

COMPARATIVE EVALUATION OF EFFECTIVENESS OF CASEIN PHOSPHOPEPTIDE AMORPHOROUS CALCIUM PHOSPHATE AND SODIUM FLUORIDE VARNISH IN DENTINE HYPERSENSITIVITY

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ABSTRACT

Objective: To determine efficacy of casein phosphopeptide amorphous calcium phosphate and sodium fluoride varnish in managing dentine hypersensitivity.

Study Design: Quasi-experimental study.

Place and Duration of Study: Foundation University College of Dentistry, Islamabad, from Jun to Nov 2020.

Methodology: Patients of both gender 20-60 years of age with ASA "American Society of Anesthesiologists physical status classification" status I (completely healthy fit patient) or status II (patient has mild systemic disease) diagnosed with dentine hypersensitivity of incisors, canines, premolars with clinical evidence of erosion, abrasion, gingival recession not requiring restorative treatment were enrolled in the study. At first visit baseline, dentine hypersensitivity was recorded by means of tactile and evaporative stimuli, response was quantified using visual analogue scale. Patients were randomly divided in two groups 1-casein phosphopeptide amorphous calcium phosphate, 2-sodium fluoride varnish desensitizing agent was applied conferring to manufacturer instructions. Visual analogue scale readings were assessed at base line and post treatment values was recorded at 7th, 15th, 30th day.

Results: Total 80 patients enrolled in the study with a mean age of 36.26 ± 8.91 years and age-range of 21-60 years. Visual analogue scale results of group-1 (n=40) were recorded at baseline as 5.9 ± 0.94, 7th day 1.9 ± 0.92, 15th day 1.4 ± 0.81 and 30th day 1.0 ± 0.71. In case of group-2 Visual Analogue Score recorded to be 6.2 ± 1.24, 3.2 ± 0.81, 3.0 ± 0.52 and 2.7 ± 1.12 at baseline, 7th, 15th, and 30th day respectively.

Conclusion: Casein phosphopeptide amorphous calcium phosphate is more effective than sodium fluoride varnish in controlling pain associated with dentine hypersensitivity.

Keywords: Casein phosphopeptide amorphous calcium phosphate, Dentine hypersensitivity, Sodium fluoride varnish.

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INTRODUCTION

Dentin hypersensitivity (DHS) is defined as a pain of short duration, sharp in character arising because of exposed dentine, in response to stimuli like tactile, evaporative and thermal.¹ Hydrodynamic theory for DHS states that pain results from alteration in fluid movement in response to stimuli mentioned above resulting in activation of nociceptors at pulp dentine interface. Cunha-Cruz *et al* reported in a recent review that the prevalence of dentinal hypersensitivity was 12.3%.²

Most frequently effected teeth are first premolars and canines, with molars being least affected. Peak prevalence is in age ranges between 30-39 years and the majority of cases are reported in individuals between 20-50 years. Combination of abrasive and erosive

tooth wear is thought to be responsible for causing DHS. Most commonly effected sites are buccal cervical regions.³ For screening prevention and monitoring of dentinal hypersensitivity in general dental practice pragmatic guidelines must be followed, that can help in successful management of such cases. Diagnosis of DHS is quiet challenging, it is important to recognize that it is essentially a diagnosis of exclusion. There are vast array of commercially available in-office and over the counter products available claiming to be effective in pain associated with DHS.⁴ Investigators have reported that DHS has an association with tooth wear pre-dominantly, however a number of etiological factors predispose to DHS these includes abrasion, abfraction wedge shaped lesions, periodontal disease, gingival recession, periodontal surgical procedures and thin gingival biotype.³

There are two specific biological processes involved, firstly-there is lesion initiation because of dentine

