Photodiagnosis and Photodynamic Therapy 27 (2019) 396–401

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

# The effects of photodynamic therapy on postoperative pain in teeth with necrotic pulps

Marcelo Santos Coelho[a,*], Larissa Vilas-Boas[a], Peter Z. Tawil[b]

[a] Faculdade de Odontologia São Leopoldo Mandic, Rua José Rocha Junqueira 13, Campinas, 13045-755, SP, Brazil
[b] University of North Carolina at Chapel Hill, Department of Endodontics School of Dentistry, University of North Carolina, 5417-J Koury Bldg, CB #7450 Chapel Hill, NC 27599-7450, United States

ARTICLE INFO

*Keywords:*
Endodontic disinfection
Laser
Methylene blue
Photodynamic therapy
Postoperative pain
Root canal therapy
Visual analogue scale

ABSTRACT

This study aimed to determine the effects of photodynamic therapy (PDT) on postoperative pain after treatments of teeth with necrotic pulps. This randomized clinical trial consisted of 60 patients who presented for treatment of asymptomatic teeth. The patients were randomly assigned into the Control Group (CG) or the PDT Group (PG). The canals were instrumented with a reciprocating instrument (50.05) under 2.5% NaOCL irrigation. After instrumentation was completed, the canals were flooded with 1.56 μM/mL of methylene blue (MB), the optical fiber was inserted to the working length and applied for 3 min (P = 100 mW, t = 3 min, E = 18 J). The device emitted PDT only for the PG. The operator and the patient were both masked to the treatment protocol. After PDT, the root canal treatment was completed and the canals were filled. A card was given to the patients to document their pain perception through the 0–10 visual analogue scale (VAS) at 24 h, 72 h, and 1-week intervals. The Mann-Whitney and Fisher´s exact tests were used for statistical analysis ($P < .05$). The average pain level for the CG was 1.33 at 24 -hs and 0.50 at 72 -hs; for the PG, the average pain level was 0.37 at 24 -h and 0 at 72 -h ($P < .05$). After 1-week there was no report of pain. PDT had a significant effect in decreasing postoperative pain at 24- and 72 -h intervals in treatment of single-rooted teeth with necrotic pulps performed in one visit.

## 1. Introduction

Root canal treatment involves the removal of vital or necrotic pulp tissue, bacteria, and its by-products. This aims to prevent apical periodontitis or to promote healing when it is present. Instrumentation of root canal along with root canal irrigation is the most important step in the disinfection of the root canal system. In some instances, root canal treatments might cause some postoperative pain [1].

Postoperative pain might be affected by several factors. Trauma of the periodontal tissues and chemical irritants can be controlled with caution during working length (WL) determination and instrumentation [2,3]. Bacterial extrusion of the remaining bacteria might also be responsible for postoperative pain, and some studies have looked at the amount of bacterial extrusion through different instrumentation kinematic motions [4]. However, no matter the kinematic used during the mechanical instrumentation, no system has been able to reach a complete sterilization of the root canal, and clinical studies have shown similar postoperative pain [5,6]. Additional steps have been proposed to enhance root canal disinfection such as calcium hydroxide dressing, lasers, as well as sonic and ultrasonic devices [7].

Recently, laser has been used in several dental protocols. Hard tissue lasers are able to melt dentin and promote ablation; soft tissue lasers might lead to biostimulation, thus improving the healing process [8]. The application of soft lasers in periodontal ligament (PDL) human cells has demonstrated to decrease cyclooxygenase and prostaglandin levels which mediates inflammation [9]. The laser photons are absorbed by mitochondrial cells releasing singlet oxygen and nitric oxide, it can also help with fibroblast proliferation, matrix synthesis and neovascularization [10].

Photodynamic therapy (PDT) is the use of a soft tissue laser that activates a photosensitizer (PS), aiming an antimicrobial activity [11]. Different PS's are used, each one in association with a specific wavelength light source. The aim is to release singlet oxygen and eradicate the bacterial DNA while being safe to mammalian cells [12]. Methylene blue (MB) is among the most used PS applied in PDT and the majority of them are associated with a light source with a wavelength from 630 to 700 nm [13]. Different studies have demonstrated that PDT is efficient to diminish the bacterial load and biofilm in vitro [14,15] and in vivo

* Corresponding author at: Rua Emilio Ribas 776 sala 13, Campinas, SP, 13025-141, Brazil.
*E-mail address:* coelho_marcelo@yahoo.com.br (M.S. Coelho).

https://doi.org/10.1016/j.pdpdt.2019.07.002
Received 22 May 2019; Received in revised form 19 June 2019; Accepted 8 July 2019
Available online 10 July 2019
1572-1000/ 

[16,17].

