Original Article

Evaluation of remineralizing effect of zinc-carbonate hydroxyapatite on the reduction of postrestorative sensitivity: A randomized controlled clinical trial

Amulya Vittal Rai, Balaram Damodar Naik

Department of Conservative Dentistry and Endodontics, SDM College of Dental Sciences and Hospital, Dharwad, Karnataka, India

Abstract

Background: The adhesive bonding ability of composite resins makes it unnecessary to remove tooth structure for retention, prevention, and convenience. However, postoperative sensitivity after placing composite restoration has been a significant problem experienced by clinicians.

Aim: The present randomized controlled trial was conducted to assess the role of dentin remineralization in the reduction of postoperative sensitivity after composite placement.

Materials and Methods: Eighty participants with occlusal carious teeth were randomly allocated to one of the four study groups, each having 20 participants, and are as follows: Group A with test group, Group A with control group, Group B with test group, and Group B with control group. Postoperative sensitivity was assessed using the Visual Analog Scale (VAS) and the United States Public Health Service (USPHS) criteria at different time intervals such as baseline, 1 week, 1 month, and 3 months. Data were analyzed using the Kruskal–Wallis ANOVA test, Mann–Whitney *U*-test, and Wilcoxon matched-pair test.

Results: All 80 participants were analyzed at the baseline, 1 week, 1 month, and the end of 3 months for the postoperative sensitivity using the VAS score and USPHS criteria. One restoration in Group A with control group reported mild sensitivity at the end of 1 week and one restoration in Group B with control group reported severe sensitivity at the end of 3 months, necessitating its replacement followed by root canal treatment. No relationship was reported between postoperative sensitivity and tooth type. There was no statistically significant difference in postoperative sensitivity in any of the treatment modalities.

Conclusion: Class I restoration using self-etch or selective-etch as well as with or without zinc-carbonate hydroxyapatite is a viable and predictable solution for the reduction of postoperative sensitivity if all the aspects of restorative techniques are considered precisely.

Keywords: Composite resin; postoperative sensitivity; remineralization; selective-etch; self-etch; zinc-carbonate hydroxyapatite

INTRODUCTION

Restorative dentistry deals with the treatment of hard tissue defects based on the priority to restore the function and esthetics without compromising the biology.[1] For many decades, amalgam has been used in clinical practice because of its good mechanical properties, easy application technique, and its acceptable cost.[2] However, on the other hand, it has been disputed over the biocompatibility of amalgam restorations because of its mercury vapor and unesthetic appearance.[3] Therefore, in many countries, the use of amalgam is declining, and these controversies lead to the development of composite resin restorations because of its higher esthetic appearance, minimal intervention, and good bonding properties to tooth structures.[4]

Address for correspondence:
Dr. Amulya Vittal Rai,
Department of Conservative Dentistry and Endodontics,
SDM College of Dental Sciences and Hospital, Sattur,
Dharwad - 580 009, Karnataka, India.
E-mail: amulyav.rai@gmail.com

Date of submission : 22.05.2022
Review completed : 31.08.2022
Date of acceptance : 09.09.2022
Published : 08.12.2022

Access this article online

Quick Response Code:

Website: www.jcd.org.in

DOI: 10.4103/jcd.jcd_300_22

How to cite this article: Rai AV, Naik BD. Evaluation of remineralizing effect of zinc-carbonate hydroxyapatite on the reduction of postrestorative sensitivity: A randomized controlled clinical trial. J Conserv Dent 2023;26:56-66.

Despite the significant improvement in material science and adhesive techniques, postoperative sensitivity following composite restorations remains the biggest challenge for practitioners. The restorative procedures required for the placement of composite resins are more complex which include etching of enamel and dentin as well as the application of acidic adhesive monomers.[5]

Patients often complain of sensitivity at different levels and intensities, with often no evidence of a failure of the restoration.[6] It was reported that postoperative sensitivity following adhesive resin restorations could be related to mechanical trauma and micro-/nanoleakage of bacteria.[7] Other studies reported that polymerization shrinkage of composite resins forms a major problem and limits its advantages such as internal stresses, debonding, and gap formation between the composite resin and tooth, leading to the deformation of restorations under occlusal stresses which transmits hydraulic pressure to the odontoblastic processes causing pain.[8,9] Postoperative sensitivity can be stated as pain in a tooth when associated with mastication or in contact with hot, cold, sweet, or sour stimuli that occur after 1 week or more posttreatment.[10]

Several strategies published in the literature tried to solve the problem of postoperative sensitivity, by using different light-curing modes,[11] different adhesive strategies,[12] applying desensitizers, cavity disinfectants before the bonding procedure,[13] and implementing different techniques for placement of posterior composite restorations.[14] Class I, Class II, and Class V composite restorations showed more failure rate than other restorations, as they are technique-sensitive procedures. Previous clinical studies have concluded that 30% of study populations present with postoperative sensitivity after composite restoration.[15]

Current adhesive systems can be successfully used in both enamel and dentin. Newer self-etch (SE) adhesive systems simultaneously etch, infiltrate, and polymerize to seal the prepared dentin.[16] This allows complete hybridization of demineralized dentin by adhesive monomers and thereby reducing postoperative sensitivity.[16,17] Selective-etch adhesive technique overcomes the main drawback of SE technique, which is suboptimal etching of mineralized enamel, by acid etching only the enamel prior to the use of adhesive.[18] It is important to notice that the success of adhesive restorative treatment relies not only on the improvement of the material properties and handling technique but also depends on the skill and knowledge that the clinician possesses regarding the material's properties, limitations, and correct use.[19]

Remineralization of enamel has gained a lot of popularity in dentistry since the 1990s after the use of casein phosphopeptide-amorphous calcium phosphate. With the advent of nanotechnology, many dentin-remineralizing agents emerged in the field of dentistry. One such dentin-remineralizing agent used in the present trial is zinc-carbonate hydroxyapatite (Zn-CHA).[15] However, the remineralizing ability of Zn-CHA has not been studied extensively and thus it is not very well known. Therefore, the main aim of the present randomized controlled trial was to assess the role of dentin remineralization in the reduction of postoperative sensitivity after composite placement. The null hypothesis was that there was no difference in the outcome between the groups with and without Zn-CHA. The second null hypothesis was that there was no difference in the clinical performance between SE and selective-etch adhesive techniques.

