



Casein Phosphopeptide and Diode Laser in Treating Dentin Hypersensitivity: A Clinical Study

Sanam Faheem^{1*}, Rimsha Qasim¹, Chander Kumar², Waqas Ahmed Farooqui³, Anam Rehman¹, Shahida Maqsood¹, Muhammad Amin Sahito⁴, Naresh Kumar^{5*}, Muhammad Sohail Zafar^{6,7,8}

¹Department of Oral Biology, Dow Dental College, Dow University of Health Sciences, Karachi, Pakistan

²Department of Periodontology, Dow Dental College, Dow University of Health Sciences, Karachi, Pakistan

³School of Public Health, Dow University of Health Sciences, Karachi, Pakistan

⁴Department of Community Dentistry, Dr Ishrat Ul Ebad Khan Institute of Oral Health Sciences, Dow University of Health Sciences, Karachi, Pakistan

⁵Department of Science of Dental Materials, Dow Dental College, Dow University of Health Sciences, Karachi, Pakistan

⁶Department of Clinical Sciences, College of Dentistry, Ajman University, Ajman, United Arab Emirates

⁷Centre of Medical and Bio-allied Health Sciences Research, Ajman University, Ajman, United Arab Emirates

⁸School of Dentistry, University of Jordan, Amman, Jordan

*Correspondence to

Sanam Faheem,
Email: Sanam.faheem@duhs.edu.pk;
Naresh Kumar,
Email: kumar.naresh@duhs.edu.pk

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Abstract

Introduction: Dentin Hypersensitivity is a clinical condition in which a patient experiences intense, short-duration pain. The ideal treatment is still a challenge that dentists face in routine practice. This research aims to determine the effectiveness of Casein phosphopeptide amorphous calcium phosphate paste (CPP-ACP) used alone or combined with a diode laser in treating dental hypersensitivity.

Methods: One hundred and twenty patients were enrolled in this randomized, double-masked clinical trial based on specific inclusion and exclusion criteria screened at the Department of Periodontology at Dow Dental College, Dow University of Health Sciences, Karachi. They were randomly assigned to one of four treatment groups: Group I: CPP-ACP paste, Group II: Diode laser only (for 100-150 seconds, on 980nm/0.5-1W laser 19J/cm), Group III: CPP-ACP paste with diode laser, Group IV: Placebo treatment. To assess pain intensity, discomfort (botheration), and tolerance, the Visual Analog Scale (VAS) was used. Patients rated their experiences on a scale from 0 to 10, with higher scores indicating greater severity. For statistical analysis, a two-way ANOVA test was applied to assess the mean difference within groups after considering the normality of data distribution. A *P* value of <0.05 was considered significant, indicating a meaningful difference between treatment effects.

Results: All treatment groups showed a significant reduction in VAS pain, botheration, and tolerance, with consistent improvement. The laser-only group (Group II) showed consistent improvement, with the most crucial change occurring immediately after the treatment among variables of VAS pain, botheration, and tolerance.

Conclusion: Diode laser therapy appears to be the most effective treatment for managing dental hypersensitivity. However, combining CPP-ACP with a diode laser is also a viable option depending on individual patient needs and preferences.

Trial Registration: ID: NCT06463938. <https://clinicaltrials.gov/study/NCT06463938>. Name of the trial registry: A Clinical Trial to Compare Lasotronix Alone or in Combination With CPP-ACP to Treat DH. Registration date: 2024-05-12.

Keywords: Dentin hypersensitivity, Non-cervical carious lesion, Laser therapy, Casein phosphopeptide paste, Toothpaste, Diode laser, Fluoride

Introduction

Dentin hypersensitivity (DH) is a clinical condition that affects quality of life by disturbing routine oral functions such as eating, speaking, or brushing teeth.¹ DH is defined as a “sharp pain of a shorter duration arising from exposed dentin in response to several chemicals and thermal or tactile stimuli that cannot be ascribed to other dental defects”.¹ The condition begins when the

dentin gets exposed, dentinal tubules are open after the erosion of overlying enamel in the crown, or there is loss of cementum in the root due to gingival recession.^{2,3} The loss of hard tissues at the cemento-enamel junction (CEJ), which is not associated with caries, is identified as a non-carious cervical lesion (NCCCL).⁴ Such lesions are frequently associated with DH in the cervical area with gingival recession.³ DH has a prevalence rate ranging from

