

Laser Photoactivated Disinfection and Microbial Reduction: A Literature Review

Rada Kazakova

Assistant Professor, DMD, PhD, Department of Prosthetic Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv
Corresponding author: Dr. Rada Kazakova, DMD, PhD, Department of Prosthetic Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv

Abstract: *Laser photoactivated disinfection is contemporary method against inflammation. Neither the dye itself, nor the laser is capable of reducing the number of bacteria as much as their combination. It is a proven alternative to the traditional methods. The main advantages of this combination, compared to the traditional treatment approaches, are its safety, proven bactericidal effect and advanced healing.*

Keywords: laser photoactivated disinfection, laser PAD, laser photodynamic therapy, laser PDT, low-level laser therapy, LLLT

1. Introduction

There is an increasing interest in combining different dyes with therapeutic lasers. Neither the dyes, nor the lasers used separately, affect bacteria, but their combination leads to singlet oxygen with a strong bactericidal effect synthesis.

Photoactivated Disinfection

Photoactivated disinfection (PAD) is a method which has already been used for treating periodontal sockets, deep carious lesions and infected root canals. [16] The laser has to work within the absorption wavelength of the dye used, which is usually within the red spectrum, with output power between 50 and 100 mW. The chosen dye is applied and left to diffuse locally for a few minutes, after which it is irradiated with the laser. Transitional coloring can be seen in the area of the dental tissues, the gingiva or the mucosa.

Photodynamic Therapy

Photodynamic therapy (PDT) can be used in addition to the mechanical causal therapy. This approach utilizes either a “cold” (low-level) or a traditional laser with a wavelength, absorbed by the dye (e.g. a diode or Nd:YAG laser). Methylene blue as a subgingival irrigant is usually placed in the sulcus. Laser wavelengths are attracted by the dye and interact with it, destroying the membranes of the bacterial cells. The light energy activated the dye, interacts with the intracellular oxygen and leads to bacteriolysis via lipid peroxidation and membrane destruction.

Aphthous Ulcers

Aphthous ulcers treatment time can be reduced and pain – alleviated immediately, by administering 4 to 6 J per lesion and 4 J per the submandibular lymph nodes on each affected side. [1, 2, 13, 20, 27] Patients prone to ulceration have to avoid toothpastes containing sodium lauryl sulfate, as it may lead to reoccurrence of the ulcers.

Inflammation

Photobiomodulation (PBM) will reduce the inflammatory process, but the inflammation type should be differentiated, as the acute is affected by higher doses and the chronic – by lower. Alleviating the pain will help the patient, but it may

also elongate the inflammatory process. The infrared dose for inflammation reduction is from 8 to 12 J/cm². [6]

Lymph system irradiation is a basic aspect of PBM for the anti-inflammatory interventions. Lim et al. conclude that when using 635-nm wavelength the existing COX-inhibitors seize COX expression and consequently COX-inhibitors inhibit PG₂ release. [5, 36] Unlike indometacin and ibuprofen, irradiation with 635-nm wavelength leads to reducing the levels of the reactive oxygen species (ROS) and mRNA expression of the cytosol and secretory phospholipase A₂ (cPLA₂ и sPLA₂). Bjordal et al. also emphasize on the PGE₂ levels reduction. [7, 8, 30, 45, 46, 47] Aimbire et al. report for a reduction of the TNF-α levels of the acute inflammation after PBM. Other researches prove the anti-inflammatory effects of PBM. [3, 4, 10, 18, 21] Steroids decrease the effect of PBM. A research compares the effect of dexamethasone and PBM and discovers similar effects. [35] Compared to the short- and long-term effects of the non-steroid anti-inflammatory drugs (NSAID), PBM looks like a good alternative, excluding the side effects of the medicaments. [2, 8] A pilot study of Abiko et al. proves that dexamethasone and PBM lead to anti-inflammatory genes expression. [2, 36] Most genes are expressed by the dexamethasone, but the ones influenced by PBM, are more favorable, compared to the others, which encode plenty of side effects.