MATERIALS AND METHODS

Study design

The study was designed as a single-site, prospective, parallel-group, double-blind, randomized controlled clinical trial. The study protocol was prepared in accordance with the Helsinki Declaration of 1975, as revised in 2000, and met the good clinical practice criteria. This clinical investigation is reported according to CONSORT guidelines.[20]

Inclusion criteria

1. Participants willing to be part of the study and ready to give written informed consent
2. Participant's age: 20–45 years
3. Teeth with vital pulp
4. Teeth having remaining dentin thickness of 1 mm.

Exclusion criteria

1. Participants not agreeable and compliant with the terms of the study
2. Teeth which were previously restored and compromised periodontal status
3. Teeth with nonvital pulp and periapical pathosis
4. Participants with parafunctional habits
5. Participants presenting with spontaneous or orofacial pain
6. Teeth with a history of orthodontic traction and which are not in normal occlusion.
7. Teeth which serve as abutment to fixed or removable prosthesis
8. Participants with systemic conditions and use of anti-inflammatory and psychotropic drugs
9. Pregnant women and lactating mothers
10. Participants with a history of deleterious habits and allergy to any of the components of the study materials.

Participants with occlusal carious teeth requesting esthetic restorations were considered for enrollment. A detailed medical and dental history was recorded to fulfill the inclusion/exclusion criteria. The oral examination was

conducted on all the subjects to exclude deep carious teeth; hence, only shallow and mid-sized carious lesions were included in the trial [Figure 1]. Tooth to be restored had to present adjacent and opposing contacts. Participants were considered suitable for the study if they responded normally to cold test and had carious lesion involving enamel and slightly extending onto dentin in the radiograph [Figure 2]. Informed consent was obtained from all the subjects after explaining to them the purpose of the study and the technical procedures that would be performed during all phases of the study. The ethical clearance was obtained from the Institutional Ethical Committee (IRB No 2018/P/CO/58). The study was approved by the Clinical Trials Registry, Government of India (CTRI/2020/05/025479).

Sample size estimation

The main outcome was the difference across groups between the mean changes in airblast test score from baseline to the end of the follow-up. From the previous study,

The expected standard deviation in Group A $= S_1 = 0.50$

The expected standard deviation in Group B $= S_2 = 0.70$

The expected mean difference $= d = 0.75$

$n = 2S^2 (Z_\alpha + Z_\beta)^2/d^2$

where

$S = S_1 + S_2/2$

$Z_\alpha = 2.58$ at 1% α-error

$Z_\beta = 1.682$ at 95% power

$d = 0.578$

Total $n = 20$ in each group to achieve 95% power and 1% α-error.

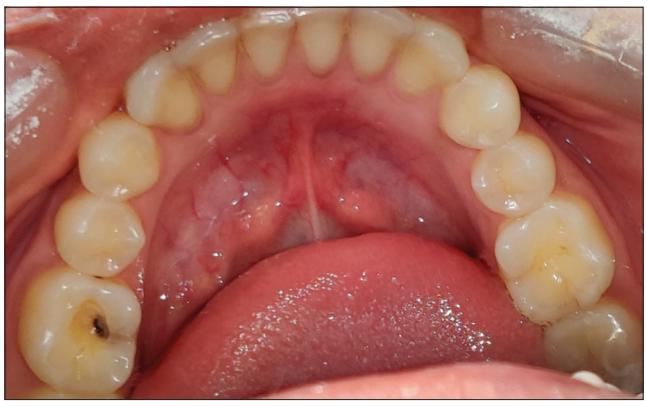

Figure 1: Preoperative occlusal photograph

In the present study, 100 participants were assessed for eligibility. Twenty participants were excluded as they did not meet the inclusion criteria. A total of 80 participants with occlusal caries were qualified to participate in the trial. Only mandibular first and second molars were selected in this study. A preoperative diagnostic digital radiograph was taken to determine the extent of caries, remaining dentin thickness, and also to rule out periapical pathologies.

Participants were randomly allotted to groups with an allocation ratio of 1:1. To ensure that the principal investigator and the study subjects were not involved in the allotment of treatment arms, random numbers were generated and allocated by an individual who was not involved in the study. Random numbers were assigned using computer-generated tables, and accordingly, participants were allotted to one of the four treatment groups. For allocation concealment, numbered containers were used. The interventions were sealed in sequentially numbered identical opaque containers according to the allocation sequence. On the day of restoration, each participant was allowed to pick up an envelope randomly. The entire study was double blinded; participants and the examiner were neither involved in the randomization process nor were they aware of the assigned group in all outcome evaluations. To maintain standardization of procedures mentioned, the entire process was performed by a single operator, who was not part of allocation concealment. There were no changes in the trial protocol from commencement to the end.

The field of operation was isolated with the application of rubber dam and conventional Class I cavity preparation was done using straight fissure bur using a high-speed handpiece with a constant depth of 2 mm as measured from the central groove using a graduated probe, with constant air and water coolant. The cavosurface angle of the prepared cavity was not beveled. Participants with

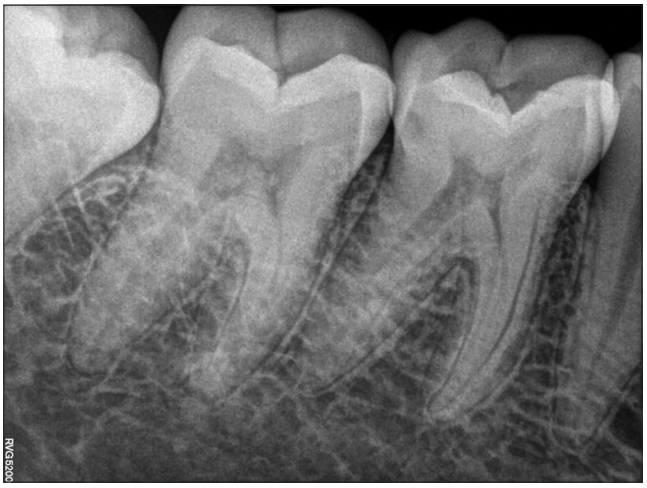

Figure 2: Preoperative diagnostic digital radiograph

cavities larger than the above dimensions were excluded from the study. Participants were then subjected to the randomization procedure and allocated to one of the treatment options to be 20 participants in every group:

- Group A with test group (Zn-CHA with SE)
- Group A with control group (SE)
- Group B with test group (Zn-CHA with selective-etch)
- Group B with control group (selective-etch).