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exposure due to loss of enamel and associated gingival recession. Secondly, once there is dentine exposure dentinal tubules are patent and exposed to oral environment. Mechanoreceptors are activated in response to minute fluid movement within the patent dentinal tubules.⁵ Clinical symptoms of DHS are quite variable in different patients, diagnosis is challenging due to subjective nature of pain. It is important to exclude any confounding factors from other orofacial pain conditions. Formulation of clear diagnosis based on sound clinical judgment is critical for successful management of clinical cases. Thorough medical and dental history must be recorded, detailed intraoral and extraoral examination is done before reaching a diagnosis. Site, onset, character, radiation of pain and associated symptoms are taken into account to formulate a treatment plan.⁶

An air blast using triple syringe or tactile stimulation using an explorer probe, together with a degree of discomfort reported by patient resulting from application of stimulus during clinical examination are acceptable to identify susceptible sites. Use of simple numeric scale visual analogue scale is used in clinical practice to record severity of pain associated with dentine hypersensitivity at baseline and to evaluate improvement over subsequent visits, this method gives pain score objectively.⁷ Dental professionals have a variety of treatment options available ranging from desensitizing agents like potassium nitrate based tooth paste as well as tubule blocking agents like strontium chloride/oxalate compounds.⁸ Remineralizing agents like sodium fluoride varnish and casein phosphopeptide amorphous calcium phosphate are novel therapeutic agents available for management of DHS.⁹

Casein phosphopeptide (CPP) is a milk derived phosphoprotein, it has the ability to bind and stabilize soluble amorphous calcium phosphate (ACP) and it provide reservoir of calcium and phosphate ions on demineralized tooth surface. In the presence of saliva, ACP dissociates into calcium and phosphate, maintaining mineral supersaturation and promoting remineralization by formation of hydroxyapatite (HA) crystals.¹⁰ The rationale of this study was to determine the effective therapeutic modality in management of DHS.

METHODOLOGY

This quasi-experimental study was carried out at Teaching Dental Institute from June to November 2020. The approval was taken from ethics research committee of the institute (ref no. AFID/R&D-5/25-2020). The sample size of 80 subjects (40 in each group) was

calculated by openEpi. Patients were enrolled in the study with two-sided confidence level(1-alpha) 95%, 80% power of detection and equal proportion of case to controls. Hypothetical proportion of controls with exposure (40) and hypothetical proportion of cases with exposure (12.3) with odds ratio (0.21) as elaborated by Cunha *et al.*² With consecutive non-probability sampling a total of 80 patients were enrolled. Group 1-casein phosphopeptide amorphous calcium phosphate (CPP ACP) (n=40) and group 2-sodium fluoride varnish (n=40).

Patients were interviewed, briefed, counselled about the procedure, and informed written consent was taken. At first appointments, a detailed history, extraoral, intraoral examination was carried out in all patients with necessary monitoring of patient vital signs. Evaluation parameters was such that we could to adhere with our inclusion and exclusion criteria, was done to ensure patient safety, which is an utmost concern in dental treatment. Careful screening of the patients for fever and symptoms consistent with COVID-19 was performed. Strict cross infection protocol was being followed.

Inclusion Criteria: Patient diagnosed with dentine hypersensitivity from both genders with an age range between 20-60 years, American Society of Anesthesiologist's (ASA) status I, or II were enrolled.

Exclusion Criteria: Non-consenting patients, mentally handicapped, pregnant and lactating females, patients with moderate-severe cardiovascular or ischemic diseases, peri-odontal disease, active root caries, internal root resorption, tongue piercing, history of bleaching treatment in last 8 weeks were excluded from the study.

At first visit, pain associated with dentine hypersensitivity was recorded by means of tactile and evaporative stimuli as baseline record. Evaporative stimuli were applied using triple syringe delivering air blast held perpendicular and 1cm away while shielding adjacent teeth with rubber dam isolation. Two consecutive readings were recorded at 5 min interval. To confirm diagnosis further tactile stimulation using periodontal probe passed perpendicular to tooth surface with apical sweeps with initial pressure of 10g and then gradually increased in increments of 10g until subject responds. Pain response was quantified using visual analog scale (VAS). Patient was provided VAS to place marking on a line of 10cm length. On this line, 0 was no pain and 10 very severe pain. Subjects were randomly allocated in 02 groups, group 1 with casein

phosphopeptide amorphous calcium phosphate (CPP-ACP), group 2 with sodium fluoride varnish. Teeth were air dried before the application of desensitizing agents. Desensitizing agent was applied over the tooth surface under rubber dam application conferring to manufacturer's instruction and left undisturbed over the tooth for 60s. Patients were advised not to rinse eat drink for 30mins after appointment. Pretreatment assessment was done at baseline and post-treatment was done on 7th, 15th and 30th day.

