





Photodynamic therapy as an adjuvant to endodontic treatment: a literature review

Terapia fotodinâmica como coadjuvante ao tratamento endodôntico: revisão de literatura

Marcus Vinícius Rabelo Santos Carvalho , Luan Oliveira de Lima , Gustavo Danilo Nascimento Lima , Nayane Chagas Carvalho Alves *

Faculty Ages, Jacobina, Bahia, BA, Brazil.

*nayanec@gmail.com

ABSTRACT

Photodynamic Therapy (PDT) has been growing in endodontics due to the excellent potential for *in vivo* root canal decontamination. This literature review aims to discuss the effectiveness of PDT in assisting as an adjuvant to endodontic treatment and the different clinical applications and their results. Thorough research was performed between March and May 2020, using the “*Terapia fotodinâmica*” and “*Endodontia*” descriptors indexed in the Descriptors in Health Sciences (DeCs) and the “Photodynamic therapy” and “Endodontics” descriptors indexed in the Medical Subject Heading Terms (MeshTerms –MeSH). The databases searched were SciELO, Pubmed, and LILACS, for publications between 2013 and 2020. In this bibliographic survey, it was selected 28 articles for a full-text analysis and used as references. The bibliographic survey showed that PDT effectively assists the endodontic treatment, offers a high potential for eliminating bacteria such as *Enterococcus faecalis*, and is little invasive and risk-free for patients. It was concluded that PDT is clearly effective, but its clinical applicability is still subject to different protocols, which requires developing a protocol for common use.

Keywords: Elimination of bacteria. Endodontics. Photodynamic therapy.

RESUMO

A Terapia Fotodinâmica (PDT) vem ganhando espaço na endodontia por demonstrar um excelente potencial de descontaminação dos canais *in vivo*. Por meio de uma revisão de literatura, o presente estudo tem como objetivo discorrer sobre a efetividade da PDT, auxiliando como coadjuvante do tratamento endodôntico, bem como as diferentes aplicações clínicas e seus resultados. Foi realizada uma minuciosa pesquisa entre os meses de março e maio do ano de 2020, em que se utilizou os descritores “Terapia fotodinâmica” e “Endodontia” indexados nos “Descritores em Ciências da Saúde” (DeCs) e “Photodynamictherapy” e “Endodontics” indexados no Medical Subject Heading Terms (MeshTerms –MeSH), nas bases de dados SciELO, Pubmed e LILACS, entre os anos de 2013 e 2020. Nesse levantamento bibliográfico, foram selecionados 28 artigos para análise do texto completo e utilizados como referências. O levantamento bibliográfico revela que a PDT em questão é comprovadamente eficaz no que diz respeito ao auxílio no tratamento endodôntico, possui grande potencial na eliminação das bactérias, como a *Enterococcus faecalis*, mostra-se pouco invasiva e livre de riscos ao paciente tratado. No mais, concluiu-se que é nítida a eficácia da PDT, no entanto, a sua aplicabilidade clínica ainda se mantém sujeita a diversos protocolos distintos, fazendo-se necessária a elaboração de um protocolo de uso comum.

Palavras-chave: Eliminação de bactérias. Endodontia. Terapia fotodinâmica.

INTRODUCTION

Endodontic pathologies are directly related to infectious microorganisms (MOs), hence, treatment success in these cases becomes strictly dependent on the complete elimination of bacterial presence, preventing episodes of pain and early loss of the compromised dental units (Trindade, Figueiredo, Steier & Weber, 2015). The natural anatomy of the root canal system (RCS) has several projections that may often present variations in the typical anatomy, which makes it hard to efficiently eliminate infections even though the current chemo-mechanical preparation (CMP) offers improvements and advances in the techniques used. It is also worth noting that intracanal medication is used to assist the CMP because the potential action against MOs is well-established, thus it tends to minimize MOs and prevent future treatment failure (Sivieri-Araujo et al., 2013).

