

Revisión de Tema

Antibacterial efficacy of photodynamic therapy in the disinfection of root canals - Integrative literature review

Eficacia antibacteriana de la terapia fotodinámica en la desinfección de canales radiculares - Revisión integrativa

Eficácia antibacteriana da terapia fotodinâmica na desinfecção de canais radiculares - Revisão integrativa da literatura

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Abstract

To evaluate the antibacterial efficacy of Photodynamic Therapy (PDT) in root canal (RC) disinfection. An integrative review of the literature was performed in diferents databases. It was selected articles published between January 2014 and January 2018, in Portuguese, English or Spanish languages, which evaluated, in a clinical trial, the antibacterial efficacy of PDT in RC disinfection. The sample consisted of 05 articles that met all the inclusion criteria, which analyzed aspects such as: sample; photosensitizer and exposure time; light source, wavelength, potency, energy and time of emission; and results. Most of the studies used single-rooted teeth and methylene blue photosensitizer with pre-irradiation time ranging from 1 to 5 minutes. The LED and the laser were the light sources used, with exposure time ranging from 40 to 240 seconds; power from 60 mW to 1000 mW; power density from 2 to 4 mW / cm²; energy of 4 to 9,6 J; and dose from 1.2 mJ / cm² to 129 J / cm². It can be concluded that, despite the heterogeneity of the protocols, there was a reduction in the bacterial populations responsible for RC infections, and it may be a supporting technique in endodontic therapy.

Keywords: Endodontics; Low-Level Light Therapy; Photodynamic Therapy; Root canal.

Resumen

Evaluar la eficacia antibacteriana de la terapia fotodinámica (TFD) en la desinfección de los conductos radiculares (CR). Se realizó una revisión bibliográfica integrativa en diferentes bases de datos. Se seleccionaron artículos publicados entre enero de 2014 y enero de 2018, en portugués, inglés o español, que evaluaron, en ensayo clínico, la eficacia antibacteriana de la TFD en la desinfección de los CR. La muestra consistió en 05 artículos que cumplieron con todos los criterios de inclusión. En estos trabajos, fueron analizados: muestra; fotosensibilizador y tiempo de exposición; fuente de luz, longitud de onda, potencia, energía y tiempo de emisión; y resultados. La mayoría de los estudios utilizaron dientes uniradulares y el fotosensibilizador de azul de metileno con un tiempo de pre-irradiación de 1 a 5 minutos. LED y láser fueron las fuentes de luz utilizadas, con tiempos de exposición que van desde 40 hasta 240 segundos; potencia de 60 mW a 1000 mW; densidad de potencia de 2 a 4 mW/cm²; energía de 4 a 9.6 J; y dosis de 1,2 mJ/cm² a 129 J/cm². Se puede concluir que, a pesar de la heterogeneidad de los protocolos, hubo una reducción en las poblaciones bacterianas responsables de las infecciones de los CR, y la TFD puede ser una técnica de apoyo en la terapia endodóntica.

Palabras clave: Endodoncia; Terapia por Láser de Baja Intensidad; Terapia fotodinámica; Conducto radicular.

Resumo

Avaliar a eficácia antibacteriana da Terapia Fotodinâmica (TFD) na desinfecção de canais radiculares (CR). Uma revisão integrativa da literatura foi realizada em diferentes bases de dados. Foram selecionados artigos publicados entre janeiro de 2014 e janeiro de 2018, nos idiomas português, inglês ou espanhol, que avaliaram, em ensaio clínico, a eficácia antibacteriana da TFD na desinfecção de CR. A amostra foi composta por 05 artigos que atenderam a todos os critérios de inclusão. Nesses trabalhos foram analisados aspectos como: amostra; fotossensibilizador e tempo de exposição; fonte de luz, comprimento de onda, potência, energia e tempo de emissão; e resultados. A maioria dos estudos utilizou dentes uniradulares e o fotossensibilizador azul de metileno com tempo de pré-irradiação variando de 1 a 5 minutos. O LED e o laser foram as fontes de luz utilizadas, com tempo de exposição variando de 40 a 240 segundos; potência de 60 mW a 1000 mW; densidade de potência de 2 a 4 mW/cm²; energia de 4 a 9,6 J; e dose de 1,2 mJ/cm² a 129 J/cm². Pode-se concluir que, apesar da heterogeneidade dos protocolos, houve uma redução nas populações bacterianas responsáveis pelas infecções dos CR, e a TFD pode ser uma técnica de suporte na terapia endodôntica.

