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ORIGINAL RESEARCH

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Effects of photobiomodulation with different application parameters on injection pain in children: a randomized clinical trial

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Abstract

Photobiomodulation (PBM) has gained increasing interest due to its effectiveness in pain reduction in various fields of dentistry. However, the number of studies evaluating the effect of PBM on injection pain in children is very limited. The aim of the study was to evaluate the efficacy of PBM with three different application parameters (doses) + topical anesthesia on reducing injection pain and to compare these results with the placebo PBM + topical anesthesia in children during supraperiosteal anesthesia administration. 160 children were randomly divided into 4 groups, 3 experimental and 1 control, with 40 subjects in each. In the experimental groups, before the anesthesia administration, PBM with a power of 0.3 W was applied for 20, 30 and 40 s in groups 1, 2 and 3, respectively. In group 4, a placebo application of laser was performed. The pain felt during the injection was assessed using the Wong-Baker Faces Pain Rating Scale (PRS), and also the Face, Legs, Activity, Cry, Consolability (FLACC) Scale. Statistical analyses were performed to evaluate the data ($p < 0.05$). The mean FLACC Scale pain scores were 3.02 $\pm$ 2.93, 2.92 $\pm$ 2.54, 2.12 $\pm$ 1.89 and 1.77 $\pm$ 1.90 for the placebo group, and Groups 1, 2, and 3, respectively. Furthermore, the mean PRS scores were 1 $\pm$ 1.03, 0.95 $\pm$ 0.98, 0.80 $\pm$ 0.822 and 0.65 $\pm$ 0.921 for the placebo group, and Groups 1, 2 and 3, respectively. The "no pain response" rate was higher in Group 3 as compared to Groups 1, 2, and placebo according to the FLACC Scale and PRS; however, no difference was found between the groups ($p = 0.109$, $p = 0.317$). Injection pain in children did not differ with placebo and PBM applied with a power of 0.3 W for 20, 30 and 40 s.

Keywords

Photobiomodulation; Children; Parameters; Injection pain; Dose

1. Introduction

Pain and dental anxiety are crucial factors affecting treatment success rates, particularly in pediatric dentistry [1]. Reducing pain and discomfort during dental therapy contributes to controlling anxiety and increasing the cooperation of children [1, 2]. Although local anesthesia is used as an important tool for this purpose, paradoxically, pain during needle insertion frequently causes non-compliance in children. Therefore, many promising approaches like acupuncture, music therapy and laser therapy have been suggested to reduce injection pain [3–5].

Photobiomodulation (PBM) therapy, formerly known as low-level laser therapy, is a non-surgical procedure for promoting tissue healing, enhancing bone repair, decreasing inflammation, and providing pain relief [5]. After it was observed that the use of not only coherent monochrome light sources (lasers) but also non-coherent light sources such as LED was effective for photo-biomodulation therapy, it has evolved into a new name in practice [6, 7].

PBM has gained increasing interest because of its effectiveness in pain reduction and pain prevention in different fields of dentistry [6–10]. It is commonly used after surgical procedures to reduce pain as wisdom tooth extraction or during the treatment of temporomandibular disorders (TMD) and prophylactically to prevent pain that may occur during the treatment of a tooth with pulpitis or injection [5, 10–13]. Inhibition of neural function appears as a mechanism for the clinical application of PBM in pain and anesthesia [14]. Although some studies have reported that pain relief with PBM can be achieved by increasing β-endorphins and nitric oxide production as well as decreasing C-fiber activity and bradykinin levels, the exact mechanism is not yet completely understood [15]. It is reported that the biological effect occurs by the absorption of light through receptors called chromophores in the tissue, and the most important chromophore responsible for this in mammalian tissues is cytochrome c oxidase (CCO) [6, 7, 16]. The hypothesis is that inhibitory nitric oxide (NO) can be dissociated from CCO, thus restoring electron transport, and increasing mitochondrial membrane potential. Another

mechanism involves the activation of light or heat-gated ion channels that are based on chromophores [16].

PBM with appropriate parameters is enabled to penetrate into tissues to stimulate biological processes [16]. The parameters used for PBM can vary depending on its purpose. Changes in those parameters such as wavelength, power energy density, exposure time, and focal spot size may result in different effects [16–18]. While optimized dosages result in a positive effect, inappropriate doses may have undesirable therapeutic consequences [16, 17]. In a study by Ramello *et al*. [18], it was reported that 4 J/cm^2 PBM application reduced the pain felt during the treatment of teeth with irreversible pulpitis. On the other hand, in the same study, it was reported that 40 J/cm^2 PBM did not have any effect on the anesthesia depth.

In the literature, a limited number of studies have been reported on utilizing PBM to prevent injection pain in adults and children. Of the 3 studies conducted on children, Uçar *et al*. [5] and Shekarchi *et al*. [19] found a positive effect, while Amrutha-Varshini *et al*. [20] obtained a negative effect. The results of the studies are inconsistent due to the differences in biostimulative effects produced by the laser parameters which show diversity. Furthermore, it is seen that the effect of PBM has been evaluated in each research by comparing the groups containing a single administration parameter in the placebo or control groups. As a result, there have been no controlled studies conducted on the effect of laser parameters used in reducing injection pain.

The goal of this current study was to evaluate the efficacy of PBM with three different application parameters + topical anesthesia on injection pain and compare it to the placebo PBM + topical anesthesia in children during supraperiosteal anesthesia administration.

