

The clinical performance of professionally dispensed bleaching gel with added amorphous calcium phosphate

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While vital bleaching with a peroxide gel generally is recognized as both safe and effective, transient dentinal hypersensitivity is a common, unpleasant side effect of the treatment. This sensation can be felt both during and immediately after treatment. Unfortunately, the etiology of bleaching-related tooth

sensitivity is neither well-understood nor easily measured¹; however, the hydrodynamic theory is a mechanism frequently cited to explain it.² According to this model, peroxide solutions introduced into the oral environment contact available dentinal surfaces and cause retraction of odontoblastic processes, resulting in rapid fluid movement inside the dentinal tubules. This ultimately manifests in stimulation of mechanoreceptors at the pulp periphery.² As a result, patients can feel a clinically evident painful sensation when such teeth are exposed to cold or pressure or even when they are at rest.

Regardless of differences in opinion regarding mechanism, the presence of tooth sensitivity too often is evi-

DISCLOSURE

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Background. The authors undertook a study to measure how the addition of amorphous calcium phosphate (ACP) to a professionally dispensed 16 percent carbamide peroxide equivalent bleaching gel affects tooth color and dentinal hypersensitivity.

Methods. The authors assigned two groups to use either the test gel containing ACP or a control gel. Both groups used their respective products for three hours daily for 14 days. At checkpoints during the treatment period, the authors studied tooth color, gingival health and three measures of hypersensitivity. They performed double-blinded clinical measurements on days three, seven, 14 and on the fifth day post-treatment.

Results. The test group demonstrated significantly lower ($P < .05$) mean thermal sensitivity scores compared with baseline (day 14: 0.21 versus 0.31; fifth posttreatment day: 0.06 versus 0.18). Tactile sensitivity also was substantially lower ($P < .05$) for test subjects (day 14: 0.26 versus 0.48; fifth posttreatment day: 0.06 versus 0.19). Furthermore, at the conclusion of the study, twice as many subjects were free of thermal sensitivity (test group, 80 percent, compared with control group, 40 percent; $P < .001$) and there was a similar significant ($P < .001$) percentage difference for tactile sensitivity. Both groups demonstrated equivalent and significant tooth color enhancement as compared with baseline (control: -7.73 shade change versus test: -8.12 ; $P < .05$).

Conclusions. This study demonstrates that ACP could be added to a 16 percent carbamide peroxide equivalent bleaching gel and result in a significant reduction of clinical measures of dentinal hypersensitivity, both during and after treatment.

Clinical Implications. The results of this study offer evidence in support of clinical decisions to treat patients with bleaching gel containing ACP when uncompromised tooth whitening efficacy is desired, yet dentinal hypersensitivity may be a concern.

Key Words. Tooth whitening; bleaching; peroxide; calcium phosphates; dentin sensitivity; tooth sensitivity; amorphous calcium phosphate; tooth remineralization.

dent for both patients and clinicians. Therefore, in an attempt to limit the discomfort felt during the tooth bleaching process, manufacturers commonly add 5 percent potassium nitrate (KNO_3) to their “sensitive-formula” gels. This is because addition of KNO_3 is the most typical way of creating antihypersensitivity toothpaste. However, this strategy fails to take into consideration that prolonged and sustained use is needed to cause a noticeable regression of pain.^{3,4}

The use of added fluorides apparently also is not the answer. The problem with this approach is that the most effective antihypersensitivity fluoride formulations use 0.4 percent stannous fluoride. This approach, however, frequently causes products to be somewhat unstable and slow-acting and can result in significant tooth discoloration.^{5,6} Hence, this ingredient is not favored for bleaching gels. Manufacturers do offer sodium fluoride formulations, but these are weak, slow-acting alternatives.

A newer approach to dentifrice-based desensitization may use a more applicable formulation strategy.^{7,8} Amorphous calcium phosphate (ACP) is a compound originally developed by the American Dental Association Foundation (ADAF) to remineralize teeth and reverse early enamel carious lesions. However, a 1999 ADAF study⁸ performed at the National Institute of Standards and Technology in Gaithersburg, Md., demonstrated that this compound also can make teeth less sensitive to hot, cold, air pressure and tactile stimulation when applied topically either by dental professionals or by patients themselves.

Another clinical study showed that ACP works via a unique method that uses amorphous calcium phosphate compounds in a carbonate solution to crystallize and form hydroxyapatite.⁹ These crystals then reportedly fill in microscopic surface defects and repair early carious lesions, as well as make teeth smoother, stronger and less sensitive. Interestingly, this agent also has been shown to minimize surface protein precipitation that can limit the ability of chromagens to bind to teeth over time.⁹ However, one requirement for maximum effectiveness is that such formulations should be stored in dual-chambered containers that separate positive and negative ion interactions until the time of introduction into the oral cavity.⁸

Hence, we were interested in determining if a professionally dispensed, commercially available 16 percent carbamide peroxide equivalent

bleaching gel delivered by dual-barrel syringe (NiteWhite Excel 3 Regular, Discus Dental, Culver City, Calif.) could be modified with an ACP-based formulation that might affect the intensity, frequency or both of dentinal hypersensitivity reactions. Furthermore, we were interested in determining if the addition of the ACP had any effect on whitening ability.