However, some bacteria such as *Enterococcus faecalis* may easily enter and stay in the dentinal tubules, causing a future problem for the treatment. This is a facultative anaerobic Gram-positive bacterium often related to treatment failure, and the numbers indicate its presence in around 22 to 77% of cases. This context requires an adjuvant therapy that can work more effectively in this and other bacteria to reduce future retreatment rates (Simões, Silva, Fernandes Neto, Batista & Catão, 2019). Photodynamic therapy (PDT) as an adjuvant to endodontic treatment significantly reduces the bacterial load of *E. faecalis* (Zorita-García et al., 2019).

For treatment optimization, PDT emerges as an adjuvant tool that has been growing in the daily clinical routine because of the high potential for canal decontamination and the satisfactory results of *in vitro* studies. Therefore, PDT has significantly reduced residual bacteria in the canal and can be used as an adjuvant to root canal disinfection (Afkhami et al., 2020). In summary, this therapy uses a photosensitizer, prioritizing non-toxic ones, and combines it with a low-intensity light source without thermal potential, becoming more effective in the decontamination process (Garcez, Roque, Murata & Hamblin, 2016). The final product of this process is a reaction that produces a reactive oxygen species, which characteristics can damage the essential intracellular molecules of the bacterium, inducing cell death by apoptosis (Almeida, Gomes, Lessa & Alves, 2019).

The oxygen element, in turn, becomes crucial for the technique because it is required in the conduits that will be exposed to therapy, which is not always achieved. The decreased concentration of this compound leads to a low bacterial reduction and renders the procedure irrelevant for disinfection. Other factors that promote good results for the technique are tissue compatibility with the photosensitizer and good light irradiation. These factors vary and do not always depend exceptionally on the proper use of the technique (Silva, Sampaio, Silva, Bravo & Cavalcanti, 2019). Hence, the present literature review aims to discuss the effectiveness of PDT in assisting as an adjuvant to endodontic treatment and the different clinical applications and their results.

MATERIAL AND METHODS

The present study is a literature review consisting of a bibliographical survey in relevant electronic databases to knowledge production in the health field: SciELO, Pubmed, and LILACS. The databases were searched in March and May 2020. The inclusion criteria were literature reviews and laboratory and clinical trials published between 2013 and 2020 in English and Portuguese. The descriptors used were "*Terapia fotodinâmica*" and "*Endodontia*" indexed in the Descriptors in Health Sciences (DeCs) and "Photodynamic therapy" OR "antimicrobial photodynamic therapy" AND "Endodontics" indexed in the Medical Subject Heading Terms (Mesh terms - MeSH). The exclusion criteria were studies that did not address the referred topic, reviews, commentary, interviews, updates, short communications, or unpublished studies. The inclusion and exclusion criteria provided 28 relevant studies on the topic, which were selected for a full-text analysis and used as references.

RESULTS AND DISCUSSION

The various reports of conventional endodontic treatment failures are directly related to permanent and residual infections from resistant bacteria (Bordea et al., 2020). Considering this problem and based on the limitations of conventional endodontic therapy, there is a current opening for starting several attempts to apply the photodynamic therapy (PDT) as an adjuvant to the treatment, based on a satisfactory clinical presentation of this method (Lima, Sousa, Melo & Silva, 2019).

The potential efficiency of PDT in eliminating and decontaminating the root canal system (RCS) is elucidated and based on three interconnected factors: a low-intensity light source (laser), a photosensitizer, and oxygen. One of the principles of PDT is using a photosensitizer absorbed by the bacterial cell, and the activated laser light is attracted by the cell wall, inducing microbial death by apoptosis (Plotino, Grande & Mercade, 2019; Stájer, Kajári, Gajdács, Musah-Eroje & Baráth, 2020).

The action mechanism occurs by transferring energy from the activated photosensitizer to the oxygen available in the RCS, where it will cause a reaction that results in the formation of different oxygen toxins (singlet oxygen and free radicals). The product of this reaction can potentially destroy proteins, lipids, and nucleic acids, among other cellular components (Silva et al., 2014).