A recent systematic review suggested that PDT is efficient as an adjunct for root canal disinfection [18]. Although it stressed its benefits, that study also emphasizes that there is a lack of clinical evidence that PDT is essential in root canal therapy. To the best of our knowledge, no study has yet investigated the influence of PDT on postoperative pain after RCT in single-rooted teeth presenting with necrotic pulps. Therefore, the aim of this randomized, double-blind clinical trial is to investigate the effects of PDT on postoperative pain in single-rooted teeth, with necrotic pulps, performed in a single visit. The null hypothesis tested is that PDT has no impact of postoperative pain.

## 2. Materials and methods

This prospective, randomized, double-blind clinical trial was approved by the Institutional Review Board and all volunteers gave their written consent after being informed about the risks and benefits of this research.

### 2.1. Sample size calculation

The sample size was based on a pilot study of 14 subjects following the same methodology. For achieving an 80% power (alpha error of 0.05) and 95% confidence of difference between the groups, a minimum of 27 volunteers in each group was deemed necessary and a goal of 30 volunteers was set for each group.

### 2.2. Patient selection and randomization

From a pool of 688 consecutively patients enrolled from June 2017 to April 2018, sixty volunteers fit the inclusion criteria and exclusion criteria (Fig. 1). Inclusion criteria were single-rooted teeth with fully developed apices, a healthy periodontal probing < 3 mm, and no mobility. Exclusion criteria were patients presenting pain prior to treatment, as well as those taking any pain relief medication or antibiotics in the previous 10 days. For diagnosis, a radiograph was taken and sensitivity testing was performed with a cold spray (EndoTest, Coltene Whaledent, Langenau, Germany) and Electric Pulp Tester (Vitality Scanner, Sybron Endo, Orange, CA). Only teeth with negative sensitivity response to cold and EPT were selected.

The volunteers were randomly divided in 2 different groups (n = 30), as follows: Control Group (CG), root canal treatment without the use of PDT, or PDT Group (PG), root canal treatment with PDT used as adjunct. Thirty charts were created for each group and were previously randomized by the dental assistant following a computerized program (random.org). The volunteers in the CG had a chart with a green dot printed, while the volunteers in the PG had a red dot in the chart (Fig. 2).

After anesthesia, rubber dam isolation was placed and the endodontic access was done with a high speed hand-piece and carbide burs. After reaching the pulp chamber, teeth were copiously irrigated with 5 mL of 2.5% sodium hypochlorite (NaOCl) through a NaviTip 31 G (Ultradent, South Jordan, UT). The canal was first carefully scouted with a size 10-k file (Dentsply Sirona, Ballaigues, Switerzland), and an estimated working length was established using an electronic apex locator (Sybron Endo, Orange, California). Following the instructions of the reciprocation system (Reciproc, VDW, Munich, Germany), once a size 30-k file reached the working length, a size 50.05 NiTi file was selected. An engine VDW Silver (VDW) was used in the "Reciproc All" setting. The file was gently moved towards the apex using an in-and-out movement with amplitude of 3–4 mm. After 3 strokes, the instrument was removed and cleaned with gauze. Using the same fashion, the file was used up to 2/3 of the estimated working length. Then, using an electronic apex locator (Sybron Endo), the final WL was established and confirmed through a radiograph to be 1 mm short of the radiographic apex. The total volume of irrigation through the instrumentation was standardized to 40 mL of NaOCl. After reaching the WL, the canals were flooded with 2.5% NaOCl and passive ultrasonic irrigation (PUI) was performed in a size 20.01 ultrasonic tip (Irrigonic, Helse Ultrasonics, Santa Rosa do Viterbo, Brazil) for 3 × 20 s, then 17% etilenediaminetetracetic acid (EDTA) was placed in the canal and remained for 3 min. Finally, 3 mL of 1.56 μM/mL MB in water solution (MMOptics, São Carlos, Brazil) was placed in the canal for 2 min.