Since there were no reports in the literature to indicate that any researchers ever had tried this, we developed our study to compare the effect of an ACP-containing bleaching gel with that of a control gel without ACP on the following factors:

- tooth color as assessed by Vita shade tabs (Vita Zahnfabrik GmbH, Bad Säckingen, Germany);
- transient dentinal hypersensitivity as assessed by thermal (air blast), tactile (Yeaple probe, Xinx Research, Portsmouth, N.H.) and self-assessed tooth sensitivity scores;
- gingival health as assessed by the Löe and Silness Gingival Index (GI).¹⁰

We carried out this study in 19 days, a period that included a two-week, once-daily treatment regimen followed by an examination at five days posttreatment to monitor color rebound and diminution of tooth sensitivity over time as described below.

MATERIALS, SUBJECTS AND METHODS

We used a parallel, double-blind, two-cell, randomized clinical study design to compare tooth color changes and differences in transient dentinal hypersensitivity. The control product was commercially available NiteWhite Excel 3 Regular (with no desensitizers), which contains 16 percent carbamide peroxide equivalent and is delivered in a dual-barrel syringe. The ACP-containing test gel we used was similar to the control gel; however, the manufacturer reformulated the individual components of the gel to incorporate the calcium ion (as CaNO_3) and the phosphate ion (as $\text{K}_4\text{P}_2\text{O}_7$) and maintain the gel's shelf stability (Table 1).

Subject qualification. We qualified 50 subjects from the New York and New Jersey area on the basis of the following criteria:

- absence of severe systemic diseases, psychological diseases or both;
- maxillary anterior tooth discoloration (equivalent to or darker than Vita shade A3);
- nonuse of any dentist-supplied or -applied vital tooth bleaching treatment in the previous six months;

TABLE 1

TREATMENT GROUPS AND PRODUCT DESCRIPTION.				
TREATMENT GROUP	PRODUCT DESCRIPTION	DURATION OF TREATMENT	MEAN AGE (YEARS) ± STANDARD DEVIATION	N (MALE: FEMALE RATIO)
Test	<ul style="list-style-type: none"> ■ 16% carbamide peroxide ■ 0.5% soluble calcium ■ Phosphate derived in part from calcium nitrate and potassium pyrophosphate ■ Dual-barrel syringe with activator 	> Three hours once daily for 14 days; follow-up at fifth day posttreatment	44.76 ± 19.7	25 (12:13)
Control	NiteWhite Excel 3 Regular* <ul style="list-style-type: none"> ■ 16% carbamide peroxide ■ No desensitizing agent ■ Dual-phase syringe with activator 	> Three hours once daily for 14 days; follow-up at fifth day posttreatment	43.64 ± 19.2	25 (13:12)

* Manufactured by Discus Dental, Culver City, Calif.

- nonuse of any in-office desensitizing agent in the previous six-month period;
- no periodontal surgery or scaling performed in the previous six months;
- the patient’s informed consent, as recommended by the ethical principles of the World Medical Association.¹¹

Moreover, the selected subjects each had six healthy maxillary anterior teeth that did not have caries, cracks or fractures; extensive or unsatisfactory restorations; restorations involving the facial surface; anterior prosthetic or orthodontic appliances; abnormal occlusal forces; periodontal pockets; or mobility. Additionally, these subjects’ teeth had no gingival recession and no type of sensitivity, regardless of the etiology.

Custom tray fabrication. Approximately five days after the screening visit, subjects returned for fabrication of a soft, full-maxillary-arch, custom bleaching tray. In each case, we took a maxillary impression with hydrophilic vinyl polysiloxane impression material, and we fabricated nonreservoir trays, according to manufacturer’s directions. Briefly summarized, these instructions called for the impressions to be poured with dental stone and then separated only after the stone had set completely. We trimmed and placed the models on the platform of a vacuum former. As the base material for the trays, we used plastic sheets that measured 0.040 inch thick and 5 × 5 inches square. We heated this material until it sagged about 1.5 to 2.0 inches from the heating element in the vacuum

former. When it was sufficiently softened, we actuated the vacuum for 30 seconds to allow for maximum model adaptation.

After tray material was cooled thoroughly, we cut and removed it from the stone model using a heated knife. We then scalloped the custom trays to 0.5 to 1.0 millimeter below the gingival margins and finished by flaming lightly with an alcohol torch to achieve smooth edges. Trays were kept cold-sterilized in a sealed bag awaiting the subjects’ return to the clinic. When they did return for baseline evaluation and product assignment, each tray was tried in the subject’s mouth and trimmed further if indicated to ensure no gingival impingement.

