The application of photothermal therapy for the treatment of periimplantitis: A literature review

ABSTRACT

Aims: The aim of this study is to review the existing literature and evaluate the clinical performance of the EmunDo technique.

Methodology: The present study was designed as a literature review of the existing publications. The search strategy included an electronic search of studies published until February 2022 and a hand search by two different investigators. Search terms were a combination of the appropriate Medical Subject Headings (MeSH) terms and free-text words in simple or multiple conjunctions.

Results: Of the 34 full-text articles examined, only 3 met all the inclusion criteria and were included in the final analysis. Photodynamic therapy with toluidine blue (630nm) and photothermal therapy (EmunDo) with infracyanine green resulted in similar rates of A. actinomycetemcomitans decrease while the use of Er:YAG laser resulted in the smallest reduction of the microbial population. No alteration on the surface of the implants was observed. The EmunDo protocol resulted in significant higher reduction of A. Actinomycetemcomitans, T. Forsythia, P. Gingivalis.

Conclusion: EmunDo treatment protocol seems to have favorable results in the microbial reduction in cases of peri-implantitis, especially in the treatment of early stages. However, due to the limitations of the existing literature, further research is required for establishing the treatment protocol and exceeding the current restrictions.

Keywords: Photothermal therapy, periimplantitis, EmunDo

1. Introduction

Dental implants have been widely used in the last decades for the rehabilitation of partial or complete edentulism. Although they have a high survival rate, there are cases that complications need to be managed. The most common complication involves inflammation of bacterial aetiology of the peri-implant soft and hard tissue, often described as peri-implant mucositis or peri-implantitis. Clinical signs of peri-implant mucositis include redness in the peri-implant tissues, oedema and bleeding and/or suppuration on probing while in peri-implantitis cases loss of alveolar bone support is observed either clinically or radiographically.[1]

However, peri-implant health can also exist in implants with reduced bone support after the treatment of peri-implantitis. Albrektsson et al were the first to describe the correlation

between microbial biofilm and peri-implant diseases.[2] Salvi et al estimated in their study the prevalence of peri-implant diseases, proving thus the high probability that an implant may need peri-implant mucositis or even periimplantitis treatment in a period of time after placement.[3] Peri-implant mucositis was estimated to have a mean prevalence rate of 43% (range: 19-65%) while peri-implantitis 22% (range: 1-47%).[3] There have been several factors reported in the literature for the development of peri-implant diseases.[4,5]

Genetical factors is proved to determine the extent and severity of the inflammatory response while the history of periodontal disease, smoking, diabetes mellitus, the presence of excess cement in the peri-implant tissues (in cement-retained restorations), as well as the presence of cardiovascular disease are other factors that seem to have a potentially negative effect on peri-implantitis.[5] For the treatment of peri-implant diseases various approaches have been proposed. Management could be surgical or non-surgical, regenerative or respective.[6]

Apart from the mechanical removal of the microbial agent using ultrasounds, manual scalers or air-polishing without raising a flap, additional methods include the use of antibiotics or antiseptics, the mechanical or chemical alteration of implant surfaces, as well as the use of dental lasers.[6,7] Neodymium lasers (Nd:YAG, Neodymium-Doped Yttrium Aluminum Garnet, 1064nm), Erbium lasers (Er:YAG, Erbium Yttrium Aluminum Garnet, 2940nm και Er,Cr:YSGG, Erbium, Chromium-Doped Yttrium Scandium Gallium Garnet, 2780nm), Carbon Dioxide lasers (CO2, Carbon Dioxide, 10600nm), as well as diode lasers (810, 940, 980, 1064nm) have been investigated.[8-10] The effectiveness of these lasers relies on their potent antibacterial effect, the elimination of bacterial toxins, the disinfection of the peri-implant pocket, the activation of hemostasis, the improvement and acceleration of the healing process through biostimulation, as well as the reduction of bacteremia.[11,12]