2. Material and method

Based on the data from a previous study [5], a minimum sample size of 35 subjects per group was calculated by utilizing G*Power software (Ver. 3.1.9.2, University of Dusseldorf, Dusseldorf, NRW, Germany). Type I error (alfa) and power (1-beta) were considered as 0.05 and 0.95, respectively. Considering the possibility of participants dropping out, the study enrolled 40 children aged 6 to 12 years old in each group (a total of 160 children). Subjects for this study were chosen according to the inclusion criteria in Table 1. Furthermore, children who had any systemic disease or were taking medication, as were children who had an allergy history to previous local anesthesia or medication, were excluded. Children with active pathology at the injection site were also excluded from the study (Table 1).

The study protocol was explained to all eligible children and their parents, and informed consent forms were obtained before beginning the study. Four subgroups consisting of 40 randomly selected patients were created for the pre-anesthesia method with random numbers generated by the computer using randomization software (Research Randomizer). The randomization and assignment of the groups were performed by a researcher who did not apply the injection or evaluate the injection pain.

Three of the groups were designated as experimental, while the fourth one was designated as the control group (placebo). Before the topical anesthetic application, the experimental groups were exposed to three different laser power settings (different application times) for the PBM, one for each group. While the power of the laser device was adjusted to 0.3 W in all 3 groups, its duration was determined as 20 s for group 1, 30 s for group 2, and 40 s for group 3. Group 4 was the placebo group, and the fiber of the laser device was kept focused on the application area before applying the topical anesthetic. Turning on the recorded sound of the laser device provided the blindness of the patient in the placebo group. The fact that PBM is a nonthermal and nonvibration process facilitated our work in creating similar application conditions for children between the experimental and control groups. PBM was performed by a different researcher than the investigator who would perform the local anesthesia application, since blindness conditions could not be provided to the groups due to the light and sound of the laser device. Then, she left the room, and the operator of the local anesthesia entered in order to apply local anesthesia. However, both the PBM practitioner and the local anesthesia practitioner remained constant throughout the study. During the PBM and placebo PBM applications, wavelength-specific protective eyeglasses (Doris CTL 2109S, Poland) were used by both the operator and the patient.

Prior to patient participation, the laser was conveniently situated, and warning notices for laser use were clearly and plainly displayed. A diode laser was used (EpiX; Biolase Technology, lnc., USA) to perform the PBM with a continuous wavelength of 940 nm in a 400 μm fiber. In noncontact mode, the fiber of the laser device was positioned 1 mm away from the application region. PBM was performed at a 0.087 cm^2 focal spot area perpendicular to the root surface. A silicon apparatus with a hole was used to keep the distance between the target tissue and the laser fiber constant. The power of the device was 0.3 W, and the energy intensity was 69 J/cm^2, 103 J/cm^2 and 138 J/cm^2 for groups 1, 2 and 3, respectively. The energy density for each group was calculated with the following formula [22]:

$H = Q/a$

H: energy density, Q: radiant energy (power × time), a: area of spot size (pi × r^2)

…J/cm^2 = …W × …s/0.087cm^2

To ensure the efficiency of the device, the output power was measured with a power meter three times throughout the research (Vega Power Meter; Ophir Photonics, 3050 North, 300 West North Logan, USA).

Following PBM, the laser operator marked the oral mucosa with a blue soft-tipped pen based on the outer edge of the silicone piece around the laser fiber to apply anesthesia on the same target area. After completing all the applications of four groups related to PBM/placebo PBM, an experienced pediatric dentist who was blinded to the study groups performed all the local anesthesia procedures. The average time (±std) from the end of laser application to the start of topical anesthesia was 17.31 + 1.26 s. Firstly, the injection site was dried, and then a topical anesthetic containing 10% lidocaine (2286026, Vemcaine Pump Spray 10% 50 mL, Vem AB, Istanbul, Turkey) was applied to the oral mucosa with a simple cotton tip applicator for 60 s. 1 mL 4% articaine

TABLE 1. Inclusion and exclusion criterias.

Subjects/Teeth	Number of Subjects
Inclusion Criteria	
1. Subjects age range of 6–12 years	
2. Subjects with high cooperation (as per the Frankl scale with a score of 3/4) [21]	
3. Subjects without medical history of systemic disease or bleeding disorder	n = 160
4. Patients who have no previous negative experience of anesthesia/dentistry	
5. Subjects having mandibular or maxillary primary first molar tooth	
6. Subjects with written informed consent which was obtained from their parents	
Exclusion Criteria	
1. Subjects requiring anesthesia application for a tooth different from first primary molar	(n = 10)
2. Subjects who were taking any medication that might affect anesthetic assessment	(n = 18)
3. Patients who have a site of active pathosis in the injection region	
4. Subjects with low cooperation (as per the Frankl scale with a score of 1/2) [21]	(n = 10)
5. Patients who have previous negative experiences with anesthesia/dentistry	(n = 14)

hydrochloride with 1/100,000 epinephrine (CLB90026, Ultracaine D-S Forte; Hoechst Canada Inc, Montreal, Quebec, Canada) was injected with a 27-gauge dental needle, and a 2 mL disposable dental syringe (Helmed, Adana, Turkey). To alleviate the children's fears, detailed explanations were given to them before each procedure in a simple and understandable manner. The PBM and injection process was explained using illustrative terms. The researcher used the modified standardized narrative approach from the American Academy of Pediatric Dentistry (AAPD) Behaviour Management Guidelines [23] and Schwartz and Kupietzky [24] to all children. Since a calm and friendly manner was maintained during the whole procedure, none of the children required any sedative or pharmaceutical therapy to complete any of the procedures.