1.3% to 92.1%, commonly affecting older adults,⁵ and the frequency of DH in patients suffering from periodontal disease is 3-57%.⁶ Studies in Pakistan report varying prevalence in different cities, with 36.4% in Karachi and 22% in Lahore.⁷ Several theories were proposed to explain the mechanism of DH. The most widely accepted theory is the hydrodynamic theory, attributing pain to fluid movement within the dentinal tubules.⁸ Ideally, these exposed dentinal tubules would be sealed or occluded to prevent fluid movement and alleviate pain.⁹ The primary treatment for DH is either blocking the dentinal tubules or chemically inhibiting the nerve impulses.¹⁰ Several methods have been introduced to occlude open dentinal tubules, either by desensitizing agents, which may cause a mechanical blockade by the precipitation of proteins in dentinal fluid, or by the use of sodium fluoride (NaF), which may cause tubular obstruction by calcium fluoride precipitation.¹¹ Casein phospho-peptide varnish and silver particles can also block dentinal tubules. The American Dental Association Council (ADAC) on Scientific Affairs and the Center of Evidence-based Dentistry recommend using silver particles to treat carious lesions as a nonrestorative treatment method.¹² These particles have been known to reduce fluid movement in dentinal tubules by narrowing their diameter.¹³ Calcium phosphate-based materials like CPP-ACP are considered potential alternative remineralizing agents with anti-carious properties. CPP-ACP has demonstrated superior remineralization effects on enamel, making it more resistant to future demineralization.¹⁴

CPP acts as a delivery agent, while ACP saturates saliva with Calcium and phosphate ions, promoting remineralization.¹⁵ The use of lasers has opened new possibilities in the treatment of DH. Theories supporting laser therapy explain that irradiation blocks pain in dentinal tubules by melting and re-crystallizing dentin or tertiary dentine production or evaporation of dentinal fluid.^{16,17} Diode lasers have been carefully designed to show high transmission in oral tissues that contain high amounts of water. The 635 nm wavelength is optimal for activating toloum chloride dye for photo-activated chemotherapy, eliminating all bacteria and biofilm without side effects.

Additionally, 200 mW power provides safe cold bio stimulation and photo disinfection within a short therapy time. Sodium fluoride (NaF) gel occludes tubules through calcium fluoride precipitation.¹⁸ Agents like potassium nitrate also show promising effects by increasing the concentration of potassium ions in nerve endings, thereby altering the nerve action potential in reducing sensory stimuli.¹⁹

Recently, DH treatment has been conducted with various types of lasers with different wavelengths, either alone or combined with desensitizing agents and varnishes, yielding effective results.^{18,20} However, to

our knowledge, limited data exist on the diode laser as a treatment modality with CPP-ACP. Therefore, this research aims to determine the effectiveness of Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) used alone or combined with diode laser therapy in reducing dentin hypersensitivity (DH).

The Null Hypothesis would state that there is no significant difference in the effectiveness of CPP-ACP and diode laser therapy when used alone or in combination as a treatment modality for dentin hypersensitivity.

Materials and Methods

Trial Design and Participants

One hundred and twenty patients were included in this randomized, double-masked clinical trial, and patient recruitment was performed in the Department of Periodontology at Dow Dental College, Dow University of Health Sciences, Karachi.

A minimum sample of 10 patients per group was calculated using PASS version 15 software (NCSS, Kaysville, Utah, USA). The sample size estimation was based on a one-way analysis of variance (ANOVA) with a 99% confidence interval, considering the mean $\pm$ SD of VAS scores at three months: Group I (CPP-ACP paste only, 2.36 ± 0.48), Group II (diode laser therapy only, 3.44 ± 0.51), Group III (combination of Groups I and II, 1.71 ± 0.45), and Group IV (control, 2.85 ± 0.35). (Ref # 21). To enhance the validity and data distribution, the sample size increased to 120 patients. However, 124 patients were recruited, 30 per group (including five patients per group expected to drop out).

Ethical approval for this study was granted by the Ethical Review Board of Dow University of Health Sciences (Reference No. IRB-2865/DUHS/Approval/2023/68), and the protocol for this parallel-group (1:1) randomized control trial was registered at the www.clinicaltrials.gov database (study identifier: NCT06463938). The study conforms to the CONSORT 2010 and CONSORT-Outcomes 2022 guidelines for trial reporting. [Figure 1](#) represents the sequential methodology of this study via the CONSORT flow diagram. Inclusion criteria were patients aged between 25 and 65 years, with at least one vital tooth with DH, no carious lesions, and no defective restorations. Exclusion criteria were patients with a history of using any desensitizing therapy for the affected tooth/teeth (in the last six months), patients taking antibiotics/anti-inflammatories, pregnant patients, patients with a history of smoking, and patients unwilling to participate.