This photodynamic therapeutical procedure is a promising approach against peri-implant diseases as it ensures the disinfection and the microbial, viral and mycotic population reduction in the oral cavity.[13] For the execution of this therapeutic protocol the local application of a photosensitiser with high binding affinity and fast accumulation ability at the target cells is needed.[14] The most popular photosensitisers are Methylene Blue (7-(dimethylamino)phenothiazin-3-ylidene-dimethylazanium; chloride) and Toluidine Blue O (7-

amino-8-methylphenothiazin-3-ylidene-dimethylazanium; chloride) with their activation being either with dental lasers or LED light bulbs.[13]

In the last years another photodynamic approach is developed enhancing more promising results.[15] The so called EmunDo protocol is a photothermal treatment that uses infracyanine green as a ptotosensitiser activated by a diode laser at a wavelength of 810nm.[16-19] Although it is a relative new treatment protocol, the results appear to be promising for the treatment of peri-implantitis in the short term and for the survival of the implant in the long term.

The aim of this study is to review the existing literature and evaluate the clinical performance of the EmunDo technique.

2. Materials and methods

The present study was designed as a literature review of the existing publications. The search strategy included an electronic search of studies published until February 2022 and a hand search by two different investigators. Search terms were a combination of the appropriate Medical Subject Headings (MeSH) terms and free-text words in simple or multiple conjunctions and were grouped as followed (peri-implantitis OR periimplantitis) AND (EmunDo OR indocyanine OR photothermal OR photodynamic OR ICG).

Additional to the subject headings criteria, the following inclusion criteria were also applied. Studies had to be in English language and focusing exclusively on the EmunDo protocol applied on implants. Reviews or meta-analyses, experimental model studies, studies in language other than English, and studies that described photodynamic treatment protocols with laser type or parameters that were different from those of the EmunDo protocol, were excluded. The final qualitative assessment was executed individually by the two researchers and only the studies that were selected by both researchers at the first screening or after consensus were used for the final analysis.

3. Results

A search of MEDLINE (PubMed) identified 140 articles. After title and abstract screening, 37 articles were excluded for not meeting the inclusion criteria or because the data could not be

extracted and 103 articles provided sufficient information. At abstract level screening 69 articles did not meet the researchers' criteria and were excluded. A full report of the remaining 34 articles was then obtained, and full screening followed. Of the 34 full-text articles examined, only 3 met all the inclusion criteria and were included in the final analysis. One double blinded randomized clinical trial and two in vitro studies provided adequate data following strictly the guidelines of the EmunDo protocol.

The first study was an in vitro study on the irradiation of implant surfaces covered by a A. actinomycetemcomitans biofilm.[20] The implants that had been included were implants with an SLA (sand-blatched, acid-etched) surface. Photodynamic therapy with toluidine blue (630nm) and photothermal therapy (EmunDo) with infracyanine green resulted in similar rates of A. actinomycetemcomitans decrease while the use of Er:YAG laser resulted in the smallest reduction of the microbial population. No alteration on the surface of the implants was observed as reported in the second included in vitro study of Saffarpour et al.[20]

In the in vivo study all patients received a mechanical debridement of the implant surface with titanium scalers and air polishing devices with sodium bicarbonate before photodynamic treatment. The EmunDo protocol resulted in significant higher reduction of A. actinomycetemcomitans, T. forsythia, P. gingivalis.[21-24] In terms of bleeding on probing ($P < 0.001$), probing pocket depth (PPD) ($P = 0.006$) and modified plaque index ($P < 0.001$), no significant differences between the investigated groups was observed.

4. Discussion

As the microbial removal from the implant surface and peri-implant pockets is crucial for the successful healing of peri-implant tissues and mechanical and chemical debridement that is widely used does not ensure the complete elimination of that microbial load from peri-implant tissues and implant surfaces, photodynamic treatment is proved to have a positive effect on the treatment of peri-implantitis. Moreover, the need for less invasive treatment methods with lower patient morbidity and less damage caused on the implant surface during the surgical procedure appears to be another major reason for the clinical application and the further development and research in the field of photodynamic laser therapy.

Among the existing photodynamic therapeutic options, the EmunDo treatment protocol seems to have promising and even better results in the microbial reduction in the treatment of peri-implantitis. It has been reported the beneficial effect against various strains such as P. gingivalis, streptococcus mutans and lactobacillus. However, the existing literature remains limited. Regarding the local or systemic use of antibiotics, the administration of different antibiotics is needed. However, they cannot reach highly effective doses within the peri-implant environment.[25,26] Not to mention the adverse effects that may cause patients with sensitivity and the development of antibiotic-resistant strains.

