periodontal treatment, the patients were recalled and were divided into test and control groups using a computer randomization table. In the control group, treatment of periodontitis consisted of a combination of mechanical debridement and irradiation with diode laser beams at a wavelength of 810 nm (Fox, A.R.C. Laser, Gmbh, Germany); in the test group, chemical debridement was combined with PDT by placing the EmunDo photosensitive material (EmunDo, A.R.C. Laser, Gmbh, Germany) within the pocket followed by irradiation with diode laser beams at a wavelength of 810 nm.

Laser Treatment/Photodynamic Therapy

Treatment was carried out with the use of diode laser beams at a wavelength of 810 nm, using the large-area handpiece and bulb fiber and bare fiber in each area. In the test group, the photosensitizer was injected into the pocket with the use of a direct blunt needle in the apico-coronal direction. After 90 seconds, the photosensitizer was rinsed away with saline solution (0.9% NaOCl). The same technique was repeated in the control group with the use of an occluded needle to blind the patients to the procedural steps. Then in both groups, the laser beams were directed toward the pockets using the following steps:

1. Transgingival irradiation: A bleaching handpiece was used for 30 seconds at a laser power of 300 mW (Figure 1A).

2. Intra-pocket irradiation: A bulb fiber measuring 300 µm in diameter was used to direct laser beams into the pocket with circular movements (300 mW, 30 seconds) (Figure 1B).

3. Elimination of granulation tissues from the infected pocket: A 300-µm bare fiber was used with circular movements (300 mW, 30 seconds) to eliminate the granulation tissues (Figure 1C).

The procedures above were repeated after 2 weeks. All the treatment procedures were carried out by a specialist who was unaware of the principle aims of the study and was

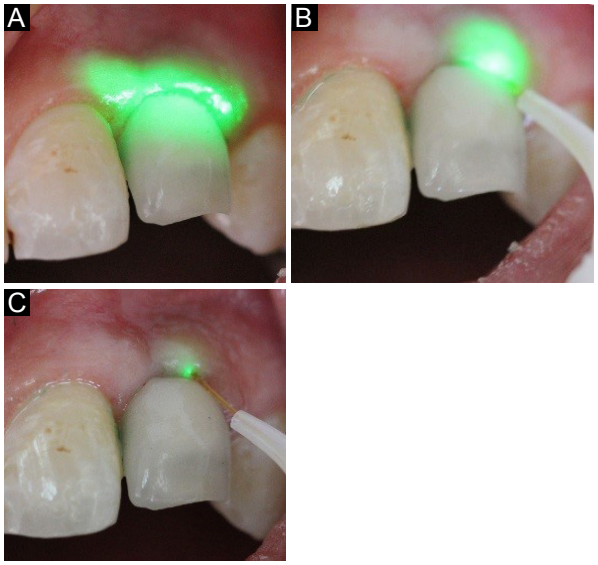

Figure 1. (**A**) Transgingival Irradiation by Bleaching Handpiece. **(B)** Intra-pocket Irradiation by a 300 µm Bare Fiber in a Circular Pattern**. (C)** limination of Granulation Tissues From the Infected Pocket Using a 300 µm Bare Fiber.

not involved in final evaluations.

During the whole laser irradiation procedures the patients and the personnel wore protective eyeglasses. From the beginning until the end of the study all the patients were examined every two weeks for any complications and to control the plaque and root surface debridement.

Clinical Measurements

The following clinical parameters were evaluated at baseline and at 6-weeks and 3-months postoperative intervals by a periodontitis who had been confirmed in relation to intra-examiner reproducibility.

Probing pocket depth (PPD): A plastic periodontal probe (Hu-Friedy, Chicago, USA), with a tip diameter of 0.5 mm, was placed with the use of 0.75-N probing force to measure the distance between the gingival margin and the sulcus depth.

PI: PI was determined with the use of modified Mombelli PI (mPI).[25]

Papilla bleeding index (BOP)[24]: Papilla PI was evaluated with the use of the same probing force and assessment of bleeding 30 seconds after probing.

Microbiologic Evaluation

Microbial samples were taken from the deepest part of each pocket at the beginning of the study and 3 months after treatment. A sterile paper point was placed in the pocket depth for 20 seconds and a cotton roll was used for isolation. Then each sample was placed in a sterile vial (pooled sample) and sent to the laboratory for the analysis of the genome. Real-time PCR was used with a conventional kit (Kiagen, USA) for the analysis of microbial samples to determine *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Treponema denticola* and *Tannerella forsythia* counts.