Study protocol and product instructions.

Following qualification determination, we enrolled subjects in the study and scheduled them for a baseline examination, which included medical history, oral soft tissue examination, Vita shade tooth color scoring, Gingival Index¹⁰ scoring and self-reported sensitivity scoring by thermal and tactile means. All examination and scoring procedures are described below.

After the baseline examinations, we randomized subjects into test and control groups, according to a stratified randomization schedule that created two balanced groups with respect to age, sex, tooth color and sensitivity scores. The evaluator of the teeth shades and sensitivity scores (M.G.) was blinded to this schedule, and the products looked identical to him and to the subjects, other than a secret product code number

known only to a co-worker (H.F.).

The evaluating clinician instructed subjects to use their assigned product according to the manufacturer's instructions as published for the commercially available control product. These directions instructed the user to wear a dentist-supplied, custom-fitted bleaching tray containing the recommended amount of gel, once daily, for a minimum of three hours (or overnight) over the course of 14 days. We standardized oral hygiene procedures by providing subjects with commercially available soft toothbrushes, unwaxed dental floss and nonwhitening toothpaste, with instructions to brush their teeth twice daily (morning and evening) for two minutes at each time. Other than using their supplied dental floss, toothpaste and toothbrush, the clinician instructed subjects to avoid use of all other oral care products.

Clinical examination of oral tissues and GI scoring. We scheduled clinical re-examinations on days three, seven and 14 as well as on the fifth day posttreatment to further assess the performance of the tested gels on teeth nos. 6 through 11. On each of those days, before examining the subjects, we updated their medical and dental histories and compliance diaries. Overall oral tissue health was the first parameter the examiner assessed at each recall examination. Specifically, he looked for and documented any present erythema, desquamation or ulceration of soft tissues. In addition, he recorded any gross changes in teeth, hard tissues or other soft tissues. He also was to note the location, size and severity of these changes.

We used a specific measure for gingival health, the Loe and Silness GI,¹⁰ at baseline, days three, seven, 14 and at five days posttreatment. For this clinical examination, the blinded examiner swept through the gingival sulcus by engaging approximately 1 to 2 mm of the gingival margin with a periodontal probe at a 45-degree angle with moderate axial pressure and sweeping from interproximal aspect to interproximal aspect along the facial aspects of the tooth. The examination procedure was well-tolerated by all subjects. The clinician measured gingivitis on Loe and Silness¹⁰ 0 to 3 scale, with 0 representing healthy tissue and 3 representing the most severe gingivitis, including tissues that spontaneously bled.

Clinical assessment of tooth color. The

same examiner assessed tooth color change at baseline and each recall visit in a treatment room with color-correct lighting (5,500 kelvin light bulbs). He placed a blue bib over the patient's clothing and did not use the dental unit light. Subjects removed lipstick (if present) and were positioned in the dental chair with their maxillary anterior teeth parallel to the floor when their tooth shade was evaluated.

We used the value-oriented Vita Classical Shade Guide tabs to determine tooth color and converted the score to a "shade score." We assigned higher scores to darker teeth and lower scores to lighter teeth in a 16-point ranking system. We calculated shade changes by determining the change in the number of shade guide units that occurred toward the lighter end of the value-oriented list of shade tabs. Although the scale is not perfectly linear, we measured the

changes as if the scale represented a continuous and approximately linear ranking, for the purpose of analysis. This model has been adopted in most tooth bleaching studies and has been acknowledged to yield "clinically relevant" data.¹²

Clinical evaluation of thermal dental hypersensitivity. A calibrated examiner

(M.G.) measured thermal sensitivity perceived by the patient by deploying a blast of air to teeth isolated with cotton rolls, from a distance of 1.0 centimeter for 1 second, as per American Dental Association-recommended guidelines.^{13,14} We used the following scale:

- 0 = absence of pain, but perceiving stimulus;
- 1 = slight pain;
- 2 = pain during application of stimulus;
- 3 = pain during application of stimulus and immediately thereafter.

Clinical evaluation of tactile dental hypersensitivity. We used a four-point scale^{13,14} to measure tactile sensitivity after a well-calibrated single examiner (M.G.) touched the labial cervical surface of anterior teeth under study with a Yeaple probe that applied a constant standardized momentary impact force (50 pounds per square centimeter). Because significant force was applied, "something" always was felt by the subject at the moment of impact, regardless of whether a tooth had dental hypersensitivity. Therefore, the measurement scale referred to any

Overall oral tissue health was the first parameter the examiner assessed at each recall examination.