Data entered and analyzed using Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables including age presented as mean and standard deviation. Qualitative variables including gender, ASA status presented in terms of frequency and percentage. Independent sample t-test was employed. The p -value of ≤ 0.05 was considered statistically significant.

RESULTS

Total 80 patients enrolled in the study with a mean age of 36.26 ± 8.91 years and age-range of 21-60 with gender distribution of male 55 (67.1%) and female 25 (30.5%). Sixty nine (84.1%) patients had American Society of Anesthesiologists (ASA) Status I whereas 11 (13.4%) were from ASA Status II (Table-II). VAS results of group 1 ($n=40$) were recorded at baseline as 5.9 ± 0.94 , 7th day 1.9 ± 0.92 , 15th day 1.4 ± 0.81 and 30th day 1.0 ± 0.71 . In case of group 2 Visual Analogue Score recorded to be 6.2 ± 1.24 , 3.2 ± 0.81 , 3.0 ± 0.52 and 2.7 ± 1.12 at baseline, 7th, 15th, and 30th day respectively (Table-II).

Table-I: Distribution of demographic profile.

Parameters		n (%)
American Society of Anesthesiologists	I	69 (84.1%)
	II	11 (13.4%)
Gender	Male	55 (67.1%)
	Female	25 (30.5%)

Table-II: Comparison of visual analog scale scores at baseline 7th, 15th, 30th day.

Parameters	Group 1 (n=40) Mean \pm SD	Group 2 (n=40) Mean \pm SD	p -value
Baseline VAS (Visual Analog Scale) score	5.9 ± 0.94	6.2 ± 1.24	0.02*
7th day VAS (Visual Analog Scale) score	1.9 ± 0.92	3.2 ± 0.81	0.70
15th day VAS (Visual Analog Scale) score	1.4 ± 0.81	$3.0 \pm .52$	0.001*
30th day VAS (Visual Analog Scale) score	1.0 ± 0.71	2.7 ± 1.12	0.001*

*Significant p -value; p -value was calculated by applying Independent sample t-test

DISCUSSION

Data analysis of research interpreted statistically significant efficacy of CPP-ACP in reducing pain associated with DHS as expressed by VAS scores at 15th day and 30th day, due to its potential for inducing remineralization of dentinal tubules. Ortiz *et al*, conducted a randomized controlled trial to determine efficacy of casein phosphopeptide-amorphous calcium phosphate fluoride (CPP-ACPF) and photo bio modulation (PBM) in the management of DHS, and effect of this management line on the health-related quality of life (HRQL). There inter-group comparison with thermal and evaporative stimuli presented that CPP-ACPF+PBM significantly reduced DHS when this treatment modality was compared with the rest of treatment options, after one-month follow-up. CPP-ACPF+PBM group showed statistically significant efficacy with a p -value ($p < 0.05$). A positive impact on the HRQL due to reduction in pain associated with dentin hypersensitivity is reported with treatment by CPP-ACPF with PBM.¹¹