A completely blind investigator objectively evaluated the behavior of the children by using the FLACC Scale [25]. The FLACC Scale is divided into 5 subgroups, each with a value between a minimum of 0 and a maximum of 2 (Fig. 1). As a result of the evaluation of each sub-parameter (1) Face, (2) Legs, (3) Activity, (4) Cry, and (5) Consolability, the total score of the FLACC Scale with a minimum of 0 and a maximum of 10 was determined. (0 = no pain, 1–3 = mild pain, 4–7 = moderate pain, and 7–10 = severe pain). Since this evaluation was made by a single researcher, this helped to ensure the reliability of the process. The researcher performed the FLACC Scale assessment on a group of 20 children who were not included in the study. The behaviors of the children, who were videotaped, were evaluated by the same researcher after an average of 1 month.

For subjective assessment, the Modified Wong-Baker FACES pain rating Scale (PRS) was used [26]. The scale has facial images ranging from smiling to crying, with ratings ranging from 0 to 3. While "0" indicates "no pain", "3" indicates "severe pain" (Fig. 2). The utilization of PRS has been previously validated in this age group [26]. Thus, in this present study, each pediatric patient was advised to mark the level of subjective pain on PRS immediately after administering the injection. The investigator responsible for evaluating the children's behavior presented the PRS to the children. All explanations were made by the same person during the study, and the evaluations were performed in a standardized manner using a script to assess the children's behaviors and feelings during the injection.

The investigators informed all the parents and children about the potential postoperative problems (*e.g.*, pain, tongue or lip biting, hematoma, and bleeding) after the therapy was completed, and they were asked to contact the investigators immediately by phone if any of the above symptoms or effects were detected.

The Statistical Package for the Social Sciences (SPSS) 20.0 (International Business Machines (IBM) Corp., Armonk, NY, USA) software package was used to conduct the statistical analysis. The intrarater reliability was calculated using the Kappa test value (κ), with the values of >0.81, 0.80–0.61, 0.60–0.41, 0.40–0.21 and <0.20 denoting the states of excellent, substantial, moderate, fair, and slight agreement, respectively. The Kolmogorov-Smirnov test was performed to check the distribution of normality. The numerical variables, which didn't distribute normally, were given as median (25th–75th percentile), and the categorical variables were presented as frequency (%). For nonnormally distributed numerical variables, the Kruskal-Wallis tests and Mann-Whitney U tests were used, and the Monte Carlo chi-square test was utilized for the analysis of the categorical variables. For testing the two-sided hypotheses, $p < 0.05$ was considered to be sufficient for indicating statistical significance.

3. Results

In the present study, a total of 212 children were examined, and 160 met the inclusion criteria. The study was conducted with children aged between 6 and 12 (8.56 ± 1.68), consisting of 75 girls and 85 boys. 52 patients were excluded due to various reasons, which have been shown in Table 1. When

Category	Scoring		
	0	1	2
Face	No expression or smile	Occasional grimace/frown, withdrawn or disinterested	Frequent/constant quivering chin, clenched jaw
Leg	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content and relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

FIGURE 1. Face, Leg, Activity, Cry, Consolability (FLACC) Scale [25].

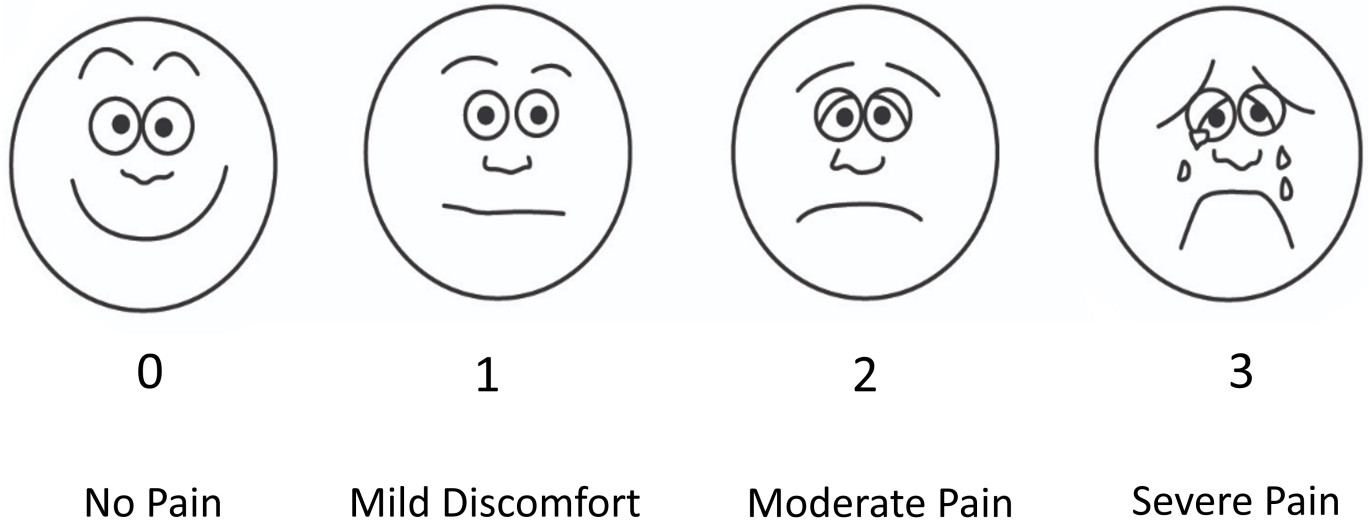

FIGURE 2. The Modified Wong-Baker FACES Pain Rating Scale (PRS) [26].

the randomized distributed participants for the control and experimental groups were evaluated in terms of homogeneity, no significant difference was observed in terms of gender and age distribution ($p = 0.516$, $p = 0.741$, respectively) (Table 2).