In their meta-analysis of 16 control groups, Chow et al. demonstrate that low-level laser therapy can reduce pain immediately in case of severe neck pain and lead to healing within 22 weeks after finishing of the treatment of patients in chronic pain. Moreover, this therapy has more favorable effect compared to taking medications. [14]

Periodontology – PAD and Microbial Reduction

Microorganisms’ level reduction is a main aim of the different procedures in everyday dental practice. The variety of protocols, which reduce the microbial number significantly, show PAD as an adjunctive therapy in infection treatment, especially in patients with resistant microorganisms and anatomical complications.

Temperature increase in high-level laser irradiation can cause denaturation of the proteins and destroy microorganisms, with high decontamination indexes. [11, 31, 32] Low-level laser therapy (LLLT) is incapable of increasing tissue temperature, which is the reason why the same antimicrobial effects as the high-level laser cannot be expected. [6, 24] Despite this limitation, soft lasers demonstrate proven microbial reduction. Their antimicrobial effect is gained through a combination of low-level lasers with external photosensitizers, which leads to highly reactive oxygen species (ROS) release. They destroy cell membranes, mitochondria and DNA, and microbial reduction is inevitable. This process is called "photoactivated disinfection" ("PAD") or "photodynamic therapy" ("PDT"). [33, 41, 42, 43, 44]

The antimicrobial capacity of PAD is used for increasing the microbial reduction in periodontal, restorative, endodontics and implantological conventional therapy. [18, 25, 38] Viral inactivation and successful treatment of infections, caused by the herpes simplex type I virus, are proven. [12, 27, 30, 46, 47]

In order to treat bacterial infections effectively, it is especially important to apply an adequate light source and a photosensitizer, capable of connecting with the target pathogen. Thus, the photosensibilisation can occur either in subgingival, or in superficial oral tissues. [5, 34, 49] The most frequently used source of photosensibilisation in dentistry is the low-level laser because it:

- Has a narrow spectral range, which allows more specific interactions with the photosensitizers;
- Can be connected with optical fibers;
- Does not lead to tissue temperature increase, as it is seen when using a polychromatic light. [5, 34]

The use of LED light is also described in the literature. [47]

There are a few photosensitizers available for PAD. The oral pathogens disinfection is in need of positively charged photosensitizers as toluidine blue and poly-L-lysine-chlorine derivatives. [26, 40] The interaction between the photosensitizers and the microorganisms occurs within a few minutes, and this incubation period has to be taken in mind before the laser irradiation. [26, 45] Figure 1 displays the use of indocyanine green as a photosensitizer.



Figure 1: Laser PAD using a diode laser and indocyanine green as a photoinitiator (EmunDo, F.O.X. Lasers).

The disadvantages of PAD include lack of standardization and established protocols. Researchers have started evaluating the antimicrobial action of PAD, the ideal light source, the most adequate photosensitizer for every bacterial species and target tissue, as well as the proper light intensity and power settings. Nevertheless, the protocols derived from the in vivo and in vitro researches, have been proved as safe and with favorable scientific results, allowing the clinical use of PAD. [13, 22]

Recent studies of Feurstein et al. have described the effect of blue light on the biofilm formation. The two main conclusions derived from this laboratory researches are about to be confirmed in vivo. The first one is that the blue light exposition of *Streptococcus mutans* affects the new formation of the biofilm, demonstrating increase of the quantity of destroyed bacteria. [13] The second one is that earlier researches show that blue light, connected with hydrogen peroxide, has strong antibacterial effect on the biofilm. [19, 20, 21, 22] There is an antibacterial synergic effect between blue light and hydrogen peroxide. The mechanism of the phototoxic effect on *S. mutans* is a mainly photochemical process, involving reactive oxygen species (ROS). The application of such light, combined with hydrogen peroxide, on an infected tooth serves as an adjunct minimally invasive treatment.