The aforementioned steps were done in both groups. At this point, both the provider and the patient were blinded. The dental assistant collected the chart that was previously selected for that patient. If a green dot was in the chart, the assistant simulated the use of the laser device (Laser Duo, MMOptics). The tip of the laser was covered with aluminum foil, the protection glasses were placed on both patient and dental assistant, and the device was applied for 3 min. All sounds of the device remained functional for both groups. If a red dot was in the chart, the assistant used the laser device placing a size 25, taper 0.04 optical fiber (MMOptics) up to the WL and moved the tip in gentle vertical motion. The laser used was used for 3 min at the following parameters: 660 nm, 100 mW, 600 J/cm$^2$ resulting in 18 J of total energy. Chart randomization, PDT application, and simulation were done by the assistant without the operator being aware of the groups. The MB blue was then removed with saline irrigation and the canal was then obturated with gutta-percha and AH Plus sealer (Dentsply, DeTrey, Konstanz, Germany) through warm vertical condensation.

### 2.3. Pain perception evaluation

The volunteers were asked to register their pain perception in a Visual Analogue Scale (VAS). The VAS consisted of a 100 mm line without any marks except by a number "0" in the beginning and a number "10" in the end. In case the patients remained pain free, they were asked to mark in the number "0"; the number "10" was used for the worst imaginable pain. All intermediate pain was registered following the volunteers' perceptions. Pain level was classified as none (0), mild (1–3), moderate (4–7), or severe (8–10). The pain perception was registered at 24 -h, 72 -h, and 1-week intervals. The volunteers were also informed that they could ask for an office visit if pain was too strong; in this scenario, the case was classified as a flare-up [19]. were also informed to take 600 mg ibuprofen every 6 h for pain relief, if necessary. The number of tablets taken by each patient was registered. Ages, genders, and smoking habits were recorded.

### 2.4. Statistical analysis

The Mann-Whitney test was used for statistical differences between the groups at each time interval. The Fischer´s exact test was applied for statistical analysis of differences in age, gender, and, smoker status. The multivariate analysis post-hoc test was performed using a logistic regression analysis. IBM SPSS 24.0 version (IBM, Armonk, NY) was used, and statistically differences were set at $P < .05$.

## 3. Results

All volunteers returned their cards after 1 week. The average age, gender, and smoking status were equally distributed among the groups. The demographic distribution of the volunteers is shown in Table 1.

The average pain level for the CG was 1.44 at the 24 -h mark, and 0.50 at the 72 -h mark. For the PG, the average pain level was 0.37 at 24 -hs and 0 at 72 -hs. These differences were statistically significant ($P < .05$). At 1 week, there was no report of pain (Table 2).

At the 24 -h interval, 91.66% of the volunteers reported no pain or mild pain. At the 72 -h interval, 96.43% of the volunteers reported no pain or mild pain. The percentage of patients that reported none, mild, moderate, or severe pain at any time interval for both groups is shown in Table 3. There was no report of flare-up.