A total of 160 local infiltration anesthesia (83 in maxilla and 77 in mandible) procedures were completed with/without PBM. None of the children in the groups reported any adverse reactions to the treatment. Based on the repeated examination of videotaped images, the Kappa value showed excellent intra-rater agreement ($\kappa > 0.80$).

The FLACC Scale scores of the groups have been shown in Table 3 and Fig. 3. The mean FLACC Scale pain scores were 3.02 ± 2.93, 2.92 ± 2.54, 2.12 ± 1.89 and 1.77 ± 1.90 for the Placebo group and Groups 1 (20 s), 2 (30 s) and 3 (40 s), respectively. The "no pain" response (0) rate was seen as the highest in Group 3 among all the groups. For all the groups except group 3, the median pain score was 2. Also, the median score for Group 3 was 1 (Table 2). Additionally, the FLACC Scale scores showed that the maximum pain score for the Placebo group and Group 1 was 10 (severe pain), and it was 7 (severe pain) and 6 (moderate) for Groups 2 and 3, respectively. However, no significant difference was found among the groups related to the FLACC pain scores ($p = 0.109$).

PRS scores have been shown in Table 3 and Fig. 4. The mean pain scores were 1 ± 1.03, 0.95 ± 0.98, 0.80 ± 0.822 and 0.65 ± 0.921 for the groups Placebo, Group 1 (20 s), 2 (30 s), and 3 (40 s), respectively. Similar to the FLACC Scale scores, no pain score (0) was seen to be the highest in Group 3 among the groups. Furthermore, while the Placebo group had the highest median score (2: moderate pain), group 3 had the lowest median score (0: no pain). For Groups 3 and 2, the median score was 1 (mild pain). However, significant difference was not found among the groups related to the PRS scores ($p = 0.317$).

PRS and FLACC scores were not affected by the age, gender

TABLE 2. Distribution of the subjects to the groups based on the age, jaw, and gender situation.

Variables	Groups				
	Group 3 (n = 40)	Group 2 (n = 40)	Group 1 (n = 40)	Placebo (n = 40)	*p* values
Gender (girls/boys)	22/18	20/20	16/24	17/23	0.516*
Age (Mean)	8.82 ± 1.50	8.52 ± 1.75	8.02 ± 1.67	8.90 ± 1.70	0.741*
Jaw (mand/max.)	18/22	19/21	21/19	19/21	0.924*

**No statistically significant difference according to the Pearson Chi-Square test (p value > 0.05).*

TABLE 3. Pain scores of the PRS and the FLACC Scale during injection pain.

	Group3 (PBM with 0.3 W/40 s)	Group 2 (PBM with 0.3 W/30 s)	Group 1 (PBM with 0.3 W/20 s)	Control (Placebo)	*p* values
PRS SORES (0–3)					
Mean ± std	0.65 ± 0.921	0.80 ± 0.822	0.95 ± 0.980	1.00 ± 1.030	0. 317*
Median	0	1	1	2	
Percentile (25/50/75)	0/1/1	0/1/1.75	0/1/1.75	0/1/2	
Minimum-maximum	0–3	0–2	0–3	0–3	
FLACC SCORES (0–10)					
Mean ± std	1.77 ± 1.90	2.12 ± 1.89	2.92 ± 2.54	3.02 ± 2.93	0.109*
Median	1	2	2	2	
Percentile (25/50/75)	0/1/3	1/2/3	1/2/5	1/2/5	
Minimum-maximum	0–6	0–7	0–10	0–10	

Abbreviations: PBM: Photobiomodulation Therapy, PRS: Wong Baker Faces Rating Scale, FLACC: Face, Legs, Activity, Crying, Consolability.
** The Kruskal-Wallis test.*

and jaw type in the experimental and placebo groups (p = 0.539, p = 0.738, p = 0.612 for PRS scores, p = 0.217, p = 0.329, p = 0.407 for FLACC scores).

4. Discussion

The present study found that the application of PBM + topical anesthesia did not differ in reducing injection pain compared to placebo PBM + topical anesthesia. Furthermore, changing the application parameters (20, 30, 40 s with 0.3 W) did not affect the injection pain either.