Palavras-chave: Endodontia; Terapia a Laser de Baixa Intensidade; Terapia Fotodinâmica; Canal Radicular.

Introduction

Pulp damage can be caused by several factors such as trauma, in cases of fracture, dislocation or parafunctional habits, such as bruxism; iatrogenic, in cases of excessive orthodontic movement and tooth bleaching; idiopathic, such as resorption; and bacterial, especially in the case of caries (1-4), which can lead to irreversible damage to the dental pulp, thus necessitating an adequate treatment of root canals (RCs). Endodontic therapy is performed to eliminate pathogenic microorganisms that are responsible for RC infections (2-4). This therapy consists of the mechanical preparation of the RCs (manual, rotational, ultrasonic) associated with chemical disinfection

using antimicrobial agents such as sodium hypochlorite and chlorhexidine (5-7), and thereafter the RCs are filled with an inert material, designed to maintain or restore the health of the periradicular tissues (5).

The success of endodontic therapy depends on the removal of all pathogens from the RC before a three-dimensional obturation (2,6). Despite the predictability of success and the use of advanced treatment techniques, residual bacteria are detectable in half of the teeth before obturation (6), due to the heterogeneity of the RC system which have accessory canals, tubules and slits (4,6,8). Therefore, although the final three-dimensional filling of the RC may deprive the bacteria of access to nutrients, the risk of failure is always present (4,6).

Infections in endodontic failures (secondary/persistent infections) are often composed of one or a few bacterial species, usually Gram-positive bacteria (9). *Enterococcus faecalis* has gained attention by its ability to persist after root canal treatment due to their ability to form biofilm on the RC wall and to invade the dentinal tubules and has been isolated from both primary and secondary infections although it has been recovered most frequently from secondary/persistent infections (2,7,10,11).

Conventional chemical irrigants are not able to eliminate *E. faecalis*, because they have a lower depth of penetration in the dentinal tubules (2). Thus, there is a need for the use of new RC disinfection techniques more effective to improve the result of endodontic treatment (4,6). In this context, photodynamic therapy (PDT) presents as a therapeutic modality that has been used as an auxiliary method in the treatment of RC. It can be used as an adjunct to the treatment of complications of antineoplastic therapy (head and neck radiotherapy and chemotherapy), for lesions with potential for malignancy, and for bacterial, viral and fungal infections (2).

In the context of endodontic therapy, PDT appears to be a complementary antimicrobial approach capable of maximizing RC disinfection, which can reduce significantly or eradicate resistant microorganisms to conventional chemical-mechanical preparation, such as *E. faecalis* (12). Moreover, this technique is considered easy to perform, painless, does not affect the periradicular tissues of the host and does not cause bacterial resistance. Thus, the present study aimed to evaluate, through an integrative review of the literature, the antibacterial efficacy of PDT in RC disinfection.

Methods

In order to meet the proposed objective, it was decided to carry out an integrative review of the literature of scientific articles published in the last five years. For this, in order to maintain the scientific and methodological rigor of the study, six guidelines pre-established in a research protocol were observed: 1) choice of theme and definition of the hypothesis or guiding questioning; 2) establishment of the criteria for inclusion and exclusion of studies for sample selection; 3) definition of the information to be extracted from the sample; 4) evaluation/critical analysis of the studies included in the sample; 5) discussion and interpretation of the results and 6) presentation of the review objectively and clearly (13).

