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Original Research

Clinical Evaluation of 532-nm Green Laser on Dentin Hypersensitivity: A Randomized Double-Blind Clinical Trial

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Abstract

Objective: The aim of this study was to evaluate the therapies of low-level green laser and chemical desensitizer in the treatment of dentin hypersensitivity (DH).
Methods: Forty-eight patients with 96 sensitive teeth were invited to participate in this clinical trial and were randomly divided into three groups. One group was treated with low-level green laser, the second group was treated with desensitizer [sodium fluoride (NaF)], and the third group acted as the placebo group and was treated with distilled water and placebo laser. The wavelength of green laser was 532 nm and the irradiance was 15 J/cm^2 per treatment site. Hypersensitivity was assessed by visual analogue scale (VAS) according to cold test and probing at baseline. Immediately, 2 weeks, and 3 months after the application of green laser, NaF, and placebo, the participants' sensitivity level was accessed by new VAS analysis.
Results: Forty-five patients with 90 teeth ($n = 15$ patients/group; 30 teeth/group) were followed up for 2 weeks and 3 months after treatment. There were significant differences in VAS scores between the placebo group and intervention group (green laser group and NaF group; analysis of variance, $p < 0.05$) at all three time points. The mean pain scores in DH reduced significantly immediately after treatment in the green laser group and NaF group when stimulated by cold and probing, whereas no significant difference was observed with these two therapies after 2 weeks ($p > 0.05$). After 3 months, mean VAS scores of the NaF group were higher than those of the green laser group ($p < 0.01$).
Conclusions: Therefore, the green laser displayed similar effectiveness as NaF in treatment of DH and could be a promising new therapy to reduce DH.

Keywords: dentin hypersensitivity, 532 nm green laser, sodium fluoride

Introduction

Dentin hypersensitivity (DH) is a common oral disease that refers to a nonspontaneous, localized, and intense pain when dentin is exposed to external stimuli such as heat, cold, touch, and osmotic pressure changes.[1] The prevalence of DH reported by Zeola et al.[2] varied from 1.3% to 92.1%, with an average rate of 33.5%. DH significantly influences patients' quality of life such as speaking, drinking, eating, and toothbrushing.[3] The mechanism of DH is still debatable, but the most widely accepted theory is the hydrodynamic theory proposed by Brannstrom.[4] Based on this theory, changes of the hydraulic fluid due to external stimuli on exposed dentinal tubules directly stimulate the extended pulp nerve receptors and odontoblasts, resulting in intense pain.

Therefore, most therapeutic products used in DH such as chemical desensitizers and high-intensity lasers are those that can effectively obstruct the tubules and reduce fluid movement. The second therapeutic strategy for DH such as potassium and low-level laser therapy acts on nerve fibers to influence the conduction of pain signal to the central nervous system.[5] Common chemical desensitizers including potassium nitrate, calcium hydroxide, sodium fluoride (NaF), glutaraldehyde, dentin sealers resins, and adhesives

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have been studied for their use in DH treatment.[6] The above applications are useful given their ability to obstruct the dentinal tubules and block transmission of stimuli by direct blockade or by formation of coagulants or insoluble calcium complexes, or protein precipitation.[7] However, not all dentinal tubule occlusion can be blocked by desensitizing agents.[8] Many desensitizing agents are unable to adhere to the dentin surface for long,[9] and the nonadherence of agents leads to exposure of the tubules. Several factors such as saliva and oral fluids result in dislocation of desensitizing agents, hence influencing the durability of treatment.[10]