Fernando *et al* conducted an in vitro study on remineralizing potential of CPP-ACP + stannous fluoride (SnF2) solution, significantly higher enamel remineralization was observed in vitro by the combined CPP-ACP + SnF2 solution compared with the CPP-ACP + NaF solution. The extent of remineralization with the CPP-ACP + SnF2 treatment was 32% greater than with the CPP-ACP + NaF treatment. CPP-ACP and SnF2 showed synergism, combination of SnF2 to CPP-ACP resulted in increased complex stability, and greater potential for ion delivery at the tooth surface this unique interaction of Sn F2 and CPP-ACP resulted in formation of Stannous ions aggregated CPP nanocomplexes, and elevated ion release and self-assembly of cross-linkage CPP nanofilaments upon contact with the tooth surface. They concluded that, the combination of CPP-ACP and SnF2 might considerably improve their efficacy in prevention and treatment DHS, finding consistent with our study. A nano-coating formed on the tooth surface drastically improves DHS.¹²

Douglas *et al*, conducted a study to evaluate, that DHS treatments were able to improve individuals' oral HRQL. DHS was assessed by evaporative, cold, and tactile stimuli, as we did in our study. Oral HRQoL was evaluated by questionnaires. In-home and in-office desensitizing agents like CPP-ACP, dentine bonding agent, potassium nitrate-based gels were used for DHS treatment. Their study reported statistically significant reduction of DHS and significant positive impact on oral HRQoL after treatment ($p < 0.05$). Studies indica-

ted decreasing of DHS and improving of oral HRQoL after DHS treatment.¹³ Alleviation of pain associated with DHS improved oral HRQoL in our patient group.

Al-Shamrani *et al*, conducted research to investigate the effect of CPP-ACP, neutral sodium fluoride gel (Flor-Opal), and nano-carbonate Apatite Paste (n-CAP), on enamel surface roughness and postoperative DHS. Their results revealed that after the application of the three surface desensitizing treatments, enamel treated with nano carbonate appetite paste showed a significant reduction in surface roughness ($p=0.002$) when compared with other two therapeutic agents. Results did not show significant effectiveness of sodium fluoride varnish in reducing DHS. Conclusion of their study was nanocarbonate Apatite Paste was considerably more effective in reducing enamel surface roughness and associated hypersensitivity.¹⁴

Dawood *et al*, conducted a study on biocompatibility and remineralization potential of CPP-ACP. Their study concluded that CPP-ACP promote mineralization by increasing bioavailability of calcium and phosphate ions needed for remineralization thereby reducing DHS. Biocompatibility of CPP-ACP was proved in this study and alkaline phosphatase activity of the osteoblast-like cells was significantly increased ($p < 0.05$) by CPP-ACP and CPP-ACFP. This material also enhanced formation of calcium mineral deposits, and the secretion of mineralization-related proteins (collagen type I and osteocalcin).¹⁵ Conclusion of this study supports our findings.

Tarique *et al*, did a comparative analysis on efficacy of three desensitizing agents i.e., 5% sodium fluoride (NaF), 5% potassium nitrate (KNO₃) and CPP-ACP in reducing DHS after in-office vital tooth bleaching. Results of their study was significant at p -value < 0.05 , thereby concluding CPP-ACP substantially reduces symptoms associated with DHS and the other two materials are having nearly the same efficacy but inferior to CPP-ACP.¹⁶ In their study sensitivity was checked on alternating days using VAS for up to one month mean was taken to evaluate the results.

Therefore, our treatment group and results were significant at p -value < 0.05 showing better efficacy of CPP-ACP over sodium fluoride varnish. A paradigm shift is emerging in dentistry and dental treatments are now aimed at providing minimally invasive and remineralization management approaches thereby conserving tooth structure.^{17,18} CPP-ACP is emerging novel material there is scarcity of literature regarding preventive, remineralizing potential of this material we

should be doing what is best available for our patients to improve their health related quality of life and to pace up with evolution in field of dentistry.

CONCLUSION

Casein phosphopeptide amorphous calcium phosphate (CPP-ACP) provides better control of symptoms when compared with sodium fluoride varnish, therefore it is an essential therapeutic modality in successful management of DHS cases.

Conflict of Interest: None.

Authors' Contribution

BA: Conception of idea, data collection, manuscript writing, MS: Conception of idea, data collection, SA: Data analysis, SR: Manuscript writing, QI: Data analysis, MW: Manuscript writing.

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Dentine Hypersensitivity

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