Surface treatment protocol

Group A with test group

After cavity preparation, the pulpal floor was coated with ethylenediaminetetraacetic acid (EDTA) solution (Smear Clear Kerr, Sybron Endo), and after 2 min, the solution was washed away. This procedure helped in removing the smear layer formed during the cavity preparation and thereby enhancing the subsequent remineralizing procedure. Later, the remineralizing agent, Zn-CHA (Biorepair, Stomysens), was applied to the pulpal floor with an applicator tip. After 5 min, the cavity was gently air-dried using a dental unit air syringe to remove the excess agent. The entire cavity was then coated with SE (Optibond All-In-One, Kerr, Sybron Endo) and scrubbed for 10 s and then the excess was removed and light-cured according to the manufacturer's instructions. The cavity was restored with ultrasonic bulk-fill composite (SonicFill, Kerr, Sybron Endo).[15]

Group A with control group

After cavity preparation, the entire cavity was then coated with SE and scrubbed for 10 s and then the excess was removed and light-cured according to the manufacturer's instructions. The cavity was restored with ultrasonic bulk-fill composite.[15]

Group B with test group

After cavity preparation, the pulpal floor was coated with EDTA solution, and after 2 min, the solution was washed away. Later, the remineralizing agent, Zn-CHA, was applied to the pulpal floor with an applicator tip. After 5 min, the cavity was gently air-dried using a dental unit air syringe to remove the excess agent. The selective-etch technique was followed in this group. Then, 37% phosphoric acid (Kerr, Sybron Endo) was applied to the cavosurface enamel first, and after 10 s, the etchant was applied to the remaining cavity. Within 5 s, the cavity was washed thoroughly with water for 1 min. The entire cavity was gently air-dried to remove the surface moisture and then coated with a bonding agent (Optibond S, Kerr, Sybron Endo). After 10 s, the excess was removed and light-cured according to the manufacturer's instructions. The cavity was restored with ultrasonic bulk-fill composite.[15]

Group B with control group

After cavity preparation, 37% phosphoric acid was applied to the cavosurface enamel first, and after 10 s, the etchant was applied to the remaining cavity. Within 5 s, the cavity was washed thoroughly with water for 1 min. The entire cavity was gently air-dried to remove the surface moisture and then coated with a bonding agent. After 10 s, the excess was removed and light-cured according to the manufacturer's instructions. The cavity was restored with ultrasonic bulk-fill composite.[15]

In all the abovementioned groups, the increments were light-cured from both the occlusal surfaces and indirectly through the cusps using *light*-emitting diode-curing light according to the manufacturer's instructions. Finally, the restoration was further polymerized for 10 s in three directions: occlusal, buccal, and lingual for complete polymerization. The finishing of the restoration was done using flame-shaped diamond-finishing burs (Shofu). Premature contacts were evaluated in both centric and eccentric by asking the participant to close lightly on a piece of articulating paper (Prodent) with the participants seated and the occlusal plane parallel to the ground. Excess composite (if present) was removed and recontoured according to the anatomical contours of the natural teeth.

Evaluation

All the practical evaluations were performed by a single investigator, who was blinded as he was not informed about the group assignment. The participants were recalled at 1 week, 1 month, and 3 months for evaluation. The examiner was trained and calibrated before the onset of the trial. There were no loses to follow-up during the trial period [Figure 3].

Airblast stimulation

A blast of air from a dental three-way syringe at a pressure between 45 and 60 psi was placed perpendicular to the tooth at a distance of 0.5 cm for 3 s with an operating temperature of approximately 19°C and any uncomfortable feeling caused by the air stimuli was recorded.[21] Adjacent teeth were isolated with cotton rolls.

The baseline and follow-up postoperative sensitivity levels were assessed using the Visual Analog Scale (VAS) and the United States Public Health Service (USPHS) criteria. Participants were given a VAS and asked to mark at a point on a linear scale marked from 0 to 10 to describe the pain experienced ranging from no pain to worst unimaginable pain. The grading of USPHS criteria are as follows: alpha – none; beta – mild, but bearable; Charlie – uncomfortable, but no replacement is necessary; and delta – painful, replacement of restoration is necessary.

RESULTS

Among the total of 100 screened participants, 80 participants met the inclusion criteria and provided

written informed consent and were recruited to the study. The first participant was included in the trial on June 9, 2020, and the last participant left the trial on October 28, 2020. Experimental protocol was implemented to all 80 participants exactly as planned and no modifications were performed. Participants attended the clinic at the time of randomization (baseline) and after 1 week, 1 month, and 3 months for follow-up. Intra-examiner reliability was almost perfect (0.97). The trial was terminated when the sample size goal was reached. None of the participants terminated the trial prematurely. No significant problems or unintended effects related or unrelated to the use of the study materials were reported.

All study subjects were healthy. The age and sex of the subjects are presented in Table 1.

Statistical analysis was carried out to participants who fulfilled the protocol in terms of eligibility, intervention, and outcome assessment.

SPSS (Statistical Package for Scientific Studies) for Windows version 20.0® was used for the statistical analysis of the present study. The nature and distribution of variables indicated that analysis by a nonparametric method was appropriate. Differences between the VAS scores for the test and control groups were analyzed using the Kruskal–Wallis test, Mann–Whitney *U*-test, and Wilcoxon matched pairs test at different time points such as baseline, 1 week, 1 month, and 3 months. In addition, differences between the scores of USPHS criteria for the test and control groups were analyzed using the Kruskal–Wallis test at different time points. The significance level of this study was set at 0.05.