PBM is a low-intensity light therapy. The effect is accepted as photochemical (nonthermal) or microthermal [27, 28]. Side effect reports related to PBM are extremely rare or non-existent, and this therapy has been approved by the FDA (and other national health agencies around the world) for different indications regarding pain management [29]. PBM treatment generally uses light at red and near-infrared (NIR) wavelengths (600–1000 nm) [27, 28]. It was determined that not only the wavelength, but also many other factors, conditions, and parameters have an influence on the therapeutic effects, including irradiance, fluence, treatment timing, and pulsing [7, 17, 27]. When the studies related to injection pain are examined, it is seen that some of them have been performed in adults (only six) [8–10, 29] and a few of them have been performed in children (only three) [5, 19, 20]. It was seen that there are differences in research protocols in terms of sample size, anesthesia application region, laser type used, application method, and parameters. One of the specific differences in the research protocol in injection pain studies is the usage of topical anesthesia when evaluating the effect of PBM. When examining studies in children, while the usage of topical anesthesia is seen in the study of Uçar *et al.* [5], it is seen that the study of Shekarchi *et al.* [19] has only evaluated the effect of PBM alone, and while two studies reported a positive effect, significance was obtained in the only study by Shekarchi *et al.* [19]. The difference in results can be attributed to the fact that the use of topical anesthesia may have overshadowed the actual effectiveness of PBM, and also that the difference in the laser parameters used may also preclude a complete comparison. Like the study by Uçar *et al.* [5], topical anesthesia was preferred to be used with PBM for the reduction of injection pain in the current research. Since managing the pain caused by a local anesthesia injection can be a critical step for gaining the initial trust of the pediatric patient in order for the treatment to continue in a positive atmosphere during subsequent visits, as well as due to the lack of a consensus on the premise that PBM use alone can reduce the injection pain,

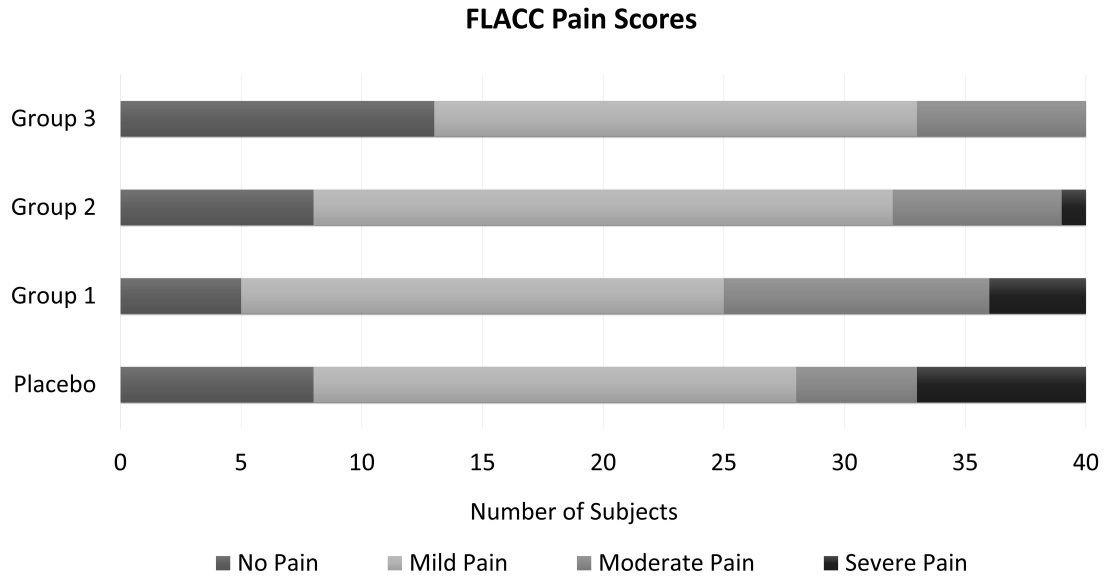

FIGURE 3. Distribution of the pain scores according to the FLACC Scale. 0: no pain, 1–3: mild pain, 4–6: moderate pain, 7–10: severe pain according to the Face, Leg, Activity, Cry, Consolability (FLACC) Scale. While the power of the laser device was adjusted to 0.3 W in all 3 groups, its duration was determined as 20 s for Group 1, 30 s for Group 2, and 40 s for Group 3. Group 4 was the placebo group.