Lasers are considered a novel and reliable treatment modality due to their fast response and repeatability.[11] High-power lasers such as Nd:YAG, Er:YAG, Er,Cr:YSGG, and CO_2 lasers can open dentinal tubules and reduce dentin permeability by melting and recrystallizing dentin.[12] The diode lasers [gallium aluminum arsenide (GaAlAs)] used as low-level laser can decrease DH-related pain likely by decreasing the dentinal fluid flow and blocking the depolarization of C-fibers to depress nerve transmission.[13] However, the reported clinical efficacy of different lasers was also quite variable.[12] Yilmaz et al.[14] suggested that GaAlAs and Er,Cr:YSGG lasers were both suitable for DH, but another study concluded that the Nd:YAG laser is more effective than Er:YAG and diode lasers.[15] Different methods and treatment parameters and programs have led to different results. Therefore, it is necessary to discover a more effective, faster-acting, and longer lasting therapy for DH. In recent years, 532-nm green lasers have been usually used to treat retinopathy and skin and mucous membrane diseases.[16] In past studies, we found low-level green laser could block nerve conduction and promote the formation of reparative dentin to reduce DH by acting on dental pulp stem cells, odontoblasts, and pulp nerve fibers. Therefore, the aim of this study was to evaluate the efficacy of low-level green laser and compare it with that of NaF in the short term and to provide a new treatment strategy for clinical DH.

Materials and Methods

Patients with more than two sensitive teeth for at least 1 month were invited to participate in this study conducted at the Peking University Hospital of Stomatology. The study was approved by the ethics committee at Peking University School and Hospital of Stomatology (PKUSSIRB-202054054) and all patients were required to sign written informed consent. Radiographic examination and thorough visual inspection using a dental mirror and probe were performed. For inclusion in the study, the subjects should not have undergone periodontal scaling in the past 2 weeks and periodontal surgery in the past 3 months and should not have taken any medication (including anti-inflammatory and analgesic) or received professional desensitization therapy in the previous 6 months. The teeth showing sensitivity were required to be without defective restorations, caries, fillings, cracks, and pulpitis. Patients with poor oral hygiene, severe periodontitis, and the teeth with wedge-shaped defects deeper than 1 mm were also excluded. Last, pregnant and lactating women (to avoid the probable side effects of the laser) and those with systemic diseases or allergies to desensitizing agents were also excluded.

We enrolled 48 participants (15 male and 33 female; mean age, 43.6 years; age range, 23–72 years) with 96 dentin-exposed teeth (40 teeth on the facial surface and 56 teeth on the occlusal surface) in this randomized controlled clinical trial. Subjects were instructed to refrain from carrying out any oral hygiene measures, eating, or drinking water at least 2 h before the evaluation. Detailed anamnesis interviews including diet, chewing habits and time, and frequency and degree of hypersensitivity were recorded before treatment. Clinical examinations were performed including oral soft tissue including soft tissue in oral and the wear position of sensitive tooth. The vitality of all experimental and adjacent teeth was checked through an electric pulp tester and recorded. Each sensitive tooth was examined in two ways cold test and probing test. Cotton rolls and suction device were applied to isolate the adjacent teeth. An ice stick was placed on the tooth being tested for 5 sec, and all the stimuli were applied on the sensitive region of the experimental tooth. The patients were asked to describe the pain intensity ranging from 0 to 10 according to a visual analogue scale (VAS). These scores were recorded as the baseline VAS score for each experimental tooth or sensitive point. Scores >2 were included to standardize the sample. After 5 min, the experimental teeth were touched by an explorer with a force of 5 g and the VAS was again recorded.

After recording the baseline VAS scores, participants were randomly assigned to three groups:

I. Green laser (532 nm; MLB-200A Nd: YAG/KTP Laser Treatment Instrument, CHONGQING JINGYU LASER TECHNOLOGY CO, LTD) and placebo (distilled water) were applied in Group A.
II. NaF (Colgate, NY, Duraphat) and green laser (532 nm) without power were applied in Group B.
III. Green laser (532 nm) without power and placebo (distilled water) were applied in Group C.

Each patient received an envelope with a number and the numbers were assigned to one of the three above-mentioned groups with unrestricted (simple) randomization. All treatments were carried out by an experienced operator with the same methods and protocols, and examinations were performed by another dentist unaware of the grouping to minimize errors and avoid bias. The patients were also blinded to the therapy received. Each subject received a single treatment and was treated without local anesthesia.