The patients were educated about the aims and design of the research. They were then asked to provide verbal and written consent, followed by a questionnaire²² for demographic details and pain type/intensity. The first investigator identified experimental teeth through clinical examination using a dental probe perpendicular to the tooth's cervical area (tactile testing), passing the

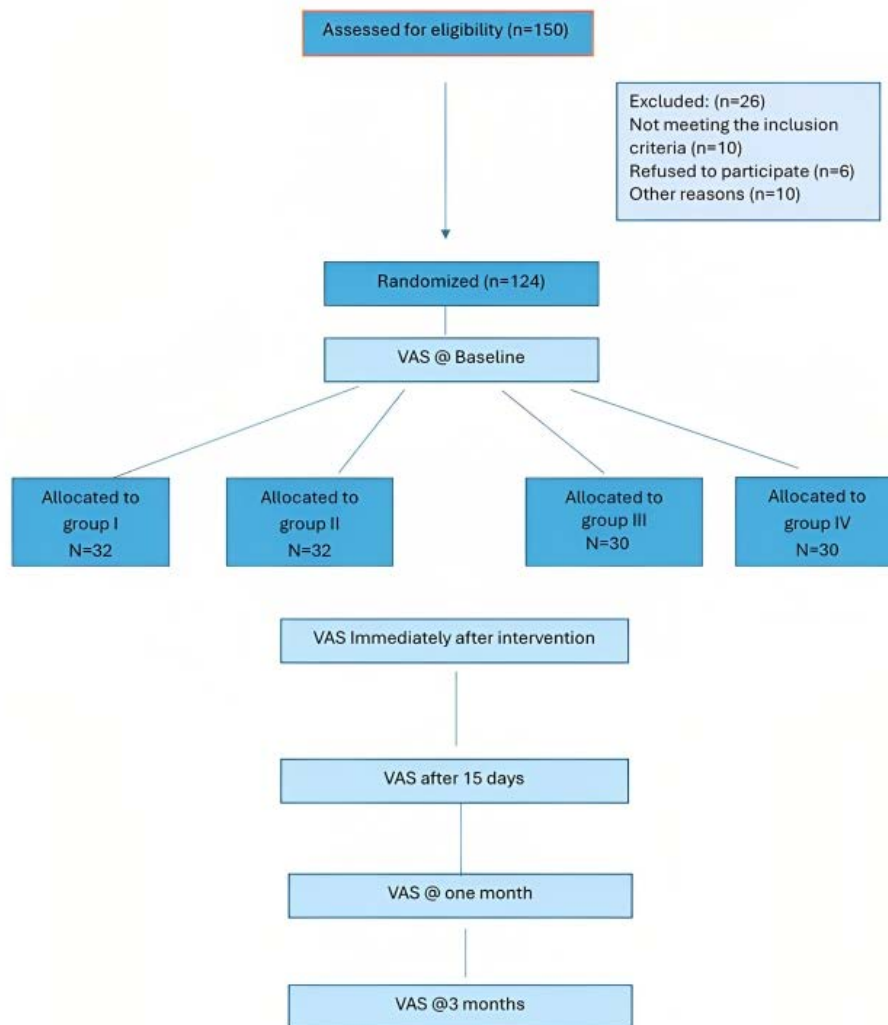


Figure 1. Consort Flowchart

cementoenamel junction to detect surface roughness. Any irregularity was declared as NCCL (non-carious cervical lesion). The vitality of all experimental teeth was checked by an electric pulp tester (Cox C-PULSE, China) to exclude pulpal pathology. The thermal evaporative stimulus was measured as the Degree of sensitivity by air blasts to a specific tooth by covering the neighboring teeth with a cotton roll to prevent false readings using the Schiff Cold Air Sensitivity Scale.^{23,24} Patients with ≥ 2 scores were included in the study. One examiner performed the air-blast sensitivity and tactile stimuli test. The second investigator asked the patient to convey their pain level using a visual analog scale (VAS) ranging from 0–10 (0: no pain and 10: unbearable pain) or categorized as mild (1–3), moderate (4–7), and severe (8–10), by using a strong air blast from a triple syringe, directed to the exposed cervical area for 1–3 seconds at 1 cm at a right angle to the buccal surface of an assigned tooth.²⁵ Only patients scoring > 3 in the VAS were included in the study. A pre-study calibration exercise was conducted to ensure consistency and reliability in pain assessment. All investigators

involved in data collection underwent a training session to standardize their use of the VAS, with anchor points for various levels of pain intensity (e.g., 0 = no pain, 10 = worst possible pain). The same anchor points were given for botheration and tolerance levels to understand the patient's pain experience comprehensively. The investigators were also trained to ask participants to rate their pain, botheration, and tolerance levels at consistent time points: either immediately post-treatment or during scheduled follow-up visits. Intra-investigator reliability was ensured by having the same investigator reassess pain levels at different time points.

Intervention

This trial was double-masked. The participants and the investigators were unaware of which treatment each participant received. A third investigator randomly assigned patients to four groups using Microsoft Excel. The program generated random numbers, which were sorted into ascending order. The participants were then assigned sequentially to Groups I–IV. The following four

treatment protocols were used:

- Group I included patients (n=32) who were only given the CPP-ACP (GC Tooth Mousse Plus) paste application. The cervical area of the tooth was dried with a cotton roll, and a generous amount of the paste was applied; the patient was instructed to let the paste stay for at least 3 minutes before washing it out. This procedure was repeated three times in 48 hours and then kept for a follow-up.
- Group II consisted of patients (n=32) who received a diode laser (*Lasotronix SMART^m 980nm/0.5-1W laser 19J/cm, Piaseczno, Poland) light for 100-150 seconds only on the cervical area of the affected tooth. This procedure was repeated three times in 48 hours, and the patients were appointed for a follow-up.
- Group III included patients (n=30) given a combination of CPP-ACP and a diode laser. A 980 nm diode laser was used with an output power of 0.5-1W delivering 19 J/cm of energy in continuous mode for 100-150 seconds. The CPP-ACP paste was first applied for 3 minutes, followed by laser irradiation. This protocol was repeated thrice within 48 hours, and the patients were then scheduled for a follow-up.
- Group IV included a control group (n=30) who received regular fluoride toothpaste as a placebo. Its active ingredient was sodium monofluorophosphate (0.76% (0.15% w/v fluoride ions). The affected tooth was dried with a cotton roll, and a generous amount of toothpaste was applied for 3 minutes. This procedure was repeated three times within 48 hours, and the patient was recommended a follow-up.

VAS values for pain, botheration (discomfort due to DH), and tolerance (how well the patient can bear discomfort due to DH) were recorded at baseline (pre-treatment), immediately post-treatment (T1), and at 15 days (T2), 30 days (T3), and three months (T4). The patients were instructed not to eat, drink, or rinse for 30 minutes post-treatment and were informed not to use any desensitizing toothpaste during follow-ups.

Statistical Analysis

Data was analyzed on IBM SPSS version 24. The normality of the data was tested for each variable. Pearson’s Chi-square assessed the association between Sex/Age and groups. For repeated outcome measures, two-way ANOVA was applied to evaluate the mean difference within the group after considering the normality of

data distribution.²⁶⁻²⁸ For Pairwise comparison, the least significant (Bonferroni) test was applied. An intention-to-treat analysis used the last-observation-carried-forward methodology to account for missing data.²⁹ The p-value of <0.05 was considered significant.

Results

Nearly all the patients completed the study. For missing data, the last-observation-carried-forward method was applied.

Reliability and inter-investigator agreement for measuring VAS scores were conducted using the Intraclass coefficient (ICC) and Cronbach’s alpha. The ICC indicated good reliability, with a single measure suggesting moderate agreement between individuals (0.663). In contrast, the average measure ICC suggested excellent agreement (0.855) with a significant F-test and p-value confirming that the measurements are reliable and consistent. Cronbach’s alpha of 0.855 suggested strong internal consistency for items being measured.

Demographic Characteristics

There were 55 males (44.4%) and 69 females (55.6%), with a mean age of 32.8±10.3 years. Sex distribution was comparable across all groups, indicating balanced randomisation. The mean age of the participants was equivalent across all groups, indicating that the study included participants of similar age on average. The standard deviation and range for age were also similar across the groups, suggesting a relatively homogeneous age distribution. (Table 1)

Power Analysis

No closely related previously published studies would be suitable for sample size calculation on the same patients. Therefore, the power of the test³⁰ was computed to support the sample size of 124 individuals (32 in the first two groups and 30 in the following two groups). The calculation was performed using the PASS version 2021 software (NCSS Statistical Software, Kaysville, UT, USA), based on the repeated-measures analysis of variance, with a regular F test, one between group factor and one within group factor at 5% level of significance, across five sessions (T). We used three outcomes (VAS pain, VAS botheration, and VAS tolerance), mean values, standard deviation (σ), and autocorrelation (ρ) in the computation of Power.

Table 1. Demographic details

Characteristics		CPP-ACP N= 32 (%)	Laser N=32 (%)	Laser + CPP-ACP N= 30(%)	Control N= 30 (%)	P value
Sex	Male	15 (23.4)	19 (29.7)	14 (21.9)	16 (25.0)	0.708c
	Female	17 (28.3)	13 (21.7)	16 (26.7)	14 (23.3)	
Age (years), mean±SD		31.9±9.59	32.8±10.3	34.1±11.0	32.2±10.7	0.846l

^c Chi-square test, ^l One-way ANOVA, SD: standard deviation.

The calculated statistical power for detecting main effects between groups ranged from 51% to 80%, with within-subject effects and interaction effects achieving powers greater than 93%, confirming sufficient sensitivity to detect meaningful differences over time and between treatment conditions.(Table 2)

This analysis supports the adequacy of our sample size (n=124; group sizes: 32, 32, 30, and 30) for robust statistical inference and ensures that our study is adequately powered to evaluate the intervention effects across treatment arms and time points.

Post-Intervention Outcome Group Measures Changes

The laser-only group (group II) consistently demonstrated superior results in reducing pain and botheration and improving tolerance to cold stimuli. The CPP-ACP paste (Group I) and the CPP-ACP paste with a diode laser (Group III) also provided significant results. The control group showed some improvement, though substantially less than the treatment groups (Table 3).