In the first stage, the theme was established from the following guiding question: "For endodontic treatment, ¿Is the antibacterial effect of PDT on root canals more effective than isolated conventional chemical-mechanical techniques?". For the next stage, the following inclusion criteria were established: scientific papers published in the period January 2014 to January 2018 in Portuguese, English or Spanish,

available in full format that evaluated the anti-bacterial efficacy of PDT in root canal disinfection in a clinical trial studies. It was used the databases Medical Publications (PubMed), Scientific Electronic Library Online (SciELO) and Latin American and Caribbean Literature in Health Sciences (LILACS). For the research, the next descriptors were used: Root canal, Photodynamic Therapy, Endodontics, Dental Pulp Diseases e Pulpectomy; obtained in accordance with Medical Subject Headings (MeSH), having Boolean operator "AND". Case studies, literature reviews, experience reports, monographs, dissertations, theses, laboratory studies and duplicate articles were excluded, as well as studies that were not related to the subject, which were performed with deciduous teeth, with microorganisms that were not bacteria and which were outside the context of endodontics. The searches were performed on January 24, 2018, with a total of 271 publications in PubMed, 07 publications in SciELO and 38 publications in LILACS, totaling 316 articles (Table 1).

Table 1. Search method for survey studies for integrative review with data from the last Five years. Campina Grande, PB, Brazil, 2018

<i>Descriptors</i>	<i>Databases</i>			
	<i>Pubmed</i>	<i>SciELO</i>	<i>LILACS</i>	<i>Total</i>
Root canal AND Photodynamic Therapy	129	04	19	152
Endodontics AND Photodynamic Therapy	118	03	17	138
Dental Pulp Diseases AND Photodynamic Therapy	14	00	01	15
Dental Pulp Necrosis AND Photodynamic Therapy	09	00	01	10
Pulpectomy AND Photodynamic Therapy	01	00	00	01
Total number of articles	271	07	38	316

After identification in the databases, the search filters were applied that concerned the period of publication and integrity of the document, and then duplicate studies were eliminated, totaling 117 articles. Then, they underwent a careful analysis of the title and abstract, leading to the exclusion of 92 articles, thus retaining 25 articles in full. Subsequent to the application of the inclusion criteria defined above, five articles were selected for review (Figure 1).