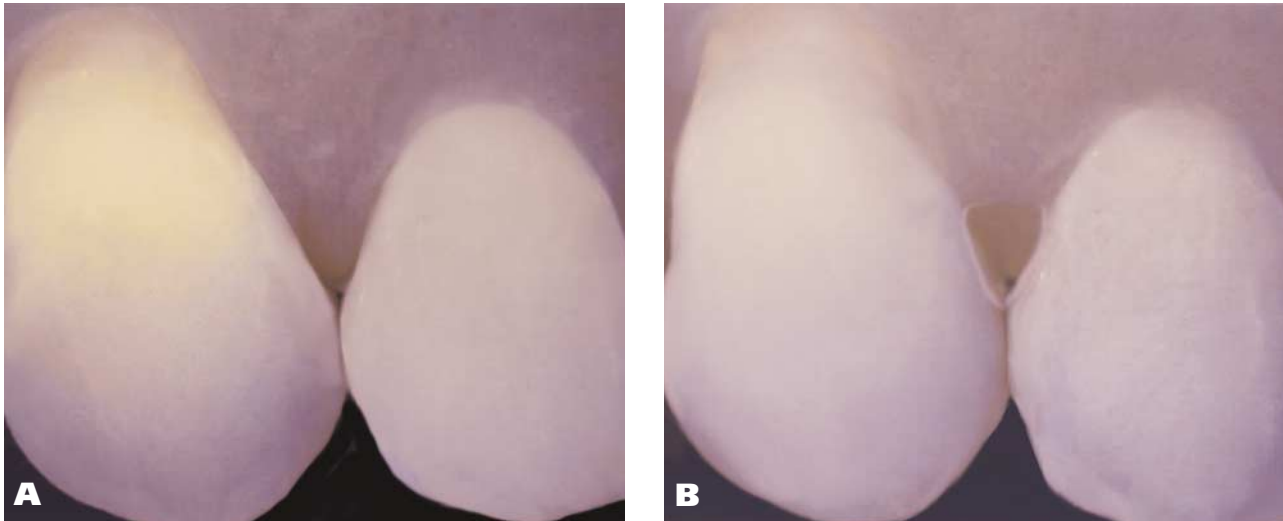


Figure 1. Two 8.3-megapixel-resolution digital images of teeth nos. 6 and 7 in a test group subject, displayed in L*a*b* (lightness, red/green, blue/yellow, respectively) mode with only the b* channel turned on. This type of image confirms that the test gel lightened teeth to a “clinically relevant”²⁰ degree. A. Baseline photograph. Tooth no. 6, Vita (Vita Zahnfabrik GmbH, Bad Säckingen, Germany) shade A3.5: 27,304 yellow pixels counted; tooth no. 7, Vita shade A3: 23,709 yellow pixels counted. B. Photograph taken at five days posttreatment. Tooth no. 6, Vita shade A2: 14,571 yellow pixels counted; tooth no. 7, Vita shade A1: 9,863 yellow pixels counted.

“residual” sensation felt immediately after the probe was removed. The examiner assigned a score of 1, 2 or 3 to correlate with descriptions of perceived “residual” slight, moderate or intense tooth pain. The examiner gave a score of 0 to teeth not having any residual painful response.

Subjective self-assessment of unstimulated tooth sensitivity. The examiner used a subjective visual analog scale (VAS) for the measurement of the intensity of “self-reported” dentinal hypersensitivity subjects experienced at each recall visit, as they sat upright in the examiner’s dental chair. Each patient’s mouth was at rest, and the teeth were not stimulated in any way. The VAS scoring sheet used a printed continuous scale of 0 through 10 points. A score of 0 referred to the absence of tooth pain at rest; a score of 10 referred to the highest level of tooth pain imaginable. The examiner instructed the subject to mark a point along the scale corresponding to the level of tooth sensitivity perceived as he or she sat “unstimulated” in the dental chair.

Digital photography. We took digital images of some teeth, primarily for internal or future promotional purposes; we did not use these images to compare the performance of the test and control products. We imported some of the images into commercially available photographic analysis software, which could highlight tooth yellowness by switching from standard red-green-blue mode to L*a*b* mode (in which L* = lightness, a* =

red/green and b* = blue/yellow) and then displaying the images using the b* (blue-yellow) channel only. A photograph displaying an example of this technique is shown in Figure 1. As shown in the figure, by counting numbers of yellow pixels, researchers could develop this technique further and test it as a potential method of measuring tooth color quantitatively as higher-definition digital cameras become available. Also, although the image in Figure 1 is shown for informational purposes only, it clearly demonstrates that teeth became much less yellow when exposed to the bleaching gels used in our study.

Statistical methods. We assessed within-treatment product effects compared with baseline using the Student *t* test for paired data. The null hypothesis for the paired *t* test states that there is no difference between baseline scores and the scores collected after treatment. In our between-treatment analyses comparing the differences in mean index scores observed between the test and control group, we used either analysis of variance or *t* test as the statistical measure. The null hypothesis for between-group comparisons was that there is no difference in the observed effect caused by either the control gel or the test gel. We tested all hypotheses at the $\alpha = .05$ level.