2. Conclusion

PAD has several advantages, compared to the traditional antimicrobial agents. It ensures faster bacteriolysis, without the need for maintaining high concentrations of the photosensitizer in the infected area, as it is when using antiseptics and antibiotics. The main advantage is its local application. PAD affects microorganisms in the area of the photosensitizer deposit, whereas systemic medications influence the whole body. Moreover, PAD does not damage or change the adjacent structures like periodontal or periapical tissues, even when a high concentration of the laser energy and the photosensitizer are applied.

References

- [1] Abbas, M., C. Zahra, M. Mahvash, F. Reza, M. Neda, A. Adriano, B. Omid, C. Nasim. Antimicrobial photodynamic therapy using diode laser activated indocyanine green as an adjunct in the treatment of chronic periodontitis: A randomized clinical trial. *Photodiag and Photodyn Ther*, Mosby Elsevier, 2016, 14:93-97.
- [2] Abiko, Y. Functional genomic study on anti-inflammatory effects by low-level laser irradiation. 8th Congress of World Federation for Laser Dentistry, Hong Kong, 2008.
- [3] Aimbire, F., R. Albertini, P. Leonardo, et al. Low-level laser therapy induces dose-dependent reduction of TNF- α levels in acute inflammation. *Photomed Laser Surg*, 2006, 24(1):33-37.
- [4] Aimbire, F., R. Albertini, RG de Magalhães, et al. Effect of PBM Ga-Al-As (685 nm) on LPS-induced inflammation of the airway and lung in the rat. *Lasers Med Sci*, 2005, 20(1):11-20.