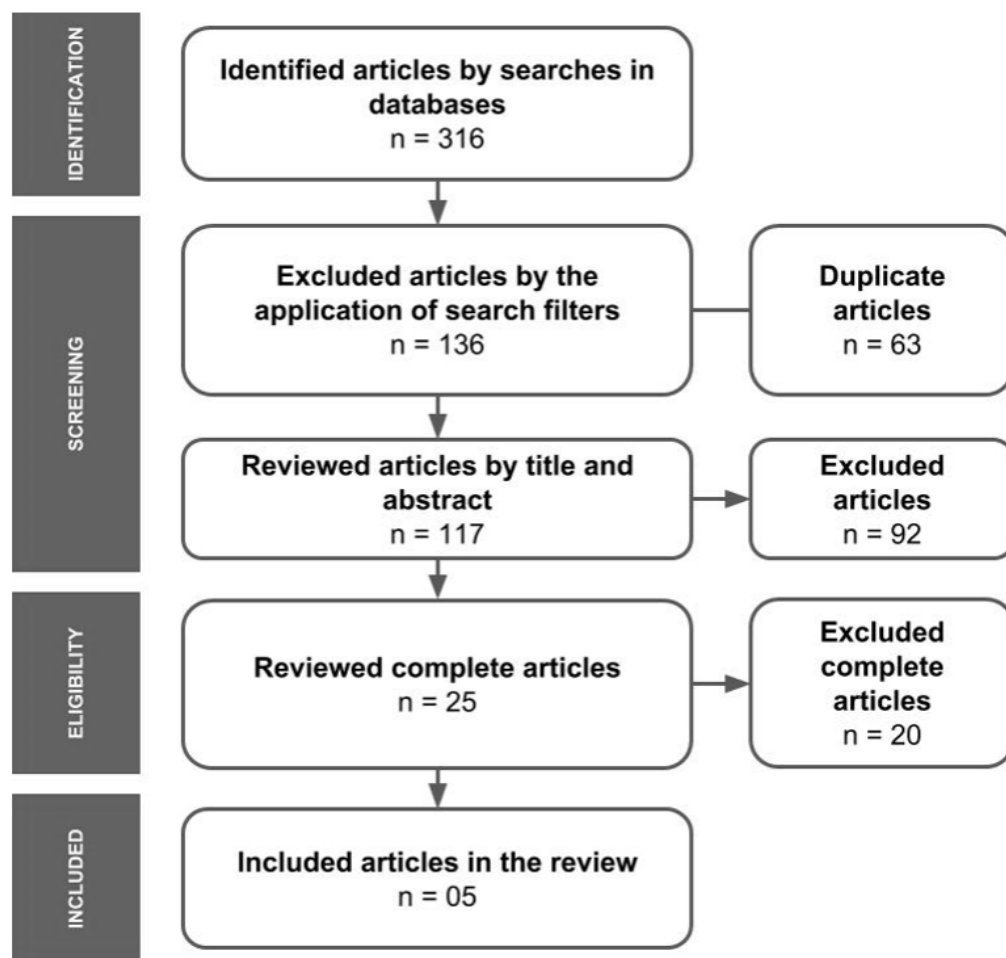


Figure 1. Flowchart of the selection process of articles included in the integrative review. Campina Grande, PB, Brazil, 2018.

For the third stage, exploratory readings were carried out to collect the pertinent information, based on the guiding question and the purpose of the study. From this, the data extracted from the text were organized in a table containing the following data: authors and year of publication; objective of the study; sample; microbiological sampling method; photosensitizer and exposure time; light source; wave-length; power; energy and time of emission and results.

With the collection of information completed, the last steps of the survey were carried out. The studies were evaluated critically and submitted to qualitative analysis. The use of frames, containing data that will be presented in the results and discussion, allowed the knowledge to be synthesized, making them more accessible. Thus, the content necessary to assess the efficacy of PDT in RC disinfection can be raised.

Results

The publications selected, from the methods described above, for evaluating the efficacy of PDT in RC disinfection are described in Tables 2 and 3.

Table 2. Information on the selected articles regarding the type of study and main objective. Campina Grande - PB, Brazil, 2018.

Title	Authors/ year	Type of study	Objective
A comparison between effect of photodynamic therapy by LED and calcium hydroxide therapy for root canal disinfection against <i>Enterococcus faecalis</i> : A randomized controlled trial	Asnaashari, M, Ashraf, H, Rahmati, A, Amini, N, 2017 (7)	Randomized controlled clinical trial	To compare the effects of calcium hydroxide therapy with PDT in addition to conventional therapy for disinfection of root canals in molars
The antimicrobial effectiveness of photodynamic therapy used as an addition to the conventional endodontic re-treatment: A clinical study	Jurič, IB, Plečko, V, Pandurić, DG, Anić, I, 2014 (18)	Randomized clinical trial	To evaluate the antimicrobial efficacy of PDT as a complement in endodontic retreatment
Antimicrobial Photodynamic Therapy Associated with Conventional Endodontic Treatment: A Clinical and Molecular Microbiological Study	Silva, CC, Chaves Júnior, SP, Pereira, GLD, Fontes, KBFDC, Antunes LAA, Póvoa, HCC et al., 2017 (19)	Clinical and molecular case-control study	To evaluate the antimicrobial effects of conventional endodontic treatment associated with PDT
Does supplemental photodynamic therapy optimize the disinfection of bacteria and endotoxins in one-visit and two-visit root canal therapy? a randomized clinical trial	Rabello, DGD, Corazza, BJM, Ferreira, LL, Santamaria, MP, Gomes, APM, Martinho, FC, 2017 (20)	Randomized controlled clinical trial	To evaluate the efficacy of PDT in the optimization of bacterial and endotoxin removal from infected root canals after one- and two-session treatments
The Antibacterial Effect of Additional Photodynamic Therapy in Failed Endodontically Treated Teeth: A Pilot Study	Asnaashari M, Homayuni H, Paymanpour P, 2016 (21)	Clinical and microbiological study	To evaluate the antibacterial effect of adjuvant PDT on teeth submitted to endodontic retreatment

The final sample for this review was composed of five scientific articles from international journals, most of them published in 2017 (60%). Regarding the type of study, two (40%) were randomized controlled clinical studies. For the studies, uni (80%) and multiradicular (20%) permanent teeth were used, 60% of which were submitted to endodontic treatment and 40% to endodontic retreatment. Regarding the number of teeth used for the sample, there was a variation of 10 to 30 units.