The mean, standard deviation, median, and interquartile range of VAS score for test and control groups of A and B are presented in Table 2. Table 3 describes the comparisons of VAS scores between all four groups, i.e. Group A with test, Group A with control, Group B with test, and Group B with control at different time points using Kruskal–Wallis test and pair-wise comparison of four groups using Mann–Whitney *U*-test. Kruskal–Wallis test and Mann–Whitney *U*-test was employed to test whether the difference between the four groups with respect to the testing parameters was statistically significant. It was found that there were no statistically significant differences between the four groups at all the time intervals.

Table 4 describes the further comparisons of VAS scores between all four groups using Friedman's test and Wilcoxon matched pairs test. It was found that there were no statistically significant differences between the baseline to 1 week, baseline to 1 month, baseline to 3 months, 1 week to 1 month, 1 week to 3 months, and 1 month to 3 months among all the test and control groups of A and B.

Table 1: Demographic chart

Variables	Group A with test group	Group A with control group	Group B with test group	Group B with control group
Age (years)				
≤24	11	9	9	11
25-34	5	7	7	5
≥35	4	4	4	4
Gender				
Male	4	6	11	10
Female	16	14	9	10

Table 2: Summary of Visual Analog Scale scores in four groups at different time points

Time points	Groups	Mean±SD	Median-IQR
Baseline	Group A with test	0.40±0.50	0.00-1.00
	Group A with control	0.45±0.51	0.00-1.00
	Group B with test	0.60±0.50	1.00-1.00
	Group B with control	0.55±0.51	1.00-1.00
1 week	Group A with test	0.65±0.49	1.00-1.00
	Group A with control	0.90±1.29	1.00-1.00
	Group B with test	0.60±0.50	1.00-1.00
	Group B with control	0.75±0.91	1.00-1.00
1 month	Group A with test	0.45±0.51	0.00-1.00
	Group A with control	0.60±0.94	0.00-1.00
	Group B with test	0.45±0.51	0.00-1.00
	Group B with control	0.55±0.51	1.00-1.00
3 months	Group A with test	0.60±0.50	1.00-1.00
	Group A with control	0.90±1.74	1.00-1.00
	Group B with test	0.60±0.50	1.00-1.00
	Group B with control	0.50±0.51	0.50-1.00

SD: Standard deviation, IQR: Interquartile range

Table 5 describes the comparisons of USPHS criteria between all four groups at different time points using Friedman's test (nonparametric test). It was found that there were no statistically significant differences between the four groups at all the time intervals.

Table 6 describes the comparisons of USPHS criteria between all four groups at different time points using Kruskal–Wallis ANOVA. It was found that there were no statistically significant differences between the four groups at all the time intervals.

DISCUSSION

With the advent of newer techniques and concepts in adhesive dentistry, there has been an increase in the frequency of replacing amalgam restorations with direct composite restorations due to esthetics and health issues.[22] However, the associated complications of composite restorations are yet to be solved, such as marginal discoloration and postoperative sensitivity, which directly attribute to polymerization shrinkage and related stress at the restoration–tooth-bonded interface.[15] Postoperative sensitivity has been attributed to the very sensitive restoration technique and the microleakage resulting either from restorative material, bonding failure, or the technique employed.[23]

Table 3: Comparison of four groups with respect to Visual Analog Scale scores at different time points by Kruskal-Wallis ANOVA

Groups	Baseline		1 week		1 month		3 months	
	Mean±SD	Median-IQR	Mean±SD	Median-IQR	Mean±SD	Median-IQR	Mean±SD	Median-IQR
Group A with test	0.40±0.50	0.00-1.00	0.65±0.49	1.00-1.00	0.45±0.51	0.00-1.00	0.60±0.50	1.00-1.00
Group A with control	0.45±0.51	0.00-1.00	0.90±1.29	1.00-1.00	0.60±0.94	0.00-1.00	0.90±1.74	1.00-1.00
Group B with test	0.60±0.50	1.00-1.00	0.60±0.50	1.00-1.00	0.45±0.51	0.00-1.00	0.60±0.50	1.00-1.00
Group B with control	0.55±0.51	1.00-1.00	0.75±0.91	1.00-1.00	0.55±0.51	1.00-1.00	0.50±0.51	0.50-1.00
H	1.9750		0.2770		0.5140		0.5220	
P	0.5780		0.9640		0.9160		0.9140	
Pair-wise comparison of four groups by Mann-Whitney *U*-test								
Group A with test versus Group A with control (*P*)	0.7868		0.8604		0.9031		0.9138	
Group A with test versus Group B with test (*P*)	0.2793		0.7868		1.0000		1.0000	
Group A with test versus Group B with control (*P*)	0.4171		0.9246		0.5885		0.5885	
Group A with control versus Group B with test (*P*)	0.4171		0.6652		0.9031		0.9138	
Group A with control versus Group B with control (*P*)	0.5885		0.7868		0.6949		0.6849	
Group B with test versus Group B with control (*P*)	0.7868		0.8711		0.5885		0.5885	

*$P<0.05$. SD: Standard deviation, IQR: Interquartile range

Table 4: Comparison of different time points with respect to Visual Analog Scale scores in four groups by Wilcoxon matched pairs test

Groups	Time points	Friedman's test (*P*-value and significance)	*t*	*Z*	*P*
Group A with test	Baseline to 1 week	0.443, not significant	40.00	1.1359	0.2560
	Baseline to 1 month		12.00	0.3381	0.7353
	Baseline to 3 months		16.50	1.1212	0.2622
	1 week to 1 month		16.50	1.1212	0.2622
	1 week to 3 months		30.00	0.2667	0.7897
	1 month to 3 months		8.00	1.0142	0.3105
Group A with control	Baseline to 1 week	0.392, not significant	3.50	1.7748	0.0759
	Baseline to 1 month		5.00	0.6742	0.5002
	Baseline to 3 months		22.00	0.9780	0.3281
	1 week to 1 month		9.00	1.5993	0.1098
	1 week to 3 months		14.00	0.0000	1.0000
	1 month to 3 months		7.00	1.1832	0.2367
Group B with test	Baseline to 1 week	0.712, not significant	39.00	0.0000	1.0000
	Baseline to 1 month		24.00	0.8002	0.4236
	Baseline to 3 months		18.00	0.0000	1.0000
	1 week to 1 month		15.00	0.8885	0.3743
	1 week to 3 months		27.50	0.0000	1.0000
	1 month to 3 months		15.00	0.8885	0.3743
Group B with control	Baseline to 1 week	0.7789, not significant	18.00	0.5331	0.5940
	Baseline to 1 month		52.50	0.0000	1.0000
	Baseline to 3 months		20.00	0.2962	0.7671
	1 week to 1 month		20.00	0.7645	0.4446
	1 week to 3 months		7.00	1.1832	0.2367
	1 month to 3 months		42.00	0.2446	0.8068