It becomes evident that techniques such as photodynamic and photothermal therapy offer promising solutions for the treatment of peri-implant diseases, even more when they are used adjacent to traditional therapeutic procedures and in combination with antibiotics or local use of chlorhexidine. The use of low-level lasers that cause minimal or no thermal damage to the adjacent healthy tissues or implant surfaces compared to high power lasers, is gaining ground in the treatment of peri-implantitis. According to the included studies photothermal therapy with the use of infracyanine green appears to have an effect on the reduction of the bacteria that are involved in peri-implant diseases, as well as towards improving the clinical parameters in the short run, while at the same time not causing damage to the implant surface.

The significant improvement of the clinical parameters and bone background shows that in cases of early peri-implantitis, this technique appears to be particularly effective. Among the limitations of the EmunDo protocol is the high cost for the clinician to obtain the equipment needed and the lack of enough controlled clinical trials that evaluate the effectiveness of this technique in combination with other peri-implantitis treatment options and in cases of different disease severity followed up overtime.

5. Conclusion

EmunDo treatment protocol seems to have favorable results in the microbial reduction in cases of peri-implantitis, especially in the treatment of early stages. However, due to the limitations of the existing literature, further research is required for establishing the treatment protocol and exceeding the current restrictions.

REFERENCES

1. Berglundh T, Armitage G, Araujo MG, et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of clinical periodontology*. Jun 2018;45 Suppl 20:S286-S291. doi:10.1111/jcpe.12957
2. Albrektsson TO, Johansson CB, Sennerby L. Biological aspects of implant dentistry: osseointegration. *Periodontol 2000*. Feb 1994;4:58-73. doi:10.1111/j.1600-0757.1994.tb00006.x
3. Salvi GE, Cosgarea R, Sculean A. Prevalence of Periimplant Diseases. *Implant Dent*. Apr 2019;28(2):100-102. doi:10.1097/ID.0000000000000872
4. Fourmousis I, Vlachos M. Genetic Risk Factors for the Development of Periimplantitis. *Implant Dent*. Apr 2019;28(2):103-114. doi:10.1097/ID.0000000000000874
5. Renvert S, Quirynen M. Risk indicators for peri-implantitis. A narrative review. *Clinical oral implants research*. Sep 2015;26 Suppl 11:15-44. doi:10.1111/clr.12636
6. Romanos GE, Javed F, Delgado-Ruiz RA, Calvo-Guirado JL. Peri-implant diseases: a review of treatment interventions. *Dent Clin North Am*. Jan 2015;59(1):157-78. doi:10.1016/j.cden.2014.08.002
7. Renvert S, Roos-Jansaker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. *Journal of clinical periodontology*. Sep 2008;35(8 Suppl):305-15. doi:10.1111/j.1600-051X.2008.01276.x
8. Romanos GE, Everts H, Nentwig GH. Effects of diode and Nd:YAG laser irradiation on titanium discs: a scanning electron microscope examination. *J Periodontol*. May 2000;71(5):810-5. doi:10.1902/jop.2000.71.5.810
9. Romanos GE, Nentwig GH. Regenerative therapy of deep peri-implant infrabony defects after CO2 laser implant surface decontamination. *The International journal of periodontics & restorative dentistry*. Jun 2008;28(3):245-55.
10. Romanos G, Ko HH, Froum S, Tarnow D. The use of CO(2) laser in the treatment of peri-implantitis. *Photomed Laser Surg*. Jun 2009;27(3):381-6. doi:10.1089/pho.2008.2280
11. Stubinger S, Etter C, Miskiewicz M, et al. Surface alterations of polished and sandblasted and acid-etched titanium implants after Er:YAG, carbon dioxide, and diode laser irradiation. *Int J Oral Maxillofac Implants*. Jan-Feb 2010;25(1):104-11.
12. Yan M, Liu M, Wang M, Yin F, Xia H. The effects of Er:YAG on the treatment of peri-implantitis: a meta-analysis of randomized controlled trials. *Lasers Med Sci*. Sep 2015;30(7):1843-53. doi:10.1007/s10103-014-1692-3
13. Takasaki AA, Aoki A, Mizutani K, et al. Application of antimicrobial photodynamic therapy in periodontal and peri-implant diseases. *Periodontol 2000*. 2009;51:109-40. doi:10.1111/j.1600-0757.2009.00302.x
14. Wilson M. Photolysis of oral bacteria and its potential use in the treatment of caries and periodontal disease. *J Appl Bacteriol*. Oct 1993;75(4):299-306. doi:10.1111/j.1365-2672.1993.tb02780.x
15. Jori G, Fabris C, Soncin M, et al. Photodynamic therapy in the treatment of microbial infections: basic principles and perspective applications. *Lasers Surg Med*. Jun 2006;38(5):468-81. doi:10.1002/lsm.20361
16. Soukos NS, Goodson JM. Photodynamic therapy in the control of oral biofilms. *Periodontol 2000*. Feb 2011;55(1):143-66. doi:10.1111/j.1600-0757.2010.00346.x