None of the studies aimed to evaluate the efficacy of PDT alone, 100% used it as a complementary method to conventional endodontic therapy. For its application, 60% used the methylene blue photosensitizer, 20% toluidine blue and 20% phenothiazinium chloride. Regarding the pre-irradiation time, there was variation between one (20%) and five (40%) minutes.

The use of red light (622-700 nm) for photoactivation of the dyes mentioned above was agreed in 100% of the studies, with a wavelength of 660 nm (60%) predominating. Despite this, the light sources used were not the same, 80% used the laser and 20% the LED light (Light Emitting Diode). Regarding the time of exposure of the light source to the photosensitizer, the studies presented different results, ranging

from 40 to 240 seconds. In addition, power was also different between the surveys, ranging from 60 mW to 1,000 mW. Likewise, it happened with energy, ranging from 4 to 9.6 J, and dose, starting from 1.2 mJ / cm² to 129 J / cm². Some studies also considered the power density, with values of 2 to 4 mW / cm².

The results obtained with the conclusion of the research showed that, in 100% of the cases, PDT functioned as a potentiator for RC disinfection when associated with conventional endodontic therapy, considerably reducing the bacterial population or, in some cases, totally eliminating it. It was also observed that PDT was more effective than other types of complementary methods, such as calcium hydroxide therapy.

Table 3. Main characteristics and results of the studies included in the integrative review.
Campina Grande - PB, Brazil, 2018

Authors/ year	Sample	Microbiological sampling method	Photosensitizer/ pre-irradiation time	Light source, wavelength, power, energy, emission time	Results
Asnaashari, M, Ashraf, H, Rahmati, A, Amini, N, 2017 (7)	Twenty multiradicular permanent teeth of twenty patients	Group 1 (n = 10): PDT after conventional endodontic treatment; Group 2 (n = 10): calcium hydroxide paste for two weeks	Toluidine blue 0.5 ml of 0.1 mg / ml 5 minutes	LED Fotosan 630 (MDD, CMS Dental Denmark, Korea), 630 nm, 2-4 mW / cm ² 1.2-4.4 mJ / cm ² and 60 seconds of exposure	PDT and calcium hydroxide therapy are effective as adjunctive methods to conventional endodontic therapy. Compared with calcium hydroxide therapy, PDT leads to a greater reduction in the number of <i>E. faecalis</i> in infected root canals
Jurič, IB, Plečko, V, Pandurić, DG, Anić, I, 2014 (18)	Twenty one uniradicular teeth submitted to endodontic retreatment of twenty one patients	Microbiological samples were collected immediately after endodontic access, after retreatment (standard therapy) and after PDT (experimental therapy)	Phenothiazinium chloride 10 mg/ mL ⁻¹ 2 minutes	Helbo laser (Helbo Photodynamic System, Bredent, Senden, Germany), 660 nm, 100 mW, 6 J and 60 seconds of exposure	PDT as adjuvant to conventional treatment led to a decrease in the number and elimination of bacterial species, with the complete elimination of bacteria in some cases
Silva, CC, Chaves Júnior, SP, Pereira, GLD, Fontes, KBFDC, Antunes LAA, Póvoa, HCC et al., 2017 (19)	Ten uniradicular permanent teeth with necrotic pulp (Control Group: 2 in maxilla and 2 in mandible; Test group: 3 in maxilla and 3 in mandible) of nine participants	Control group and test group: before chemical-mechanical instrumentation (sample A); after chemical-mechanical instrumentation (Sample B); after PDT, exclusively in the test group; before root canal filling (sample D)	Methylene blue 100 µg/ mL 5 minutes	Laser diode (Laser Duo, MMOptics, São Carlos, SP, Brazil), 660 nm, 100 mW, 4 J and 40 seconds of exposure	PDT can be used as an effective complementary therapy in endodontic treatment, resulting in a significant reduction in the incidence of <i>E. faecalis</i>