VAS Pain

The laser-only group (Group II) showed consistent improvement, with the most significant change occurring immediately after the treatment (55.1%, $P<0.001$), increasing to 63% in three months ($P<0.001$). The CPP-ACP paste with a diode laser (Group III) also showed consistent improvement at all time points. The CPP-ACP paste (Group I) also showed tremendous change, with the most considerable improvement observed after three months (61%, $P<0.001$). The control group showed moderate improvement, with the most significant improvement of 64% in three months ($P<0.001$). (Table 3)

VAS Botheration

The laser-only group (group II) showed consistent improvement, with the most prominent improvement observed immediately after the treatment (58%, $P<0.001$); however, the CPP-ACP paste with a diode laser (Group III) also showed improvement, with the most significant improvement observed immediately after the treatment (52%, $P<0.001$). The CPP-ACP paste

Table 2. Power analysis for outcome

Outcome	MSE _{Between}	MSE _{Within}	ρ	σ	Power		
					Between	Within	Interaction
VAS Pain	6.25	0.59	0.66	1.31	51%	>99%	42%
VAS Botheration	4.37	0.56	0.58	1.15	77%	>99%	99%
VAS Tolerance	4.502	0.677	0.53	1.20	80%	>99%	93%

Table 3. Comparison of Pain, botheration and tolerance across different treatment groups

Outcome Measures	CPP-ACP (N=32)			Laser Only (N=32)			Laser + CPP-ACP (N=30)			Control (N=30)		
Sessions	Mean $\pm$ SD	Δ (P-value¥)	Imp (%)	Mean $\pm$ SD	Δ (P-value¥)	Imp (%)	Mean $\pm$ SD	Δ (P-value¥)	Imp (%)	Mean $\pm$ SD	Δ (P-Value¥)	Imp (%)
VAS Pain												
Baseline	7.6 $\pm$ 1.5	-	-	7.3 $\pm$ 1.4	-	-	7.8 $\pm$ 1.2	-	-	7.4 $\pm$ 1.4	-	-
Immediate after	3.9 $\pm$ 1.5	3.6 (<0.001)	49.3	3.3 $\pm$ 1.3	3.9 (<0.001)	55.1	4.3 $\pm$ 1.6	3.6 (<0.001)	47.0	3.8 $\pm$ 1.4	3.6 (<0.001)	49.5
After 15 days	3.5 $\pm$ 1.3	4.1 (<0.001)	55.2	2.9 $\pm$ 0.8	4.3 (<0.001)	58.9	3.6 $\pm$ 1.4	4.2 (<0.001)	54.2	3.3 $\pm$ 1.5	4.1 (<0.001)	55.5
After 1 month	3.1 $\pm$ 1.5	4.4 (<0.001)	60.0	2.7 $\pm$ 0.8	4.6 (<0.001)	62.1	3.5 $\pm$ 1.4	4.3 (<0.001)	55.0	3.0 $\pm$ 1.3	4.4 (<0.001)	59.3
After 3 months	3.0 $\pm$ 1.5	4.6 (<0.001)	61.4	2.7 $\pm$ 0.7	4.6 (<0.001)	62.6	3.1 $\pm$ 1.1	4.7 (<0.001)	60.2	2.7 $\pm$ 1.0	4.7 (<0.001)	63.6
VAS Botheration												
Baseline	7.1 $\pm$ 1.6	-	-	6.5 $\pm$ 1.1	-	-	6.8 $\pm$ 1.2	-	-	6.6 $\pm$ 1.6	-	-
Immediate after	3.7 $\pm$ 1.3	3.4 (<0.001)	48.2	2.8 $\pm$ 1.2	3.7 (<0.001)	57.9	3.3 $\pm$ 1.3	3.4 (<0.001)	52.1	3.9 $\pm$ 1.2	2.8 (<0.001)	34.5
After 15 days	3.2 $\pm$ 1.3	3.9 (<0.001)	55.5	2.5 $\pm$ 0.9	3.9 (<0.001)	60.9	3.3 $\pm$ 1.2	3.5 (<0.001)	51.9	3.2 $\pm$ 1.3	3.4 (<0.001)	45.2
After 1 month	2.9 $\pm$ 1.1	4.2 (<0.001)	59.2	2.3 $\pm$ 0.6	4.3 (<0.001)	64.4	2.9 $\pm$ 1.1	3.8 (<0.001)	56.1	2.8 $\pm$ 0.9	3.8 (<0.001)	53.3
After 3 months	2.8 $\pm$ 1.1	4.3 (<0.001)	60.0	2.3 $\pm$ 0.6	4.3 (<0.001)	65.2	3.3 $\pm$ 0.9	3.6 (<0.001)	52.0	2.6 $\pm$ 0.9	4.1 (<0.001)	57.0
VAS Tolerance												
Baseline	6.7 $\pm$ 1.5	-	-	6.3 $\pm$ 1.2	-	-	6.6 $\pm$ 1.2	-	-	6.5 $\pm$ 0.9	-	-
Immediate after	4.1 $\pm$ 2.4	2.7 (<0.001)	38.1	2.6 $\pm$ 0.9	3.7 (<0.001)	57.7	3.2 $\pm$ 1.3	3.4 (<0.001)	52.6	3.4 $\pm$ 1.3	3.2 (<0.001)	49.3
After 15 days	3.3 $\pm$ 1.3	3.4 (<0.001)	51.9	2.4 $\pm$ 0.7	3.9 (<0.001)	61.3	3.0 $\pm$ 1.1	3.6 (<0.001)	53.8	2.8 $\pm$ 1.3	3.7 (<0.001)	58.3
After 1 month	2.9 $\pm$ 1.2	3.8 (<0.001)	57.0	2.3 $\pm$ 0.6	4.1 (<0.001)	63.1	2.9 $\pm$ 0.9	3.7 (<0.001)	56.0	2.7 $\pm$ 1.1	3.9 (<0.001)	59.9
After 3 months	2.8 $\pm$ 1.2	3.9 (<0.001)	59.0	2.3 $\pm$ 0.6	4.1 (<0.001)	63.1	2.9 $\pm$ 1.0	3.7 (<0.001)	55.5	2.6 $\pm$ 0.9	4.0 (<0.001)	61.0