17. Roncati M, Lucchese A, Carinci F. Non-surgical treatment of peri-implantitis with the adjunctive use of an 810-nm diode laser. *J Indian Soc Periodontol*. Nov 2013;17(6):812-5. doi:10.4103/0972-124X.124531
18. Boehm TK, Ciancio SG. Diode laser activated indocyanine green selectively kills bacteria. *J Int Acad Periodontol*. Jul 2011;13(2):58-63.
19. Birang E, Talebi Ardekani MR, Rajabzadeh M, Sarmadi G, Birang R, Gutknecht N. Evaluation of Effectiveness of Photodynamic Therapy With Low-level Diode Laser in Nonsurgical Treatment of Peri-implantitis. *J Lasers Med Sci*. Summer 2017;8(3):136-142. doi:10.15171/jlms.2017.25
20. Saffarpour A, Nozari A, Fekrazad R, Saffarpour A, Heibati MN, Iranparvar K. Microstructural Evaluation of Contaminated Implant Surface Treated by Laser, Photodynamic Therapy, and Chlorhexidine 2 percent. *Int J Oral Maxillofac Implants*. Sep/Oct 2018;33(5):1019-1026. doi:10.11607/jomi.6325
21. Fekrazad R, Khoei F, Bahador A, Hakimiha N. Comparison of different modes of photo-activated disinfection against Porphyromonas gingivalis: An in vitro study. *Photodiagnosis Photodyn Ther*. Dec 2020;32:101951. doi:10.1016/j.pdpdt.2020.101951
22. Fekrazad R, Karamifar K, Bahador A. Comparison of antibacterial effect of photodynamic therapy using indocyanine green (Emundo) with 2% metronidazole and 2% chlorhexidine gel on Porphyromonas gingivalis (an in-vitro study). *Photodiagnosis Photodyn Ther*. Sep 2016;15:28-33. doi:10.1016/j.pdpdt.2016.04.003
23. Ahrari F, Shahabi M, Fekrazad R, et al. Antimicrobial photodynamic therapy of Lactobacillus acidophilus by indocyanine green and 810-nm diode laser. *Photodiagnosis Photodyn Ther*. Dec 2018;24:145-149. doi:10.1016/j.pdpdt.2018.08.013
24. Fekrazad R, Khoei F, Hakimiha N, Bahador A. Photoelimination of Streptococcus mutans with two methods of photodynamic and photothermal therapy. *Photodiagnosis Photodyn Ther*. Dec 2013;10(4):626-31. doi:10.1016/j.pdpdt.2013.07.002
25. Socransky SS, Haffajee AD. Dental biofilms: difficult therapeutic targets. *Periodontol 2000*. 2002;28:12-55. doi:10.1034/j.1600-0757.2002.280102.x
26. Walker CB. The acquisition of antibiotic resistance in the periodontal microflora. *Periodontol 2000*. Feb 1996;10:79-88. doi:10.1111/j.1600-0757.1996.tb00069.x