Authors/ year	Sample	Microbiological sampling method	Photosensitizer/ pre-irradiation time	Light source, wavelength, power, energy, emission time	Results
Rabello, DGD, Corazza, BJM, Ferreira, LL, Santamaria, MP, Gomes, APM, Martinho, FC, 2017 (20)	Twenty four unirradicular teeth of twenty four patients	Samples collected before and after root canal treatment in the treatment group of a visit (12) - PDT 120 seconds after mechanical chemical preparation with reciprocating system + 2.5% NaOCl + EDTA 17%; and of two visits (12) - PDT 14 days after medication between visits	Methylene blue 0.1 mg/ ml 1 minute	Laser diode (Laser Duo, MMOptics, São Carlos, SP, Brazil), 660 nm, 60 mW, 129 J / cm ² and 120 seconds of exposure	PDT optimized disinfection of root canals in one session, but not in two, with calcium hydroxide medication. Despite the modality of treatment, supplemental PDT was not effective against endotoxins
Asnaashari M, Homayuni H, Paymanpour P, 2016 (21)	Thirty unirradicular permanent teeth submitted to endodontic retreatment of twenty seven participants	Three microbiological samples: 1. After root canal depletion; 2. After chemical-mechanical preparation; 3. After application of the PDT	Methylene blue 50 mg/ mL 2 minutes	Laser diode (BWTEK Inc, Newark, DE), 665 nm, 1000 mW, 9.6 J and 240 seconds of exposure	PDT can be effective being used as an additional disinfection method for the root canal, especially in the endodontically treated teeth.

Discussion

During endodontic treatment, the use of chemical agents for the elimination of microorganisms that colonize RCs is indispensable. However, the deep invasion of bacteria in the dentin tubules and the formation of biofilms are the main difficulties for a complete disinfection, since the commonly used irrigating solutions are not able to eliminate persistent microorganisms (4). Therefore, the role of PDT in this context has been widely tested both *in vitro* studies (2-4,6) and *ex vivo* (14,15), as it is believed that this therapeutic form is capable of destroying more resistant bacteria.

The word "photodynamic" refers to the effect of the activation of light on living organisms. Starting from the same principle, PDT can be described as a treatment that uses light sources to activate a photosensitizing agent in the presence of oxygen. This therapeutic modality has been shown to be effective in the treatment of periodontal diseases and oral disorders with malignant potential such as leukoplakia and malignant oral lesions such as squamous cell carcinoma (7).

PDT uses a photoactivated dye (photosensitizer) which, in the presence of oxygen, is activated in the light exposure of a specific wavelength (2,9,16). The energy that is transferred from the activated photosensitizer to the available oxygen results in the formation of oxygen in the form of free radicals that are toxic species of oxygen (2,4,16). These reactive chemical species can damage proteins, lipids, nucleic acids and other cellular components, causing disintegration of target cells (2). Thus, bacteria such as *E. faecalis*, which have a relatively porous membrane, built on a thick layer of peptidoglycans and lipoteichoic acid, promote a greater diffusion of the photosensitizer to the bacterium, facilitating its destruction (4). The main advantage of this technique is that the production of heat is minimal, without causing side effects,

since its action is based on photochemical events (2). Several photosensitizers have been submitted to observation. Toluidine blue, a basic thiazine metachromatic dye, is one of the most used in PDT to eliminate endodontic bacteria (4). Another one that is being used is methylene blue, an organic dye belonging to the phenothiazine family, as it has well established photosensitizing properties. In addition, its hydrophilicity, associated with its low molecular weight and positive charge, allows its passage through the channels of protein in the outer membrane of Gram-negative bacteria (2). In the present review, most of the included studies used methylene blue as a photosensitizer.