- [5] Bevilacqua, IM, RA Nicolau, S. Khouri, et al. The impact of photodynamic therapy on the viability of *Streptococcus mutans* in a planktonic culture. *Photomed Laser Surg*, 20007, 25:513-518.
- [6] Bhatti, M. A. MacRobert, S. Meghji, et al. A study of the uptake of toluidine blue O by *Porphyromonas gingivalis* and the mechanism of lethal photosensitization. *Photochem Photobiol*, 1998, 68:370-376.
- [7] Bjordal, JM, AE Ljunggren, A. Klovning, L. Slordal. NSAIDs including coxibs, probably do more harm than good, and paracetamol is ineffective for hip OA. *Ann Rheum Dis*, 2005, 64(4):655-656.
- [8] Bjordal, JM, RA Lopes-Marting, VV Iversen. A randomized, placebo-controlled trial of low-level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations. *Br J Sports Med*, 2006, 40(1):76-80.
- [9] Bonsor, SJ, GJ Pearson. Current clinical applications of photoactivated disinfection in restorative dentistry. *Dent Update*, 2006, 33(3):143-144, 147-150, 153.
- [10] Bortone, F., HA Santos, R. Albertini, et al. Low level laser therapy modulates kinin receptors mRNA expression in the subplantar muscle of rat paw subjected to carrageenan-induced inflammation. *Int Immunopharmacol*, 2008, 8(2):206-210.
- [11] Braun, A., C. Dehn, F. Krause, S. Jepsen. Short-term clinical effects of adjunctive antimicrobial photodynamic therapy in periodontal treatment: a randomized clinical trial. *J Clin Periodontol*, 2008, 35(10):877-884.
- [12] Chan, Y., CH Lai. Bactericidal effect of different laser wavelengths in periodontopathic germs in photodynamic therapy. *Lasers Med Sci*, 2003, 18:51-55.
- [13] Chebath-Taub, D., D. Steinberg, JD Featherstone, O. Feuerstein. Influence of blue light on *Streptococcus mutans* re-organization in biofilm. *J Photochem Photobiol B*, 2012, 116:75-78.
- [14] Chow, RT, MI Johnson, RA Lopes-Martins, JM Bjordal. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomized placebo or active-treatment controlled trials. *Lancet*, 1009, 374:1897-1908.
- [15] Christodoulide, N., D. Nikolidakis, P. Chondros, et al. Photodynamic therapy as an adjunct to non-surgical periodontal treatment: a randomized, controlled clinical trial. *J Periodontol*, 2008, 79:1638-1644.
- [16] Convissar, RA. Principles and practice of laser dentistry. Ed. 2. Elsevier Mosby, 2015.
- [17] Daniell MD, Hill JS. A history of photodynamic therapy. *Aust NZ Surg* 1991; 61; (5):340-348.
- [18] Dickers, B., L. Lamard, A. Peremans, et al. Temperature rise during photo-activated disinfection of root canals. *Lasers Med Sci*, 2009, 24:81-85.
- [19] Fekrazad, R., A. Mir, V. Barghi, M. Shams-Ghahfarokhi. Eradication of *C. albicans* and *T. rubrum* with photoactivated indocyanine green, Citrus aurantifolia essential oil and fluconazole. *Photodiag and Photodyn Ther*, Mosby Elsevier, 2015, 12:289-297.
- [20] Fekrazad, R., F. Khoei, N. Hakimiha, A. Bahador. Photoelimination of *Streptococcus mutans* with two methods of photodynamic and photothermal therapy. *Photodiag and Photodyn Ther*, Mosby Elsevier, 2013, 10:626-631.
- [21] Fekrazad, R., VG Barghi, A. Mir, M. Shams-Ghahfarokhi. In vitro photodynamic inactivation of *Candida albicans* by phenothiazine dye (new methylene blue) and Indocyanine green (EminDo®). *Photodiag and Photodyn Ther*, Mosby Elsevier, 2015, 12:52-57.
- [22] Feuerstein, O., D. Moreinos, D. Steinberg. Synergic antibacterial effect between visible light and hydrogen peroxide on *Streptococcus mutans*. *J Antimicrob Chemother*, 2006, 57(5):872-876, Feuerstein, O., Light therapy: complementary antibacterial treatment of oral biofilm. *Adv Dent res*, 2012, 24(2):103-107.
- [23] Giusti, JS, L. Santos-Pino, AC Pizzolito, et al. Antimicrobial photodynamic action on dentine using light-emitting diode light source. *Photomed Laser Surg*, 2008, 26:281-287, Hayek, RR, NS Araujo, MA Gioso, et al. Comparative study between the effects of photodynamic therapy and conventional therapy on microbial reduction in ligature-induced peri-implantitis in dogs. *J Periodontol*, 2005, 76:1275-1281.
- [24] Harris, F., LK Chatfield, DA Phoenix. Phenothiazinium based photosensitisers – photodynamic agents with a multiplicity of cellular targets and clinical applications. *Curr Drug Targets*, 2005, 6:615-627.
- [25] Ishikawa, I., A. Aoki, AA Takasaki. Potential applications of erbium:YAG laser in periodontics. *J Periodont Res*, 2004, 39:275-285.
- [26] Jori, G., C. Fabris, M. Soncin, et al. Photodynamic therapy in the treatment of microbial infections: basic principles and perspective applications. *Lasers Surg Med*, 2006, 38:468-481.
- [27] Komerik, N., H. Nakanishi, AJ MacRobert, et al. In vivo killing of *Porphyromonas gingivalis* by toluidine blue-mediated photosensitization in an animal model. *Antimicrob Agents Chemother*, 2003, 47:932-940.
- [28] Kosarieh, E., SS Khavas, A. Rahimi, N. Chiniforush, N. Gutknecht. The comparison of penetration depth of two different photosensitizers in root canals with and without smear layer: An in vitro study. *Photodiag and Photodyn Ther*, Mosby Elsevier, 2016, 13:10-14.
- [29] Lim, W., S. Lee, I. Kim, et al. The anti-inflammatory mechanism of 635 nm light-emitting diode irradiation compared with existing COX inhibitors. *Laser Surg Med*, 2007, 39:614-621.
- [30] Malik, Z., J. Hanania, Y. Nitzan. Bactericidal effects of photoactivated porphyrins: an alternative approach to antimicrobial drugs. *J Photochem Photobiol B*, 1990, 5:281-293.
- [31] Meire, MA, K. De Prijk, T. Coenye, et al. Effectiveness of different laser systems to kill *Enterococcus faecalis* in aqueous suspension and in an infected tooth model. *Int Endod J*, 2009, 42(4):351-359.
- [32] Morselli, M. et al. Effects of very low energy-density treatment of joint pain by CO2 laser. *Laser Surg Med*, 1985, 5(5):150-153.
- [33] Popova, E., S. Dimitrov, H. Kissov, A. Vlahova, I. Angelov, V. Mantareva, V. Kussovski. Photodynamic destruction of *Candida albicans* on complete dentures with porphyrins and phthalocyanines. – 14th Congress of BASS. 9th Scientific Congress of BgDA, Varna, Bulgaria, 6-9 May, 2009. Abstract Book, p. 82.