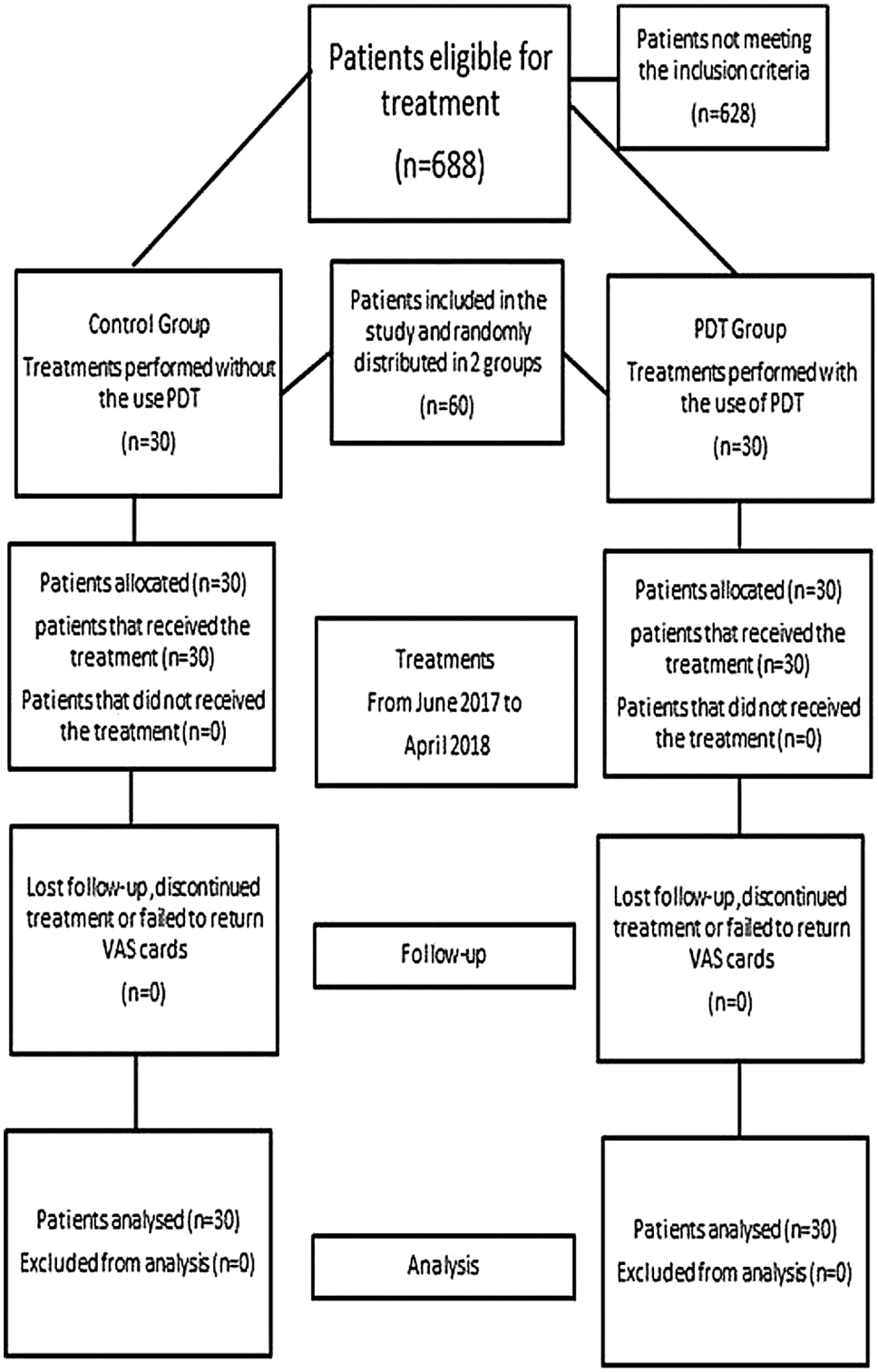


**Fig. 1.** Flowchart of patients' allocation and randomization.

The average number of tablets taken for pain medication was 0.77 ± 2.11 for the CG and 0.13 ± 0.43 for the PG. These findings were not statistically significant ($P > .05$).

## 4. Discussion

The present study aimed to assess the impact of PDT on post-operative pain in treatments performed in single-rooted teeth presenting with necrotic pulps performed in a single visit. presenting with pre-operative pain were not included, as it is defined that previous pain impacts the postoperative status [20]. All canals were kept patent with a small instrument (size 10-K file) and the WL was determined with the apex locator and confirmed through a radiograph to be 1 mm short of the radiographic apex. Care was taken to avoid over-instrumentation because, as shown in a previous study, it might increase postoperative pain [21]. The volunteers were randomly assigned to both groups, so control of age and gender was not done. These variables could have impacted the results; however, the distribution of male and female