In Group A subjects, the sensitive teeth were irradiated by the 532-nm green laser at an intensity of 15 J/cm^2 (parameters given in Table 1). The laser was placed at a distance of 5 mm from the tooth surface and applied on the exposed dental position continually for 5 min. The adjacent teeth

Table 1. Parameters of Light Equipment

Wavelength	*Mode*	*Fluence rate (mW/cm^2)*	*Output power (mW)*
532 nm	CW	47	150
Tip diameter (mm)	*Distance (mm)*	*Treatment time (min)*	*Frequency*
10	5	5	1

CW, continuous wave.

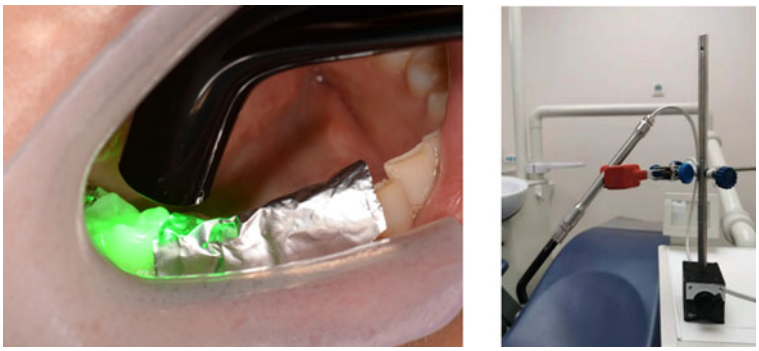

FIG. 1. Patient received irradiation of the 532-nm green laser with a distance of 5 mm and the shelf was used to hold the laser in the same position.

were covered with opaque tinfoil (Fig. 1). After irradiation for 30 min, the placebo was applied on the teeth for 5 min. In Group B, patients received irradiation of the 532-nm green laser, but the power was turned off. After 30 min, NaF was carefully applied to the sensitive tooth to ensure that the desensitizer made complete contact with the sensitive area left for 5 min. Thirty minutes later, the surface of the tested tooth was dried lightly with compressed air and rinsed thoroughly with water. In Group C, the operator only pretended to irradiate patients' teeth, without laser activation. Then, a placebo was applied according to the same protocol with NaF. All participants were instructed to avoid rinsing their mouths, chewing food, or brushing for at least 30 min, 3 h, and 12 h, respectively, after the treatment. When the study was terminated, patients in Group C were recalled to receive desensitizer application for DH.

During the study, patients were required to maintain good oral hygiene (brushing teeth twice a day and using dental floss three times a day) and not allowed to use any anti-hypersensitivity medication or mouthwash. The participants were followed up at 2 weeks and 3 months after the treatment. The teeth were examined with an ice stick and re-probing as described earlier, and the VAS scores were obtained. Four scores were recorded for each patient at four time points: baseline, immediately after treatment, 2 weeks after treatment, and 3 months after treatment. The soft tissue and pulp vitality were examined repeatedly in each review. Radiological examination of experimental teeth was conducted at the 3 months review.

Statistical analysis

All statistical analyses were performed using SPSS (IBM SPSS Statistics 20, Armonk, NY). The VAS mean value was calculated to assess the effect of DH, and analysis of variance was used to compare the consistency of VAS values at baseline and at the three points after intervention in different groups. The descriptive statistics are presented as mean ± standard deviation. Chi-square test was taken to identify the relationship between gender and DH. p-Value ≤0.05 was considered to indicate statistical significance.

Results

In this study, 48 participants with 96 teeth received treatment for DH. Of these, 45 patients with 90 teeth ($n = 15$ patients/group; 30 teeth/group) aged 23–72 years (mean: 45.8 years) were followed up for 2 weeks and 3 months after treatment with a follow-up rate ∼93.8%. The age and gender distributions of the three study groups are displayed in Table 2.