*$P<0.05$

The postulated theory for postoperative sensitivity following composite restorations includes gap formation which predisposes to microleakage. Microleakage, in turn, causes compression of the restoration during loading, causing fluid to be forced in and out from underneath the restoration causing pain. Therefore, the current theory of pulpal tooth pain dictates that any change in the hydraulic pressure within the dentinal tubules stimulates the pain receptors within the pulp, thereby causing pain.[24]

A sequence of cuspal displacement takes place during an adhesive procedure. Drying and bonding produce rapid cuspal contraction and slight cuspal expansion, respectively, whereas light curing of resin induces gradual but extensive cuspal contraction, which persists after light curing. Therefore, the above effects as well as large, rapid fluid movement, cuspal displacement during restoration, and postcuring might have implications for postoperative sensitivity.[25]

Table 5: Comparison of four groups with respect to the United States Public Health Service criteria at different time points by Friedman's test

UPHCS	Groups				Total
	A test (%)	A control (%)	B test (%)	B control (%)	
Baseline					
0	19 (25.0)	19 (25.0)	19 (25.0)	19 (25.0)	76 (100.0)
1	0	0	0	0	0
1 week					
0	19 (25.7)	18 (24.3)	19 (25.7)	18 (24.3)	74 (100.0)
1	0	1 (50.0)	0	1 (50.)	2 (100.0)
USPHS_1 month					
0	19 (25.3)	18 (24.0)	19 (25.3)	19 (25.3)	75 (100.0)
1	0	1 (100.0)	0	0	1 (100.0)
USPHS_3 months					
0	19 (25.3)	18 (24.0)	19 (25.3)	19 (25.3)	75 (100.0)
1	0	1 (100.0)	0	0	1 (100.0)
Friedman's test (*P*-value, significance)	$	0.392, not significant	$	0.392, not significant	-

*$P<0.05$. $: No changes observed in the group across the timeline, USPHS: United States Public Health Service

The advantage of choosing hydroxyapatite particles with the smallest possible dimensions was discovered more than three decades ago. In fact, Hefferren, since 1976, has shown that increased remineralization occurs, especially with apatite particle sizes <4 mm.[21] In this study, Zn-CHA nanocrystals were used which led to remineralization/repair of the surface by deposition of a hydroxyapatite-rich coating. Concerning its nano-sized bioactive components, those gaps in the dentinal tubules could be sealed completely with plugs within a few minutes until the regeneration of a mineralized layer has occurred within a few hours.[21] Besides, its high surface area permits the release of more calcium and phosphate ions at low concentrations.[24]

Biomimetic zinc-CHA (Zn-CHA) has been synthesized with a stoichiometric Ca/P molar ratio of about 1.7 ± 0.1, containing 4 ± 1 wt% of carbonate ions, prevalently replacing phosphate groups, while 1% of Ca^{2+} ions are substituted by Zn^{2+}. Both the synthesized biomimetic Zn-CHA and human enamel apatite not only contain a similar carbonate amount but also have been shown to promote carbonate substitution to the phosphate and/or hydroxyl group. This is very much similar to the synthetic and biological CHA nanocrystals.[26]

In the present study, even after a follow-up of 3 months, all the treatment groups were primarily effective in decreasing the scores of VAS and USPHS criteria for measuring postoperative sensitivity. There were no statistically significant differences between all the four groups such as Group A with test, Group A with control, Group B with test, and Group B with control in VAS scores and USPHS criteria at different time intervals when compared with nonparametric tests. Therefore, the null hypothesis was accepted.

In the present trial, participants aged between 20 and 45 were considered; this is because dentin is neither too young nor old and has a good remineralizing potential. Smear Clear (17% EDTA) was used to disturb the smear layer and make the surface active for dentin remineralization.[27,28]

In order to minimize variation in the restorative technique in the current study, all the restorative procedures were carried out by a single operator. Furthermore, in order to avoid bias in the distribution of tooth type, mandibular 1st and 2nd molars were considered in the present study.

According to the previous study by Yousaf *et al*.,[29] postoperative sensitivity was typically reported by the patients during the 1st week after the restorative procedure with a reduction in incidence over a period of time. Therefore, in order to minimize recall bias in the current study, the re-evaluation was done at baseline, after 1 week, 1 month, and 3 months. The 3-month evaluation period that was assigned for the current study might have provided a more reasonable scenario for testing the effectiveness of the investigated remineralizing agent. This evaluation period gave them more time to block the incompletely sealed dentinal tubules present in the hybridized layer, thus decreasing postoperative sensitivity over longer periods.

Class I cavities were considered in the present trial because of the higher incidence of reported postoperative sensitivity in the literature, which could be attributed to the configuration factor or C factor. This C factor is the ratio between the numbers of bonded walls versus unbonded walls in a prepared cavity. In Class I cavities, the C factor is the highest (5/1); therefore, the higher the C factor, the higher is the stress resulting from polymerization shrinkage.[5]

One out of 20 participants in Group B with the control group presented with sensitivity 7 days after the restorative procedure. A possible explanation might be related to the enamel marginal sealing and the occlusal adjustments accomplished after the treatment. Nevertheless, 1 out of

Table 6: Comparison of four groups with respect to the United States Public Health Service criteria at different time points by Kruskal-Wallis ANOVA

Groups	Alpha				Bravo				Charlie				Delta			
	BL	1 week	1 month	3 months	BL	1 week	1 month	3 months	BL	1 week	1 month	3 months	BL	1 week	1 month	3 months
Group A with test	20	20	20	20	0	0	0	0	0	0	0	0	0	0	0	0
Group A with control	20	19	19	19	0	1	0	0	0	0	1	0	0	0	0	1
Group B with test	20	20	20	20	0	0	0	0	0	0	0	0	0	0	0	0
Group B with control	20	19	20	20	0	1	0	0	0	0	0	0	0	0	0	0
H	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
P	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000