An *in vitro* study by Afkhami et al. (17), used an unusual photosensitizer, green indocyanine, which has low toxicity in the host tissue, high absorption in the near-infrared spectrum and is effective in the elimination of fungi and bacteria. In this study, in order to compare the efficacy of different disinfection methods to decrease the count of *E. faecalis* in CR, the authors concluded that the application of diode laser (810nm) associated with indocyanine green did not have adequate antimicrobial activity for use as adjuvant in endodontic treatments. On the other hand, when associated with silver nanoparticles, they could be used as coadjuvants in the disinfection of the CR system (17).

Regarding the light source, the low-power laser, in the red wavelength can be used for this, since it produces a monochromatic beam with specific wavelength to activate the photosensitizer (7). Another source used in association with dyes is the LED, also known as light emitting diode. Compared to the previous light source, it is considered more profitable, because it has a lower cost and consumes less energy. In addition, it is safer and easier to use, being an option that has recently become more desirable (7,11). Most photosensitizers are activated by light between 630 and 700nm, characterizing the red color in the electromagnetic spectrum (4,5). Accordingly, all studies included in this review used red light for the dye activation.

Asnaashari et al. (11) in an *in vitro* study compared the effects of these two types of light emitters for PDT on RC disinfection. For this, they used anterior teeth infected with *E. faecalis*, and the photosensitizer used was toluidine blue. In conclusion, they verified that the LED light was more effective in relation to the laser. Despite this statement, the wavelength used in this study (810nm) is different from that conventionally used in other experimental studies using laser and/or LED (4,6,7,14,15,18-21).

In order to analyze the efficacy of PDT in the different areas of dentistry, light sources of low intensity are used, but there is no consensus regarding the adequate power for its application (7,18-20). In contrast to the conventional protocols, Asnaashari et al. (21) carried out a clinical pilot study to evaluate the effect of PDT on intraradicular biofilm after endodontic retreatment, in which the Methylene Blue photosensitizer and a diode laser unit were used 665nm light with output power of 1W. The authors found good results using this power (21), but it does not apply to PDT. It is likely that the antimicrobial effect has been given due to the increase in temperature above the lethal values for the bacterial cell structures as observed in the study by Bago et al. (22). In him, an *ex vivo* experiment was conducted comparing the antimicrobial activity of high intensity pulse diode laser irradiation (975nm, 2W), PDT (Toluidine Blue, 660nm, 100mW), 30-gauge syringe irrigation with 2.5% sodium hypochlorite (NaOCl, 60 s) and sonic agitation of NaOCl with the EndoActivator system (60 s) on *E. faecalis*. Finally, they concluded that the pulse diode laser and NaOCl syringe irrigation alone were the least efficient therapies in reducing the root canal infection.

In the *in vitro* studies, although PDT protocols are the most varied, all suggest that this technique is effective as an aid to chemical irrigators and mechanical methods in the disinfection of RC (2-4,6,23). In relation to the *ex vivo* studies, there is also a diversity of protocols, and all suggest the use of PDT as a coadjuvant in the disinfection of RCs, although there is no complete disinfection of these (8,14,15,24,25). Nevertheless, in these types of studies there are limitations, such as using very specific bacterial biofilms.

All clinical trial studies included in this review concluded that PDT may be an adjuvant therapy in the treatment of RCs. However, there is variation of protocols, photosensitizers and pre-irradiation time. In addition, further studies involving teeth with large curvatures and multiradicular are required. Our sample had only one study that used multiradicular teeth (7). Further clinical trial studies with longer longitudinal follow-up periods are needed to demonstrate the efficacy of this promising technique in the disinfection of the RC system and to also show the possible adverse events associated with PDT to prove that its use is truly feasible.

Conclusions

The present integrative review allowed us to identify both the already consolidated points and the lack of standardization of protocols currently applied in clinical studies of PDT in the context of Endodontics. Despite this, these methods have shown promise in reducing the bacterial populations responsible for RC infections and can be used as adjuvants to conventional endodontic therapy and are more effective than when used alone. In view of the evidence found, it is believed that further studies are necessary to establish complete and standardized protocols, since the information available in the literature is very limited. In addition, knowledge regarding disadvantages and contraindications is also relevant, but is not addressed by the studies.

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