The mean baseline VAS scores of the three groups for cold and probing stimulation are presented in Tables 3 and 4. There was no significant difference noted (cold stimulation: 6.6 ± 1.4/6.2 ± 2.0/6.7 ± 1.4, probing stimulation: 5.3 ± 1.6/5.1 ± 1.8/5.4 ± 1.6). Before treatment, the maximal VAS score was 8 (probing test) and 10 (cold test); the minimal pain level was 2 (probing test) and 5 (cold test), and the mean score of all participants was 5.3 (probing test) and 6.5 (cold test; Tables 5 and 6). For the evaluation of pain over the course of time, each group was analyzed separately. There were significant differences before treatment and immediately after treatment in VAS scores for Group A ($p < 0.01/p < 0.01$) and Group B ($p < 0.01/p < 0.01$) both in the probing and cold tests. This result showed that low-level green laser and NaF reduced pain level in DH. No change in sensitivity was detected for the placebo group; the mean VAS scores changed from 5.4 to 5.3 (probing test) and from 6.7 to 6.1 (cold test). This suggested that placebo was not helpful to alleviate pain in DH.

The mean scores of the green laser group (1.8 ± 1.8/1.9 ± 1.4) and NaF group (1.9 ± 2.2/2.0 ± 1.3) were significantly different than those of the placebo group immediately after treatment (5.3 ± 1.6/6.1 ± 1.7). However, intragroup score comparisons showed no statistically significant differences for the two time points (immediately and after 2 weeks) in the Groups A and B ($p > 0.05$). At the 3-month follow-up, the mean VAS score of the NaF group (3.3 ± 1.4/3.2 ± 0.9) was higher than that of the green laser group (1.5 ± 1.1/1.6 ± 1.4; $p < 0.01$). The mean scores of the placebo group were similar at all three time points.

TABLE 2. THE DISTRIBUTION OF AGE AND GENDER OF THE GREEN LASER GROUP, DOLOFLUORIDE GROUP, AND PLACEBO GROUP

	Gender			*Age (years)*	
Groups	*Male*	*Female*	n	*Range*	*Mean ± SD*
Green laser	4	11	30	26–63	47.4 ± 13.1
Dolofluoride	6	9	30	23–72	43.6 ± 13.5
Placebo	4	11	30	26–65	46.2 ± 11.7
Total	14	31	90	23–72	43.6 ± 12.5

SD, standard deviation.

Table 3. Mean Visual Analogue Scale Scores and Standard Deviation at Baseline, Immediately, and at 2 Weeks and 3 Months After Treatment with Green Laser, Dolofluoride, and Placebo Groups for the Probe Test

	Baseline	*Immediately*	*2 weeks later*	*3 months later*
Green laser	5.3 ± 1.6^{a}	1.8 ± 1.8^{b}	1.5 ± 1.2^{b}	1.5 ± 1.1^{b}
Dolofluoride	5.1 ± 1.8^{a}	1.9 ± 2.2^{b}	1.8 ± 1.2^{b}	1.9 ± 1.5^{c}
Placebo	5.4 ± 1.6^{a}	5.3 ± 1.6^{a}	5.4 ± 1.6^{a}	5.3 ± 1.7^{a}

Identical letters in table indicate that values are not statistically different ($p > 0.05$). [All values marked with ''a'' are not statistically different from each other. All values marked with ''b'' are not statistically different from each other. All values marked with ''a'' are statistically different from those of ''b.'' The values marked ''c'' are statistically different from those of ''a'' and ''b''].

Table 4. Mean Visual Analogue Scale Scores and Standard Deviation at Baseline, Immediately, and at 2 Weeks and 3 Months After Treatment with Green Laser, Dolofluoride, and Placebo Groups for the Cold Test

	Baseline	*Immediately*	*2 weeks*	*3 months*
Green laser	6.6 ± 1.4^{a}	1.9 ± 1.4^{b}	1.6 ± 1.2^{b}	1.6 ± 1.4^{b}
Dolofluoride	6.2 ± 2.0^{a}	2.0 ± 1.3^{b}	2.2 ± 0.9^{b}	1.9 ± 0.8^{c}
Placebo	6.7 ± 1.4^{a}	6.1 ± 1.7^{a}	6.0 ± 1.8^{a}	5.9 ± 1.7^{a}

Identical letters in table indicate that values are not statistically different ($p > 0.05$). [All values marked with ''a'' are not statistically different from each other. All values marked with ''b'' are not statistically different from each other. All values marked with ''a'' are statistically different from those of ''b.'' The values marked ''c'' are statistically different from those of ''a'' and ''b''].