*$P<0.05$. BL: Baseline

20 participants in Group A with control group presented sensitivity 90 days after the restorative procedures, requiring replacement of the restoration followed by root canal treatment. This may have been associated with the material and restorative technique. It could also be related to the stresses generated by polymerization of the resin material at the bonded interfaces and/or by possible accelerated degradation of the adhesive system.[19] Besides, it is important to emphasize that the occurrence of postoperative sensitivity was low because the criteria used for the selection of participants and cavity preparations were standardized. Therefore, the best conditions for the placement of restoration avoiding bacterial contamination and occlusal interferences can individually or entirely contribute to the lowest incidence of postoperative sensitivity.[19]

As there are very few studies available in the literature regarding the use of Zn-CHA used in the form of varnish, this remineralizing agent used in other forms is considered for the purpose of outcome comparison. Results were compared wherever possible and should be interpreted with caution.

The first double-blind clinical randomized trial by Orsini *et al*. in 2010[30] compared the desensitizing efficacy using a sodium fluoride/potassium nitrate dentifrice and a new dentifrice containing carbonate/hydroxyapatite nanocrystals. This study demonstrated the efficacy of Zn-CHA toothpaste in significantly reducing dentin hypersensitivity after 4 and 8 weeks, supporting its utility in clinical practice. Moreover, a further recent randomized clinical trial by the same authors[31] showed that this effect of Zn-CHA could be exerted after only 3 days of treatment.

The result of the present trial is in accordance with the previous studies by Huang *et al*. that showed a significant remineralizing effect on enamel for nHA solutions[32,33] and also for nHA toothpaste.[34] A noncomparative 8-week clinical study by Al Asmari and Khan[35] concluded that dentifrice based on Zn-CHA nanocrystals is capable of remineralization and reducing or controlling DH. A drop in the Schiff Sensitivity Scale score was achieved using desensitizing toothpaste containing Zn-CHA. An *in vitro* study by Alessandri Bonetti *et al*.[36] demonstrated that the use of a Zn-CHA-containing toothpaste was found to be able to protect stripped enamel surfaces from demineralization.

A comparative *in vivo* study by Lelli *et al*.[26] concluded that on SEM-EDAX, XRD, and Fourier-transform infrared spectroscopy observations, the Zn-CHA toothpaste demonstrated an appreciable formation of a biomimetic CHA coating on the enamel surface. Furthermore, these synthetic nanostructured CHA microcrystals were consistent with a mineral biomimetic apatitic deposition, which does not alter the chemical-physical properties of the enamel.

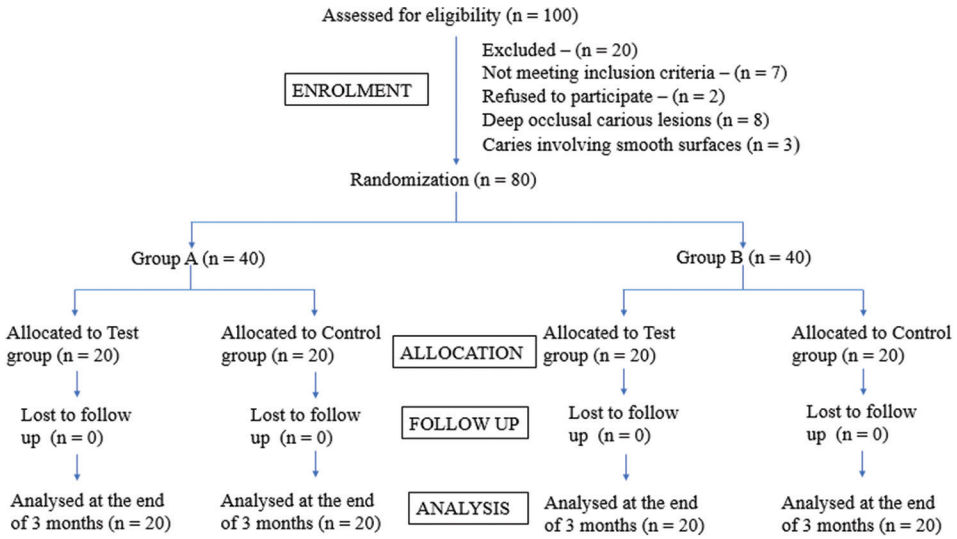

Figure 3: Flowchart of participants throughout the trial

Another *in vivo* and *in vitro* study by Bossù *et al*.[21] evaluated the enamel remineralization and repair results of biomimetic hydroxyapatite toothpaste. It was concluded that the use of nanostructured microparticles in biomimetic hydroxyapatite toothpaste was proven to have a higher potential of remineralization of the enamel. Therefore, biomimetic hydroxyapatite nanocrystals became a valuable preventive measure against caries, especially for high-risk individuals.

Whereas, a recent *in situ* study by Souza *et al*.[37] demonstrated that experimental nHA paste (not a toothpaste) was not able to decrease enamel demineralization. Another *in vitro* study by Esteves-Oliveira *et al*.[38] concluded that the nanohydroxyapatite-containing toothpaste could not significantly inhibit caries progression in a bacteria-free and demineralizing pH-cycling model.

Prevention of postoperative sensitivity has been related to the ability to seal the gaps and open dentinal tubules that are present at the interface between the dentin adhesive and the dentin.[24] However, advances in dentin-bonding systems have minimized the incidence of postoperative sensitivity after composite resin restorations.

The main disadvantages associated with etch-and-rinse adhesive systems are potential contamination when washing the acid etchant, longer etching times, and overdrying the dentin.[17] Overdrying of dentin can lead to the collapse of collagen meshwork in conditioned dentin, which may lead to postoperative sensitivity and a decrease in bond strength. In attempts to decrease the number of steps, decrease in chairside time and subsequent more chances of procedure errors like potential overdrying in dentin bonding has led to the development of SE adhesives.[29] However, the inherently acidic SE systems have more water in their composition making them highly susceptible to hydrolysis and disintegration over time.[39,40]

A study by Francis *et al*.[41] showed that there was no significant difference in postsensitivity between total-etch and selective-etch techniques at baseline, immediately after treatment, 24 h, and 2 weeks after treatment. Moreover, the results of this study are in accordance with similar *in vivo* studies. A study by Perdigão *et al*.[42] found no statistically significant difference in postoperative sensitivity between 30 restorations placed using SE and 36 restorations placed using total-etch adhesive systems.