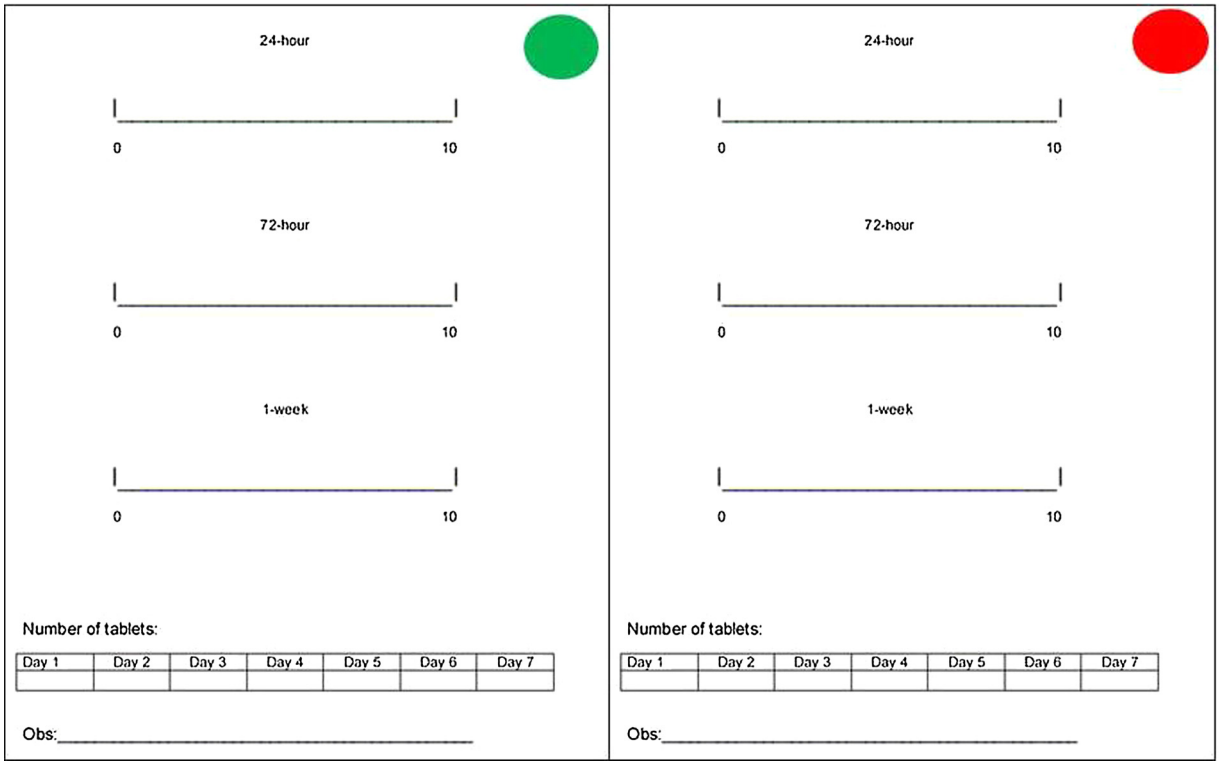


**Fig. 2.** Visual analogue scale and daily record of tablets, the green dot indicating control group, and the red dot indicating PDT Group.

**Table 1**
Demographic aspects and tooth distribution of patients in CG and PG.

| | Control | PDT |
|---|---|---|
| Mean age | 46.97 ± 13.23 | 46.73 ± 16.30 |
| Male patients | 12 | 10 |
| Smokers | 3 | 3 |
| Maxillary incisor | 14 | 14 |
| Mandibular incisor | 3 | 6 |
| Maxillary canine | 4 | 1 |
| Mandibular canine | 1 | – |
| Maxillary premolar | 2 | 4 |
| Mandibular premolar | 6 | 5 |

**Table 2**
Average, mean (standard deviation) pain level in both groups at 3 different time-intervals.

| | Control | PDT | p-value |
|---|---|---|---|
| 24 hours | 1.44 (2.09) | 0.37 (0.81) | 0.037* |
| 72 hours | 0.5 (1.61) | 0 (0) | 0.021* |
| 1 week | 0 (0) | 0 (0) | > 0.999 |

* *Statistically significant at P < .05.*

**Table 3**
Percentage (%) of patients presenting with none, mild, moderate, or severe pain at the 3 time-intervals evaluated.

| | | Control | PDT |
|---|---|---|---|
| 24 hours | none | 56.66 | 80 |
| | mild | 26.66 | 20 |
| | moderate | 16.66 | 0 |
| | severe | 0 | 0 |
| 72 hours | none | 83.33 | 100 |
| | mild | 10 | 0 |
| | moderate | 3.33 | 0 |
| | severe | 3.33 | 0 |
| 1 week | none | 100 | 100 |
| | mild | 0 | 0 |
| | moderate | 0 | 0 |
| | severe | 0 | 0 |

volunteers was similar in both groups, and age of volunteers was not statistically different [2,22].