Chi-square test was used to investigate the relationship between gender and DH. The mean VAS scores of female and male patients are displayed in Table 6. There was no statistically significant difference between male and female patients, which suggested that the patient's gender did not influence the effect of a chosen therapy for DH. After treatment, all teeth were examined for pulp vitality, and no adverse reactions or complications were detected. Soft tissues were normal without ulceration and/or erosion. Radiological examination performed after 3 months showed no abnormalities.

Discussion

With increased life expectancy and behavioral changes, DH has become a common clinical problem over the past 20 years.[17] Epidemiological studies have suggested an increased prevalence of DH in recent years. In 2008,[18] a cross-sectional survey on DH investigated the prevalence and influencing factors of DH in six cities of China. The results showed that 29.7% of the total survey population were diagnosed with DH and the incidence of DH in women (35.9%) was significantly higher than that in men (23.4%). There was also a worrying prevalence of DH in Brazil, where almost one in five adolescents had DH. A North American study showed that subjects with DH had, on average, 3.5 sensitive teeth. Therefore, it is necessary to seek a safe and long-lasting therapy for DH.

Duraphat contains 5% NaF as a desensitizer and can block dentin tubules; hence, it is used in the treatment of DH to alleviate the symptoms.[13,19] Many researchers have shown that NaF had a positive effect on DH treatment.[20–22] Suri et al.[23] conducted a study to compare the effectiveness of 5% topical NaF varnish and 980-nm GaAlAs diode laser, wherein the 5% topical NaF varnish showed better effectiveness than the GaAlAs laser alone and the combination of 5% NaF and 980-nm GaAlAs laser. Therefore, Duraphat can be considered as a noninvasive treatment option for DH.

Table 5. Range of Visual Analogue Scale Scores at Baseline, Immediately, and at 2 Weeks and 3 Months After Treatment of Laser, Dolofluoride, and Placebo Groups for Probing and Cold Tests

	Mean VAS scores of probing test				*Mean VAS scores of cold test*			
Groups	*Baseline*	*Immediately*	*2 weeks*	*3 months*	*Baseline*	*Immediately*	*2 weeks*	*3 months*
Green laser	2–8	0–5	0–5	0–4	5–10	0–5	0–4	0–4
Dolofluoride	2–9	0–5	0–5	0–5	5–10	0–5	0–4	0–5
Placebo	3–9	3–9	4–8	3–9	5–10	5–10	5–10	5–10

VAS, visual analogue scale.

Table 6. Mean Visual Analogue Scale Scores and Standard Deviation at Baseline, Immediately, and at 2 Weeks and 3 Months After Treatment Based on Patient's Gender

	Baseline		*Immediately*		*2 weeks later*		*3 months later*	
	Probing	*Cold*	*Probing*	*Cold*	*Probing*	*Cold*	*Probing*	*Cold*
Female	5.3 ± 1.7	6.4 ± 1.7	2.9 ± 2.1	3.2 ± 2.3	3.2 ± 1.9	2.9 ± 2.3	3.4 ± 2.1	3.4 ± 2.2
Male	5.2 ± 1.9	6.7 ± 1.7	2.6 ± 2.3	3.8 ± 2.6	2.7 ± 2.1	4.0 ± 2.6	3.4 ± 2.1	4.0 ± 2.2