Browning *et al*. evaluated postoperative sensitivity at 13 weeks after treatment and found no significant difference between the total-etch and SE technique.[43] Another study by Scotti *et al*. evaluated the influence of a three-step total-etch versus two-step SE adhesive system on immediate postoperative sensitivity and found that there was no statistically significant difference between the two groups.[44] A meta-analysis by Krithikadatta of clinical trials on comparison of different clinical outcomes of composite restoration placed with SE and total-etch reported that there was no significant difference in postoperative sensitivity.[45]

Composite resin was cured indirectly through the cusps, to minimize the deleterious effects of polymerization shrinkage stresses on the marginal integrity of the composite restorations and also on the microscopic integrity of the adhesive bond to dentin.[26]

The VAS method was used to evaluate POS in the current study. This offers participants a wider range of responses and more uniform instructions by avoiding descriptors such as mild, moderate, and severe, which can be interpreted

quite differently from one participant to another. It also provides a more accurate and effective statistical test than other tests based on the fixed categories. Besides, it has the ability to detect minor changes in pain intensities over time or due to treatment.[26]

The present trial has a few limitations which must be discussed. When the dentin is prepared closer to the pulp, the tubule density, and diameter increase, thus increasing both the volume and flow of pulpal fluid (hydrodynamic effects) when teeth are subjected to stimuli[26] which is perceived by subjects as pain. Therefore, moderate-to-deep cavities should be compared for further evaluation.

This trial has a relatively small sample size. However, this is unlikely to be true because the differences across treatment groups for all measures in all tests are definitively small in absolute and relative terms.

This trial has a relatively shorter follow-up. Therefore, further long-term follow-up studies should be conducted to assess the clinical parameters before recommending their routine application in dentistry.

CONCLUSION

Within the limitations of the present study, it can be concluded that there was no significant difference in the postoperative sensitivity between SE and selective-etch adhesive systems. Furthermore, Class I composite restorations following the use of Zn-CHA effectively prevented postoperative sensitivity, thereby demonstrating Zn-CHA as a novel agent to repair and remineralize dental hard tissues.

It is suggested that the dental practitioner should have a clear understanding of the basic principles and have adequate training for proper clinical application of adhesive systems and composite restorations. Following a standardized protocol and handling the materials based on the manufacturer's instructions can help minimize postoperative sensitivity in Class I composite restorations.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Al-Nahlawi T, Altaki Z, Abbood D. Post-operative sensitivity of class I, II amalgam and composite resin restorations: Clinical evaluation in an undergraduate program. Int Dent Med J Adv Res 2015;1:1-4.
2. Bjørklund G. The history of dental amalgam. Tidsskr Nor Laegeforen 1989;109:3582-5.
3. Uçar Y, Brantley WA. Biocompatibility of dental amalgams. Int J Dent 2011;2011:981595.
4. Sutalo J. Composite materials in aesthetic dentistry. Lijec Vjesn 1991;113:187-90.
5. Sabbagh J, Fahd JC, McConnell RJ. Post-operative sensitivity and posterior composite resin restorations: A review. Dent Update 2018;45:207-213.
6. Akpata ES, Sadiq W. Post-operative sensitivity in glass-ionomer versus adhesive resin-lined posterior composites. Am J Dent 2001;14:34-8.
7. Brännström M. Infection beneath composite resin restorations: Can it be avoided? Oper Dent 1987;12:158-63.
8. Eick JD, Welch FH. Polymerization shrinkage of posterior composite resins and its possible influence on postoperative sensitivity. Quintessence Int 1986;17:103-11.
9. Jordan RE, Suzuki M, Boksman L. Posterior composite restorations -where do we stand? Ont Dent 1985;62:13-4, 17-8, 20.
10. Berkowitz GS, Horowitz AJ, Curro FA, Craig RG, Ship JA, Vena D, *et al.* Postoperative hypersensitivity in class I resin-based composite restorations in general practice: Interim results. Compend Contin Educ Dent 2009;30:356-8, 360, 362-3.
11. Alomari Q, Omar R, Akpata E. Effect of LED curing modes on postoperative sensitivity after class II resin composite restorations. J Adhes Dent 2007;9:477-81.
12. Coelho-de-Souza FH, Klein-Júnior CA, Camargo JC, Beskow T, Balestrin MD, Demarco FF. Double-blind randomized clinical trial of posterior composite restorations with or without bevel: 6-month follow-up. J Contemp Dent Pract 2010;11:001-8.
13. Hajizadeh H, Ghavamnasiri M, Majidinia S. Randomized clinical evaluation of the effect of chlorhexidine on postoperative sensitivity of posterior composite resin restorations. Quintessence Int 2013;44:793-8.
14. Costa T, Rezende M, Sakamoto A, Bittencourt B, Dalzochio P, Loguercio AD, *et al.* Influence of adhesive type and placement technique on postoperative sensitivity in posterior composite restorations. Oper Dent 2017;42:143-54.
15. Vejai Vekaash CJ, Venkatesh KV, Kumar Reddy TV, Devaraj K. A novel method to reduce postoperative sensitivity after composite restoration: A triple-blinded *in vivo* study. J NTR Univ Health Sci 2018;7:19-22.
16. Van Meerbeek B, Yoshihara K, Yoshida Y, Mine A, De Munck J, Van Landuyt KL. State of the art of self-etch adhesives. Dent Mater 2011;27:17-28.
17. Masarwa N, Mohamed A, Abou-Rabii I, Abu Zaghlan R, Steier L. Longevity of self-etch dentin bonding adhesives compared to etch-and-rinse dentin bonding adhesives: A systematic review. J Evid Based Dent Pract 2016;16:96-106.
18. Suzuki T, Takamizawa T, Barkmeier WW, Tsujimoto A, Endo H, Erickson RL, *et al.* Influence of etching mode on enamel bond durability of universal adhesive systems. Oper Dent 2016;41:520-30.
19. Briso AL, Mestrener SR, Delício G, Sundfeld RH, Bedran-Russo AK, de Alexandre RS, *et al.* Clinical assessment of postoperative sensitivity in posterior composite restorations. Oper Dent 2007;32:421-6.
20. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. Trials 2010;11:32.
21. Bossù M, Saccucci M, Salucci A, Di Giorgio G, Bruni E, Uccelletti D, *et al.* Enamel remineralization and repair results of biomimetic hydroxyapatite toothpaste on deciduous teeth: An effective option to fluoride toothpaste. J Nanobiotechnology 2019;17:17.
22. Mjör IA, Moorhead JE, Dahl JE. Selection of restorative materials in permanent teeth in general dental practice. Acta Odontol Scand 1999;57:257-62.
23. Nash RW, Lowe RA, Leinfelder K. Using packable composites for direct posterior placement. J Am Dent Assoc 2001;132:1099-104.
24. Aboelenein AZ, Riad MI, Haridy MF. Effect of a self-etch adhesive containing nanobioglass on postoperative sensitivity of posterior composite restorations – A randomized trial. Open Access Maced J Med Sci 2019;7:2313-20.
25. Ratih DN, Palamara JE, Messer HH. Dentinal fluid flow and cuspal displacement in response to resin composite restorative procedures. Dent Mater 2007;23:1405-11.
26. Lelli M, Putignano A, Marchetti M, Foltran I, Mangani F, Procaccini M, *et al.* Remineralization and repair of enamel surface by biomimetic Zn-carbonate hydroxyapatite containing toothpaste: A comparative *in vivo* study. Front Physiol 2014;5:333.
27. Nakabayashi N, Ashizawa M, Nakamura M. Identification of a resin-dentin hybrid layer in vital human dentin created *in vivo*: Durable bonding to vital dentin. Quintessence Int 1992;23:135-41.
28. Pashley DH. Smear layer: Overview of structure and function. Proc Finn Dent Soc 1992;88 Suppl 1:215-24.
29. Yousaf A, Aman N, Manzoor MA, Shah JA, Dilrasheed. Postoperative sensitivity of self etch versus total etch adhesive. J Coll Physicians Surg Pak 2014;24:383-6.