The photochemical process of PDT causes two types of mechanisms: type I, based on electron transfer; and type II, based on energy transfer. In the entire reaction, mechanism type I is responsible for only 5% of the set, forming oxidized products. The other 95% are from mechanism type II, which is wanted and responsible for inducing cell apoptosis, considering that it does not damage the adjacent tissues, differing from the necrotic process (Schaeffer, D'Aviz, Ghiggi & Klassmann, 2019). This makes PDT a safe and effective therapy because, by inducing apoptosis in which cell death is programmed with shrinkage and phagocytized by macrophages, it prevents cell lysis and cytoplasmic content overflow and consequent tissue lesions (Lacerda, Alfenas & Campos, 2014).

This promising expectation caused PDT studies to focus on the mode of using the technique, testing several dyes and light and laser emitters. Studies show that blue dyes such as methylene blue associated with laser with a wavelength near 633 nm present favorable results for microbial reduction. The crucial part of this technique is to excite the photosensitizer in the target with a minimum surround effect because it is not a thermal therapy. However, variations in time, intensity, and amount of photosensitizer may lead to different results. Therefore, the efficiency of this therapy depends on biological factors: selectivity and retention of the photosensitizer and oxygen concentration in the medium; physical factors: the light flux that reaches the treatment region and the transfer of excitation energy of the photosensitizer; and chemical factors: molecule oxidizing effect and life span (Asnaashari, Godiny, Azari-Marhabi, Tabatabaei & Barati, 2016).

Concerning the biological factor, it is worth mentioning the pre-irradiation time, which is the time before therapy when the root canals receive the photosensitizer. This time is vital for the target cells to effectively absorb the material applied before being exposed to irradiation. In endodontic cases, this time interval called pre-irradiation time ranges from 2 up to 5 minutes (Sivieri-Araujo et al., 2013).

Considering that oxygen is also essential to this therapy, using optical fiber attached to the laser tip is suggested to ensure a satisfactory oxygen presence during PDT, making helical movements from the apical to the cervical aspect within the root canal system throughout the process. These movements with optical fiber will agitate the photosensitizer, which will ensure the reoxygenation of the medium, thus increasing the available oxygen. Moreover, using optical fiber contributes to distributing the light better in the canal treated (Lacerda et al., 2014).

The literature shows that the conventional endodontic treatment combined with PDT is more effective in root canal disinfection. A recent systematic review confirmed the efficacy of PDT in removing endodontic biofilms from infected root canals (Bordea et al., 2020). The PDT is a technique of easy and fast clinical application that satisfactorily reduces the microbial load conservatively, without tissue lesions.

Several factors contribute to the results of PDT, such as the type, dose, application time, and location of the photosensitizer; oxygen availability; and parameters related to the light source, including wavelength (nm), power density (mW/cm^2), and energy flux (J/cm^2). They may significantly interfere with the results according to the variables (Chrepa, Kotsakis, Pagonis & Hargreaves, 2014; Borsatto et al., 2015).

To analyze potential morphological changes, Lacerda, Lima, Lacerda, and Campos (2016) used two groups of teeth, in which one was subjected to conventional endodontic treatment and did not receive PDT, and the other received PDT (toluidine blue base previously applied for 5 minutes before irradiation combined with a low-level red diode laser of approximately 660 nm, which was also activated for 5 minutes continuously using optical fiber). At the end of the study, after analyzing the teeth, the control group presented a higher smear layer retention, and the teeth that received PDT presented a considerable opening of the dentinal tubules, which is not concerning compared to the benefits of the technique (Lacerda, Lima, Lacerda & Campos, 2016).

However, a similar study by Menezes, Prado, Gomes, Gusman and Simão (2017) performed PDT with methylene blue as the photosensitizer, complying with a pre-irradiation time of 2 minutes, and activated by a diode laser of 100 W and 660 nm, in a 90-second interval. The authors showed that the treatment morphologically changed the dentin, inducing a lower bond strength of the AH Plus and MTA Fillapex cements used in the study (Menezes et al., 2017).