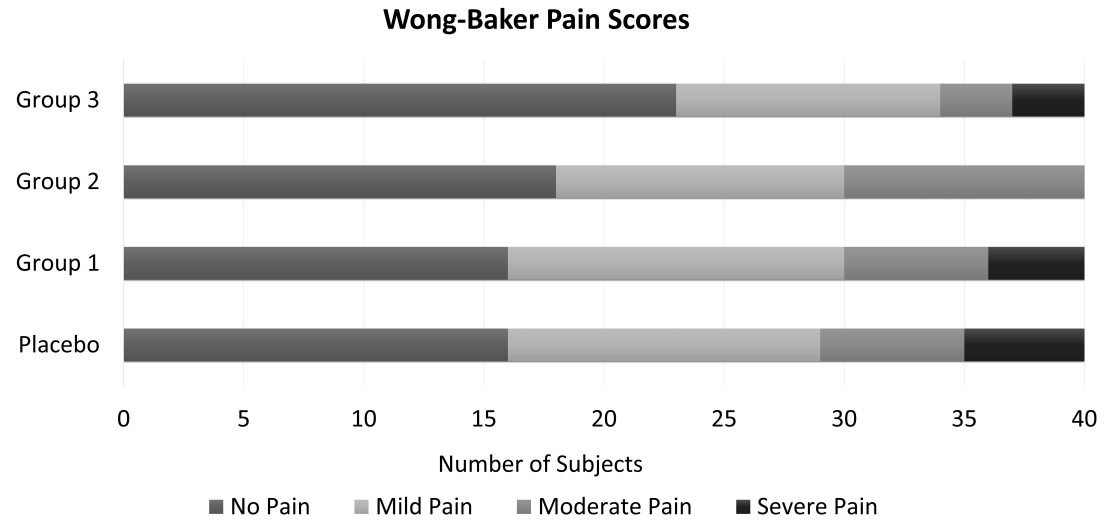

FIGURE 4. Distribution of the pain scores according to the Modified Wong-Baker FACES Pain Rating Scale (PRS). 0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain according to the PRS Scale. While the power of the laser device was adjusted to 0.3 W in all 3 groups, its duration was determined as 20 s for Group 1, 30 s for Group 2, and 40 s for Group 3. Group 4 was the placebo group.

PBM was not chosen to be used without topical anesthesia.

Of the various laser-related parameters described in the literature, wavelength (range, 660 to 980 nm), irradiation time (range, 20 s to 3 min), and power rate (range, 30 mW to 300 mW) are the only parameters that have been fully reported in injection pain related researches [5, 8, 9, 20, 30–32]. They have prevented the interpretation of laser efficiency and the repetition of the used parameters due to incomplete use. Ghabraei *et al.* [30] performed the only study in adults that reported all parameters, including contact mode or distance from the target tissue. They evaluated injection pain in the maxillary anterior region using the following laser parameters in the contact mode: wavelength, 980 nm; power, 300 mW; energy density, 15.62 J/cm^2; total energy, 6 J; irradiation time, 20 s; and surface area, 0.384 cm^2. However, they concluded that PBM with these parameters was not superior to placebo in decreasing pain. In children, only Uçar *et al.* [5] reported all the parameters using a wavelength of 810 nm, a power of 300 mW (0.3 W) for a duration of 20 s, and an energy density of 69 J/cm^2 without contact mode. Similarly, no decrease was observed in pain values with objective assessment. Thus, only two studies provided all parameters, and both reported that the desired PBM effect was not achieved [5, 30]. Since there is limited research and no consensus regarding the parameters to reduce injection pain in children and adults, we performed the present study to provide more insights into this literature gap.

In regard to injection pain studies, the lowest and highest energy density reported was 4 J/cm^2 and 69 J/cm^2 by Ghaderi *et al*. [31] and Uçar *et al*. [5], respectively. Ghaderi *et al*. [31] reported that a laser with 4 J/cm^2 resulted in a negative effect and increased injection pain rather than a decrease in pain. Although positive effects were reported in studies with higher energy densities, the expected level was not reached [5, 30]. Thus, in this study, we aimed to obtain a positive effect at a desired level by increasing the energy density. The highest reported value (69 J/cm^2) was increased by gradually increasing the application time of the laser. Since data on higher energy doses were not available, energy was increased cautiously, taking into account that the investigated cohort consisted of children. In addition, care was taken to not exceed the highest power (300 mW) described in the literature [30].

The maximum application time in the literature was 3 minutes [8]. It was found that the application time increased as energy density and power decreased [8, 9]. PBM was performed by Jagtab *et al*. [8] for 3 minutes using a power of 60 mW and by Sattayut *et al*. [9] for 2 minutes using a power of 30 mW and an energy intensity of 27.69 J/cm^2. Although a positive result was reported in the first study [8], a negative result was observed in the second [9]. However, both studies had missing parameters. In studies where the energy density was reported as 300 mW, the application time was limited to 20 seconds [5, 30]. As an exception, only a 1-minute application using 300 mW power was reported in a study by Amrutha-Varshini *et al*. [20]. Although they obtained negative results, they are the only ones to have used pulse mode for PBM on the reduction of injection pain. Thus, it is not possible to interpret the findings in terms of application time effects and results. In this present study, based on existing literature, 20 sec was used as the minimal application time, which was increased gradually to increase the energy density and evaluate the effect of increasing time on pain prevention.

A 940 nm diode laser was applied with a 0.3 W power with three different application times (20, 30, 40 s) and energy densities (69 J/cm^2, 103 J/cm^2, and 138 J/cm^2). Although the expected effect was not achieved, we found that the increase in energy with time led to a decrease in pain scores. The pain scores were lower in the PBM application groups as compared to the placebo group. The maximum number of "no pain" scores were detected in the group with the PBM applied for 40 s. A biphasic dose response was previously thought to be responsible for the effect of PBM on pain [27]. It was observed that a very low dose of light doesn't have any discernible effect, while a larger dose can have a positive effect until a plateau is reached [33]. If the dose is increased beyond the plateau threshold, then the benefit progressively decreases until the baseline (no effect) is reached [33]. At this point, any further increase in the light dose will lead to damage to the tissue [28, 33]. However, Cronshaw *et al*. [28] recently suggested that the multi-phasic biological response is more suitable for explaining PBM-induced analgesia's cellular basis than the biphasic-dose response. It is proposed that this may involve the activity of a class of mitochondrial transmembrane proteins called uncoupling proteins. Furthermore, it is proposed that this may induce the heat stress protein (HSP) response and that intracellular microthermal inclines may be of significance in PBM pain relief. This means, that while the biostimulation effect of a relatively low dose of light causes a positive effect, the reversible photoinhibition of a higher dose of light (until damage begins in the tissue) can also cause a positive effect on the reduction of pain as well [28, 33]. Pain reduction with increased energy density and time may result from the multi-phasic biological response to PBM.