30. Orsini G, Procaccini M, Manzoli L, Giuliodori F, Lorenzini A, Putignano A. A double-blind randomized-controlled trial comparing the desensitizing efficacy of a new dentifrice containing carbonate/hydroxyapatite nanocrystals and a sodium fluoride/potassium nitrate dentifrice. J Clin Periodontol 2010;37:510-7.
31. Orsini G, Procaccini M, Manzoli L, Sparabombe S, Tiriduzzi P, Bambini F, *et al*. A 3-day randomized clinical trial to investigate the desensitizing properties of three dentifrices. J Periodontol 2013;84:e65-73.
32. Huang S, Gao S, Cheng L, Yu H. Remineralization potential of nano-hydroxyapatite on initial enamel lesions: An *in vitro* study. Caries Res 2011;45:460-8.
33. Huang SB, Gao SS, Yu HY. Effect of nano-hydroxyapatite concentration on remineralization of initial enamel lesion *in vitro*. Biomed Mater 2009;4:034104.
34. Colombo M, Mirando M, Rattalino D, Beltrami R, Chiesa M, Poggio C. Remineralizing effect of a zinc-hydroxyapatite toothpaste on enamel erosion caused by soft drinks: Ultrastructural analysis. J Clin Exp Dent 2017;9:e861-8.
35. Al Asmari D, Khan MK. Evaluate efficacy of desensitizing toothpaste containing zinc-carbonate hydroxyapatite nanocrystals: Non-comparative eight-week clinical study. J Int Soc Prev Community Dent 2019;9:566-70.
36. Alessandri Bonetti G, Pazzi E, Zanarini M, Marchionni S, Checchi L. The effect of zinc-carbonate hydroxyapatite versus fluoride on enamel surfaces after interproximal reduction. Scanning 2014;36:356-61.
37. Souza BM, Comar LP, Vertuan M, Fernandes Neto C, Buzalaf MA, Magalhães AC. Effect of an experimental paste with hydroxyapatite nanoparticles and fluoride on dental demineralisation and remineralisation *in situ*. Caries Res 2015;49:499-507.
38. Esteves-Oliveira M, Santos NM, Meyer-Lueckel H, Wierichs RJ, Rodrigues JA. Caries-preventive effect of anti-erosive and nano-hydroxyapatite-containing toothpastes *in vitro*. Clin Oral Investig 2017;21:291-300.
39. Moszner N, Salz U, Zimmermann J. Chemical aspects of self-etching enamel-dentin adhesives: A systematic review. Dent Mater 2005;21:895-910.
40. Nishiyama N, Tay FR, Fujita K, Pashley DH, Ikemura K, Hiraishi N, *et al.* Hydrolysis of functional monomers in a single-bottle self-etching primer-correlation of 13C NMR and TEM findings. J Dent Res 2006;85:422-6.
41. Francis T, Sakkir N, Soe HH, Yeow TY, Hwe HZ, Tze AL. Postoperative sensitivity of selective-etch and total-etch techniques in composite resin restorations: An *in vivo* study. J Clin Diagn Rest 2020;14:ZC01-4.
42. Perdigão J, Geraldeli S, Hodges JS. Total-etch versus self-etch adhesive: Effect on postoperative sensitivity. J Am Dent Assoc 2003;134:1621-9.
43. Browning WD, Blalock JS, Callan RS, Brackett WW, Schull GF, Davenport MB, *et al.* Postoperative sensitivity: A comparison of two bonding agents. Oper Dent 2007;32:112-7.
44. Scotti N, Bergantin E, Giovannini R, Delbosco L, Breschi L, Migliaretti G, *et al.* Influence of multi-step etch-and-rinse versus self-etch adhesive systems on the post-operative sensitivity in medium-depth carious lesions: An *in vivo* study. Am J Dent 2015;28:214-8.
45. Krithikadatta J. Clinical effectiveness of contemporary dentin bonding agents. J Conserv Dent 2010;13:173-83.