RESULTS

All 50 subjects completed the 19-day study. One male patient in the control group lacked canine

TABLE 2

SUMMARY OF RESULTS: GINGIVAL INDEX SCORES* AND ORAL TISSUE EXAMINATION.

TREATMENT GROUP	GINGIVAL INDEX SCORES (± STANDARD DEVIATION)			ORAL TISSUE EXAMINATION RESULTS
	Baseline	Treatment Day 14	Treatment Day 19	
Test	0.33 ± 0.11	0.42 ± 0.13	0.47 ± 0.15	Within normal limits for all examinations and for all subjects
Control	0.32 ± 0.08	0.46 ± 0.12	0.44 ± 0.12	Within normal limits for all examinations and for all subjects

* Using the scale developed by Loe and Silness.¹⁰

teeth and had in their place first premolar teeth. These premolars had been moved to their current anterior location through orthodontic treatment 20 years before. Therefore, we counted these premolar teeth as teeth nos. 6 and 11 for the purpose of this study. No subjects missed any recall appointments, and all subjects were paid for their participation.

Tables 2 and 3 show the mean demographic data for the 50 subjects enrolled and the mean baseline scores for both the test gel and control gel groups for all clinical parameters measured. We noted no statistical differences for any of the parameters ($P > .05$) at baseline, which indicates that the groups were balanced before the study's treatment protocol began.

Oral tissue health. Oral hard- and soft-tissue visual examinations revealed no significant oral soft-tissue pathology in either group, neither at baseline nor at any of the recall evaluations. Therefore, on the basis of what we know about the safety record of the commercially available control product, and the safety record of ACP-based products in general, we believe that the test gel formulation is likely to be a safe product for use if prescribed by a dentist using the manufacturer's printed recommendations and directions.¹⁵ However, additional safety testing still is recommended before the product's commercial release.

GI scores. The baseline Loe and Silness GI score for the control gel group was $0.32 \pm$ a standard deviation (SD) of .08; the test group had a similar mean score of 0.33 ± 0.11 . At the conclusion of two weeks, the control group's GI mean score was 0.46 ± 0.12 , and the test group's GI mean score was 0.42 ± 0.13 . These results were not significantly different from the groups'

respective baseline scores and also not significantly different from each other. Similar parity was seen at the five-day-posttreatment examination and again was not statistically different ($P > .05$). Table 2 shows all baseline, two-week and five-day-post-treatment GI mean scores for both groups.

Tooth color assessment. The data we used in the statistical analysis were the shade scores of the maxillary anterior teeth \pm SD grouped by means for each evaluation day. The bar graph in Figure 2 compares the change in shade score from baseline on days three, seven, 14 and the fifth day posttreatment. Student *t* test indicated that for all tooth color measurements, and for both the control and test groups, tooth color after treatment always was significantly lighter than baseline color ($P < .001$). By day 14, the test group showed an overall improvement of 8.17 units and the control group showed an improvement of 7.73 units (on a 16-point scale). Although the test group's mean improvement was 0.44 units higher than the control group's mean, it was not statistically better ($P > .05$). However, most importantly, the data indicate that the addition of ACP did not influence the whitening efficacy of the gel negatively; in fact, the trend was the opposite.

Dentinal hypersensitivity. We used three measures of dentinal hypersensitivity to provide as much evidence as possible for our examination of the effects of ACP on tooth sensitivity. Table 3 offers a comparison of pretreatment and post-treatment sensitivity levels for each method of assessment. That table and Figure 3 (page 390) show that statistically significant and clinically relevant differences in sensitivity scores were found in favor of the test group gel.

Furthermore, we measured antihypersensitivity efficacy as the percentage of subjects who

TABLE 3

TEST GROUP VERSUS CONTROL GROUP: SUMMARY OF MEAN CLINICAL SCORES ± STANDARD ERROR OF THE MEAN (SEM) AND COMPARISON WITH BASELINE SCORES.								
MEASUREMENT POINT	VITA* SHADE		THERMAL SENSITIVITY		TACTILE SENSITIVITY		SELF-REPORTED SENSITIVITY	
	Control Group	Test Group	Control Group	Test Group	Control Group	Test Group	Control Group	Test Group
Baseline Mean ± SEM	10.12 ± 0.82	10.20 ± 0.91	0.27 ± 0.04	0.26 ± 0.07	0.39 ± 0.05	0.39 ± 0.05	0.35 ± 0.07	0.29 ± 0.09
Day 14 Mean ± SEM	2.39 ± 0.49 [†]	2.03 ± 0.58 [†]	0.58 ± 0.06	0.47 ± 0.05	0.87 ± 0.06	0.65 ± 0.08	1.29 ± 0.17	1.14 ± 0.20
Change from baseline	7.73	8.17	0.31	0.21 [‡]	0.48	0.26 [‡]	0.91	0.85
Day 19 Mean ± SEM	2.59 ± 0.39 [†]	2.26 ± 0.47 [†]	0.45 ± 0.05	0.32 ± 0.04	0.57 ± 0.05	0.45 ± 0.07	0.40 ± 0.14	0.35 ± 0.18
Change from baseline	7.53	7.94	0.18	0.06 [‡]	0.19	0.06 [‡]	0.05	0.06