In most of the studies evaluating the effectiveness of PBM on injection pain, no information was given about how the blindness of the researcher and the patient was achieved due to the sound and light generated during the operation of the laser [8, 9]. The device's sound was previously recorded on a mobile phone and then played back to blind the children to the process in the present study. Since the light was intraorally applied, they could not see the application itself, hence the blindness to the process could be fully achieved. However, blindness could not be achieved with the placebo and control groups since the laser operator was aware of its sound, application time, and light effect. Nevertheless, this problem was attempted to be overcome in a similar manner to the methodologies of previous studies by Shekarchi *et al*. [19] and Tuk *et al*. [10] by choosing the laser operator and injection operator as different persons.

Regarding age and gender differences, no significant differences were found in the pain scores reported by males and females as well as by any age group. This finding is in agreement with the results of previous studies by Uçar *et al*. [5] and Seraj *et al*. [34].

On the other hand, we did not include patients younger than 6 years due to potential uncooperative behaviors. Since the maximum age limit in our pediatric dental clinic was 12, a 12-year-old group was also included. Although previous injection pain studies included children aged 6–12 years [35], this could be considered a limitation in our study that might have led to reporting different pain scores in this age range. However, this limitation was partly overcome by the fact that pain scores were evaluated with both objective and subjective scales. In addition, since the first primary molar teeth are usually exfoliated in children aged 11–12, there were very few patients in this age range.

5. Conclusions

In the present study, PBM with different parameters (0.3 W; 20, 30, 40 s) + topical anesthesia was not found to be different in reducing injection pain compared to placebo + topical anesthesia in children. Additional research is needed to determine how different application parameters, injection techniques, and individual characteristics (children/adults) influence the effectiveness of PBM on injection pain.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

AUTHOR CONTRIBUTIONS

ME, EK, ÜŞE and ÖPK—material preparation, data collection, and analysis were performed. ME and EK—write the first draft of the manuscript. ÜŞE and ME—edit the first draft of the manuscript. All authors contributed to the study conception and design. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The protocol of this prospective, randomized, single-center, triple-blind, parallel-controlled, clinical trial was approved by the Biruni University's Clinical Research Ethics Committee (KAEK-62-22-09) in accordance with the principles stated in the Helsinki Declaration, prior to the treatment. Inform consent was obtained from all of the participants and their parents.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Shetty V, Suresh LR, Hegde AM. Effect of virtual reality distraction on pain and anxiety during dental treatment in 5- to 8-year-old children. Journal of Clinical Pediatric Dentistry. 2019; 43: 97–102.

[2] Garret-Bernardin A, Cantile T, D'Antò V, Galanakis A, Fauxpoint G, Ferrazzano GF, *et al*. Pain experience and behavior management in pediatric dentistry: a comparison between traditional local anesthesia and the wand computerized delivery system. Pain Research and Management. 2017; 2017: 1–6.

[3] Rangel CRG, Pinheiro SL. Laser acupuncture and intravascular laser irradiation of blood for management of pediatric dental anxiety. Journal of Oral Science. 2021; 63: 355–357.

[4] Ribeiro MKA, Alcântara-Silva TRM, Oliveira JCM, Paula TC, Dutra JBR, Pedrino GR, *et al*. Music therapy intervention in cardiac autonomic modulation, anxiety, and depression in mothers of preterms: randomized controlled trial. BMC Psychology. 2018; 6: 57.

[5] Uçar G, Şermet Elbay Ü, Elbay M. Effects of low level laser therapy on injection pain and anesthesia efficacy during local anesthesia in children: a randomized clinical trial. International Journal of Paediatric Dentistry. 2022; 32: 576–584.

[6] Hamblin MR. Photobiomodulation or low-level laser therapy. Journal of Biophotonics. 2016; 9: 1122–1124.

[7] Heiskanen V, Hamblin MR. Photobiomodulation: lasers *vs.* light emitting diodes? Photochemical & Photobiological Sciences. 2018; 17: 1003–1017.

[8] Jagtap B, Bhate K, Magoo S, S N S, Gajendragadkar KS, Joshi S. Painless injections-a possibility with low level laser therapy. Journal of Dental Anesthesia and Pain Medicine. 2019; 19: 159–165.

[9] Sattayut S. Low intensity laser for reducing pain from anesthetic palatal injection. Photomedicine and Laser Surgery. 2014; 32: 658–662.

[10] Tuk JGC, van Wijk AJ, Mertens IC, Keleş Z, Lindeboom JAH, Milstein DMJ. Analgesic effects of preinjection low-level laser/light therapy (LLLT) before third molar surgery: a double-blind randomized controlled trial. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2017; 124: 240–247.

[11] Ayyildiz S, Emir F, Sahin C. Evaluation of low-level laser therapy in TMD patients. Case Reports in Dentistry. 2015; 2015: 1–6.

[12] Topçuoğlu HS, Akpınar B. The effect of low-level laser therapy on the success rate of inferior alveolar nerve blocks in mandibular molars with symptomatic irreversible pulpitis: a randomized clinical trial. International Endodontic Journal. 2021; 54: 1720–1726.