Statistical Analysis

Means and standard deviations of clinical and microbial variables were determined in each group. Data were analyzed with SPSS 20. Kruskal-Wallis test was used to compare non-parametric data (PPD and BOP) between the groups. Mann-Whitney test was used for two-by-two comparison of the groups.

Friedman's and Wilcoxon tests were used to determine differences in mean clinical parameters at baseline and 6-week and 3-month intervals. Wilcoxon test was used to compare microbial variables between the groups at baseline and 3-month postoperative interval ($\alpha = 0.05$).

Results

Forty implants with primary peri-implantitis in 20 patients were included in the study. All the patients completed the 3-month period of the study. Healing was uneventful in all the cases, without pain, burning sensation or unpleasant feelings. The mean bone loss at the beginning of the study in the laser and PDT groups was 1.02 ± 0.47 and 1.45 ± 0.84 mm, respectively. Independent *t* test did not reveal any significant difference in the mean bone loss between the two groups ($P = 0.56$).

Table 1 presents the results of clinical parameters at baseline and at 6-week and 3-month postoperative intervals and their changes (Δ0-6 w, Δ0-3 m).

There were no significant differences between the 2 groups at baseline and 6 weeks and 3 months after the therapeutic procedures; however, there was significant decrease in all the clinical parameters after treatment ($P \leq 0.006$).

Table 2 presents the results of two-by-two comparisons of the clinical parameters during the whole study period. As shown in the table, all the parameters exhibited significant differences at 6-week and 3-month intervals except for the mean of probing depth in the control group and the mean of bleeding index in the test group.

Table 3 presents the counts of periodontopathogens in the cultures at different time intervals and treatment groups. As shown in the table, laser significantly only decreased *P. gingivalis* counts ($P = 0.015$), and differences in *A. actinomycetemcomitans* counts were at significance threshold ($P = 0.061$). On the other hand, laser + EmunDo significantly decreased *A. actinomycetemcomitans* ($P = 0.022$), *T. forsythi*a ($P = 0.038$) and *P. gingivalis* ($P = 0.050$) counts. Mann-Whitney test did not reveal any significant difference in changes in bacterial counts before and after treatment between the treatment modalities ($P_{A. actinomycetemcomitans} = 0.846$, $P_{P. gingivalis} = 0.503$, $P_{P. intermedia} = 0.682$, $P_{T. denticola} = 0.399$ and $P_{T. forsythia} = 0.199$). Therefore, based on the results, the 2 treatment modalities had similar effects on bacteria.

Discussion

The results of the present study showed significant decrease in the means of PPD, BOP and mPI clinical parameters at

Table 1. The Results of Clinical Parameters at Baseline, 6 Weeks and 3 Months After Treatment And Their Changes (Δ0-6 w, Δ0-6 m)

Clinical Parameter	Time Interval	Group Test	Group Control	*P* Value[a]
PPD (mm)	Baseline	4.06 ± 0.78	4.02 ± 0.67	0.872
	6 Weeks	2.95 ± 0.89	2.87 ± 0.81	0.782
	3 Months	2.75 ± 0.84	2.69 ± 0.77	0.807
	P value (repeated measures ANOVA)	0.001	0.006	
mPI Mean score	Baseline	1.25 ± 0.64	1.01 ± 0.91	0.929
	6 Weeks	0.65 ± 0.49	0.60 ± 0.75	0.709
	3 Months	0.35 ± 0.49	0.25 ± 0.44	0.709
	P value (Friedman)	<0.001	<0.001	
BOP Mean score	Baseline	1.85 ± 0.87	2.00 ± 0.86	0.845
	6 Weeks	0.55 ± 0.69	0.85 ± 0.67	0.217
	3 Months	0.50 ± 0.61	0.35 ± 0.59	0.929
	P value (Friedman)	<0.001	<0.001	

[a]Independent *t* test for PPD, Mann-Whitney for mPI and BOP.