Δ : mean difference; ¥P-value on comparison using repeated measures two-way ANOVA with post hoc (Bonferroni) test.

only showed substantial improvement, with an enormous improvement of 59% in three months ($P < 0.001$). The control group showed moderate improvement, with the most significant improvement of 57% in three months ($P < 0.001$). (Table 3)

VAS Tolerance

The laser-only group (Group II) showed consistent improvement, with the most considerable improvement observed immediately after the treatment (58%, $P < 0.001$) and at three months (63%, $P < 0.001$). CPP-ACP showed significant improvement, with an enormous improvement of 59% in 3 months ($P < 0.001$). CPP-ACP paste with a diode laser also showed an improvement of 55.5% in three months ($P < 0.001$). The control group showed moderate improvement, with the most considerable improvement of 61% at three months ($P < 0.001$). (Table 3)

Comparison of Outcome Measures Between Groups

The laser-only group (Group II) was the only treatment group that consistently showed differences compared to the control group, and that was associated with a reduction in both pain and botheration. (Table 4)

VAS Pain

Differences were observed immediately after the treatment ($\Delta = -0.487$, $P = > 0.99$) and after 1 month ($\Delta = -0.281$, $P = 0.99$), suggesting that the laser-only group (Group II) experienced a noticeable reduction in pain compared to the control group. Differences were observed immediately after the treatment ($\Delta = 0.467$, $P = > 0.99$) and after 1 month ($\Delta = 0.5$, $P = 0.791$), suggesting that the CPP-ACP paste with diode laser group experienced increased pain compared to the control group. (Table 4)

VAS Botheration

A significant difference was observed in VAS botheration

immediately after the treatment ($\Delta = -1.085$, $P = 0.005$), suggesting that the laser-only group (Group II) experienced a significant reduction in botheration compared to the control group. A significant difference in group III was also observed in VAS botheration after 3 months ($\Delta = 0.600$, $P = 0.070$). (Table 4).

VAS Tolerance

Differences were observed immediately after the treatment ($\Delta = -0.742$, $P = 0.435$) and after 1 month ($\Delta = -0.417$, $P = 0.632$), suggesting that the laser-only group experienced a noticeable reduction in tolerance compared to the control group. (Table 4).

Partial Eta Squared for VAS Comaprison

All three outcome measures (VAS Pain, VAS Botheration, and VAS Tolerance) showed substantial session effects ($\eta^2_p > 0.80$), indicating that significant changes occurred over time regardless of group assignment. Also, the results revealed that all treatments substantially improved DH symptoms across sessions, emphasising the importance of time-dependent therapeutic effects (Table 5).

The group effect sizes for all outcomes were small to moderate (ranging from $\eta^2_p = 0.051$ to $\eta^2_p = 0.093$). The highest group effect was observed for VAS Tolerance ($\eta^2_p = 0.093$), which may suggest that the combined therapy had a slightly more pronounced impact on patients' tolerance to hypersensitivity (Table 5).

Discussion

Dentin hypersensitivity is a chronic condition characterized by intense, short-lasting pain. This condition disrupts routine oral functions and impedes oral hygiene, leading to plaque accumulation, periodontal disease progression, gingival recession, and root exposure.³¹ Various treatment modalities have been proposed, but no gold standard has been established yet.^{21,32} Laser treatments are either high

Table 4. Intra-group Comparison of VAS scores over time for different treatment modalities