Standardization of shaping in different anatomies is a great challenge. The use of a single file reciprocating instrument in single rooted teeth aimed to promote the same apical size in all canals. A previous *in vivo* study demonstrated that, in treatment of necrotic teeth, kinematics is not relevant for postoperative pain [6]. Recently, Cruz-Junior et al. [21] showed low incidence of pain in treatments performed with single-file reciprocating instruments up to size 40. Our study used an instrumentation protocol similar to that study, however enlarging up to size 50. It has been suggested that a larger apical preparation size could lead to a decrease in the bacterial load [23]. Thus, the overall finding that 91.66% of the patients reporting no pain to mild pain at any time interval of our study was higher than previously reported 82.22% by Cruz-Junior et al. [21]. The larger apical preparation could have played a role in reducing the bacterial load and leading to less postoperative pain.

After endodontic procedures, strong pain or swelling might occur, characterizing a flare-up, and possibly requiring an unscheduled office visit [19]. Similar to previous studies, the data herein presented showed no incidence of flare-up [24]; other studies also reported a low incidence of flare-ups [25]. Moreover, there was no difference in the number of tablets taken between the CG and PG. The overall incidence of pain in the present study was low; however, only the control group reported moderate (24- and 72-h interval) or severe pain (72-h interval). When PDT was applied, only mild pain was reported at the 24-h interval, and all patients were pain-free at the 72-h interval. The average pain level of patients that underwent the PDT protocol was lower in the initial postoperative days. It took 1 week until no difference was seen between the groups. The lower incidence of pain observed at the 24- and 72-h intervals in PG might be due to the PDT

application, thus the null hypothesis was not accepted.

Nunes et al. [26] demonstrated that the *enterococcus faecalis* biofilm is reduced with root canal instrumentation and irrigation with 1% NaOCl, regardless of the use of PDT. Conversely, other study showed the effectiveness of PDT in reducing the biofilm and the bacterial load [15]. The optical fiber helps to propagate the light inside the root canal, enhancing disinfection [27]. In an *in vivo* study, Garcez et al showed bacteria free canals after using a PDT protocol associating 660 nm light source delivered by an optical fiber [16]. Decreasing the bacterial load should lead to less bacterial extrusion and remnants, consequently decreasing pain perception. Similarly, to Garcez et al, we might infer that, in the present study, the PDT group presented a smaller bacterial load than NaOCl irrigation alone. Therefore, the PDT group presented less postoperative pain at 24- and 72 -h intervals when compared to NaOCl irrigation without PDT.

Low-level laser therapy is claimed to possess anti-inflammatory properties, and decrease prostaglandin levels, edema, and pain [28]. A meta-analysis showed its efficacy to reduce acute and chronic neck pain [29]. Bramante et al. reported the use of 660 nm light source as an adjunct in the healing process of a case of NaOCl extrusion [8]. Recently, Arslan et al. [30] demonstrated that 970 nm diode laser reduced postoperative pain in the first 4 days of root canal retreatment. In both studies, the laser was applied close to the soft tissues aiming biostimulation rather than disinfection. In the present study, the canals were instrumented up to the size 50.05; consequently, the size 25.04 optical fiber that conducts the light source could reach the full WL. Additionally, patency was achieved in all cases of the present study, allowing the light to propagate through the foramen. Vaarkamp et al. [31] demonstrated that 632 nm wavelength light can scatter through more than 2 mm of dentine. A previous study has demonstrated the ability of a 645 nm wavelength (similar to the 660 nm used in this study) in promoting the increase expression of genes involved in healing of human cells [32]. Thus, we can hypothesize that in the present study the laser irradiation could have reached periapical tissues increasing cell proliferation and neovascularization [10]. In another recent study, PDT was applied with a similar protocol to our study in mandibular molars resulting in better healing of periapical healing but no difference in postoperative pain was reported [33]. Nonetheless, while our study used single-rooted straight root canals, de Miranda et al used mandibular molars which are more challenging to standardize.

Currently, there is no standardized photosensitizer for the use along with the 660 nm light source when applying PDT in endodontics. Garcez et al [27] used polyethylenimine chlorin(e6) as a photosensitizer and a diode laser as a light source for 4 min in an *in vivo* study or, MB for 30 s in an *in vitro* model [14]. Another study used phenothiazin-5-ium,3,7-bis(dimethylamino)-,chloride and applied the light source for 60 s [15]. While there is no agreement about the ideal protocol, the present study used MB (1.56 μM/mL) and applied the light for 3 min as suggested by the manufacturer. Future studies should consider different PDT protocols and their impacts on postoperative pain. In addition, long-term outcomes, assessing periapical status of treatments performed with PDT, are highly desirable. The low cost and risks of such treatment should encourage future research also in teeth presenting more complex anatomies.