Table 2. The Results of Two-by-Two Comparisons of The Clinical Parameters During the Whole Study Period

Clinical Parameter	Time Interval	Test Group		Control Group	
		Δ	*P* Value[a]	Δ	*P* Value[a]
PPD (mm)	0-6w	1.11 ± 1.04	<0.001	1.15 ± 0.91	<0.001
	6w-3m	0.20 ± 0.64	0.039	0.19 ± 0.69	0.087
	0-3m	1.31 ± 1.16	<0.001	1.34 ± 1.08	<0.001
mPI Mean score	0-6w	1.30 ± 0.98	0.003	1.15 ± 0.74	0.012
	6w-3m	0.05 ± 0.60	0.014	0.50 ± 0.51	0.035
	0-3m	1.35 ± 0.87	<0.001	1.65 ± 0.93	0.002
BOP Mean score	0-6w	0.60 ± 0.68	<0.001	0.50 ± 0.76	<0.001
	6w-3m	0.30 ± 0.47	0.705	0.35 ± 0.67	0.002
	0-3m	0.90 ± 0.55	<0.001	0.85 ± 0.93	<0.001

[a]Paired *t* test for PPD and Wilcoxon for BOP and mPI.

Table 3. The Mean Counts of Periodontopathogens in Microbial Cultures in Terms of Time Intervals and Treatment Groups

Group	Bacteria	Before*	After*	Mean Difference*	*P* Value (Wilcoxon)
Laser	*A. actinomycetemcomitans*	1.12 ± 0.86	0.61 ± 0.62	-0.51 ± 0.85	0.061
	P. gingivalis	1.68 ± 1.50	1.03 ± 1.44	-0.64 ± 0.90	0.015
	P. intermedia	1.27 ± 1.11	0.65 ± 1.19	-0.62 ± 1.35	0.091
	T. denticola	0.48 ± 0.55	0.28 ± 0.44	-0.20 ± 0.46	0.26
	T. forsythia	0.31 ± 0.55	0.15 ± 0.27	-0.16 ± 0.57	0.481
Laser + EmunDo	*A. actinomycetemcomitans*	0.91 ± 0.80	0.47 ± 0.64	0.64 ± 0.44-	0.022
	P. gingivalis	1.42 ± 1.49	0.70 ± 0.99	1.49 ± 0.72-	0.050
	P. intermedia	1.04 ± 1.30	0.39 ± 0.58	1.59 ± 0.65-	0.182
	T. denticola	0.53 ± 0.63	0.21 ± 0.46	0.71 ± 0.32-	0.085
	T. forsythia	0.43 ± 0.55	0.14 ± 0.24	0.55 ± 0.29-	0.038

6-week and 3-month postoperative intervals compared to baseline in both groups; however, there were no significant difference between the two groups. In relation to BOP, PDT did not result in a significant difference after 3 months compared to the 6-week interval; however, such a difference was significant in the laser group. Therefore, there was no significant change after 3 months compared to 6-week interval. However, contrary to BOP, PPD exhibited greater decrease in the laser group; in this context, after 3 months no significant difference was observed compared to the 6-week interval. In addition, there were significant differences in PI between the three time intervals in both groups. It shows that during the study period, the oral hygiene of patients has improved.

On the other hand, the results of the present study showed no significant difference in decreasing bacterial counts between the two treatment modalities; the two techniques decreased all the bacterial counts, but eliminated none. Therefore, it can be concluded that both treatment modalities were effective in decreasing the counts of periodontopathogens. However, during the follow-ups in the present study, the differences were significant in the laser group only in relation to *P. gingivalis*; the differences were at significance threshold in relation to *A. actinomycetemcomitans*. In addition, in the PDT group, *A. actinomycetemcomitans*, *P. gingivalis* and *T. forsythia* counts decreased significantly.

Salvi et al[26] showed that mechanical debridement alone

around implants with carbon fiber curettes resulted in a decrease in inflammation severity in the mucosa and a decrease in pocket depth. However, many other studies, including that of Birang et al,[27] have shown that the use of diode laser or chlorhexidine gel, as adjunctive techniques, is more effective than mechanical debridement alone in the treatment of chronic periodontitis, concluding that if routine mechanical debridement is combined with diode laser or chlorhexidine gel, it will be more effective in improving the clinical and microbiologic parameters. Gojkov-Vakelic et al[28] showed that use of diode laser beams decreased the number of active pathogens in periodontal pockets. On the other hand, the results of studies done by Moritz et al[29] and Angelov et al[30] showed that treatment with diode laser might improve periodontal pockets and periodontal parameters. In a case report, Roncati et al[1] showed that the use of diode laser resulted in a decrease in probing depth and in a negative BOP around implants. Therefore, given the results of previous studies in relation to the effect of diode laser on decreasing periodontal pathogens and similarity between the microbial agents in periodontitis and peri-implantitis, in the present study, diode laser with a wavelength of 810 nm was used to improve peri-implantitis parameters. In addition, considering reports on the light absorption and florescence properties of different dyes, it was shown that excitation of these materials with light results in destructive effects in biologic systems.[31]

Von Tappeiner[32] showed that these reactions can result in the destruction of protozoa. Blum[33] and Spikes and Livingston[34] believed that PDT function depended on activated photoreactions in which the oxygen molecule takes part, resulting in photosensitized dye oxidation.