Group / Measure	Baseline Δ	P value	Immediate After Δ	P value	After 15 Days Δ	P value	After 1 Month Δ	P value	After 3 Months Δ	P value
CPP-ACP										
VAS Pain	0.196	> 0.99	0.138	> 0.99	0.169	> 0.99	0.125	> 0.99	0.333	> 0.99
VAS Bother	0.460	> 0.99	-0.148	> 0.99	0.019	> 0.99	0.104	> 0.99	0.277	> 0.99
VAS Tolerance	0.185	> 0.99	0.696	0.550	0.513	0.455	0.302	> 0.99	0.246	> 0.99
Laser Only										
VAS Pain	-0.085	> 0.99	-0.487	> 0.99	-0.362	> 0.99	-0.281	> 0.99	-0.010	> 0.99
VAS Bother	-0.133	> 0.99	-1.085	0.005	-0.669	0.142	-0.583	0.111	-0.379	0.615
VAS Tolerance	-0.221	> 0.99	-0.742	0.435	-0.425	0.841	-0.417	0.632	0.317	> 0.99
Laser+CPP-ACP (labeled as "Laser+Mouse")										
VAS Pain	0.467	> 0.99	0.467	> 0.99	0.333	> 0.99	0.500	0.791	0.467	0.689
VAS Bother	0.133	> 0.99	-0.533	0.609	0.067	> 0.99	0.133	> 0.99	0.600	0.070
VAS Tolerance	0.067	> 0.99	-0.167	> 0.99	0.233	> 0.99	0.200	> 0.99	0.333	> 0.99

Δ : mean difference. * P -value on comparison using repeated measures two-way ANOVA with a post hoc (Bonferroni) test.

Table 5. Effect size for outcomes using RM ANOVA

Outcome Measure	Sessions (η^2_p)	Groups (η^2_p)	Session $\times$ Group Interaction (η^2_p)
VAS Pain	0.867	0.051	0.013
VAS Botheration	0.844	0.089	0.055
VAS Tolerance	0.808	0.093	0.041

power, such as Er: YAG, Nd: YAG, or diode lasers, which reduce or seal dentinal tubules by heat generation, or low power like photobiomodulation (PBM), also sealing dentinal tubules by the cellular stimulation of odontoblasts in tertiary dentin.^{33,34,35} Toothpaste remains one of the most widely available over-the-counter treatments. These pastes may contain desensitizing agents such as strontium chloride, fluoride, and potassium nitrate, as well as newer formulations containing calcium sodium phosphosilicate (Novamin or Sensodyne Repair), or remineralizing agents like MI Paste with Casein Phosphopeptide Amorphous Calcium Phosphate (CPP-ACP), which is claimed to produce the best results.^{15,36} The present clinical research aimed to determine the efficacy of Casein Phosphopeptide Paste (CPP-ACP) used alone or in combination with a diode laser, involving four intervention groups. Airblast and tactile stimulation were used to accurately measure hypersensitivity levels, as reported by Clark and Troullous et al.³⁷

The results showed that all treatment modalities provided comparable clinical improvements with pain reduction, as found in a study by Madhavan et al. and Femiano et al.^{18,38} In this study, group II (Diode Laser) proved to be the most effective treatment, with consistent improvement and a 63% reduction in pain and botheration at three months ($P < 0.001$). These findings align with those of Gogkov-Vukelic et al.,³⁹ Hashim et al.⁴⁰, and Monadder et al., who reported successful management of dentin hypersensitivity pain with diode laser therapy, showing consistent reductions in the VAS up to six months.⁴¹ Tabatabaei et al. demonstrated a significant decrease in DH pain immediately after the treatment; however, no significant change was observed at three- or six-month follow-ups.³⁶ Raichur et al. also found significant results, with an 85% reduction in the pain score when directly irradiated using a diode laser.⁴² Laser energy promotes the formation of sclerotic dentin, which may aid in tubular occlusion. In vitro, studies have shown that a small dose of laser can melt dentin and create a double-layer structure that narrows the lumen of dentinal tubules. The immediate pain relief may be due to the depressed nerve transmission of C-fibers.²¹

Group III (CPP-ACP paste with a diode laser) did not show statistically significant differences compared to the control for managing DH, which is in conflict with a study by Demydova et al., who reported the highest results with propolis combined with a diode laser.²¹ Ortiz et al. obtained

similar results when using Casein Phosphopeptide Paste combined with Photobiomodulation (PBM).⁴³ Femiano et al. found that combining a diode laser (810 nm, 5W) with a VivaSens desensitizing agent¹⁸ was the most effective treatment, as compared to using these treatments alone, opposing the findings of this research. A plausible explanation lies in the sequence of application and the biochemical mechanism of VivaSens, which contains potassium nitrate, which reduces the excitability of nerves, and its combination with lasers might be more effective. In contrast, Amorphous Calcium Phosphate CPP-ACP paste works under the remineralization principle, upon interaction with saliva, and dissociates calcium and phosphate ions in an amorphous state, creating a supersaturated environment. These ions precipitate and occlude dentinal tubules by binding to phosphorylated collagen fibers in inter tubular dentin, leading to apatite formation and narrowing of lumen, thereby reducing hypersensitivity.⁴³⁻⁴⁵ The use of a laser can further enhance the process of tubule occlusion and surface modification.