* Manufactured by Vita Zahnfabrik GmbH, Bad Säckingen, Germany.
[†] Color significantly lighter than baseline color (Student *t* test; *P* > .05).
[‡] Sensitivity response significantly lower than among control subjects (Student *t* test; *P* > .05).

returned to baseline comfort levels at different intervals. This analysis showed that use of the test gel resulted in a significantly higher percentage of subjects who returned to baseline pain-free status at both day 14 (end of treatment) and at the fifth day post-treatment. Figure 4 shows that five days after treatment had ceased, a significantly greater (*P* < .001) percentage of ACP gel group subjects (80 percent) than control subjects (40 percent) returned to baseline thermal tooth sensitivity scores. Likewise, comfortable baseline tactile sensitivity levels were reached by a higher percentage of test subjects than of control subjects (64 versus 52 percent; *P* < .001).

Furthermore, as per Table 3 and Figure 3, the test group demonstrated significantly lower (*P* < .05) mean thermal sensitivity scores ($\Delta_{\text{TEST-14}} = 0.21$ units and $\Delta_{\text{TEST-POSTTX}} = 0.06$) compared with corresponding control group scores ($\Delta_{\text{CONTROL-14}} = 0.31$ and $\Delta_{\text{CONTROL-POSTTX}} = 0.18$). The tactile sensitivity scores also were statistically lower (*P* < .05) among test group subjects (Table 3).

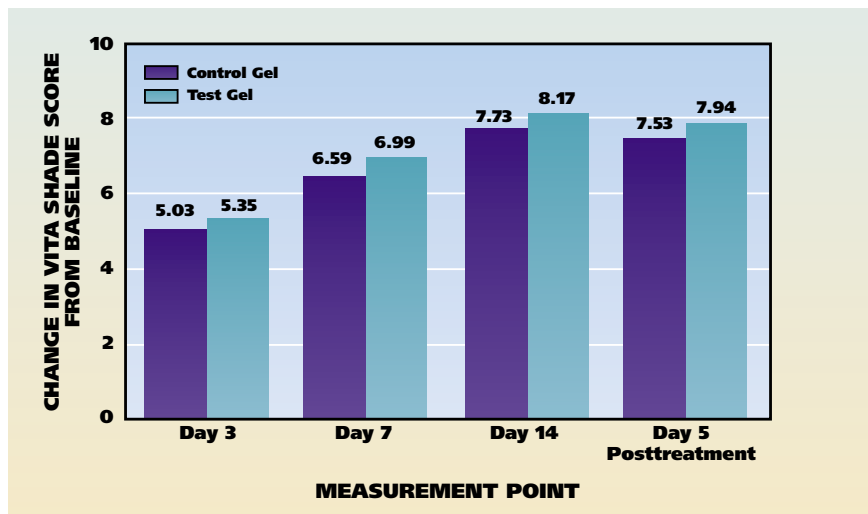


Figure 2. A bar graph comparing the control and test groups' tooth color score improvement from baseline at days three, seven, 14 and fifth day posttreatment. Baseline scores were control group, $\mu = 10.12$; test group, $\mu = 10.20$. Vita shade tabs are manufactured by Vita Zahnfabrik GmbH, Bad Säckingen, Germany.

However, the subjective, self-reported data were not as strong as the above-referenced objective data, but still trending or statistically in favor of the test group results. At day seven, the control group had mean visual analog scores that were 2.02 ± 0.20 units higher than at baseline, while the test group's mean score was 25 percent lower and statistically better (*P* < .01). Day 14 posttreatment results did not achieve the same