There is controversy over the effect of PDT. The majority of reports indicate that PDT only results in decreasing the inflammation severity and there is insufficient evidence in relation to the effect of PDT on periodontitis.[35-37] Shibli et al[38] showed the effect of PDT on the pathogens within periodontal pockets. Meisel and Kocher[20] showed that the use of photosensitizing dyes and their activation with laser beams might result in the destruction of pathogens responsible for periodontal diseases and peri-implantitis. Gursoy et al[39] suggested that PDT might be an appropriate tool in superficial and local infections, and although it cannot be an alternative for antimicrobial agents, it might facilitate the treatment of oral infections. Therefore, considering the results of studies on the effect of PDT on periodontal pathogens, periodontal infections and peri-implantitis, in the present study PDT was applied in the test group and its effects were compared with those of laser therapy (LT) alone in the control group.

Schar et al[2] compared the effects of PDT and during therapy with minocycline on peri-implantitis. The results showed that both treatment modalities were similarly effective in decreasing inflammation of the peri-implant mucosa.

Bassetti et al[40] compared drug therapy with minocycline and PDT for the treatment of peri-implantitis. A follow-up of 12 months showed a significant decrease in the number of sites with BOP, a decrease in probing depth and a decrease in *P. gingivalis* and *T. forsythia* counts, with no significant difference between the 2 groups.

The results of the present study in relation to a decrease in mucosal inflammation, a decrease in BOP and PPD and a decrease in bacterial colony counts are consistent with those of studies by Schar et al[2] and Bassetti et al.[40] Therefore, it can be concluded that treatment with laser, drug therapy and treatment with laser in association with photosensitizing dyes yield similar results in the treatment of peri-implantitis. On the other hand, based on the results of the present study only *P. gingivalis* counts in the control group and *A. actinomycetemcomitans*, *P. gingivalis* and *T. forsythia* counts in the test group decreased significantly; in this context, the bacterial species were similar to those in the study carried out by Bassetti et al.[40]

In a study, the effect of PDT with toluidine blue on periodontopathogens and biofilm on tooth surfaces was evaluated and it was reported that the use of diode laser beams at a wavelength of 830 nm in association with the use of toluidine blue within periodontal pockets was effective in destroying bacteria and it might be a reliable alternative for antimicrobial treatment in periodontitis.[41] Therefore, the results of the present study are consistent with studies carried on by Shibli et al,[38] Kocher and Mecisel[20] and the study mentioned above. PDT with a combination of laser and EmunDo dye resulted in destruction of bacteria and in a decrease in bacterial counts, indicating that the type of the dye does not influence the antibacterial effect and the presence of a different photosensitizing dye results in similar antibacterial effects. On the other hand, there was no significant difference between the use of laser beams alone and in association with a photosensitizing agent in the present study. Therefore, it can be concluded that dye does not have a major role in the antimicrobial effect of laser and laser alone is responsible for the antibacterial effect.

One of the limitations of the present study was the absence of comparisons between mechanical treatment alone and the two modalities of treatment with laser beams. In addition, another limitation was the lack of comparison of the results with the drug therapy technique. It is suggested that a similar study be carried out with a larger sample size in order to compare the effects of mechanical treatment, drug therapy and the use of laser beams.

Conclusion

Based on the results of this study, 810-nm laser beams alone and in association with photo-sensitizing dye resulted in improvements in the clinical and microbiological parameters around implants with peri-implantitis during the short follow-up periods of the study, with no significant difference between the 2 groups.

Ethical Considerations

The present randomized clinical trial study was registered at the Iranian Clinical Trials website under the code

IRCT2017030932749N2 (http://irct.ir) and was approved by the Ethics Committee of Isfahan University of Medical Sciences under the code 394383.

Conflict of Interests

None.

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