- [34] Prates, RA, AM Jr Yamada, LC Suzuki, et al. Bactericidal effect of malachite green and red laser on *Actinobacillus actinomycetemcomitans*. J Photochem Photobiol B, 2007, 86:70-76.
- [35] RA Lopes-Martins, R. Albertini, PS Lopes-Martins, et al. Steroids receptor antagonist Mifepristone inhibits the anti-inflammatory effects of photoradiation. Photomed Laser Surg, 2006, 24(2):197-201.
- [36] Reis, SR, AP Medrado, AM Marchionni, et al. Effect of 670-nm laser therapy and dexamethasone on tissue repair: a histological and ultrastructural study. Photomed Laser Surg, 2008, 26(4):307-313.
- [37] Schillenburg, H., S. Hobo, LD Whitsett. Fundamentals of fixed prosthodontics, Quintessence, 2012, Chicago, ed 4, pp 319-320.
- [38] Schoop, U., W. Kluger, A. Moritz, et al. Bactericidal effect of different laser systems in the deep layers of dentin. Lasers Surg Med, 2004, 35:111-116.
- [39] Smetana, Z., E. Ben-Hur, E. Mendelson, et al. Herpes simplex virus proteins are damaged following photodynamic inactivation with phthalocyanines. J Photochem Photobiol B, 1998, 44:77-83.
- [40] Soukos, NS, MR Hamblin, T. Hasan. The effect of charge on cellular uptake and phototoxicity of polylysine chlorin(e6) conjugates. Photochem Photobiol, 1997, 65:723-729.
- [41] Vlahova A., Chr. Kissov, E. Popova. Photodynamic disinfection of dental impressions as a new competitive method to the conventional cleansing procedures. Journal of Analytical Oncology, Dec 2012, Vol. 1, No. 2, 187 – 191.
- [42] Vlahova, A., Chr. Kissov, E. Popova, G. Todorov. Photodynamic disinfection of dentures. American Journal of Infectious Diseases and Microbiology, 2013, Vol. 1, No. 2, 34-37.
- [43] Vlahova, A., Chr. Kissov, E. Popova. Photodynamic disinfection of dental impressions and dentures. LAP Lambert Academic Publishing, Saarbrücken, Germany, 2013, ISBN 978-3-659-46063-0.
- [44] Vlahova. A., Chr. Kisov, E. Popova, I. Haydushka, V. Mantareva – A new method for photodynamic disinfection of prosthetic constructions and impressions in prosthetic dentistry - Folia Medica, v.54, 2012, 1, 51 – 57.
- [45] Wainwright, M. Photodynamic antimicrobial chemotherapy (PACT). J Antimicrob Chemother, 1998, 42:13-28.
- [46] William, JA, GJ Pearson, MJ Colles, M. Wilson. The photoactivated antibacterial action of toluidine blue O in a collagen matrix and in carious dentine. Caries Res, 2004, 38(6):530-536.
- [47] Wood, S., B. Nattress, J. Kirkham, et al. An in vitro study of the use of photodynamic therapy for the treatment of natural oral plaque biofilms formed in vivo. J Photochem Photobiol B, 1999, 50:1-7.