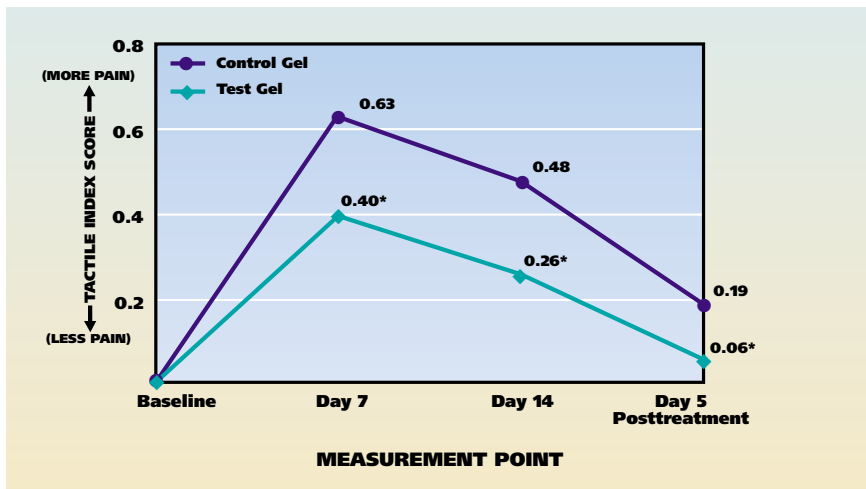


Figure 3. A line graph comparing the control and test groups' differences in tactile sensitivity from baseline at days seven, 14 and fifth day post-treatment. (Baseline scores were control group, $\mu = 0.39$; test group, $\mu = 0.39$.) The test group shows a statistically significant lesser degree of sensitivity compared with the control group at all points asterisked ($P < .05$).

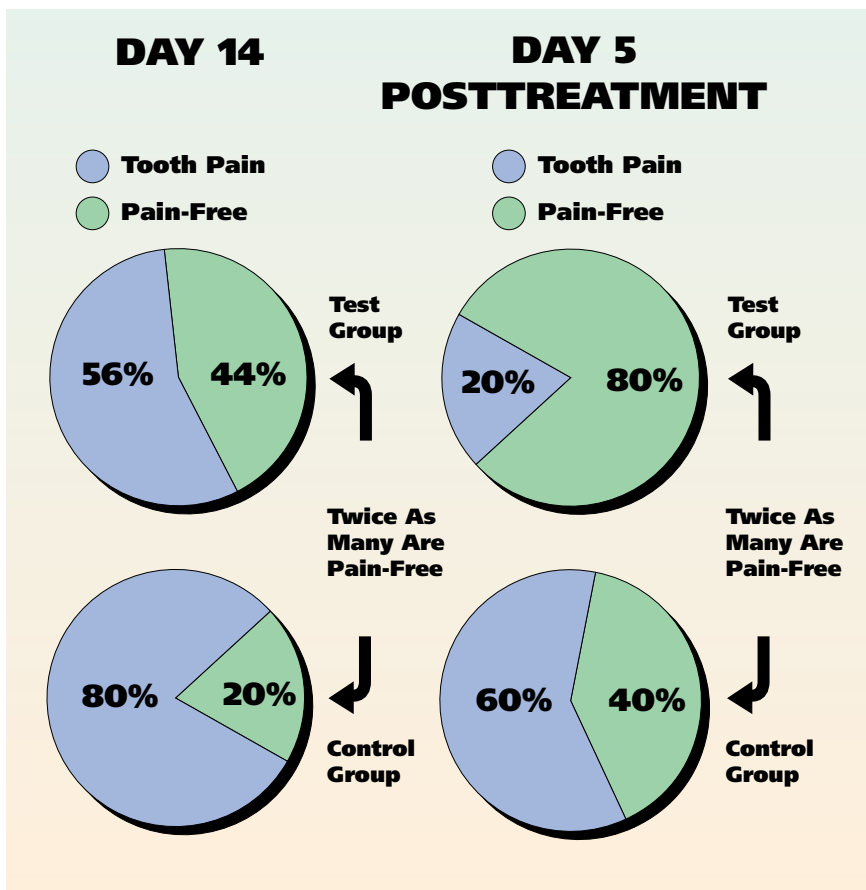


Figure 4. A series of pie charts showing that at day 14 and fifth day post-treatment, a much higher percentage of test group subjects than of control group subjects returned to baseline thermal tooth sensitivity scores. At both time points, the percentage is significantly different ($P < .001$). Five days posttreatment, twice as many test group subjects as control group subjects no longer were uncomfortable.

level of statistical significance, though the trend still was higher for the test group. At the fifth day posttreatment, the mean change from baseline was nearly identical (Table 3).

DISCUSSION

Transient dentinal hypersensitivity has been attributed to the permeation of the bleaching agent into the pulp,¹ and it is a side effect that is present in as many as 78 percent of all people who undergo tray-based tooth-whitening treatments.¹⁶⁻¹⁹ Traditionally, if they anticipate that a patient might be likely to develop sensitivity, dental professionals have prescribed bleaching gels with a standard desensitizing agent.¹ Unfortunately, the available formulations used to control bleaching sensitivity have achieved only limited success.²⁰

Despite the obvious need for better products, there has been little progress in the development of new formulations, at least in part because it is objectively difficult to measure the effectiveness of any new ideas. Pain or discomfort is a subjective sensation that is complicated to quantify, and measurement of its gradual elimination by a desensitizing agent remains an elusive target. Numerous investigators have tried to define dentinal sensitivity,²¹⁻²⁴ but their results show that large sample sizes are required to overcome measurement inaccuracies between patients and observers, and that this makes it difficult to achieve an acceptable statistical power of greater than 80 percent.