Conclusion

Within the limitations of this study, it can be concluded that PDT was efficient in reducing postoperative pain in single-visit root canal treatment of teeth with necrotic pulps. The number of tablets taken for pain relief was not affected by PDT.

## References


[1] A. Arias, M. Azabal, J.J. Hidalgo, J.C. de la Macorra, Relationship between post-endodontic pain, tooth diagnostic factors, and apical patency, J. Endod. 35 (2009) 189–192.

[2] A. Arias, J.C. de la Macorra, J.J. Hidalgo, M. Azabal, Predictive models of pain following root canal treatment: a prospective clinical study, Int. Endod. J. 46 (2013) 784–793.

[3] H. Arslan, Y. Guven, E. Karatas, E. Doganay, Effect of the simultaneous working length control during root canal preparation on postoperative pain, J. Endod. 43 (2017) 1422–1427.

[4] J.M. Tinoco, G. De-Deus, E.M. Tinoco, F. Saavedra, R.A. Fidel, L.M. Sassone, Apical extrusion of bacteria when using reciprocating single-file and rotary multifile instrumentation systems, Int. Endod. J. 47 (2014) 560–566.

[5] M.A. Neves, J.C. Provenzano, I.N. Rocas, J.F. Siqueira, Clinical antibacterial effectiveness of root canal preparation with reciprocating single-instrument or continuously rotating multi-instrument systems, J. Endod. 42 (2016) 25–29.

[6] J.B. Relvas, M.M. Bastos, A.A. Marques, A.D. Garrido, E.C. Sponchiado, Assessment of postoperative pain after reciprocating or rotary NiTi instrumentation of root canals: a randomized, controlled clinical trial, Clin. Oral Investig. 20 (2016) 1987–1993.

[7] M. Granevik Lindstrom, E. Wolf, H. Fransson, The antibacterial effect of Nd:YAG laser treatment of teeth with apical periodontitis: a randomized controlled trial, J. Endod. 43 (2017) 857–863.

[8] C.M. Bramante, J.A. Duque, B.C. Cavenago, R.R. Vivan, A.S. Bramante, Use of a 660-nm laser to aid in the healing of necrotic alveolar mucosa caused by extruded sodium hypochlorite: a case report, J. Endod. 41 (2015) 1899–1902.

[9] N. Shimizu, M. Yamaguchi, T. Goseki, Y. Shibata, H. Takiguchi, T. Iwasawa, Y. Abiko, Inhibition of prostaglandin E2 and interleukin 1- production by low-power laser irradiation in stretched human periodontal ligament cells, J. Dent. Res. 74 (1995) 1382–1388.

[10] M. Goyal, S. Makkar, S. Pasricha, Low level laser therapy in dentistry, Int. J. Laser Dent. 3 (2013) 82–88.

[11] A.C. Trindade, J.A. De Figueiredo, L. Steier, J.B. Weber, Photodynamic therapy in endodontics: a literature review, Photomed. Laser Surg. 33 (2015) 175–182.

[12] Y. Xu, M.J. Young, R.A. Battaglino, L.R. Morse, C.R. Fontana, Endodontic antimicrobial photodynamic therapy: safety assessment in mammalian cell cultures, J. Endod. 35 (2009) 1567–1572.

[13] H. Gursoy, C. Ozcakir-Tomruk, J. Tanalp, S. Yilmaz, Photodynamic therapy in dentistry: a literature review, Clin. Oral Investig. 17 (2013) 1113–1125.

[14] P. Diogo, C. Fernandes, F. Caramelo, M. Mota, I.M. Miranda, Antimicrobial photodynamic therapy against endodontic enterococcus faecalis and candida albicans mono and mixed biofilms in the presence of photosensitizers: a comparative study with classical endodontic irrigants, Front. Microbiol. 8 (2017) 498.

[15] D. Hoedke, C. Enseleit, D. Gruner, H. Dommisch, S. Schlafer, Effect of photodynamic therapy in combination with various irrigation protocols on an endodontic multispecies biofilm ex vivo, Int. Endod. J. 51 (2018) 23–34.

[16] A.S. Garcez, S.C. Nunez, M.R. Hamblim, H. Suzuki, M.S. Ribeiro, Photodynamic therapy associated with conventional endodontic treatment in patients with antibiotic-resistant microflora: a preliminary report, J. Endod. 36 (2010) 1463-1266.