The development of laser technology in dentistry provides new therapeutic possibilities for DH. Low-power laser works through photobiomodulation, including promoting DNA and RNA synthesis, changing pH values inside and outside the cell, accelerating metabolism and protein production, and promoting enzyme activities, all of which block pain signal transduction.[13] Some studies found that low-power laser revealed interaction with dental pulp, causing an increase in the metabolic activity of odontoblast cells, and promoting the production of tertiary dentin;[24,25] this was also proven by Tate et al.[26] Karu et al.[27,28] suggested that low-power lasers of 635 and 808 nm could be absorbed by cytochrome c oxidase on the mitochondrial respiratory chain, which could increase cellular aerobic respiration and produce more adenosine triphosphate (ATP). However, the effect of 808-nm laser on DH is slow (>1 month) and some studies showed that the effect of 808-nm laser on some patients was not obvious.[28] In this study, the pain level was decreased immediately after laser application, which revealed that the 532-nm laser came into effect instantly. Aranha et al.[29] mentioned that patients always complained of pain within 1 week after treatment with laser for DH. Most patients in the green laser group in this study felt that the pain level was acceptable after 3 months.

The low-power green laser has been widely used in clinical medicine such as treating erythematous skin lesions with lower energy and multiple passes,[30] removing a wide array of tattoo pigments[31] and treating retinopathy of prematurity.[32] Previous experiments have demonstrated the safety of green light in the treatment of skin and mucosa; however, there were no studies on the treatment of DH with 532 nm green laser. Zach and Cohen[33] believed that when pulp cavity temperature rises by 5.5°C, 15% pulp necrosis occurs. Kimura et al.[13] suggested that if the laser equipment is set to correct parameters, the temperature in the pulp cavity will rise by <5°C, so that healthy pulp tissue is not thermally injured. In the previous experiment, the researcher measured pulp temperature irradiated by 532-nm green light *in vitro*. There was no change of temperature in pulp cavity at an output power of 15 J/cm^2, with an application time of 5 min and a distance of 5 mm. Therefore, low-energy green light did not cause an increase in intramedullary temperature. In our recent study, the 532-nm laser was harmless to dental pulp stem cells, dental pulp fibroblasts, and rat dental pulp tissue.

In our previous study, we found photosensitive protein Opsin4 was expressed in human dental pulp stem cells and rat odontoblast cells and that 532 nm green light could affect the expression level of Opsin4. Wang et al.[34] found that 540 nm green light could regulate calcium influx through Opsin4 and TRPV1 calcium channels on human adipose-derived stem cells (hASCs). Therefore, we speculated there was similar process on odontoblast cells or myelin-free C-type sensory nerve terminals, which led to cell depolarization and reduction of ATP release, resulting in an immediate analgesic effect. The 540- and 520-nm green light could stimulate osteoblast differentiation of hASCs and human bone marrow stem cells (hBMSCs) by Opsin4 and TRPV1.[35] In addition, our research group found that green light can accelerate the osteogenic differentiation of hBMSCs by activating the mitogen-activated protein kinase-extracelluar regulated protein kinases (MAPK-ERK) signal pathway. Therefore, we speculate that green light may also promote osteoblast differentiation of dental pulp stem cells to odontoblast cells by interaction of Opsin4, TRPV1, and MAPK-ERK signaling pathway, and produce reparative dentin to maintain the therapeutic effect on DH for a long period.

However, further studies are required to better understand the mechanism of 532-nm green light laser. Besides, additional studies are also needed to evaluate the long-term stability of green laser for DH. Comparing the effects between green light high-power laser and exploring which type of DH is more effective with green laser are some of the potential future research directions.

Conclusions

Treatments performed with green laser and NaF were both equally effective in decreasing DH pain in the short-term evaluation (2 weeks) and the effect of green laser was more stable after 3 months. Therefore, 532-nm green laser was considered a reliable method for DH. However, additional studies are needed to further observe the clinical outcomes of desensitization by using green laser for a longer follow-up duration.

Authors' Contributions

S.N.H. carried out experiments, analyzed data, and wrote the article. L.T.Y. and M.Q.W. carried out experiments. Y.G.W. and Y.S.Z. conceived and designed the study.

Author Disclosure Statement

No competing financial interests exist.

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