When a new category of desensitizing agent, ACP, was identified in the literature,⁸ it seemed to us to have high promise as a solution to this ongoing problem. Unlike the other desensitizers, ACP rapidly obliterates the dentinal tubules by rapid precipitation of calcium phosphate crystals on the surface and

also inside the dentinal tubules.^{7,9} It also may have the ability to directly depolarize nerve endings⁷; however, this hypothesis requires further study.

On the basis of the above findings, we postulated that the addition of ACP to gels used for bleaching of vital teeth might mitigate sensitivity in a rapid and significant manner without affecting whitening efficacy.

Our data demonstrate that the 16 percent carbamide peroxide equivalent gel with ACP can significantly lower ($P < .05$) sensitivity scores, as gauged by several different methods of assessment. Furthermore, even after treatment had ceased, we recorded a continued significant improvement ($P < .05$) in tactile and thermal sensitivity responses. Additionally, we saw no decrease in whitening efficacy in either group after two weeks. At the end of treatment, subjects in the ACP gel group had teeth lightened to the same extent as the control group (respectively, -8.17 versus -7.73 shades; $P > .05$). Therefore, we conclude that the two products have similar ability to lighten teeth.

Considered from a slightly different point of view, the results consistently show that the test ACP formulation had a positive effect on reducing bleaching-related tooth sensitivity. Five days after treatment had ceased, a significantly greater ($P < .001$) percentage of ACP gel group subjects (80 percent) returned to baseline thermal tooth sensitivity scores compared with control group subjects (40 percent) (Figure 3). Likewise, greater numbers of test group subjects returned to baseline tactile sensitivity levels (64 versus 52 percent; $P < .001$) compared with the control subjects treated with the non-ACP gel. Since our data showed a decrease in both thermal and tactile sensitivity, we believe that these data are good predictors of what “real-world” clinicians might find once the ACP gel is available commercially.

We believe that these results are highly clinically relevant, because comparing tooth sensitivity levels offers an alternative method of distinguishing among various tooth-bleaching products, which typically cite very similar whitening benefits (in the range of six to eight Vita shades). As clinicians survey the dental landscape and decide which services they will offer, their choice likely will be driven by pro-

cedures that produce safe and satisfactory results, while also producing happy patients who are willing to refer friends and family. Common sense leads us to conclude that when patients are unable to make practice choices based on technical differences in treatment modality, subjective factors such as their comfort and lack of pain become paramount. Patients easily can relate to these sensations, and they will gravitate naturally toward practices offering whitening procedures that are more comfortable.

In our study—and not surprisingly—our data indicate that during the course of tooth bleaching treatment, the bleaching induced a mild sensitivity reaction in some subjects. However, these data also show that the ACP bleaching gel caused these sensations to be statistically milder and shorter in duration than the bleaching carried out without ACP. However, before deciding on our overall conclusions listed below, we have taken into consideration that there is a high degree of difficulty in accurately measuring sensitivity. We know that it is possible that we introduced bias simply by asking patients to evaluate a perception of sensitivity that they otherwise might have ignored.

Furthermore, our data are not correlated with those of a patient satisfaction study, so it is not possible to conclude that patients would choose one product over the other. Therefore, we encourage further research into sensitivity measurement so that a more objective metric can be repeated at multiple clinical sites.

Yet, despite the above considerations, we believe that these shortcomings are overcome by the redundancy afforded us by using three measurement methods and also by the repeated favorable results measured universally in favor of the test gel. Also in some cases, the differences between the groups are quite large and statistically significant ($P < .001$).

Our conclusions also are based on the belief that if patients are unable to distinguish between whitening technologies, they will use whitening efficacy and sensitivity as their means for discriminating between practices using different whitening products. Thus, a quicker return to baseline sensitivity scores without sacrificing whitening efficacy probably will become a more

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The results consistently show that the test formulation had a positive effect on reducing bleaching-related tooth sensitivity.

important parameter for judging clinical success of whitening products.

Thus, this study indicates that the use of a 16.0 percent carbamide peroxide equivalent bleaching gel containing amorphous calcium phosphate delivered by a dual-barrel syringe may be a clinically effective and safe method of whitening teeth. Furthermore, data indicate that this new formulation results in less overall tooth sensitivity during treatment and much faster relief of bleaching-related transient hypersensitivity pain over the immediate five days after treatment has ceased.

CONCLUSION

This is the first study to show that ACP added to a 16 percent carbamide peroxide equivalent gel formulation can be a clinically advantageous formulation, benefiting both patients and clinicians. While we recognize the inherent difficulty in measuring dentinal sensitivity, we nonetheless believe that our longitudinal analyses demonstrate that dual-chamber bleaching products containing ACP may be a significant advance in tray-based bleaching gel technology that produces whitening efficacy equal to that of, with less sensitivity than, comparable formulations without ACP. ■

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