[17] D.G.D. Rabello, B.J.M. Corazza, L.L. Ferreira, M.P. Santamaria, A.P.M. Gomes, F.C. Martinho, Does supplemental photodynamic therapy optimize the disinfection of bacteria and endotoxins in one-visit and two-visit root canal therapy? A randomized clinical trial, Photodiagnosis Photodyn, Ther. 19 (2017) 205–211.

[18] V. Chrepa, G.A. Kotsakis, T.C. Pagonis, K.M. Hargreaves, The effect of photodynamic therapy in root canal disinfection: a systematic review, J. Endod. 40 (2014) 891–898.

[19] J.F. Siqueira, Microbial causes of endodontic flare-ups, Int. Endod. J. 36 (2003) 453–463.

[20] M. Torabinejad, J.D. Kettering, J.C. McGraw, R.R. Cummings, T.G. Dwyer, T.S. Tobias, Factors associated with endodontic interappointment emergencies of teeth with necrotic pulps, J. Endod. 14 (1988) 261–266.

[21] J.A. Cruz Junior, M.S. Coelho, A.S. Kato, N. Vivacqua-Gomes, C.E. Fontana, The effect of foraminal enlargement of necrotic teeth with the reciproc system on postoperative pain: a prospective and randomized clinical trial, J. Endod. 42 (2016) 8–11.

[22] M.E. Robinson, J.L. Riley, C.D. Myers, R.K. Papas, E.A. Wise, Gender role expectations of pain: relationship to sex differences in pain, J. Pain 2 (2001) 251–257.

[23] S.J. Card, A. Sigurdsson, D. Orstavik, M. Trope, The effectiveness of increased apical enlargement in reducing intracanal bacteria, J. Endod. 28 (2002) 779–783.

[24] E.J. Silva, K. Menaged, N. Ajuz, M.R. Monteiro, T.S. Coutinho-Filho, Postoperative pain after foraminal enlargement in anterior teeth with necrosis and apical periodontitis: a prospective and randomized clinical trial, J. Endod. 39 (2013) 173–176.

[25] Vde O. Alves, Endodontic flare-ups: a prospective study, Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 110 (2010) 68–72.

[26] M.R. Nunes, I. Mello, G.C. Franco, J.M. de Medeiros, S.S. Dos Santos, Effectiveness of photodynamic therapy against enterococcus faecalis, with and without the use of an intracanal optical fiber: an in vitro study, Photomed. Laser Surg. 29 (2011) 803–808.

[27] A.S. Garcez, E.R. Fregnani, H.M. Rodriguez, S.C. Nunez, C.P. Sabino, The use of optical fiber in endodontic photodynamic therapy. Is it really relevant? Lasers Med. Sci. 28 (2013) 79–85.

[28] R. Albertini, A.B. Villaverde, F. Aimbire, M.A. Salgado, J.M. Bjordal, Anti-inflammatory effects of low-level laser therapy (LLLT) with two different red wavelengths (660 nm and 684 nm) in carrageenan-induced rat paw edema, J.Photochem. Photobiol. B. 89 (2007) 50–55.

[29] R.T. Chow, M.I. Johnson, R.A. Lopes-Martins, J.M. Bjordal, Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials, Lancet 374 (2009) 1897–1908.

[30] H. Arslan, E. Doganay, E. Karatas, M.A. Unlu, H.M.A. Ahmed, Effect of low-level laser therapy on postoperative pain after root canal retreatment: a preliminary

placebo-controlled, triple-blind, randomized clinical trial, J. Endod. 43 (2017) 1765–1769.
[31] J. Vaarkamp, J.J. ten Bosch, E.H. Verdonschot, Propagation of light through human dental enamel and dentine, Caries Res. 29 (1995) 8–13.
[32] Z. Lou, C. Zhang, T. Gong, C. Xue, A. Scholp, J.J. Jiang, Wound-healing effects of 635-nm low-level laser therapy on primary human vocal fold epithelial cells: an in vitro study, Lasers Med. Sci. 34 (2019) 547–557.
[33] R.G. de Miranda, A.P.V. Colombo, Clinical and microbiological effectiveness of photodynamic therapy on primary endodontic infections: a 6-month randomized clinical trial, Clin. Oral Investig. 22 (2018) 1751–1761.