[13] Ghabraei S, Chiniforush N, Bolhari B, Aminsobhani M, Khosarvi A. The effect of photobiomodulation on the depth of anesthesia during endodontic treatment of teeth with symptomatic irreversible pulpitis (double blind randomized clinical trial). Journal of Lasers in Medical Sciences. 2018; 9: 11–14.

[14] Chow RT, Armati PJ. Photobiomodulation: implications for anesthesia and pain relief. Photomedicine and Laser Surgery. 2016; 34: 599–609.

[15] Chen Y, Chen XL, Zou XL, Chen SZ, Zou J, Wang Y. Efficacy of low-level laser therapy in pain management after root canal treatment or retreatment: a systematic review. Lasers in Medical Science. 2019; 34: 1305–1316.

[16] Hamblin MR. Mechanisms and mitochondrial redox signaling in photobiomodulation. Photochemistry and Photobiology. 2018; 94: 199–212.

[17] Zein R, Selting W, Hamblin MR. Review of light parameters and photobiomodulation efficacy: dive into complexity. Journal of Biomedical Optics. 2018; 23: 1–17.

[18] Ramalho KM, de Souza LMP, Tortamano IP, Adde CA, Rocha RG, de Paula Eduardo C. A randomized placebo-blind study of the effect of low power laser on pain caused by irreversible pulpitis. Lasers in Medical Science. 2016; 31: 1899–1905.

[19] Shekarchi F, Nokhbatolfoghahaei H, Chiniforush N, Mohaghegh S, Haeri Boroojeni HS, Amini S, *et al*. Evaluating the preemptive analgesic effect of photo-biomodulation therapy on pain perception during local anesthesia injection in children: a split-mouth triple-blind randomized controlled clinical trial. Photochemistry and Photobiology. 2022; 98: 1195–1200.

[20] AmruthaVarshini I, Penmatsa C. Effectiveness of pre-cooling the injection site, laser biostimulation, and topical local anesthetic gel in reduction of local anesthesia injection pain in children. International Journal of Clinical Pediatric Dentistry. 2021; 14: 81–83.

[21] Frankl S, Shiere F, Fogels H. Should the parent remain with the child in the dental operatory? ASDC Journal of Dentistry for Children. 1962; 29: 150–163.

[22] Murphy L. Pediatric laser dentistry: a user's guide. British Dental Journal. 2011; 211: 613.

[23] American Academy of Pediatric Dentistry. Behavior guidance for the pediatric dental patient. The reference manual of pediatric dentistry. American Academy of Pediatric Dentistry: Chicago, Ill. 2022; 321–339.

[24] Schwartz S, Kupietzky A. Local anesthesia. In Wright GZ, Kupietzky A (ed.). Behavior management in dentistry for children (pp. 107–124). 2nd edn. Wiley: New York. 2014.

[25] Willis MH, Merkel SI, Voepel-Lewis T, Malviya S. FLACC behavioral pain assessment scale: a comparison with the child's self-report. Pediatric Nursing. 2003; 29: 195–198.

[26] Wong DL, Baker CM. Pain in children: comparison of assessment scales. Pediatric Nursing. 1988; 14: 9–17.

[27] Tsai S, Hamblin MR. Biological effects and medical applications of infrared radiation. Journal of Photochemistry and Photobiology B: Biology. 2017; 170: 197–207.

[28] Cronshaw M, Parker S, Arany P. Feeling the heat: evolutionary and microbial basis for the analgesic mechanisms of photobiomodulation therapy. Photobiomodulation, Photomedicine, and Laser Surgery. 2019; 37: 517–526.

[29] de Sousa MVP, Kawakubo M, Ferraresi C, Kaippert B, Yoshimura EM, Hamblin MR. Pain management using photobiomodulation: Mechanisms, location, and repeatability quantified by pain threshold and neural biomarkers in mice. Journal of Biophotonics. 2018; 11: e201700370.

[30] Ghabraei S, Bolhari B, Nashtaie HM, Noruzian M, Niavarzi S,

Chiniforush N. Effect of photobiomodulation on pain level during local anesthesia injection: a randomized clinical trial. Journal of Cosmetic and Laser Therapy. 2020; 22: 180–184.

[31] Ghaderi F, Ghaderi R, Davarmanesh M, Bayani M, Arabzade Moghadam S. Pain management during needle insertion with low level laser. European Journal of Paediatric Dentistry. 2016; 17: 151–154.

[32] Kermanshah H, Chiniforush N, Kolahdouz Mohammadi M, Motevasselian F. Effect of photobiomodulation therapy with 915 nm diode laser on pain perception during local anesthesia of maxillary incisors: a randomized controlled trial. Photochemistry and Photobiology. 2022; 98: 1471–1475.

[33] Huang YY, Chen AC, Carroll JD, Hamblin MR. Biphasic dose response in low level light therapy. Dose-Response. 2009; 7: 358–383.

[34] Seraj B, Ghadimi S, Hakimiha N, Kharazifard MJ, Hosseini Z. Assessment of photobiomodulation therapy by an 8l0-nm diode laser on the reversal of soft tissue local anesthesia in pediatric dentistry: a preliminary randomized clinical trial. Lasers in Medical Science. 2020; 35: 465–471.

[35] Elbay ÜŞ, Elbay M, Kaya E, Cilasun Ü. Intraligamentary and supraperiosteal anesthesia efficacy using a computer controlled delivery system in mandibular molars. Journal of Clinical Pediatric Dentistry. 2016; 40: 193–199.

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