The present clinical research found that group I (where CPP-ACP paste was applied at baseline 3 times in the first 48 hours only) showed consistent improvement, with a maximum of 61% ($P < 0.001$) at three months. However, this was inconsistent with the findings of Madhavan et al., who reported that CPP-ACP showed minimal effectiveness in reducing DH pain.³⁸ However, Tung et al. evaluated the clinical effectiveness of CPP-ACP as a therapeutic agent (in the form of chemically induced precipitation) for DH treatment.⁴⁶ Satish and Kidiyur et al. also assessed the in vitro effects of CPP-ACP, showing that crystal-like deposits occluded many dentinal tubules after the initial application of the paste was used twice daily for 7 days.⁴⁵

This study also showed moderate improvement in the control group, consistent with findings from Al Habashneh et al who reported a significant reduction in the VAS scale for DH patients after applying Colgate triclosan/herbal toothpaste.⁴⁷ Studies indicate that fluoride toothpaste only modestly affects DH pain because fluoride ions do not directly occlude dentinal tubules. Instead, the presence of calcium or phosphorus from saliva or specific proteins may play a role in desensitization.^{48,49} The present research demonstrated that fluoridated toothpaste may help relieve DH pain when consistently applied to cervical lesions. Previous research has also discussed the role of a placebo, which has significantly reduced the VAS.⁵⁰ West et al. have also acknowledged that a placebo can act as an intervention and reduce the VAS, possibly through the Hawthorne effect, which is more of a behavioral response of participants due to their awareness of being observed in the study. Hence, they maintain their oral hygiene, which could enhance natural desensitization.⁵¹⁻⁵³ Placebo effects may also be enhanced by positive communication

between the patient and the dentist, which is considered a mixture of physiological and psychological interaction between them, as the patient's belief in the treatment's value can lead to pain relief due to endorphin release.⁵⁴

Based on the data from this study, the null hypothesis (no significant difference in the effectiveness of CPP-ACP or diode laser when used alone compared to when used in combination as a treatment modality for dentin hypersensitivity) was rejected, and the alternate hypothesis (there is a significant difference in effectiveness when used alone) was accepted.

Eventually consistent improvement in VAS pain, botheration, and tolerance was observed in nearly all treatment groups. This research has explored the versatility of the VAS by measuring botheration, tolerance, and pain to quantify DH's broader impact in everyday life. These scales were also used to understand the effectiveness of treatment in terms of patients' satisfaction.

This study has limitations such as shorter follow-up duration, limited sample size, potential bias in pain assessment as pain remains subjective, and no direct evaluation of dentine microstructure to reveal tubular occlusion. This study demonstrated promising results in consistently improving DH pain across all groups. Group III showed no significant results; a Type II error remains possible, where an actual effect may exist but was not detected due to insufficient power. Future studies with larger sample sizes, greater statistical power, and different laser wavelengths are necessary to analyze and understand the exact mechanisms of DH pain relief. Additionally, reversing the treatment sequence in group III could help assess its impact on the effectiveness of this combination. Nonetheless, the current study's findings provide a solid foundation for further investigation into the sequencing of these treatments to optimise patient outcomes.

Conclusion

Based on the study results, the diode laser therapy demonstrated consistently superior outcomes in reducing pain and botheration and improving tolerance to cold stimuli compared to the other treatment modalities. Statistically significant improvements were observed in the laser-only group immediately after the treatment and at the 3-month follow-up, with reductions in pain, botheration, and tolerance scores. The combination modalities also showed improvements, but these were not significantly different from the control group, suggesting that the combination did not outperform the laser-only treatment in consistent effectiveness.

Authors' Contribution

Conceptualization: Sanam Faheem.

Data curation: Rimsha Qasim, Anam Rehman.

Formal analysis: Waqas Ahmed Farooqui.

Investigation: Anam Rehman, Muhammad Amin Sahito, Chander Kumar.

Methodology: Sanam Faheem, Rimsha Qasim, Chander Kumar.

Project administration: Sanam Faheem, Shahida Maqsood.

Resources: Chander Kumar.

Software: Waqas Ahmed Farooqui, Muhammad Amin Sahito.

Supervision: Shahida Maqsood, Naresh Kumar.

Validation: Anam Rehman.

Visualization: Chander Kumar, Shahida Maqsood.

Writing-original draft: Sanam Faheem, Rimsha Qasim.

Writing-review & editing: Muhammad Sohail Zafar, Naresh Kumar.

Competing Interests

The authors declare no conflicts of interest.

Data Availability Statement

The data presented in this study are available on request from the corresponding author.

Ethical Approval

The Institutional Review Board of Dow University of Health Sciences, Karachi, Pakistan, approved this study. (Ref: IRB-2932/ DUHS/ Approval/2023/68). Moreover, the trial was registered at <https://clinicaltrials.gov/study/NCT06463938> (ID: NCT06463938) on 12 May 2024.

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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