In a broader perspective, Yildirim et al. (2013) compared the auxiliary treatment using 5% sodium hypochlorite to PDT with different application times (1, 2, and 4 minutes). The PDT technique with methylene blue irradiated by a 660-nm laser showed that both methods were efficient in suppressing *Enterococcus faecalis*. Moreover, 1 minute was sufficient for the therapy because there was no difference in action compared to the groups with a longer irradiation time (Yildirim et al., 2013).

However, Xhevdet et al. (2014) performed PDT in three teeth groups, applying the HELBO photosensitizer irradiated with a laser of the same brand, with 660 nm and 100 mW of power. The irradiation intervals were 1, 3, and 5 minutes, and the group with a longer exposure time eliminated more bacteria and fungi, followed by the 3-minute group, and lastly by the lowest exposure time, which was below the others, contradicting the previous study (Xhevdet et al., 2014).

Bumb et al. (2014) verified 20 dental units in two groups, in which one was treated only conventionally, and the other was associated with PDT. In this case, the therapy was based on methylene blue irradiated for 10 minutes with a 910-nm laser. At the end of the process and after the cycle of an entire day, the therapy was satisfactory as an adjuvant in reducing microorganisms in the infected canal, reaching 96.7% of elimination (Bumb et al., 2014).

Furthermore, Asnaashari, Ashraf, Rahmati and Amini (2017) associated drug therapy in their study to assess the antimicrobial effect of PDT compared to the calcium hydroxide therapy. The PDT used toluidine blue as the photosensitizer with irradiation based on a diode LED (660 nm and 200 mW) for 60 seconds. Finally, the study showed that both therapies were efficient as an adjuvant to endodontic treatment, but PDT showed higher potential for *Enterococcus faecalis* elimination (Asnaashari et al., 2017).

Leading the technique to more complex cases, Lima et al. (2019) decided to use PDT as a treatment adjuvant due to the persistence of a fistula after four conventional endodontic treatment sessions in a perforated dental element. Hence, they used a dual red laser of 660 nm and 18 J of power for 180 seconds in each conduit instrumented with methylene blue at 0.05%. Thirty days after ending the therapy, the fistula regressed and allowed obturation. After one year of follow-up, there was no symptomatology, and the perforated region showed bone neoformation (Lima et al., 2019).

Still on the subject of complexities, Martinelli, Andrade, Limoeiro, Valladão and Braitt (2019) analyzed the use of PDT for endodontic retreatment in a single session. The clinical application used Chimiolux methylene blue at 0.05%, complying with the 5 minutes before irradiation and later irradiated with a Therapy XT laser device for an 80-second interval. At the end of the therapy, the photosensitizer was removed with 5 ml of 6% NaOCl and obturated. After 10 months of follow-up,

there were signs of bone repair in the apical region and no clinical signs and symptoms (Martinelli et al., 2019).

Contrary to all the previous studies that used the methylene blue dye technique, Sebrão, Bezerra, França, Ferreira and Westphalen (2017) compared two photosensitizers in PDT. One group used methylene blue at 0.01% with irradiation by a red laser (660 nm), and another group used rose bengal irradiated by a green laser (532 nm). The study showed that, in these proportions, after one day, the rose photosensitizer associated with a green laser stood out in this comparison for eliminating *Enterococcus faecalis* better (Sebrão et al., 2017).

Tooth color change is a disadvantage of PDT. For instance, an *in vitro* study reported that photosensitizers change tooth color and did not show differences between groups using methylene blue and toluidine blue dyes because both belong to the phenothiazines family (Costa et al., 2016).

CONCLUSION

Based on the literature discussed, photodynamic therapy (PDT) is a proven effective technique, little invasive, and risk-free for patients. The PDT is effective in eliminating bacteria such as *Enterococcus faecalis* without causing bacterial resistance, thus becoming an important auxiliary tool for conventional treatment. It was concluded that PDT is clearly effective, but its clinical applicability is still subject to different protocols, which requires developing a protocol for common use.

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